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Authors	Author address	Title	Publication	Abstract
[No authors listed]		Supplements for Chronic Fatigue Syndrome?	P T. 2016 Sep;41(9):587-8.	
Ablin JN(1), Häuser W(2).	(1)Institute of Rheumatology, Tel Aviv Sourasky Medical Center & Tel Aviv University Faculty of Medicine, Israel. (2)Department of Internal Medicine I, Klinikum Saarbrücken, 66119 Saarbrücken, Germany & Department of Psychosomatic Medicine & Psychotherapy, Technische Universität München, 81865 München, Germany.	Fibromyalgia syndrome: novel therapeutic targets.	165. Pain Manag. 2016 May;6(4):371-81.	Fibromyalgia syndrome (FMS) is a chronic disorder characterized by widespread pain and tenderness, accompanied by disturbed sleep, chronic fatigue and multiple additional functional symptoms. FMS continues to pose an unmet need regarding pharmacological treatment and many patients fail to achieve sufficient relief from existing treatments. As FMS is considered to be a condition in which pain amplification occurs within the CNS, therapeutic interventions, both pharmacological and otherwise, have revolved around attempts to influence pain processing in the CNS. In the current review, we present an update on novel targets in the search for effective treatment of FMS.
Ablin JN(1), Zohar AH(2), Zaraya-Blum R(2), Buskila D(3).	(1) Institute of Rheumatology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. (2) Department of Clinical Psychology, Ruppin Academic Center , Israel. (3)Department of Medicine H, Soroka Medical Center, Beer Sheva, Israel; Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer	Distinctive personality profiles of fibromyalgia and chronic fatigue syndrome patients	PeerJ. 2016 Sep 13;4:e2421.	OBJECTIVE: The current study is an innovative exploratory investigation, aiming at identifying differences in personality profiles within Fibromyalgia Syndrome (FMS) and Chronic Fatigue Syndrome (CFS) patients. METHOD: In total, 344 participants (309 female, 35 male) reported suffering from FMS and/or CFS and consented to participate in the study. Participants were recruited at an Israeli FM/CFS patient meeting held in May 2013, and through an announcement posted on several social networks. Participants were asked to complete a research questionnaire, which included FMS criteria and severity scales, and measures of personality, emotional functioning, positivity, social support and subjective assessment of general health. In total, 204 participants completed the research questionnaire (40.7% attrition rate). RESULTS: A cluster analysis produced two distinct clusters, which differed significantly on psychological variables, but did not differ on demographic variables or illness severity. As compared to cluster number 2 (N = 107), participants classified into cluster number 1 (N = 97) showed a less adaptive pattern, with higher levels of Harm Avoidance and Alexithymia; higher prevalence of Type D personality; and lower levels of Persistence (PS), Reward dependence (RD), Cooperation, Self-directedness (SD), social support and positivity. CONCLUSION: The significant pattern of results indicates at least two distinct personality profiles of FM and CFS patients. Findings from this research may help

	Sheva, Israel.			improve the evaluation and treatment of FM and CFS patients, based on each patient's unique needs, psychological resources and weaknesses, as proposed by the current trend of personalized medicine.
Adamczyk-Sowa M(1), Sowa P(2), Adamczyk J(3), Niedziela N(4), Misiolek H(5), Owczarek M(4), Zwirska-Korczala K(3).	(1)Department of Neurology in Zabrze, Medical University of Silesia, Zabrze, Poland. m.adamczyk.sowa@gmail.com. (2)ENT Department in Zabrze, Medical University of Silesia, Zabrze, Poland. (3)Department of Physiology in Zabrze, Medical University of Silesia, Zabrze, Poland. (4)Department of Neurology in Zabrze, Medical University of Silesia, Zabrze, Poland. (5)Department of Anaesthesiology and Intensive Therapy, Medical University of Silesia, Katowice, Poland.	Effect of melatonin supplementation on plasma lipid hydroperoxides, homocysteine concentration and chronic fatigue syndrome in multiple sclerosis patients treated with interferons-beta and mitoxantrone.	J Physiol Pharmacol. 2016 Apr;67(2):235-42.	Multiple sclerosis (MS) prevalence is higher in geographic regions with less sunlight exposure. Melatonin participates in the effects of sunlight in healthy individuals and could play a role in MS pathophysiology. Melatonin crosses the blood-brain barrier and exerts antioxidative, immunomodulatory, and anti-inflammatory effects. Chronic fatigue syndrome concerns 80 - 90% MS patients. The pathophysiology of chronic fatigue syndrome is unknown, however activation of immune, inflammatory, oxidative and nitrosative stress mechanisms and plasma lipid peroxide elevation was reported. Homocysteine increases plasma lipid hydroperoxides levels. The aim was to determine the effect of melatonin supplementation on chronic fatigue syndrome in MS patients and evaluate plasma lipid hydroxyperoxides (LHP) and homocysteine concentrations as a potential biochemical fatigue biomarkers. Into a case-control prospective study 102 MS patients divided according receiving immunomodifying MS treatment into groups: RRMS-pretreated, RRMS-INF-beta, SP/PPMS-mitoxantrone, RRMS-relapse were enrolled. Patients were supplemented with melatonin over 90 days. Plasma LHP, homocysteine concentration, brain MRI and fatigue score were examined. Results show that LHP concentrations were significantly higher in all studied MS groups vs.CONTROLS: In all MS patient groups melatonin application resulted in significant decrease in plasma LHP concentrations. Plasma homocysteine concentration was similar in healthy people, RRMS-pretreated, RRMS-INF-beta and SP/PP-MS-mitoxantrone groups. However, in the RRMS-relapse group plasma levels of homocysteine were significantly higher compared to the RRMS-pretreated group. There were no significant differences in plasma homocysteine concentration in the studied groups before and after melatonin application. The fatigue score was significantly lower in RRMS pretreated group compared to RRMS-INF-beta and SP/PP MS-mitoxantrone treated patients. Plasma lipid hydroxyperoxides could be potential biochemical chronic fatigue syndrome biomarker in MS patients and homocysteine could be a potential marker of acute phase of MS. Melatonin exerts beneficial effects in MS patients based on its' proved antioxidative properties.
Afifi TO(1), MacMillan HL(2), Boyle M(2), Cheung K(1), Taillieu T(1), Turner S(1), Sareen J(1).	(1)University of Manitoba. (2)McMaster University.	Child abuse and physical health in adulthood.	Health Rep. 2016 Mar 16;27(3):10-8.	BACKGROUND: A large literature exists on the association between child abuse and mental health, but less is known about associations with physical health. The study objective was to determine if several types of child abuse were related to an increased likelihood of negative physical health outcomes in a nationally representative sample of Canadian adults. DATA AND METHODS: Data are from the 2012 Canadian Community Health Survey-Mental Health (n = 23,395). The study sample was representative of the Canadian population aged 18 or older. Child physical abuse, sexual abuse, and exposure to intimate partner violence were assessed in relation to self-perceived general health and 13 self-reported, physician-diagnosed physical conditions. RESULTS: All child abuse

				types were associated with having a physical condition (odds ratios = 1.4 to 2.0) and increased odds of obesity (odds ratios = 1.2 to 1.4). Abuse in childhood was associated with arthritis, back problems, high blood pressure, migraine headaches, chronic bronchitis/emphysema/COPD, cancer, stroke, bowel disease, and chronic fatigue syndrome in adulthood, even when sociodemographic characteristics, smoking, and obesity were taken into account (odds ratios = 1.1 to 2.6). Child abuse remained significantly associated with back problems, migraine headaches, and bowel disease when further adjusting for mental conditions and other physical conditions (odds ratios = 1.2 to 1.5). Sex was a significant moderator between child abuse and back problems, chronic bronchitis/emphysema/COPD, cancer, and chronic fatigue syndrome, with slightly stronger effects for women than men. INTERPRETATION: Abuse in childhood was associated with increased odds of having 9 of the 13 physical conditions assessed in this study and reduced self-perceived general health in adulthood. Awareness of associations between child abuse and physical conditions is important in the provision of health care.
Albrecht PJ, Rice FL.		Fibromyalgia syndrome pathology and environmental influences on afflictions with medically unexplained symptoms.	Rev Environ Health. 2016 Jun 1;31(2):281-94.	Fibromyalgia syndrome (FMS) is a clinical disorder predominant in females with unknown etiology and medically unexplained symptoms (MUS), similar to other afflictions, including irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), post-traumatic stress disorder (PTSD), Gulf War illness (GFI), and others. External environmental stimuli drive behavior and impact physiologic homeostasis (internal environment) via autonomic functioning. These environments directly impact the individual affective state (mind), which feeds back to regulate physiology (body). FMS has emerged as a complex disorder with pathologies identified among neurotransmitter and enzyme levels, immune/cytokine functionality, cortical volumes, cutaneous innervation, as well as an increased frequency among people with a history of traumatic and/or emotionally negative events, and specific personality trait profiles. Yet, quantitative physical evidence of pathology or disease etiology among FMS has been limited (as with other afflictions with MUS). Previously, our group published findings of increased peptidergic sensory innervation associated with the arterio-venous shunts (AVS) in the glabrous hand skin of FMS patients, which provides a plausible mechanism for the wide-spread FMS symptomology. This review focuses on FMS as a model affliction with MUS to discuss the implications of the recently discovered peripheral innervation alterations, explore the role of peripheral innervation to central sensitization syndromes (CSS), and examine possible estrogen-related mechanisms through which external and internal environmental factors may contribute to FMS etiology and possibly other afflictions with MUS.
Ali S(1), Matcham F(2), Irving K(3), Chalder T(4).	(1)Chronic Fatigue Research and Treatment Unit, South London and Maudsley	Fatigue and psychosocial variables in autoimmune rheumatic disease and chronic fatigue syndrome:	J Psychosom Res. 2017 Jan;92:1-8.	OBJECTIVE: Fatigue is common in autoimmune rheumatic diseases (ARD). This study compared symptom-related cognitions, beliefs, behaviours, quality of sleep, lack of acceptance and distress in participants with ARD such as rheumatoid arthritis (RA), seronegative spondyloarthropathy (SpA), and connective tissue disease (CTD), and

	NHS Foundation Trust, London, United Kingdom. (2)Institute of Psychiatry, Psychology and Neuroscience, Department of Psychological Medicine, King's College London. (3)Rheumatology, Kings College Hospital NHS Foundation Trust, London, United Kingdom. (4)Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London. Electronic address: trudie.chalder@kcl.ac.uk.	A cross-sectional comparison.		participants with chronic fatigue syndrome (CFS). METHODS: 303 participants with RA, SpA, CTD and CFS completed questionnaire measures of fatigue, social adjustment, cognitive-behavioural responses, lack of acceptance, distress and quality of sleep. The RA, SpA and CTD groups were first compared with each other. They were then combined into one group and compared with the CFS group. RESULTS: There were no statistically significant differences between the RA, SpA or CTD groups for any of the measures. The CFS group was more fatigued, reported more distress and sleep disturbance and had worse social adjustment than the ARD group after adjustment for age and illness duration. After adjustment for fatigue, age, and illness duration, the CFS group scored more highly on lack of acceptance and avoidance/resting behaviour while the ARD group showed significantly higher levels of catastrophizing, damage beliefs, and symptom focusing than the CFS group. CONCLUSION: Fatigue in rheumatic diseases may be perpetuated by similar underlying transdiagnostic processes. The ARD and CFS groups showed similarities but also key differences in their responses to symptoms. Specific aspects of treatment may need to be tailored towards each group. For example, lack of acceptance and avoidance behaviour may be particularly important in perpetuating fatigue in CFS.
Altman D(1), Iliadou AN(2), Lundholm C(2), Milsom I(3), Pedersen NL(2).	(1)Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden; Division of Obstetrics and Gynecology, Department of Clinical Science, Danderyd Hospital, Karolinska Institutet, Stockholm, Sweden. Electronic address: daniel.altman@ki.se. (2)Department of Medical Epidemiology	Somatic Comorbidity in Women with Overactive Bladder Syndrome.	J Urol. 2016 Aug;196(2):473-7.	PURPOSE: We explore the influence of co-occurring somatic illnesses on prevalent overactive bladder in women of premenopausal age. MATERIALS AND METHODS: Data for the present study were derived from a nationwide survey on complex diseases among all twins in the Swedish Twin Registry born 1959 to 1985. The present study was limited to female twins participating in the survey (12,850). Generalized estimating equations were used to estimate odds ratios with 95% CIs. Environmental and genetic influences were assessed in co-twin control analysis. RESULTS: Generalized estimating equations analysis showed a significant association between overactive bladder and migraine (OR 1.34, 95% CI 1.15-1.57), fibromyalgia (1.83, 1.54-2.18), chronic fatigue (1.81, 1.49-2.19) and eating disorders (1.56, 1.24-1.96). There was also a significant association with allergic disorders including asthma (1.24, 1.01-1.52) and eczema (1.22, 1.04-1.43). Among reproductive disorders, urinary tract infections (1.60, 1.40-1.84), dysmenorrhea (1.53, 1.33-1.76) and pelvic pain (1.60, 1.31-1.94) showed the strongest association with overactive bladder. Results from co-twin control analysis indicated that the significant associations observed in generalized estimating equations analysis were influenced by environmental and genetic factors without a common pathway model.

	and Biostatistics, Karolinska Institutet, Stockholm, Sweden. (3)Departments of Obstetrics and Gynecology at Sahlgrenska Academy, University of Gothenburg and Sahlgrenska University Hospital, Gothenburg, Sweden.			CONCLUSIONS: Our results suggest a multifactorial and complex pathogenesis of overactive bladder in which associations between various somatic illnesses and overactive bladder may be affected by environmental and genetic factors.
Antcliff D(1), Campbell M, Woby S, Keeley P.	(1)*The Pennine Acute Hospitals NHS Trust, Physiotherapy Department, North Manchester General Hospital, Manchester, M8 5RB, UK †School of Nursing, Midwifery and Social Work, University of Manchester, Manchester, M13 9PL, UK ‡The Pennine Acute Hospitals NHS Trust, Research and Development Department, North Manchester General Hospital, Manchester, M8 5RB, UK §Department of Health Sciences, University of Huddersfield, Huddersfield, HD1 3DH, UK.	Activity Pacing is Associated with Better and Worse Symptoms for Patients with Long-term Conditions.	Clin J Pain. 2016 Jun 17.	BACKGROUND: Activity pacing has been associated with both improved and worsened symptoms, and its role in reducing disability among patients with long-term conditions has been questioned. However, existing studies have measured pacing according to uni-dimensional subscales, and therefore the empirical evidence for pacing as a multifaceted construct remains unclear. We have developed a 26-item Activity Pacing Questionnaire (APQ-26) for chronic pain/fatigue containing five themes of pacing: activity adjustment, activity consistency, activity progression, activity planning and activity acceptance. OBJECTIVE: To assess the associations between the five APQ-26 pacing themes and symptoms of pain, physical fatigue, depression, avoidance and physical function. METHODS: Cross-sectional questionnaire design study. Data analysed using multiple regression. PARTICIPANTS: 257 adult patients with diagnoses of chronic low back pain, chronic widespread pain, fibromyalgia and chronic fatigue syndrome/myalgic encephalomyelitis. RESULTS: Hierarchical multiple regression showed that activity adjustment was significantly associated with increased physical fatigue, depression and avoidance, but decreased physical function (all P≤0.030). Activity consistency was associated with decreased pain, physical fatigue, depression and avoidance but increased physical function (all P≤0.003). Activity planning was associated with reduced physical fatigue (P=0.025) and activity acceptance was associated with increased avoidance (P=0.036). CONCLUSION: Some APQ-26 pacing themes were associated with worse symptoms and others with symptom improvement. Specifically, pacing themes involving adjusting/reducing activities were associated with worse symptoms, whereas pacing themes involving undertaking consistent activities were associated with improved symptoms. Future study will explore the causality of these associations to add clarification regarding the effects of pacing on patients' symptoms.
Antcliff D(1), Keeley P(2),	(1)The Pennine Acute Hospitals NHS Trust,	Exploring patients' opinions of activity pacing	Physiotherapy. 2016 Sep;102(3):300-7.	OBJECTIVE: Despite the frequent recommendation of activity pacing as a coping strategy for patients with chronic pain and/or fatigue, pacing is interpreted in different

Campbell M(3), Woby S(4), McGowan L(5).	Physiotherapy Department, North Manchester General Hospital, Manchester M8 5RB, UK; School of Nursing, Midwifery and Social Work, University of Manchester, Manchester M13 9PL, UK. Electronic address: Deborah.Antcliff@pat.nhs.uk. (2)Department of Health Sciences, University of Huddersfield, Huddersfield HD1 3DH, UK. (3)School of Nursing, Midwifery and Social Work, University of Manchester, Manchester M13 9PL, UK. (4)The Pennine Acute Hospitals NHS Trust, Research and Development Department, North Manchester General Hospital, Manchester M8 5RB, UK. (5)School of Healthcare, Baines Wing, University of Leeds, Leeds LS2 9JT, UK.	and a new activity pacing questionnaire for chronic pain and/or fatigue: a qualitative study.		ways and there is an absence of a widely accepted pacing scale. We have developed a new Activity Pacing Questionnaire (APQ). The aims of this study were to explore patients' views and beliefs about the concept of pacing, together with the acceptability of the APQ. DESIGN: Qualitative pragmatic study using semi-structured telephone interviews. Data were analysed using Framework analysis. PARTICIPANTS: 16 adult patients attending secondary care physiotherapy out-patient departments were recruited via purposive sampling. Diagnoses included chronic low back pain, chronic widespread pain, fibromyalgia and chronic fatigue syndrome/myalgic encephalomyelitis. FINDINGS: Pacing emerged as a multifaceted concept from participants' descriptions. The implementation of pacing was influenced by participants' age, the presence of co-morbidities and participants' emotions. The APQ was found to be generally acceptable in comparison to two existing pacing subscales. Participants undertook activities using quota/symptom-contingent approaches. Four behavioural typologies emerged: Task avoidance, Task persistence, Task fluctuation (boom-bust) and Task modification (activity pacing). CONCLUSIONS: The APQ appears to be easy to complete, and acceptable to patients who are attending physiotherapy for the management of long-term conditions. It emerged that individual patients implemented different pacing facets to varying degrees, and that different behavioural typologies were apparent. The relationships between behavioural typologies and facets of pacing warrant further investigation to facilitate the development of effective tailored pacing interventions.
Aoki R(1), Kobayashi N(2), Suzuki G(3), Kuratsune H(4),	(1)Department of Psychiatry, The Jikei University School of Medicine, 3-25-8	Human herpesvirus 6 and 7 are biomarkers for fatigue, which distinguish between physiological	Biochem Biophys Res Commun. 2016 Sep 9;478(1):424-30.	Fatigue reduces productivity and is a risk factor for lifestyle diseases and mental disorders. Everyone experiences physiological fatigue and recovers with rest. Pathological fatigue, however, greatly reduces quality of life and requires therapeutic interventions. It is therefore necessary to distinguish between the two but there has

Shimada K(2), Oka N(2), Takahashi M(2), Yamadera W(5), Iwashita M(5), Tokuno S(6), Nibuya M(7), Tanichi M(7), Mukai Y(8), Mitani K(9), Kondo K(2), Ito H(5), Nakayama K(5).	Nishi-Shimbashi, Minato-ku, Tokyo 105-8461, Japan. Electronic address: ryo-fcb@jikei.ac.jp. (2)Department of Virology, The Jikei University School of Medicine, 3-25-8 Nishi-Shimbashi, Minato-ku, Tokyo 105-8461, Japan. (3)Flight Crew Operations and Technology Unit, Japan Aerospace Exploration Agency Houston Office, 18050 Saturn Lane, Suite 310, Houston, TX 77058, USA. (4)Clinical Center for Fatigue Science, Osaka City University Graduate School of Medicine, Osaka, Japan; Department of Health Science, Faculty of Health Science for Welfare, Kansai University of Welfare Sciences, Osaka, Japan. (5)Department of Psychiatry, The Jikei University School of Medicine, 3-25-8 Nishi-Shimbashi, Minato-ku, Tokyo 105-8461, Japan. (6)Department of Defense Medicine,	fatigue and pathological fatigue.		been no biomarker for this. We report on the measurement of salivary human herpesvirus (HHV-) 6 and HHV-7 as biomarkers for quantifying physiological fatigue. They increased with military training and work and rapidly decreased with rest. Our results suggested that macrophage activation and differentiation were necessary for virus reactivation. However, HHV-6 and HHV-7 did not increase in obstructive sleep apnea syndrome (OSAS), chronic fatigue syndrome (CFS) and major depressive disorder (MDD), which are thought to cause pathological fatigue. Thus, HHV-6 and HHV-7 would be useful biomarkers for distinguishing between physiological and pathological fatigue. Our findings suggest a fundamentally new approach to evaluating fatigue and preventing fatigue-related diseases.

	National Defense Medical College, Tokorozawa, Saitama, Japan. (7)Department of Psychiatry, National Defense Medical College, Tokorozawa, Saitama, Japan. (8)Military Medicine Research Unit, Test and Evaluation Command, Japan Ground Self Defense Force, Setagaya, Tokyo, Japan. (9)Department of Internal Medicine, Japan Self-Defense Force Central Hospital, Setagaya, Tokyo, Japan.			
Arslan E(1), Yildiz S(2), Albayrak Y(3,)(4), Koklukaya E(5,)(6).	(1)Department of Electrical and Electronics Engineering, Faculty of Engineering, Sakarya University, Sakarya, Turkey. (2)Department of Physical Medicine and Rehabilitation, Egirdir Bone & Joint Disease Treatment and Rehabilitation Hospital, Isparta, Turkey. (3)Department of Electrical and Electronics Engineering, Faculty of	Rule based fuzzy logic approach for classification of fibromyalgia syndrome.	Australas Phys Eng Sci Med. 2016 Jun;39(2):501-15.	Fibromyalgia syndrome (FMS) is a chronic muscle and skeletal system disease observed generally in women, manifesting itself with a widespread pain and impairing the individual's quality of life. FMS diagnosis is made based on the American College of Rheumatology (ACR) criteria. However, recently the employability and sufficiency of ACR criteria are under debate. In this context, several evaluation methods, including clinical evaluation methods were proposed by researchers. Accordingly, ACR had to update their criteria announced back in 1990, 2010 and 2011. Proposed rule based fuzzy logic method aims to evaluate FMS at a different angle as well. This method contains a rule base derived from the 1990 ACR criteria and the individual experiences of specialists. The study was conducted using the data collected from 60 inpatient and 30 healthy volunteers. Several tests and physical examination were administered to the participants. The fuzzy logic rule base was structured using the parameters of tender point count, chronic widespread pain period, pain severity, fatigue severity and sleep disturbance level, which were deemed important in FMS diagnosis. It has been observed that generally fuzzy predictor was 95.56 % consistent with at least of the specialists, who are not a creator of the fuzzy rule base. Thus, in diagnosis classification where the severity of FMS was classified as well, consistent findings were obtained from the comparison of interpretations and experiences of specialists and the fuzzy logic approach. The study proposes a rule base, which could eliminate the shortcomings

	Engineering, Akdeniz University, Antalya, Turkey. yalbayrak@akdeniz.edu.tr. (4)Sakarya University, Sakarya, Turkey. yalbayrak@akdeniz.edu.tr. (5)Sakarya University, Sakarya, Turkey. (6)Department of Electrical and Electronics Engineering, Faculty of Engineering, Gazi University, Ankara, Turkey.			of 1990 ACR criteria during the FMS evaluation process. Furthermore, the proposed method presents a classification on the severity of the disease, which was not available with the ACR criteria. The study was not limited to only disease classification but at the same time the probability of occurrence and severity was classified. In addition, those who were not suffering from FMS were evaluated for their conditions in other patient groups.
Atkins C(1), Wilson AM(2).	(1)Norwich Medical School, University of East Anglia, Norwich, Norfolk, UK c.atkins@uea.ac.uk. (2)Norwich Medical School, University of East Anglia, Norwich, Norfolk, UK.	Managing fatigue in sarcoidosis - A systematic review of the evidence.	Chron Respir Dis. 2016 Aug 9. pii: 1479972316661926.	Fatigue is a common manifestation of sarcoidosis, often persisting without evidence of disease activity. First-line therapies for sarcoidosis have limited effect on fatigue. This review aimed to assess the treatment options targeting sarcoidosis-associated fatigue. Medline and Web of Science were searched in November 2015; the bibliographies of these papers, and relevant review papers, were also searched. Studies were included if they reported on the efficacy of interventions (both pharmacological and non-pharmacological) on fatigue scores in sarcoidosis patients. Eight studies were identified that fulfilled the inclusion criteria. These studies evaluated six different interventions (infliximab, adalimumab, ARA 290, methylphenidate, armodafinil and exercise programmes). There is evidence to support a treatment effect of anti-tumour necrosis factor (TNF)-αtherapies (adalimumab and infliximab) and neurostimulants (methylphenidate and armodafinil), but within five of the studies, the risk of bias was high within most domains and the remaining three studies included only small numbers of participants and were short in duration. Trial evidence for treating fatigue as a manifestation of sarcoidosis is limited and requires further investigation. Anti-TNF-α therapies may be beneficial in patients with organ-threatening disease. Neurostimulants have some trial evidence supporting improvements in fatigue but further investigation is needed before they can be recommended.
Baday M(1), Calamak S(1), Durmus NG(2,)(3), Davis	(1)Canary Center at Stanford for Cancer Early Detection, Radiology	Integrating Cell Phone Imaging with Magnetic Levitation (i-LEV) for Label-Free Blood Analysis	Small. 2016 Mar 2;12(9):1222-9.	There is an emerging need for portable, robust, inexpensive, and easy-to-use disease diagnosis and prognosis monitoring platforms to share health information at the point-of-living, including clinical and home settings. Recent advances in digital health technologies have improved early diagnosis, drug treatment, and personalized

RW(2,)(3,)(4), Steinmetz LM(3,)(4), Demirci U(1).	Department, School of Medicine, Stanford University, CA, 94304, USA. (2)Department of Biochemistry, School of Medicine, Stanford University, CA, 94304, USA. (3)Stanford Genome Technology Center, Stanford University, CA, 94304, USA. (4)Department of Genetics, School of Medicine, Stanford University, CA, 94304, USA.	at the Point-of-Living.		medicine. Smartphones with high-resolution cameras and high data processing power enable intriguing biomedical applications when integrated with diagnostic devices. Further, these devices have immense potential to contribute to public health in resource-limited settings where there is a particular need for portable, rapid, label-free, easy-to-use, and affordable biomedical devices to diagnose and continuously monitor patients for precision medicine, especially those suffering from rare diseases, such as sickle cell anemia, thalassemia, and chronic fatigue syndrome. Here, a magnetic levitation-based diagnosis system is presented in which different cell types (i.e., white and red blood cells) are levitated in a magnetic gradient and separated due to their unique densities. Moreover, an easy-to-use, smartphone incorporated levitation system for cell analysis is introduced. Using our portable imaging magnetic levitation (i-LEV) system, it is shown that white and red blood cells can be identified and cell numbers can be quantified without using any labels. In addition, cells levitated in i-LEV can be distinguished at single-cell resolution, potentially enabling diagnosis and monitoring, as well as clinical and research applications.
Bakken IJ(1), Tveito K(2), Aaberg KM(2,)(3), Ghaderi S(2), Gunnes N(2), Trogstad L(2), Magnus P(2), Stoltenberg C(2,)(4), Håberg SE(2).	(1)Norwegian Institute of Public Health, PO Box 4404, Nydalen, Oslo, 0403, Norway. inger.johanne.bakken @fhi.no. (2)Norwegian Institute of Public Health, PO Box 4404, Nydalen, Oslo, 0403, Norway. (3)The National Center for Epilepsy, Oslo University Hospital, Oslo, Norway. (4)Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway.	Comorbidities treated in primary care in children with chronic fatigue syndrome / myalgic encephalomyelitis: A nationwide registry linkage study from Norway.	BMC Fam Pract. 2016 Sep 2;17(1):128.	BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a complex condition. Causal factors are not established, although underlying psychological or immunological susceptibility has been proposed. We studied primary care diagnoses for children with CFS/ME, with children with another hospital diagnosis (type 1 diabetes mellitus [T1DM]) and the general child population as comparison groups. METHODS: All Norwegian children born 1992-2012 constituted the study sample. Children with CFS/ME (n = 1670) or T1DM (n = 4937) were identified in the Norwegian Patient Register (NPR) (2008-2014). Children without either diagnosis constituted the general child population comparison group (n = 1337508). We obtained information on primary care diagnoses from the Norwegian Directorate of Health. For each primary care diagnosis, the proportion and 99 % confidence interval (CI) within the three groups was calculated, adjusted for sex and age by direct standardization. RESULTS: Children with CFS/ME were more often registered with a primary care diagnosis of weakness/general tiredness (89.9 % [99 % CI 88.0 to 91.8 %]) than children in either comparison group (T1DM: 14.5 % [99 % CI: 13.1 to 16.0 %], general child population: 11.1 % [99 % CI: 11.0 to 11.2 %]). Also, depressive disorder and anxiety disorder were more common in the CFS/ME group, as were migraine, muscle pain, and infections. In the 2 year period prior to the diagnoses, infectious mononucleosis was registered for 11.1 % (99 % CI 9.1 to 13.1 %) of children with CFS/ME and for 0.5 % (99 % CI (0.2 to 0.8 %) of children with T1DM. Of children with CFS/ME, 74.6 % (1292/1670) were registered with a prior primary care diagnosis of weakness / general tiredness. The time span from the first primary care diagnosis of weakness / general tiredness to the specialist health care diagnosis of CFS/ME was 1 year or longer for

				47.8 %. CONCLUSIONS: This large nationwide registry linkage study confirms that the clinical picture in CFS/ME is complex. Children with CFS/ME were frequently diagnosed with infections, supporting the hypothesis that infections may be involved in the causal pathway. The long time span often observed from the first diagnosis of weakness / general tiredness to the diagnosis of CFS/ME might indicate that the treatment of these patients is sometimes not optimal.
Band R, Barrowclough C, Caldwell K, Emsley R, Wearden A.		Activity Patterns in Response to Symptoms in Patients Being Treated for Chronic Fatigue Syndrome: An Experience Sampling Methodology Study.	Health Psychol. 2016 Nov 7.	Objective: Cognitive-behavioral models of chronic fatigue syndrome (CFS) propose that patients respond to symptoms with 2 predominant activity patterns-activity limitation and all-or-nothing behaviors-both of which may contribute to illness persistence. The current study investigated whether activity patterns occurred at the same time as, or followed on from, patient symptom experience and affect. Method: Twenty-three adults with CFS were recruited from U.K. CFS services. Experience sampling methodology (ESM) was used to assess fluctuations in patient symptom experience, affect, and activity management patterns over 10 assessments per day for a total of 6 days. Assessments were conducted within patients' daily life and were delivered through an app on touchscreen Android mobile phones. Multilevel model analyses were conducted to examine the role of self-reported patient fatigue, pain, and affect as predictors of change in activity patterns at the same and subsequent assessment. Results: Current experience of fatigue-related symptoms and pain predicted higher patient activity limitation at the current and subsequent assessments whereas subjective wellness predicted higher all-or-nothing behavior at both times. Current pain predicted less all-or-nothing behavior at the subsequent assessment. In contrast to hypotheses, current positive affect was predictive of current activity limitation whereas current negative affect was predictive of current all-or-nothing behavior. Both activity patterns varied at the momentary level. Conclusions: Patient symptom experiences appear to be driving patient activity management patterns in line with the cognitive-behavioral model of CFS. ESM offers a useful method for examining multiple interacting variables within the context of patients' daily life. (PsycINFO Database Record
Band R(1,)(2), Barrowclough C(1), Emsley R(3), Machin M(4), Wearden AJ(1).	(1)School of Psychological Sciences & Manchester Centre for Health Psychology, University of Manchester, UK. (2)Centre for Applications of Health Psychology, University of Southampton, UK. (3)Centre for Biostatistics, Institute	Significant other behavioural responses and patient chronic fatigue syndrome symptom fluctuations in the context of daily life: An experience sampling study.	Br J Health Psychol. 2016 Sep;21(3):499-514.	OBJECTIVE: Significant other responses to patients' symptoms are important for patient illness outcomes in chronic fatigue syndrome (CFS/ME); negative responses have been associated with increased patient depression, whilst increased disability and fatigue have been associated with solicitous significant other responses. The current study aimed to examine the relationship between significant other responses and patient outcomes within the context of daily life. DESIGN: Experience Sampling Methodology (ESM). METHOD: Twenty-three patients with CFS/ME and their significant others were recruited from specialist CFS/ME services. Sixty momentary assessments, delivered using individual San Francisco Android Smartphones, were conducted over a period of 6 days. All participants reported on affect, dyadic contact, and significant other responses to the patient. Patients reported on symptom severity, disability, and activity management strategies. RESULTS: Negative significant other responses were associated

	of Population Health, University of Manchester, UK. (4)Centre for Health Informatics, Institute of Population Health, University of Manchester, UK.			with increased patient symptom severity and distress reported at the same momentary assessment; there was evidence of a potentially mediating role of concurrent distress on symptom severity. Patient-perceived solicitous responses were associated with reduced patient activity and disability reported at the same momentary assessment. Lagged analyses indicate that momentary associations between significant other responses and patient outcomes are largely transitory; significant other responses were not associated with any of the patient outcomes at the subsequent assessment. CONCLUSION: The results indicate that significant other responses are important influences on the day-to-day experience of CFS/ME. Further research examining patient outcomes in association with specific significant other behavioural responses is warranted and future interventions that target such significant other behaviours may be beneficial. Statement of contribution What is already known on this subject? The existing literature has identified that significant other responses are important with respect to patient outcomes in CFS/ME. In particular, when examined cross-sectionally and longitudinally, negative and solicitous significant other responses are associated with poorer illness outcomes. This study is the first to examine the momentary associations between negative and solicitous responses, as reported by the patient and significant other, and patient-reported outcomes. An ESM paradigm was used to assess these temporal relationships within the context of participants' daily life. What does this study add? Negative responses were associated with increased momentary patient distress and symptoms. Perceived solicitousness was associated with activity limitation but less perceived disability. The impact of significant other responses on patient outcomes was found to be transitory.
Band R(1), Chadwick E(2), Hickman H(2), Barrowclough C(3), Wearden A(3).	(1)School of Psychological Sciences & Manchester Centre for Health Psychology, University of Manchester, UK; Academic unit of Psychology & Centre for Applications of Health Psychology, University of Southampton, UK. Electronic address: r.j.band@soton.ac.uk. (2)Academic unit of Psychology & Centre for Applications of	Assessing the reliability of the five minute speech sample against the Camberwell family interview in a chronic fatigue syndrome sample.	Compr Psychiatry. 2016 May;67:9-12.	PURPOSE: The current study aimed to examine the reliability of the Five Minute Speech Sample (FMSS) for assessing relative Expressed Emotion (EE) compared with the Camberwell Family Interview (CFI) in a sample of relatives of adult patients with Chronic Fatigue Syndrome (CFS). METHOD: 21 relatives were recruited and completed both assessments. The CFI was conducted first for all participants, with the FMSS conducted approximately one month later. Trained raters independently coded both EE measures; high levels of rating reliability were established for both measures. Comparisons were conducted for overall EE status, emotional over-involvement (EOI) and criticism. FINDINGS: The distribution of high and low-EE was equivalent across the two measures, with the FMSS correctly classifying EE is 71% of cases (n=15). The correspondence between the FMSS and CFI ratings was found to be non-significant for all categorical variables. However, the number of critical comments made by relatives during the FMSS significantly correlated with the number of critical comments made during the CFI. The poorest correspondence between the measures was observed for the EOI dimension. CONCLUSION: The findings suggest that the FMSS may be a useful screening tool for identifying high-EE, particularly criticism, within a sample of relatives of patients with CFS. However, the two measures should not be assumed equivalent,

	Health Psychology, University of Southampton, UK. (3)School of Psychological Sciences & Manchester Centre for Health Psychology, University of Manchester, UK.			and the CFI should be used where possible, particularly with respect to understanding EOI.
Bansal AS(1,)(2).	(1)Department of Immunology and Allergy, St. Helier Hospital, Carshalton, Surrey, SM5 1AA, UK. Amolak.Bansal@esth.nhs.uk. (2)The Sutton CFS Service, Sutton Hospital, Cotswold Rd, Sutton, SM2 5NF, UK. Amolak.Bansal@esth.nhs.uk.	Investigating unexplained fatigue in general practice with a particular focus on CFS/ME.	BMC Fam Pract. 2016 Jul 19;17:81.	Unexplained fatigue is not infrequent in the community. It presents a number of challenges to the primary care physician and particularly if the clinical examination and routine investigations are normal. However, while fatigue is a feature of many common illnesses, it is the main problem in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). This is a poorly understood condition that is accompanied by several additional symptoms which suggest a subtle multisystem dysfunction. Not infrequently it is complicated by sleep disturbance and alterations in attention, memory and mood.Specialised services for the diagnosis and management of CFS/ME are markedly deficient in the UK and indeed in virtually all countries around the world. However, unexplained fatigue and CFS/ME may be confidently diagnosed on the basis of specific clinical criteria combined with the normality of routine blood tests. The latter include those that assess inflammation, autoimmunity, endocrine dysfunction and gluten sensitivity. Early diagnosis and intervention in general practice will do much to reduce patient anxiety, encourage improvement and prevent expensive unnecessary investigations.There is presently an on-going debate as to the precise criteria that best confirms CFS/ME to the exclusion of other medical and psychiatric/psychological causes of chronic fatigue. There is also some disagreement as to best means of investigating and managing this very challenging condition. Uncertainty here can contribute to patient stress which in some individuals can perpetuate and aggravate symptoms. A simple clinical scoring system and a short list of routine investigations should help discriminate CFS/ME from other causes of continued fatigue.
Barbour AG(1).	(1)Departments of Medicine and Microbiology & Molecular Genetics, University of California, Irvine.	"Lyme": Chronic Fatigue Syndrome by Another Name?	Clin Infect Dis. 2016 Jan 1;62(1):134-5.	Comment on Clin Infect Dis. 2015 Oct 1;61(7):1084-91.
Barboza KC(1), Salinas LM(2), Sahebjam F(2), Jesudian AB(3),	(1)Department of Medicine, New York University Langone Medical Center, New	Impact of depressive symptoms and hepatic encephalopathy on health-related quality of	Metab Brain Dis. 2016 Aug;31(4):869-80.	Depression, common in chronic medical conditions, and hepatic encephalopathy (HE), a reversible neuropsychiatric syndrome due to liver dysfunction, are associated with impaired health-related quality of life (HRQOL) in cirrhosis and hepatitis C (HCV). This study investigated the impact of depression and HE on HRQOL in cirrhotic patients with

Weisberg IL(4), Sigal SH(2).	York City, NY, USA. katherine.barboza@nyumc.org. (2)Division of Gastroenterology, Department of Medicine, New York University Langone Medical Center, New York City, NY, USA. (3)Center for Liver Disease and Transplantation, New York Presbyterian Weill Cornell Medical Center, New York, NY, USA. (4)Division of Gastroenterology, Department of Medicine, New York University Langone Medical Center, New York City, New York, USA.	life in cirrhotic hepatitis C patients.		HCV. A convenience sample of 43 ambulatory patients, with varying degrees of cirrhosis secondary to HCV, was prospectively enrolled in this study. Participants were assessed for any current depressive, fatigue, and daytime sleepiness symptoms and underwent a psychometric evaluation to determine the presence of HE symptoms. Participants reported current HRQOL on general health and liver disease-specific questionnaires. Diagnosis and current health status were confirmed via medical records. The associations between disease severity, depressive symptoms, HE, fatigue, and daytime sleepiness were measured. Predictors of HRQOL in this sample were determined. Depressive symptoms (70 %) and HE (77 %) were highly prevalent in this sample, with 58 % actively experiencing both conditions at the time of study participation. A significant positive association was found between depressive symptoms and HE severity (P = .05). Depressive symptoms were significantly associated with fatigue (P < .001), daytime sleepiness (P < .001), general HRQOL (P < .001), and disease-specific HRQOL (P < .001). HE was significantly associated with fatigue (P = .02), general HRQOL (P < .001), and disease-specific HRQOL (P < .001). Depressive symptoms and HE were significant predictors of reduced HRQOL (P < .001), with depressive symptoms alone accounting for 58.8 % of the variance. Depressive symptoms and HE accounted for 68.0 % of the variance. Findings suggest a possible pathophysiological link between depression and HE in cirrhosis, and potentially a wider-reaching benefit of treating minimal and overt HE than previously appreciated.
Bårdsen K(1), Nilsen MM(2), Kvaløy JT(3), Norheim KB(4), Jonsson G(5), Omdal R(6).	(1)Research Department, Stavanger University Hospital, Stavanger, Norway. (2)International Research Institute of Stavanger, Stavanger, Norway. (3)Research Department, Stavanger University Hospital, Stavanger, Norway Department of Mathematics and Natural Sciences, University of Stavanger, Stavanger,	Heat shock proteins and chronic fatigue in primary Sjögren's syndrome.	Innate Immun. 2016 Apr;22(3):162-7.	Fatigue occurs frequently in patients with cancer, neurological diseases and chronic inflammatory diseases, but the biological mechanisms that lead to and regulate fatigue are largely unknown. When the innate immune system is activated, heat shock proteins (HSPs) are produced to protect cells. Some extracellular HSPs appear to recognize cellular targets in the brain, and we hypothesize that fatigue may be generated by specific HSPs signalling through neuronal or glial cells in the central nervous system. From a cohort of patients with primary Sjögren's syndrome, 20 patients with high and 20 patients with low fatigue were selected. Fatigue was evaluated with a fatigue visual analogue scale. Plasma concentrations of HSP32, HSP60, HSP72 and HSP90α were measured and analysed to determine if there were associations with the level of fatigue. Plasma concentrations of HSP90α were significantly higher in patients with high fatigue compared with those with low fatigue, and there was a tendency to higher concentrations of HSP72 in patients with high fatigue compared with patients with low fatigue. There were no differences in concentrations of HSP32 and HSP60 between the high- and low-fatigue groups. Thus, extracellular HSPs, particularly HSP90α, may signal fatigue in chronic inflammation. This supports the hypothesis that fatigue is generated by cellular defence mechanisms.

	Norway. (4)Clinical Immunology Unit, Department of Internal Medicine, Stavanger University, Hospital, Stavanger, Norway. (5)Department of Medical Biochemistry, Stavanger University Hospital, Stavanger, Norway. (6)Clinical Immunology Unit, Department of Internal Medicine, Stavanger University, Hospital, Stavanger, Norway Department of Medical Science, Faculty of Medicine and Dentistry, University of Bergen, Bergen, Norway roald.omdal@sus.no.			
Barnden LR(1), Kwiatek R(2), Crouch B(3), Burnet R(4), Del Fante P(5).	(1)Department of Nuclear Medicine, The Queen Elizabeth Hospital, Woodville, SA 5011, Australia; National Centre for NeuroImmunology and Emerging Diseases, Griffith University, Gold Coast, QLD 4222, Australia. (2)Division of Medical Subspecialities, Lyell McEwin Hospital, Elizabeth, SA 5112, Australia.	Autonomic correlations with MRI are abnormal in the brainstem vasomotor centre in Chronic Fatigue Syndrome.	Neuroimage Clin. 2016 Mar 31;11:530-7.	Autonomic changes are often associated with the chronic fatigue syndrome (CFS), but their pathogenetic role is unclear and brain imaging investigations are lacking. The vasomotor centre and, through it, nuclei in the midbrain and hypothalamus play a key role in autonomic nervous system regulation of steady state blood pressure (BP) and heart rate (HR). In this exploratory cross-sectional study, BP and HR, as indicators of autonomic function, were correlated with volumetric and T1- and T2-weighted spin-echo (T1w and T2w) brain MRI in 25 CFS subjects and 25 normal controls (NC). Steady state BP (systolic, diastolic and pulse pressure) and HR in two postures were extracted from 24 h blood pressure monitoring. We performed (1) MRI versus autonomic score interaction-with-group regressions to detect locations where regression slopes differed in the CFS and NC groups (collectively indicating abnormality in CFS), and (2) MRI regressions in the CFS and NC groups alone to detect additional locations with abnormal correlations in CFS. Significant CFS regressions were repeated controlling for anxiety and depression (A&D). Abnormal regressions were detected in nuclei of the brainstem vasomotor centre, midbrain reticular formation and hypothalamus, but also in limbic nuclei involved in stress responses and in prefrontal white matter. Group

	(3)Department of Nuclear Medicine, The Queen Elizabeth Hospital, Woodville, SA 5011, Australia. (4)Endocrinology Department, Royal Adelaide Hospital, Adelaide, SA 5000, Australia. (5)Healthfirst Network, Woodville, SA 5011, Australia.			comparisons of CFS and NC did not find MRI differences in these locations. We propose therefore that these regulatory nuclei are functioning correctly, but that two-way communication between them is impaired in CFS and this affects signalling to/from peripheral effectors/sensors, culminating in inverted or magnified correlations. This single explanation for the diverse abnormal correlations detected here consolidates the conclusion for a brainstem/midbrain nerve conduction deficit inferred earlier (Barnden et al., 2015). Strong correlations were also detected in isolated NC regressions.
Bayliss K(1), Riste L(2), Band R(3), Peters S(4), Wearden A(4), Lovell K(5), Fisher L(6), Chew-Graham CA(7).	(1)Public Programmes, Central Manchester University Hospitals NHS Foundation Trust, University of Manchester, Manchester Academic Health Science Centre, Manchester, UK. kerin.bayliss@manchester.ac.uk. (2)Centre for Primary Care, Institute of Population Health, University of Manchester, Manchester, UK. (3)School of Psychology, University of Southampton, Southampton, UK. (4)School of Psychological Sciences, University of Manchester, Manchester, UK. (5)School of Nursing,	Implementing resources to support the diagnosis and management of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) in primary care: A qualitative study.	BMC Fam Pract. 2016 Jun 4;17:66.	BACKGROUND: Previous research has highlighted that many GPs lack the confidence and knowledge to diagnose and manage people with CFS/ME. Following the development of an online training module for GPs, and an information pack and DVD for patients, this study explored the extent to which these resources can be implemented in routine primary care. METHODS: Semi structured qualitative interviews were completed with patients and GPs across North West England. All interviews were transcribed and analysed using open exploratory thematic coding. Following this thematic analysis, the authors conducted a further theory-driven analysis of the data guided by Normalisation Process Theory. RESULTS: When used in line with advice from the research team, the information resource and training were perceived as beneficial to both patients and GPs in the diagnosis and management of CFS/ME. However, 47 % of patients in this study did not receive the information pack from their GP. When the information pack was used, it was often incomplete, sent in the post, and GPs did not work with patients to discuss the materials. Only13 out of 21 practices completed the training module due to time pressures and the low priority placed on low prevalence, contentious, hard to manage conditions. When the module was completed, many GPs stated that it was not feasible to retain the key messages as they saw so few patients with the condition. Due to the complexity of the condition, GPs also believed that the diagnosis and management of CFS/ME should take place in a specialist care setting. CONCLUSION: While barriers to the implementation of training and resources for CFS/ME remain, there is a need to support CFS/ME patients to access reliable, evidence based information outside primary care. Our findings suggest that future research should develop an online resource for patients to support self-management.

	Midwifery and Social Work, University of Manchester, Manchester, UK. (6)National School for Primary Care Research, University of Manchester, Manchester, UK. (7)Primary Care and Health Sciences and National School for Primary Care Research, Keele University, Keele, Staffordshire, UK.			
Bazzichi L(1), Giacomelli C(2), Consensi A(2), Atzeni F(3), Batticciotto A(4), Di Franco M(5), Casale R(6), Sarzi-Puttini P(4).	(1)Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy. l.bazzichi@gmail.com. (2)Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy. (3)IRCCS Galeazzi Orthopaedic Institute, Milan, Italy. (4)Rheumatology Unit, L. Sacco University Hospital of Milan, Italy. (5)Department of Internal Medicine and Medical Specialities, Division of Rheumatology, Sapienza University of Rome, Italy.	One year in review 2016: fibromyalgia.	Clin Exp Rheumatol. 2016 Mar-Apr;34(2 Suppl 96):S145-9. Epub 2016 Apr 22.	Fibromyalgia (FM) syndrome is a chronic disease with unknown aetiology, characterised by widespread pain, fatigue and other functional symptoms. We reviewed the literature of the past year to underline the recent progress in the etiopathogenesis, assessment and therapies of this syndrome, evaluating the articles published between January 2015 and January 2016.

	(6)Habilita, Care & Research Rehabilitation Institutes, EFIC Pain School, Department of High Technology Rehabilitation & Pain Rehabilitation Unit, Zingonia di Ciserano (Bergamo), Italy.			
Benor D(1), Rossiter-Thornton J(2), Toussaint L(3).	(1)Energy Medicine University, Mill Valley, CA, USA db@danielbenor.com. (2)Toronto, Ontario, Canada. (3)Luther College, Decorah, IA, USA.	A Randomized, Controlled Trial of Wholistic Hybrid Derived From Eye Movement Desensitization and Reprocessing and Emotional Freedom Technique (WHEE) for Self-Treatment of Pain, Depression, and Anxiety in Chronic Pain Patients.	J Evid Based Complementary Altern Med. 2016 Jul 18. pii: 2156587216659400. [Epub ahead of print]	In this pilot study, a convenience sample of 24 chronic pain patients (17 with chronic fatigue syndrome/fibromyalgia) were randomized into WHEE treatment and wait-list control groups for 6 weeks. Assessments of depression, anxiety, and pain were completed before, during, and at 1 and 3 months after treatment. Wait-listed patients then received an identical course of WHEE and assessments. WHEE decreased anxiety ($P < .5$) and depression ($P < .05$) compared with the control group. The wait-list-turned-WHEE assessments demonstrated decreased pain severity ($P < .05$) and depression ($P < .04$) but not pain interference or anxiety. WHEE appears a promising method for pain, anxiety, and depression in patients with chronic pain, compared to standard medical care alone. Though a small pilot study, the present results suggest that further research appears warranted. An incidental finding was that a majority of patients with chronic pain had suffered psychological trauma in childhood and/or adulthood.
Bezzina OM(1), Gallagher P(1), Mitchell S(2), Bowman SJ(3), Griffiths B(2), Hindmarsh V(2), Hargreaves B(2), Price EJ(4), Pease CT(5), Emery P(5), Lanyon P(6), Bombardieri M(7), Sutcliffe N(8), Pitzalis C(7), Hunter J(9), Gupta M(9), McLaren J(10), Cooper AM(11,)(12),	(1)Institute of Neuroscience, Newcastle University.	Subjective and Objective Measures of Dryness Symptoms in Primary Sjögren's Syndrome - Capturing the discrepancy.	Arthritis Care Res (Hoboken). 2016 Dec 19.	BACKGROUND: There is a weak relationship between subjective symptoms and objective markers of disease activity in individuals with Primary Sjögren's Syndrome (PSS). This presents a significant barrier to developing treatments if modifying disease markers does not translate into reduced perception of symptoms. Little is known about the reasons for this discrepancy. OBJECTIVES: To develop a novel method for capturing the discrepancy between objective tests and subjective dryness symptoms (a 'Sensitivity' scale) and to explore predictors of dryness Sensitivity. METHODS: Archive data from the UK Primary Sjogren's Syndrome Registry (n=681) was used. Patients were classified on a scale from -5 (stoical) to +5 (sensitive) depending on the degree of discrepancy between their objective and subjective symptoms classes. Sensitivity scores were correlated with demographic variables, disease-related factors and symptoms of pain, fatigue, anxiety and depression. RESULTS: Patients were on average relatively stoical for both dryness symptoms (ocular mean±s.d. -0.42±2.2, oral mean±s.d. -1.24±1.6). Twenty-seven percent of patients were classified 'sensitive' to ocular dryness in contrast to 9% for oral dryness. Hierarchical regression analyses identified the strongest predictor of ocular dryness was self-reported pain and the strongest predictor of oral dryness was self-reported fatigue. CONCLUSIONS: Ocular and oral dryness sensitivity can be classified on a continuous scale. The two symptom

Regan M(13), Giles IP(14), Isenberg DA(14), Vadivelu S(15), Coady D(16), Dasgupta B(17), McHugh NJ(18), Young-Min SA(12), Moots RJ(19), Gendi N(20), Akil M(21), MacKay K(22); UK Primary Sjögren's Syndrome Registry, Ng WF(2,)(23), Robinson LJ(1).				types are predicted by different variables. A large number of factors remain to be explored that may impact on symptom-sensitivity in PSS and the proposed method could be used to identify relatively sensitive and stoical patients for future studies.
Bhatia R(1), Kizilbash SJ(2), Ahrens SP(2), Killian JM(3), Kimmes SA(2), Knoebel EE(2), Muppa P(2), Weaver AL(3), Fischer PR(4).	(1)Mayo Medical School, Rochester, MN. (2)Mayo Medical School, Rochester, MN; Division of General Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN. (3)Mayo Medical School, Rochester, MN; Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, MN. (4)Mayo Medical School, Rochester, MN; Division of General Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN. Electronic address:	Outcomes of Adolescent-Onset Postural Orthostatic Tachycardia Syndrome.	J Pediatr. 2016 Jun;173:149-53.	OBJECTIVES: To determine the clinical course of adolescent-onset postural orthostatic tachycardia syndrome (POTS) and to assess health-related quality of life, 2-10 years after diagnosis. STUDY DESIGN: Pediatric patients, 13-18 years of age, diagnosed with POTS at Mayo Clinic, Rochester, from 2003 to 2010 were mailed a questionnaire if they were at least 18 years of age at the time of the mailing. The primary outcome measures were norm-based, age- and sex-adjusted, 36-Item Short Form Health Survey physical composite score and mental composite score. RESULTS: The survey was mailed to 502 patients with a response rate of 34% (n = 172). The mean duration from diagnosis to survey completion was 5.4 (SD, 1.9) years; the mean age of the respondents at the time of the survey was 21.8 (2.2) years. The responders were predominantly females (84% vs 68% of nonresponders; P < .001). Only 33 (19%) respondents reported complete resolution of symptoms, and an additional 51% reported persistent but improved symptoms, and 28 (16%) had only intermittent symptoms. The majority (71%) consider their health at least "good." The mean physical composite score was significantly lower than the population norm (mean [SD], 36.6 [15.8] vs 50; P < .001), however, the corresponding mean mental composite score was normal (50.1 [11.2]). CONCLUSIONS: Overall, 86% of adolescents with POTS report resolved, improved, or just intermittent symptoms, when assessed via questionnaire at an average of 5 years after initial treatment. Patients with persistent symptoms have more physical than mental health concerns.

	fischer.phil@mayo.edu.			
Billing-Ross P(1), Germain A(2), Ye K(3), Keinan A(4), Gu Z(5), Hanson MR(6).	(1)Division of Nutritional Sciences, Cornell University, Ithaca, NY, 14853, USA. pdb87@cornell.edu. (2)Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, 14853, USA. ag297@cornell.edu. (3)Department of Biological Statistics and Computational Biology, Cornell University, Ithaca, NY, 14853, USA. ky297@cornell.edu. (4)Department of Biological Statistics and Computational Biology, Cornell University, Ithaca, NY, 14853, USA. ak735@cornell.edu. (5)Division of Nutritional Sciences, Cornell University, Ithaca, NY, 14853, USA. zg27@cornell.edu. (6)Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, 14853, USA. mrh5@cornell.edu.	Mitochondrial DNA variants correlate with symptoms in myalgic encephalomyelitis/chronic fatigue syndrome.	J Transl Med. 2016 Jan 20;14:19.	BACKGROUND: Mitochondrial dysfunction has been hypothesized to occur in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), a disease characterized by fatigue, cognitive difficulties, pain, malaise, and exercise intolerance. We investigated whether haplogroup, single nucleotide polymorphisms (SNPs), or heteroplasmy of mitochondrial DNA (mtDNA) were associated with health status and/or symptoms. METHODS: Illumina sequencing of PCR-amplified mtDNA was performed to analyze sequence and extent of heteroplasmy of mtDNAs of 193 cases and 196 age- and gender-matched controls from DNA samples collected by the Chronic Fatigue Initiative. Association testing was carried out to examine possible correlations of mitochondrial sequences with case/control status and symptom constellation and severity as reported by subjects on Short Form-36 and DePaul Symptom Questionnaires. RESULTS: No ME/CFS subject exhibited known disease-causing mtDNA mutations. Extent of heteroplasmy was low in all subjects. Although no association between mtDNA SNPs and ME/CFS vs. healthy status was observed, haplogroups J, U and H as well as eight SNPs in ME/CFS cases were significantly associated with individual symptoms, symptom clusters, or symptom severity. CONCLUSIONS: Analysis of mitochondrial genomes in ME/CFS cases indicates that individuals of a certain haplogroup or carrying specific SNPs are more likely to exhibit certain neurological, inflammatory, and/or gastrointestinal symptoms. No increase in susceptibility to ME/CFS of individuals carrying particular mitochondrial genomes or SNPs was observed.

Błaut-Jurkowska J(1), Jurkowski M(1).	(1)Non-public Health Care Center, Kłaj, Poland.	[Post-Lyme disease syndrome]. [Article in Polish]	Pol Merkur Lekarski. 2016 Feb;40(236):129-33.	Lyme disease is a chronic infectious disease caused by the bacteria, spirochete of the Borrelia type. Skin, nervous system, musculoskeletal system and heart may be involved in the course of the disease. The prognosis for properly treated Lyme disease is usually good. However, in about 5% of patients so called Post-Lyme disease syndrome (PLSD) develops. It is defined as a syndrome of subjective symptoms persisting despite proper treatment of Borrelia burgdorferi infection. The most common symptoms include: fatigue, muscle and joint pain, and problems with memory and concentration. Pathogenesis of PLDS remains unknown. The differential diagnosis should include neurological, rheumatic and mental diseases. Till now there is no causative treatment of PLDS. In relieving symptom rehabilitation, painkillers, anti-inflammatory and antidepressants medicines are recommended. Emotional and psychological supports are also necessary. Non-specific symptoms reported by patients with post- Lyme disease syndrome raise the suspicion of other pathologies. This can lead to misdiagnosis and implementation of unnecessary, potentially harmful to the patient's therapy. An increase in tick-borne diseases needs to increase physicians awareness of these issues.
Blease C(1,)(2), Carel H(3), Geraghty K(4).	(1)School of Philosophy, University College Dublin, Dublin, Ireland. (2)Program in Placebo Studies, Harvard Medical School, Harvard University, Boston, USA. (3)School of Philosophy, University of Bristol, Bristol, UK. (4)Centre for Primary Care, University of Manchester, Manchester, UK.	Epistemic injustice in healthcare encounters: evidence from chronic fatigue syndrome.	J Med Ethics. 2016 Dec 5. pii: medethics-2016-103691.	Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) remains a controversial illness category. This paper surveys the state of knowledge and attitudes about this illness and proposes that epistemic concerns about the testimonial credibility of patients can be articulated using Miranda Fricker's concept of epistemic injustice. While there is consensus within mainstream medical guidelines that there is no known cause of CFS/ME, there is continued debate about how best to conceive of CFS/ME, including disagreement about how to interpret clinical studies of treatments. Against this background, robust qualitative and quantitative research from a range of countries has found that many doctors (and medical students) display uncertainty about whether CFS/ME is real, which may result in delays in diagnosis and treatment for patients. Strikingly, qualitative research evinces that patients with CFS/ME often experience suspicion by healthcare professionals, and many patients vocally oppose the effectiveness, and the conceptualisation, of their illness as psychologically treatable. We address the intersection of these issues and healthcare ethics, and claim that this state of affairs can be explained as a case of epistemic injustice (2007). We find evidence that healthcare consultations are fora where patients with CFS/ME may be particularly vulnerable to epistemic injustice. We argue that the (often unintentional) marginalisation of many patients is a professional failure that may lead to further ethical and practical consequences both for progressive research into CFS/ME, and for ethical care and delivery of current treatments among individuals suffering from this debilitating illness.
Blockmans D(1), Persoons P(2).	(1)a Department of General Internal Medicine , University	Long-term methylphenidate intake in chronic fatigue syndrome.	Acta Clin Belg. 2016 Dec;71(6):407-414. Epub 2016 Jun 27.	OBJECTIVE: Concentration disturbances are frequent in chronic fatigue syndrome (CFS). In a placebo-controlled double-blind crossover study, methylphenidate over 4 weeks was superior to placebo in the relief of fatigue and concentration disturbance. This

	Hospital Gasthuisberg , Leuven , Belgium. (2)b Department of Psychiatry , University Hospital Gasthuisberg , Leuven , Belgium.			observational study describes the effect of long-term methylphenidate intake on fatigue, concentration, and daily life activities, as reported by the patients themselves. METHODS: A questionnaire was sent to all CFS patients who were prescribed methylphenidate at the general internal medicine department of a university hospital between August 2004 and February 2007, for possible improvement of concentration difficulties and fatigue. RESULTS: Out of 194 consecutive patients, 149 (76.8%) sent the questionnaire back. At the time of the questionnaire, 65.3% had stopped the intake of methylphenidate, 34.7% still took it daily or occasionally. Among the patients who continued methylphenidate, 48% reported an at least 50% improvement of fatigue, and 62% reported an at least 50% improvement of concentration difficulties. This continued intake of methylphenidate resulted in more working hours in these patients. Side effects (agitation, palpitations, and dry mouth) were reported significantly more in patients who had stopped methylphenidate than in those who still took it. CONCLUSION: The long-term intake of methylphenidate by CFS patients with concentration difficulties has a positive effect in about one out of three patients.
Boggero IA, Rojas-Ramirez MV, de Leeuw R, Carlson CR.		Satisfaction with Life in Orofacial Pain Disorders: Associations and Theoretical Implications.	J Oral Facial Pain Headache. 2016 Spring;30(2):99-106.	AIMS: To test if patients with masticatory myofascial pain, local myalgia, centrally mediated myalgia, disc displacement, capsulitis/synovitis, or continuous neuropathic pain differed in self-reported satisfaction with life. The study also tested if satisfaction with life was similarly predicted by measures of physical, emotional, and social functioning across disorders. METHODS: Satisfaction with life, fatigue, affective distress, social support, and pain data were extracted from the medical records of 343 patients seeking treatment for chronic orofacial pain. Patients were grouped by primary diagnosis assigned following their initial appointment. Satisfaction with life was compared between disorders, with and without pain intensity entered as a covariate. Disorder-specific linear regression models using physical, emotional, and social predictors of satisfaction with life were computed. RESULTS: Patients with centrally mediated myalgia reported significantly lower satisfaction with life than did patients with any of the other five disorders. Inclusion of pain intensity as a covariate weakened but did not eliminate the effect. Satisfaction with life was predicted by measures of physical, emotional, and social functioning, but these associations were not consistent across disorders. CONCLUSIONS: Results suggest that reduced satisfaction with life in patients with centrally mediated myalgia is not due only to pain intensity. There may be other factors that predispose people to both reduced satisfaction with life and centrally mediated myalgia. Furthermore, the results suggest that satisfaction with life is differentially influenced by physical, emotional, and social functioning in different orofacial pain disorders.
Boissoneault J(1), Letzen J(1), Lai S(2), O'Shea A(1), Craggs J(1),	(1)Department of Clinical and Health Psychology, University of Florida.	Abnormal resting state functional connectivity in patients with chronic fatigue syndrome: an	Magn Reson Imaging. 2016 May;34(4):603-8.	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a debilitating disorder characterized by severe fatigue and neurocognitive dysfunction. Recent work from our laboratory and others utilizing arterial spin labeling functional magnetic resonance imaging (ASL) indicated that ME/CFS patients have lower resting

Robinson ME(1), Staud R(3).	(2)Department of Radiation Oncology, and Human Imaging Core of Clinical and Translational Science Institute, University of Florida. (3)Department of Medicine, University of Florida. Electronic address: staudr@ufl.edu.	arterial spin-labeling fMRI study.		state regional cerebral blood flow (rCBF) in several brain areas associated with memory, cognitive, affective, and motor function. This hypoperfusion may underlie ME/CFS pathogenesis and may result in alterations of functional relationships between brain regions. The current report used ASL to compare functional connectivity of regions implicated in ME/CFS between patients and healthy controls (HC). METHODS: Participants were 17 ME/CFS patients (Mage=48.88years, SD=12) fulfilling the 1994 CDC criteria and 17 age/sex matched HC (Mage=49.82years, SD=11.32). All participants underwent T1-weighted structural MRI as well as a 6-min pseudo-continuous arterial spin labeling (pCASL) sequence, which quantifies CBF by magnetically labeling blood as it enters the brain. Imaging data were preprocessed using SPM 12 and ASL tbx, and seed-to-voxel functional connectivity analysis was conducted using the CONN toolbox. All effects noted below are significant at $p<0.05$ with cluster-wise FDR correction for multiple comparisons. RESULTS: ME/CFS patients demonstrated greater functional connectivity relative to HC in bilateral superior frontal gyrus, ACC, precuneus, and right angular gyrus to regions including precuneus, right postcentral gyrus, supplementary motor area, posterior cingulate gyrus, and thalamus. In contrast, HC patients had greater functional connectivity than ME/CFS in ACC, left parahippocampal gyrus, and bilateral pallidum to regions including right insula, right precentral gyrus, and hippocampus. Connectivity of the left parahippocampal gyrus correlated strongly with overall clinical fatigue of ME/CFS patients. CONCLUSION: This is the first ASL based connectivity analysis of patients with ME/CFS. Our results demonstrate altered functional connectivity of several regions associated with cognitive, affective, memory, and higher cognitive function in ME/CFS patients. Connectivity to memory related brain areas (parahippocampal gyrus) was correlated with clinical fatigue ratings, providing supporting evidence that brain network abnormalities may contribute to ME/CFS pathogenesis.
Boissoneault J(1), Letzen J(1), Lai S(2), Robinson ME(1), Staud R(3).	(1) Department of Clinical and Health Psychology, University of Florida, Gainesville, FL, USA. (2) Department of Radiation Oncology, University of Florida, Gainesville, FL, USA. (3) Department of Medicine, University of Florida, Gainesville, FL, USA. staudr@ufl.edu.	Static and dynamic functional connectivity in patients with chronic fatigue syndrome: use of arterial spin labelling fMRI.	Clin Physiol Funct Imaging. 2016 Sep 28.	Studies using arterial spin labelling (ASL) have shown that individuals with chronic fatigue syndrome (CFS) have decreased regional cerebral blood flow, which may be associated with changes in functional neural networks. Indeed, recent studies indicate disruptions in functional connectivity (FC) at rest in chronically fatigued patients including perturbations in static FC (sFC), that is average FC at rest between several brain regions subserving neurocognitive, motor and affect-related networks. Whereas sFC often provides information of functional network reorganization in chronic illnesses, investigations of temporal changes in functional connectivity between multiple brain areas may shed light on the dynamic characteristics of brain network activation associated with such maladies. We used ASL fMRI in 19 patients with CFS and 15 healthy controls (HC) to examine both static and dynamic changes in FC among several a priori selected brain regions during a fatiguing cognitive task. HC showed greater increases than CFS in static FC (sFC) between insula and temporo-occipital structures and between precuneus and thalamus/striatum. Furthermore, inferior

				frontal gyrus connectivity to cerebellum, occipital and temporal structures declined in HC but increased in CFS. Patients also showed lower dynamic FC (dFC) between hippocampus and right superior parietal lobule. Both sFC and dFC correlated with task-related fatigue increases. These data provide the first evidence that perturbations in static and dynamic FC may underlie chronically fatigued patients' report of task-induced fatigue. Further research will determine whether such changes in sFC and dFC are also characteristic for other fatigued individuals, including patients with chronic pain, cancer and multiple sclerosis.
Brady E(1), Segar J, Sanders C.	(1)Centre for Primary Care, University of Manchester, Manchester, United Kingdom. ellen.brady1987@gmail.com.	"I Always Vet Things": Navigating Privacy and the Presentation of Self on Health Discussion Boards Among Individuals with Long-Term Conditions.	J Med Internet Res. 2016 Oct 13;18(10):e274.	BACKGROUND: The ethics of research into online communities is a long-debated issue, with many researchers arguing that open-access discussion groups are publically accessible data and do not require informed consent from participants for their use for research purposes. However, it has been suggested that there is a discrepancy between the perceived and actual privacy of user-generated online content by community members. OBJECTIVE: There has been very little research regarding how privacy is experienced and enacted online. The objective of this study is to address this gap by qualitatively exploring the expectations of privacy on Internet forums among individuals with long-term conditions. METHODS: Semistructured interviews were conducted with 20 participants with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and 21 participants with type 1 and 2 diabetes mellitus, and were analyzed using thematic analysis. Participants were recruited via online and offline routes, namely forums, email lists, newsletters, and face-to-face support groups. RESULTS: The findings indicate that privacy online is a nebulous concept. Rather than individuals drawing a clear-cut distinction between what they would and would not be comfortable sharing online, it was evident that these situations were contextually dependent and related to a number of unique and individual factors. CONCLUSIONS: Interviewees were seen to carefully manage how they presented themselves on forums, filtering and selecting the information that they shared about themselves in order to develop and maintain a particular online persona, while maintaining and preserving an acceptable level of privacy.
Brække Norheim K(1), Imgenberg-Kreuz J(2), Jonsdottir K(3), Janssen EA(3), Syvänen AC(2), Sandling JK(4), Nordmark G(5), Omdal R(6).	(1)Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Stavanger, Norway katnorheim@gmail.com. (2)Molecular Medicine and Science for Life Laboratory,	Epigenome-wide DNA methylation patterns associated with fatigue in primary Sjögren's syndrome.	Rheumatology (Oxford). 2016 Jun;55(6):1074-82.	OBJECTIVE: Chronic fatigue is a common, disabling and poorly understood phenomenon. Recent studies indicate that epigenetic mechanisms may be involved in the expression of fatigue, a prominent feature of primary SS (pSS). The aim of this study was to investigate whether DNA methylation profiles of whole blood are associated with fatigue in patients with pSS. METHODS: Forty-eight pSS patients with high (n = 24) or low (n = 24) fatigue as measured by a visual analogue scale were included. Genome-wide DNA methylation was investigated using the Illumina HumanMethylation450 BeadChip array. After quality control, a total of 383 358 Cytosine-phosphate-Guanine (CpG) sites remained for further analysis. Age, sex and differential cell count estimates were included as covariates in the association model. A false discovery rate-corrected P < 0.05 was considered significant, and a cut-off of 3% average difference in methylation

	Department of Medical Sciences, Uppsala University, Uppsala, Sweden. (3)Department of Pathology, Stavanger University Hospital, Stavanger, Norway. (4)Molecular Medicine and Science for Life Laboratory, Department of Medical Sciences, Uppsala University, Uppsala, Sweden Rheumatology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden. (5)Rheumatology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden. (6)Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Stavanger, Norway.			levels between high- and low-fatigue patients was applied. RESULTS: A total of 251 differentially methylated CpG sites were associated with fatigue. The CpG site with the most pronounced hypomethylation in pSS high fatigue annotated to the SBF2-antisense RNA1 gene. The most distinct hypermethylation was observed at a CpG site annotated to the lymphotoxin alpha gene. Functional pathway analysis of genes with differently methylated CpG sites in subjects with high vs low fatigue revealed enrichment in several pathways associated with innate and adaptive immunity. CONCLUSION: Some genes involved in regulation of the immune system and in inflammation are differently methylated in pSS patients with high vs low fatigue. These findings point to functional networks that may underlie fatigue. Epigenetic changes could constitute a fatigue-regulating mechanism in pSS.
Braley TJ(1), Boudreau EA(2,)(3,)(4).	(1)University of Michigan Department of Neurology, Multiple Sclerosis and Sleep Disorders Centers, 1500 E. Medical Center Dr, C728 Med-Inn Building, Ann	Sleep Disorders in Multiple Sclerosis	Curr Neurol Neurosci Rep. 2016 May;16(5):50. .	Recent studies suggest that individuals with multiple sclerosis (MS) are at increased risk for sleep disturbances and that sleep disturbances contribute to fatigue and other chronic symptoms in MS. Although fatigue occurs commonly in people with MS, this symptom is often attributed to MS-specific pathology. Consequently, sleep disorders are often unrecognized and untreated in this population. Timely diagnosis and treatment of sleep problems in MS offer a new opportunity to ameliorate some of the daytime fatigue experienced by patients with MS. To increase this opportunity, the practitioner should be comfortable performing basic screening for common sleep

	Arbor, MI, USA. (2)Department of Neurology, Oregon Health & Science University, 3181 SW Sam Jackson Park Road L226, Portland, OR, 97239-3098, USA. boudreau@ohsu.edu. (3)Department of Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, 3181 SW Sam Jackson Park Road L226, Portland, OR, 97239-3098, USA. boudreau@ohsu.edu. (4)Portland VA Medical Center, P3-ECOE, 3710 SW US Veterans Hospital Road, Portland, OR, 97239, USA. boudreau@ohsu.edu.			complaints among patients with MS. The objectives of this review are to summarize the latest relevant data on sleep disorders in MS and offer a helpful approach to the identification and workup of the most common sleep problems in this population. Unexplored research avenues and opportunities to address important questions at the interface of sleep and MS are also discussed.
Brenu EW(1), Broadley S(2), Nguyen T(3), Johnston S(3), Ramos S(1), Staines D(1), Marshall-Gradisnik S(3).	(1)The National Centre for Neuroimmunology and Emerging Diseases, Griffith Health Institute, Griffith University, Gold Coast, Australia. (2)School of Medicine, Griffith University, Gold Coast, Australia. (3)The National Centre for Neuroimmunology and Emerging	A Preliminary Comparative Assessment of the Role of CD8+ T Cells in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and Multiple Sclerosis.	J Immunol Res. 2016;2016:9064529.	Background. CD8+ T cells have putative roles in the regulation of adaptive immune responses during infection. The purpose of this paper is to compare the status of CD8+ T cells in Multiple Sclerosis (MS) and Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). Methods. This preliminary investigation comprised 23 CFS/ME patients, 11 untreated MS patients, and 30 nonfatigued controls. Whole blood samples were collected from participants, stained with monoclonal antibodies, and analysed on the flow cytometer. Using the following CD markers, CD27 and CD45RA (CD45 exon isoform 4), CD8+ T cells were divided into naïve, central memory (CM), effector memory CD45RA- (EM), and effector memory CD45RA+ (EMRA) cells. Results. Surface expressions of BTLA, CD127, and CD49/CD29 were increased on subsets of CD8+ T cells from MS patients. In the CFS/ME patients CD127 was significantly decreased on all subsets of CD8+ T cells in comparison to the nonfatigued controls. PSGL-1 was significantly reduced in the CFS/ME patients in comparison to the nonfatigued controls. Conclusions. The results suggest significant deficits in the

	Diseases, Griffith Health Institute, Griffith University, Gold Coast, Australia; School of Medical Science, Griffith University, Gold Coast, Australia.			expression of receptors and adhesion molecules on subsets of CD8+ T cells in both MS and CFS/ME patients. These deficits reported may contribute to the pathogenesis of these diseases. However, larger sample size is warranted to confirm and support these encouraging preliminary findings.
Brewer J(1), Thrasher JD(2), Hooper D(3).	(1)Plaza Infectious Disease and St. Luke's Hospital, 4320 Wornall Road, Suite 440, Kansas City, MO 64111, USA. jbrewer@plazamedicine.com. (2)Citrus Heights, CA 95610, USA. toxicologist1@msn.com. (3)RealTime Laboratories, Carrollton, TX 75010, USA. dhooper@realtimelab.com.	Reply to Comment on Detection of Mycotoxin in Patients with Chronic Fatigue Syndrome. Toxins 2013, 5, 605-617" by Mark J. Mendell.	Toxins (Basel). 2016 Nov 7;8(11). pii: E325.	The authors of [1] have received further correspondence from Mark J. Mendell [2] concerning the above paper.[..].
Brewer J(1), Thrasher JD(2), Hooper D(3).	(1)Plaza Infectious Disease and St. Luke's Hospital, 4320 Wornall Road, Suite 440, Kansas City, MO 64111, USA. jbrewer@plazamedicine.com. (2)Citrus Heights, CA 95610, USA. toxicologist1@msn.com. (3)RealTime Laboratories, Carrollton, TX 75010, USA.	Reply to Comment on Detection of Mycotoxins in Patients with Chronic Fatigue Syndrome Toxins 2013, 5, 605-617 by John W. Osterman, M.D.	Toxins (Basel). 2016 Nov 7;8(11). pii: E323.	This paper [1] was an observational case study.[..].

	dhooper@realtimelab.com.			
Brigden A(1), Beasant L(1), Hollingworth W(1), Metcalfe C(2), Gaunt D(2), Mills N(1), Jago R(3), Crawley E(1).	(1)School of Social and Community Medicine, University of Bristol, Bristol, UK. (2)Bristol Randomised Trials Collaboration & School of Social and Community Medicine, University of Bristol, Bristol, UK. (3)Centre for Exercise, Nutrition & Health Sciences, School for Policy Studies, Bristol, UK.	Managed Activity Graded Exercise iN Teenagers and pre-Adolescents (MAGENTA) feasibility randomised controlled trial: study protocol.	BMJ Open. 2016 Jul 4;6(7):e011255.	INTRODUCTION: Paediatric chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is a relatively common and disabling condition, yet there is a limited evidence base for treatment. There is good evidence that graded exercise therapy is moderately effective in adults with CFS/ME, but there is little evidence for the effectiveness, cost-effectiveness, acceptability or best method of delivery for paediatric CFS/ME. This study aims to investigate the acceptability and feasibility of carrying out a multicentre randomised controlled trial investigating the effectiveness of graded exercise therapy compared with activity management for children/teenagers who are mildly or moderately affected with CFS/ME. METHODS AND ANALYSIS: 100 paediatric patients (8-17 years) with CFS/ME will be recruited from 3 specialist UK National Health Service (NHS) CFS/ME services (Bath, Cambridge and Newcastle). Patients will be randomised (1:1) to receive either graded exercise therapy or activity management. Feasibility analysis will include the number of young people eligible, approached and consented to the trial; attrition rate and treatment adherence; questionnaire and accelerometer completion rates. Integrated qualitative methods will ascertain perceptions of feasibility and acceptability of recruitment, randomisation and the interventions. All adverse events will be monitored to assess the safety of the trial. ETHICS AND DISSEMINATION: The trial has received ethical approval from the National Research Ethics Service (South West-Frenchay 15/SW/0124). TRIAL REGISTRATION NUMBER: ISRCTN23962803; Pre-results.
Broadbent S(1), Coutts R.	(1)School of Health and Human Sciences, Southern Cross University, Lismore, NSW, AUSTRALIA.	Graded versus Intermittent Exercise Effects on Lymphocytes in Chronic Fatigue Syndrome.	Med Sci Sports Exerc. 2016 Sep;48(9):1655-63.	PURPOSE: There is increasing evidence of immune system dysfunction in chronic fatigue syndrome (CFS), but little is known of the regular exercise effects on immune cell parameters. This pilot study investigated the effects of graded and intermittent exercise on CD4 lymphocyte subset counts and activation compared with usual care. METHODS: Twenty-four CFS patients (50.2 ± 10 yr) were randomized to graded exercise (GE), intermittent exercise (IE), or usual care (UC) groups; 18 sedentary non-CFS participants (50.6 ± 10 yr) were controls (CTL) for blood and immunological comparisons. Outcome measures were pre- and postintervention flow cytometric analyses of circulating lymphocyte subset cell counts; expression of CD3, CD4, CD25, and CD134; full blood counts; and V˙O2peak. RESULTS: Preintervention, CD3 cell counts, and expression of CD4, CD25, CD134, and CD4CD25CD134 were significantly lower in GE, IE, and UC compared with CTL ($P < 0.05$). Total lymphocyte concentration was significantly lower in GE and IE groups compared with CTL. There were significant postintervention increases in i) expression of CD4 and CD4CD25CD134 for GE and IE, but CD25 and CD134 for IE only; ii) circulating counts of CD3 and CD4 for GE, and CD3, CD4, CD8, CD3CD4CD8, CD3CD16CD56, CD19, and CD45 for IE; iii) neutrophil concentration for GE; and iv) V˙O2peak and elapsed test time for IE and GE, V˙Epeak for IE. CONCLUSIONS: Twelve weeks of GE and IE training significantly improved CD4

				lymphocyte activation and aerobic capacity without exacerbating CFS symptoms. IE may be a more effective exercise modality with regard to enhanced CD4 activation in CFS patients.
Burfeind KG(1), Michaelis KA(1), Marks DL(2).	(1)Papé Family Pediatric Research Institute, Oregon Health & Science University, Portland, OR, USA; MD/PhD Program, Oregon Health & Science University, Portland, OR, USA. (2)Papé Family Pediatric Research Institute, Oregon Health & Science University, Portland, OR, USA. Electronic address: marksd@ohsu.edu.	The central role of hypothalamic inflammation in the acute illness response and cachexia.	Semin Cell Dev Biol. 2016 Jun;54:42-52.	When challenged with a variety of inflammatory threats, multiple systems across the body undergo physiological responses to promote defense and survival. The constellation of fever, anorexia, and fatigue is known as the acute illness response, and represents an adaptive behavioral and physiological reaction to stimuli such as infection. On the other end of the spectrum, cachexia is a deadly and clinically challenging syndrome involving anorexia, fatigue, and muscle wasting. Both of these processes are governed by inflammatory mediators including cytokines, chemokines, and immune cells. Though the effects of cachexia can be partially explained by direct effects of disease processes on wasting tissues, a growing body of evidence shows the central nervous system (CNS) also plays an essential mechanistic role in cachexia. In the context of inflammatory stress, the hypothalamus integrates signals from peripheral systems, which it translates into neuroendocrine perturbations, altered neuronal signaling, and global metabolic derangements. Therefore, we will discuss how hypothalamic inflammation is an essential driver of both the acute illness response and cachexia, and why this organ is uniquely equipped to generate and maintain chronic inflammation. First, we will focus on the role of the hypothalamus in acute responses to dietary and infectious stimuli. Next, we will discuss the role of cytokines in driving homeostatic disequilibrium, resulting in muscle wasting, anorexia, and weight loss. Finally, we will address mechanisms and mediators of chronic hypothalamic inflammation, including endothelial cells, chemokines, and peripheral leukocytes.
Calle Gómez Á(1), Delgado Díez B(1), Campillo I López F(1), Salmerón Ruiz MA(2), Casas Rivero J(1).	(1)Unidad de Medicina de la Adolescencia, Hospital Universitario La Paz, Madrid, España. (2)Unidad de Medicina de la Adolescencia, Hospital Universitario La Paz, Madrid, España. Electronic address: mariasalmeronruiz@gmail.com.	[Chronic fatigue syndrome in adolescents]. [Article in Spanish]	An Pediatr (Barc). 2016 Dec;85(6):318-320.	
Campion P(1).	(1) University of Hull. E-mail: p.d.campion@hull.ac.uk.	Chronic fatigue syndrome: is the biopsychosocial model responsible for patient dissatisfaction and	Br J Gen Pract. 2016 Oct;66(651):511.	

		harm?		
Casson SM(1), Sandler C, Bogg T, Lloyd A, Barry B.	(1)1University New South Wales, Australia, Sydney, Australia. 2University of New South Wales & Neuroscience Research Australia, Sydney, Australia.	Capturing Activity Pacing in People with Chronic Fatigue Syndrome Using Actigraphy: 422 Board #259 June 1, 9: 30 AM - 11: 00 AM.	Med Sci Sports Exerc. 2016 May;48(5 Suppl 1):118.	
Castro-Marrero J(1), Sáez-Francàs N(2), Segundo MJ(3), Calvo N(4), Faro M(5), Aliste L(5), Fernández de Sevilla T(5), Alegre J(5).	(1)CFS Clinical Unit, Vall d'Hebron University Hospital Research Institute, Universitat Autònoma de Barcelona, 08035, Barcelona, Spain. Electronic address: jesus.castro@vhir.org. (2)Psychiatry Unit, Sant Rafael Hospital (FIDMAG), 08035, Barcelona, Spain; Psychiatry Department, Vall d'Hebron University Hospital (CIBERSAM), Universitat Autònoma de Barcelona, 08035, Barcelona, Spain. (3)Vitae Natural Nutrition, S.L., Sant Cugat del Vallès, 08172, Barcelona, Spain. (4)Psychiatry Department, Vall d'Hebron University Hospital (CIBERSAM), Universitat Autònoma de Barcelona, 08035, Barcelona, Spain.	Effect of coenzyme Q10 plus nicotinamide adenine dinucleotide supplementation on maximum heart rate after exercise testing in chronic fatigue syndrome - A randomized, controlled, double-blind trial.	Clin Nutr. 2016 Aug;35(4):826-34.	BACKGROUND & AIMS: Chronic Fatigue Syndrome (CFS) is a complex condition, characterized by severe disabling fatigue with no known cause, no established diagnostic tests, and no universally effective treatment. Several studies have proposed symptomatic treatment with coenzyme Q10 (CoQ10) and nicotinamide adenine dinucleotide (NADH) supplementation. The primary endpoint was to assess the effect of CoQ10 plus NADH supplementation on age-predicted maximum heart rate (max HR) during a cycle ergometer test. Secondary measures included fatigue, pain and sleep. METHODS: A proof-of-concept, 8-week, randomized, controlled, double-blind trial was conducted in 80 CFS patients assigned to receive either CoQ10 plus NADH supplementation or matching placebo twice daily. Maximum HR was evaluated at baseline and at end of the run-in period using an exercise test. Fatigue, pain and sleep were evaluated at baseline, and then reassessed at 4- and 8-weeks through self-reported questionnaires. RESULTS: The CoQ10 plus NADH group showed a significant reduction in max HR during a cycle ergometer test at week 8 versus baseline (P = 0.022). Perception of fatigue also showed a decrease through all follow-up visits in active group versus placebo (P = 0.03). However, pain and sleep did not improve in the active group. Coenzyme Q10 plus NADH was generally safe and well tolerated. CONCLUSIONS: Our results suggest that CoQ10 plus NADH supplementation for 8 weeks is safe and potentially effective in reducing max HR during a cycle ergometer test and also on fatigue in CFS. Further additional larger controlled trials are needed to confirm these findings. Clinical trial registrationThis trial was registered at clinicaltrials.gov as NCT02063126.

	(5)CFS Clinical Unit, Vall d'Hebron University Hospital Research Institute, Universitat Autònoma de Barcelona, 08035, Barcelona, Spain.			
Cathébras P(1).	(1)Service de médecine interne, CHU de Saint-Étienne, 42055 Saint-Étienne cedex 2, France. Electronic address: pascal.cathebras@chu-st-etienne.fr.	[What's in a name? New and older labels for chronic fatigue]. [Article in French]	Rev Med Interne. 2016 Dec;37(12):791-795.	
Chacko A(1), Staines DR(2), Johnston SC(1), Marshall-Gradisnik SM(1).	(1)School of Medical Science, Griffith University, QLD, Australia.; The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, QLD, Australia. (2)The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, QLD, Australia.	Dysregulation of Protein Kinase Gene Expression in NK Cells from Chronic Fatigue Syndrome/Myalgic Encephalomyelitis Patients.	Gene Regul Syst Bio. 2016 Aug 28;10:85-93.	BACKGROUND: The etiology and pathomechanism of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) are unknown. However, natural killer (NK) cell dysfunction, in particular reduced NK cytotoxic activity, is a consistent finding in CFS/ME patients. Previous research has reported significant changes in intracellular mitogen-activated protein kinase pathways from isolated NK cells. The purpose of this present investigation was to examine whether protein kinase genes have a role in abnormal NK cell intracellular signaling in CFS/ME. METHOD: Messenger RNA (mRNA) expression of 528 protein kinase genes in isolated NK cells was analyzed (nCounter GX Human Kinase Kit v2 (XT); NanoString Technologies) from moderate (n = 11; age, 54.9 ± 10.3 years) and severe (n = 12; age, 47.5 ± 8.0 years) CFS/ME patients (classified by the 2011 International Consensus Criteria) and nonfatigued controls (n = 11; age, 50.0 ± 12.3 years). RESULTS: The expression of 92 protein kinase genes was significantly different in the severe CFS/ME group compared with nonfatigued controls. Among these, 37 genes were significantly upregulated and 55 genes were significantly downregulated in severe CFS/ME patients compared with nonfatigued controls. CONCLUSIONS: In severe CFS/ME patients, dysfunction in protein kinase genes may contribute to impairments in NK cell intracellular signaling and effector function. Similar changes in protein kinase genes may be present in other cells, potentially contributing to the pathomechanism of this illness.
Chan J S M(1,)(2), Li A(3,)(4,)(5), Ng SM(1), Ho R T H(1,)(2), Xu A(6,)(7,)(8), Yao	(1)Centre on Behavioral Health, Faculty of Social Science, The University of Hong	Adiponectin potentially contributes to the anti-depressive effects of Baduanjin Qigong exercise in women with chronic	Cell Transplant. 2016 Dec 7.	Our recent study demonstrates that adiponectin signaling plays a significant role in mediating physical exercise-exerted effects on hippocampal neurogenesis and antidepression in mice. Whether the findings can be translated to humans remains unknown. This study aimed to investigate the effects of Baduanjin Qigong exercise on adiponectin, and evaluate whether adiponectin is involved in the anti-

TJ(9), Wang XM(2), So KF(3,)(4,)(5), Chan C L W(1,)(2).	Kong, Hong Kong SAR, China. (2)Department of Social Work and Social Administration, Faculty of Social Science, The University of Hong Kong, Hong Kong Special AdministrationRegion (Hong Kong SAR), China. (3)Guangdong-Hong Kong-Macau Institute of CNS Regeneration, Guangdong Key Laboratory of Brain Function and Diseases, Jinan University, Guangzhou, China (4)Departments of Ophthalmology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China (5)State Key Laboratory of Brain and Cognitive Sciences, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China (6)Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong	fatigue syndrome-like illness.		depressive effects of Qigong exercise on chronic fatigue syndrome (CFS)-like illness. This is a randomized, waitlist-controlled trial. One hundred and eight female participants were randomly assigned to either Qigong exercise or waitlist groups. Sixteen 1.5-hour Qigong lessons were conducted. Outcome measures were taken at three time points. Baseline adiponectin levels were negatively associated with body weight, body mass index, waist circumference, hip circumference and waist/hip ratio in women with CFS-like illness. Compared with waitlist control, Qigong exercise significantly reduced anxiety and depressive symptoms, and significantly raised plasma adiponectin levels (median = 0.8 vs. -0.1, $p < 0.05$). More interestingly, increases in adiponectin level following Qigong exercise were associated with decreases in depression score for the Qigong group ($r = - 0.38$, $p = 0.04$). Moreover, adjusted linear regression analysis further identified Qigong exercise and change in adiponectin level as the significant factors accounting for reduction of depressive symptoms. Baduanjin Qigong significantly increased adiponectin level in females with CFS-like illness. Decreases in depressive symptoms were associated with increases in adiponectin levels following Qigong exercise, indicating that the potential contribution of adiponectin to Qigong exercise-elicited anti-depressive effects in human subjects. .

	Kong SAR, China (7)Department of Pharmacology and Pharmacy, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China (8)State Key Laboratory of Pharmaceutical Biotechnology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, China (9)Department of Biostatistics, Harvard C.H. Chan School of Public Health, Cambridge, MA, USA			
Chelimsky G(1), Kovacic K(1), Simpson P(2), Nugent M(2), Basel D(3), Banda J(1), Chelimsky T(4).	(1)Center for Pediatric Neurogastroenterology, Motility, and Autonomic Disorders, Medical College of Wisconsin, Milwaukee, WI. (2)Division of Quantitative Health Sciences, Medical College of Wisconsin, Milwaukee, WI. (3)Division of Pediatric Genetics, Medical College of Wisconsin, Milwaukee, WI. (4)Center for Pediatric	Benign Joint Hypermobility Minimally Impacts Autonomic Abnormalities in Pediatric Subjects with Chronic Functional Pain Disorders.	J Pediatr. 2016 Oct;177:49-52.	OBJECTIVE: To determine if children with benign joint hypermobility (BJH) syndrome and chronic functional pain disorders have more autonomic dysfunction. STUDY DESIGN: Retrospective chart review study of pediatric patients seen in the pediatric neurogastroenterology and autonomic clinic who underwent autonomic testing and had either a Beighton score of ≥6 and met Brighton criteria for BJH (with BJH) or a score of ≤2 (no BJH). RESULTS: Twenty-one female subjects (10 without BJH) met inclusion criteria; 64% of BJH had diagnosis confirmed by genetics consultation. We evaluated for postural tachycardia syndrome, syncope, orthostatic intolerance, and orthostatic hypotension. None of these diagnoses, as well as baseline heart rate, peak heart rate in first 10 minutes of head up tilt (P = .35 and P = .61, respectively), and sudomotor index (suggestive of autonomic neuropathy) (P = .58), showed differences between the groups. Age of onset of symptoms was also similar (P = .61) (BJH vs without BJH: median [range]:15.6 years [12.9-17.5] vs 15.4 years [11.1-18.2]). There was no difference between groups in complaints of migraine, chronic nausea, chronic fatigue, lightheadedness, dizziness, fainting >3 times/lifetime, delayed onset of sleep, irritable bowel syndrome, dyspepsia, abdominal migraine, functional abdominal pain, constipation, or fibromyalgia. CONCLUSIONS: Children with chronic functional pain disorders and BJH have autonomic testing findings and comorbid features compared

	Neurogastroenterology, Motility, and Autonomic Disorders, Medical College of Wisconsin, Milwaukee, WI; Department of Neurology, Medical College of Wisconsin, Milwaukee, WI.			with a similar cohort of subjects without BJH, suggesting that BJH is not the driver of the autonomic and comorbid disorders.
Chen CH(1), Yang TY, Lin CL, Chen CS, Lin WM, Kuo CN, Lin MC, Kao CH.	(1)From the Department of Medical Laboratory Science and Biotechnology (CHC); Molecular and Genomic Epidemiology Center, China Medical University Hospital, China Medical University, Taichung (T-YY); Division of Nephrology, Department of Internal Medicine, Changhua Christian Hospital, Changhua (T-YY); Management Office for Health Data, China Medical University Hospital (C-LL); College of Medicine (C-LL); Division of Chinese Trauma, China Medical University Hospital, China Medical University, Taichung (C-SC);	Dry Eye Syndrome Risks in Patients With Fibromyalgia: A National Retrospective Cohort Study.	Medicine (Baltimore). 2016 Jan;95(4):e2607.	The coexistence of fibromyalgia (FM) and dry eye syndrome (DES) has been previously reported. However, there are few studies on how patients with FM may develop concomitant DES. Patients with chronic widespread pain, like FM, chronic fatigue syndrome, and irritable bowel syndrome (IBS), was concerned for the rheumatic or psychosomatic disorders which might adequately reflect the long-term risk of DES. We retrieved data on FM patients from the National Health Insurance Research Database of Taiwan covering the years 2000 to 2011. Our FM population consisted of 25,777 patients versus 103,108 patients in the non-FM group: the overall incidence of DES in these populations was 7.37/10,000 and 4.81/10,000, respectively. Male FM patients had a higher incidence of DES, with a 1.39-fold DES risk for males and a 1.45-fold for females after adjustment for confounding factor. Notably, FM patients aged ≤49 years had an elevated 80% risk of DES compared with the non-FM group. Without comorbidities, FM patients had an approximately 1.40-fold risk of DES than those without FM. The additive effects of FM and IBS or FM and sleep disturbance were pointed out that the risk for DES would be elevated when the FM patients with IBS or sleep disturbance. FM patients have a higher incidence of DES than that of non-FM patients. They carry long-term DES risks from a relatively young age, particularly those with psychiatric problems. Risk stratification for a timely psychiatric medication intervention and risk modifications are not intended.

	Department of Diagnostic Radiology, Chang Gung Memorial Hospital, Chiayi (W-ML); Chang Gung University, Taoyuan (W-ML); Kau-Tang Traditional Medical Hospital, Taichung (C-NK); Department of Nuclear Medicine, I-Shou University, Kaohsiung (M-GL); Department of Nuclear Medicine and PET Center, China Medical University Hospital (C-HK); and Graduate Institute of Clinical Medical Science and School of Medicine, College of Medicine, China Medical University, Taichung, Taiwan (C-HK).			
Chen Y(1), Shergis JL(2), Wu L(1), Yu X(1), Zeng Q(3), Xu Y(3), Guo X(4), Zhang AL(2), Xue CC(5), Lin L(6).	(1)Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, Guangdong Province, China; Department of Respiratory Medicine, Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, Guangdong Province, China. (2)China-Australia International Research Centre for	A systematic review and meta-analysis of the herbal formula Buzhong Yiqi Tang for stable chronic obstructive pulmonary disease.	Complement Ther Med. 2016 Dec;29:94-108.	OBJECTIVE: To systematically evaluate the efficacy and safety of Buzhong Yiqi Tang (BZYQT) for stable chronic obstructive pulmonary disease (COPD). METHODS: Three electronic English databases (PubMed, EMBASE and CENTRAL) and four Chinese databases (CBM, CNKI, CQVIP and WFMO) were searched from their inceptions until 30th June 2016. Participants were diagnosed with COPD according to the Chinese Medical Association's COPD diagnosis and treatment guidelines or Global Initiative for Chronic Obstructive Lung Disease (GOLD), and were in stable stage. Randomized controlled trials (RCTs) of oral BZYQT, alone or combined with conventional treatment, compared with conventional treatment alone or plus placebo were included in the review. Clinical improvement and the six-minute walking test (6MWT) were the primary outcome measures. The secondary outcome measures were defined as forced expiratory volume in one second (FEV1), forced vital capacity (FVC), respiratory muscle strength index with maximum inspiratory pressure (MIP), COPD Assessment Test (CAT), and frequency of acute exacerbations. To assess risk of bias the Cochrane, Risk of Bias

	Chinese Medicine, School of Health and Biomedical Sciences, RMIT University, Melbourne, Australia. (3)Department of Respiratory Medicine, Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, Guangdong Province, China. (4)Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, Guangdong Province, China. (5)Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, Guangdong Province, China; China-Australia International Research Centre for Chinese Medicine, School of Health and Biomedical Sciences, RMIT University, Melbourne, Australia. Electronic address: charlie.xue@rmit.edu.au. (6)Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, Guangdong Province, China; Department of Respiratory Medicine, Guangdong Provincial Hospital of Chinese			tool was used, and statistical analysis was performed using RevMan 5.3.0 software. RESULTS: Sixteen studies (1400 participants) were included. The results of meta-analysis indicated patients receiving BZYQT alone or BZYQT in combination with conventional treatment showed a significant increase in clinical improvement (RR 1.25, 95% CI 1.18 to 1.33, I(2)=0%), enhanced exercise capacity 6MWT (MD 51.22m, 95% CI 45.56 to 56.89, I(2)=44%), improved lung function FVC (L) (MD 0.26 liters, 95% CI 0.18 to 0.33, I(2)=37%), reduced respiratory muscle fatigue MIP (MD 0.46 liters, 95% CI 0.11 to 0.80, I(2)=0%), and improved quality of life CAT (MD -2.56 points, 95% CI -3.40 to -1.72, I(2)=0%) when compared with conventional treatment alone, or plus placebo. BZYQT also showed small but significant improvements in FEV1% and decreased acute exacerbations of COPD. Four studies reported that no adverse events occurred, other studies did not mention adverse events. The finding should be considered with caution because the included studies had methodological shortfalls. CONCLUSIONS: BZYQT improves clinically important outcomes for patients with stable COPD, such as improved clinical symptoms, exercise capacity, lung function and quality of life. Moreover, it has an excellent safety profile. However further evaluation is needed to validate these preliminary findings in high quality RCTs.

	Medicine, Guangzhou, Guangdong Province, China; Guangdong Provincial Key Laboratory of Clinical Research on Traditional Chinese Medicine Syndrome, Guangzhou, Guangdong Province, China. Electronic address: drlinlin620@163.com.			
Chi A(1), Zhang Y(2), Kang Y(2), Shen Z(2).	(1)Laboratory of Nutrition and Hygiene, Shaanxi Normal University, Xi'an 710119, China. Electronic address: 381686871@qq.com. (2)Laboratory of Nutrition and Hygiene, Shaanxi Normal University, Xi'an 710119, China.	Metabolic mechanism of a polysaccharide from Schisandra chinensis to relieve chronic fatigue syndrome.	Int J Biol Macromol. 2016 Dec;93(Pt A):322-332.	Schisandra chinensis fruits are a famous traditional Chinese medicine to treat all kinds of fatigue. This study aimed to investigate the therapeutic effect and metabolic mechanism of a polysaccharide (SCP) from Schisandra chinensis fruits on chronic fatigue syndrome (CFS). SCP was isolated and the physicochemical properties were analyzed. A CFS model of rats was established and the urinary metabonomic studies were performed using gas chromatography time-of-flight mass spectrometry (GC-TOF-MS) in combination with multivariate statistical analysis. The results showed that SCP is a protein-bound polysaccharide. The amino acid composition of SCP consisted of 12 amino acids. The growth and the behaviors of the rats in the CFS model group were worse than those in the control group and improved after SCP treatment. Analysis of the GC-TOF-MS revealed that twelve metabolites were significantly changed, and six metabolites were oppositely and significantly changed after the SCP treatment. The TCA cycle metabolic pathways and the alanine, aspartate and glutamate metabolism were identified as significant metabolic pathways involved with SCP. The therapeutic mechanism of SCP against CFS was partially due to the restoration of these disturbed pathways.
Chiauzzi E(1), DasMahapatra P(2), Cochin E(2), Bunce M(3), Khoury R(3), Dave P(3).	(1)PatientsLikeMe, Inc., 160 Second Street, Cambridge, MA, 02142, USA. echiauzzi@patientslikeme.com. (2)PatientsLikeMe, Inc., 160 Second Street, Cambridge, MA, 02142, USA. (3)Genenetech, South	Factors in Patient Empowerment: A Survey of an Online Patient Research Network.	200. Patient. 2016 Dec;9(6):511-523.	BACKGROUND: Providers and healthcare organizations have begun recognizing the importance of patient empowerment as a driver of patient-centered care. Unfortunately, most studies have investigated empowerment with single diseases. Identifying factors of empowerment across conditions and populations would enable a greater understanding of this construct. OBJECTIVE: The purpose of this study was to understand empowerment in relation to health information-seeking, interactions with providers and peers, and healthcare access in chronic disease patients. This study also sought to identify key empowerment factors and their association with patient characteristics. METHODS: Participants were recruited through PatientsLikeMe, an online research platform where patients share their personal and medical history data. Patients completed an online survey that assessed self-reported health behavior (e.g.

	San Francisco, CA, USA.			knowledge-seeking, experiences with healthcare providers, and peer interactions) and healthcare access. An exploratory factor analysis identified key empowerment domains. Domain level sum scores and sum of all domains (total score) were compared across patient characteristics and diseases. RESULTS: Overall, 3988 participants were included in the study, with the majority actively involved in their healthcare, but many cited difficulties with matching their treatment goals with those of their physician (34 %) and spending sufficient time with the physician (36 %). Factor analysis identified two domains-Positive Patient-Provider Interaction, and Knowledge and Personal Control-that explained >60 % of the overall variance in the observed variables. Mean total empowerment scores for patients with a primary complaint of Parkinson's disease (61.8) and multiple sclerosis (60.3) were significantly greater than fibromyalgia (55.3) and chronic fatigue syndrome (54.8). Patients who were older, male, more educated, and insured also reported significantly greater levels of empowerment. CONCLUSIONS: The two domains of empowerment identified in this study are consistent with previous studies, but the differences in empowerment levels across diseases suggest a need for further studies on disease-related attributes of empowerment. Future research should examine the pathways for empowerment, as well as the relationship between empowerment domains and clinical outcomes.
Choi HH(1), Cho YS(1).	(1)Department of Internal Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea.	Fecal Microbiota Transplantation: Current Applications, Effectiveness, and Future Perspectives	256. Clin Endosc. 2016 May;49(3):257-65. .	Fecal microbiota transplantation (FMT) is the infusion of liquid filtrate feces from a healthy donor into the gut of a recipient to cure a specific disease. A fecal suspension can be administered by nasogastric or nasoduodenal tube, colonoscope, enema, or capsule. The high success rate and safety in the short term reported for recurrent Clostridium difficile infection has elevated FMT as an emerging treatment for a wide range of disorders, including Parkinson's disease, fibromyalgia, chronic fatigue syndrome, myoclonus dystopia, multiple sclerosis, obesity, insulin resistance, metabolic syndrome, and autism. There are many unanswered questions regarding FMT, including donor selection and screening, standardized protocols, long-term safety, and regulatory issues. This article reviews the efficacy and safety of FMT used in treating a variety of diseases, methodology, criteria for donor selection and screening, and various concerns regarding FMT.
Chouard CH(1).	(1)a ENT Department & AudioPhonoProsthesis Laboratory of the Paris-Saint-Antoine Hospital , Paris , France Paris.	Did Napoleon suffer from chronic rhonchopathy?	45. Acta Otolaryngol. 2016 Nov 9:1-4.	CONCLUSION: If Napoleon had been treated, Europa would then have doubtless been different, and perhaps would not have known the last two World wars. OBJECTIVES: This study plans to demonstrate that Napoleon very probably suffered from Chronic Rhonchopathy. BACKGROUND: Between 1983-1993, the author led their ENT department of CHU Saint-Antoine to contribute in the knowledge of chronic snoring and Obstructive Sleep Apneas Syndrome (OSAS), and to define the treatment of their consequences. As a result of these efforts, in Paris in 1987 the First International Congress on Chronic Rhonchopathy was organized. Obstructive Sleep Apnoea Syndrome (OSAS) is caused by anatomical and intermittent obstruction of the upper airway, which impedes passage of air to the lungs during sleep. Recent literature

				demonstrates that chronic snoring frequently precedes this obstruction by several years, and always accompanies this syndrome. All life long, there is a severity increasing continuum between more light snoring and more severe OSAS, i.e. Pickwick Syndrome. This continuum is described as a new disease called Chronic Rhonchopathy. This term was never discussed; since 2006, it has been implicitly recognized. MATERIALS AND METHOD: Napoleon would sleep very little. He used to wake up in the night and then grasp the chance to work. Brief sleeping time in day repaired his fatigue. He also had a short and thick neck. In the last quarter of his life he had progressively suffered from obesity, daily involuntary sleepiness, and his intellectual capabilities had been undoubtedly decreasing. In the vast literature concerning Napoleon's behavior, the author brought together the clinical elements which could be due to this disease. This study looked for the morphological peculiarities of this OSAS in sculpture and painting, that had the Emperor as the model. RESULTS: Napoleon presented surely diurnal somnolence, asthenia, obesity, neck shortness, retrognatia, and nasal pathology. He did not suffer from these troubles while he was young. On the contrary, he took advantage of his multiple awakenings, doubtlessly due to apnea occurring during his paradoxical sleep, to deal with some of his main masterpieces, e.g. the French Code Civil. With age, the Emperor's chronic rhonchopathy became more severe. If he had benefitted of modern treatments, maybe Moskowa would not have been a French defeat and Waterloo would have been a victory for France.
Ciregia F(1), Kollipara L(2), Giusti L(1), Zahedi RP(2), Giacomelli C(3), Mazzoni MR(1), Giannaccini G(1), Scarpellini P(4), Urbani A(5,)(6), Sickmann A(2,)(7,)(8), Lucacchini A(1), Bazzichi L(3).	(1) Department of Pharmacy, University of Pisa, Pisa, Italy. (2) Leibniz-Institut für Analytische Wissenschaften-ISAS, Dortmund, Germany. (3) Division of Rheumatology, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy. (4) Division of Psychiatry, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy. (5) Istituto di Biochimica e Biochimica Clinica,	Bottom-up proteomics suggests an association between differential expression of mitochondrial proteins and chronic fatigue syndrome.	89. Transl Psychiatry. 2016 Sep 27;6(9):e904.	Chronic fatigue syndrome (CFS) is a debilitating and complex disorder characterized by unexplained fatigue not improved by rest. An area of investigation is the likely connection of CFS with defective mitochondrial function. In a previous work, we investigated the proteomic salivary profile in a couple of monozygotic twins discordant for CFS. Following this work, we analyzed mitochondrial proteins in the same couple of twins. Nano-liquid chromatography electrospray ionization mass spectrometry (nano-LC-MS) was used to study the mitochondria extracted from platelets of the twins. Subsequently, we selected three proteins that were validated using western blot analysis in a big cohort of subjects (n=45 CFS; n=45 healthy), using whole saliva (WS). The selected proteins were as follows: aconitate hydratase (ACON), ATP synthase subunit beta (ATPB) and malate dehydrogenase (MDHM). Results for ATPB and ACON confirmed their upregulation in CFS. However, the MDHM alteration was not confirmed. Thereafter, seeing the great variability of clinical features of CFS patients, we decided to analyze the expression of our proteins after splitting patients according to clinical parameters. For each marker, the values were actually higher in the group of patients who had clinical features similar to the ill twin. In conclusion, these results suggest that our potential markers could be one of the criteria to be taken into account for helping in diagnosis. Furthermore, the identification of biomarkers present in particular subgroups of CFS patients may help in shedding light upon the complex entity of CFS. Moreover, it could help in developing tailored treatments.

	Università Cattolica, Rome, Italy. (6) Proteomics and Metabonomics Unit, IRCCS-Fondazione Santa Lucia, Rome, Italy. (7) Department of Chemistry, College of Physical Sciences, University of Aberdeen. Aberdeen, UK. (8)Medizinische Fakultät, Medizinische Proteom-Center, Ruhr-Universität Bochum, Bochum, Germany.			
Clark JE(1), Fai Ng W(2), Watson S(1), Newton JL(3).	(1)Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK. (2)Faculty of Medical Sciences, Institute of Cellular Medicine, Newcastle University, Clinical Academic Office, 3rd Floor, William Leech Building, Newcastle upon Tyne NE2 4HH, UK. (3)Faculty of Medical Sciences, Institute of Cellular Medicine, Newcastle University, Clinical Academic Office, 3rd Floor, William Leech Building, Newcastle upon Tyne NE2 4HH, UK Newcastle	The aetiopathogenesis of fatigue: unpredictable, complex and persistent.	277. Br Med Bull. 2016 Mar;117(1):139-48.	BACKGROUND: Chronic fatigue syndrome is a common condition characterized by severe fatigue with post-exertional malaise, impaired cognitive ability, poor sleep quality, muscle pain, multi-joint pain, tender lymph nodes, sore throat or headache. Its defining symptom, fatigue is common to several diseases. AREAS OF AGREEMENT: Research has established a broad picture of impairment across autonomic, endocrine and inflammatory systems though progress seems to have reached an impasse. AREAS OF CONTROVERSY: The absence of a clear consensus view of the pathophysiology of fatigue suggests the need to switch from a focus on abnormalities in one system to an experimental and clinical approach which integrates findings across multiple systems and their constituent parts and to consider multiple environmental factors. GROWING POINTS: We discuss this with reference to three key factors, non-determinism, non-reductionism and self-organization and suggest that an approach based on these principles may afford a coherent explanatory framework for much of the observed phenomena in fatigue and offers promising avenues for future research. AREAS TIMELY FOR DEVELOPING RESEARCH: By adopting this approach, the field can examine issues regarding aetiopathogenesis and treatment, with relevance for future research and clinical practice.

	Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK julia.newton@newcastle.ac.uk julia.newton@ncl.ac.uk.			
Clark LV(1), McCrone P, Ridge D, Cheshire A, Vergara-Williamson M, Pesola F, White PD.	(1)Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, United Kingdom. l.clark@qmul.ac.uk.	Graded Exercise Therapy Guided Self-Help Trial for Patients with Chronic Fatigue Syndrome (GETSET): Protocol for a Randomized Controlled Trial and Interview Study.	170. JMIR Res Protoc. 2016 Jun 8;5(2):e70.	BACKGROUND: Chronic fatigue syndrome, also known as myalgic encephalomyelitis (CFS/ME), is characterized by chronic disabling fatigue and other symptoms, which are not explained by an alternative diagnosis. Previous trials have suggested that graded exercise therapy (GET) is an effective and safe treatment. GET itself is therapist-intensive with limited availability. OBJECTIVE: While guided self-help based on cognitive behavior therapy appears helpful to patients, Guided graded Exercise Self-help (GES) is yet to be tested. METHODS: This pragmatic randomized controlled trial is set within 2 specialist CFS/ME services in the South of England. Adults attending secondary care clinics with National Institute for Health and Clinical Excellence (NICE)-defined CFS/ME (N=218) will be randomly allocated to specialist medical care (SMC) or SMC plus GES while on a waiting list for therapist-delivered rehabilitation. GES will consist of a structured booklet describing a 6-step graded exercise program, supported by up to 4 face-to-face/telephone/Skype™ consultations with a GES-trained physiotherapist (no more than 90 minutes in total) over 8 weeks. The primary outcomes at 12-weeks after randomization will be physical function (SF-36 physical functioning subscale) and fatigue (Chalder Fatigue Questionnaire). Secondary outcomes will include healthcare costs, adverse outcomes, and self-rated global impression change scores. We will follow up all participants until 1 year after randomization. We will also undertake qualitative interviews of a sample of participants who received GES, looking at perceptions and experiences of those who improved and worsened. RESULTS: The project was funded in 2011 and enrolment was completed in December 2014, with follow-up completed in March 2016. Data analysis is currently underway and the first results are expected to be submitted soon. CONCLUSIONS: This study will indicate whether adding GES to SMC will benefit patients who often spend many months waiting for rehabilitative therapy with little or no improvement being made during that time. The study will indicate whether this type of guided self-management is cost-effective and safe. If this trial shows GES to be acceptable, safe, and comparatively effective, the GES booklet could be made available on the Internet as a practitioner and therapist resource for clinics to recommend, with the caveat that patients also be supported with guidance from a trained physiotherapist. The pragmatic approach in this trial means that GES findings will be generalizable to usual National Health Service (NHS) practice. TRIAL REGISTRATION: International Standard Randomized Controlled Trial Number (ISRTCTN):

				22975026; http://www.isrctn.com/ISRCTN22975026 (Archived by WebCite at http://www.webcitation.org/6gBK00CUX).
Colaris MJ(1,)(2), de Boer M(1,)(2), van der Hulst RR(1,)(2), Cohen Tervaert JW(3,)(4).	(1)Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands. (2)Reconstructive, Plastic and Hand Surgery, Maastricht University Medical Center, Maastricht, The Netherlands. (3)Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands. jw.cohentervaert@maastrichtuniversity.nl. (4)Clinical and Experimental Immunology, Reinaert Clinic, Maastricht, The Netherlands. jw.cohentervaert@maastrichtuniversity.nl.	Two hundreds cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature.	141. Immunol Res. 2016 Jul 13.	In this study, we compared one hundred patients with autoimmune/inflammatory syndrome induced by adjuvants (ASIA) due to silicone implant incompatibility syndrome diagnosed in 2014 in Maastricht, the Netherlands, with one hundred historical patients with adjuvant breast disease diagnosed in the Baylor College of Medicine, Houston, USA, between 1985 and 1992. Similarities and differences between these two cohorts were identified to determine whether the spectrum of silicone-related disease changed during the last 30 years. Patients with complaints possibly due to silicone-filled breast implants were prospectively examined in the Reinaert Clinic, Maastricht, the Netherlands between January 2014 and October 2014. All patients were evaluated for the fulfilment of ASIA criteria. Results were compared to results of the Baylor College cohort and 18 other reviewed historical cohorts. Clinical manifestations between the Maastricht and Baylor College cohorts were comparable. Fatigue was observed in 98 current patients and in 95 historical patients. Arthralgia was observed in 91 versus 81 historical patients. Myalgia was observed in 54 versus 91 patients. Cognitive impairment was observed in 78 versus 81 patients, pyrexia was observed in 64 versus 52 patients, sicca complaints in 73 versus 72 patients and severe neurological manifestations in 20 versus 32 patients. From the 54 patients who underwent removal of their silicone breast implant, 50 % (n = 27) of the patients experienced improvement of complaints after explantation of the implant. Also, in the 18 reviewed historical cohorts, similar clinical manifestations were described. Our findings suggest that no major changes were present in the observed clinical manifestations between the Maastricht and Baylor College cohorts. Also, despite changes in the principal constituents of the silicone implants during the past fifty years, silicone remained an adjuvant that may 'bleed' and subsequently may be a chronic stimulus to the immune system resulting in similar clinical manifestations as observed in the Maastricht cohort, the Baylor College cohort and 18 other large cohorts of patients. We therefore conclude that silicone-related disease has not changed during the last 30 years.
Collatz A(1), Johnston SC(2), Staines DR(2), Marshall-Gradisnik SM(2).	(1)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia; School of Medical Sciences, Griffith University, Gold Coast, QLD,	A Systematic Review of Drug Therapies for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.	180. Clin Ther. 2016 Jun;38(6):1263-1271.e9.	PURPOSE: The pathogenesis of chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is complex and remains poorly understood. Evidence regarding the use of drug therapies in CFS/ME is currently limited and conflicting. The aim of this systematic review was to examine the existing evidence on the efficacy of drug therapies and determine whether any can be recommended for patients with CFS/ME. METHODS: MEDLINE, EMBASE, and PubMed databases were searched from the start of their records to March 2016 to identify relevant studies. Randomized controlled trials focusing solely on drug therapy to alleviate and/or eliminate chronic fatigue symptoms were included in the review. Any trials that considered graded exercise therapy, cognitive behavior therapy, adaptive pacing, or any other nonpharmaceutical treatment plans were excluded. The inclusion criteria were examined to ensure that

	Australia. Electronic address: ansel.collatz@griffithuni.edu.au. (2)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia; School of Medical Sciences, Griffith University, Gold Coast, QLD, Australia.			study participants met specific CFS/ME diagnostic criteria. Study size, intervention, and end point outcome domains were summarized. FINDINGS: A total of 1039 studies were identified with the search terms; 26 studies met all the criteria and were considered suitable for review. Three different diagnostic criteria were identified: the Holmes criteria, International Consensus Criteria, and the Fukuda criteria. Primary outcomes were identified as fatigue, pain, mood, neurocognitive dysfunction and sleep quality, symptom severity, functional status, and well-being or overall health status. Twenty pharmaceutical classes were trialed. Ten medications were shown to be slightly to moderately effective in their respective study groups ($P < 0.05$). IMPLICATIONS: These findings indicate that no universal pharmaceutical treatment can be recommended. The unknown etiology of CFS/ME, and complications arising from its heterogeneous nature, contributes to the lack of clear evidence for pharmaceutical interventions. However, patients report using a large number and variety of medications. This finding highlights the need for trials with clearly defined CFS/ME cohorts. Trials based on more specific criteria such as the International Consensus Criteria are recommended to identify specific subgroups of patients in whom treatments may be beneficial.
Collin SM(1), Nikolaus S(2), Heron J(3), Knoop H(2), White PD(4), Crawley E(3).	(1)School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, UK. Electronic address: simon.collin@bristol.ac.uk. (2)Expert Centre for Chronic Fatigue, Radboud University Medical Centre Nijmegen, The Netherlands. (3)School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, UK. (4)Wolfson Institute of Preventive Medicine, Barts and the London	Chronic fatigue syndrome (CFS) symptom-based phenotypes in two clinical cohorts of adult patients in the UK and The Netherlands.	304. J Psychosom Res. 2016 Feb;81:14-23.	OBJECTIVE: Studies have provided evidence of heterogeneity within chronic fatigue syndrome (CFS), but few have used data from large cohorts of CFS patients or replication samples. METHODS: 29 UK secondary-care CFS services recorded the presence/absence of 12 CFS-related symptoms; 8 of these symptoms were recorded by a Dutch tertiary service. Latent Class Analysis (LCA) was used to assign symptom profiles (phenotypes). Regression models were fitted with phenotype as outcome (in relation to age, sex, BMI, duration of illness) and exposure (in relation to comorbidities and patient-reported measures). RESULTS: Data were available for 7041 UK and 1392 Dutch patients. Almost all patients in both cohorts presented with post-exertional malaise, cognitive dysfunction and disturbed/unrefreshing sleep, and these 3 symptoms were excluded from LCA. In UK patients, six phenotypes emerged: 'full' polysymptomatic (median 8, IQR 7-9 symptoms) 32.8%; 'pain-only' (muscle/joint) 20.3%; 'sore throat/painful lymph node' 4.5%; and 'oligosymptomatic' (median 1, IQR 0-2 symptoms) 4.7%. Two 'partial' polysymptomatic phenotypes were similar to the 'full' phenotype, bar absence of dizziness/nausea/palpitations (21.4%) or sore throat/painful lymph nodes (16.3%). Women and patients with longer duration of illness were more likely to be polysymptomatic. Polysymptomatic patients had more severe illness and more comorbidities. LCA restricted to 5 symptoms recorded in both cohorts indicated 3 classes (polysymptomatic, oligosymptomatic, pain-only), which were replicated in Dutch data. CONCLUSIONS: Adults with CFS may have one of 6 symptom-based phenotypes associated with sex, duration and severity of illness, and comorbidity. Future research needs to determine whether phenotypes predict treatment outcomes, and require different treatments.

	School of Medicine and Dentistry, Queen Mary University of London, London, UK.			
Collin SM(1), Norris T(1), Nuevo R(1), Tilling K(2), Joinson C(1), Sterne JA(2), Crawley E(3).	(1)School of Social & Community Medicine and Centre for Child & Adolescent Health, University of Bristol, Bristol, United Kingdom. (2)School of Social & Community Medicine and. (3)School of Social & Community Medicine and Centre for Child & Adolescent Health, University of Bristol, Bristol, United Kingdom esther.crawley@bristol.ac.uk.	Chronic Fatigue Syndrome at Age 16 Years.	301. Pediatrics. 2016 Feb;137(2):e20153434.	BACKGROUND: In the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort, chronic disabling fatigue lasting ≥6 months affected 1.3% of 13-year-olds, was equally common in boys and girls, and became more prevalent with increasing family adversity. METHODS: ALSPAC data were used to estimate the prevalence of chronic fatigue syndrome (CFS) at age 16 years, defined by parental report of unexplained disabling fatigue lasting ≥6 months. We investigated gender and a composite 14-item family adversity index as risk factors. School absence data were obtained from the National Pupil Database. Multiple imputation was used to address bias caused by missing data. RESULTS: The prevalence of CFS was 1.86% (95% confidence interval [CI]: 1.47 to 2.24). After excluding children with high levels of depressive symptoms, the prevalence was 0.60% (95% CI: 0.37 to 0.84). Authorized school absences were much higher (mean difference: 35.6 [95% CI: 26.4 to 44.9] half-day sessions per academic year) and reported depressive symptoms were much more likely (odds ratio [OR]: 11.0 [95% CI: 5.92 to 20.4]) in children with CFS than in those without CFS. Female gender (OR: 1.95 [95% CI: 1.33 to 2.86]) and family adversity (OR: 1.20 [95% CI: 1.01 to 1.42] per unit family adversity index) were also associated with CFS. CONCLUSIONS: CFS affected 1.9% of 16-year-olds in a UK birth cohort and was positively associated with higher family adversity. Gender was a risk factor at age 16 years but not at age 13 years or in 16-year-olds without high levels of depressive symptoms.
Copeland SM(1).	(1)CauseHealth Project, Norwegian University of Life Sciences, Ås, Norway.	Unexpected findings and promoting monocausal claims, a cautionary tale.	168. J Eval Clin Pract. 2016 Jun 10.	Stories of serendipitous discoveries in medicine incorrectly imply that the path from an unexpected observation to major discovery is straightforward or guaranteed. In this paper, I examine a case from the field of research about chronic fatigue syndrome (CFS). In Norway, an unexpected positive result during clinical care has led to the development of a research programme into the potential for the immunosuppressant drug rituximab to relieve the symptoms of CFS. The media and public have taken up researchers' speculations that their research results indicate a causal mechanism for CFS - consequently, patients now have great hope that 'the cause' of CFS has been found, and thus, a cure is sure to follow. I argue that a monocausal claim cannot be correctly asserted, either on the basis of the single case of an unexpected, although positive, result or on the basis of the empirical research that has followed up on that result. Further, assertion and promotion of this claim will have specific harmful effects: it threatens to inappropriately narrow the scope of research on CFS, might misdirect research altogether, and could directly and indirectly harm patients. Therefore, the CFS case presents a cautionary tale, illustrating the risks involved in drawing a theoretical hypothesis from an unexpected observation. Further, I draw attention to the tendency in contemporary clinical research with CFS to promote new research directions on the

				basis of reductive causal models of that syndrome. Particularly, in the case of CFS research, underdetermination and causal complexity undermine the potential value of a monocausal claim. In sum, when an unexpected finding occurs in clinical practice or medical research, the value of following up on that finding is to be found not in the projected value of a singular causal relationship inferred from the finding but rather in the process of research that follows.
Costabel U, Wessendorf TE, Bonella F.		[Epidemiology and Clinical Presentation of Sarcoidosis]. [Article in German]	131. Klin Monbl Augenheilkd. 2016 Jul 25.	Sarcoidosis is a systemic disease of unknown aetiology. Typical histology shows epithelioid cell granulomas, and typical immunopathology enhanced Th1 type immune responses in the involved organs. The disease occurs worldwide, but more frequently in northern countries than in the south. In Germany, the incidence is estimated to be 10 per 100,000, and the prevalence 44-48 per 100,000. Sarcoidosis usually affects adults under 50 years of age, but can also be seen in children, adolescents and in the elderly. Women are more frequently affected than men. Familial clusters can occur. The clinical presentation of sarcoidosis varies widely and depends on the manifestations in the individual organ. Systemic symptoms include fatigue, night sweats, weight loss, fever, arthralgia and myalgia. Organ-specific symptoms include cough and dyspnoea, with pulmonary involvement, headache and palsy in neurosarcoidosis, arrhythmias and heart failure in cardiac sarcoidosis, and manifold skin lesions with skin involvement. Relapses are rarely seen in acute sarcoidosis, whereas the chronic form tends to relapse more frequently. Löfgren's syndrome, a specific phenotype of acute sarcoidosis, is characterised by bihilar lymphadenopathy, ankle arthritis and erythema nodosum. Chronic sarcoidosis can be asymptomatic, despite radiological changes, which may be extensive. By definition, sarcoidosis has become chronic after 2 years of disease with ongoing signs of activity. The long-term prognosis is generally good, but depends on the different organ manifestations and complications.
Cottrell DJ.		Fifteen-minute consultation: Medically unexplained symptoms.	294. Arch Dis Child Educ Pract Ed. 2016 Jun;101(3):114-8.	Medically unexplained symptoms are common and not always easy to manage. A wide range of symptoms may be presented and anxiety in the child, family and paediatrician about the possibility of a missed serious organic diagnosis may hamper effective management. Evidence-based approaches to a number of different presenting problems share a number of components. A model for assessment and management based on clinical experience and this evidence base is described.
Crépeaux G(1), Eidi H(2), David MO(3), Baba-Amer Y(4), Tzavara E(5), Giros B(5), Authier FJ(4), Exley C(6), Shaw CA(7), Cadusseau	(1)Inserm U955 E10, Université Paris Est Créteil (UPEC), Créteil, France; Ecole Nationale Vétérinaire d'Alfort, Maisons-Alfort, France. Electronic address: guillemette.crepeaux	Non-linear dose-response of aluminium hydroxide adjuvant particles: Selective low dose neurotoxicity.	24. Toxicology. 2017 Jan 15;375:48-57.	Aluminium (Al) oxyhydroxide (Alhydrogel(®)), the main adjuvant licensed for human and animal vaccines, consists of primary nanoparticles that spontaneously agglomerate. Concerns about its safety emerged following recognition of its unexpectedly long-lasting biopersistence within immune cells in some individuals, and reports of chronic fatigue syndrome, cognitive dysfunction, myalgia, dysautonomia and autoimmune/inflammatory features temporally linked to multiple Al-containing vaccine administrations. Mouse experiments have documented its capture and slow transportation by monocyte-lineage cells from the injected muscle to lymphoid organs and eventually the brain. The present study aimed at evaluating mouse brain function

J(8), Gherardi RK(4).	@vet-alfort.fr. (2)Inserm U955 E10, Université Paris Est Créteil (UPEC), Créteil, France; Inserm U1204, Université Evry Val d'Essonne (UEVE), Evry, France. (3)Inserm U1204, Université Evry Val d'Essonne (UEVE), Evry, France. (4)Inserm U955 E10, Université Paris Est Créteil (UPEC), Créteil, France. (5)Inserm U1130, CNRS UMR 8246, UPMC UM CR18, Paris, France. (6)Birchall Centre, Keele University, Staffordshire, UK. (7)Department of Ophthalmology, University of British Columbia, Vancouver, BC, Canada. (8)Inserm U955 E10, Université Paris Est Créteil (UPEC), Créteil, France; Faculté des Sciences &Technologies UPEC, Créteil, France.			and Al concentration 180days after injection of various doses of Alhydrogel(®) (200, 400 and 800µg Al/kg of body weight) in the tibialis anterior muscle in adult female CD1 mice. Cognitive and motor performances were assessed by 8 validated tests, microglial activation by Iba-1 immunohistochemistry, and Al level by graphite furnace atomic absorption spectroscopy. An unusual neuro-toxicological pattern limited to a low dose of Alhydrogel(®) was observed. Neurobehavioural changes, including decreased activity levels and altered anxiety-like behaviour, were observed compared to controls in animals exposed to 200µg Al/kg but not at 400 and 800µg Al/kg. Consistently, microglial number appeared increased in the ventral forebrain of the 200µg Al/kg group. Cerebral Al levels were selectively increased in animals exposed to the lowest dose, while muscle granulomas had almost completely disappeared at 6 months in these animals. We conclude that Alhydrogel(®) injected at low dose in mouse muscle may selectively induce long-term Al cerebral accumulation and neurotoxic effects. To explain this unexpected result, an avenue that could be explored in the future relates to the adjuvant size since the injected suspensions corresponding to the lowest dose, but not to the highest doses, exclusively contained small agglomerates in the bacteria-size range known to favour capture and, presumably, transportation by monocyte-lineage cells. In any event, the view that Alhydrogel(®) neurotoxicity obeys "the dose makes the poison" rule of classical chemical toxicity appears overly simplistic.
Cvejic E(1), Birch RC(1), Vollmer-Conna U(2).	(1)School of Psychiatry, University of New South Wales Medicine, Sydney, 2052, NSW, Australia. (2)School of	Cognitive Dysfunction in Chronic Fatigue Syndrome: a Review of Recent Evidence.	234. Curr Rheumatol Rep. 2016 May;18(5):24.	Cognitive difficulties represent a common and debilitating feature of the enigmatic chronic fatigue syndrome (CFS). These difficulties manifest as self-reported problems with attention, memory, and concentration and present objectively as slowed information processing speed particularly on complex tasks requiring sustained attention. The mechanisms underlying cognitive dysfunction remain to be established; however, alterations in autonomic nervous system activity and cerebral blood flow

	Psychiatry, University of New South Wales Medicine, Sydney, 2052, NSW, Australia. ute@unsw.edu.au.			have been proposed as possibilities. Heterogeneity in the experience of cognitive impairment, as well as differences in the methods utilised to quantify dysfunction, may contribute to the difficulties in establishing plausible biological underpinnings. The development of a brief neurocognitive battery specifically tailored to CFS and adoption by the international research community would be beneficial in establishing a profile of cognitive dysfunction. This could also provide better insights into the underlying biological mechanisms of cognitive dysfunction in CFS and enhance the development of targeted treatments.
Cvejic E(1), Lloyd AR(2), Vollmer-Conna U(3).	(1)School of Psychiatry, University of New South Wales, Australia. Electronic address: e.cvejic@unsw.edu.au. (2)Inflammation and Infection Research Centre, School of Medical Sciences, University of New South Wales, Australia. Electronic address: a.lloyd@unsw.edu.au. (3)School of Psychiatry, University of New South Wales, Australia. Electronic address: ute@unsw.edu.au.	Neurocognitive improvements after best-practice intervention for chronic fatigue syndrome: Preliminary evidence of divergence between objective indices and subjective perceptions.	242. Compr Psychiatry. 2016 Apr;66:166-75.	BACKGROUND: Neurocognitive difficulties are commonly reported by patients suffering from chronic fatigue syndrome (CFS). Moderate improvements from 'best practice' therapy are promising, but to date reported efficacy is based entirely on subjective measures. This is problematic, given the well-documented divergence between subjective perceptions and actual neurocognitive performance, including in this patient group. MATERIAL AND METHODS: Subjective and objective measures of neurocognitive performance were obtained from 25 patients with well-characterized CFS before and after the completion of a 12-week graded-activity program incorporating a cognitive training component. Additionally, self-reported symptoms, cardiac autonomic activity (a relevant biomarker of stress responsivity), and their relation to neurocognitive improvements were examined. RESULTS: Substantive post-intervention improvements in subjective ($p=0.006$) and objective (including faster responses speeds and greater accuracy, $p's<0.001$) neurocognitive performance were documented. Participants also demonstrated reduced autonomic reactivity to the cognitive challenge at follow-up ($p's\leq0.01$). These improvements were accompanied by improvements in symptom ratings ($p's\leq0.01$). However, subjective ratings of neurocognitive difficulties, and CFS-related symptoms were not linked to objective performance improvements. CONCLUSIONS: These initial data provide the first evidence of objective neurocognitive performance improvements accompanied by a significant reduction in responsiveness in stress-related neural pathways consequent to cognitive-behavioral/graded exercise therapy programs. These findings provide support for the effectiveness of such programs in remediating clinical status. These promising findings warrant further investigation, including replication in a larger sample utilizing more controlled study designs.
Dahan H, Shir Y, Nicolau B, Keith D, Allison P.		Self-Reported Migraine and Chronic Fatigue Syndrome Are More Prevalent in People with Myofascial vs Nonmyofascial Temporomandibular Disorders.	299. J Oral Facial Pain Headache. 2016 Winter;30(1):7-13.	AIMS: To compare the number of comorbidities and the prevalence of five specific comorbidities in people who have temporomandibular disorders (TMD) with or without myofascial pain. METHODS: This cross-sectional study included 180 patients seeking TMD treatment in Boston and Montreal hospitals. A self-administered questionnaire was used to collect information on sociodemographic and behavioral factors, as well as the presence of the following five comorbidities: migraine, chronic fatigue syndrome, irritable bowel syndrome, interstitial cystitis, and restless leg syndrome. TMD was diagnosed using the Research Diagnostic Criteria for TMD. Chi-square and Student t

				tests were used for categorical and continuous variables, respectively, to test for differences between myofascial (n = 121) and nonmyofascial (n = 59) TMD groups. Multiple logistic regression analysis was used to compare the type and number of self-reported comorbidities in both groups, controlling for confounding variables. RESULTS: The following were found to be significantly higher in the myofascial TMD group than in the nonmyofascial TMD group: self-reported migraine (55% vs 28%, P = .001), chronic fatigue syndrome (19% vs 5%, P = .01), and the mean total number of comorbidities (1.30 vs 0.83, P = .01). CONCLUSION: Individuals with myofascial TMD had a higher prevalence of self-reported migraine and chronic fatigue syndrome than those with nonmyofascial TMD.
Dahan S(1), Tomljenovic L(2), Shoenfeld Y(3).	(1)Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer, Israel Sackler Faculty of Medicine, Tel Aviv University, Israel. (2)Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada. (3)Zabludowicz Center for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer, Israel Sackler Faculty of Medicine, Tel Aviv University, Israel Shoenfel@post.tau.ac.il.	Postural Orthostatic Tachycardia Syndrome (POTS)--A novel member of the autoimmune family.	288. Lupus. 2016 Apr;25(4):339-42.	Postural orthostatic tachycardia syndrome (POTS) is a heterogeneous disorder of the autonomic nervous system in which a change from the supine position to an upright position causes an abnormally large increase in heart rate or tachycardia (30 bpm within 10 min of standing or head-up tilt). This response is accompanied by a decrease in blood flow to the brain and hence a spectrum of symptoms associated with cerebral hypoperfusion. Many of these POTS-related symptoms are also observed in chronic anxiety and panic disorders, and therefore POTS is frequently under- and misdiagnosed.
Daniels J(1,)(2), Loades ME(3).	(1) Department of Psychology, University of Bath, Bath, UK. j.daniels@bath.ac.uk. (2) Bristol Chronic Fatigue Syndrome/ME	A Novel Approach to Treating CFS and Co-morbid Health Anxiety: A Case Study.	78. Clin Psychol Psychother. 2016 Oct 6.	OBJECTIVES: Chronic Fatigue Syndrome (CFS) is a debilitating condition that affects 0.2-0.4% of the population. First-line treatments are Cognitive Behaviour Therapy or graded exercise therapy; however, these treatments yield only moderate effect sizes. Emerging research suggests that anxiety about health may be common in CFS. Health anxiety treatment models demonstrate good therapeutic outcomes; however, these models have yet to be applied to CFS. This paper describes the application of a novel

	Service, Southmead Hospital, Bristol, UK. j.daniels@bath.ac.uk. (3)Department of Psychology, University of Bath, Bath, UK.			cognitive behavioural approach to the treatment of both physical and anxiety related symptoms in a patient with CFS and, furthermore, presents a conceptual hypothesis regarding the mutually maintaining relationship between these two co-occurring conditions. DESIGN: A single-case design was used, with pre-data, post-data and follow-up data. The cognitive behavioural model of health anxiety was adapted and delivered as an eight-session intervention. The intervention was driven by an individualized formulation developed collaboratively with the patient. RESULTS: The application of this approach generated reliable and clinically significant reductions in physical and psychological symptoms, which were maintained at 12-month follow-up. The participant no longer fulfilled the criteria for CFS or health anxiety following eight treatment sessions. The treatment approach was found to be agreeable to the patient. All treatment hypotheses were supported. CONCLUSIONS: An adapted cognitive behavioural approach to treating CFS and health anxiety yields positive results and shows promise for application to the broader CFS population. ESSAGES: Chronic Fatigue Syndrome (CFS) is a debilitating condition that is difficult to treat successfully; first-line recommended treatments achieve only moderate effect sizes. Anxiety, particularly about health, is reported to be common in CFS. However, anxiety is not specifically targeted within treatment and may negatively influence outcome due to the potentially mutually maintaining nature of these complex conditions. The present study demonstrates that an integrated treatment approach designed to encompass physical and psychological symptoms yields reliable and clinically significant outcomes in 50% of time recommend for first line treatments. Results reflected non-case level status for both CFS and health anxiety at end of treatment, in addition to reductions across all clinical measures. This study demonstrates the fundamental importance of an individualized, rather than generic, treatment approach to complex cases; the 'meaning' of experience is a central tenet within a cognitive approach that should be reflected in treatment.
Davis S(1).	(1), is in private practice in Minneapolis, Minnesota, and the research director for Living Matrix, Inc.	Reversal of Irritable Bowel Syndrome, Sleep Disturbance, and Fatigue With an Elimination Diet, Lifestyle Modification, and Dietary Supplements: A Case Report.	14. Integr Med (Encinitas). 2016 Oct;15(5):60-66.	BACKGROUND: A 53-y-old Caucasian patient presented in August 2015 with chief complaints of irritable bowel syndrome (IBS; gas/bloating, gastroesophageal reflux), fatigue, and sleep disturbances. He also noted a history of chronic sinusitis, seasonal allergies, multiple chemical sensitivities, and right knee pain (3 surgeries). His primary care physician, in 2014, diagnosed prediabetes based on an elevated hemoglobin A1c and high-sensitivity C-reactive protein, which was treated with diet and lifestyle modification. CASE/INTERVENTION: In the course of 6 mo, the patient was treated using an elimination diet, lifestyle modifications, botanicals, and dietary supplements. By addressing the underlying cause of issues, his symptoms decreased and quality of life increased, resulting in the resolution of his IBS symptoms, improved sleep, and increased energy levels. CONCLUSION: This case illustrates the potential diagnostic importance of early testing for gut microbiome imbalances and gastrointestinal infections in the management of IBS as well as the usefulness of a systems-based

				approach for diagnostic assessment and management of a complex chronic case.
de Biase S(1), Valente M(2), Gigli GL(2).	(1)Neurology Unit, Department of Experimental and Clinical Medical Sciences, University of Udine Medical School, Udine, Italy. (2)Neurology Unit, Department of Experimental and Clinical Medical Sciences, University of Udine Medical School, Udine, Italy; Department of Neurosciences, Santa Maria della Misericordia University Hospital, Udine, Italy.	Intractable restless legs syndrome: role of prolonged-release oxycodone-naloxone.	253. Neuropsychiatr Dis Treat. 2016 Feb 23;12:417-25.	Restless legs syndrome (RLS) is a common neurological disorder characterized by an irresistible urge to move the legs accompanied by uncomfortable sensations that occur at night or at time of rest. Pharmacological therapy should be limited to patients who suffer from clinically relevant symptoms. Chronic RLS is usually treated with either a dopamine agonist (pramipexole, ropinirole, rotigotine) or an α2δ calcium-channel ligand (gabapentin, gabapentin enacarbil, pregabalin). Augmentation is the main complication of long-term dopaminergic treatment, and frequently requires a reduction of current dopaminergic dose or a switch to non-dopaminergic medications. Opioids as monotherapy or add-on treatment should be considered when alternative satisfactory regimens are unavailable and the severity of symptoms warrants it. In a recent Phase III trial, oxycodone-naloxone prolonged release (PR) demonstrated a significant and sustained effect on patients with severe RLS inadequately controlled by previous treatments. The adverse-event profile was consistent with the safety profile of opioids. The most frequent adverse events were fatigue, constipation, nausea, headache, hyperhidrosis, somnolence, dry mouth, and pruritus. Adverse events were usually mild or moderate in intensity. No cases of augmentation were reported. Oxycodone-naloxone PR is approved for the second-line symptomatic treatment of adults with severe to very severe idiopathic RLS after failure of dopaminergic treatment. Further studies are needed to evaluate if oxycodone-naloxone PR is equally efficacious as a first-line treatment. Moreover, long-term comparative studies between opioids, dopaminergic drugs and α2δ ligands are needed.
De Gucht V(1), Garcia FK(2), den Engelsman M(2), Maes S(2).	(1)Health, Medical, and Neuropsychology Unit, Leiden University, Wassenaarseweg 52, P.O. BOX 955, 2300 RB, Leiden, Netherlands. degucht@fsw.leidenuniv.nl. (2)Health, Medical, and Neuropsychology Unit, Leiden University, Wassenaarseweg 52, P.O. BOX 955, 2300 RB, Leiden, Netherlands.	Differences in Physical and Psychosocial Characteristics Between CFS and Fatigued Non-CFS Patients, a Case-Control Study.	268. Int J Behav Med. 2016 Oct;23(5):589-94.	PURPOSE: The main research question is: "Do CFS patients differ from fatigued non-CFS patients with respect to physical, cognitive, behavioral, social, and emotional determinants?" In addition, group differences in relevant outcomes were explored. METHOD: Patients who met the Centers for Disease Control (CDC) criteria for CFS were categorized as CFS; these patients were mainly recruited via a large Dutch patient organization. Primary care patients who were fatigued for at least 1 month and up to 2 years but did not meet the CDC criteria were classified as fatigued non-CFS patients. Both groups were matched by age and gender (N = 192 for each group). RESULTS: CFS patients attributed their fatigue more frequently to external causes, reported a worse physical functioning, more medical visits, and a lower employment rate. The results of a multiple logistic regression analysis showed that patients who believe that their fatigue is associated with more severe consequences, that their fatigue will last longer and is responsible for more additional symptoms are more likely to be classified as CFS, while patients who are more physically active and have higher levels of "all or nothing behavior" are less likely to be classified as having CFS. CONCLUSION: A longitudinal study should explore the predictive value of the above factors for the transition from medically unexplained fatigue to CFS in order to develop targeted interventions for primary care patients with short-term fatigue complaints.

de Korwin JD(1), Chiche L(2), Banovic I(3), Ghali A(4), Delliaux S(5), Authier FJ(6), Cozon G(7), Hatron PY(8), Fornasieri I(9), Morinet F(10).	(1)Faculté de médecine, université de Lorraine, département de médecine interne et d'immunologie clinique, CHU de Nancy, hôpital de Brabois-BPC, rue du Morvan, 54511 Vandœuvre-lès-Nancy cedex, France. Electronic address: jd.dekorwin@chu-nancy.fr. (2)Service de médecine interne, hôpital européen, 6, rue Désirée-Clary, 13003 Marseille, France. (3)UPRES PSY-NCA, EA 4700, UFR des sciences de l'homme et de la société, rue Lavoisier, 76821 Mont-Saint-Aignan, France. (4)Pôle cardiovasculaire et thoracique, laboratoire de physiologie respiratoire - explorations à l'exercice, hôpital Nord, AP-HM, Aix-Marseille université, MD, DS-ACI, UMR 2, 13915 Marseille, France. (5)Service de médecine interne,	[Chronic fatigue syndrome: A new disorder?] [Article in French]	174. Rev Med Interne. 2016 Dec;37(12):811-819.	More than 30 years after its individualization, chronic fatigue syndrome (CFS) remains a debilitating condition for the patient and a confusing one to the physicians, both because of diagnostic difficulties and poorly codified management. Despite the numerous work carried out, its pathophysiology remains unclear, but a multifactorial origin is suggested with triggering (infections) and maintenance (psychological) factors as well as the persistence of inflammatory (low grade inflammation, microglial activation…), immunologic (decrease of NK cells, abnormal cytokine production, reactivity to a variety of allergens, role of estrogens…) and muscular (mitochondrial dysfunction and failure of bioenergetic performance) abnormalities at the origin of multiple dysfunctions (endocrine, neuromuscular, cardiovascular, digestive…). The complexity of the problem and the sometimes contradictory results of available studies performed so far are at the origin of different pathophysiological and diagnostic concepts. Based on a rigorous analysis of scientific data, the new American concept of Systemic Disease Exertion Intolerance proposed in 2015 simplifies the diagnostic approach and breaks with the past and terminologies (CFS and myalgic encephalomyelitis). It is still too early to distinguish a new disease, but this initiative is a strong signal to intensify the recognition and management of patients with CFS and stimulate research.

	CHU d'Angers, 4, rue Larrey, 49933 Angers cedex 09, France. (6)Centre de référence des maladies neuromusculaires, CHU Henri-Mondor, DHU Pepsy, AP-HP, Inserm U955-Eq.10 « biologie du système neuromusculaire », faculté de médecine de Créteil, 94000 Créteil, France. (7)Immunologie clinique, hôpital Édouard-Herriot-Pavillon F, UFR de médecine Lyon-Est, université Claude-Bernard-Lyon-1, 69437 Lyon cedex 03, France. (8)Service de médecine interne, centre national de référence maladies rares, CHU Huriez, place de Verdun, 59037 Lille, France. (9)Université de Strasbourg, faculté de psychologie, 12, rue Goethe, 67000 Strasbourg, France. (10)Pôle biologie-pathologie-physiologie, hôpital Saint-Louis, AP-HP, université Paris-			

	Diderot-Paris-7, 1, avenue Vellefaux, 75010 Paris, France.			
Dehghan M(1), Schmidt-Wilcke T(2), Pfleiderer B(3), Eickhoff SB(4,)(5), Petzke F(6), Harris RE(7), Montoya P(8), Burgmer M(1).	(1)Department of Psychosomatics and Psychotherapy, University Hospital Münster, Münster, Germany. (2)Department of Neurology, Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil, Ruhr Universität Bochum, Bochum, Germany. (3)Department of Clinical Radiology, University Hospital Münster, Münster, Germany. (4)Institute of Neuroscience and Medicine (INM-1), Research Center Jülich, Germany. (5)Institute of Clinical Neuroscience and Medical Psychology, Heinrich-Heine University, Düsseldorf, Germany. (6)Department of Anesthesiology, Pain Medicine, University Hospital Göttingen, Göttingen, Germany. (7)Department of Anesthesiology, Chronic Pain and	Coordinate-based (ALE) meta-analysis of brain activation in patients with fibromyalgia.	281. Hum Brain Mapp. 2016 May;37(5):1749-58.	There are an increasing number of neuroimaging studies that allow a better understanding of symptoms, neural correlates and associated conditions of fibromyalgia. However, the results of these studies are difficult to compare, as they include a heterogeneous group of patients, use different stimulation paradigms, tasks, and the statistical evaluation of neuroimaging data shows high variability. Therefore, this meta-analytic approach aimed at evaluating potential alterations in neuronal brain activity or structure related to pain processing in fibromyalgia syndrome (FMS) patients, using quantitative coordinate-based "activation likelihood estimation" (ALE) meta-analysis. 37 FMS papers met the inclusion criteria for an ALE analysis (1,264 subjects, 274 activation foci). A pooled ALE analysis of different modalities of neuroimaging and additional analyses according functional and structural changes indicated differences between FMS patients and controls in the insula, amygdala, anterior/mid cingulate cortex, superior temporal gyrus, the primary and secondary somatosensory cortex, and lingual gyrus. Our analysis showed consistent results across FMS studies with potential abnormalities especially in pain-related brain areas. Given that similar alterations have already been demonstrated in patients with other chronic pain conditions and the lack of adequate control groups of chronic pain subjects in most FMS studies, it is not clear however, whether these findings are associated with chronic pain in general or are unique features of patients with FMS. Hum Brain Mapp 37:1749-1758, 2016. © 2016 Wiley Periodicals, Inc.

	Fatigue Research, University of Michigan, Michigan. (8)Research Institute of Health Sciences, University of Balearic Islands, Palma, Spain.			
Denman M.		Review: Exercise therapy reduces fatigue in chronic fatigue syndrome.	195. Ann Intern Med. 2016 May 17;164(10):JC55.	
Densham S(1), Williams D(2), Johnson A(2), Turner-Cobb JM(3).	(1)Department of Psychology, University of Bath, Claverton Down, Bath, UK. (2)The Royal National Hospital for Rheumatic Diseases, Royal United Hospitals Bath, NHS Foundation Trust, Bath, UK. (3)Department of Psychology, University of Bath, Claverton Down, Bath, UK. Electronic address: julie.turner-cobb@bath.edu.	Enhanced psychological flexibility and improved quality of life in chronic fatigue syndrome/myalgic encephalomyelitis.	117. J Psychosom Res. 2016 Sep;88:42-7.	OBJECTIVE: Psychological Flexibility (PF) is a relatively new concept in physical health. It can be defined as an overarching process of being able to accept the presence of wanted/unwanted experiences, choosing whether to change or persist in behaviour in response to those experiences. Associations between processes of PF and quality of life (QoL) have been found in long-term health conditions such as chronic pain, PF has not yet been applied to Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). METHODS: Changes in PF, fatigue severity and QoL were examined in one hundred and sixty-five patients with CFS/ME engaged in a six-week outpatient interdisciplinary group treatment programme. Participants were assessed using a series of self-report measures at the start of the start (T1) and end of a six-week programme (T2) and at six months follow up (T3). RESULTS: Significant changes in PF and QoL were observed from pre-treatment (T1) to post treatment follow-up (T2 and T3); changes in fatigue severity were observed from T1 to T3 only. Controlling for fatigue severity, changes in the PF dimension of activity/occupational engagement were associated with improvement in QoL at six month follow up (T3) but not at six weeks post programme (T2). CONCLUSION: Findings indicate an interdisciplinary group treatment approach for people with CFS/ME may be associated with improved QoL, processes of PF and fatigue severity, supporting a link between PF and long term health conditions. Results highlight links between PF and patient QoL in CFS/ME and the value of interdisciplinary treatment approaches in this patient population.
Devine M, Taylor S, Renton T.		Chronic post-surgical pain following the placement of dental implants in the maxilla: A case series.	163. Eur J Oral Implantol. 2016;9 Suppl 1(2):179-86.	PURPOSE: To present ten cases of chronic post-surgical neuropathic pain (CPSP) arising after placement of maxillary dental implants, in order to raise awareness of this potential complication of treatment. MATERIALS AND METHODS: Data collected from the case notes of consecutive patients presenting to the orofacial pain clinic, with neuropathic pain arising after placement of maxillary dental implants. RESULTS: Nine out of 10 patients were female, with an average age 55.4 years. Six patients had a significant medical history (depression, peripheral neuropathic pain, irritable bowel syndrome and fibromyalgia). Six patients had single implants placed, four had multiple implants. Four patients experienced pain during implant placement. Onset of pain was immediate in nine patients. Pain intensity (visual analogue scale) ranged from 2 to 9

				(average 5.6). Pain was constant in all patients. Exacerbating factors included stress, tiredness, low mood and cold weather. Implants were removed in two patients however pain did not resolve. Pain management was complex; including medication (anti-epileptics and tricyclic antidepressants), Botox injections and cognitive behavioural therapy, however pain did not completely resolve in nine cases. CONCLUSIONS: Persistent pain after dental implant placement may occur with no apparent organic cause and without any neurosensory deficits. Practitioners must be aware of chronic post-surgical neuropathic pain as a possible complication of implant placement, particularly in patients with a significant medical history. Consideration should be given as to whether these patients are suitable for implant rehabilitation. Patients reporting very severe and prolonged postoperative pain following implant surgery should be considered at risk of CPSP and referred to a specialist in orofacial pain.
Ding WH(1), Li W, Chen XY, Shi JJ.	(1)Department of Orthodontics, Hospital of Stomatology, College of Medicine, Zhejiang University, Hangzhou 310006, China.	[The study of genistein attenuating genioglossus muscle fatigue under chronic intermittent hypoxia]. [Article in Chinese]	307. Zhonghua Kou Qiang Yi Xue Za Zhi. 2016 Jan;51(1):46-50.	OBJECTIVE: To investigate the effects of genistein on genioglossus muscle function and nuclear factor erythroid 2 related factor 2(Nrf-2)/antioxidant responsive element(ARE) signaling pathway in rats under chronic intermittent hypoxia(CIH) condition in order to find medication treatment of obstructive sleep apnea/hyponea syndrome. METHODS: Thirty female Sprague-Dawley(SD) rats (8 weeks old) were randomly(random number table) divided into three groups 1 week after ovariectomy: control group(NC group), CIH group, and CIH+genistein treatment group(T group). Rats in the latter two groups were exposed to CIH for 8 h/d for 5 weeks. Electrophysiological method was used to detect the change of genioglossus muscle function, and real-time reverse transcription(RT)-PCR and Western blotting were used to determine the level of Nrf-2 gene and protein. RESULTS: Compared to NC group, the contractive properties of genioglossus muscle fatigue test at every time set was significantly decreased in CIH group($P<0.05$). Compared to CIH group, the contractive properties was significantly increased in T group($P<0.05$). The level of Nrf-2 gene and protein were less in CIH group(0.54±0.11 and 0.35±0.13) than in NC group(1.00±0.001.00±0.00)($P<0.05$). Compared to CIH group the level of Nrf-2 gene and protein were increased in T group (0.76 ± 0.16 and 0.63 ± 0.14) ($P<0.05$), however, it was still less than the level in NC group($P<0.05$). CONCLUSIONS: CIH attenuates genioglossus muscle fatigue resistance under chronic intermittent hypoxia through Nrf-2/ARE signaling pathway. Genistein protects genioglossus muscle function through up-regulation of the level of Nrf-2 gene and protein.
Dixon EA(1), Benham G(2), Sturgeon JA(3), Mackey S(3), Johnson KA(3), Younger J(3,)(4).	(1)Department of Anesthesia, Division of Pain Management, Stanford University School of Medicine, 1070 Arastradero Rd.,	Development of the Sensory Hypersensitivity Scale (SHS): a self-report tool for assessing sensitivity to sensory stimuli.	276. J Behav Med. 2016 Jun;39(3):537-50.	Sensory hypersensitivity is one manifestation of the central sensitization that may underlie conditions such as fibromyalgia and chronic fatigue syndrome. We conducted five studies designed to develop and validate the Sensory Hypersensitive Scale (SHS); a 25-item self-report measure of sensory hypersensitivity. The SHS assesses both general sensitivity and modality-specific sensitivity (e.g. touch, taste, and hearing). 1202 participants (157 individuals with chronic pain) completed the SHS, which

	Suite 200, Palo Alto, CA, 94304, USA. eadixon@stanford.edu. (2)Department of Psychological Science, University of Texas Rio Grande Valley, Edinburg, TX, USA. (3)Department of Anesthesia, Division of Pain Management, Stanford University School of Medicine, 1070 Arastradero Rd., Suite 200, Palo Alto, CA, 94304, USA. (4)Department of Psychology, Department of Anesthesiology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, USA.			demonstrated an adequate overall internal reliability (Cronbach's alpha) of 0.81, suggesting the tool can be used as a cross-modality assessment of sensitivity. SHS scores demonstrated only modest correlations (Pearson's r) with depressive symptoms (0.19) and anxiety (0.28), suggesting a low level of overlap with psychiatric complaints. Overall SHS scores showed significant but relatively modest correlations (Pearson's r) with three measures of sensory testing: cold pain tolerance (-0.34); heat pain tolerance (-0.285); heat pain threshold (-0.271). Women reported significantly higher scores on the SHS than did men, although gender-based differences were small. In a chronic pain sample, individuals with fibromyalgia syndrome demonstrated significantly higher SHS scores than did individuals with osteoarthritis or back pain. The SHS appears suitable as a screening measure for sensory hypersensitivity, though additional research is warranted to determine its suitability as a proxy for central sensitization.
Dusser P(1), Hentgen V(2), Neven B(3), Koné-Paut I(4).	(1)Service de rhumatologie pédiatrie, CHU Kremlin Bicêtre, AP-HP, 78, rue du Général-Leclerc, 94270 Le Kremlin-Bicêtre, France; Centre de référence des maladies auto-inflammatoires (MAI), 94270 Le Kremlin-Bicêtre, France. Electronic address: perrine.dusser@aphp.fr. (2)Centre de	Is colchicine an effective treatment in periodic fever, aphtous stomatitis, pharyngitis, cervical adenitis (PFAPA) syndrome?	224. Joint Bone Spine. 2016 Jul;83(4):406-11.	INTRODUCTION: PFAPA syndrome is the most frequent periodic fever syndrome in non-Mediterranean patients. The pathogenesis is unclear and the treatment is purely symptomatic and not standardized. The aim of this study was to assess colchicine's efficacy as prophylactic treatment in PFAPA syndrome and to identify factors able to predict response to treatment. METHODS: We performed a retrospective, multicentric, cohort study of PFAPA patients under colchicine prophylaxis. PFAPA diagnosis was established according to Feder's criteria. Medical records were reviewed and analyzed for demographic, clinical and laboratory data. We distinguished one responder's group, defined as patients who had no more or twice fewer crises under colchicine and another one of non-responders. Subgroup analyses were performed using non-parametric Mann-Whitney test for quantitative data and calculating odds ratio and confidence interval for qualitative data. Difference between the two groups was considered significant for P-value<0.05 or a confidence interval different from 1. RESULTS-CONCLUSION: Twenty children, 65% of whom were boys, were analyzed. Their mean age at disease onset was 2.3±1.5 years. Among the nine responder patients, five were MEFV (71%) heterozygotes: M694V mutation in four and V726A once.

	référence des maladies auto-inflammatoires (MAI), 94270 Le Kremlin-Bicêtre, France; Service de pédiatrie générale, centre hospitalier, hôpital André-Mignot, centre hospitalier Versailles, 78150 Le Chesnay, France. (3)Unité d'immunologie-hématologie et rhumatologie pédiatriques, CHU de Paris, hôpital Necker-Enfants-Malades, AP-HP, 75015 Paris, France. (4)Service de rhumatologie pédiatrie, CHU Kremlin Bicêtre, AP-HP, 78, rue du Général-Leclerc, 94270 Le Kremlin-Bicêtre, France; Centre de référence des maladies auto-inflammatoires (MAI), 94270 Le Kremlin-Bicêtre, France.			Heterozygous MEFV gene mutation tended to be more frequent in the responders group (71% versus 43%; OR=0.3 [0.03-2.7]). Non-responder patients had more chronic fatigue (82% versus 33%; OR=9 [1,14-71]) and had more oral aphtosis (82% versus 11%; OR=36 [1,7-141]) than the responders ones. Although not significant, colchicine treatment appeared more effective in patients with less complete PFAPA phenotype and MEFV heterozygosity.
Edwards JC(1), McGrath S(2), Baldwin A(3), Livingstone M(4), Kewley A(5).	(1)Division of Medicine, University College London , London , UK. (2)Monmouth , UK. (3)Bristol , UK. (4)Cognac , France. (5)Adelaide , Australia.	The biological challenge of myalgic encephalomyelitis/chronic fatigue syndrome: a solvable problem.	181. Fatigue. 2016 Apr 2;4(2):63-69. Epub 2016 Apr 28.	

Evrensel A(1), Ceylan ME(1).	(1)Department of Psychiatry, Uskudar University, Istanbul, Turkey.	Fecal Microbiota Transplantation and Its Usage in Neuropsychiatric Disorders.	126. Clin Psychopharmacol Neurosci. 2016 Aug 31;14(3):231-7.	Fecal microbiota transplantation has a 1700-year history. This forgotten treatment method has been put into use again during the last 50 years. The interest in microbiota-gut-brain axis and fecal microbiota transplantation is rapidly increasing. New evidence is obtained in the etiopathogenesis of neuropsychiatric disorders. There is a large number of experimental and clinical researches in the field of gut-brain axis. There is limited information on fecal microbiota transplantation. Despite this, initial results are promising. It is commonly used in the treatment of gastrointestinal diseases such as Clostridium difficile infection, Crohn's disease, ulcerative colitis. It is also experimentally used in the treatment of metabolic and autoimmune diseases. There are case reports that it is effective in the treatment of autism, Parkinson's disease, multiple sclerosis, chronic fatigue syndrome and irritable bowel syndrome. Its implementation is easy, and it is a cheap and reliable treatment method. However, the long-term risks are unknown. Additionally, standard application protocols have not yet been established. There are a lot of questions to be answered. A university in Turkey has got official permission this year, and started to apply fecal microbiota transplantation. In this review, neuropsychiatric areas of use of fecal microbiota transplantation have been discussed in the light of the current information.
Fan AP(1), Kosik RO(2), Xu GT(3), Cai Q(3), Lien S(4), Huang L(3), Zhao X(3), Zhang X(5), Wang Y(5), Chen Q(6).	(1)School of Medicine, National Yang-Ming University, Taiwan. Electronic address: fan_angela@hotmail.com. (2)Stanford Medical School, San Francisco, CA, USA. (3)Tongji University School of Medicine, Shanghai, China. (4)School of Medicine, National Yang-Ming University, Taiwan. (5)Dean and Vice President, Qiqihar Medical University, Qiqihar, China. (6)Chancellor and Party Chief, Nanjing Medical University, Nanjing, China.	Factors associated with professionalism in Chinese medical students: an exploratory cross-sectional study.	16. Lancet. 2016 Oct;388 Suppl 1:S32.	BACKGROUND: Professionalism is a central part of medical practice, and medical organisations worldwide have mandated training on this topic for future medical doctors. In China, national guidelines were developed to make explicit expectations that were once implicit. Medical education reform over the past decade has emphasised topics such as medical humanities, life-long learning, and patient-centered learning in an effort to increase the professionalism of future physicians. Although the importance of teaching professionalism has been well recognised, few studies have evaluated its implementation at Chinese medical schools. METHODS: We recruited medical students from three medical schools deemed to be representative of different regions in China (Tongji University School of Medicine, Shanghai (national); Nanjing Medical University, Jiangsu (provincial); Qiqihar Medical University, Heilongjiang (local)). We used the Jefferson Scale of Physician Empathy- Student Version (JSPES), Chinese version of the General Health Questionnaire, Center for Epidemiologic Studies Depression Scale (CES-D), Chronic Fatigue Syndrome assessment, and other personality and social status instruments to collect cross-sectional data. Statistical analyses were done using SPSS (version 20). Ethical approval was obtained by the Institutional Review Board of National Yang-Ming University. FINDINGS: We recruited 914 participants to the study. The mean JSPES score of the total population was 105 (SD 20). National university (Tongji) medical students (109 [18]), female medical students (107 [20]), and medical students who had not yet reached their third year of medical school (110 [17]) had significantly higher levels of professionalism than those in their third year or above (99 [17]). Professionalism and empathy were significantly associated with chronic fatigue syndrome: those who had higher scores in professionalism scored less for

				chronic fatigue syndrome (Pearson Correlation, -0·203; p<0·0001. Professionalism was synergistically associated with personality, general health, and depression (p<0·0001). Statistically significant differences in personality (p<0·0001), general health (p=0·002), depression (p=0·001), and chronic fatigue syndrome (p<0·0001) were also found between students from the three universities. INTERPRETATION: Chinese medical students in general have a positive disposition towards professionalism. Level of professionalism is highly associated with chronic fatigue syndrome, so medical educators should pay attention to curricular burden and provide support mechanisms aimed at reducing student stress. FUNDING: Republic of China Ministry of Science and Technologygrant MOST104-2511-S-010-003.
Faro M(1), Sàez-Francás N(2), Castro-Marrero J(2), Aliste L(2), Fernández de Sevilla T(2), Alegre J(2).	(1)EAP CAP Terrassa Nord, Consorci Sanitari de Terrassa, Barcelona, España. Electronic address: 34174mfc@comb.cat. (2)Unidad de Fatiga Crónica, Servicio de Medicina Interna, Hospital Universitario Vall d'Hebron, Barcelona, España.	Gender differences in chronic fatigue syndrome. [Article in English, Spanish]	357. Reumatol Clin. 2016 Mar-Apr;12(2):72-7.	BACKGROUND AND OBJECTIVES: Chronic fatigue syndrome (CFS) is a chronic condition that predominantly affects women. To date, there are few epidemiologic studies on CFS in men. The objective of the study was to assess whether there are gender-related differences in CFS, and to define a clinical phenotype in men. PATIENTS AND METHODS: A prospective, cross-sectional cohort study was conducted including CFS patients at the time of diagnosis. Sociodemographic data, clinical variables, comorbid phenomena, fatigue, pain, anxiety/depression, and health quality of life, were assessed in the CFS population. A comparative study was also conducted between genders. RESULTS: The study included 1309 CFS patients, of which 119 (9.1%) were men. The mean age and symptoms onset were lower in men than women. The subjects included 30% single men vs. 15% single women, and 32% of men had specialist work vs. 20% of women. The most common triggering factor was an infection. Widespread pain, muscle spasms, dizziness, sexual dysfunction, Raynaud's phenomenon, morning stiffness, migratory arthralgias, drug and metals allergy, and facial oedema were less frequent in men. Fibromyalgia was present in 29% of men vs. 58% in women. The scores on physical function, physical role, and overall physical health of the SF-36 were higher in men. The sensory and affective dimensions of pain were lower in men. CONCLUSIONS: The clinical phenotype of the men with CFS was young, single, skilled worker, and infection as the main triggering agent. Men had less pain and less muscle and immune symptoms, fewer comorbid phenomena, and a better quality of life.
Feliu-Soler A(1,)(2), Borràs X(3), Peñarrubia-María MT(4,)(5), Rozadilla-Sacanell A(6), D'Amico F(7), Moss-Morris R(8), Howard MA(9), Fayed N(10), Soriano-	(1)Teaching, Research & Innovation Unit, Parc Sanitari Sant Joan de Déu, C/Dr. Antoni Pujadas 42, 08830, Sant Boi de Llobregat, Barcelona, Spain. a.feliu@pssjd.org.	Cost-utility and biological underpinnings of Mindfulness-Based Stress Reduction (MBSR) versus a psychoeducational programme (FibroQoL) for fibromyalgia: a 12-month randomised controlled trial (EUDAIMON study).	262. BMC Complement Altern Med. 2016 Feb 27;16:81.	BACKGROUND: The EUDAIMON study focuses on fibromyalgia syndrome (FMS), a prevalent chronic condition characterized by pain, fatigue, cognitive problems and distress. According to recent reviews and meta-analyses, Mindfulness-Based Stress Reduction (MBSR) is a promising therapeutic approach for patients with FMS. The measurement of biomarkers as part of the analysis of MBSR effects would help to identify the neurobiological underpinnings of MBSR and increase our knowledge of FMS pathophysiology. The main objectives of this 12-month RCT are: firstly, to examine the effectiveness and cost-utility for FMS patients of MBSR as an add-on to treatment as usual (TAU) versus TAU + the psychoeducational programme FibroQoL, and versus TAU only; secondly, to examine pre-post differences in brain structure and function, as well

Mas C(11,)(12,)(13), Puebla-Guedea M(14,)(15), Serrano-Blanco A(16,)(17), Pérez-Aranda A(18), Tuccillo R(19), Luciano JV(20,)(21).				as levels of specific inflammatory markers in the three study arms and; thirdly, to analyse the role of some psychological variables as mediators of 12-month clinical outcomes. METHODS: Effectiveness, cost-utility, and neurobiological analyses performed alongside a 12-month RCT. The participants will be 180 adult patients with FMS recruited at the Sant Joan de Déu hospital (St. Boi de Llobregat, Spain), randomly allocated to one of the three study arms: TAU + MBSR vs. TAU + FibroQol vs. TAU. A comprehensive assessment to collect functional, quality of life, distress, costs, and psychological variables will be conducted pre-, post-intervention, and at 12-month post-intervention. Fifty per cent of study participants will be evaluated at pre- and post-treatment using Voxel-Based Morphometry, Diffusion Tensor Imaging, pseudo-continuous Arterial Spin Labeling, and resting state fMRI. A cytokine multiplex kit of high-sensitivity will be applied (cytokines IL-6, IL-8, IL-10 + high-sensitivity CRP test). DISCUSSION: The findings obtained from this RCT will indicate whether MBSR is potentially cost-effective for FMS and contribute to knowledge of any brain and inflammatory changes associated with MBSR in FMS patients. Specifically, we will determine whether there are morphometric and functional changes associated with participation in MBSR in brain regions related to meta-awareness, body awareness, memory consolidation-reconsolidation, emotion regulation and in networks postulated to underpin the sensory-discriminative, cognitive-evaluative and affective-motivational aspects of the pain experience. TRIAL REGISTRATION: NCT02561416 . Registered 23 September 2015.
Fenouillet E(1,)(2), Vigouroux A(3), Steinberg JG(1), Chagvardieff A(4), Retornaz F(5), Guieu R(1), Jammes Y(6,)(7).	(1)DS-ACI UMR MD2, Faculty of Medicine, Aix-Marseille University, Bd. Pierre Dramard, 13916, Marseille Cedex 20, France. (2)CNRS, Institut des Sciences Biologiques, Marseille, France. (3)Clinical Respiratory Physiology Laboratory, Nord Hospital, Marseille, France. (4)Emergency Unit, Nord Hospital, Marseille, France. (5)Internal Medicine Department, European Hospital,	Association of biomarkers with health-related quality of life and history of stressors in myalgic encephalomyelitis/chronic fatigue syndrome patients.	107. J Transl Med. 2016 Aug 31;14:251.	BACKGROUND: Myalgic encephalomyelitis chronic fatigue syndrome (ME/CFS) is a common debilitating disorder associated with an intense fatigue, a reduced physical activity, and an impaired quality of life. There are no established biological markerof the syndrome. The etiology is unknown and its pathogenesis appears to be multifactorial. Various stressors, including intense physical activity, severe infection, and emotional stress are reported in the medical history of ME/CFS patients which raises the question whether any physiological and biological abnormalities usually found in these patients could be indicative of the etiology and/or the quality-of-life impairment. METHODS: Thirty-six patients and 11 age-matched healthy controls were recruited. The following variables that appear to address common symptoms of ME/CFS were studied here: (1) muscle fatigue during exercise has been investigated by monitoring the compound muscle action potential (M-wave); (2) the excessive oxidative stress response to exercise was measured via two plasma markers (thiobarbituric acid reactive substances: TBARS; reduced ascorbic-acid: RAA); (3) a potential inflammatory component was addressed via expression of CD26 on peripheral blood mononuclear cells; (4) quality-of-life impairment was assessed using the London Handicap Scale (LHS) and the Medical Outcome Study Short Form-36 (SF-36). The medical history of each patient, including the presence of stressors such as intense sports practice, severe acute infection and/or severe emotional stress was

	Marseille, France. (6)DS-ACI UMR MD2, Faculty of Medicine, Aix-Marseille University, Bd. Pierre Dramard, 13916, Marseille Cedex 20, France. yves.jammes@univ-amu.fr. (7)Clinical Respiratory Physiology Laboratory, Nord Hospital, Marseille, France. yves.jammes@univ-amu.fr.			documented. RESULTS: We observed that: (1) there were striking differences between cases and controls with regard to three biological variables: post-exercise M-wave, TBARS variations and CD26-expression at rest; (2) each of these three variables correlated with the other two; (3) abnormalities in the biomarkers associated with health-related quality of life: the LHS score was negatively correlated with the exercise-induced TBARS increase and positively correlated with CD26-expression while the pain component of SF-36 was negatively correlated with CD26-expression; (4) the TBARS increase and the M-wave decrease were the highest, and the CD26-expression level the lowest in patients who had been submitted to infectious stressors. CONCLUSION: In ME/CFS patients, severe alterations of the muscle excitability, the redox status, as well as the CD26-expression level are correlated with a marked impairment of the quality-of-life. They are particularly significant when infectious stressors are reported in the medical history.
Fernie BA(1), Murphy G(2), Wells A(3), Nikčević AV(4), Spada MM(5).	(1)King's College London,Institute of Psychiatry,Psychology and Neuroscience, and Cascaid,South London and Maudsley NHS Foundation Trust,UK. (2)Royal Free Hampstead NHS Foundation Trust,London,UK. (3)University of Manchester,UK. (4)Kingston University,Kingston upon Thames,UK. (5)London South Bank University,UK.	Treatment Outcome and Metacognitive Change in CBT and GET for Chronic Fatigue Syndrome.	364. Behav Cogn Psychother. 2016 Jul;44(4):397-409.	BACKGROUND: Studies have reported that Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) are effective treatments for Chronic Fatigue Syndrome (CFS). METHOD: One hundred and seventy-one patients undertook a course of either CBT (n = 116) or GET (n = 55) and were assessed on a variety of self-report measures at pre- and posttreatment and follow-up. AIMS: In this paper we present analyses on treatment outcomes for CBT and GET in routine clinical practice and evaluate whether changes on subscales of the Metacognitions Questionnaire-30 (MCQ-30) predict fatigue severity independently of changes in other covariates, and across the two treatment modalities. RESULTS: Both CBT and GET were equally effective at decreasing fatigue, anxiety, and depression, and at increasing physical functioning. Changes on the subscales of the MCQ-30 were also found to have a significant effect on fatigue severity independently of changes in other covariates and across treatment modalities. CONCLUSION: The findings from the current study suggest that CFS treatment protocols for CBT and GET, based on those from the PACE trial, achieve similar to poorer outcomes in routine clinical practice as in a RCT.
Ferré A(1).	(1)Unidad del Sueño, Servicio Neurofisiología Clínica, Hospital Quirón, Barcelona, España. Electronic	Chronic fatigue syndrome and sleep disorders: clinical associations and diagnostic difficulties. [Article in English, Spanish]	273. Neurologia. 2016 Feb 11. pii: S0213-4853(16)00010-4.	INTRODUCTION: Chronic fatigue syndrome (CFS) is characterised by the presence of intractable fatigue and non-restorative sleep, symptoms which are also very prevalent in multiple diseases and appear as side effects of different drugs. Numerous studies have shown a high prevalence of sleep disorders in patients with CFS. However, non-restorative sleep and fatigue are frequently symptoms of the sleep disorders themselves, so primary sleep disorders have to be ruled out in many cases of CFS.

	address: doctorferre@gmail.com.			DEVELOPMENT: This review was performed using a structured search of the MeSH terms ([Sleep]+[Chronic fatigue syndrome]) in the PubMed database. CONCLUSION: Identifying primary sleep disorders in patients meeting diagnostic criteria for CFS will allow for a more comprehensive treatment approach involving new diagnostic and therapeutic strategies that may improve quality of life for these patients.
Finsterer J(1), Zarrouk-Mahjoub S(2).	(1)Krankenanstalt Rudolfstiftung, Postfach 20, 1180, Vienna, Austria. fifigs1@yahoo.de. (2)Genomics Platform, Pasteur Institute of Tunis, Tunis, Tunisia.	Is chronic fatigue syndrome truly associated with haplogroups or mtDNA single nucleotide polymorphisms?	162. J Transl Med. 2016 Jun 18;14(1):182.	
Fitzcharles MA(1,)(2), Baerwald C(3), Ablin J(4), Häuser W(5,)(6).	(1)Division of Rheumatology, McGill University Health Centre, Quebec, Canada. (2)Alan Edwards Pain Management Unit, McGill University Health Center, Quebec, Canada. (3)Department Internal Medicine, Neurology and Dermatology, Clinic for Gastroenterology and Rheumatology, Universitätsklinikum Leipzig, Leipzig, Germany. (4)Institute of Rheumatology, Tel Aviv Sourasky Medical Center and Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. (5)Department Internal Medicine I,	Efficacy, tolerability and safety of cannabinoids in chronic pain associated with rheumatic diseases (fibromyalgia syndrome, back pain, osteoarthritis, rheumatoid arthritis): A systematic review of randomized controlled trials.	311. Schmerz. 2016 Feb;30(1):47-61.	BACKGROUND: In the absence of an ideal treatment for chronic pain associated with rheumatic diseases, there is interest in the potential effects of cannabinoid molecules, particularly in the context of global interest in the legalization of herbal cannabis for medicinal use. METHODS: A systematic search until April 2015 was conducted in Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, www.cannabis-med.org and clinicaltrials.gov for randomized controlled trials with a study duration of at least 2 weeks and at least ten patients per treatment arm with herbal cannabis or pharmaceutical cannabinoid products in fibromyalgia syndrome (FMS), osteoarthritis (OA), chronic spinal pain, and rheumatoid arthritis (RA) pain. Outcomes were reduction of pain, sleep problems, fatigue and limitations of quality of life for efficacy, dropout rates due to adverse events for tolerability, and serious adverse events for safety. The methodology quality of the randomized controlled trials (RCTs) was evaluated by the Cochrane Risk of Bias Tool. RESULTS: Two RCTs of 2 and 4 weeks duration respectively with nabilone, including 71 FMS patients, one 4-week trial with nabilone, including 30 spinal pain patients, and one 5-week study with tetrahydrocannbinol/cannabidiol, including 58 RA patients were included. One inclusion criterion was pain refractory to conventional treatment in three studies. No RCT with OA patients was found. The risk of bias was high for three studies. The findings of a superiority of cannabinoids over controls (placebo, amitriptyline) were not consistent. Cannabinoids were generally well tolerated despite some troublesome side effects and safe during the study duration. CONCLUSIONS: Currently, there is insufficient evidence for recommendation for any cannabinoid preparations for symptom management in patients with chronic pain associated with rheumatic diseases.

	Klinikum Saarbrücken, Winterberg 1, Saarbrucken, Germany. whaeuser@klinikum-saarbruecken.de. (6)Department of Psychosomatic Medicine and Psychotherapy, Technische Universität München, Munich, Germany. whaeuser@klinikum-saarbruecken.de.			
Fluge Ø(1), Mella O(2), Bruland O(3), Risa K(1), Dyrstad SE(4), Alme K(1), Rekeland IG(1), Sapkota D(1), Røsland GV(4), Fosså A(5), Ktoridou-Valen I(1), Lunde S(1), Sørland K(1), Lien K(6), Herder I(6), Thürmer H(7), Gotaas ME(8), Baranowska KA(8), Bohnen LM(9), Schäfer C(9), McCann A(10), Sommerfelt K(11), Helgeland L(12), Ueland PM(13), Dahl O(2), Tronstad	(1)Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway.	Metabolic profiling indicates impaired pyruvate dehydrogenase function in myalgic encephalopathy/chronic fatigue syndrome.	5. JCI Insight. 2016 Dec 22;1(21):e89376.	Myalgic encephalopathy/chronic fatigue syndrome (ME/CFS) is a debilitating disease of unknown etiology, with hallmark symptoms including postexertional malaise and poor recovery. Metabolic dysfunction is a plausible contributing factor. We hypothesized that changes in serum amino acids may disclose specific defects in energy metabolism in ME/CFS. Analysis in 200 ME/CFS patients and 102 healthy individuals showed a specific reduction of amino acids that fuel oxidative metabolism via the TCA cycle, mainly in female ME/CFS patients. Serum 3-methylhistidine, a marker of endogenous protein catabolism, was significantly increased in male patients. The amino acid pattern suggested functional impairment of pyruvate dehydrogenase (PDH), supported by increased mRNA expression of the inhibitory PDH kinases 1, 2, and 4; sirtuin 4; and PPARδ in peripheral blood mononuclear cells from both sexes. Myoblasts grown in presence of serum from patients with severe ME/CFS showed metabolic adaptations, including increased mitochondrial respiration and excessive lactate secretion. The amino acid changes could not be explained by symptom severity, disease duration, age, BMI, or physical activity level among patients. These findings are in agreement with the clinical disease presentation of ME/CFS, with inadequate ATP generation by oxidative phosphorylation and excessive lactate generation upon exertion.

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Friedberg F(1), Coronel J(2), Seva V(2), Adamowicz JL(2), Napoli A(2).	(1)Stony Brook University, USA fred.friedberg@stonybrookmedicine.edu. (2)Stony Brook University, USA.	Participant attributions for global change ratings in unexplained chronic fatigue and chronic fatigue syndrome.	373. J Health Psychol. 2016 May;21(5):690-8.	The purpose of this mixed methods study was to identify participants' attributions for their global impression of change ratings in a behavioral intervention for unexplained chronic fatigue and chronic fatigue syndrome. At 3-month follow-up, participants (N = 67) were asked "Why do you think you are (improved, unchanged, worse)?" Improved patients pointed to specific behavioral changes, unchanged patients referred to a lack of change in lifestyle, and worsened patients invoked stress and/or specific life events. Identifying patient perceptions of behaviors associated with patient global impression of change-rated improvement and non-improvement may assist in developing more effective management strategies in clinical care.
Fukuda S(1,)(2,)(3), Nojima J(4), Kajimoto O(5), Yamaguti K(3,)(6), Nakatomi Y(3,)(6), Kuratsune H(1,)(3,)(6), Watanabe Y(2,)(3).	(1)University of Kansai Welfare Sciences, 3-11-1 Asahigaoka, Kashiwara, Osaka, 582-0026, Japan. (2)RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-Minamimachi, Chuo-Ku, Kobe, Hyogo, 650-0047, Japan. (3)Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abenoku, Osaka City, Osaka, 545-8585, Japan. (4)Yamaguchi University Graduate School of Medicine, 1-1-1 Minamiogushi, Ube City, Yamaguchi, 755-8505, Japan. (5)Department of Medical Science on Fatigue, Osaka City University Graduate	Ubiquinol-10 supplementation improves autonomic nervous function and cognitive function in chronic fatigue syndrome.	209. Biofactors. 2016 Jul 8;42(4):431-40.	The aim of this study was to evaluate the benefit of oral ubiquinol-10 supplementation in CFS patients using an open-label study and a randomized, double-blinded, placebo-controlled (RCT) study. Twenty patients with CFS were randomly enrolled in an 8-week open-label oral ubiquinol-10 (150 mg ubiquinol-10/day) study. The patients and the attending physicians were not blinded to the supplementation. Forty-three patients with CFS were randomly assigned to receive either ubiquinol-10 (150 mg/day) or placebo every day for 12 weeks. The patients and the attending physicians were blinded to the supplementation, and a total of 31 patients (N = 17 in the ubiquinol group and 14 in the placebo group) completed the study. The beneficial effects of ubiquinol-10 were observed in the open-label study we conducted prior to the RCT. The RCT results suggest that supplementation with ubiquinol-10 for 12 weeks is effective for improving several CFS symptoms. © 2016 BioFactors, 42(4):431-440, 2016.

	School of Medicine, 1-4-3 Asahimachi, Abenoku, Osaka City, Osaka, 545-8585, Japan. (6)Department of Endocrinology, Metabolism and Molecular Medicine, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abenoku, Osaka City, Osaka, 545-8585, Japan.			
Fukuda S(1), Nojima J(2), Motoki Y(2), Yamaguti K(3), Nakatomi Y(3), Okawa N(4), Fujiwara K(4), Watanabe Y(5), Kuratsune H(6).	(1)University of Kansai Welfare Sciences, Kashiwara, Osaka 582-0026, Japan; RIKEN Center for Life Science Technologies, Kobe, Hyogo 650-0047, Japan; Department of Physiology, Osaka City University Graduate School of Medicine, Osaka 545-8585, Japan. Electronic address: sfukuda@fuksi-kagk-u.ac.jp. (2)Department of Laboratory Science, Yamaguchi University Graduate School of Medicine, Yamaguchi 755-8505, Japan. (3)Department of Physiology, Osaka City University Graduate School of Medicine,	A potential biomarker for fatigue: Oxidative stress and anti-oxidative activity.	184. Biol Psychol. 2016 Jul;118:88-93.	We sought to determine whether oxidative stress and anti-oxidative activity could act as biomarkers that discriminate patients with chronic fatigue syndrome (CFS) from healthy volunteers at acute and sub-acute fatigue and resting conditions. We calculated the oxidative stress index (OSI) from reactive oxygen metabolites-derived compounds (d-ROMs) and the biological antioxidant potential (BAP). We determined changes in d-ROMs, BAP, and OSI in acute and sub-acute fatigue in two healthy groups, and compared their values at rest between patients with CFS (diagnosed by Fukuda 1994 criteria) and another group of healthy controls. Following acute fatigue in healthy controls, d-ROMs and OSI increased, and BAP decreased. Although d-ROMs and OSI were significantly higher after sub-acute fatigue, BAP did not decrease. Resting condition yielded higher d-ROMs, higher OSI, and lower BAP in patients with CFS than in healthy volunteers, but lower d-ROMs and OSI when compared with sub-acute controls. BAP values did not significantly differ between patients with CFS and controls in the sub-acute condition. However, values were significantly higher than in the resting condition for controls. Thus, measured of oxidative stress (d-ROMS) and anti-oxidative activity (BAP) might be useful for discriminating acute, sub-acute, and resting fatigue in healthy people from patients with CFS, or for evaluating fatigue levels in healthy people.

	Osaka 545-8585, Japan; Department of Endocrinology, Metabolism and Molecular Medicine, Osaka City University Graduate School of Medicine, Osaka 545-8585, Japan. (4)University of Kansai Welfare Sciences, Kashiwara, Osaka 582-0026, Japan. (5)RIKEN Center for Life Science Technologies, Kobe, Hyogo 650-0047, Japan; Department of Physiology, Osaka City University Graduate School of Medicine, Osaka 545-8585, Japan. (6)University of Kansai Welfare Sciences, Kashiwara, Osaka 582-0026, Japan; RIKEN Center for Life Science Technologies, Kobe, Hyogo 650-0047, Japan; Department of Physiology, Osaka City University Graduate School of Medicine, Osaka 545-8585, Japan; Department of Endocrinology, Metabolism and Molecular Medicine, Osaka City University Graduate School of			

	Medicine, Osaka 545-8585, Japan.			
Gamp M(1), Renner B(2).	(1)University of Konstanz, Germany. martina.gamp@uni-konstanz.de. (2)University of Konstanz, Germany.	Pre-Feedback Risk Expectancies and Reception of Low-Risk Health Feedback: Absolute and Comparative Lack of Reassurance.	59. Appl Psychol Health Well Being. 2016 Nov;8(3):364-385.	BACKGROUND: Personalised health-risk assessment is one of the most common components of health promotion programs. Previous research on responses to health risk feedback has commonly focused on the reception of bad news (high-risk feedback). The reception of low-risk feedback has been comparably neglected since it is assumed that good news is reassuring and readily received. However, field studies suggest mixed responses to low-risk health feedback. Accordingly, we examine whether pre-feedback risk expectancies can mitigate the reassuring effects of good news. METHODS: In two studies (N = 187, N = 565), after assessing pre-feedback risk expectancies, participants received low-risk personalised feedback about their own risk of developing (the fictitious) Tucson Chronic Fatigue Syndrome (TCFS). Study 2 also included peer TCFS risk status feedback. Afterwards, self- and peer-related risk perception for TCFS was assessed. RESULTS: In both studies, participants who expected to be at high risk but received good news (unexpected low-risk feedback) showed absolute lack of reassurance. Specifically, they felt at significantly greater TCFS risk than participants who received expected good news. Moreover, the unexpected low-risk group even believed that their risk was as high as (Study 1) or higher (Study 2) than that of their peers (comparative lack of reassurance). CONCLUSION: Results support the notion that high pre-feedback risk expectancies can mitigate absolute and comparative reassuring effects of good news.
García-Álvarez L(1), Pérez-Matute P(1), Blanco JR(1), Ibarra V(1), Oteo JA(2).	(1)Infectious Diseases Department, Hospital San Pedro-Center for Biomedical Research of La Rioja (CIBIR), Logroño, La Rioja, Spain. (2)Infectious Diseases Department, Hospital San Pedro-Center for Biomedical Research of La Rioja (CIBIR), Logroño, La Rioja, Spain. Electronic address: jaoteo@riojasalud.es.	High prevalence of asymptomatic carriers of Tropheryma whipplei in different populations from the North of Spain.	331. Enferm Infecc Microbiol Clin. 2016 Jun-Jul;34(6):340-5.	INTRODUCTION: Tropheryma whipplei is the causative agent of Whipple disease. T. whipplei has also been detected in asymptomatic carriers with a very different prevalence. To date, in Spain, there are no data regarding the prevalence of T. whipplei in a healthy population or in HIV-positive patients, or in chronic fatigue syndrome (CFS). Therefore, the aim of this work was to assess the prevalence of T. whipplei in stools in those populations. METHODS: Stools from 21 HIV-negative subjects, 65 HIV-infected, and 12 CFS patients were analysed using real time-PCR. HIV-negative and positive subjects were divided into two groups, depending on the presence/absence of metabolic syndrome (MS). Positive samples were sequenced. RESULTS: The prevalence of T. whipplei was 25.51% in 98 stool samples analysed. Prevalence in HIV-positive patients was significantly higher than in HIV-negative (33.8% vs. 9.09%, p=0.008). Prevalence in the control group with no associated diseases was 20%, whereas no positive samples were observed in HIV-negative patients with MS, or in those diagnosed with CFS. The prevalence observed in HIV-positive patients without MS was 30.35%, and with MS it was 55.5%. The number of positive samples varies depending on the primers used, although no statistically significant differences were observed. CONCLUSIONS: There is a high prevalence of asymptomatic carriers of T. whipplei among healthy and in HIV-infected people from Spain. The role of T. whipplei in HIV patients with MS is unclear, but the prevalence is higher than in other populations.

Garus-Pakowska A(1), Leśniewska A(1), Gaszyńska E(1), Szatko F(1).	(1)Department of Hygiene and Health Promotion, Medical University of Łódź, Łódź, Poland.	Occupational exposure and health problems among Polish denturists: a population-based study in Łódź province.	239. Int Dent J. 2016 Aug;66(4):237-46.	OBJECTIVE: The aim of this study was to analyse the potential health effects of occupational exposure of denturists in the Łódź province. METHODS: The survey was performed among 103 denturists working in 24 dental laboratories in the Łódź province using the questionnaire prepared by the authors. RESULTS: The most common health problems associated with work (occurring daily or at least once a week) were: back pain (69.8%); chronic fatigue syndrome (61.6%); irritation, itching and rashes on the hands (51.2%); restlessness and aggression (43.0%); and watery and itchy eyes (41.9%). Psychosocial and ergonomic hazards associated with work organisation (72.2%) were the most common work environment factors related to the denturist profession. CONCLUSIONS: Analyses of denturists' occupational exposure in the Łódź province and epidemiological estimates of the health effects suggest the need for preventive measures.
Gay CW(1), Robinson ME(1), Lai S(2), O'Shea A(1), Craggs JG(1), Price DD(3), Staud R(4).	(1)1 Department of Clinical & Health Psychology, University of Florida College of Medicine , Gainesville, Florida. (2)2 Department of Radiation Oncology & Neurology, University of Florida College of Medicine , Gainesville, Florida. (3)3 Department of Maxillo-Facial Surgery, University of Florida College of Medicine , Gainesville, Florida. (4)4 Department of Medicine, University of Florida College of Medicine , Gainesville, Florida.	Abnormal Resting-State Functional Connectivity in Patients with Chronic Fatigue Syndrome: Results of Seed and Data-Driven Analyses.	339. Brain Connect. 2016 Feb;6(1):48-56.	Although altered resting-state functional connectivity (FC) is a characteristic of many chronic pain conditions, it has not yet been evaluated in patients with chronic fatigue. Our objective was to investigate the association between fatigue and altered resting-state FC in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Thirty-six female subjects, 19 ME/CFS and 17 healthy controls, completed a fatigue inventory before undergoing functional magnetic resonance imaging. Two methods, (1) data driven and (2) model based, were used to estimate and compare the intraregional FC between both groups during the resting state (RS). The first approach using independent component analysis was applied to investigate five RS networks: the default mode network, salience network (SN), left frontoparietal networks (LFPN) and right frontoparietal networks, and the sensory motor network (SMN). The second approach used a priori selected seed regions demonstrating abnormal regional cerebral blood flow (rCBF) in ME/CFS patients at rest. In ME/CFS patients, Method-1 identified decreased intrinsic connectivity among regions within the LFPN. Furthermore, the FC of the left anterior midcingulate with the SMN and the connectivity of the left posterior cingulate cortex with the SN were significantly decreased. For Method-2, five distinct clusters within the right parahippocampus and occipital lobes, demonstrating significant rCBF reductions in ME/CFS patients, were used as seeds. The parahippocampal seed and three occipital lobe seeds showed altered FC with other brain regions. The degree of abnormal connectivity correlated with the level of self-reported fatigue. Our results confirm altered RS FC in patients with ME/CFS, which was significantly correlated with the severity of their chronic fatigue.
Gelonch O(1), Garolera M(2), Valls J(3), Rosselló L(4), Pifarré J(5).	(1)Clinical Research Group for Brain, Cognition and Behavior, Consorci Sanitari de Terrassa, Terrassa, Spain;	Executive function in fibromyalgia: Comparing subjective and objective measures.	243. Compr Psychiatry. 2016 Apr;66:113-22.	BACKGROUND: There is evidence to suggest the existence of an executive dysfunction in people diagnosed with fibromyalgia, although there are certain inconsistencies between studies. Here, we aim to compare executive performance between patients with fibromyalgia and a control group by using subjective and objective cognitive tests, analyzing the influence of patient mood on the results obtained, and studying associations between the two measures. METHOD: 82 patients diagnosed with

	University of Lleida, Spain. (2)Clinical Research Group for Brain, Cognition and Behavior, Consorci Sanitari de Terrassa, Terrassa, Spain; Neuropsychology Unit, Hospital de Terrassa, Consorci Sanitari de Terrassa, Terrassa, Spain. (3)Institute of Biomedical Research of Lleida, IRB-Lleida, Spain. (4)Rheumatology Section, Fibromyalgia and Chronic Fatigue Syndrome Unit, Hospital Universitari de Santa Maria, Lleida, Spain. (5)University of Lleida, Spain; Institute of Biomedical Research of Lleida, IRB-Lleida, Spain. Electronic address: pifarre1@comll.cat.			fibromyalgia and 42 healthy controls, matched by age and years of education, were assessed using the Behavioral Rating Inventory of Executive Function - Adult Version (BRIEF-A) as a subjective measure of executive functioning. A selection of objective cognitive tests were also used to measure a series of executive functions and to identify symptoms of depression and anxiety. RESULTS: Patients with fibromyalgia perceived greater difficulties than the control group on all of the BRIEF-A scales. However, after adjustments were made for depression and anxiety the only differences that remained were those associated with the working memory scale and the Metacognition and Global Executive Composite index. In the case of the objective cognitive tests, a significantly worse overall performance was evidenced for the fibromyalgia patients. However, this also disappeared when adjustments were made for depression and anxiety. After this adjustment, fibromyalgia patients only performed significantly worse for the interference effect in the Stroop Test. Although there were no significant associations between most of the objective cognitive tests and the BRIEF-A scales, depression and anxiety exhibited strong associations with almost all of the BRIEF-A scales and with several of the objective cognitive tests. CONCLUSIONS: Patients with fibromyalgia showed executive dysfunction in subjective and objective measures, although most of this impairment was associated with mood disturbances. Exceptions to this general rule were observed in the impairment of working memory evidenced on the BRIEF-A scale and the inhibition impairment exhibited by the interference effect from the Stroop Test. The two types of measurement provide different yet complementary information.
Geoffroy PA(1), Micoulaud Franchi JA(2), Lopez R(3), Poirot I(4), Brion A(5), Royant-Parola S(6), Etain B(7).	(1) U1144, case 15, faculté de pharmacie, Inserm, 4, avenue de l'Observatoire, 75006 Paris, France; UMR-S 1144, université Paris Descartes, 75006 Paris, France; UMR-S 1144, université Paris Diderot, Sorbonne Paris Cité, 75013 Paris,	[How to characterize and treat sleep complaints in bipolar disorders?] [Article in French]	91. Encephale. 2016 Sep 23. pii: S0013-7006(16)30180-4.	OBJECTIVES: Sleep complaints are very common in bipolar disorders (BD) both during acute phases (manic and depressive episodes) and remission (about 80 % of patients with remitted BD have poor sleep quality). Sleep complaints during remission are of particular importance since they are associated with more mood relapses and worse outcomes. In this context, this review discusses the characterization and treatment of sleep complaints in BD. METHODS: We examined the international scientific literature in June 2016 and performed a literature search with PubMed electronic database using the following headings: "bipolar disorder" and ("sleep" or "insomnia" or "hypersomnia" or "circadian" or "apnoea" or "apnea" or "restless legs"). RESULTS: Patients with BD suffer from sleep and circadian rhythm abnormalities during major depressive episodes (insomnia or hypersomnia, nightmares, nocturnal and/or early awakenings, non-

	France; GH Saint-Louis-Lariboisière-F.-Widal, pôle de psychiatrie et de médecine addictologique, AP-HP, 75475 Paris cedex 10, France; Fondation FondaMental, 94000 Créteil, France. Electronic address: pierrealexis.geoffroy @aphp.fr. (2) USR CNRS 3413 SANPSY, université de Bordeaux, CHU Pellegrin, 33076 Bordeaux, France; Service d'explorations fonctionnelles du système nerveux, clinique du sommeil, CHU de Bordeaux, place Amélie-Raba-Léon, 33076 Bordeaux, France. (3) Centre national de référence narcolepsie et hypersomnie idiopathique, CHU Gui-De-Chauliac, 34000 Montpellier, France; U1061, Inserm, 34000 Montpellier, France. (4) Pôle de psychiatrie, médecine légale et médecine en milieu pénitencière, unité de sommeil de			restorative sleep) and manic episodes (insomnia, decreased need for sleep without fatigue), but also some of these abnormalities may persist during remission. These remission phases are characterized by a reduced quality and quantity of sleep, with a longer sleep duration, increased sleep latency, a lengthening of the wake time after sleep onset (WASO), a decrease of sleep efficiency, and greater variability in sleep/wake rhythms. Patients also present frequent sleep comorbidities: chronic insomnia, sleepiness, sleep phase delay syndrome, obstructive sleep apnea/hypopnea syndrome (OSAHS), and restless legs syndrome (RLS). These disorders are insufficiently diagnosed and treated whereas they are associated with mood relapses, treatment resistance, affect cognitive global functioning, reduce the quality of life, and contribute to weight gain or metabolic syndrome. Sleep and circadian rhythm abnormalities have been also associated with suicidal behaviors. Therefore, a clinical exploration with characterization of these abnormalities and disorders is essential. This exploration should be helped by questionnaires and documented on sleep diaries or even actimetric objective measures. Explorations such as ventilatory polygraphy, polysomnography or a more comprehensive assessment in a sleep laboratory may be required to complete the diagnostic assessment. Treatments obviously depend on the cause identified through assessment procedures. Treatment of chronic insomnia is primarily based on non-drug techniques (by restructuring behavior and sleep patterns), on psychotherapy (cognitive behavioral therapy for insomnia [CBT-I]; relaxation; interpersonal and social rhythm therapy [IPSRT]; etc.), and if necessary with hypnotics during less than four weeks. Specific treatments are needed in phase delay syndrome, OSAHS, or other more rare sleep disorders. CONCLUSIONS: BD are defined by several sleep and circadian rhythm abnormalities during all phases of the disorder. These abnormalities and disorders, especially during remitted phases, should be characterized and diagnosed to reduce mood relapses, treatment resistance and improve BD outcomes.

	psychiatrie adulte, hôpital Fontan 1, CHRU de Lille, 59037 Lille, France. (5) Réseau Morphée, 92380 Garches, France. (6) Réseau Morphée, 92380 Garches, France; Clinique du Château, 92380 Garches, France. (7)U1144, case 15, faculté de pharmacie, Inserm, 4, avenue de l'Observatoire, 75006 Paris, France; UMR-S 1144, université Paris Descartes, 75006 Paris, France; UMR-S 1144, université Paris Diderot, Sorbonne Paris Cité, 75013 Paris, France; GH Saint-Louis-Lariboisière-F.-Widal, pôle de psychiatrie et de médecine addictologique, AP-HP, 75475 Paris cedex 10, France; Fondation FondaMental, 94000 Créteil, France.			
Georgin-Lavialle S(1), Gaillard R(2), Moura D(3), Hermine O(4).	(1)Service de médecine Interne, Hôpital Tenon, Université Pierre et Marie Curie, Assistance Publique-Hôpitaux de Paris,	Mastocytosis in adulthood and neuropsychiatric disorders.	226. Transl Res. 2016 Aug;174:77-85.e1.	Patients with mastocytosis can display various disabling general and neuropsychological symptoms among one third of them, including general signs such as fatigue and musculoskeletal pain, which can have a major impact on quality of life. Neurological symptoms are less frequent and mainly consist of acute or chronic headache (35%), rarely syncopes (5%), acute onset back pain (4%), and in a few cases, clinical and radiological symptoms resembling or allowing the diagnosis of multiple sclerosis (1.3%). Headaches are associated with symptoms related to mast cell activation syndrome

	Paris, France. (2)Laboratoire de "Physiopathologie des maladies Psychiatriques", Centre de Psychiatrie et Neurosciences U894, INSERM; Université Paris Descartes, Sorbonne Paris Cité, Paris, France; Service de Psychiatrie, Centre Hospitalier Sainte-Anne, Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine Paris Descartes, Paris, France; Human Histopathology and Animal Models, Infection and Epidemiology Department, Institut Pasteur, Paris, France. (3)Centre de référence des mastocytoses, Université Paris Descartes, Sorbonne, Paris Cité, Hôpital Necker Enfants malades, Paris, France. (4)Centre de référence des mastocytoses, Université Paris Descartes, Sorbonne, Paris Cité, Hôpital			(flushes, prurit, and so forth) and more frequently present as migraine (37.5%), with often aura (66%). Depression-anxiety like symptoms can occur in 40% to 60% of the patients and cognitive impairment is not rare (38.6%). The pathophysiology of these symptoms could be linked to tissular mast cell infiltration or to mast cell mediators release or both. The tryptophan metabolism could be involved in mast cell-induced neuroinflammation through indoleamine-2,3-dioxygenase activation. Treatments targeting mast cell may be useful to target neuropsychological features associated with mastocytosis, including tyrosine kinase inhibitors.

	Necker Enfants malades, Paris, France; INSERM U1163 and CNRS ERL 8254 and Laboratory of Physiopathology and Treatment of Hematological Disorders Hôpital Necker-Enfants malades, Institut Imagine, Paris, France; Service d'hématologie adulte, Université Paris Descartes, Sorbonne, Paris Cité, Assistance Publique-Hôpitaux de Paris, Institut Imagine, Hôpital Necker-Enfants malades, Paris, France. Electronic address: ohermine@gmail.com.			
Geraghty KJ, Esmail A.		Chronic fatigue syndrome: is the biopsychosocial model responsible for patient dissatisfaction and harm?	128. Br J Gen Pract. 2016 Aug;66(649):437-8.	
Geraghty KJ(1), Blease C(2).	(1) University of Manchester, UK keith.geraghty@manchester.ac.uk. (2)University of Leeds, UK.	Cognitive behavioural therapy in the treatment of chronic fatigue syndrome: A narrative review on efficacy and informed consent.	96. J Health Psychol. 2016 Sep 15. pii: 1359105316667798.	Cognitive behavioural therapy is increasingly promoted as a treatment for chronic fatigue syndrome. There is limited research on informed consent using cognitive behavioural therapy in chronic fatigue syndrome. We undertook a narrative review to explore efficacy and to identify the salient information that should be disclosed to patients. We found a complex theoretical model underlying the rationale for psychotherapy in chronic fatigue syndrome. Cognitive behavioural therapy may bring about changes in self-reported fatigue for some patients in the short term, however there is a lack of evidence for long-term benefit or for improving physical function and cognitive behavioural therapy may cause distress if inappropriately prescribed. Therapist effects and placebo effects are important outcome factors.

Geraghty KJ(1).	(1)The University of Manchester, UK keith.geraghty@manchester.ac.uk.	'PACE-Gate': When clinical trial evidence meets open data access.	54. J Health Psychol. 2016 Nov 1. pii: 1359105316675213.	Science is not always plain sailing and sometimes the voyage is across an angry sea. A recent clinical trial of treatments for chronic fatigue syndrome (the PACE trial) has whipped up a storm of controversy. Patients claim the lead authors overstated the effectiveness of cognitive behavioural therapy and graded exercise therapy by lowering the thresholds they used to determine improvement. In this extraordinary case, patients discovered that the treatments tested had much lower efficacy after an information tribunal ordered the release of data from the PACE trial to a patient who had requested access using a freedom of information request.
Gherardi RK(1), Aouizerate J(1), Cadusseau J(2), Yara S(2), Authier FJ(3).	(1)Garches-Necker-Mondor-Hendaye Reference Centre for Neuromuscular Diseases, 94000 Créteil, France; Expert Centre for Neuromuscular Pathology, Henri-Mondor Hospital, AP-HP, 51, avenue du Maréchal-de-Lattre-de-Tassigny, 94000 Créteil, France; Inserm U955-Team 10 "Biology of Neuromuscular System" Paris Est-Créteil University, Créteil, France. (2)Garches-Necker-Mondor-Hendaye Reference Centre for Neuromuscular Diseases, 94000 Créteil, France; Inserm U955-Team 10 "Biology of Neuromuscular System" Paris Est-Créteil University, Créteil, France.	Aluminum adjuvants of vaccines injected into the muscle: Normal fate, pathology and associated disease.	258. Morphologie. 2016 Jun;100(329):85-94.	Aluminum oxyhydroxide (Alhydrogel(®)) is a nano-crystalline compound forming aggregates that has been introduced in vaccine for its immunologic adjuvant effect in 1926. It is the most commonly used adjuvant in human and veterinary vaccines but mechanisms by which it stimulates immune responses remain ill-defined. Although generally well tolerated on the short term, it has been suspected to occasionally cause delayed neurologic problems in susceptible individuals. In particular, the long-term persistence of aluminic granuloma also termed macrophagic myofasciitis is associated with chronic arthromyalgias and fatigue and cognitive dysfunction. Safety concerns largely depend on the long biopersistence time inherent to this adjuvant, which may be related to its quick withdrawal from the interstitial fluid by avid cellular uptake; and the capacity of adjuvant particles to migrate and slowly accumulate in lymphoid organs and the brain, a phenomenon documented in animal models and resulting from MCP1/CCL2-dependant translocation of adjuvant-loaded monocyte-lineage cells (Trojan horse phenomenon). These novel insights strongly suggest that serious re-evaluation of long-term aluminum adjuvant phamacokinetics and safety should be carried out.

	(3)Garches-Necker-Mondor-Hendaye Reference Centre for Neuromuscular Diseases, 94000 Créteil, France; Expert Centre for Neuromuscular Pathology, Henri-Mondor Hospital, AP-HP, 51, avenue du Maréchal-de-Lattre-de-Tassigny, 94000 Créteil, France; Inserm U955-Team 10 "Biology of Neuromuscular System" Paris Est-Créteil University, Créteil, France. Electronic address: authier@u-pec.fr.			
Giloteaux L(1), Goodrich JK(1,)(2), Walters WA(1,)(2), Levine SM(3), Ley RE(1,)(2), Hanson MR(4).	(1)Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, USA. (2)Department of Microbiology, Cornell University, Ithaca, NY, USA. (3)Private Practice, New York, NY, USA. (4)Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, USA. mrh5@cornell.edu.	Reduced diversity and altered composition of the gut microbiome in individuals with myalgic encephalomyelitis/chronic fatigue syndrome.	158. Microbiome. 2016 Jun 23;4(1):30.	BACKGROUND: Gastrointestinal disturbances are among symptoms commonly reported by individuals diagnosed with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). However, whether ME/CFS is associated with an altered microbiome has remained uncertain. Here, we profiled gut microbial diversity by sequencing 16S ribosomal ribonucleic acid (rRNA) genes from stool as well as inflammatory markers from serum for cases (n = 48) and controls (n = 39). We also examined a set of inflammatory markers in blood: C-reactive protein (CRP), intestinal fatty acid-binding protein (I-FABP), lipopolysaccharide (LPS), LPS-binding protein (LBP), and soluble CD14 (sCD14). RESULTS: We observed elevated levels of some blood markers for microbial translocation in ME/CFS patients; levels of LPS, LBP, and sCD14 were elevated in ME/CFS subjects. Levels of LBP correlated with LPS and sCD14 and LPS levels correlated with sCD14. Through deep sequencing of bacterial rRNA markers, we identified differences between the gut microbiomes of healthy individuals and patients with ME/CFS. We observed that bacterial diversity was decreased in the ME/CFS specimens compared to controls, in particular, a reduction in the relative abundance and diversity of members belonging to the Firmicutes phylum. In the patient cohort, we find less diversity as well as increases in specific species often reported to be pro-inflammatory species and reduction in species frequently described as anti-inflammatory. Using a

				machine learning approach trained on the data obtained from 16S rRNA and inflammatory markers, individuals were classified correctly as ME/CFS with a cross-validation accuracy of 82.93 %. CONCLUSIONS: Our results indicate dysbiosis of the gut microbiota in this disease and further suggest an increased incidence of microbial translocation, which may play a role in inflammatory symptoms in ME/CFS.
Giloteaux L(1), Hanson MR(1), Keller BA(2).	(1) Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, USA. (2)Department of Exercise & Sport Sciences, Ithaca College, School of Health Sciences & Human Performance, Ithaca, NY, USA.	A Pair of Identical Twins Discordant for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Differ in Physiological Parameters and Gut Microbiome Composition.	77. Am J Case Rep. 2016 Oct 10;17:720-729.	BACKGROUND Patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) present with profound fatigue, flu-like symptoms, pain, cognitive impairment, orthostatic intolerance, and post-exertional malaise (PEM), and exacerbation of some or all of the baseline symptoms. CASE REPORT We report on a pair of 34-year-old monozygotic twins discordant for ME/CFS, with WELL, the non-affected twin, and ILL, the affected twin. Both twins performed a two-day cardiopulmonary exercise test (CPET), pre- and post-exercise blood samples were drawn, and both provided stool samples for biochemical and molecular analysis. At peak exertion for both CPETs, ILL presented lower VO2peak and peak workload compared to WELL. WELL demonstrated normal reproducibility of VO2@ventilatory/anaerobic threshold (VAT) during CPET2, whereas ILL experienced an abnormal reduction of 13% in VAT during CPET2. A normal rise in lactate dehydrogenase (LDH), creatine kinase (CK), adrenocorticotropic hormone (ACTH), cortisol, creatinine, and ferritin content was observed following exercise for both WELL and ILL at each CPET. ILL showed higher increases of resistin, soluble CD40 ligand (sCD40L), and soluble Fas ligand (sFasL) after exercise compared to WELL. The gut bacterial microbiome and virome were examined and revealed a lower microbial diversity in ILL compared to WELL, with fewer beneficial bacteria such as Faecalibacterium and Bifidobacterium, and an expansion of bacteriophages belonging to the tailed dsDNA Caudovirales order. CONCLUSIONS Results suggest dysfunctional immune activation in ILL following exercise and that prokaryotic viruses may contribute to mucosal inflammation and bacterial dysbiosis. Therefore, a two-day CPET and molecular analysis of blood and microbiomes could provide valuable information about ME/CFS, particularly if applied to a larger cohort of monozygotic twins.
Gilron I(1), Chaparro LE, Tu D, Holden RR, Milev R, Towheed T, DuMerton-Shore D, Walker S.	(1)Departments of aAnesthesiology and Perioperative Medicine and bBiomedical and Molecular Sciences, Queen's University, Kingston, Canada cUniversity of Toronto, Department of Anesthesia, University of Toronto,	Combination of pregabalin with duloxetine for fibromyalgia: a randomized controlled trial.	248. Pain. 2016 Jul;157(7):1532-40.	Fibromyalgia is a syndrome characterized by chronic widespread pain and associated with sleep disturbance, depression, fatigue, and cognitive dysfunction. Polypharmacy is commonly used, but supportive evidence is limited. Most fibromyalgia trials focus primarily on pain reduction with monotherapy. This trial compares a pregabalin-duloxetine combination to each monotherapy. Using a randomized, double-blind, 4-period crossover design, participants received maximally tolerated doses of placebo, pregabalin, duloxetine, and pregabalin-duloxetine combination-for 6 weeks. Primary outcome was daily pain (0-10); secondary outcomes included global pain relief, Fibromyalgia Impact Questionnaire, SF-36 survey, Medical Outcomes Study Sleep Scale, Beck Depression Inventory (BDI-II), adverse events, and other measures. Of 41 participants randomized, 39 completed ≥2 treatments. Daily pain during placebo, pregabalin, duloxetine, and combination was 5.1, 5.0, 4.1, and 3.7, respectively (P <

	Toronto, Canada dPublic Health Sciences eMathematics and Statistics fPsychology and gPsychiatry, Queen's University, Kingston, Canada hDivision of Rheumatology, Department of Medicine Queen's University, Kingston, ON, Canada iDepartment of Anesthesiology and Perioperative Medicine, Queen's University, Kingston, Canada.			0.05 only for combination vs placebo, and pregabalin). Participants (%) reporting ≥moderate global pain relief were 18%, 39%, 42%, and 68%, respectively (P < 0.05 for combination vs placebo, pregabalin, and duloxetine). Fibromyalgia Impact Questionnaire scores were 42.9, 37.4, 36.0, and 29.8, respectively (P < 0.05 for combination vs placebo, pregabalin, and duloxetine). SF-36 scores were 50.2, 55.7, 56.0, and 61.2, respectively (P < 0.05 for combination vs placebo, pregabalin, and duloxetine). Medical Outcomes Study Sleep Scale scores were 48.9, 35.2, 46.1, and 32.1, respectively (P < 0.05 only for combination vs placebo, and duloxetine). BDI-II scores were 11.9, 9.9, 10.7, and 8.9, respectively (P < 0.05 only for combination vs placebo). Moderate-severe drowsiness was more frequent during combination vs placebo. Combining pregabalin and duloxetine for fibromyalgia improves multiple clinical outcomes vs monotherapy. Continued research should compare this and other combinations to monotherapy for fibromyalgia.
Gimeno Pi I(1), Guitard Sein-Echaluce ML(2), Rosselló Aubach L(3), Torres Puig-Gros J(4), Fernández Solà J(5).	(1)Centro de Atención Primaria 1er de Maig. Institut Català de la Salut. Lleida, España igimeno.lleida.ics@gencat.cat. (2)Facultad de Enfermería y Fisioterapia. Universidad de Lleida, Lleida. España. (3)Unidad de Reumatología. Hospital Universitario Santa María. Lleida. España. (4)Servicio de Vigilancia Epidemiológica. Departamento de Salud. Lleida. España. (5)Unidad de Fatiga	Stressful Events in the Onset of Chronic Fatigue Syndrome. [Article in English, Spanish; Abstract available in Spanish from the publisher]	114. Rev Esp Salud Publica. 2016 Aug 18;90:e1-7.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is a complex and multifactorial disease. Stressful situations experienced could be related to the presentation of the disease. Few studies have determined which factors could trigger CFS. The main objective of this study was to explore the stressful situations which can be associated with CFS presentation. METHODS: Retrospective observational case-control study with CFS diagnosed patients according to the Fukuda's criteria. Controls were matched to cases by sex, age and educational level with a 1:1 ratio. Participants aged between 18 and 75 years from the province of Lleida. Information was obtained through personal questionnaires. The measure of association was the odds ratio. RESULTS: In total, 77 cases and 77 controls were included. Association found between stressful life events and presentation of disease were pregnancy ORa=31.7 (CI95%:2.2-456.7), spousal abuse ORa= 10.2 (CI95%:1.2-88.4) and mobbing ORa=6.9 (CI95%:1.3-36.9), eating disorders=7.5 (CI95%:1.3-42.1), car accident ORa=5.5 (CI95%:1.7-17 9), economic problems ORa=5.1 (CI95%:2.1-12.6) and changes in sleep habits ORa=2.8 (CI95%:1.1-7.5). CONCLUSIONS: Stressful life events as pregnancy, spousal abuse, mobbing, eating disorders, car accident, economic problems and changes in sleep habits felt by those affected must be taken into consideration when compiling background information related to the onset of Chronic Fatigue Syndrome. Adequate identification of these stressful life events in risk people could contribute to early diagnosis of Chronic Fatigue Syndrome.

	Crónica. Hospital Clínic. Universidad de Barcelona. España.			
Godts D(1), Moorkens G(2,)(3), Mathysen DG(4,)(2).	(1)From the Antwerp University Hospital, Department of Ophthalmology, Edegem (Antwerp); godts@uza.be. (2)University of Antwerp, Faculty of Medicine and Health Sciences, Wilrijk (Antwerp). (3)Antwerp University Hospital, Department of Internal Medicine, Edegem (Antwerp), Belgium. (4)From the Antwerp University Hospital, Department of Ophthalmology, Edegem (Antwerp).	Binocular Vision in Chronic Fatigue Syndrome.	60. Am Orthopt J. 2016 Jan;66(1):92-97.	INTRODUCTION AND PURPOSE: To compare binocular vision measurements between Chronic Fatigue Syndrome (CFS) patients and healthy controls. METHODS: Forty-one CFS patients referred by the Reference Centre for Chronic Fatigue Syndrome of the Antwerp University Hospital and forty-one healthy volunteers, matched for age and gender, underwent a complete orthoptic examination. Data of visual acuity, eye position, fusion amplitude, stereopsis, ocular motility, convergence, and accommodation were compared between both groups. RESULTS: Patients with CFS showed highly significant smaller fusion amplitudes ($P < 0.001$), reduced convergence capacity ($P < 0.001$), and a smaller accommodation range ($P < 0.001$) compared to the control group. CONCLUSION: In patients with CFS binocular vision, convergence and accommodation should be routinely examined. CFS patients will benefit from reading glasses either with or without prism correction in an earlier stage compared to their healthy peers. Convergence exercises may be beneficial for CFS patients, despite the fact that they might be very tiring. Further research will be necessary to draw conclusions about the efficacy of treatment, especially regarding convergence exercises. To our knowledge, this is the first prospective study evaluating binocular vision in CFS patients.
Goebel A(1).	(1)Pain Research Institute, Department of Translational Medicine, University of Liverpool, and The Walton Centre NHS Foundation Trust, Liverpool, L9 7AL, UK. Electronic address: andreasgoebel@rocketmail.com.	Autoantibody pain.	270. Autoimmun Rev. 2016 Jun;15(6):552-7.	As autoantibodies bind to target tissues, Fc-region dependent inflammation can induce pain via mediators exciting nociceptors. But recently another possibility has emerged, where autoantibody binding to nociceptors can directly cause pain, without inflammation. This is thought to occur as a result of Fab-region mediated modification of nerve transduction, transmission, or neuropeptide release. In three conditions, complex regional pain syndrome, anti-voltage gated potassium channel complex autoimmunity, and chronic fatigue syndrome, all associated with no or only little inflammation, initial laboratory-, and clinical trial-results have suggested a potential role for autoantibody-mediated mechanisms. More research assessing the pathogenic roles of autoantibodies in these and other chronic pain conditions is required. The concept of autoantibody-mediated pain offers hope for the development of novel therapies for currently intractable pains.
Goldsmith KA(1), Chalder T(2), White PD(3), Sharpe M(4), Pickles A(5).	(1) Biostatistics & Health Informatics Department, Institute of Psychiatry, Psychology &	Measurement error, time lag, unmeasured confounding: Considerations for longitudinal estimation of	94. Stat Methods Med Res. 2016 Sep 19. pii: 0962280216666111.	Clinical trials are expensive and time-consuming and so should also be used to study how treatments work, allowing for the evaluation of theoretical treatment models and refinement and improvement of treatments. These treatment processes can be studied using mediation analysis. Randomised treatment makes some of the assumptions of mediation models plausible, but the mediator-outcome relationship could remain

	Neuroscience, King's College London, London, UK kimberley.goldsmith@kcl.ac.uk. (2) Academic Department of Psychological Medicine, Weston Education Centre, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. (3) Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine, Queen Mary University, London, UK. (4) Psychological Medicine Research, Department of Psychiatry, University of Oxford, Oxford, UK. (5)Biostatistics & Health Informatics Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK.	the effect of a mediator in randomised clinical trials.		subject to bias. In addition, mediation is assumed to be a temporally ordered longitudinal process, but estimation in most mediation studies to date has been cross-sectional and unable to explore this assumption. This study used longitudinal structural equation modelling of mediator and outcome measurements from the PACE trial of rehabilitative treatments for chronic fatigue syndrome (ISRCTN 54285094) to address these issues. In particular, autoregressive and simplex models were used to study measurement error in the mediator, different time lags in the mediator-outcome relationship, unmeasured confounding of the mediator and outcome, and the assumption of a constant mediator-outcome relationship over time. Results showed that allowing for measurement error and unmeasured confounding were important. Contemporaneous rather than lagged mediator-outcome effects were more consistent with the data, possibly due to the wide spacing of measurements. Assuming a constant mediator-outcome relationship over time increased precision.
Goldsmith LP, Dunn G, Bentall RP, Lewis SW, Wearden AJ.		Correction: Therapist Effects and the Impact of Early Therapeutic Alliance on Symptomatic Outcome in Chronic Fatigue Syndrome.	177. PLoS One. 2016 Jun 1;11(6):e0157199. Erratum for PLoS One. 2015 Dec 14;10(12):e0144623.	

Goldsmith LP, Dunn G, Bentall RP, Lewis SW, Wearden AJ.		Correction: Therapist Effects and the Impact of Early Therapeutic Alliance on Symptomatic Outcome in Chronic Fatigue Syndrome.	190. PLoS One. 2016 May 18;11(5):e0156120 Erratum for PLoS One. 2015 Dec 14;10(12):e0144623.	
Gopaluni S(1), Sherif M, Ahmadouk NA.	(1)Department of Nephrology, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, UK, CB2 0QQ.	Interventions for chronic kidney disease-associated restless legs syndrome.	47. Cochrane Database Syst Rev. 2016 Nov 7;11:CD010690.	BACKGROUND: Restless legs syndrome (RLS) is defined as the spontaneous movement of the limbs (mainly legs) associated with unpleasant, sometimes painful sensation which is relieved by moving the affected limb. Prevalence of RLS among people on dialysis has been estimated between 6.6% and 80%. RLS symptoms contribute to impaired quality of life and people with RLS are shown to have increased cardiovascular morbidity and mortality.Various pharmacological and non-pharmacological interventions have been used to treat primary RLS. However, the evidence for use of these interventions in people with chronic kidney disease (CKD) is not well established. The agents used in the treatment of primary RLS may be limited by the side effects in people with CKD due to increased comorbidity and altered drug pharmacokinetics. OBJECTIVES: The aim of this review was to critically look at the benefits, efficacy and safety of various treatment options used in the treatment of RLS in people with CKD and those undergoing renal replacement therapy (RRT). We aimed to define different group characteristics based on CKD stage to assess the applicability of a particular intervention to an individual patient. SEARCH METHODS: We searched the Cochrane Kidney and Transplant Specialised Register to 12 January 2016 through contact with the Information Specialist using search terms relevant to this review. SELECTION CRITERIA: Randomised controlled trials (RCT) and quasi-RCTs that assessed the efficacy of an intervention for RLS in adults with CKD were eligible for inclusion. Studies investigating idiopathic RLS or RLS secondary to other causes were excluded. DATA COLLECTION AND ANALYSIS: Two authors independently assessed studies for eligibility and conducted risk of bias evaluation. Results were expressed as risk ratios (RR) and their 95% confidence intervals (CI) for dichotomous outcomes, and mean difference (MD) and 95% CI for continuous outcomes. MAIN RESULTS: We included nine studies enrolling 220 dialysis participants. Seven studies were deemed to have moderate to high risk of bias. All studies were small in size and had a short follow-up period (two to six months). Studies evaluated the effects of six different interventions against placebo or standard treatment. The interventions studied included aerobic resistance exercise, gabapentin, ropinirole, levodopa, iron dextran, and vitamins C and E (individually and in combination).Aerobic resistance exercise showed a significant reduction in severity of RLS compared to no exercise (2 studies, 48 participants: MD -7.56, 95% CI -14.20 to -0.93; I(2) = 65%), and when compared to exercise with no resistance (1 study, 24 participants: MD -11.10, 95% CI -17.11 to -5.09), however there was no significant reduction when compared to ropinirole (1 study, 22 participants): MD -0.55, 95% CI -

				6.41 to 5.31). There were no significant differences between aerobic resistance exercise and either no exercise or ropinirole in the physical or mental component summary scores (using the SF-36 form). Improvement in sleep quality varied. There was no significant difference in subjective sleep quality between exercise and no exercise; however one study reported a significant improvement with ropinirole compared to resistance exercise (MD 3.71, 95% CI 0.89 to 6.53). Using the Epworth Sleepiness Scale there were no significant differences between resistance exercise and no exercise, ropinirole, or exercise with no resistance. Two studies reported there were no adverse events and one study did not mention if there were any adverse events. In one study, one patient in each group dropped out but the reason for dropout was not reported. Two studies reported no adverse events and one study did not report adverse events.Gabapentin was associated with reduced RLS severity when compared to placebo or levodopa, and there was a significant improvement in sleep quality, latency and disturbance reported in one study when compared to levodopa. Three patients dropped out due to lethargy (2 patients), and drowsiness, syncope and fatigue (1 patient).Because of a short duration of action, rebound and augmentation were noted with levodopa treatment even though it conferred some benefit in reducing the symptoms of RLS. Reported adverse events were severe vomiting, agitation after caffeine intake, headaches, dry mouth, and gastrointestinal symptoms.One study (25 participants) reported iron dextran reduced the severity of RLS at weeks one and two, but not at week four. Vitamins C, E and C plus E (1 study, 60 participants) helped the symptoms of RLS with minimal side effects (nausea and dyspepsia) but more evidence is needed before any conclusions can be drawn. AUTHORS' CONCLUSIONS: Given the small size of the studies and short follow-up, it can only be concluded that pharmacological interventions and intra-dialytic exercise programs have uncertain effects on RLS in haemodialysis patients. There have been no studies performed in non-dialysis CKD, peritoneal dialysis patients, or kidney transplant recipients. Further studies are warranted before any conclusions can be drawn. Aerobic resistance exercise and ropinirole may be suitable interventions for further evaluation.
Gotts ZM(1), Newton JL(2,)(3), Ellis JG(1), Deary V(1).	(1)Faculty of Health and Life Sciences, Northumbria University, Newcastle-Upon-Tyne, UK. (2)Institute of Cellular Medicine, Medical School, Newcastle University & Newcastle Hospitals NHS Foundation Trust,	The experience of sleep in chronic fatigue syndrome: A qualitative interview study with patients.	367. Br J Health Psychol. 2016 Feb;21(1):71-92.	OBJECTIVES: Sleep disturbances are common in chronic fatigue syndrome (CFS), and one of the key symptom complaints, yet it has been neglected by previous qualitative research. The aim was to explore the specific role of sleep in patients' experience of their illness. DESIGN: A qualitative semi-structured interview format facilitated a detailed and open exploration of sleep, and the extent to which its management and problems were linked to the lived experience of CFS. METHODS: Eleven semi-structured interviews were conducted with individuals with CFS. Data were transcribed verbatim and analysed thematically, to explore and describe patients' experience of their sleep, and its impact on their condition. RESULTS: Sleep emerged as a key aspect of the illness experience, and its management and effect on daytime functioning was a central pre-occupation for all 11 participants; all of them saw sleep as playing a critical role in their

	UK. (3)UK NIHR Biomedical Research Centre in Ageing, Newcastle-Upon-Tyne, UK.			illness through either maintaining or exacerbating existing symptoms. Exploration of individual experiences presented three overarching themes: (1) sleep pattern variability over illness course and from day to day; (2) effect of sleep on daytime functioning; and (3) attempts at coping and sleep management. CONCLUSIONS: Each patient with CFS has a unique experience of sleep. Despite the differing narratives regarding the role of sleep in CFS, all participants held the belief that sleep is a vital process for health and well-being which has had a direct bearing on the course and progression of their CFS. Also, every participant regarded their sleep as in some way 'broken' and in need of management/repair. Patients' insights demonstrate sleep-specific influences on their CFS, and the impact of disturbed sleep should be a consideration for clinical and research work. STATEMENT OF CONTRIBUTION: What is already known on this subject? Sleep disturbances are common in CFS, and one of the key symptom complaints, yet it has been neglected by previous qualitative research. Ontology of CFS is a matter of dispute, with models ranging from the biological to the psychological competing to explain symptomatology in this illness. A qualitative study has the potential to add some clarity to the debate by making the patients' lived experience of the condition, and their own understanding of it, the focus of research. What this study adds? Coping and attempts at managing sleep problems in CFS adds to the 'illness burden' experienced by patients. Disturbed sleep is universally seen by patients with CFS as impacting on other daytime symptoms. Broken sleep may contribute to a biopsychosocial cycle that serves to maintain this illness.
Goulart R(1), Pessoa C(2), Lombardi I Junior(3).	(1)Post-Graduate Interdisciplinary Program in Health Sciences, Universidade Federal de São Paulo, Santos, SP, Brazil. Electronic address: rubens_goulart@yahoo.com. (2)Rehabilitation and Physiotherapy Service, Prefeitura Municipal de Santos, Santos, SP, Brazil. (3)The Human Movement Sciences Department, Universidade Federal de São Paulo, Santos, SP, Brazil.	Psychological aspects of juvenile fibromyalgia syndrome: a literature review. [Article in English, Portuguese]	173. Rev Bras Reumatol Engl Ed. 2016 Jan-Feb;56(1):69-74.	Juvenile fibromyalgia syndrome (JFMS) is a non-inflammatory chronic pain condition that occurs mainly in girls aged 9-15 years. JFMS is characterized by constant widespread pain in different parts of the body, poor sleep quality, daytime sleepiness and an altered mood. Concomitant psychological and organic factors result in a diminished capacity to cope with pain. The quality of life of individuals with chronic pain and their caregivers is severely restricted and the occurrence of symptoms of anxiety and depression is common in this population. The aim of the present study was to perform a systematic review of the literature on psychosocial factors related to JFMS. The findings reveal differences in opinion between patients and family members regarding the effect of the condition, as mothers tend to classify JFMS as more severe than the patients themselves. Individuals with JFMS seem to share the same personality traits and there seems to be a type of family environment that is favorable to the occurrence of this condition. Psychological and functional aspects should be treated with methods that can help patients and family members alter their coping strategies regarding day-to-day problems, attenuate the dysfunctional consequences of pain and fatigue and diminish the risk of catastrophizing that individuals submitted to constant pain develop in relation to their surrounding environment.

Grape HE(1), Solbrække KN(1), Kirkevold M(1), Mengshoel AM(1).	(1)a Faculty of Medicine , Institute of Health and Society, University of Oslo , Blindern , Oslo , Norway.	Tiredness and fatigue during processes of illness and recovery: A qualitative study of women recovered from fibromyalgia syndrome.	27. Physiother Theory Pract. 2017 Jan;33(1):31-40.	Fibromyalgia syndrome (FMS), a chronic musculoskeletal pain condition, is often accompanied by fatigue. In this study, inspired by narrative approaches to health and illness, we explore how women who have regained their health after FMS describe tiredness along a storyline from before they fell ill, through their illness, recovery process, and present-day health. The data derive from qualitative interviews with eight Norwegian women who previously suffered from FMS but who no longer had the condition at the time of interview. We undertook a narrative analysis to understand the complexity of the stories about tiredness and fatigue and on this basis identified a storyline based on four sub-narratives: 1) Alarming but ignored tiredness (before illness); 2) paralyzing fatigue (during illness); 3) making sense of fatigue (recovery process); and 4) integrating tiredness into life (today). The findings highlight participants' different understandings and meanings of tiredness and fatigue and the ways in which these link past, present, and future. Significantly, a clear distinction between tiredness and fatigue was not always found. Overall, the storyline that emerges from the narratives is about balancing tiredness/fatigue with everyday life, and how this unfolds in different ways across the span of FMS, from falling ill to recovering and regaining health.
Grosman-Rimon L(1,)(2,)(3), Clarke H(4,)(3), Mills PB(5,)(6), Chan AK(5,)(6), Rathbone AT(7), Kumbhare D(1,)(2,)(3).	(1)Canada. (2)University Health NetworkCanada. (3)University of TorontoCanada. (4)Toronto General HospitalCanada. (5)University of British ColumbiaCanada. (6)GF Strong Rehabilitation CentreCanada. (7)Western UniversityCanada.	Clinicians' perspective of the current diagnostic criteria for myofascial pain syndrome.	33. J Back Musculoskelet Rehabil. 2016 Nov 11.	INTRODUCTION: Myofascial pain syndrome (MPS) is one of the most common chronic musculoskeletal pain disorders. However, MPS is often under-diagnosed. The purpose of this study was to characterize practicing clinicians' perspectives of the current diagnostic criteria for MPS. METHODS: A cross-sectional study design was used with a self-administered questionnaire. The questionnaire evaluated clinicians' perspective of the current diagnostic criteria for MPS. The sample population (n= 119) consisted of 40% family physicians, 31% physical medicine (PM) and rehabilitation specialists, 11% rheumatologists, 10% emergency room (ER) physicians, and 8% anesthesiologists specializing in chronic pain. RESULTS: Our findings demonstrated that participating clinicians agree that ''point tenderness'' and ''pain reproduction'' are criteria for MPS. In contrast, the clinicians do not consider ''autonomic symptoms'' as an important criterion for MPS. The anesthesiologists view ''restricted range of motion'' as a criterion for MPS more than the other groups, and they tend to consider ''referred pain'' and ''pain reproduction'' as criteria. Physical medicine and rehabilitation specialists and anesthesiologists tend to view ''local twitch response'' more as a criterion for MPS compared with the other groups. Most groups of clinicians consider ''weakness without atrophy'' as an important MPS criterion except for family physicians. It is important to note that ''poor sleep'', ''daytime fatigue'' and ''cognitive symptoms'', which are not considered as MPS symptoms, are often mistaken for MPS among practicing clinicians. CONCLUSION: Our findings suggest that the diagnostic criteria are not well known, highlighting the need for an expert consensus to determine the importance of each criterion for MPS diagnosis.
Grue J(1).	(1)University of Oslo,	ILLNESS IS WORK:	291. Health (London).	The concept of careers has an extensive history in the sociology of health and illness.

	Norway jangrue@gmail.com.	Revisiting the concept of illness careers and recognizing the identity work of patients with ME/CFS.	2016 Jul;20(4):401-12.	Among other things, the notion of a career has been used to describe the changing identities of patients diagnosed with mental illness, to identify distinct stages in the progression of various illnesses, and to recognize the cooperative efforts of hospitalized patients. However, the career concept may be reanalyzed as part of an analytical metaphor that makes salient both the agency of people with illnesses and the social structures in which they are enmeshed. This metaphor, ILLNESS IS WORK, can valorize and aid understanding of the identity work and actions of patients with chronic illnesses, particularly illnesses with a low degree of social recognition and medical prestige such as myalgic encephalopathy and chronic fatigue syndrome.
Guillamo E(1), Barbany JR, Blazquez A, Delicado MC, Ventura JL, Javierre C.	(1)Department of Physiological Sciences II, Exercise Physiology Unit, School of Medicine, University of Barcelona, Barcelona, Spain - eguillamo@ub.edu.	Physical effects of a reconditioning program me in a group of chronic fatigue syndrome patients.	167. J Sports Med Phys Fitness. 2016 May;56(5):579-86.	BACKGROUND: Physical exercise can be part of treatment in patients with chronic fatigue syndrome (CFS), where the aim would be to improve strength and endurance through increasing physical exercise (intensity and time) without aggravating symptomatology. The present study examines the effectiveness of a reconditioning programme (focusing on strength, endurance, balance and propioception) for achieving maximum functional capacity according to the clinical status of CFS patients. METHODS: Sixty-eight patients with CFS were randomly assigned to two groups: a control group (CG) comprising 22 patients and an active group (AG) of 46 patients, the latter being invited to take part in a functional reconditioning programme based on 12 weeks of laboratory training followed by a further 12-week home training period. Functional assessments were as follows: before (I) and after (II) the laboratory training and after (III) the home training. RESULTS: In the AG, 22 patients (67%) completed the intervention (laboratory) stage and 20 finished the whole protocol (61%). Patients in the AG showed improved static and dynamic balance, as well as significantly greater maximum strength ($F=7.059$, $P<0.05$). Differences in resistance strength were also observed, with the AG showing a 19.9% improvement between functional assessments I and II ($P=0.04$). We do not found changes in the CG. CONCLUSIONS: A physical exercise programme of this kind might offer CFS patients the opportunity to improve their strength, balance and quality of life, there being only a very small risk of relapse and none of the adverse effects of other treatments.
Gunn SR(1), Gunn GG(1), Mueller FW(2).	(1)Department of Genomic Pathology, Targeted Genomics, San Antonio, TX, USA. (2)Family Practice, Huebner Family Medicine, San Antonio, TX, USA.	Reversal of Refractory Ulcerative Colitis and Severe Chronic Fatigue Syndrome Symptoms Arising from Immune Disturbance in an HLA-DR/DQ Genetically Susceptible Individual with Multiple Biotoxin Exposures.	198. Am J Case Rep. 2016 May 11;17:320-5.	BACKGROUND: Patients with multisymptom chronic conditions, such as refractory ulcerative colitis (RUC) and chronic fatigue syndrome (CFS), present diagnostic and management challenges for clinicians, as well as the opportunity to recognize and treat emerging disease entities. In the current case we report reversal of co-existing RUC and CFS symptoms arising from biotoxin exposures in a genetically susceptible individual. CASE REPORT: A 25-year-old previously healthy male with new-onset refractory ulcerative colitis (RUC) and chronic fatigue syndrome (CFS) tested negative for autoimmune disease biomarkers. However, urine mycotoxin panel testing was positive for trichothecene group and air filter testing from the patient's water-damaged rental house identified the toxic mold Stachybotrys chartarum. HLA-DR/DQ testing revealed a multisusceptible haplotype for development of chronic inflammation, and serum

				chronic inflammatory response syndrome (CIRS) biomarker testing was positive for highly elevated TGF-beta and a clinically undetectable level of vasoactive intestinal peptide (VIP). Following elimination of biotoxin exposures, VIP replacement therapy, dental extractions, and implementation of a mind body intervention-relaxation response (MBI-RR) program, the patient's symptoms resolved. He is off medications, back to work, and resuming normal exercise. CONCLUSIONS: This constellation of RUC and CFS symptoms in an HLA-DR/DQ genetically susceptible individual with biotoxin exposures is consistent with the recently described CIRS disease pathophysiology. Chronic immune disturbance (turbatio immuno) can be identified with clinically available CIRS biomarkers and may represent a treatable underlying disease etiology in a subset of genetically susceptible patients with RUC, CFS, and other immune disorders.
Hackett KL(1,)(2), Lambson RL(3), Strassheim V(1), Gotts Z(4), Deary V(1,)(5), Newton JL(6,)(7).	(1)CRESTA Fatigue Clinic, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. (2)Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK. (3)Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK. (4)Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK. (5)Department of Psychology, Northumbria University, Newcastle upon Tyne, UK. (6)CRESTA Fatigue Clinic, Newcastle upon Tyne Hospitals NHS Foundation Trust,	A concept mapping study evaluating the UK's first NHS generic fatigue clinic.	349. Health Expect. 2016 Oct;19(5):1138-49.	IMPORTANCE: Fatigue is a significant and debilitating symptom affecting 25% of the population. It occurs in those with a range of chronic diseases, can be idiopathic and in 0.2-0.4% of the UK population occurs in combination with other symptoms that together constitute chronic fatigue syndrome (CFS). Until recently, NHS clinical services only focussed upon CFS and excluded the majority of fatigued patients who did not meet the CFS diagnostic criteria. The CRESTA Fatigue interdisciplinary clinic was established in 2013 in response to this unmet need. OBJECTIVE: To identify the service needs of the heterogeneous group of patients accessing the CRESTA Fatigue Clinic, to prioritize these needs, to determine whether each is being met and to plan targeted service enhancements. DESIGN: Using a group concept mapping approach, we objectively identified the shared understanding of service users accessing this novel clinic. SETTING: NHS Clinics for Research & Service in Themed Assessment (CRESTA) Fatigue Clinic, Newcastle Upon Tyne, UK. PARTICIPANTS: Patients (n = 30) and referrers (n = 10) to the CRESTA Fatigue Clinic contributed towards a statement generation exercise to identify ways the clinic could support service users to improve their quality of life. Patients (n = 46) participated in the sorting and rating task where resulting statements were sorted into groups similar in meaning and rated for 'importance' and 'current success'. MAIN OUTCOME AND MEASURE: We mapped the needs of patients attending the CRESTA Fatigue Clinic and identified which high-priority needs were being successfully met and which were not. RESULTS: Multidimensional scaling and hierarchical cluster analysis depicted the following eight themed clusters from the data which related to various service-user requirements: 'clinic ethos', 'communication', 'support to self-manage', 'peer support', 'allied health services', 'telemedicine', 'written information' and 'service operation'. Service improvement targets were identified within value bivariate plots of the statements. CONCLUSION AND RELEVANCE: Service development concepts were grouped into thematic clusters and prioritized for both importance and current success. The resulting concept maps depict where the CRESTA Fatigue Clinic successfully addresses issues which matter to patients and highlights areas for service enhancement. Unmet needs of patients have been identified in a

	Newcastle upon Tyne, UK. julia.newton@newcastle.ac.uk. (7)Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK. julia.newton@newcastle.ac.uk.			rigorous service evaluation, and these are currently being addressed in collaboration with a service-user group.
Hall KT(1,)(2), Kossowsky J(2,)(3,)(4), Oberlander TF(5), Kaptchuk TJ(2,)(6,)(7), Saul JP(8), Wyller VB(9), Fagermoen E(10), Sulheim D(11), Gjerstad J(12), Winger A(13), Mukamal KJ(2,)(6).	(1)Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA. (2)Harvard Medical School, Boston, MA, USA. (3)Department of Anesthesiology Perioperative and Pain Medicine, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA. (4)Department of Clinical Psychology and Psychotherapy, University of Basel, Basel, Switzerland. (5)Child and Family Research Institute, Department of Pediatrics, and School of Population and Public Health, University of British Columbia, Vancouver, British Columbia,	Genetic variation in catechol-O-methyltransferase modifies effects of clonidine treatment in chronic fatigue syndrome.	130. Pharmacogenomics J. 2016 Oct;16(5):454-60.	Clonidine, an α2-adrenergic receptor agonist, decreases circulating norepinephrine and epinephrine, attenuating sympathetic activity. Although catechol-O-methyltransferase (COMT) metabolizes catecholamines, main effectors of sympathetic function, COMT genetic variation effects on clonidine treatment are unknown. Chronic fatigue syndrome (CFS) is hypothesized to result in part from dysregulated sympathetic function. A candidate gene analysis of COMT rs4680 effects on clinical outcomes in the Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial (NorCAPITAL), a randomized double-blinded clonidine versus placebo trial, was conducted (N=104). Patients homozygous for rs4680 high-activity allele randomized to clonidine took 2500 fewer steps compared with placebo (Pinteraction=0.04). There were no differences between clonidine and placebo among patients with COMT low-activity alleles. Similar gene-drug interactions were observed for sleep (Pinteraction=0.003) and quality of life (Pinteraction=0.018). Detrimental effects of clonidine in the subset of CFS patients homozygous for COMT high-activity allele warrant investigation of potential clonidine-COMT interaction effects in other conditions.

	Canada. (6)Division of General Medicine and Primary Care, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA. (7)Program in Placebo Studies, Beth Israel Deaconess Medical Center, Boston, MA, USA. (8)Division of Cardiology, Department of Pediatrics, Medical University of South Carolina, Charleston, SC, USA. (9)Department of Paediatrics, Akershus University Hospital, Lørenskog, Norway. (10)Department of Anesthesiology and Critical Care, Oslo University Hospital, Oslo, Norway. (11)Department of Pediatrics, Lillehammer County Hospital, Brumunddal, Norway. (12)National Institute of Occupational Health, Department, Oslo, Norway. (13)Department of Nursing and Health			

	Promotion, Faculty of Health, Oslo University College of Applied Sciences, Oslo, Norway.			
Hansen AH(1,)(2), Lian OS(3).	(1)Faculty of Health Sciences, Department of Community Medicine, University of Tromsø - The Arctic University of Norway, 9037, Tromsø, Norway. anne.helen.hanzen@gmail.com. (2)University Hospital of North Norway, PO box 35, 9038, Tromsø, Norway. anne.helen.hanzen@gmail.com. (3)Faculty of Health Sciences, Department of Community Medicine, University of Tromsø - The Arctic University of Norway, 9037, Tromsø, Norway.	Experiences of general practitioner continuity among women with chronic fatigue syndrome/myalgic encephalomyelitis: a cross-sectional study.	37. BMC Health Serv Res. 2016 Nov 14;16(1):650.	BACKGROUND: Continuity of care is important for patients with chronic illness in need of coordinated healthcare services from multiple providers. Little is known about how patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) experience continuity of GP care. This study explores how women with CFS/ME experience GP care across the three dimensions of continuity: informational, management, and relational continuity. METHODS: This cross-sectional study uses questionnaire data collected from members of The Norwegian ME Association. Descriptive statistics and logistic regressions were used to estimate experiences of continuity, and associations with age, education, self-rated degree of CFS/ME, duration of the GP relation (GP duration), and number of GP visits for CFS/ME-related issues during the previous year (GP frequency). RESULTS: Almost two-thirds of participants reported positive experiences across all three dimensions of GP continuity of care; 64.4% for informational, 64.1% for management, and 77.2% for relational continuity. Lower educational attainment was associated with more negative experiences of informational continuity (primary school only compared to university educated: odds ratio [OR] 0.12, confidence interval [CI] 0.03-0.49, p = 0.003). Compared to participants aged 40-59 years, those aged 60+ years were significantly less likely to have experienced poor (negative) management continuity (OR 0.25, CI 0.09-0.76, p = 0.014). A GP relationship of three or more years was associated with positive experiences of relational continuity (OR 2.32, CI 1.09-4.95, p = 0.030). Compared to those with moderate CFS/ME, those who graded their CFS/ME as severe or very severe were significantly more likely to have negative experiences of relational continuity (OR 0.38, CI 0.14-0.99, p = 0.047). CONCLUSIONS: A large proportion of participants experienced all three aspects of continuity of GP care (especially the relational dimension) positively. Informational and management continuity scores were moderately lower. Our results suggest greater emphasis on information giving, feedback, and better coordination of care to be good strategies for practice improvement for this patient group.
Hansen AH(1), Lian OS(2).	(1)Faculty of Health Sciences, Department of Community Medicine, UiT The Arctic University of Norway and Norwegian Centre for	How do women with chronic fatigue syndrome/myalgic encephalomyelitis rate quality and coordination of healthcare services? A cross-sectional study.	231. BMJ Open. 2016 Apr 4;6(4):e010277.	OBJECTIVE: To test the association between self-rated health and self-rated degree of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), and CFS/ME patients' assessment of quality of primary care, specialist care and coordination of care. DESIGN: Cross-sectional study. SETTING: Self-reported questionnaire data from women members of The Norwegian ME Association obtained in 2013. PARTICIPANTS: 431 women with CFS/ME aged 16-73 years. MAIN OUTCOME MEASURE: The participants' assessment of quality in primary care, specialist care and in coordination of care

	Integrated Care and Telemedicine, University Hospital of North Norway, Tromsø, Norway. (2)Faculty of Health Sciences, Department of Community Medicine, UiT The Arctic University of Norway, Tromsø, Norway.			(good/very good or poor/very poor). Main explanatory variables: self-rated health and self-rated degree of CFS/ME. RESULTS: Quality of care was rated poor by 60.6% in primary care, by 47.7% in specialist care, and by 71.2% regarding coordination of care. Poorer self-rated health increased the probability of rating quality in primary care poor, particularly among women 40 years and over (OR 2.38, 95% CI 1.63 to 3.49), women with university education (OR 2.57, CI 1.68 to 3.94), and owing to less frequent general practitioner (GP) visits (OR 2.46, CI 1.60 to 3.78). Poorer self-rated health increased the probability of rating quality poor in specialist care (OR 1.38, CI 1.05 to 1.82), but not in coordination of care. A more severe CFS/ME was associated with a higher probability of rating quality in primary care poor (OR 0.61, CI 0.38 to 0.93). Frequent visitors and those with a long GP relationship were less likely to report primary care quality as poor. CONCLUSIONS: A large proportion of women with CFS/ME rated quality of care poor/very poor in primary care, specialist care and in coordination of care. The dissatisfaction was higher for primary care than for specialist care. Overall, poorer self-rated health and a more severe CFS/ME were associated with lower quality scores in primary and specialist care, but not in coordination of care. Healthcare services, as assessed by women with CFS/ME, do have a large potential for improvement.
Hanson MR(1), Gu Z(2), Keinan A(3), Ye K(3), Germain A(4), Billing-Ross P(2).	(1)Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, 14853, USA. mrh5@cornell.edu. (2)Division of Nutritional Sciences, Cornell University, Ithaca, NY, 14853, USA. (3)Department of Biological Statistics and Computational Biology, Cornell University, Ithaca, NY, 14853, USA. (4)Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY, 14853, USA.	Association of mitochondrial DNA variants with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) symptoms.	9. J Transl Med. 2016 Dec 20;14(1):342.	Earlier this year, we described an analysis of mitochondrial DNA (mtDNA) variants in myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) patients and healthy controls. We reported that there was no significant association of haplogroups or singe nucleotide polymorphisms (SNPs) with disease status. Nevertheless, a commentary about our paper appeared (Finsterer and Zarrouk-Mahjoub. J Transl Med14:182, 2016) that criticized the association of mtDNA haplogroups with ME/CFS, a conclusion that was absent from our paper. The aforementioned commentary also demanded experiments that were outside of the scope of our study, ones that we had suggested as follow-up studies. Because they failed to consult a published and cited report describing the cohorts we studied, the authors also cast aspersions on the method of selection of cases for inclusion. We reiterate that we observed statistically significant association of mtDNA variants with particular symptoms and their severity, though we observed no association with disease status.
Hardcastle SL(1), Brenu EW(1),	(1)a National Centre for Neuroimmunology	Severity Scales for Use in Primary Health Care to	370. Health Care Women Int. 2016 Jun;37(6):671-	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a physical and cognitive disabling illness, characterized by severe fatigue and a range of physiological

Johnston S(1), Staines D(2), Marshall-Gradisnik S(1).	and Emerging Diseases, Griffith Health Centre , School of Medical Science, Griffith University , Gold Coast , Queensland , Australia. (2)b National Centre for Neuroimmunology and Emerging Diseases, Griffith Health Centre, School of Medical Science , Griffith University; and Queensland Health, Gold Coast Public Health Unit , Gold Coast , Queensland , Australia.	Assess Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.	86.	symptoms, that primarily affects women. The immense variation in clinical presentation suggests differences in severity based on symptomology and physical and cognitive functional capacities. In this article, we examine a number of severity scales used in assessing severity of patients with CFS/ME and the clinical aspects of CFS/ME severity subgroups. The use of severity scales may be important in CFS/ME because it permits the establishment of subgroups that may improve accuracy in both clinical and research settings.
Harris K(1), Band RJ(2), Cooper H(3), Macintyre VG(3), Mejia A(4), Wearden AJ(3).	(1)School of Psychological Sciences and Manchester Centre for Health Psychology, University of Manchester, UK. kamelia.harris@manchester.ac.uk. (2)Centre for Applications of Health Psychology, University of Southampton, UK. (3)School of Psychological Sciences and Manchester Centre for Health Psychology, University of Manchester, UK. (4)Institute for Scientific Research	Distress in significant others of patients with chronic fatigue syndrome: A systematic review of the literature.	176. Br J Health Psychol. 2016 Nov;21(4):881-893.	PURPOSE: The objective of this study was to systematically review existing empirical research assessing levels and correlates of distress in significant others of patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). METHODS: Systematic searches in CINAHL, Web of Science and PsycINFO were conducted in August 2014. The search was repeated in January 2015 to check for newly published articles. Studies published in English with quantitative, qualitative, or mixed designs exploring distress, poor subjective health, poor mental health, reduced quality of life and well-being, and symptoms of depression and anxiety in significant others (>18 years) of children and adults with CFS/ME were included. Quality appraisal of included studies was carried out. Quantitative and qualitative studies were summarized separately. RESULTS: Six articles met eligibility criteria. Two quantitative studies with significant others of adult patients, and one quantitative and two mixed-methods studies with significant others of child patients showed moderate to high levels of distress. One qualitative study (adult patients) found minimal evidence of distress and that acceptance of CFS/ME was related to better adjustment. In the quantitative and mixed-methods studies, significant others who attributed some level of responsibility for symptoms to the patient, or who were female, or whose partners had poorer mental health, had higher levels of distress. CONCLUSIONS: The small number of studies to date, the contrary evidence from a qualitative study, and the limited data available on levels of distress in significant others of patients with CFS/ME mean that our conclusion that distress levels

	and High Technology Services, City of Knowledge, Clayton, Panama.			are elevated is provisional. We recommend that future qualitative studies focus on this particular topic. Further longitudinal studies exploring correlates of distress within the context of a predictive theoretical model would be helpful. Statement of contribution What is already known on this subject? Chronic fatigue syndrome (CFS/ME) entails considerable economic, social, and personal costs. Uncertainties exist around diagnosis and management. This may lead to particular difficulties for significant others trying to support patients. What does this study add? Few studies have examined distress and its correlates in significant others of people with CFS/ME. Significant others report elevated levels of distress on quantitative measures.
Harris S(1), Gilbert M(2), Beasant L(2), Linney C(3), Broughton J(2), Crawley E(2).	(1)1 South Wales Doctoral Programme in Clinical Psychology, Cardiff University, UK. (2)2 Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, UK. (3)3 Department of Psychology, Durham University, UK.	A qualitative investigation of eating difficulties in adolescents with chronic fatigue syndrome/myalgic encephalomyelitis.	187. Clin Child Psychol Psychiatry. 2017 Jan;22(1):128-139.	BACKGROUND: An estimated 10% of children and adolescents with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) experience eating difficulties; however, little is known about why these difficulties develop, what the impact is or how to manage them. METHODS: Semi-structured interviews were conducted with adolescents (aged 12-17 years) attending a specialist service who have a primary diagnosis of CFS/ME and experience nausea, abdominal pain and/or eating difficulties. A total of 11 adolescents were interviewed (eight female, mean age: 15 years). Transcripts were analysed thematically using techniques of constant comparison which commenced soon after data collection and informed further interview protocols. RESULTS: Adolescents perceived their eating difficulties were caused by abdominal symptoms, being too fatigued to eat and changes to their senses of taste and smell. Some of the adolescents recognised how their eating difficulties were exacerbated and maintained by psychological factors of low mood and anxiety. The adolescents eating difficulties had a negative impact on their weight, fatigue, socialising and family life. They perceived helpful interventions to include modifying their diets, families adjusting and also medical interventions (e.g. medication). Adolescents identified that early education and support about diet and eating habits would have been helpful. CONCLUSIONS: If adolescents diagnosed with CFS/ME develop eating difficulties, this has a significant impact on their quality of life, illness and on their families. Not eating increases fatigue, low mood and anxiety which further exacerbates the eating difficulties. Clinicians should screen for eating difficulties in those with symptoms of nausea and abdominal pain, warn adolescents and their families of the risk of developing eating difficulties and provide interventions and support as early as possible.
Harvey JM(1), Broderick G(2,)(3,)(4), Bowie A(5), Barnes ZM(1), Katz BZ(6), O'Gorman MR(7),	(1)Department of Medicine, University of Miami, Miami, FL, USA. (2)Department of Medicine, University of Miami, Miami, FL, USA.	Tracking post-infectious fatigue in clinic using routine Lab tests.	211. BMC Pediatr. 2016 Apr 26;16:54.	BACKGROUND: While biomarkers for chronic fatigue syndrome (CFS) are beginning to emerge they typically require a highly specialized clinical laboratory. We hypothesized that subsets of commonly measured laboratory markers used in combination could support the diagnosis of post-infectious CFS (PI-CFS) in adolescents following infectious mononucleosis (IM) and help determine who might develop persistence of symptoms. METHODS: Routine clinical laboratory markers were collected prospectively in 301 mono-spot positive adolescents, 4 % of whom developed CFS (n = 13). At 6, 12, and

Vernon SD(8), Fletcher MA(9), Klimas NG(9), Taylor R(10).	gbroderick@nova.edu. (3)Institute for Neuro Immune Medicine, Nova Southeastern University, University Park Plaza, 3440 South University, Fort Lauderdale, 33328, FL, USA. gbroderick@nova.edu. (4)University of Alberta, Edmonton, AB, Canada. gbroderick@nova.edu. (5)University of Alberta, Edmonton, AB, Canada. (6)Ann & Robert H Lurie Children's Hospital of Chicago, Chicago, IL, USA. (7)Children's Hospital Los Angeles, Los Angeles, CA, USA. (8)Solve ME/CFS Initiative, Charlotte, NC, USA. (9)Institute for Neuro Immune Medicine, Nova Southeastern University, University Park Plaza, 3440 South University, Fort Lauderdale, 33328, FL, USA. (10)University of Illinois at Chicago, Chicago, IL, USA.			24 months post-diagnosis with IM, 59 standard tests were performed including metabolic profiling, liver enzyme panel, hormone profiles, complete blood count (CBC), differential white blood count (WBC), salivary cortisol, and urinalysis. Classification models separating PI-CFS from controls were constructed at each time point using stepwise subset selection. RESULTS: Lower ACTH levels at 6 months post-IM diagnosis were highly predictive of CFS (AUC p = 0.02). ACTH levels in CFS overlapped with healthy controls at 12 months, but again showed a trend towards a deficiency at 24 months. Conversely, estradiol levels depart significantly from normal at 12 months only to recover at 24 months (AUC p = 0.02). Finally, relative neutrophil count showed a significant departure from normal at 24 months in CFS (AUC p = 0.01). Expression of these markers evolved differently over time between groups. CONCLUSIONS: Preliminary results suggest that serial assessment of stress and sex hormones as well as the relative proportion of innate immune cells measured using standard clinical laboratory tests may support the diagnosis of PI-CFS in adolescents with IM.
Hawkes N(1).		Online CBT is trialled for children with chronic fatigue syndrome.	57. BMJ. 2016 Oct 31;355:i5860.	
Hilpüsch F.		[Prednisolone against	245. Tidsskr Nor	

		myalgic encephalomyelitis/chronic fatigue syndrome?]. [Article in Norwegian]	Laegeforen. 2016 Mar 15;136(5):397.	
Hod K(1), Ringel-Kulka T, Martin CF, Maharshak N, Ringel Y.	(1)Departments of *Epidemiology and Preventive Medicine, School of Public Health §Gastroenterology and Liver Diseases, Tel Aviv Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel Departments of †Medicine, Division of Gastroenterology and Hepatology ‡Maternal and Child Health, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC.	High-sensitive C-Reactive Protein as a Marker for Inflammation in Irritable Bowel Syndrome	363. J Clin Gastroenterol. 2016 Mar;50(3):227-32. .	BACKGROUND: Recent studies demonstrated low-grade inflammation in patients with irritable bowel syndrome (IBS). However, these studies have been relatively small and do not enable examination of this factor in different subtypes of IBS and the possibility of confounding effects of comorbidities that may be associated with inflammatory responses. GOALS: To investigate the association between high-sensitive C-reactive protein (hs-CRP) and the diagnosis of IBS, IBS subtypes, symptoms' severity, and IBS-associated comorbidities. STUDY: This cross-sectional study uses data from a large matched case-control study of IBS subjects and healthy controls (HC). hs-CRP levels were measured in all subjects. IBS diagnosis was determined by Rome III criteria, negative screening blood tests, and normal colonoscopy. Subjects were evaluated for IBS severity and associated pain and psychological comorbidities. RESULTS: A total of 242 IBS patients and 244 HC were studied. Median hs-CRP levels in the IBS group were significantly higher than in HC (1.80; interquartile range, 0.7 to 4.04 mg/L vs. 1.20, interquartile range, 0.5 to 2.97 mg/L respectively, P<0.006). Levels were highest in IBS-D patients with greater disease severity. Hs-CRP levels mildly correlated with symptoms severity (r=0.169, P=0.009); this correlation was stronger for the IBS-D patients (r=0.27, P=0.006). IBS was a significant independent predictor (P=0.025) for higher hs-CRP levels, whereas other pain and psychological comorbidities were not. CONCLUSIONS: Given these observations of cross-sectional differences in hs-CRP between IBS subtypes and severity, independent of pain and comorbidities, more research is needed to explore a possible role of low-grade inflammation in the pathogenesis and/or clinical presentation of IBS.
Holmøy T.		Re: Kronisk utmattelsessyndrom/myalgisk encefalopati--sykdomsmekanismer, diagnostikk og behandling. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2016 Feb 9;136(3):204-5. Comment on Tidsskr Nor Laegeforen. 2015 Dec 15;135(23-24):2172-5.	
Hornig M(1,)(2), Gottschalk G(3), Peterson DL(3), Knox KK(4,)(5), Schultz AF(1), Eddy ML(1), Che X(1), Lipkin WI(1,)(2,)(6).	(1)Center for Infection and Immunity, Columbia University Mailman School of Public Health, New York, NY, USA. (2)Department of Epidemiology,	Cytokine network analysis of cerebrospinal fluid in myalgic encephalomyelitis/chronic fatigue syndrome.	365. Mol Psychiatry. 2016 Feb;21(2):261-9.	Myalgic encephalomyelitis/chronic fatigue syndrome is an unexplained debilitating disorder that is frequently associated with cognitive and motor dysfunction. We analyzed cerebrospinal fluid from 32 cases, 40 subjects with multiple sclerosis and 19 normal subjects frequency-matched for age and sex using a 51-plex cytokine assay. Group-specific differences were found for the majority of analytes with an increase in cases of CCL11 (eotaxin), a chemokine involved in eosinophil recruitment. Network analysis revealed an inverse relationship between interleukin 1 receptor antagonist and colony-stimulating factor 1, colony-stimulating factor 2 and interleukin 17F, without

	Columbia University Mailman School of Public Health, New York, NY, USA. (3)Sierra Internal Medicine at Incline Village, Incline Village, NV, USA. (4)Coppe Healthcare Solutions, Waukesha, WI, USA. (5)Simmaron Research, Incline Village, NV, USA. (6)Departments of Pathology and Neurology, College of Physicians and Surgeons, Columbia University, New York, NY, USA.			effects on interleukin 1α or interleukin 1β, suggesting a disturbance in interleukin 1 signaling. Our results indicate a markedly disturbed immune signature in the cerebrospinal fluid of cases that is consistent with immune activation in the central nervous system, and a shift toward an allergic or T helper type-2 pattern associated with autoimmunity.
Horwood S(1), Anglim J(1), Tooley G(1).	(1)a School of Psychology , Deakin University , Victoria , Australia.	Statistically modelling the relationships between Type D personality and social support, health behaviors and symptom severity in chronic illness groups.	240. Psychol Health. 2016 Sep;31(9):1047-63.	OBJECTIVE: The study aimed to develop a predictive model of how Type D personality influences health behaviours, social support and symptom severity and assess its generalisability to a range of chronic illnesses. DESIGN: Participants were classified as either healthy (n = 182) or having a chronic illness (n = 207). Participants completed an online survey measuring Type D and a range of health-related variables. Chronic illness participants were classified as having either a functional somatic syndrome (i.e. chronic fatigue syndrome or fibromyalgia), where the underlying pathological processes were unclear, or illnesses such as type 2 diabetes, osteoarthritis or rheumatoid arthritis, where the causes are well understood. MAIN OUTCOME MEASURES: Outcome measures were health behaviours, social support and both physical and psychological symptoms. RESULTS: The rate of Type D was higher in chronic illness participants (53%) than in healthy controls (39%). Negative affectivity (NA) and social inhibition (SI) both correlated with outcome measures, although NA was generally the stronger predictor. Using NA and SI as independent subscales led to superior prediction of health outcomes than using categorical or continuous representations. CONCLUSION: Findings suggest that the relationship between Type D and health outcomes may generalise across different chronic illnesses.
Howard Tripp N(1), Tarn J(2), Natasari A(2),	(1)Musculoskeletal Research Group, Institute of Cellular	Fatigue in primary Sjögren's syndrome is associated with lower	124. RMD Open. 2016 Jul 19;2(2):e000282.	OBJECTIVES: This article reports relationships between serum cytokine levels and patient-reported levels of fatigue, in the chronic immunological condition primary Sjögren's syndrome (pSS). METHODS: Blood levels of 24 cytokines were measured in

Gillespie C(3), Mitchell S(4), Hackett KL(2), Bowman SJ(5), Price E(6), Pease CT(7), Emery P(7), Lanyon P(8), Hunter J(9), Gupta M(9), Bombardieri M(10), Sutcliffe N(10), Pitzalis C(10), McLaren J(11), Cooper A(12), Regan M(13), Giles I(14), Isenberg DA(14), Saravanan V(15), Coady D(16), Dasgupta B(17), McHugh N(18), Young-Min S(19), Moots R(20), Gendi N(21), Akil M(22), Griffiths B(4), Lendrem DW(1), Ng WF(1).	Medicine, Newcastle University, Newcastle-upon-Tyne, UK; Newcastle-upon-Tyne NHS Foundation Trust, Newcastle-upon-Tyne, UK. (2)Musculoskeletal Research Group , Institute of Cellular Medicine, Newcastle University , Newcastle-upon-Tyne , UK. (3)Department of Mathematics and Statistics , Newcastle University , Newcastle-upon-Tyne , UK. (4)Newcastle-upon-Tyne NHS Foundation Trust , Newcastle-upon-Tyne , UK. (5)University Hospital Birmingham , Birmingham , UK. (6)Great Western Hospitals NHS Foundation Trust , Swindon , UK. (7)Section of Musculoskeletal Disease, NIHR Leeds Musculoskeletal Biomedical Research Unit , Leeds Institute of Molecular Medicine, University of Leeds, Leeds Teaching Hospitals Trust , Leeds , UK.	levels of proinflammatory cytokines.		159 patients with pSS from the United Kingdom Primary Sjögren's Syndrome Registry and 28 healthy non-fatigued controls. Differences between cytokines in cases and controls were evaluated using Wilcoxon test. Patient-reported scores for fatigue were evaluated, classified according to severity and compared with cytokine levels using analysis of variance. Logistic regression was used to determine the most important predictors of fatigue levels. RESULTS: 14 cytokines were significantly higher in patients with pSS (n=159) compared to non-fatigued healthy controls (n=28). While serum levels were elevated in patients with pSS compared to healthy controls, unexpectedly, the levels of 4 proinflammatory cytokines-interferon-γ-induced protein-10 (IP-10) (p=0.019), tumour necrosis factor-α (p=0.046), lymphotoxin-α (p=0.034) and interferon-γ (IFN-γ) (p=0.022)-were inversely related to patient-reported levels of fatigue. A regression model predicting fatigue levels in pSS based on cytokine levels, disease-specific and clinical parameters, as well as anxiety, pain and depression, revealed IP-10, IFN-γ (both inversely), pain and depression (both positively) as the most important predictors of fatigue. This model correctly predicts fatigue levels with reasonable (67%) accuracy. CONCLUSIONS: Cytokines, pain and depression appear to be the most powerful predictors of fatigue in pSS. Our data challenge the notion that proinflammatory cytokines directly mediate fatigue in chronic immunological conditions. Instead, we hypothesise that mechanisms regulating inflammatory responses may be important.

	(8)Nottingham University Hospitals NHS Trust , Nottingham , UK. (9)Gartnavel General Hospital , Glasgow , UK. (10)Barts Health NHS Trust & Barts and the London School of Medicine & Dentistry , London , UK. (11)NHS Fife, Whyteman's Brae Hospital , Kirkaldy , UK. (12)Royal Hampshire County Hospital , Winchester , UK. (13)Royal Derby Hospital , Derby , UK. (14)University College London Hospitals NHS Foundation Trust , London , UK. (15)Queen Elizabeth Hospital , Gateshead , UK. (16)Sunderland Royal Hospital , Sunderland , UK. (17)Southend University Hospital , Westcliff-on-sea , UK. (18)Royal National Hospital for Rheumatic Diseases , Bath , UK. (19)Portsmouth Hospitals NHS Trust , Portsmouth , UK. (20)Aintree University Hospitals , Liverpool , UK. (21)Basildon			

	Hospital , Basildon , UK. (22)Royal Hallamshire Hospital , Sheffield , UK.			
Huang L(1), Kutch JJ, Ellingson BM, Martucci KT, Harris RE, Clauw DJ, Mackey S, Mayer EA, Schaeffer AJ, Apkarian AV, Farmer MA.	(1)aDepartment of Physiology, Feinberg School of Medicine, Northwestern University, Chicago, IL, USAbDivision of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA, USAcOppenheimer Center for Neurobiology of Stress and Pain, David Geffen School of Medicine, University of California-Los Angeles, Los Angeles, CA, USAdDepartments of Anesthesiology, Perioperative and Pain Medicine, Division of Pain Medicine, Stanford University Medical Center, Stanford, CA, USAeDepartment of Anesthesiology, and the Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI, USAfDepartment of Urology, Northwestern	Brain white matter changes associated with urological chronic pelvic pain syndrome: multisite neuroimaging from a MAPP case-control study.	38. Pain. 2016 Dec;157(12):2782-2791.	Clinical phenotyping of urological chronic pelvic pain syndromes (UCPPSs) in men and women have focused on end organ abnormalities to identify putative clinical subtypes. Initial evidence of abnormal brain function and structure in male pelvic pain has necessitated large-scale, multisite investigations into potential UCPPS brain biomarkers. We present the first evidence of regional white matter (axonal) abnormalities in men and women with UCPPS, compared with positive (irritable bowel syndrome, IBS) and healthy controls. Epidemiological and neuroimaging data were collected from participants with UCPPS (n = 52), IBS (n = 39), and healthy sex- and age-matched controls (n = 61). White matter microstructure, measured as fractional anisotropy (FA), was examined by diffusion tensor imaging. Group differences in regional FA positively correlated with pain severity, including segments of the right corticospinal tract and right anterior thalamic radiation. Increased corticospinal FA was specific and sensitive to UCPPS, positively correlated with pain severity, and reflected sensory (not affective) features of pain. Reduced anterior thalamic radiation FA distinguished patients with IBS from those with UCPPS and controls, suggesting greater microstructural divergence from normal tract organization. Findings confirm that regional white matter abnormalities characterize UCPPS and can distinguish between visceral diagnoses, suggesting that regional axonal microstructure is either altered with ongoing pain or predisposes its development.

	University, Feinberg School of Medicine, Chicago, IL, USAgDepartments of Surgery and Anesthesia, Northwestern University, Feinberg School of Medicine, Chicago, IL, USA.			
Hughes A(1), Hirsch C(1), Chalder T(2), Moss-Morris R(3).	(1)Psychology Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK. (2)Department of Psychological Medicine, Weston Education Centre, King's College London, UK. (3)Psychology Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK. Rona.moss-morris@kcl.ac.uk.	Attentional and interpretive bias towards illness-related information in chronic fatigue syndrome: A systematic review	159. Br J Health Psychol. 2016 Nov;21(4):741-763. .	PURPOSE: Chronic fatigue syndrome (CFS) is characterized by severe and debilitating fatigue. Studies based on self-report measures suggest negative illness representations, related symptom interpretations, and heightened symptom focusing are maintaining factors of fatigue. This study reviews studies which have investigated these cognitive biases using experimental methods, to (1) review the evidence for information processing biases in CFS; (2) determine the nature of these biases, that is the stages cognitive biases occur and for what type of stimuli; and (3) provide directions for future methodologies in this area. METHODS: Studies were included that measured attention and interpretation bias towards negative and illness-related information in people with CFS and in a comparison group of healthy controls. PubMed, Ovid, CINAHL, PsycINFO, Web of Science, and EThOS were searched until December 2014. RESULTS: The evidence for cognitive biases was dependent on the methodology employed as well as the type and duration of the stimuli presented. Modified Stroop studies found weak evidence of an attentional bias in CFS populations, whereas visual-probe studies consistently found an attentional bias in CFS groups for health-threatening information presented for 500 ms or longer. Interpretative bias studies which required elaborative processing, as opposed to a spontaneous response, found an illness-related interpretive bias in the CFS group compared to controls. CONCLUSIONS: Some people with CFS have biases in the way they attend to and interpret somatic information. Such cognitive processing biases may maintain illness beliefs and symptoms in people with CFS. This review highlights methodological issues in experimental design and makes recommendations to aid future research to forge a consistent approach in cognitive processing research. Statement of contribution What is already known on this subject? Studies based on self-report measures suggest negative illness representations, related symptom interpretations, and heightened symptom focusing contribute to the maintenance of chronic fatigue. Experimental studies in other clinical populations, such as patients with anxiety, depression, and chronic pain, have identified illness-specific biases in how information is implicitly attended to and interpreted, which has a causal role in these conditions. What does this study add? This is the first review of implicit cognitive processes in chronic fatigue syndrome (CFS). Sustained attention and negative

				interpretations of somatic information may reinforce negative illness beliefs. Cognitive processes have a role to play in the cognitive behavioural model of CFS.
Hughes AM(1), Chalder T(2), Hirsch CR(1), Moss-Morris R(1).	(1)Psychology Department,King's College London,Institute of Psychiatry, Psychology and Neuroscience,London, UK. (2)Department of Psychological Medicine,King's College London,London,UK.	An attention and interpretation bias for illness-specific information in chronic fatigue syndrome.	28. Psychol Med. 2016 Nov 29:1-13.	BACKGROUND: Studies have shown that specific cognitions and behaviours play a role in maintaining chronic fatigue syndrome (CFS). However, little research has investigated illness-specific cognitive processing in CFS. This study investigated whether CFS participants had an attentional bias for CFS-related stimuli and a tendency to interpret ambiguous information in a somatic way. It also determined whether cognitive processing biases were associated with co-morbidity, attentional control or self-reported unhelpful cognitions and behaviours. METHOD: A total of 52 CFS and 51 healthy participants completed self-report measures of symptoms, disability, mood, cognitions and behaviours. Participants also completed three experimental tasks, two designed specifically to tap into CFS salient cognitions: (i) visual-probe task measuring attentional bias to illness (somatic symptoms and disability) v. neutral words; (ii) interpretive bias task measuring positive v. somatic interpretations of ambiguous information; and (iii) the Attention Network Test measuring general attentional control. RESULTS: Compared with controls, CFS participants showed a significant attentional bias for fatigue-related words and were significantly more likely to interpret ambiguous information in a somatic way, controlling for depression and anxiety. CFS participants had significantly poorer attentional control than healthy individuals. Attention and interpretation biases were associated with fear/avoidance beliefs. Somatic interpretations were also associated with all-or-nothing behaviour and catastrophizing. CONCLUSIONS: People with CFS have illness-specific biases which may play a part in maintaining symptoms by reinforcing unhelpful illness beliefs and behaviours. Enhancing adaptive processing, such as positive interpretation biases and more flexible attention allocation, may provide beneficial intervention targets.
Hughes AM(1), Gordon R(1), Chalder T(1), Hirsch CR(1), Moss-Morris R(2).	(1) Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK. (2) Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK. rona.moss-morris@kcl.ac.uk.	Maximizing potential impact of experimental research into cognitive processes in health psychology: A systematic approach to material development.	92. Br J Health Psychol. 2016 Nov;21(4):764-780.	BACKGROUND: There is an abundance of research into cognitive processing biases in clinical psychology including the potential for applying cognitive bias modification techniques to assess the causal role of biases in maintaining anxiety and depression. Within the health psychology field, there is burgeoning interest in applying these experimental methods to assess potential cognitive biases in relation to physical health conditions and health-related behaviours. Experimental research in these areas could inform theoretical development by enabling measurement of implicit cognitive processes that may underlie unhelpful illness beliefs and help drive health-related behaviours. However, to date, there has been no systematic approach to adapting existing experimental paradigms for use within physical health research. Many studies fail to report how materials were developed for the population of interest or have used untested materials developed ad hoc. The lack of protocol for developing stimuli specificity has contributed to large heterogeneity in methodologies and findings. PURPOSE: In this article, we emphasize the need for standardized methods for stimuli development and replication in experimental work, particularly as it extends beyond its

				original anxiety and depression scope to other physical conditions. METHOD: We briefly describe the paradigms commonly used to assess cognitive biases in attention and interpretation and then describe the steps involved in comprehensive/robust stimuli development for attention and interpretation paradigms using illustrative examples from two conditions: chronic fatigue syndrome and breast cancer. CONCLUSIONS: This article highlights the value of preforming rigorous stimuli development and provides tools to aid researchers engage in this process. We believe this work is worthwhile to establish a body of high-quality and replicable experimental research within the health psychology literature. Statement of contribution What is already known on this subject? Cognitive biases (e.g., tendencies to attend to negative information and/or interpret ambiguous information in negative ways) have a causal role in maintaining anxiety and depression. There is mixed evidence of cognitive biases in physical health conditions and chronic illness; one reason for this may be the heterogeneous stimuli used to assess attention and interpretation biases in these conditions. What does this study add? Steps for comprehensive/robust stimuli development for attention and interpretation paradigms are presented. Illustrative examples are provided from two conditions: chronic fatigue syndrome and breast cancer. We provide tools to help researchers develop condition-specific materials for experimental studies.
Husa P.		[Extrahepatic manifestations of HCV infection]. [Article in Czech]	76. Vnitr Lek. 2016 Fall;62(Suppl2):18-22.	Extrahepatic manifestations of hepatitis C virus infection (HCV) are very common. The most common of these is mixed cryoglobulinaemia. Anti-HCV antibodies and viral ribonucleic acid, HCV RNA, can be found in the cryoprecipitates, together with the rheumatoid factor. Cryoglobulins consist of a complex of immunoglobulins that in vitro precipitate upon the cooling bellow the human body temperature. Vasculitis is caused by the deposition of such immune complexes in the small blood vessels. A link with the HCV infection is considered to be established with membranoproliferative glomerulonephritis, leukocytoclastic vasculitis, lymphoproliferative disorders (in particular B cell lymphoma), Sjögren and sicca syndrome, lichen planus, porfyria cutanea tarda and diabetes mellitus. Very probable is the relationship of chronic HCV infection and thyroid disease, arthralgias, otherwise unexplained fatigue and autoimmune hepatitis.Key words: direct acting antivirals - extrahepatic manifestations - chronic hepatitis C - mixed cryoglobulinaemia.
Huth TK(1,)(2), Brenu EW(1,)(2), Ramos S(1,)(2), Nguyen T(1,)(2), Broadley S(3,)(4), Staines D(1,)(2), Marshall-Gradisnik S(1,)(2).	(1)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, Qld, Australia. (2)School of Medical	Pilot Study of Natural Killer Cells in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis and Multiple Sclerosis.	344. Scand J Immunol. 2016 Jan;83(1):44-51.	Patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and multiple sclerosis (MS) suffer from debilitating fatigue which is not alleviated by rest. In addition to the fatigue-related symptoms suffered by patients with CFS/ME and MS, dysfunction of the immune system and, in particular, reduced natural killer (NK) cell cytotoxic activity has also been reported in CFS/ME and MS. The purpose of this pilot study was to compare NK cellular mechanisms in patients with CFS/ME and MS to investigate potential dysfunctions in the NK cell activity pathway. Flow cytometry protocols assessed CD56(dim) CD16(+) and CD56(bright) CD16(+/-) NK cell expression of adhesion molecules, NK activating and inhibiting receptors, NK cell maturation and lytic

	Science, Griffith University, Southport, Qld, Australia. (3)School of Medicine, Griffith University, Southport, Qld, Australia. (4)Gold Coast University Hospital, Southport, Qld, Australia.			proteins. All participants in this study were female and included 14 patients with CFS/ME, nine patients with MS and 19 non-fatigued controls. The patient groups and the non-fatigued controls were not taking any immunosuppressive or immune-enhancing medications. In the MS cohort, KIR2DL5 was significantly increased on CD56(bright) CD16(+/-) NK cells and expression of CD94 was significantly increased on CD56(dim) CD16(+) NK cells in comparison with the controls. Co-expression of CD57 and perforin was significantly increased on CD56(dim) CD16(+) NK cells from patients with CFS/ME compared to the MS and non-fatigued control participants. The results from this pilot study suggest that NK cells from patients with CFS/ME and MS may have undergone increased differentiation in response to external stimuli which may affect different mechanisms in the NK cell cytotoxic activity pathway.
Huth TK(1,)(2), Staines D(3,)(4), Marshall-Gradisnik S(3,)(4).	(1)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, QLD, Australia. teilah.huth@griffithuni.edu.au. (2)School of Medical Science, Griffith University, Southport, QLD, Australia. teilah.huth@griffithuni.edu.au. (3)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, QLD, Australia. (4)School of Medical Science, Griffith University, Southport, QLD, Australia.	ERK1/2, MEK1/2 and p38 downstream signalling molecules impaired in CD56 dim CD16+ and CD56 bright CD16 dim/- natural killer cells in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis patients.	217. J Transl Med. 2016 Apr 21;14:97.	BACKGROUND: Natural Killer (NK) cell effector functions are dependent on phosphorylation of the mitogen-activated protein kinases (MAPK) pathway to produce an effective immune response for the clearance of target cells infected with viruses, bacteria or malignantly transformed cells. Intracellular signals activating NK cell cytokine production and cytotoxic activity are propagated through protein phosphorylation of MAPKs including MEK1/2, ERK1/2, p38 and JNK. Reduced NK cell cytotoxic activity is consistently reported in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) patients and intracellular signalling by MAPK in NK cells remains to be investigated. Therefore, the purpose of this paper was to investigate MAPK downstream signalling molecules in NK cell phenotypes from CFS/ME patients. METHODS: Flow cytometric protocols were used to measure phosphorylation of the MAPK pathway in CD56(bright)CD16(dim/-) and CD56(dim)CD16(+) NK cells following stimulation with K562 tumour cells or phorbol-12-myristate-13-acetate plus ionomycin. NK cell cytotoxic activity, degranulation, lytic proteins and cytokine production were also measured as markers for CD56(bright)CD16(dim/-) and CD56(dim)CD16(+) NK cell function using flow cytometric protocols. RESULTS: CFS/ME patients (n = 14) had a significant decrease in ERK1/2 in CD56(dim)CD16(+) NK cells compared to the non-fatigued controls (n = 11) after incubation with K562 cells. CD56(bright)CD16(dim/-) NK cells from CFS/ME patients had a significant increase in MEK1/2 and p38 following incubation with K562 cells. CONCLUSIONS: This is the first study to report significant differences in MAPK intracellular signalling molecules in CD56(dim)CD16(+) and CD56(bright)CD16(dim/-) NK cells from CFS/ME patients. The current results highlight the importance of intracellular signalling through the MAPK pathway for synergistic effector function of CD56(dim)CD16(+) and CD56(bright)CD16(dim/-) NK cells to ensure efficient clearance of target cells. In CFS/ME patients, dysfunctional MAPK signalling may contribute to reduced NK cell cytotoxic activity.
Huth TK(1), Brenu	(1)National Centre for	Killer Cell	154. Gene Regul Syst Bio.	Killer cell immunoglobulin-like receptor (KIR) genes encode for activating and inhibitory

EW(1), Staines DR(1), Marshall-Gradisnik SM(1).	Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, QLD, Australia.; School of Medical Science, Griffith University, Southport, QLD, Australia.	Immunoglobulin-like Receptor Genotype and Haplotype Investigation of Natural Killer Cells from an Australian Population of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis Patients.	2016 Jun 19;10:43-9.	surface receptors, which are correlated with the regulation of Natural Killer (NK) cell cytotoxic activity. Reduced NK cell cytotoxic activity has been consistently reported in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) patients, and KIR haplotypes and allelic polymorphism remain to be investigated. The aim of this article was to conduct a pilot study to examine KIR genotypes, haplotypes, and allelic polymorphism in CFS/ME patients and nonfatigued controls (NFCs). Comparison of KIR and allelic polymorphism frequencies revealed no significant differences between 20 CFS/ME patients and 20 NFCs. A lower frequency of the telomeric A/B motif ($P < 0.05$) was observed in CFS/ME patients compared with NFCs. This pilot study is the first to report the differences in the frequency of KIR on the telomeric A/B motif in CFS/ME patients. Further studies with a larger CFS/ME cohort are required to validate these results.
Iacob E(1), Light AR(1), Donaldson GW(1), Okifuji A(1), Hughen RW(1), White AT(1), Light KC(1).	(1)University of Utah, Salt Lake City.	Gene Expression Factor Analysis to Differentiate Pathways Linked to Fibromyalgia, Chronic Fatigue Syndrome, and Depression in a Diverse Patient Sample	360. Arthritis Care Res (Hoboken). 2016 Jan;68(1):132-40. .	OBJECTIVE: To determine if independent candidate genes can be grouped into meaningful biologic factors, and whether these factors are associated with the diagnosis of chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS), while controlling for comorbid depression, sex, and age. METHODS: We included leukocyte messenger RNA gene expression from a total of 261 individuals, including healthy controls (n = 61), patients with FMS only (n = 15), with CFS only (n = 33), with comorbid CFS and FMS (n = 79), and with medication-resistant (n = 42) or medication-responsive (n = 31) depression. We used exploratory factor analysis (EFA) on 34 candidate genes to determine factor scores and regression analysis to examine whether these factors were associated with specific diagnoses. RESULTS: EFA resulted in 4 independent factors with minimal overlap of genes between factors, explaining 51% of the variance. We labeled these factors by function as 1) purinergic and cellular modulators, 2) neuronal growth and immune function, 3) nociception and stress mediators, and 4) energy and mitochondrial function. Regression analysis predicting these biologic factors using FMS, CFS, depression severity, age, and sex revealed that greater expression in factors 1 and 3 was positively associated with CFS and negatively associated with depression severity (Quick Inventory for Depression Symptomatology score), but not associated with FMS. CONCLUSION: Expression of candidate genes can be grouped into meaningful clusters, and CFS and depression are associated with the same 2 clusters, but in opposite directions, when controlling for comorbid FMS. Given high comorbid disease and interrelationships between biomarkers, EFA may help determine patient subgroups in this population based on gene expression.
Ihsan M(1,)(2), Watson G(3), Abbiss CR(4).	(1)Sports Physiology Department, Singapore Sports Institute, 3 Stadium Drive, Singapore, 397630, Singapore.	What are the Physiological Mechanisms for Post-Exercise Cold Water Immersion in the Recovery from Prolonged Endurance and	269. Sports Med. 2016 Aug;46(8):1095-109.	Intense training results in numerous physiological perturbations such as muscle damage, hyperthermia, dehydration and glycogen depletion. Insufficient/untimely restoration of these physiological alterations might result in sub-optimal performance during subsequent training sessions, while chronic imbalance between training stress and recovery might lead to overreaching or overtraining syndrome. The use of post-exercise cold water immersion (CWI) is gaining considerable popularity among athletes

	Ihsan_Abdullah@sport.gov.sg. (2)Centre for Exercise and Sport Science Research, School of Exercise and Health Sciences, Edith Cowan University, Perth, Australia. Ihsan_Abdullah@sport.gov.sg. (3)School of Human Life Sciences, University of Tasmania, Launceston, TAS, Australia. (4)Centre for Exercise and Sport Science Research, School of Exercise and Health Sciences, Edith Cowan University, Perth, Australia.	Intermittent Exercise?		to minimize fatigue and accelerate post-exercise recovery. CWI, through its primary ability to decrease tissue temperature and blood flow, is purported to facilitate recovery by ameliorating hyperthermia and subsequent alterations to the central nervous system (CNS), reducing cardiovascular strain, removing accumulated muscle metabolic by-products, attenuating exercise-induced muscle damage (EIMD) and improving autonomic nervous system function. The current review aims to provide a comprehensive and detailed examination of the mechanisms underpinning acute and longer term recovery of exercise performance following post-exercise CWI. Understanding the mechanisms will aid practitioners in the application and optimisation of CWI strategies to suit specific recovery needs and consequently improve athletic performance. Much of the literature indicates that the dominant mechanism by which CWI facilitates short term recovery is via ameliorating hyperthermia and consequently CNS mediated fatigue and by reducing cardiovascular strain. In contrast, there is limited evidence to support that CWI might improve acute recovery by facilitating the removal of muscle metabolites. CWI has been shown to augment parasympathetic reactivation following exercise. While CWI-mediated parasympathetic reactivation seems detrimental to high-intensity exercise performance when performed shortly after, it has been shown to be associated with improved longer term physiological recovery and day to day training performances. The efficacy of CWI for attenuating the secondary effects of EIMD seems dependent on the mode of exercise utilised. For instance, CWI application seems to demonstrate limited recovery benefits when EIMD was induced by single-joint eccentrically biased contractions. In contrast, CWI seems more effective in ameliorating effects of EIMD induced by whole body prolonged endurance/intermittent based exercise modalities.
Ilhan B(1), Can M(2), Alibaz-Oner F(3), Yilmaz-Oner S(3), Polat-Korkmaz O(1), Ozen G(3), Mumcu G(4), Maradit Kremers H(5), Direskeneli H(3).	(1)Department of Internal Medicine, School of Medicine, Marmara University, Istanbul, Turkey. (2)Department of Rheumatology, Fatih Sultan Mehmet Education and Research Hospital, Istanbul, Turkey. (3)Department of Rheumatology, School of Medicine, Marmara University, Istanbul, Turkey. (4)Faculty of	Fatigue in patients with Behcet's syndrome: relationship with quality of life, depression, anxiety, disability and disease activity.	264. Int J Rheum Dis. 2016 Feb 23.	OBJECTIVES: Fatigue is a common symptom of chronic inflammatory diseases. The objective of this study was to investigate fatigue in patients with Behcet's syndrome (BS) and to examine the relationship between fatigue and disease activity, quality of life, anxiety and depression. METHODS: This is a cross-sectional study of 123 BS patients and 71 healthy controls in Turkey. All subjects completed the Multidimensional Assessment of Fatigue (MAF) questionnaire, Short form-36 (SF-36), Hospital Anxiety and Depression (HADS) scale and Health Assessment Questionnaire (HAQ). Disease activity among BS patients was assessed using the Behcet Syndrome Activity Scale (BSAS) and the physician's global assessment (PGA). RESULTS: BS patients had significantly higher MAF, HADS-depression (HADS-D) and HADS-anxiety (HADS-A) scores than the healthy controls ($P < 0.001$). Both the physical and mental components of the SF-36 scale were impaired in BS patients ($P = 0.0001$). BS patients with active disease, depression and anxiety had significantly higher MAF scores compared to BS patients without active disease, depression and anxiety ($P = 0.0001$). MAF scores showed positive correlations with HADS-A, HADS-D, HAQ scores and negative correlations with SF-36 mental and physical components. In regression analyses, depression, anxiety and

	Health Sciences, Marmara University, Istanbul, Turkey. (5)Department of Epidemiology, Mayo Clinic, Rochester, Minnesota, USA.			physical dysfunction were significantly associated with fatigue, after adjusting for age, sex, SF-36 physical and mental scores, HAQ, HADS-A, HADS-D and BSAS scores ($P < 0.05$). Decreases in SF-36 physical and mental scores were significant predictive factors for high MAF score in healthy controls ($P < 0.05$). CONCLUSIONS: Fatigue is common in clinically active BS patients compared with healthy controls and inactive BS patients. Depression, anxiety and physical dysfunction were significantly associated with fatigue.
Illegems J(1), Moorkens G, Van Den Eede F.	(1)Behaviour Therapy Division for Fatigue and Functional Symptoms, Antwerp University Hospital, Edegem, Belgium.	Group Cognitive Behaviour Therapy for Chronic Fatigue Syndrome.	120. Psychother Psychosom. 2016;85(5):308.	
Imamura S(1), Narita S(2), Nishikomori R(3), Tsuruta H(1), Numakura K(1), Maeno A(1), Saito M(1), Inoue T(1), Tsuchiya N(1), Nanjo H(4), Heike T(3), Satoh S(1,)(5), Habuchi T(1).	(1)Department of Urology, Akita University School of Medicine, 1-1-1 Hondo, Akita, 010-8543, Japan. (2)Department of Urology, Akita University School of Medicine, 1-1-1 Hondo, Akita, 010-8543, Japan. nari6202@gipc.akita-u.ac.jp. (3)Department of Pediatrics, Kyoto University Graduate School of Medicine, Kyoto, Japan. (4)Department of Pathology, Akita University Hospital, Akita, Japan. (5)Center for Kidney Disease and Transplantation, Akita University Hospital, Akita, Japan.	Secondary bladder amyloidosis with familial Mediterranean fever in a living donor kidney transplant recipient: a case report.	68. BMC Res Notes. 2016 Oct 19;9(1):473.	BACKGROUND: Secondary bladder amyloidosis is an extremely rare disease, resulting from a chronic systematic inflammatory disorder associated with amyloid deposits. Although uncommon in Japan, familial Mediterranean fever (FMF) is a hereditary autoinflammatory disease characterized by recurrent episodes of fever of short duration and serositis and is frequently associated with systemic amyloidosis. Here, we present a case of a Japanese patient complaining of fever and macroscopic hematuria after a living donor renal transplantation. Consequently, he was diagnosed with secondary bladder amyloidosis with FMF. CASE PRESENTATION: A 64-year-old Japanese male received a living ABO-incompatible kidney transplant from his wife. The postoperative clinical course was normal, and the patient was discharged 21 days after the transplantation with a serum creatinine level of 0.78 mg/dl. The patient frequently complained of general fatigue and fever of unknown origin. Six months later, the patient presented with continuous general fatigue, macroscopic hematuria, and fever. Cystoscopic examination of the bladder showed an edematous region with bleeding, and a transurethral biopsy revealed amyloid deposits. His wife stated that the patient had a recurrent high fever since the age of 40 years and that his younger brother was suspected to have a familial autoinflammatory syndrome; thus, the patient was also suspected to have a familial autoinflammatory syndrome. Based on his brother's medical history and the genetic tests, which showed a homozygous mutation (M694V/M694V) for the Mediterranean fever protein, he was diagnosed with FMF. Although colchicine treatment for FMF was planned, the patient had an untimely death due to heart failure. We re-evaluated the pathological findings of the various tissue biopsies obtained during the treatment after the renal transplantation. Immunohistochemistry revealed amyloid deposits in the bladder region, renal allograft, and myocardium and the condition was diagnosed as AA amyloidosis associated with FMF. CONCLUSION: We presented a case of systemic amyloidosis with FMF, involving the bladder region, myocardium, and renal allograft, diagnosed after renal

				transplantation. Bladder amyloidosis should be considered in patients with macroscopic hematuria, particularly in the kidney transplant recipients with idiopathic chronic renal disease. Diagnosis of secondary bladder amyloidosis may result in the early detection of underlying diseases, which may contribute to patient prognosis.
Ingman T(1), Ali S(1), Bhui K(1), Chalder T(2).	(1)Tom Ingman, MSc, King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK; Sheila Ali, MSc, Chronic Fatigue Research and Treatment Unit, South London and Maudsley NHS Foundation Trust, London, UK; Kamaldeep Bhui, MD, FRCPsych, Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; Trudie Chalder, PhD, King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK. (2)Tom Ingman, MSc, King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK; Sheila Ali, MSc, Chronic Fatigue Research and Treatment Unit, South	Chronic fatigue syndrome: comparing outcomes in White British and Black and minority ethnic patients after cognitive-behavioural therapy.	289. Br J Psychiatry. 2016 Sep;209(3):251-6.	BACKGROUND: Cognitive-behavioural therapy (CBT) is one of the most promising treatments for chronic fatigue syndrome (CFS). It is unclear whether CBT is effective for Black and minority ethnic (BME) groups. AIMS: To assess the effectiveness of CBT in BME patients compared with White British patients presenting to a specialist CFS service. METHOD: Data from 67 (19.0%) BME participants and 285 (81.0%) White British participants referred to a specialist CFS service in the UK were collected at baseline and after CBT treatment. RESULTS: Pairwise comparisons revealed that both BME participants and White British participants significantly improved on measures of fatigue severity (P<0.001), physical functioning (P<0.001) and work/social adjustment (P<0.001). Independent samples t-tests showed that BME participants improved despite exhibiting significantly higher baseline damage beliefs (P = 0.009), catastrophising (P = 0.024), all-or-nothing behaviour (P = 0.036) and avoidance/resting behaviour (P = 0.001), compared with White British participants. CONCLUSIONS: To our knowledge, this study is the first to indicate that CBT is effective for treating CFS in a group of patients from diverse BME backgrounds.

	London and Maudsley NHS Foundation Trust, London, UK; Kamaldeep Bhui, MD, FRCPsych, Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; Trudie Chalder, PhD, King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK trudie.chalder@kcl.ac.uk.			
Jackson H(1), MacLeod AK(2).	(1)Royal Holloway, University of London, London, UK. hj0305@gmail.com. (2)Royal Holloway, University of London, London, UK.	Well-being in Chronic Fatigue Syndrome: Relationship to Symptoms and Psychological Distress.	71. Clin Psychol Psychother. 2016 Oct 13.	OBJECTIVE: There is growing recognition in psychology that wellness is more than the absence of disease and distress. Well-being has been defined in numerous ways. Two dominant models include Diener, Eunkook, Suh, Lucas and Smith's (1999) model of subjective well-being (SWB) and Ryff's (1989) model of psychological well-being (PWB). In contrast to the abundance of research investigating negative constructs and psychopathology in chronic fatigue syndrome (CFS), there has been a paucity of positive psychology studies. This study had two aims: to examine PWB and SWB and their relationship to symptoms in CFS and to compare PWB scores in a subgroup of the CFS sample to a matched control group. METHOD: Chronic fatigue syndrome participants (n = 60) completed self-report scales of PWB, SWB, fatigue, anxiety and depression. PWB scores in a subgroup of the CFS sample (n = 42) were compared with those of a matched nonclinical control group (n = 42). RESULTS: Correlations between scales of symptoms and well-being were complex. Well-being dimensions were largely independent of physical components of fatigue but strongly related to psychological components of fatigue and psychological distress. Multiple regression indicated that five dimensions of well-being uniquely predicted symptomatology. Compared with the control group, the CFS group scored significantly lower on five of Ryff's six PWB dimensions, with particularly marked deficits in personal growth, environmental mastery and self-acceptance. CONCLUSION: This multidimensional assessment of well-being advances our understanding of CFS and offers new treatment targets. Future

				research must investigate whether interventions targeting theses well-being deficits can boost the efficacy of symptom-focused treatments. KEY PRACTITIONER MESSAGES: Previous psychological research into CFS has largely focused on the identification of negative constructs and CBT, a treatment that targets evidenced-based negative constructs, has demonstrated efficacy in reducing levels of fatigue and disability. However, the majority of people continue to experience psychiatric symptoms and excessive levels of fatigue post-treatment. Finding ways to enhance the efficacy of existing treatments is a clinical priority. There is evidence to suggest that in clinical populations, standard CBT is effective at reducing negative affect and thinking but fails to enhance low levels of positive affect and thinking, implying treatments may be more effective if they promote positive functioning alongside a reduction of negative functioning. Multidimensional models of well-being suggest that well-being is not a single phenomenon, and different psychological disorders may be characterized by varying well-being deficit profiles. Psychological well-being was found to be diminished in CFS participants compared with controls, with particularly marked deficits in personal growth, environmental mastery and self-acceptance, suggesting that these may be particularly important treatment targets. Well-being dimensions within the CFS group were largely independent of physical symptoms but strongly related to psychological symptoms, suggesting what may be causing low levels of well-being in CFS is largely psychological factors and the general impact of living with a chronic illness rather than symptom levels per se.
Jafry NM(1).	(1) ME sufferer, author of The State of Me (HarperCollins, 2008). E-mail: nmjk48@yahoo.co.uk.	Chronic fatigue syndrome and the biopsychosocial model	83. Br J Gen Pract. 2016 Oct;66(651):511.	
Janse A(1), Wiborg JF(1), Bleijenberg G(1), Tummers M(1), Knoop H(1).	(1)Expert Center for Chronic Fatigue, Radboud University Medical Center.	The efficacy of guided self-instruction for patients with idiopathic chronic fatigue: A randomized controlled trial.	257. J Consult Clin Psychol. 2016 May;84(5):377-88.	OBJECTIVE: To determine the efficacy of a cognitive-behavioral intervention for patients meeting U.S. Centers for Disease Control and Prevention (CDC) criteria for idiopathic chronic fatigue (ICF). ICF is thought to be a less severe disorder than chronic fatigue syndrome (CFS). The intervention consisted of a booklet with self-instructions combined with e-mail contact with a therapist. METHOD: Randomized controlled trial conducted at an outpatient facility. All patients suffered from severe and persistent fatigue with moderate impairment levels or fewer than 4 additional symptoms. Patients were randomly allocated to either guided self-instruction or a wait-list control group. Primary outcome measures were fatigue severity assessed with the Checklist Individual Strength and level of overall impairment assessed with the Sickness Impact Profile. Outcome measures were assessed prior to randomization and following treatment or wait-list control group. RESULTS: One hundred patients were randomly allocated to the intervention or a wait-list control group and 95 completed second assessment. An intention-to-treat analysis showed significant treatment effects for fatigue severity (-

				8.98, 95% confidence interval [CI] [-13.99, -3.97], Cohen's d = 0.68, p < .001) and for overall impairment (-317.19, 95% CI [-481.70, -152.68], Cohen's d = 0.53, p < .01) in favor of the intervention. The number of additional symptoms and overall impairment at baseline did not moderate posttreatment fatigue severity. Baseline overall impairment moderated posttreatment impairment. CONCLUSIONS: Patients with ICF can be treated effectively with a minimal intervention. This is relevant as ICF is more prevalent than CFS and treatment capacity is limited.
Jara LJ(1,)(2), Izquierdo E(3,)(4), Medina G(5,)(6).	(1)Direction of Education and Research, Hospital de Especialidades Centro Médico La Raza, Instituto Mexicano del Seguro Social, Seris/Zaachila S/N, Colonia La Raza, Mexico City, Mexico. luis_jara_quezada@hotmail.com. (2)Universidad Nacional Autónoma de México, Mexico City, Mexico. luis_jara_quezada@hotmail.com. (3)Rheumatology Department, Hospital de Especialidades Centro Médico La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico. (4)Universidad Peruana Cayetano Heredia, Lima, Peru. (5)Universidad Nacional Autónoma de México, Mexico City, Mexico.	Is the immune neuroendocrine system the connection between epipharyngitis and chronic fatigue syndrome induced by HPV vaccine? : Editorial.	101. Immunol Res. 2016 Sep 7.	

	(6)Clinical Research Unit, Hospital de Especialidades Centro Médico La Raza, Instituto Mexicano del Seguro Social, Mexico City, Mexico.			
Jason LA(1), McManimen S(1), Sunnquist M(1), Brown A(1), Furst J(1), Newton JL(2), Strand EB(3).	(1)Center for Community Research, DePaul University, Chicago, IL USA. (2)Newcastle University. (3)Oslo University Hospital.	Case definitions integrating empiric and consensus perspectives.	221. Fatigue. 2016;4(1):1-23. Epub 2016 Jan 19.	BACKGROUND: There has been considerable controversy regarding how to name and define the illnesses known as myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS). The IOM report has proposed a new clinical criteria and name for this illness, but aspects of these recommendations have been scrutinized by patients and scientists. PURPOSE: It is possible that both empiric and consensus approaches could be used to help settle some of these diagnostic challenges. Using patient samples collected in the United States, Great Britain, and Norway (N=556), the current study attempted to categorize patients using more general as well as more restricted case definitions. RESULTS: Overall, the outcomes suggest that there might be four groupings of patients, with the broadest category involving those with chronic fatigue (N=62), defined by 6 or more months of fatigue which can be cannot be explained by medical or psychiatric conditions. A second category involves those patients that have chronic fatigue that can be explained by a medical or psychiatric condition (N=47). A third category involves more specific criteria that have been posited both by the IOM report, a Canadian Clinical Case criteria, a ME-ICC criteria and a more empiric approach. These efforts have specified domains of substantial reductions of activity, post-exertional malaise, neurocognitive impairment, and sleep dysfunction (N=346). Patients with these characteristics were more functionally impaired than those meeting just chronic fatigue criteria, $p < .05$. Finally, those meeting even more restrictive ME criteria proposed by Ramsay, identified a smaller and even more impaired group, $p < .05$. DISCUSSION: The advantages of using such empirical and consensus approaches to develop reliable classification and diagnostic efforts are discussed.
Jason LA(1), Sunnquist M(2), Brown A(2), Evans M(2), Newton JL(3).	(1)Center for Community Research, DePaul University, USA ljason@depaul.edu. (2)Center for Community Research, DePaul University, USA. (3)Institute for Ageing and Health, Newcastle University,	Are Myalgic Encephalomyelitis and chronic fatigue syndrome different illnesses? A preliminary analysis.	374. J Health Psychol. 2016 Jan;21(1):3-15.	Considerable discussion has transpired regarding whether chronic fatigue syndrome is a distinct illness from Myalgic Encephalomyelitis. A prior study contrasted the Myalgic Encephalomyelitis International Consensus Criteria with the Fukuda and colleagues' chronic fatigue syndrome criteria and found that the Myalgic Encephalomyelitis International Consensus Criteria identified a subset of patients with greater functional impairment and physical, mental, and cognitive problems than the larger group who met Fukuda and colleagues' criteria. The current study analyzed two discrete data sets and found that the Myalgic Encephalomyelitis International Consensus Criteria identified more impaired individuals with more severe symptomatology.

	UK.			
Jepsen JR(1), Rasmussen HB.	(1) Centre of Maritime Health and Society, Institute of Public Health, University of Southern Denmark, Esbjerg, Denmark Department of Occupational Medicine, Hospital of Southwestern Jutland, Esbjerg, Denmark. jriis@cmss.sdu.dk.	The metabolic syndrome among Danish seafarers: a follow-up study.	86. Int Marit Health. 2016;67(3):129-36.	BACKGROUND: The metabolic syndrome (MS) represents a cluster of risk factors related to insulin resistance. Metabolic syndrome is a strong risk factor for chronic metabolic and cardiovascular diseases and is related to nutritional factors, sleep patterns, work-related stress, fatigue, and physical activity - all of which are critical issues at sea. We have previously demonstrated a MS prevalence of 24.2% in Danish seafarers. This study aimed to follow the trend of MS after 2 years' intervention. MATERIALS AND METHODS: Out of 524 Danish seafarers (mean age 37.7 years) who underwent medical fit-for-duty examination by seamen's doctors at baseline, 141 seafarers (mean age 41.3 years) were tracked and re-examined after 2 years. At baseline all participants received general advice regarding lifestyle issues. Seafarers with MS were additionally given specific advice regarding treatment. The seafarers provided questionnaire information about their workplace on board, about treatment of hyperlipidaemia, hypertension, and about previously diagnosed type 2-diabetes. In order to define MS, we collected data about waist circumference, blood pressure, triglycerides, HDL-cholesterol, and fasting plasma glucose. RESULTS: Out of 35 (26.5%) seafarers who fulfilled the criteria for MS at follow-up, 18 had MS at baseline while 9 were incident cases. Two seafarers with MS at baseline ceased to qualify for this condition at follow-up. The prevalence of seafarers with MS at follow-up represents a minimal estimate because a proportion could not be assessed due to missing fasting blood tests. Smoking and alcohol consumption was not reduced. CONCLUSIONS: In spite of the intervention, the prevalence of MS increased in this group of seafarers. This study indicates the limitations of individual health promotion and the need for corporate actions.
Johnson AD(1), Cohn CS(2).	(1)Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota, USA john4613@umn.edu. (2)Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota, USA.	Xenotropic Murine Leukemia Virus-Related Virus (XMRV) and the Safety of the Blood Supply.	151. Clin Microbiol Rev. 2016 Oct;29(4):749-57.	In 2006, a new virus, xenotropic murine leukemia virus-related virus (XMRV), was discovered in a cohort of U.S. men with prostate cancer. Soon after this initial finding, XMRV was also detected in samples from patients with chronic fatigue syndrome (CFS). The blood community, which is highly sensitive to the threat of emerging infectious diseases since the HIV/AIDS crisis, recommended indefinite deferral of all blood donors with a history of CFS. As XMRV research progressed, conflicting results emerged regarding the importance of this virus in the pathophysiology of prostate cancer and/or CFS. Molecular biologists traced the development of XMRV to a recombination event in a laboratory mouse that likely occurred circa 1993. The virus was propagated via cell lines derived from a tumor present in this mouse and spread through contamination of laboratory samples. Well-controlled experiments showed that detection of XMRV was due to contaminated samples and was not a marker of or a causal factor in prostate cancer or CFS. This paper traces the development of XMRV in the prostate and CFS scientific communities and explores the effect it had on the blood community.
Johnston S(1,)(2),	(1)School of Medical	A targeted genome	39. BMC Med Genet. 2016	BACKGROUND: Chronic Fatigue Syndrome, also known as Myalgic Encephalomyelitis

Staines D(3), Klein A(4,)(3), Marshall-Gradisnik S(4,)(3).	Science, Griffith University, Gold Coast, Australia. samantha.johnston@griffith.edu.au. (2)The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, Gold Coast, QLD, 4222, Australia. samantha.johnston@griffith.edu.au. (3)The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, Gold Coast, QLD, 4222, Australia. (4)School of Medical Science, Griffith University, Gold Coast, Australia.	association study examining transient receptor potential ion channels, acetylcholine receptors, and adrenergic receptors in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.	Nov 11;17(1):79.	(CFS/ME) is a debilitating condition of unknown aetiology. It is characterized by a range of physiological effects including neurological, sensory and motor disturbances. This study examined candidate genes for the above clinical manifestations to identify single nucleotide polymorphism (SNP) alleles associated with CFS/ME compared with healthy controls. METHODS: DNA was extracted and whole genome genotyping was performed using the HumanOmniExpress BeadChip array. Gene families for transient receptor potential ion channels, acetylcholine receptors, and adrenergic receptors, and acetylcholinesterase were targeted. The frequency of each SNP and their association between CFS/ME and healthy controls was examined using Fisher's exact test, and to adjust for multiple testing, False Detection Rate (FDR) and Bonferroni corrections were applied ($p < 0.05$). RESULTS: The study included 172 participants, consisting of 95 Fukuda defined CFS/ME patients (45.8 ± 8.9; 69 % female) and 77 healthy controls (42.3 ± 10.3; 63 % female). A total of 950 SNPs were included for analysis. 60 significant SNPs were associated with CFS/ME compared with healthy controls. After applying FDR and Bonferroni corrections, SNP rs2322333 in adrenergic receptor α1 (ADRA1A) was higher in CFS/ME compared with healthy controls (45.3 % vs. 23.4 %; $p = 0.059$). The genotype class that was homozygous minor (AA) was substantially lower in CFS/ME compared with healthy controls (4.2 % vs. 24.7 %). CONCLUSIONS: This study reports for the first time the identification of ADRA1A and a possible association between CFS/ME and genotype classes. Further examination of the functional role of this class of adrenergic receptors may elucidate the cause of particular clinical manifestations observed in CFS/ME.
Johnston SC(1), Staines DR(2), Marshall-Gradisnik SM(1).	(1)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Parklands, QLD, Australia; School of Medical Sciences, Griffith University, Parklands, QLD,	Epidemiological characteristics of chronic fatigue syndrome/myalgic encephalomyelitis in Australian patients.	169. Clin Epidemiol. 2016 May 17;8:97-107.	BACKGROUND: No epidemiological investigations have previously been conducted in Australia according to the current clinical definitions of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). The aim of this study was to describe sociodemographic and illness characteristics of Australian patients with CFS/ME. METHODS: A cross-sectional survey on the medical history of patients enrolled in an Australian CFS/ME research database between April 2013 and April 2015. Participants were classified according to Fukuda criteria and International Consensus Criteria. RESULTS: A total of 535 patients diagnosed with CFS/ME by a primary care physician were identified. The mean age of all patients was 46.4 years (standard deviation 12.0); the majority were female (78.61%), Caucasian, and highly educated. Of these, 30.28% met Fukuda criteria. A further 31.96% met both Fukuda criteria and International

	Australia. (2)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Parklands, QLD, Australia.			Consensus Criteria. There were 14.58% reporting chronic fatigue but did not meet criteria for CFS/ME and 23.18% were considered noncases due to exclusionary conditions. Within those meeting CFS/ME criteria, the most common events prior to illness included cold or flu, gastrointestinal illness, and periods of undue stress. Of the 60 symptoms surveyed, fatigue, cognitive, and short-term memory symptoms, headaches, muscle and joint pain, unrefreshed sleep, sensory disturbances, muscle weakness, and intolerance to extremes of temperature were the most commonly occurring symptoms (reported by more than two-thirds of patients). Significant differences in symptom occurrence between Fukuda- and International Consensus Criteria-defined cases were also identified. CONCLUSION: This is the first study to summarize sociodemographic and illness characteristics of a cohort of Australian CFS/ME patients. This is vital for identifying potential risk factors and predictors associated with CFS/ME and for guiding decisions regarding health care provision, diagnosis, and management.
Kakuda W(1), Momosaki R, Yamada N, Abo M.	(1)Department of Rehabilitation Medicine, The Jikei University School of Medicine, Japan.	High-frequency rTMS for the Treatment of Chronic Fatigue Syndrome: A Case Series.	26. Intern Med. 2016;55(23):3515-3519. Epub 2016 Dec 1.	Structural and functional abnormalities of the prefrontal cortex seem to correlate with fatigue in patients with chronic fatigue syndrome (CFS). We consecutively applied facilitatory high-frequency repetitive transcranial magnetic stimulation (rTMS) to the dorsolateral prefrontal cortex (DLPFC) of seven CFS patients over three days. Five patients completed the 3-day protocol without any adverse events. For the other two patients, we had to reduce the stimulation intensity in response to mild adverse reactions. In most of the patients, treatment resulted in an improvement of fatigue symptoms. High-frequency rTMS applied over the DLPFC can therefore be a potentially useful therapy for CFS patients.
Kapur N(1), Webb R(2).	(1)Centre for Suicide Prevention, Centre for Mental Health and Safety, Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester M13 9PL, UK. Electronic address: nav.kapur@manchester.ac.uk. (2)Centre for Suicide Prevention, Centre for Mental Health and Safety, Institute of Brain,	Suicide risk in people with chronic fatigue syndrome.	274. Lancet. 2016 Apr 16;387(10028):1596-7.	Comment on Lancet. 2016 Apr 16;387(10028):1638-43.

	Behaviour and Mental Health, University of Manchester, Manchester M13 9PL, UK.			
Karageorgas T(1), Fragioudaki S(1), Nezos A(1), Karaiskos D(1), Moutsopoulos HM(1), Mavragani CP(1).	(1)National and Kapodistrian University of Athens, Athens, Greece.	Fatigue in Primary Sjögren's Syndrome: Clinical, Laboratory, Psychometric, and Biologic Associations.	350. Arthritis Care Res (Hoboken). 2016 Jan;68(1):123-31.	OBJECTIVE: To identify independent contributors of fatigue in primary Sjögren's syndrome (SS) patients, taking into account clinical, laboratory, and psychological features, and to explore the potential role of interferon (IFN)-induced gene indoleamine 2,3-dioxygenase (IDO-1), anti-21-hydroxylase (anti-21[OH]) antibodies, and soluble BAFF. METHODS: Detailed clinical and laboratory characteristics were recorded for 106 primary SS patients. The Functional Assessment of Chronic Illness Therapy-Fatigue, Zung Depression Scale, State-Trait Anxiety Inventory, Eysenck Personality Questionnaire Scale, and Athens Insomnia Scale were adopted to assess fatigue, depression, anxiety, and sleep disturbances, respectively. Peripheral whole blood expression levels of IDO-1, as well as type I and II IFN-induced genes were calculated using quantitative reverse transcriptase-polymerase chain reaction. Serum anti-21(OH) antibodies and soluble BAFF levels were determined by a radioimmunoassay and an enzyme-linked immunosorbent assay, respectively. Univariate and multivariate models were performed to identify determinants of fatigue. RESULTS: Fatigue was detected in 32 of 106 (30.2%) primary SS patients. In univariate analysis, fatigue was associated with arthralgias/myalgias, fibromyalgia hydroxychloroquine therapy, both state and trait anxiety scores, depression, and neuroticism, as well as impaired sleep patterns. Multivariate analysis revealed neuroticism (odds ratio [OR] 6.9, [95% confidence interval (95% CI) 1.7-28.0]), depression (OR 3.0 [95% CI 0.8-11.0]), and fibromyalgia (OR 5.5 [95% CI 1.1-27.7]) as independent fatigue contributors. Soluble BAFF levels, anti-21(OH) autoantibodies, and IDO-1 messenger RNA expression did not significantly differ between fatigued and nonfatigued primary SS patients. CONCLUSION: Depression, neuroticism, and fibromyalgia play a major role in primary SS-associated fatigue and should be addressed in clinical practice, with active collaboration between rheumatologists and mental health professionals. Further studies are warranted in order to explore underlying pathophysiologic pathways that might explain fatigue in the setting of primary SS.
Karras S(1), Rapti E(2), Matsoukas S(3), Kotsa K(4).	(1)First Department of Internal Medicine, Division of Endocrinology and Metabolism, AHEPA Hospital, Thessaloniki 54636, Greece. karraspiros@yahoo.gr.	Vitamin D in Fibromyalgia: A Causative or Confounding Biological Interplay?	172. Nutrients. 2016 Jun 4;8(6). pii: E343.	Fibromyalgia (FM) is a chronic syndrome with an increasing prevalence, characterized by widespread musculoskeletal pain in combination with a variety of cognitive symptoms and fatigue. A plethora of scientific evidence that has accumulated during the last decades, resulted in a significant improvement of the understanding of the pathophysiology of the disease. However, current therapeutic approaches in patients with FM remains a multidimensional approach including patient education, behavioral therapy, exercise, pain management, and relief of chronic symptoms, rather than the use drug therapies, based on the mechanisms of disease development. Vitamin D, a fat-

	(2)First Department of Internal Medicine, Division of Endocrinology and Metabolism, AHEPA Hospital, Thessaloniki 54636, Greece. raptieleni8@gmail.com. (3)First Department of Internal Medicine, Division of Endocrinology and Metabolism, AHEPA Hospital, Thessaloniki 54636, Greece. mastparkour@hotmail.com. (4)First Department of Internal Medicine, Division of Endocrinology and Metabolism, AHEPA Hospital, Thessaloniki 54636, Greece. kalmanthou@yahoo.gr.			soluble vitamin derived mainly from skin synthesis through ultraviolet radiation, has been recognized to manifest a plethora of extraskeletal actions, apart from its fundamental role in skeletal and calcium homeostasis, including modulation of cell growth, neuromuscular actions, and potential anti-inflammatory properties. Recent findings indicate that hypovitaminosis D to be highly prevalent in patients with FM. Supplementation studies are limited so far, indicating potential beneficial effects on pain and severity of the disease, however specific recommendations are lacking. This review aims to summarize and critically appraise data regarding the pathophysiological interplay between vitamin D and FM, available results from observational and supplementation studies so far, with a clinical discourse on current knowledge gaps and future research agenda.
Karsan N(1), Prabhakar P(2), Goadsby PJ(3).	(1)Headache Group, Department of Basic and Clinical Neuroscience, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK. (2)Department of Paediatric Neurology, Great Ormond Hospital for Children	Characterising the premonitory stage of migraine in children: a clinic-based study of 100 patients in a specialist headache service.	63. J Headache Pain. 2016 Dec;17(1):94. Epub 2016 Oct 21.	BACKGROUND: The premonitory stage of migraine attacks, when symptomatology outside of pain can manifest hours to days before the onset of the headache, is well recognised. Such symptoms have been reported in adults in a number of studies, and have value in predicting an impending headache. These symptoms have not been extensively studied in children. We aimed to characterise which, if any, of these symptoms are reported in children seen within a Specialist Headache Service. METHODS: We reviewed clinic letters from the initial consultation of children and adolescents seen within the Specialist Headache Service at Great Ormond Street Hospital between 1999 and 2015 with migraine in whom we had prospectively assessed clinical phenotype data. We randomly selected 100 cases with at least one premonitory symptom recorded in the letter. For these patients, the age at headache onset, presence of family history of headache, headache diagnosis, presence of episodic syndromes which may be associated with headache, developmental milestones,

	NHS Foundation Trust, London, UK. (3)NIHR-Wellcome Trust King's Clinical Research Facility, King's College Hospital, London, SE5 9PJ, UK. peter.goadsby@kcl.ac.uk.			gestation at birth, mode of delivery and presence of premonitory symptoms occurring before or during headache were recorded. RESULTS: Of the 100 patients selected, 65 % were female. The age range of the patients was 18 months to 15 years at the time of headache onset. The most common diagnosis was chronic migraine in 58 %, followed by episodic migraine (29 %), New Daily Persistent Headache with migrainous features (8 %) and hemiplegic migraine (5 %). A history of infantile colic was noted in 31 % and was the most common childhood episodic syndrome associated with migraine. The most common premonitory symptoms recorded were fatigue, mood change and neck stiffness. The commonest number of reported premonitory symptoms was two. CONCLUSION: Premonitory symptoms associated with migraine are reported in children as young as 18 months, with an overall clinical phenotype comparable to adults. Better documentation of this stage will aid parents and clinicians to better understand the phenotype of attacks, better recognise migraine and thus initiate appropriate management. Larger studies with a broader base are warranted to understand the extent and implications of these symptoms for childhood and adolescent migraine.
Kasapoğlu Aksoy M(1), Altan L(1,)(2), Ökmen Metin B(1).	(1)a Department of Physical Medicine and Rehabilitation , Sağlık Bilimleri University Bursa Yüksek Ihtisas Training and Research Hospital , Bursa , Turkey and. (2)b Department of Physical Medicine and Rehabilitation , Uludağ University Medicine Faculty , Bursa , Turkey.	The relationship between balance and vitamin 25(OH)D in fibromyalgia patients.	34. Mod Rheumatol. 2016 Dec 9:1-7.	INTRODUCTION: Fibromyalgia syndrome (FMS) is a chronic disease characterized by diffuse pain of unknown cause, fatigue, sleep disorders, cognitive dysfunction, and sensitivity. Fibromyalgia was shown to be associated with balance problems and increased incidence of falls. There are many theoretical mechanisms related to the impact of vitamin D on postural control. The aim of the current study was to investigate the relationship between vitamin 25(OH)D levels and pain, balance and daily activities in patients with FMS. METHOD: Patients aged 35-65 years who were diagnosed with FMS according to 1990 ACR diagnostic criteria were screened. Seventy patients diagnosed with FMS and 60 healthy controls with comparable age and gender were included in the study. Fibromyalgia impact scale (FIQ), Berg Balance Scale (BBS), the Nottingham Health Profile (NHP), and visual analog scale (VAS) were applied to the subjects. The subjects were divided into two groups by vitamin 25(OH)D level being above or below 30 ng/ml. RESULTS: A statistically significant difference was established between VAS, BBS value and all NHP subscale and NHP total values of FMS patients and those of healthy control group. The relationship between BBS and the level of vitamin 25(OH)D of all participants was investigated, a positive statistically significant relationship was found with Vit-D at $r = 0.481$ level ($p < 0.05$). CONCLUSION: It was observed that low vitamin D levels affected balance in both FMS group and healthy control group. It should be kept in mind that vitamin D level is likely to negatively affect balance and VAS values in FMS.
Keating EM(1,)(2), Antiel RM(3), Weiss KE(3), Wallace	(1)Mayo Clinic, Rochester, MN, USA ekeating@alumni.nd.edu. (2)Baylor College	Parental Perceptions of Pediatric Pain and POTS-Related Disability.	17. Clin Pediatr (Phila). 2016 Dec 8. pii: 0009922816681137.	Adolescents with postural orthostatic tachycardia syndrome (POTS) often have pain and functional impairment. This study evaluated how parental attributions of children's symptoms relate to child functional impairment. Adolescents with chronic pain and clinical symptoms suggestive of autonomic dysfunction (fatigue, dizziness, nausea) that

D(4), Antiel SJ(3), Fischer PR(3), Junghans-Rutelonis AN(3), Harbeck-Weber C(3).	of Medicine/Texas Children's Hospital, Houston, TX, USA. (3)Mayo Clinic, Rochester, MN, USA. (4)Children's Mercy Hospital, Kansas City, MO, USA.			attended a multidisciplinary chronic pain clinic completed measures of depression, anxiety, and functioning (n = 141). Parents of 114 of these patients completed the Parent Pain Attribution Questionnaire (PPAQ), a measure indicating the extent they believe physical and psychosocial factors account for their child's health condition. Patients were retrospectively grouped as to whether or not they had significant POTS on tilt table testing (n = 37). Greater parental attribution to physical causes was associated with increased levels of functional disability whether patients had POTS (r = 0.45, P = .006) or not (r = 0.25, P = .03). These results suggest that providers should advocate a more comprehensive family-oriented rehabilitative approach to treatment.
Keech A(1), Vollmer-Conna U(2), Barry BK(3), Lloyd AR(4).	(1) School of Medical Sciences, University of New South Wales Sydney, NSW, Australia. (2) School of Psychiatry, University of New South Wales Sydney, NSW, Australia. (3) School of Medical Sciences, University of New South WalesSydney, NSW, Australia; Neuroscience Research AustraliaSydney, NSW, Australia. (4)Inflammation and Infection Research Centre, School of Medical Sciences, University of New South Wales Sydney, NSW, Australia.	Gene Expression in Response to Exercise in Patients with Chronic Fatigue Syndrome: A Pilot Study.	79. Front Physiol. 2016 Sep 22;7:421. eCollection 2016.	Chronic fatigue syndrome (CFS) is a debilitating disorder of unknown pathogenesis, characterized by fatigue, which is exacerbated after minimal exercise. We examined the effect of a single bout of aerobic exercise on leucocyte mRNA expression of genes putatively linked to exaggerated afferent signaling as an under-pinning of the fatigue state. A carefully-characterized sample of patients with CFS (N = 10) and healthy matched control participants (N = 12) were included. Participant ratings of fatigue and other symptoms, as well as blood samples, were obtained at baseline, and five other time-points up to 72 h after 25 min of moderate-intensity cycling exercise. Leucocyte mRNA of 19 metabolite-sensing, adrenergic, immune, and neurotransmission genes was examined using quantitative polymerase chain reaction. Patients with CFS reported substantial fatigue, functional impairment, and poor sleep at baseline (all $p < 0.02$), and exercise immediately induced worsened patients' fatigue (effect size, ES = 1.17). There were no significant changes in gene expression after exercise and patients did not differ from control participants at any time point. Higher levels of expression of ficolin (FCN1) and a purinergic receptor (P2RX4) in patients with CFS were found when all time points were combined. Patients with CFS did not show significant exercise-induced changes in leucocyte mRNA of 19 metabolite-sensing, adrenergic, immune and neurotransmission genes despite a prominent exacerbation of fatigue.
Keijmel SP(1), Raijmakers RP(2), Bleeker-Rovers CP(3), van der Meer JW(4), Netea MG(5), Schoffelen T(6),	(1)Radboud Expertise Centre for Q Fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical	Altered interferon-γ response in patients with Q-fever fatigue syndrome.	298. J Infect. 2016 Apr;72(4):478-85.	OBJECTIVES: Whether immunological mechanisms underlie Q-fever fatigue syndrome (QFS) remains unclear. For acute Q-fever, the antigen-specific interferon-γ (IFNγ) response may be a useful tool for diagnosis, and the IFNγ/interleukin(IL)-2 production ratio may be a marker for chronic Q-fever and treatment monitoring. Here we explored the specific IFNγ production and IFNγ/IL-2 ratio in QFS patients. METHODS: IFNγ and IL-2 production were tested in ex-vivo stimulated whole blood of QFS patients (n = 20), and compared to those previously determined in seropositive controls (n = 135), and

van Deuren M(7).	center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands; Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Stephan.Keijmel@radboudumc.nl. (2)Radboud Expertise Centre for Q Fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands; Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Ruud.Raijmakers@radboudumc.nl. (3)Radboud Expertise Centre for Q Fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical			chronic Q-fever patients (n = 28). Also, the correlation between patient characteristics and IFNγ, IL-2, and IFNγ/IL-2 ratio was determined. RESULTS: QFS patients were younger ($p < 0.001$), but gender distribution was similar to seropositive controls and chronic Q-fever patients. Coxiella burnetii Nine Mile stimulation revealed a higher IFNγ production in QFS (median 319.5 pg/ml) than in seropositive controls (120 pg/ml, $p < 0.01$), but comparable to chronic Q-fever (2846 pg/ml). The IFNγ/IL-2 ratio was similar to that in seropositive controls, but lower than in chronic Q-fever patients ($p < 0.01$). Symptom duration was positively correlated with IL-2 production, and negatively correlated with the IFNγ/IL-2 ratio. CONCLUSIONS: These results point to an altered cell-mediated immunity in QFS, and suggest a different immune response than in chronic Q-fever.

	center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands; Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Chantal.Bleeker-Rovers@radboudumc.nl. (4)Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Jos.vanderMeer@radboudumc.nl. (5)Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Mihai.Netea@radboudumc.nl. (6)Radboud Expertise Centre for Q Fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical center, P.O. Box 9101,			

	6500 HB, Nijmegen, The Netherlands; Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Teske.Schoffelen@radboudumc.nl. (7)Department of Internal Medicine, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Electronic address: Marcel.vanDeuren@radboudumc.nl.			
Kempke S(1), Luyten P(1), Mayes LC(2), Van Houdenhove B(3), Claes S(3).	(1)Faculty of Psychology and Educational Sciences, University of Leuven. (2)Yale Child Study Center, Yale Medical School, Yale University. (3)Department of Psychiatry, University Psychiatric Center, University of Leuven.	Self-critical perfectionism predicts lower cortisol response to experimental stress in patients with chronic fatigue syndrome.	321. Health Psychol. 2016 Mar;35(3):298-307.	OBJECTIVE: Previous studies have suggested that self-critical perfectionism (SCP) may play a role in the development and maintenance of Chronic Fatigue Syndrome (CFS). In this study we investigated whether SCP is related to a hypofunction of the hypothalamic-pituitary-adrenal (HPA) axis, which has been shown to be a key factor in the pathophysiology of CFS. METHOD: We conducted a quasi-experimental study to examine the association between SCP (as measured with the Depressive Experiences Questionnaire) and stress reactivity in a sample of 41 female CFS patients. Participants were exposed to the Trier Social Stress Test (TSST). Both subjective stress and salivary cortisol levels were measured until 90 min after the TSST. We also examined the relationship between stress reactivity and illness characteristics (i.e., duration and severity of symptoms). RESULTS: The results showed that SCP was associated with increased subjective stress reactivity, but with decreased HPA-axis reactivity as indicated by a blunted cortisol response to the TSST. Furthermore, we found an inverse relationship between cortisol reactivity and symptom severity. There was no relationship between cortisol reactivity and illness duration. CONCLUSION: Our findings suggest that SCP is associated with loss of resilience of the neurobiological stress response system in CFS.
Kidd E(1), Brown	(1)Center for	The Relationship between	214. Diagnostics (Basel).	Chronic fatigue syndrome (CFS) is a debilitating illness, but it is unclear if patient age

A(2), McManimen S(3), Jason LA(4), Newton JL(5), Strand EB(6).	Community Research, DePaul University, 990 W. Fullerton Ave. Suite 3100, Chicago, IL 60614, USA. ekidd3118@gmail.com. (2)Center for Community Research, DePaul University, 990 W. Fullerton Ave. Suite 3100, Chicago, IL 60614, USA. abrown57@depaul.edu. (3)Center for Community Research, DePaul University, 990 W. Fullerton Ave. Suite 3100, Chicago, IL 60614, USA. smcmanim@depaul.edu. (4)Center for Community Research, DePaul University, 990 W. Fullerton Ave. Suite 3100, Chicago, IL 60614, USA. ljason@depaul.edu. (5)Clinical Medicine, Newcastle University, Newcastle NE2 4HH, England. julia.newton@newcastle.ac.uk. (6)Division of Medicine, Oslo University Hospital, 0450 Oslo, Norway. lbstr@ous-hf.no.	Age and Illness Duration in Chronic Fatigue Syndrome.	2016 Apr 22;6(2). pii: E16.	and illness duration might affect symptoms and functioning of patients. In the current study, participants were categorized into four groups based upon age (under or over age 55) and illness duration (more or less than 10 years). The groups were compared on functioning and symptoms. Findings indicated that those who were older with a longer illness duration had significantly higher levels of mental health functioning than those who were younger with a shorter or longer illness duration and the older group with a shorter illness duration. The results suggest that older patients with an illness duration of over 10 years have significantly higher levels of mental health functioning than the three other groups. For symptoms, the younger/longer illness duration group had significantly worse immune and autonomic domains than the older/longer illness group. In addition, the younger patients with a longer illness duration displayed greater autonomic and immune symptoms in comparison to the older group with a longer illness duration. These findings suggest that both age and illness duration need to be considered when trying to understand the influence of these factors on patients.
Kim J(1), Ku B(1), Kim KH(1).	(1)KM Fundamental Research Division, Korea Institute of	Validation of the qi blood yin yang deficiency questionnaire on chronic	205. Chin Med. 2016 May 2;11:24. .	BACKGROUND: Chronic fatigue (CF) reflects an imbalance of inter-organ functions or of the four essential physiological components qi, blood (xue), yin, and yang. CF can be subdivided into different patterns. However, there are no diagnostic methods for CF.

	Oriental Medicine, 1672 Yuseongdae-ro, Yuseong-gu, Daejeon, 34054 Republic of Korea.	fatigue		This study aimed to clinically validate a pattern identification method by identifying correlations between CF and responses to the qi blood yin yang deficiency questionnaire (QBYY-Q). METHODS: Participants were recruited between May and June 2014 through the Kyung Hee University Korean Medicine hospital website and via posters and comprised 129 CF patients diagnosed with the United States Centers for Disease Control and Prevention (1994) criteria. Participants who had organic diseases that explained the CF were excluded. A total of 159 participants were asked to complete the QBYY-Q, the fatigue severity scale, and the Chalder fatigue scale. The latter two questionnaires were used to assess convergent validity with the QBYY-Q. Among the 129 CF participants, 70 and 59 had chronic fatigue syndrome and idiopathic chronic fatigue, respectively. Two Korean medical doctors independently assessed participants' qi, blood, yin, and yang deficiency patterns using QBYY deficiency pattern identification guidelines. Based on the results of a preliminary study of the QBYY-Q, we selected 32 reliable items for symptoms corresponding to each deficiency pattern. The items were used to estimate internal consistency and construct validity. Multinomial logistic regression analysis was performed for scores on each deficiency pattern. RESULTS: The data were means and standard deviations or numbers of participants and proportions for continuous and categorical variables, respectively. A statistical significance level of $P < 0.05$ was assumed. The QBYY-Q showed satisfactory internal consistency. Explanatory factor analysis extracted two factors for each deficiency pattern. The percentages of explained variance for qi, blood, yin, and yang deficiency were 45.1, 58.0, 52.2, and 63.4 %, respectively. Each QBYY-Q deficiency score was positively associated with each corresponding deficiency pattern. Qi deficiency was used as a reference category. Odds ratios of blood, yin, and yang deficiency were 10.97, 10.69, and 14.64, respectively. CONCLUSION: The QBYY-Q was suitable for estimating the influences of qi, blood, yin, and yang deficiencies in CF. Trial registration This trial was registered with the Korean Clinical Trial Register (KCT0001199).
Koçyiğit BF(1), Gür A(2), Altındağ Ö(2), Akyol A(2), Gürsoy S(2).	(1)Department of Physical Medicine and Rehabilitation, Gaziantep University Faculty of Medicine, Gaziantep, Turkey. bfk2701@hotmail.com. (2)Department of Physical Medicine and Rehabilitation, Gaziantep University Faculty of Medicine, Gaziantep, Turkey.	Comparison of education and balneotherapy efficacy in patients with fibromyalgia syndrome: A randomized, controlled clinical study.	183. Agri. 2016 Apr;28(2):72-8.	OBJECTIVES: Fibromyalgia is a disease characterized by chronic, widespread pain. Pharmacological and non-pharmacological treatment methods are used. The aim of the present study was to determine the effect of balneotherapy on treatment of fibromyalgia syndrome, compared with education alone. METHODS: A total of 66 patients diagnosed with fibromyalgia syndrome were randomly separated into balneotherapy and control groups. Patients in both groups were informed about fibromyalgia syndrome. In addition, the balneotherapy group received 21 sessions of spa treatment with 34.8 °C thermomineral water, attending the spa 5 days a week. Patients were evaluated by visual analogue scale, tender point count, fibromyalgia impact questioning, and modified fatigue impact scale at initiation of treatment on the 15th day, 1st month, 3rd month, and 6th month. Evaluations were performed by the same doctor. RESULTS: Statistically significant improvement was detected in all parameters, compared to starting evaluation, in both groups. Most improved results

				among all parameters were observed in the balneotherapy group on the first 3-month follow-up. In addition, all parameters beyond tender point count and modified fatigue impact were improved on 6-month follow-up. CONCLUSION: It was concluded that addition of balneotherapy to patient education has both short- and long-term beneficial effects on female patients with fibromyalgia.
Kraus MA(1), Fluck RJ(2), Weinhandl ED(3), Kansal S(4), Copland M(5), Komenda P(6), Finkelstein FO(7).	(1)Indiana University Medical School, Indianapolis, IN. (2)Department of Renal Medicine, Royal Derby Hospital, Derby, United Kingdom. (3)Department of Pharmaceutical Care and Health Systems, College of Pharmacy, University of Minnesota, Minneapolis, MN. Electronic address: wein0205@umn.edu. (4)Department of Nephrology and Hypertension, Cleveland Clinic, Cleveland, OH. (5)Division of Nephrology, University of British Columbia, Vancouver, Canada. (6)Section of Nephrology, Department of Medicine, University of Manitoba, Winnipeg, Canada; Department of Community Health Sciences, University of Manitoba, Winnipeg,	Intensive Hemodialysis and Health-Related Quality of Life.	62. Am J Kidney Dis. 2016 Nov;68(5S1):S33-S42.	Diminished health-related quality of life (HRQoL) is common in dialysis patients and associated with increased risks for morbidity and mortality. Patients may present limitations in both physical and mental HRQoL. Poor physical HRQoL may be defined by limited physical function, role limitations due to physical health, dissatisfaction with physical ability, and impaired mobility. Sleep disorders such as obstructive sleep apnea, restless legs, and fatigue are typical manifestations of poor physical HRQoL in dialysis patients. Poor mental HRQoL may be defined by depressive thinking, lack of positive affect, anxiety, and feelings of social isolation. The prevalence of depression is high in dialysis patients. Intensive hemodialysis (HD) can positively address HRQoL. In 3 randomized clinical trials, relative to conventional HD, intensive HD increased physical and mental component summary scores from the 36-Item Short-Form Health Survey (SF-36), although individual treatment effects of daily nocturnal HD were not statistically significant. In another large prospective study, initiation of short daily HD therapy was followed after 12 months by improvements in all SF-36 domains, sleep quality, and restless legs symptoms. In a small study of nocturnal HD, apnea and hypopnea episodes per hour decreased by almost 70% after conversion from conventional HD. Intensive HD is also associated with a large reduction in postdialysis recovery time. In contrast, 2 randomized clinical trials failed to demonstrate statistically significant effects of intensive HD on the Beck Depression Inventory score despite a significant decrease in Beck Depression Inventory score in the prospective study of short daily HD. Furthermore, intensive HD may not improve objective physical performance and can increase burden on caregivers in the home setting. In conclusion, intensive HD potentially can address both physical and mental aspects of poor HRQoL relative to conventional HD. However, more studies are needed to understand the effects of intensive HD, including specific schedules, on HRQoL.

	Canada; Seven Oaks General Hospital Renal Program, Winnipeg, Canada. (7)Yale University School of Medicine, New Haven, CT.			
Kreijne JE(1), Lie MR(2), Vogelaar L(2), van der Woude CJ(2).	(1)Department of Gastroenterology & Hepatology, Erasmus MC, Rotterdam, The Netherlands j.kreijne@erasmusmc.nl. (2)Department of Gastroenterology & Hepatology, Erasmus MC, Rotterdam, The Netherlands.	Practical Guideline for Fatigue Management in Inflammatory Bowel Disease.	342. J Crohns Colitis. 2016 Jan;10(1):105-11.	During active inflammatory bowel disease (IBD) fatigue is a common symptom, which seems related to active gut inflammation. However, even in remission many patients suffer from fatigue that negatively affects quality of life and work productivity. Currently, robust knowledge on the pathogenesis and treatment of IBD-related fatigue is lacking. In order to alleviate the burden of IBD-related fatigue, a systematic approach is mandatory. We propose a fatigue attention cycle to enhance identification, evaluation and management of fatigued IBD patients. The benefits of the cycle are twofold. Firstly, it allows the systematic and uniform identification of patients with severe fatigue, in turn allowing tailored non-pharmacological and pharmacological interventions. Secondly, uniform identification of such patients creates a well-defined patient base to investigate the underlying pathogenesis of fatigue, resulting in a greater understanding of this debilitating phenomenon and possibly resulting in the discovery of predictive factors and new treatment interventions.
Lago Blanco E(1), Puiguriguer Ferrando J(2), Rodríguez Enríquez M(3), Agüero Gento L(3), Salvà Coll J(4), Pizà Portell MR(3).	(1)Sección de Psicología Clínica, Servicio de Psiquiatría, Hospital Universitario Son Espases, Mallorca, España. Electronic address: eva.lago@ssib.es. (2)Sección de Toxicología, Servicio de Urgencias, Hospital Universitario Son Espases, Mallorca, España. (3)Sección de Psicología Clínica, Servicio de Psiquiatría, Hospital Universitario Son Espases, Mallorca, España. (4)Servicio de Psiquiatría, Hospital	[Multiple chemical sensitivity: Clinical evaluation of the severity and psychopathological profile]. [Article in Spanish]	326. Med Clin (Barc). 2016 Feb 5;146(3):108-11.	INTRODUCTION AND OBJECTIVE: Multiple chemical sensitivity (MCS) is a multisystem disorder of controversial etiology, affecting some subjects when exposed to chemicals at no harmful concentrations. The objective of this paper is to describe the epidemiological, clinical and psychological features of a sample of patients with MCS for further specific group treatment. PATIENS AND METHOD: Descriptive study of patients diagnosed with MCS in a toxicology unit. We administered the Quick Environmental Exposure and Sensitivity Inventory, the structured interview SCID-II, the anxiety scale HAS and the type A personality test, PCTA. RESULTS: Seventy-three patients were included. The mean age was 52,6 years (range 33-77; SD 9.29). Sixty-six were females (90.4%). Fifty-three percent were classified as i-ii and ii grade. Sixty-one patients (83%) presented some type of comorbidity, mainly chronic pain, fibromyalgia and chronic fatigue. They exhibited higher levels of anxiety (average score of 19.2), prevalence of phobic-avoidant traits of personality and type A behavior in 31.1%. CONCLUSIONS: MCS affects middle-aged women with comorbidities (chronic pain, fibromyalgia and chronic fatigue) and high anxiety and avoidance behaviors. This preliminary analysis should help provide a specific therapeutic approach to these patients.

	Universitario Son Espases, Mallorca, España.			
Lai JS(1), Beaumont JL(1), Diaz J(2), Khan S(2), Cella D(1).	(1)Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois. (2)Novartis Pharma AG, Basel, Switzerland.	Validation of a short questionnaire to measure symptoms and functional limitations associated with hand-foot syndrome and mucositis in patients with metastatic renal cell carcinoma.	338. Cancer. 2016 Jan 15;122(2):287-95.	BACKGROUND: Hand-foot syndrome and mucositis/stomatitis are frequent adverse events (AEs) of treatment with tyrosine kinase inhibitors in cancer therapy. Quality-of-life instruments that measure the functional consequences of these AEs are needed to assess the impact of therapeutic interventions and to guide patient care. The Hand-Foot and Mucositis Symptom and Impact Questionnaire (HAMSIQ [formerly the Supplementary Quality of Life Questionnaire]) was used in the COMPARZ trial (Pazopanib vs Sunitinib in the Treatment of Locally Advanced and/or Metastatic Renal Cell Carcinoma [national clinical trial no. NCT00720941]) and the PISCES study (Patient Preference Study of Pazopanib vs Sunitinib in Advanced or Metastatic Kidney Cancer [clinicaltrials.gov NCT01064310]) to assess mouth/throat and hand/foot soreness symptoms and subsequent limitations in patients receiving pazopanib or sunitinib for metastatic renal cell carcinoma. The objective of the current analysis was to validate the HAMSIQ using data from the PISCES study. METHODS: The HAMSIQ was administered in the PISCES study at baseline and every 2 weeks over two 10-week periods to patients who were receiving pazopanib or sunitinib. Data from the first 10-week period were used to assess the feasibility, validity, and responsiveness of the HAMSIQ. RESULTS: In total, ≥85% of 169 patients completed the HAMSIQ (excluding the item concerning days off work). Correlations among items within the same limitation subscale generally were high (Cronbach $\alpha \geq .80$). HAMSIQ limitation scores differentiated patients according to their baseline performance status and severity of soreness. Small-to-moderate correlations were observed for the symptoms/limitation scores and for changes from baseline scores between the HAMSIQ and the Functional Assessment of Chronic Illness Therapy fatigue survey. The HAMSIQ demonstrated responsiveness to changes in clinical status and the development of hand-foot syndrome AEs over time. CONCLUSIONS: The HAMSIQ is a feasible, valid, reliable, and responsive instrument for assessing the impact of hand-foot syndrome and mucositis in patients receiving tyrosine kinase inhibitors. Cancer 2016;122:287-295. © 2015 American Cancer Society.
Lami MJ(1), Martínez MP(2), Sánchez AI(2), Miró E(2), Diener FN(1), Prados G(3), Guzmán MA(3).	(1)Department of Personality, Assessment, and Psychological Treatment, Faculty of Psychology, University of Granada, Granada, Spain. (2)Mind, Brain and Behavior	Gender Differences in Patients with Fibromyalgia Undergoing Cognitive-Behavioral Therapy for Insomnia: Preliminary Data.	292. Pain Pract. 2016 Feb;16(2):E23-34.	Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome that significantly affects patients' quality of life. Its main symptoms are pain, fatigue, and sleep disturbances.AIM: The aim of this study was to assess the efficacy of cognitive-behavioral therapy for insomnia (CBT-I) in men and women with FM and compare sleep and clinical features between both genders. METHODS: Fifteen women and 13 men were selected to participate in nine weekly CBT-I sessions that involved completing several self-reported questionnaires at pretreatment, post-treatment, and follow-up. Patients were recruited from the Rheumatology Service and Pain Unit of Hospital and a fibromyalgia association. Group psychotherapy was performed at clinical unit of the

	Research Center (CIMCYC), University of Granada, Granada, Spain. (3)Internal Medicine Service, Virgen de las Nieves University Hospital, and Rheumatology Service, Virgen de las Nieves University Hospital, Granada, Spain.			Faculty of Psychology. RESULTS: Both groups showed significant clinical and statistical improvements in sleep quality and the main symptoms associated with FM (ie, pain intensity, fatigue, anxiety, pain catastrophizing, and pain-related anxiety). Differential treatment responsiveness between sexes was observed. Male group exhibited significant changes at post-treatment in sleep disturbances and pain-related anxiety and catastrophizing. The female group showed post-treatment improvements in sleep latency, general fatigue, and depression, which persisted at follow-up. CONCLUSIONS: Differential responses to treatment between men and women were observed in some sleep- and pain-related variables. Outcomes show the needed to design different treatments for men and women with FM is discussed.
Landi A(1), Broadhurst D(2), Vernon SD(3), Tyrrell DL(4), Houghton M(5).	(1)Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, Canada. Electronic address: landi@ualberta.ca. (2)Department of Medicine, Katz Group Centre for Pharmacy & Health, University of Alberta, Edmonton, AB T6G 2E1, Canada. (3)Bateman Horne Center, 1002 E. South Temple, Suite 408, Salt Lake City, UT 84102, USA. (4)Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, Canada. (5)Li Ka Shing Institute of Virology, Department of Medical Microbiology	Reductions in circulating levels of IL-16, IL-7 and VEGF-A in myalgic encephalomyelitis/chronic fatigue syndrome.	329. Cytokine. 2016 Feb;78:27-36.	Recently, differences in the levels of various chemokines and cytokines were reported in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) as compared with controls. Moreover, the analyte profile differed between chronic ME/CFS patients of long duration versus patients with disease of less than 3years. In the current study, we measured the plasma levels of 34 cytokines, chemokines and growth factors in 100 chronic ME/CFS patients of long duration and in 79 gender and age-matched controls. We observed highly significant reductions in the concentration of circulating interleukin (IL)-16, IL-7, and Vascular Endothelial Growth Factor A (VEGF-A) in ME/CFS patients. All three biomarkers were significantly correlated in a multivariate cluster analysis. In addition, we identified significant reductions in the concentrations of fractalkine (CX3CL1) and monokine-induced-by-IFN-γ (MIG; CXCL9) along with increases in the concentrations of eotaxin 2 (CCL24) in ME/CFS patients. Our data recapitulates previous data from another USA ME/CFS cohort in which circulating levels of IL-7 were reduced. Also, a reduced level of VEGF-A was reported previously in sera of patients with Gulf War Illness as well as in cerebral spinal fluid samples from a different cohort of USA ME/CFS patients. To our knowledge, we are the first to test for levels of IL-16 in ME/CFS patients. In combination with previous data, our work suggests that the clustered reduction of IL-7, IL-16 and VEGF-A may have physiological relevance to ME/CFS disease. This profile is ME/CFS-specific since measurement of the same analytes present in chronic infectious and autoimmune liver diseases, where persistent fatigue is also a major symptom, failed to demonstrate the same changes. Further studies of other ME/CFS and overlapping disease cohorts are warranted in future.

	and Immunology, Canada. Electronic address: michael.houghton@ualberta.ca.			
Landmark L, Lindgren RM, Sivertsen B, Magnus P, Conradi S, Thorvaldsen SN, Stanghelle JK.		Chronic fatigue syndrome and experience with the Lightning Process.	247. Tidsskr Nor Laegeforen. 2016 Mar 15;136(5):396.	
Larun L(1), Brurberg KG, Odgaard-Jensen J, Price JR.	(1)Norwegian Insitute of Public Health, Postboks 4404 Nydalen, Oslo, Norway, N-0403.	Exercise therapy for chronic fatigue syndrome.	156. Cochrane Database Syst Rev. 2016 Jun 24;(6):CD003200.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterised by persistent, medically unexplained fatigue, as well as symptoms such as musculoskeletal pain, sleep disturbance, headaches and impaired concentration and short-term memory. CFS presents as a common, debilitating and serious health problem. Treatment may include physical interventions, such as exercise therapy, which was last reviewed in 2004. OBJECTIVES: The objective of this review was to determine the effects of exercise therapy (ET) for patients with CFS as compared with any other intervention or control.• Exercise therapy versus 'passive control' (e.g. treatment as usual, waiting-list control, relaxation, flexibility).• Exercise therapy versus other active treatment (e.g. cognitive-behavioural therapy (CBT), cognitive treatment, supportive therapy, pacing, pharmacological therapy such as antidepressants).• Exercise therapy in combination with other specified treatment strategies versus other specified treatment strategies (e.g. exercise combined with pharmacological treatment vs pharmacological treatment alone). SEARCH METHODS: We searched The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR), the Cochrane Central Register of Controlled Trials (CENTRAL) and SPORTDiscus up to May 2014 using a comprehensive list of free-text terms for CFS and exercise. We located unpublished or ongoing trials through the World Health Organization (WHO) International Clinical Trials Registry Platform (to May 2014). We screened reference lists of retrieved articles and contacted experts in the field for additional studies SELECTION CRITERIA: Randomised controlled trials involving adults with a primary diagnosis of CFS who were able to participate in exercise therapy. Studies had to compare exercise therapy with passive control, psychological therapies, adaptive pacing therapy or pharmacological therapy. DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, risk of bias assessments and data extraction. We combined continuous measures of outcomes using mean differences (MDs) and standardised mean differences (SMDs). We combined serious adverse reactions and drop-outs using risk ratios (RRs). We calculated an overall effect size with 95% confidence intervals (CIs) for

				each outcome. MAIN RESULTS: We have included eight randomised controlled studies and have reported data from 1518 participants in this review. Three studies diagnosed individuals with CFS using the 1994 criteria of the Centers for Disease Control and Prevention (CDC); five used the Oxford criteria. Exercise therapy lasted from 12 to 26 weeks. Seven studies used variations of aerobic exercise therapy such as walking, swimming, cycling or dancing provided at mixed levels in terms of intensity of the aerobic exercise from very low to quite rigorous, whilst one study used anaerobic exercise. Control groups consisted of passive control (eight studies; e.g. treatment as usual, relaxation, flexibility) or CBT (two studies), cognitive therapy (one study), supportive listening (one study), pacing (one study), pharmacological treatment (one study) and combination treatment (one study). Risk of bias varied across studies, but within each study, little variation was found in the risk of bias across our primary and secondary outcome measures.Investigators compared exercise therapy with 'passive' control in eight trials, which enrolled 971 participants. Seven studies consistently showed a reduction in fatigue following exercise therapy at end of treatment, even though the fatigue scales used different scoring systems: an 11-item scale with a scoring system of 0 to 11 points (MD -6.06, 95% CI -6.95 to -5.17; one study, 148 participants; low-quality evidence); the same 11-item scale with a scoring system of 0 to 33 points (MD -2.82, 95% CI -4.07 to -1.57; three studies, 540 participants; moderate-quality evidence); and a 14-item scale with a scoring system of 0 to 42 points (MD -6.80, 95% CI -10.31 to -3.28; three studies, 152 participants; moderate-quality evidence). Serious adverse reactions were rare in both groups (RR 0.99, 95% CI 0.14 to 6.97; one study, 319 participants; moderate-quality evidence), but sparse data made it impossible for review authors to draw conclusions. Study authors reported a positive effect of exercise therapy at end of treatment with respect to sleep (MD -1.49, 95% CI -2.95 to -0.02; two studies, 323 participants), physical functioning (MD 13.10, 95% CI 1.98 to 24.22; five studies, 725 participants) and self-perceived changes in overall health (RR 1.83, 95% CI 1.39 to 2.40; four studies, 489 participants). It was not possible for review authors to draw conclusions regarding the remaining outcomes.Investigators compared exercise therapy with CBT in two trials (351 participants). One trial (298 participants) reported little or no difference in fatigue at end of treatment between the two groups using an 11-item scale with a scoring system of 0 to 33 points (MD 0.20, 95% CI -1.49 to 1.89). Both studies measured differences in fatigue at follow-up, but neither found differences between the two groups using an 11-item fatigue scale with a scoring system of 0 to 33 points (MD 0.30, 95% CI -1.45 to 2.05) and a nine-item Fatigue Severity Scale with a scoring system of 1 to 7 points (MD 0.40, 95% CI -0.34 to 1.14). Serious adverse reactions were rare in both groups (RR 0.67, 95% CI 0.11 to 3.96). We observed little or no difference in physical functioning, depression, anxiety and sleep, and we were not able to draw any conclusions with regard to pain, self-perceived changes in overall health, use of health service resources and drop-out rate.With regard

				to other comparisons, one study (320 participants) suggested a general benefit of exercise over adaptive pacing, and another study (183 participants) a benefit of exercise over supportive listening. The available evidence was too sparse to draw conclusions about the effect of pharmaceutical interventions. AUTHORS' CONCLUSIONS: Patients with CFS may generally benefit and feel less fatigued following exercise therapy, and no evidence suggests that exercise therapy may worsen outcomes. A positive effect with respect to sleep, physical function and self-perceived general health has been observed, but no conclusions for the outcomes of pain, quality of life, anxiety, depression, drop-out rate and health service resources were possible. The effectiveness of exercise therapy seems greater than that of pacing but similar to that of CBT. Randomised trials with low risk of bias are needed to investigate the type, duration and intensity of the most beneficial exercise intervention.
Larun L(1), Brurberg KG, Odgaard-Jensen J, Price JR.	(1)Primary Health Care Unit, Norwegian Knowledge Centre for the Health Services, PO Box 7004, St Olav's plass, Oslo, Norway, N-0130.	Exercise therapy for chronic fatigue syndrome.	287. Cochrane Database Syst Rev. 2016 Feb 7;2:CD003200.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterised by persistent, medically unexplained fatigue, as well as symptoms such as musculoskeletal pain, sleep disturbance, headaches and impaired concentration and short-term memory. CFS presents as a common, debilitating and serious health problem. Treatment may include physical interventions, such as exercise therapy, which was last reviewed in 2004. OBJECTIVES: The objective of this review was to determine the effects of exercise therapy (ET) for patients with CFS as compared with any other intervention or control.• Exercise therapy versus 'passive control' (e.g. treatment as usual, waiting-list control, relaxation, flexibility).• Exercise therapy versus other active treatment (e.g. cognitive-behavioural therapy (CBT), cognitive treatment, supportive therapy, pacing, pharmacological therapy such as antidepressants).• Exercise therapy in combination with other specified treatment strategies versus other specified treatment strategies (e.g. exercise combined with pharmacological treatment vs pharmacological treatment alone). SEARCH METHODS: We searched The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR), the Cochrane Central Register of Controlled Trials (CENTRAL) and SPORTDiscus up to May 2014 using a comprehensive list of free-text terms for CFS and exercise. We located unpublished or ongoing trials through the World Health Organization (WHO) International Clinical Trials Registry Platform (to May 2014). We screened reference lists of retrieved articles and contacted experts in the field for additional studies SELECTION CRITERIA: Randomised controlled trials involving adults with a primary diagnosis of CFS who were able to participate in exercise therapy. Studies had to compare exercise therapy with passive control, psychological therapies, adaptive pacing therapy or pharmacological therapy. DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, risk of bias assessments and data extraction. We combined continuous measures of outcomes using mean differences (MDs) and standardised mean differences (SMDs). We combined serious adverse reactions and drop-outs using risk ratios (RRs). We calculated an overall effect size with 95% confidence intervals (CIs) for

				each outcome. MAIN RESULTS: We have included eight randomised controlled studies and have reported data from 1518 participants in this review. Three studies diagnosed individuals with CFS using the 1994 criteria of the Centers for Disease Control and Prevention (CDC); five used the Oxford criteria. Exercise therapy lasted from 12 to 26 weeks. Seven studies used variations of aerobic exercise therapy such as walking, swimming, cycling or dancing provided at mixed levels in terms of intensity of the aerobic exercise from very low to quite rigorous, whilst one study used anaerobic exercise. Control groups consisted of passive control (eight studies; e.g. treatment as usual, relaxation, flexibility) or CBT (two studies), cognitive therapy (one study), supportive listening (one study), pacing (one study), pharmacological treatment (one study) and combination treatment (one study). Risk of bias varied across studies, but within each study, little variation was found in the risk of bias across our primary and secondary outcome measures.Investigators compared exercise therapy with 'passive' control in eight trials, which enrolled 971 participants. Seven studies consistently showed a reduction in fatigue following exercise therapy at end of treatment, even though the fatigue scales used different scoring systems: an 11-item scale with a scoring system of 0 to 11 points (MD -6.06, 95% CI -6.95 to -5.17; one study, 148 participants; low-quality evidence); the same 11-item scale with a scoring system of 0 to 33 points (MD -2.82, 95% CI -4.07 to -1.57; three studies, 540 participants; moderate-quality evidence); and a 14-item scale with a scoring system of 0 to 42 points (MD -6.80, 95% CI -10.31 to -3.28; three studies, 152 participants; moderate-quality evidence). Serious adverse reactions were rare in both groups (RR 0.99, 95% CI 0.14 to 6.97; one study, 319 participants; moderate-quality evidence), but sparse data made it impossible for review authors to draw conclusions. Study authors reported a positive effect of exercise therapy at end of treatment with respect to sleep (MD -1.49, 95% CI -2.95 to -0.02; two studies, 323 participants), physical functioning (MD 13.10, 95% CI 1.98 to 24.22; five studies, 725 participants) and self-perceived changes in overall health (RR 1.83, 95% CI 1.39 to 2.40; four studies, 489 participants). It was not possible for review authors to draw conclusions regarding the remaining outcomes.Investigators compared exercise therapy with CBT in two trials (351 participants). One trial (298 participants) reported little or no difference in fatigue at end of treatment between the two groups using an 11-item scale with a scoring system of 0 to 33 points (MD 0.20, 95% CI -1.49 to 1.89). Both studies measured differences in fatigue at follow-up, but neither found differences between the two groups using an 11-item fatigue scale with a scoring system of 0 to 33 points (MD 0.30, 95% CI -1.45 to 2.05) and a nine-item Fatigue Severity Scale with a scoring system of 1 to 7 points (MD 0.40, 95% CI -0.34 to 1.14). Serious adverse reactions were rare in both groups (RR 0.67, 95% CI 0.11 to 3.96). We observed little or no difference in physical functioning, depression, anxiety and sleep, and we were not able to draw any conclusions with regard to pain, self-perceived changes in overall health, use of health service resources and drop-out rate.With regard

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Larun L(1), Brurberg KG(2), Odgaard-Jensen J(3), Price JR(4).	(1)Norwegian Insitute of Public Health, Postboks 4404 Nydalen, Oslo, Norway, N-0403. (2)Unit for Primary Care and Clinical Procedures, Norwegian Institute of Public Health, PO Box 4404, Nydalen, Oslo, Norway, 0403. (3)Biometrics, Link Medical Research AS, Box 4382 Nydalen, Oslo, Norway, N-0402. (4)Department of Psychiatry, University of Oxford, The Warneford Hospital, Headington, Oxford, UK, OX3 7JX.	Exercise therapy for chronic fatigue syndrome.	10. Cochrane Database Syst Rev. 2016 Dec 20;12:CD003200.	Update of Cochrane Database Syst Rev. 2016 Jun 24;(6):CD003200. BACKGROUND: Chronic fatigue syndrome (CFS) is characterised by persistent, medically unexplained fatigue, as well as symptoms such as musculoskeletal pain, sleep disturbance, headaches and impaired concentration and short-term memory. CFS presents as a common, debilitating and serious health problem. Treatment may include physical interventions, such as exercise therapy, which was last reviewed in 2004. OBJECTIVES: The objective of this review was to determine the effects of exercise therapy (ET) for patients with CFS as compared with any other intervention or control.• Exercise therapy versus 'passive control' (e.g. treatment as usual, waiting-list control, relaxation, flexibility).• Exercise therapy versus other active treatment (e.g. cognitive-behavioural therapy (CBT), cognitive treatment, supportive therapy, pacing, pharmacological therapy such as antidepressants).• Exercise therapy in combination with other specified treatment strategies versus other specified treatment strategies (e.g. exercise combined with pharmacological treatment vs pharmacological treatment alone). SEARCH METHODS: We searched The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR), the Cochrane Central Register of Controlled Trials (CENTRAL) and SPORTDiscus up to May 2014 using a comprehensive list of free-text terms for CFS and exercise. We located unpublished or ongoing trials through the World Health Organization (WHO) International Clinical Trials Registry Platform (to May 2014). We screened reference lists of retrieved articles and contacted experts in the field for additional studies SELECTION CRITERIA: Randomised controlled trials involving adults with a primary diagnosis of CFS who were able to participate in exercise therapy. Studies had to compare exercise therapy with passive control, psychological therapies, adaptive pacing therapy or pharmacological therapy. DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, risk of bias assessments and data extraction. We combined continuous measures of outcomes using mean differences (MDs) and standardised mean differences (SMDs). We combined serious adverse reactions and drop-outs using risk

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				changes in overall health, use of health service resources and drop-out rate.With regard to other comparisons, one study (320 participants) suggested a general benefit of exercise over adaptive pacing, and another study (183 participants) a benefit of exercise over supportive listening. The available evidence was too sparse to draw conclusions about the effect of pharmaceutical interventions. AUTHORS' CONCLUSIONS: Patients with CFS may generally benefit and feel less fatigued following exercise therapy, and no evidence suggests that exercise therapy may worsen outcomes. A positive effect with respect to sleep, physical function and self-perceived general health has been observed, but no conclusions for the outcomes of pain, quality of life, anxiety, depression, drop-out rate and health service resources were possible. The effectiveness of exercise therapy seems greater than that of pacing but similar to that of CBT. Randomised trials with low risk of bias are needed to investigate the type, duration and intensity of the most beneficial exercise intervention.
Larun L(1), Odgaard-Jensen J, Price JR, Brurberg KG.	(1)Primary Health Care Unit, Norwegian Knowledge Centre for the Health Services, Oslo, Norway - ela@nokc.no.	An abridged version of the Cochrane review of exercise therapy for chronic fatigue syndrome.	345. Eur J Phys Rehabil Med. 2016 Apr;52(2):244-52. Epub 2015 Sep 16.	BACKGROUND: Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME) is estimated to affect between 2 in 1000 and 2 in 100 adults depending on how diagnostic criteria are applied. Patients with CFS have long-lasting fatigue in addition to symptoms including muscle pain, concentration and sleep problems. These symptoms cause significant disability and distress to the people affected. This review is an update of a previous Cochrane review (2004) that showed that exercise therapy was a promising treatment for adults with CFS. AIM: The aim of this systematic review was to determine the effects of exercise therapy for patients with CFS. DESIGN: Systematic review. SETTING: Health care settings. POPULATION: Participants over 18 years with a primary diagnosis of CFS, able to attend an outpatient clinic for exercise therapy, were included. METHODS: We searched electronic databases, including SPORTDiscus, up to May 2014 using a comprehensive list of free-text terms for CFS and exercise. Randomized clinical trials from all health care settings with participants over 18 years with a primary diagnosis of CFS, able to attend an outpatient clinic for exercise therapy, were included. We have included 8 randomized clinical studies that reported data from 1518 participants. Seven studies used aerobic exercise such as walking, swimming, or cycling and one study used non-aerobic exercise. The exercise therapies lasted between 12 and 26 weeks. Meta-analysis was done when appropriate. RESULTS: Exercise therapy was more effective at reducing fatigue than "passive" treatments or no treatment at end of treatment. Exercise therapy also had a positive effect on people's daily physical functioning, sleep quality and self-rated overall health. Nearly twice as many patients reported improvement self-rated overall health after exercise therapy (40 per 100) compared to standard treatment (22 per 100). The evidence was too sparse and/or of too low quality to conclude if exercise therapy has an effect on pain, quality of life, anxiety or depression. Exercise therapy was not found to worsen symptoms for people with CFS, while serious side effects were rare in all exercise and comparison groups. CONCLUSIONS: Patiens

				with CFS may generally benefit from and feel less fatigued following exercise therapy, and no evidence suggests that exercise therapy may worsen outcomes. CLINICAL REHABILITATION IMPACT: Exercise therapy should be considered.
Lawson N(1), Hsieh CH(1), March D(2), Wang X(1).	(1)Department of Neurosurgery, Stanford University School of Medicine, Stanford, CA, USA. (2)Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA.	Elevated Energy Production in Chronic Fatigue Syndrome Patients.	69. J Nat Sci. 2016;2(10). pii: e221.	Chronic Fatigue Syndrome (CFS) is a debilitating disease characterized by physical and mental exhaustion. The underlying pathogenesis is unknown, but impairments in certain mitochondrial functions have been found in some CFS patients. To thoroughly reveal mitochondrial deficiencies in CFS patients, here we examine the key aspects of mitochondrial function in blood cells from a paired CFS patient-control series. Surprisingly, we discover that in patients the ATP levels are higher and mitochondrial cristae are more condensed compared to their paired controls, while the mitochondrial crista length, mitochondrial size, shape, density, membrane potential, and enzymatic activities of the complexes in the electron transport chain remain intact. We further show that the increased ATP largely comes from non-mitochondrial sources. Our results indicate that the fatigue symptom in this cohort of patients is unlikely caused by lack of ATP and severe mitochondrial malfunction. On the contrary, it might be linked to a pathological mechanism by which more ATP is produced by non-mitochondrial sources.
Leblebici B(1), Özelsancak R(2), Yılmaz EE(1), Doruk P(1).	(1)Department of Physical Medicine and Rehabilitation, Baskent University Faculty of Medicine, Adana Medical and Research Center, Adana, Turkey. (2)Department of Nephrology, Baskent University Faculty of Medicine, Adana Medical and Research Center, Adana, Turkey.	Fibromyalgia syndrome in Turkish hemodialysis patients.	356. Hemodial Int. 2016 Jan;20(1):106-10.	The aim of our study was to evaluate the frequency of fibromyalgia syndrome (FMS) in hemodialysis (HD) patients and to assess whether this syndrome is associated with gender, age, duration of HD, or various laboratory parameters. This study was composed of 221 chronic HD patients (99 females and 122 males), and we recorded each participant's age, gender, causes of kidney failure, HD duration, education level, and symptoms related to FMS, which was diagnosed according to the 2010 American College of Rheumatology criteria. We documented the laboratory parameters for all patients. In addition, patients with FMS filled out the Fibromyalgia Impact Questionnaire. Twenty-two patients met the diagnostic criteria for FMS (9%), and there were no statistically significant differences related to age, gender, or HD duration between FMS and non-FMS groups ($P > 0.05$). In addition, the education levels were lower in patients diagnosed with FMS ($P < 0.05$), and there were statistically significant differences related to sleep disturbance, fatigue, and cognitive symptoms between the two groups ($P < 0.05$) as well. However, their laboratory parameters were similar ($P > 0.05$). There was a higher prevalence of FMS in HD patients than in the general population. Sleep disturbances, fatigue, education level, and cognitive symptoms were associated with FMS, but there was no correlation between the laboratory parameters and this condition.
Lee JH(1,)(2), Kim JE(1,)(2,)(3), Jang YJ(1,)(4), Lee CC(5), Lim TG(1,)(2), Jung SK(1,)(4), Lee	(1)WCU Biomodulation Major, Department of Agricultural Biotechnology and Center for Food and	Dehydroglyasperin C suppresses TPA-induced cell transformation through direct inhibition of MKK4 and PI3K.	366. Mol Carcinog. 2016 May;55(5):552-62.	Bioactive natural compounds from plant-derived sources have received substantial interest due to their potential therapeutic and preventive effects toward various human diseases. Licorice (Glycyrrhiza), a frequently-used component in traditional oriental medicines, has been incorporated into recipes not only to enhance taste, but also to treat various conditions including inflammation, chronic fatigue syndrome, and even cancer. Dehydroglyasperin C (DGC) is a major isoflavone found in the root of

E(1,)(6), Lim SS(7), Heo YS(8), Seo SG(1,)(2), Son JE(1,)(2), Kim JR(1,)(2), Lee CY(5,)(9), Lee HJ(3), Lee KW(1,)(2,)(3,)(10).	Bioconvergence, Seoul National University, Seoul, Republic of Korea. (2)Advanced Institutes of Convergence Technology, Seoul National University, Suwon, Republic of Korea. (3)Research Institute of Bio Food Industry, Institute of Green Bio Science and Technology, Seoul National University, Pyeongchang, Republic of Korea. (4)Division of Creative Food Science for Health, Korea Food Research Institute, Seongnam, Republic of Korea. (5)Department of Food Science and Technology, Cornell University, Ithaca, NY, 14456, USA. (6)Traditional Alcoholic Beverage Research Team, Korea Food Research Institute, Seongnam, Republic of Korea. (7)Department of Food Science and Nutrition, Hallym University, Chuncheon, Republic of Korea.			licorice. In the present study, we investigated the cancer chemopreventive effect of DGC and the underlying molecular mechanisms involved, by analyzing its effects on 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced neoplastic cell transformation and cyclooxygenase (COX)-2 expression in JB6 P+ mouse epidermal cells. DGC treatment attenuated TPA-induced activator protein-1 (AP-1) and nuclear factor-κB (NF-κB) transcriptional activation, two major regulators of TPA-induced cell transformation, and COX-2 expression. TPA-induced phosphorylation of p38, JNK1/2 and Akt was also suppressed by DGC. Kinase assay data revealed that DGC inhibited the kinase activity of MKK4 and PI3K and this outcome was due to direct physical binding with DGC. Notably, DGC bound directly to MKK4 and PI3K in an ATP-competitive manner. Taken together, these results suggest that DGC exhibits cancer chemopreventive potential via its inhibitory effect on TPA-induced neoplastic cell transformation and COX-2 modulation through regulation of the MKK4 and PI3K pathways.

	(8)Department of Chemistry, Konkuk University, Seoul, Republic of Korea. (9)Department of Biochemistry, King Abdulaziz University, Jeddah, SA. (10)Institute on Aging, Seoul National University, Seoul, Republic of Korea.			
Lewith G(1), Stuart B(2), Chalder T(3), McDermott C(2), White PD(4).	(1)Primary Care and Population Sciences, University of Southampton, UK. Electronic address: gl3@soton.ac.uk. (2)Primary Care and Population Sciences, University of Southampton, UK. (3)Academic Department of Psychological Medicine, King's College London, Weston Education Centre, London, UK. (4)Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine, Queen Mary University, London, UK.	Complementary and alternative healthcare use by participants in the PACE trial of treatments for chronic fatigue syndrome.	140. J Psychosom Res. 2016 Aug;87:37-42.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is characterised by persistent fatigue, disability and a range of other symptoms. The PACE trial was randomised to compare four non-pharmacological treatments for patients with CFS in secondary care clinics. The aims of this sub study were to describe the use of complementary and alternative medicine (CAM) in the trial sample and to test whether CAM use correlated with an improved outcome. METHOD: CAM use was recorded at baseline and 52weeks. Logistic and multiple regression models explored relationships between CAM use and both patient characteristics and trial outcomes. RESULTS: At baseline, 450/640 (70%) of participants used any sort of CAM; 199/640 (31%) participants were seeing a CAM practitioner and 410/640 (64%) were taking a CAM medication. At 52weeks, those using any CAM fell to 379/589 (64%). Independent predictors of CAM use at baseline were female gender, local ME group membership, prior duration of CFS and treatment preference. At 52weeks, the associated variables were being female, local ME group membership, and not being randomised to the preferred trial arm. There were no significant associations between any CAM use and fatigue at either baseline or 52weeks. CAM use at baseline was associated with a mean (CI) difference of 4.10 (1.28, 6.91; p=0.024) increased SF36 physical function score at 52weeks, which did not reach the threshold for a clinically important difference. CONCLUSION: CAM use is common in patients with CFS. It was not associated with any clinically important trial outcomes.
Loades ME(1), Sheils EA(1), Crawley E(2).	(1) Department of Psychology, University of Bath, Bath, UK.	Treatment for paediatric chronic fatigue syndrome or myalgic	73. BMJ Open. 2016 Oct 11;6(10):e 012271.	OBJECTIVES: At least 30% of young people with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) also have symptoms of depression. This systematic review aimed to establish which treatment approaches for depression are effective and

	(2)School of Social and Community Medicine, University of Bristol, Bristol, UK.	encephalomyelitis (CFS/ME) and comorbid depression: a systematic review.		whether comorbid depression mediates outcome. SETTING: A systematic review was undertaken. The search terms were entered into MEDLINE, EMBASE, PsycInfo and the Cochrane library. PARTICIPANTS: Inclusion and exclusion criteria were applied to identify relevant papers. Inclusion criteria were children age <18, with CFS/ME, defined using CDC, NICE or Oxford criteria, and having completed a valid assessment for depression. RESULTS: 9 studies were identified which met the inclusion criteria, but none specifically tested treatments for paediatric CFS/ME with depression and none stratified outcome for those who were depressed compared with those who were not depressed. There is no consistent treatment approach for children with CFS/ME and comorbid depression, although cognitive-behavioural therapy for CFS/ME and a multicomponent inpatient programme for CFS/ME have shown some promise in reducing depressive symptoms. An antiviral medication in a small scale, retrospective, uncontrolled study suggested possible benefit. CONCLUSIONS: It is not possible to determine what treatment approaches are effective for depression in paediatric CFS/ME, nor to determine the impact of depression on the outcome of CFS/ME treatment. Young people with significant depression tend to have been excluded from previous treatment studies.
Loebel M(1), Grabowski P(2), Heidecke H(3), Bauer S(2), Hanitsch LG(2), Wittke K(2), Meisel C(4), Reinke P(5), Volk HD(6), Fluge Ø(7), Mella O(8), Scheibenbogen C(6).	(1)Institute for Medical Immunology, Charité University Medicine Berlin, Campus Virchow, Berlin, Germany. Electronic address: madlen.loebel@charite.de. (2)Institute for Medical Immunology, Charité University Medicine Berlin, Campus Virchow, Berlin, Germany. (3)CellTrend GmbH, Luckenwalde, Brandenburg, Germany. (4)Institute for Medical Immunology, Charité University Medicine Berlin, Campus Virchow, Berlin,	Antibodies to β adrenergic and muscarinic cholinergic receptors in patients with Chronic Fatigue Syndrome.	341. Brain Behav Immun. 2016 Feb;52:32-9.	Infection-triggered disease onset, chronic immune activation and autonomic dysregulation in CFS point to an autoimmune disease directed against neurotransmitter receptors. Autoantibodies against G-protein coupled receptors were shown to play a pathogenic role in several autoimmune diseases. Here, serum samples from a patient cohort from Berlin (n=268) and from Bergen with pre- and post-treatment samples from 25 patients treated within the KTS-2 rituximab trial were analysed for IgG against human α and β adrenergic, muscarinic (M) 1-5 acetylcholine, dopamine, serotonin, angiotensin, and endothelin receptors by ELISA and compared to a healthy control cohort (n=108). Antibodies against β2, M3 and M4 receptors were significantly elevated in CFS patients compared to controls. In contrast, levels of antibodies against α adrenergic, dopamine, serotonin, angiotensin, and endothelin receptors were not different between patients and controls. A high correlation was found between levels of autoantibodies and elevated IgG1-3 subclasses, but not with IgG4. Further patients with high β2 antibodies had significantly more frequently activated HLA-DR+ T cells and more frequently thyreoperoxidase and anti-nuclear antibodies. In patients receiving rituximab maintenance treatment achieving prolonged B-cell depletion, elevated β2 and M4 receptor autoantibodies significantly declined in clinical responder, but not in non-responder. We provide evidence that 29.5% of patients with CFS had elevated antibodies against one or more M acetylcholine and β adrenergic receptors which are potential biomarkers for response to B-cell depleting therapy. The association of autoantibodies with immune markers suggests that they activate B and T cells expressing β adrenergic and M acetylcholine receptors. Dysregulation of acetylcholine and adrenergic signalling could also explain various clinical symptoms of CFS.

	Germany; Labor Berlin GmbH, Immunology Department, Charité University Medicine Berlin, Campus Virchow, Berlin, Germany. (5)Department of Nephrology, Charité University Medicine Berlin, Germany; Berlin-Brandenburg Center for Regenerative Therapies (BCRT), Charité University Medicine Berlin, Germany. (6)Institute for Medical Immunology, Charité University Medicine Berlin, Campus Virchow, Berlin, Germany; Berlin-Brandenburg Center for Regenerative Therapies (BCRT), Charité University Medicine Berlin, Germany. (7)Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway. (8)Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway;			

	Department of Clinical Science, University of Bergen, Bergen, Norway.			
Loganovsky K(1), Perchuk I(1), Marazziti D(2).	(1)a State Institution "National Research Center for Radiation Medicine of the National Academy of Medical Sciences of Ukraine" , Kyiv , Ukraine. (2)b Dipartimento di Medicina Clinica e Sperimentale, Section of Psychiatry, University of Pisa , Pisa , Italy.	Workers on transformation of the shelter object of the Chernobyl nuclear power plant into an ecologically-safe system show qEEG abnormalities and cognitive dysfunctions: A follow-up study.	362. World J Biol Psychiatry. 2016 Dec;17(8):600-607. Epub 2015 May 23.	OBJECTIVES: The present study aimed at assessing bioelectric activity and cognitive functions in the workers on the conversion project of the "Shelter" object (SO) of the Chernobyl nuclear power plant into an environmentally safe system. METHODS: A total of 196 men were included and examined before (t0) and after (t1) working on the SO in the period 2004-2008. They underwent a qEEG and a battery of neuropsychological and psychiatric assessments. RESULTS: At t1, the organized type of qEEG shifted towards the disorganized one. An increase of spectral δ-power in the left frontotemporal area, of θ- and α-power in the left temporal area, with redistribution of α-activity to the front and reduction of dominant frequency in the left temporal area, were registered. Further, neurocognitive tests revealed the presence of mild cognitive disorders at t1. Interestingly, those subjects previously exposed to radiation with no consequences, were more resistant to these detrimental effects. CONCLUSIONS: Taken together, the disturbances observed may be considered as cognitive symptoms of a chronic fatigue syndrome resulting from the exposure to ionizing radiation. Simple and non-invasive assessments, such as those performed by us, may be helpful to detect early brain changes caused by the presence of radiological risk factors.
Loy BD(1), O'Connor PJ, Dishman RK.	(1)1Department of Neurology, Oregon Health and Science University, Portland, OR; 2Department of Kinesiology, University of Georgia, Athens, GA.	Effect of Acute Exercise on Fatigue in People with ME/CFS/SEID: A Meta-analysis.	192. Med Sci Sports Exerc. 2016 Oct;48(10):2003-12.	PURPOSE: A prominent symptom of myalgic encephalomyelitis, chronic fatigue syndrome, or systemic exertion intolerance disease (ME/CFS/SEID) is persistent fatigue that is worsened by physical exertion. Here the population effect of a single bout of exercise on fatigue symptoms in people with ME/CFS/SEID was estimated and effect moderators were identified. METHODS: Google Scholar was systematically searched for peer-reviewed articles published between February 1991 and May 2015. Studies were included where people diagnosed with ME/CFS/SEID and matched control participants completed a single bout of exercise and fatigue self-reports were obtained before and after exercise. Fatigue means, standard deviations, and sample sizes were extracted to calculate effect sizes and the 95% confidence interval. Effects were pooled using a random-effects model and corrected for small sample bias to generate mean Δ. Multilevel regression modeling adjusted for nesting of effects within studies. Moderators identified a priori were diagnostic criteria, fibromyalgia comorbidity, exercise factors (intensity, duration, and type), and measurement factors. RESULTS: Seven studies examining 159 people with ME/CFS/SEID met inclusion criteria, and 47 fatigue effects were derived. The mean fatigue effect was Δ = 0.73 (95% confidence interval = 0.24-1.23). Fatigue increases were larger for people with ME/CFS/SEID when fatigue was measured 4 h or more after exercise ended rather than during or immediately after exercise ceased. CONCLUSIONS: This preliminary evidence indicates that acute exercise increases fatigue in people with ME/CFS/SEID more than that in

				control groups, but effects were heterogeneous between studies. Future studies with no-exercise control groups of people with ME/CFS/SEID are needed to obtain a more precise estimate of the effect of exercise on fatigue in this population.
Lunde S(1), Kristoffersen EK(2,)(3), Sapkota D(1,)(4), Risa K(1), Dahl O(1,)(3), Bruland O(1,)(5), Mella O(1,)(3), Fluge Ø(1).	(1)Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway. (2)Department of Immunology and Transfusion Medicine, Haukeland University Hospital, Bergen, Norway. (3)Department of Clinical Science, University of Bergen, Haukeland University Hospital, Bergen, Norway. (4)Department of Clinical Medicine, University of Bergen, Haukeland University Hospital, Bergen, Norway. (5)Department of Medical Genetics and Molecular Medicine, Haukeland University Hospital, Bergen, Norway.	Serum BAFF and APRIL Levels, T-Lymphocyte Subsets, and Immunoglobulins after B-Cell Depletion Using the Monoclonal Anti-CD20 Antibody Rituximab in Myalgic Encephalopathy/Chronic Fatigue Syndrome.	113. PLoS One. 2016 Aug 18;11(8):e0161226.	Myalgic Encephalopathy/Chronic Fatigue Syndrome (ME/CFS) is a disease of unknown etiology. We have previously suggested clinical benefit from B-cell depletion using the monoclonal anti-CD20 antibody rituximab in a randomized and placebo-controlled study. Prolonged responses were then demonstrated in an open-label phase-II study with maintenance rituximab treatment. Using blood samples from patients in the previous two clinical trials, we investigated quantitative changes in T-lymphocyte subsets, in immunoglobulins, and in serum levels of two B-cell regulating cytokines during follow-up. B-lymphocyte activating factor of the tumor necrosis family (BAFF) in baseline serum samples was elevated in 70 ME/CFS patients as compared to 56 healthy controls ($p = 0.011$). There were no significant differences in baseline serum BAFF levels between patients with mild, moderate, or severe ME/CFS, or between responders and non-responders to rituximab. A proliferation-inducing ligand (APRIL) serum levels were not significantly different in ME/CFS patients compared to healthy controls at baseline, and no changes in serum levels were seen during follow-up. Immunophenotyping of peripheral blood T-lymphocyte subsets and T-cell activation markers at multiple time points during follow-up showed no significant differences over time, between rituximab and placebo groups, or between responders and non-responders to rituximab. Baseline serum IgG levels were significantly lower in patients with subsequent response after rituximab therapy compared to non-responders ($p = 0.03$). In the maintenance study, slight but significant reductions in mean serum immunoglobulin levels were observed at 24 months compared to baseline; IgG 10.6-9.5 g/L, IgA 1.8-1.5 g/L, and IgM 0.97-0.70 g/L. Although no functional assays were performed, the lack of significant associations of T- and NK-cell subset numbers with B-cell depletion, as well as the lack of associations to clinical responses, suggest that B-cell regulatory effects on T-cell or NK-cell subsets are not the main mechanisms for the observed improvements in ME/CFS symptoms observed in the two previous trials. The modest increase in serum BAFF levels at baseline may indicate an activated B-lymphocyte system in a subgroup of ME/CFS patients.
Maddali Bongi S(1), Paoletti G(2), Calà M(3), Del Rosso A(4), El Aoufy K(5), Mikhaylova S(6).	(1)Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Viale Largo Brambilla 3, 50134 Florence,	Efficacy of rehabilitation with Tai Ji Quan in an Italian cohort of patients with Fibromyalgia Syndrome.	122. Complement Ther Clin Pract. 2016 Aug;24:109-15.	BACKGROUND: Fibromyalgia Syndrome (FMS) is characterized by musculoskeletal pain, muscle tenderness leading to disability, impaired quality of life (QoL), fatigue and it is accompanied by sleep disorders and psychological distress. Mind body therapies (MBT), such as Tai Ji Quan (TJQ), use different techniques to facilitate the ability of the mind to influence disease characteristics and symptoms. Some studies showed that TJQ, in patients with rheumatic diseases, particularly FMS, improved QoL, disability and psychological distress. OBJECTIVES: To evaluate the efficacy of TJQ on disability, QoL, fatigue, sleep and psychological distress in an Italian cohort of FMS patients. METHODS:

	Italy. Electronic address: susanna.maddalibongi@gmail.com. (2)Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Viale Largo Brambilla 3, 50134 Florence, Italy. Electronic address: gianlucapaoletti@hotmail.com. (3)Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Viale Largo Brambilla 3, 50134 Florence, Italy. Electronic address: micha.wip@libero.it. (4)Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Viale Largo Brambilla 3, 50134 Florence, Italy. Electronic address: angela.delrosso@fastwebnet.it. (5)Department of			We enrolled 44 FMS patients: 22 patients (Experimental Group) participated to a course of Tai Ji Quan style of (2/week for 16 weeks); 22 patients (Control Group) participated to an educational course about FMS (2/week for 16 weeks). At baseline (T0) and at the end of treatment (T1), patients were assessed for disability [Fibromyalgia Impact Questionnaire (FIQ), Health Assessment Questionnaire (HAQ)], Quality of Life [Short-Form 36 (SF36)], fatigue [Functional Assessment of Chronic Illness-Fatigue (FACIT-F)], pain [Widespread Pain Index (WPI)], tenderness [Tender Points (TP)], Sleep Quality [Pittsburgh Sleep Quality Index (PSQI)] and mood disorders [Hospital Anxiety and Depression Scale (HADS)]. RESULTS: At T1 versus T0, patients of the Experimental Group showed a significant improvement in FIQ, FACIT, SF36 (Summary Physical Index, Physical activity, physical role, bodily pain, general health, vitality, emotional role limitations), in WPI, TP, PSQI (total, sleep duration, and sleep disturbance) and HADS (total score and anxiety subscale), while Patients in the Control Group did not improve in any parameter. CONCLUSIONS: In FMS patients TJQ, if performed by an expert physiotherapist, should be regarded as an effective rehabilitation method.

	Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Viale Largo Brambilla 3, 50134 Florence, Italy. Electronic address: khadija.ela92@gmail.com. (6)Department of Experimental and Clinical Medicine, Division of Rheumatology, University of Florence, Viale Largo Brambilla 3, 50134 Florence, Italy. Electronic address: svetlana.mkh@gmail.com.			
Mallet M(1), King E(1), White PD(2).	(1)Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK. (2)Wolfson Institute of Preventive Medicine, Barts and the London School of medicine and Dentistry, Queen Mary University of London, London, UK. Electronic address: p.d.white@qmul.ac.uk.	A UK based review of recommendations regarding the management of chronic fatigue syndrome.	118. J Psychosom Res. 2016 Sep;88:33-5.	OBJECTIVES: Chronic fatigue syndrome (CFS) is a controversial illness, with apparent disagreements between medical authorities and patient support organisations regarding safe and effective treatments. The aim of this study was to measure the extent of different views regarding treatments, comparing patient support organisations and medical authorities in the UK. METHODS: Two independent raters analysed two groups of resources: UK patient support websites and both medical websites and textbooks. A 5-point Likert scale was developed with the question 'With what strength does the source recommend these treatments?' The various treatments were divided into the following four groups: complementary and alternative medicine (CAM), pharmacological, rehabilitative, and pacing therapies. RESULTS: There were significant differences between the scores for patient support organisations and medical sources for all 4 treatment groups. The results for supporting CAM were 74% (patient group) vs 16% (medical source) ($p<0.001$), 71% vs 42% for pharmacological ($p=0.01$), 28% vs 94% for rehabilitative ($p<0.001$) and 91% vs 50% for pacing treatments ($p=0.001$). CONCLUSIONS: There were substantially different treatment recommendations between patient support organisations and medical sources. Since expectations can determine response to treatment, these different views may reduce the engagement in and effectiveness of rehabilitative therapies recommended by

				national guidelines and supported by systematic reviews.
Maltese PE(1), Venturini L(2), Poplavskaya E(3), Bertelli M(4), Cecchin S(4), Granato M(4), Nikulina SY(3), Salmina A(3), Aksyutina N(3), Capelli E(5), Ricevuti G(2), Lorusso L(6).	(1)MAGI Non-Profit Human Medical Genetics Institute, Rovereto, TN, Italy paolo.maltese@assomagi.org. (2)Cellular Pathophysiology and Clinical Immunology Laboratory, Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy. (3)Department of Internal Diseases N.1, Krasnoyarsk State Medical University, Krasnoyarsk, Russia. (4)MAGI Non-Profit Human Medical Genetics Institute, Rovereto, TN, Italy. (5)Immunology and Genetic Analysis Laboratory, Department of Earth and Environmental Sciences, University of Pavia, Pavia, Italy. (6)Department of Neurology, Mellino Mellini Hospital, Chiari, BS, Italy.	Genetic evaluation of AMPD1, CPT2, and PGYM metabolic enzymes in patients with chronic fatigue syndrome.	115. Genet Mol Res. 2016 Jul 29;15(3).	Chronic fatigue syndrome (CFS) is a disease that can seriously impair one's quality of life; patients complain of excessive fatigue and myalgia following physical exertion. This disease may be associated with abnormalities in genes affecting exercise tolerance and physical performance. Adenosine monophosphate deaminase (AMPD1), carnitine palmitoyltransferase II (CPT2), and the muscle isoform of glycogen phosphorylase (PYGM) genes provide instructions for producing enzymes that play major roles in energy production during work. The aim of this study was to look for evidence of genotype-associated excessive muscle fatigue. Three metabolic genes (AMPD1, CPT2, and PYGM) were therefore fully sequenced in 17 Italian patients with CFS. We examined polymorphisms known to alter the function of these metabolic genes, and compared their genotypic distributions in CFS patients and 50 healthy controls using chi-square tests and odds ratios. One-way analysis of variance with F-ratio was carried out to determine the associations between genotypes and disease severity using CF scores. No major genetic variations between patients and controls were found in the three genes studied, and we did not find any association between these genes and CFS. In conclusion, variations in AMPD1, CPT2, and PGYM genes are not associated with the onset, susceptibility, or severity of CFS.
Mandal T(1), Aydın Ş(2), Kanmaz D(3), Karasulu AL(3), Aras G(3), Tuncay	(1)Department of Chest Diseases, Yedikule Chest Diseases and Chest Surgery Training and	To what extent and why are COPD and Willis-Ekbom disease associated?	179. Sleep Breath. 2016 Sep;20(3):1021-7.	AIM: Willis-Ekbom disease (RLS/WED) is common in chronic obstructive pulmonary disease (COPD). Patients with RLS/WED have poorer quality of sleep and more fatigue and depressive symptoms. The prevalence of RLS/WED in patients with COPD has been reported to vary between 29.1 and 36.8 %. However, during exacerbation, the prevalence can increase up to 54 %. These rates are higher than those seen in general

E(3).	Research Hospital, 34020, Zeytinburnu, Istanbul, Turkey. tugbamandal160@hotmail.com. (2)Department of Neurology, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, Zeytinburnu, Istanbul, Turkey. (3)Department of Chest Diseases, Yedikule Chest Diseases and Chest Surgery Training and Research Hospital, 34020, Zeytinburnu, Istanbul, Turkey.			population. We have not enough knowledge regarding the association between RLS and COPD. In this study, we aimed to determine the frequency of RLS in patients with stable COPD without comorbid conditions. In addition, we also aimed to determine possible related causative factors. METHOD: We included 80 COPD patients without comorbid conditions who presented to our outpatient clinic between April 2013 and September 2013 for RLS/WED evaluation. Three cases that have polyneuropathy and one case that refused undergoing electromyography (EMG) examination were excluded from the study. Demographic data, P-A chest X-rays, pulmonary function tests (PFT), biochemical parameters (including hemogram), and dyspnea scales were evaluated for each patient. In addition, the RLS/WED rating scale and Epworth Sleep Scale (ESS) were applied. Further, each patient diagnosed with RLS/WED underwent a detailed neurological examination (performed by a neurologist) and an EMG examination to rule out polyneuropathy. RESULTS: Out of 76 COPD cases included in our study, 26.3 % (n = 20) were diagnosed with RLS/WED (mean age 60.4 ± 7.5 years, 20 males). The cases with RLS/WED had significantly lower body mass index (BMI) than cases without RLS/WED ($p = 0.009$). There were no significant differences between cases with and without RLS/WED with respect to PFT, dyspnea scales, and arterial blood gas values. However, ESS was significantly different ($p = 0.016$). There were no significant differences in RLS/WED scores and mean hs-CRP levels between COPD stages ($p = 0.424$; $p = 0.518$, respectively), while ESS was significantly different ($p = 0.016$). ESS was significantly higher in stage B COPD than in stages A and D ($p = 0.005$, $p = 0.008$, respectively). Based on our model, we found that exacerbations and iron binding capacity (UIBC) were predictive factors for RLS/WED ($p < 0.100$) CONCLUSION: RLS/WED is a common disease in cases with stable COPD. Despite our hypothesis suggesting that the prevalence of RLS/WED in COPD is related with systemic inflammation, we did not find a significant association between hs-CRP and COPD cases with RLS/WED. However, we did find that UIBC is a predictive factor for the development of RLS/WED. Nonetheless, further studies are needed to understand the relationships between UIBC, low BMI, and the development of RLS/WED in COPD.
Maroti D(1), Molander P(2,)(3), Bileviciute-Ljungar I(1,)(2).	(1) Department of Clinical Sciences, Karolinska Institutet and Department of Rehabilitation Medicine, Danderyd Hospital, Stockholm, Sweden. (2) Department of Medical and Health Sciences, Linköping	Differences in alexithymia and emotional awareness in exhaustion syndrome and chronic fatigue syndrome	85. Scand J Psychol. 2017 Feb;58(1):52-61. .	Symptoms of Exhaustion Syndrome (ES) and Chronic Fatigue Syndrome (CFS) are overlapping and create difficulties of differential diagnosis. Empirical studies comparing ES and CFS are scarce. This study aims to investigate if there are any emotional differences between ES and CFS. This cross-sectional study compared self-reported alexithymia and observer-rated emotional awareness in patients with ES (n = 31), CFS (n = 38) and healthy controls (HC) (n = 30). Self-reported alexithymia was measured with the Toronto Alexithymia Scale-20 (TAS-20) and emotional awareness with an observer-rated performance test, the Level of Emotional Awareness Scale (LEAS). Additionally, depression and anxiety were scored by the Hospital Anxiety and Depression Scale (HADS). Results show that patients with ES expressed higher self-reported alexithymia in the TAS-20 compared to HC, but had similar emotional

	University and Region Östergotland, Linköping, Sweden. (3)Department of Behavioral Sciences and Learning, Linköping University, Linköping, Sweden.			awareness capacity in the observer-rated performance test, the LEAS. Patients with CFS expressed more difficulties in identifying emotions compared to HCs, and performed significantly worse in the LEAS-total and spent more time completing the LEAS as compared to HC. Correlation and multiple regressions analyses revealed that depression and anxiety positively correlated with and explained part of the variances in alexithymia scores, while age and group explained the major part of the variance in LEAS. Findings of this study indicate that emotional status is different in patients with ES and CFS with respect to both self-reported alexithymia and observer-rated emotional awareness. Emotional parameters should be approached both in clinical investigation and psychotherapy for patients with ES and CFS.
Marshall-Gradisnik S(1,)(2), Johnston S(3,)(2), Chacko A(3,)(2), Nguyen T(3,)(2), Smith P(2), Staines D(3,)(2).	(1)School of Medical Science, Griffith University, Gold Coast, QLD, Australia s.marshall-gradisnik@griffith.edu.au. (2)The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD Australia. (3)School of Medical Science, Griffith University, Gold Coast, QLD, Australia.	Single nucleotide polymorphisms and genotypes of transient receptor potential ion channel and acetylcholine receptor genes from isolated B lymphocytes in myalgic encephalomyelitis/chronic fatigue syndrome patients.	40. J Int Med Res. 2016 Nov 10. pii: 0300060516671622.	OBJECTIVE: The pathomechanism of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is unknown; however, a small subgroup of patients has shown muscarinic antibody positivity and reduced symptom presentation following anti-CD20 intervention. Given the important roles of calcium (Ca(2+)) and acetylcholine (ACh) signalling in B cell activation and potential antibody development, we aimed to identify relevant single nucleotide polymorphisms (SNPs) and genotypes in isolated B cells from CFS/ME patients. METHODS: A total of 11 CFS/ME patients (aged 31.82 ± 5.50 years) and 11 non-fatigued controls (aged 33.91 ± 5.06 years) were included. Flow cytometric protocols were used to determine B cell purity, followed by SNP and genotype analysis for 21 mammalian TRP ion channel genes and nine mammalian ACh receptor genes. SNP association and genotyping analysis were performed using ANOVA and PLINK analysis software. RESULTS: Seventy-eight SNPs were identified in nicotinic and muscarinic acetylcholine receptor genes in the CFS/ME group, of which 35 were in mAChM3. The remaining SNPs were identified in nAChR delta (n = 12), nAChR alpha 9 (n = 5), TRPV2 (n = 7), TRPM3 (n = 4), TRPM4 (n = 1) mAChRM3 2 (n = 2), and mAChRM5 (n = 3) genes. Nine genotypes were identified from SNPs in TRPM3 (n = 1), TRPC6 (n = 1), mAChRM3 (n = 2), nAChR alpha 4 (n = 1), and nAChR beta 1 (n = 4) genes, and were located in introns and 3' untranslated regions. Odds ratios for these specific genotypes ranged between 7.11 and 26.67 for CFS/ME compared with the non-fatigued control group. CONCLUSION: This preliminary investigation identified a number of SNPs and genotypes in genes encoding TRP ion channels and AChRs from B cells in patients with CFS/ME. These may be involved in B cell functional changes, and suggest a role for Ca(2+) dysregulation in AChR and TRP ion channel signalling in the pathomechanism of CFS/ME.
Marshall-Gradisnik S(1), Huth T(1), Chacko A(1), Johnston S(1), Smith P(2), Staines D(2).	(1)School of Medical Science, Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia;	Natural killer cells and single nucleotide polymorphisms of specific ion channels and receptor genes in myalgic encephalomyelitis/chronic	216. Appl Clin Genet. 2016 Mar 31;9:39-47.	AIM: The aim of this paper was to determine natural killer (NK) cytotoxic activity and if single nucleotide polymorphisms (SNPs) and genotypes in transient receptor potential (TRP) ion channels and acetylcholine receptors (AChRs) were present in isolated NK cells from previously identified myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) patients. SUBJECTS AND METHODS: A total of 39 ME/CFS patients (51.69±2 years old) and 30 unfatigued controls (47.60±2.39 years old) were included in

	National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia. (2)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Gold Coast, QLD, Australia.	fatigue syndrome.		this study. Patients were defined according to the 1994 Centers for Disease Control and Prevention criteria. Flow cytometry protocols were used to examine NK cytotoxic activity. A total of 678 SNPs from isolated NK cells were examined for 21 mammalian TRP ion channel genes and for nine mammalian AChR genes via the Agena Bioscience iPlex Gold assay. SNP association and genotype was determined using analysis of variance and Plink software. RESULTS: ME/CFS patients had a significant reduction in NK percentage lysis of target cells (17%±4.68%) compared with the unfatigued control group (31%±6.78%). Of the 678 SNPs examined, eleven SNPs for TRP ion channel genes (TRPC4, TRPC2, TRPM3, and TRPM8) were identified in the ME/CFS group. Five of these SNPs were associated with TRPM3, while the remainder were associated with TRPM8, TRPC2, and TRPC4 (P<0.05). Fourteen SNPs were associated with nicotinic and muscarinic AChR genes: six with CHRNA3, while the remainder were associated with CHRNA2, CHRNB4, CHRNA5, and CHRNE (P<0.05). There were sixteen genotypes identified from SNPs in TRP ion channels and AChRs for TRPM3 (n=5), TRPM8 (n=2), TRPC4 (n=3), TRPC2 (n=1), CHRNE (n=1), CHRNA2 (n=2), CHRNA3 (n=1), and CHRNB4 (n=1) (P<0.05). CONCLUSION: We identified a number of SNPs and genotypes for TRP ion channels and AChRs from isolated NK cells in patients with ME/CFS, suggesting these SNPs and genotypes may be involved in changes in NK cell function and the development of ME/CFS pathology. These anomalies suggest a role for dysregulation of Ca(2+) in AChR and TRP ion channel signaling in the pathomechanism of ME/CFS.
McCarthy J(1).	(1)David Grant Medical Center Family Medicine Residency Program - Travis Air Force Base, 101 Bodin Circle, Travis AFB, California 94535.	Myalgias and Myopathies: Fibromyalgia.	313. FP Essent. 2016 Jan;440:11-5.	Fibromyalgia is a syndrome of chronic widespread pain typically accompanied by fatigue, nonrestorative sleep, cognitive dysfunction, and mood disorders. As defined by the 2010 American College of Rheumatology criteria, fibromyalgia affects approximately 5% of the population and is the second most common disorder, after osteoarthritis, for which patients are referred to rheumatology subspecialists. These criteria provide a framework for diagnosing fibromyalgia that does not require tender points and incorporates other symptoms of the syndrome in addition to pain. Extensive laboratory tests and imaging are not required to diagnose fibromyalgia. A patient-centered, multimodal approach that includes patient education, behavioral therapy, a graded exercise program, and pharmacotherapy should be used for patients with fibromyalgia. Prescribers must be mindful of adverse drug effects and should tailor therapy to the individual patient. Strong evidence of benefit exists for tricyclic antidepressants, cyclobenzaprine, and serotonin-norepinephrine reuptake inhibitors in fibromyalgia management, whereas nonsteroidal anti-inflammatory drugs and opioids have limited proven benefit. Fibromyalgia can cause significant disability and loss of function. Family physicians are well equipped to direct the multimodal care of patients with fibromyalgia.
McManimen SL(1), Sunnquist ML(1), Jason	(1)DePaul University, USA. (2)DePaul University, USA	Deconstructing post-exertional malaise: An exploratory factor	112. J Health Psychol. 2016 Aug 24. pii: 1359105316664139.	Post-exertional malaise is a cardinal symptom of myalgic encephalomyelitis and chronic fatigue syndrome. There are two differing focuses when defining post-exertional malaise: a generalized, full-body fatigue and a muscle-specific fatigue. This study aimed

LA(2).	ljason@depaul.edu.	analysis.		to discern whether post-exertional malaise is a unified construct or whether it is composed of two smaller constructs, muscle fatigue and generalized fatigue. An exploratory factor analysis was conducted on several symptoms that assess post-exertional malaise. The results suggest that post-exertional malaise is composed of two empirically different experiences, one for generalized fatigue and one for muscle-specific fatigue.
McNicholas WT(1).	(1)Department of Respiratory and Sleep Medicine, St. Vincent's University Hospital, Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Dublin, Ireland.	Chronic obstructive pulmonary disease and obstructive sleep apnoea-the overlap syndrome.	267. J Thorac Dis. 2016 Feb;8(2):236-42.	Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) are highly prevalent disorders and the co-existence of both disorders, termed the overlap syndrome, affects at least 1% of the adult population. Patients with the overlap syndrome typically experience more pronounced nocturnal oxygen desaturation and there is a high prevalence of pulmonary hypertension in such patients. Recent evidence suggests that the prevalence of each disorder together is higher than might be predicted by simple prevalence statistics, although the evidence is not clear-cut in this regard. Sleep itself can have several negative effects in patients with COPD. Sleep quality is diminished with reduced amounts of slow wave and rapid-eye-movement (REM) sleep, which may contribute to daytime symptoms such as fatigue and lethargy. Furthermore, normal physiological adaptations during sleep that result in mild hypoventilation in normal subjects are more pronounced in COPD, which can result in clinically important nocturnal oxygen desaturation. Management of sleep disorders in patients with COPD should address both sleep quality and disordered gas exchange. Non-invasive pressure support is beneficial in selected cases, particularly during acute exacerbations associated with respiratory failure, and is particularly helpful in patients with the overlap syndrome. There is limited evidence of benefit from pressure support in the chronic setting in COPD patients without OSA.
Meeus M(1,)(2,)(3,)(4), Ickmans K(5,)(6,)(7,)(8), Struyf F(5,)(6), Kos D(6,)(9,)(10), Lambrecht L(11), Willekens B(12), Cras P(12), Nijs J(5,)(6,)(7,)(8).	(1)Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium. mira.meeus@ugent.be. (2)Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp,	What is in a name? Comparing diagnostic criteria for chronic fatigue syndrome with or without fibromyalgia.	371. Clin Rheumatol. 2016 Jan;35(1):191-203.	The current study had two objectives. (1) to compare objective and self-report measures in patients with chronic fatigue syndrome (CFS) according to the 1994 Center for Disease Control (CDC) criteria, patients with multiple sclerosis (MS), and healthy controls, and (2) to contrast CFS patients who only fulfill CDC criteria to those who also fulfill the criteria for myalgic encephalomyelitis (ME), the 2003 Canadian criteria for ME/CFS, or the comorbid diagnosis of fibromyalgia (FM). One hundred six participants (48 CFS patients diagnosed following the 1994 CDC criteria, 19 MS patients, and 39 healthy controls) completed questionnaires assessing symptom severity, quality of life, daily functioning, and psychological factors. Objective measures consisted of activity monitoring, evaluation of maximal voluntary contraction and muscle recovery, and cognitive performance. CFS patients were screened whether they also fulfilled ME criteria, the Canadian criteria, and the diagnosis of FM. CFS patients scored higher on symptom severity, lower on quality of life, and higher on depression and kinesiophobia and worse on MVC, muscle recovery, and cognitive performance compared to the MS patients and the healthy subjects. Daily activity levels were also lower compared to healthy subjects. Only one difference was found between those fulfilling the ME criteria

	Antwerp, Belgium. mira.meeus@ugent.be. (3)Pain in Motion International Research Group, . mira.meeus@ugent.be. (4)Rehabilitation Sciences and Physiotherapy, Ghent University, Campus Heymans (UZ) 3 B3, De Pintelaan 185, Ghent, Belgium. mira.meeus@ugent.be. (5)Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium. (6)Pain in Motion International Research Group. (7)Departments of Human Physiology and & Rehabilitation Sciences, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium. (8)Department of Physiotherapy and Rehabilitation, University Hospital Brussels, Brussel, Belgium. (9)Division of Occupational Therapy,			and those who did not regarding the degree of kinesiophobia (lower in ME), while comorbidity for FM significantly increased the symptom burden. CFS patients report more severe symptoms and are more disabled compared to MS patients and healthy controls. Based on the present study, fulfillment of the ME or Canadian criteria did not seem to give a clinically different picture, whereas a diagnosis of comorbid FM selected symptomatically worse and more disabled patients.

	Artesis Plantijn University College Antwerp, Antwerp, Belgium. (10)Rehabilitation Sciences, KU Leuven, Leuven, Belgium. (11)Private practice for internal medicine, Ghent, Belgium. (12)Department of Neurology, Faculty of Medicine, University and University Hospital Antwerp, Antwerp, Belgium.			
Mendell MJ(1).	(1)California Department of Public Health, Richmond, CA 94804, USA. Mark.Mendell@cdph.ca.gov.	Comment on Detection of Mycotoxins in Patients with Chronic Fatigue Syndrome Toxins 2013, 5, 605-617.	42. Toxins (Basel). 2016 Nov 7;8(11). pii: E324.	The paper by Brewer et al. (2013) has a key methodologic flaw [1].[..].
Mensah F(1), Bansal A(2), Berkovitz S(3), Sharma A(1), Reddy V(1), Leandro MJ(1), Cambridge G(1).	(1)Department of Rheumatology Research, Division of Medicine, University College of London. (2)Department of Immunology, Epsom and St Helier University Hospitals NHS Trust. (3)Department of Neurology, Royal London Hospital of Integrated Medicine, London, UK.	Extended B cell phenotype in patients with myalgic encephalomyelitis/chronic fatigue syndrome: a cross-sectional study.	328. Clin Exp Immunol. 2016 May;184(2):237-47.	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a heterogeneous condition of unknown aetiology characterized by multiple symptoms including fatigue, post-exertional malaise and cognitive impairment, lasting for at least 6 months. Recently, two clinical trials of B cell depletion therapy with rituximab (anti-CD20) reported convincing improvement in symptoms. A possible but undefined role for B cells has therefore been proposed. Studies of the relative percentages of B cell subsets in patients with ME/CFS have not revealed any reproducible differences from healthy controls (HC). In order to explore whether more subtle alterations in B cell subsets related to B cell differentiation exist in ME/CFS patients we used flow cytometry to immunophenotype $CD19^+$ B cells. The panel utilized immunoglobulin (Ig)D, CD27 and CD38 (classical B cell subsets) together with additional markers. A total of 38 patients fulfilling Canadian, Centre for Disease Control and Fukuda ME/CFS criteria and 32 age- and sex-matched HC were included. We found no difference in percentages of classical subsets between ME/CFS patients and HC. However, we observed an increase in frequency ($P < 0{\cdot}01$) and expression (MFI; $P = 0{\cdot}03$) of CD24 on total B cells, confined to IgD^+ subsets. Within memory subsets, a higher frequency of $CD21^+$ $CD38^-$ B cells (> 20%) was associated with the presence of ME/CFS [odds ratio: 3·47 (1·15-10·46); $P = 0{\cdot}03$] compared with HC, and there was a negative correlation with disease duration. In

				conclusion, we identified possible changes in B cell phenotype in patients with ME/CFS. These may reflect altered B cell function and, if confirmed in other patient cohorts, could provide a platform for studies based on clinical course or responsiveness to rituximab therapy.
Menzies V(1), Thacker LR 2nd(2), Mayer SD(3), Young AM(4), Evans S(5), Barstow L(6).	(1)School of Nursing, Virginia Commonwealth University, Richmond, VA, USA vsmenzies@vcu.edu. (2)School of Nursing, Virginia Commonwealth University, Richmond, VA, USA. (3)Department of Pharmacotherapy and Outcomes Science, School of Pharmacy, Virginia Commonwealth University, Richmond, VA, USA. (4)University of Virginia Health Systems, Charlottesville, VA, USA. (5)University of Colorado Hospital, Aurora, CO, USA. (6)Mission Hospitals, Asheville, NC, USA.	Polypharmacy, Opioid Use, and Fibromyalgia: A Secondary Analysis of Clinical Trial Data.	134. Biol Res Nurs. 2016 Jul 18. pii: 1099800416657636.	The major therapeutic approach for treating fibromyalgia (FM), a chronic widespread pain syndrome, is pharmacotherapy-centered symptom management. Complexity of treatment often leads to multiple medication prescriptions. While there is no current alternative to the probable need for polypharmacy in this patient population, there remains concern related to potential side effects and adverse drug events. In this secondary analysis of data on medications taken collected from two parent studies, all medications were broken down into the following categories: opioid, nonopioid, antidepressant, anticonvulsant, muscle relaxant, and benzodiazepine. The impact on pain severity and pain interference of these medication categories as well as perceived stress, fatigue, and depression scores was assessed. Baseline pain severity ($p = .0106$) and pain interference ($p = .0002$) were significantly correlated with opioid use as compared to nonopioid use. A multivariate regression with backward elimination resulted in a model for pain severity with one significant predictor variable, fatigue ($p < .0001$); pain interference had three significant predictor variables: opioid use ($p = .04$), fatigue ($p < .0001$), and depression ($p = .04$). While future studies should further address the utility of opioids and examine the role of polypharmacy as part of symptom management strategies for individuals with FM, study findings suggest that, for those who suffer chronic widespread pain as the predominant symptom experience, a challenge equally as perplexing for nurses and nursing research alike as managing the pain lies in addressing the fatigue and depression in this patient population.
Menzies V(1).	(1)Victoria Menzies is an associate professor in the Department of Adult Health and Nursing Systems, Virginia Commonwealth University School of Nursing, Richmond.	Fibromyalgia Syndrome: Current Considerations in Symptom Management.	324. Am J Nurs. 2016 Jan;116(1):24-32; quiz 33, 41.	Fibromyalgia syndrome (FMS), one of the most common rheumatic disorders, is estimated to affect up to 15 million people in the United States, 80% to 90% of whom are women. The syndrome is characterized by the presence of chronic widespread pain and various concurrent symptoms, which may include fatigue, cognitive disturbances (memory problems, difficulty concentrating, confusion), distressed mood (anxiety, depression), nonrestorative sleep, and muscular stiffness. Symptom management appears to be best addressed using a multimodal approach, with treatment strategies tailored to the individual. While medication may provide adequate symptom relief for some patients, experts generally recommend integrating both pharmacologic and

	Contact author: vsmenzies@vcu.edu. The author and planners have disclosed no potential conflicts of interest, financial or otherwise.			nonpharmacologic approaches. Some patients may benefit from the adjunctive use of complementary and alternative medicine (CAM) modalities. Because symptom remission is rare and medication adverse effects can complicate symptom management, well-informed nursing care practices and patient education are essential. This article describes the existing treatment guidelines, discusses pharmacologic and nonpharmacologic approaches (including CAM-based modalities), and outlines nursing approaches aimed at enhancing patient self-management.
Merkies IS(1), Kieseier BC.	(1)Department of Neurology, Maastricht University Medical Centre, Maastricht, The Netherlands.	Fatigue, Pain, Anxiety and Depression in Guillain-Barré Syndrome and Chronic Inflammatory Demyelinating Polyradiculoneuropathy.	223. Eur Neurol. 2016;75(3-4):199-206.	BACKGROUND: In the clinical evaluation of patients with Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), scant attention is paid to symptoms such as fatigue, pain and anxiety/depression. We aimed at addressing seminal studies that focused on the burden of these symptoms and their impact on quality of life (QoL) in these conditions. SUMMARY: Fatigue, pain, and anxiety/depression are increasingly being recognized in patients with GBS and CIDP, although their pathophysiological provenance remains unknown. Fatigue and pain are significant in terms of prevalence and intensity, may be a presenting symptom, and can persist for years after apparent functional recovery, suggesting residual injury. Anxiety/depression has also been examined although studies are limited. Despite their negative impact on QoL, the long-term dynamics of these symptoms in patients with GBS and particularly CIDP receiving therapy in routine clinical practice have not been systematically evaluated. Such observations formed the basis for the ongoing (GAMEDIS) studies evaluating the effect of Gamunex on fatigue and depression in patients with CIDP, of which some preliminary data are presented. KEY MESSAGES: Strength and sensory deficits are the main areas of focus in patients with GBS and CIDP, but they do not explain the total reduction in QoL, suggesting the possible role of other complaints. A more comprehensive approach to patient care demands that factors such as pain, fatigue and anxiety/depression receive greater attention. The non-interventional GAMEDIS studies are expected to provide valuable insight into the long-term effectiveness of Gamunex in everyday practice.
Miglis MG(1), Muppidi S(2), Feakins C(2), Fong L(2), Prieto T(2), Jaradeh S(2).	(1)Division of Autonomic Neurology, Stanford University Medical Center, 211 Quarry Rd, 2nd Fl, MC 5992, Stanford, CA, 94305, USA. mmiglis@stanford.edu. (2)Division of Autonomic Neurology, Stanford University Medical Center, 211	Sleep disorders in patients with postural tachycardia syndrome.	320. Clin Auton Res. 2016 Feb;26(1):67-73.	OBJECTIVE: Patients with postural tachycardia syndrome (POTS) often describe symptoms of fatigue, sleepiness, and lack of refreshing sleep. We aimed to provide further objective measures of sleep in patients with POTS. METHODS: POTS patients (n = 18) were selected based on autonomic testing and evaluation at our center. Controls (n = 16) of similar age, gender, and BMI were selected from new patients referred to the Stanford Sleep Disorders Clinic for any sleep-related complaint. All patients underwent polysomnography and completed several sleep questionnaires and a 2-week sleep diary. RESULTS: POTS patients and control subjects were of similar age (27 ± 10.2 vs. 29 ± 5.4 years, p = 0.92) and Body Mass Index (21 ± 3.8 vs. 24 ± 4.1, p = 0.14). The majority of subjects in both groups were females (72 % POTS vs. 81 % controls). POTS patients scored higher on subjective fatigue scales but not sleepiness scales. POTS patients scored in the normal range on the BDI and the "evening" category on the MEQ.

	Quarry Rd, 2nd Fl, MC 5992, Stanford, CA, 94305, USA.			Their sleep diaries were not different from controls. With the exception of mild OSA, slightly reduced %REM and prolonged REM latency, their PSG data were normal and no different from controls. CONCLUSIONS: It is unlikely that the sleep-related complaints of POTS patients are the result of a primary sleep disorder unique to POTS. We propose that a combination of factors such as body fatigue, chronic pain, and other somatic symptoms common in POTS patients might be the underlying reason for sleep-related symptoms in POTS.
Miller RR(1), Uyaguari-Diaz M(2), McCabe MN(2), Montoya V(2), Gardy JL(1,)(2), Parker S(3), Steiner T(4), Hsiao W(5,)(6), Nesbitt MJ(7), Tang P(8), Patrick DM(1,)(2); CCD Study Group.	(1)School of Population and Public Health, University of British Columbia, Vancouver, British Columbia, Canada. (2)British Columbia Centre for Disease Control, Vancouver, British Columbia, Canada. (3)Centre for Health Evaluation and Outcome Sciences, Vancouver, British Columbia, Canada. (4)Department of Medicine, University of British Columbia, Vancouver, British Columbia, Canada. (5)British Columbia Public Health Microbiology and Reference Laboratory, Vancouver, British Columbia, Canada. (6)Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, British Columbia, Canada. (7)Coastal	Metagenomic Investigation of Plasma in Individuals with ME/CFS Highlights the Importance of Technical Controls to Elucidate Contamination and Batch Effects.	56. PLoS One. 2016 Nov 2;11(11):e0165691.	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating disease causing indefinite fatigue. ME/CFS has long been hypothesised to have an infectious cause; however, no specific infectious agent has been identified. We used metagenomics to analyse the RNA from plasma samples from 25 individuals with ME/CFS and compare their microbial content to technical controls as well as three control groups: individuals with alternatively diagnosed chronic Lyme syndrome (N = 13), systemic lupus erythematosus (N = 11), and healthy controls (N = 25). We found that the majority of sequencing reads were removed during host subtraction, thus there was very low microbial RNA content in the plasma. The effects of sample batching and contamination during sample processing proved to outweigh the effects of study group on microbial RNA content, as the few differences in bacterial or viral RNA abundance we did observe between study groups were most likely caused by contamination and batch effects. Our results highlight the importance of including negative controls in all metagenomic analyses, since there was considerable overlap between bacterial content identified in study samples and control samples. For example, Proteobacteria, Firmicutes, Actinobacteria, and Bacteriodes were found in both study samples and plasma-free negative controls. Many of the taxonomic groups we saw in our plasma-free negative control samples have previously been associated with diseases, including ME/CFS, demonstrating how incorrect conclusions may arise if controls are not used and batch effects not accounted for.

	Genomics Inc., Burnaby, British Columbia, Canada. (8)Department of Pathology, Sidra Medical and Research Center, Doha, Qatar.			
Milrad SF(1), Hall DL(2), Jutagir DR(1), Lattie EG(3), Ironson GH(1), Wohlgemuth W(4), Nunez MV(5), Garcia L(6), Czaja SJ(6), Perdomo DM(6), Fletcher MA(5), Klimas N(5), Antoni MH(7).	(1)Department of Psychology, University of Miami, 5665 Ponce de Leon Blvd., Miami, FL 33133, USA. (2)Department of Psychiatry, Massachusetts General Hospital/Harvard Medical School, 55 Fruit St., Boston, MA 02114, USA. (3)Department of Preventive Medicine, Northwestern University Feinberg School of Medicine, 680 N Lake Shore Dr. Suite 1400, Chicago, IL 60611, USA. (4) Department of Sleep Medicine, Miami Veteran Affairs Hospital, 1201 NW 16th St, Miami, FL 33125, USA. (5) Institute for Neuro Immune Medicine, Nova Southeastern University, 8501 SW 124th Ave #111, Miami, FL 33183, USA.	Poor sleep quality is associated with greater circulating pro-inflammatory cytokines and severity and frequency of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) symptoms in women.	2. J Neuroimmunol. 2016 Dec 14.	OBJECTIVE: Poor sleep quality has been linked to inflammatory processes and worse disease outcomes in the context of many chronic illnesses, but less is known in conditions such as chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). This study examines the relationships between sleep quality, pro-inflammatory cytokines, and CFS/ME symptoms. METHODS: Sixty women diagnosed with CFS/ME were assessed using the Pittsburgh Sleep Quality Index (PSQI), Fatigue Symptom Inventory (FSI) and Center for Disease Control and Prevention (CDC)-based CFS/ME symptom questionnaires. Circulating plasma pro-inflammatory cytokine levels were measured by ELISA. Multiple regression analyses examined associations between sleep, cytokines and symptoms, controlling for age, education, and body mass index. RESULTS: Poor sleep quality (PSQI global score) was associated with greater pro-inflammatory cytokine levels: interleukin-1β (IL-1β) (β=0.258, p=0.043), IL-6 (β=0.281, p=0.033), and tumor necrosis factor-alpha (TNF-α) (β=0.263, p=0.044). Worse sleep quality related to greater fatigue severity (β=0.395, p=0.003) and fatigue-related interference with daily activities (β=0.464, p<0.001), and more severe and frequent CDC-defined core CFS/ME symptoms (β=0.499, p<0.001, and β=0.556, p<0.001, respectively). CONCLUSIONS: Results underscore the importance of managing sleep-related difficulties in this patient population. Further research is needed to identify the etiology of sleep disruptions in CFS/ME and mechanistic factors linking sleep quality to symptom severity and inflammatory processes.

	(6) Department of Psychiatry and Behavioral Sciences, University of Miami, 1120 NW 14th St., Miami, FL 33136, USA. (7) Department of Psychology, University of Miami, 5665 Ponce de Leon Blvd., Miami, FL 33133, USA. Electronic address: mantoni@miami.edu.			
Mitchell WM(1).	(1)a Department of Pathology, Microbiology & Immunology , Vanderbilt University , Nashville , USA.	Efficacy of rintatolimod in the treatment of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).	230. Expert Rev Clin Pharmacol. 2016 Jun;9(6):755-70.	Chronic fatigue syndrome/ Myalgic encephalomyelitis (CFS/ME) is a poorly understood seriously debilitating disorder in which disabling fatigue is an universal symptom in combination with a variety of variable symptoms. The only drug in advanced clinical development is rintatolimod, a mismatched double stranded polymer of RNA (dsRNA). Rintatolimod is a restricted Toll-Like Receptor 3 (TLR3) agonist lacking activation of other primary cellular inducers of innate immunity (e.g.- cytosolic helicases). Rintatolimod also activates interferon induced proteins that require dsRNA for activity (e.g.- 2'-5' adenylate synthetase, protein kinase R). Rintatolimod has achieved statistically significant improvements in primary endpoints in Phase II and Phase III double-blind, randomized, placebo-controlled clinical trials with a generally well tolerated safety profile and supported by open-label trials in the United States and Europe. The chemistry, mechanism of action, clinical trial data, and current regulatory status of rintatolimod for CFS/ME including current evidence for etiology of the syndrome are reviewed.
Miwa K(1).	(1)Miwa Naika Clinic, Toyama, Japan. Electronic address: info@miwa-naika.com.	Down-regulation of renin-aldosterone and antidiuretic hormone systems in patients with myalgic encephalomyelitis/chronic fatigue syndrome.	143. J Cardiol. 2016 Jul 8. pii: S0914-5087(16)30120-4.	BACKGROUND: Central nervous system dysfunction associated with myalgic encephalomyelitis (ME) has been postulated as the cause of chronic fatigue syndrome (CFS). A small heart or reduced left ventricular volume with reduced cardiac output has been reported to be common in patients with ME. The main circulatory blood volume regulators may be down-regulated. METHODS: Plasma levels of the neurohumoral factors that regulate circulatory blood volume were determined in 18 patients with ME and 15 healthy subjects (Controls). RESULTS: The echocardiographic examination revealed that the mean values for the left ventricular end-diastolic diameters, stroke volume index, and cardiac index as well as the mean blood pressure were all significantly smaller in the ME group than in the Controls. The mean plasma renin activity (1.6±1.0ng/ml/h vs. 2.5±1.5ng/ml/h, p=0.06) was considerably lower in the ME group than in the Controls. Both the mean plasma aldosterone (104±37pg/ml vs. 157±67pg/ml, p=0.004) and antidiuretic hormone (ADH) (2.2±1.0pg/ml vs.

				3.3±1.5pg/ml, p=0.02) concentrations were significantly lower in the ME group than in the Controls. Desmopressin (120µg), a synthetic version of arginine vasopressin, was orally administered for five successive days to 10 patients with ME. In five patients (50%), the symptoms of orthostatic intolerance during a 10min active standing test were ameliorated in association with a significant increase in urinary osmotic pressure and decrease in heart rate. Furthermore, in five patients (50%), the performance status scores for the activities of daily living were improved. CONCLUSIONS: Both the renin-aldosterone and ADH systems were down-regulated despite the existence of reduction in cardiac preload and output in patients with ME. Desmopressin improved symptoms in half of the patients.
Miwa K(1).	(1)Department of Internal Medicine, Miwa Naika Clinic, 1-4-3 Shintomicho, Toyama, 930-0002, Japan. info@miwa-naika.com.	Variability of postural orthostatic tachycardia in patients with myalgic encephalomyelitis and orthostatic intolerance.	346. Heart Vessels. 2016 Sep;31(9):1522-8.	Central nervous system dysfunction with myalgic encephalomyelitis (ME) has been suggested as the main cause of chronic fatigue syndrome. Fluctuation of the symptom severity and hierarchy is a characteristic feature in ME patients. The characteristics of the sympathetic activation may differ between the "good days" and "bad days" in them. Twenty-four ME patients with orthostatic intolerance underwent a conventional 10-min active standing test and echocardiography both on a "good day" and a "bad day", defined according to the severity of their symptoms. The mean heart rate at rest was significantly higher on the "bad days" than on the "good days". During the standing test on a "bad day", 5 patients (21 %) failed to maintain an upright posture for 10 min, whereas on a "good day" all the 24 patients maintained it. Postural orthostatic tachycardia (POT) (increase in heart rate ≥30 beats/min) or severe POT (heart rate ≥120 beats/min) was observed on the "bad days" in 10 patients (43 %) who did not suffer from the severe tachycardia on the "good days", suggesting the exaggerated sympathetic nervous activation. In contrast, POT did not occur or severe POT was attenuated on the "bad days" in 5 patients (21 %) who developed POT or severe POT on the "good days", suggesting the impaired sympathetic activation. Echocardiography revealed significantly lower mean values of both the left ventricular end-diastolic diameter and stroke volume index on the "bad days" compared with the "good days". In conclusion, in ME patients with orthostatic intolerance, the exaggerated activation of the sympathetic nervous system while standing appears to switch to the impaired sympathetic activation after the system is loaded with the additional accentuated stimuli associated with the preload reduction.
Mizuno K(1), Kawatani J(2), Tajima K(3), Sasaki AT(4), Yoneda T(5), Komi M(6), Hirai T(7), Tomoda A(8), Joudoi T(9),	(1) Pathophysiological and Health Science Team, RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-minamimachi, Chuo-ku, Kobe, Hyogo 650-	Low putamen activity associated with poor reward sensitivity in childhood chronic fatigue syndrome.	80. Neuroimage Clin. 2016 Sep 26;12:600-606. eCollection 2016.	Motivational signals influence a wide variety of cognitive processes and components of behavioral performance. Cognitive dysfunction in patients with childhood chronic fatigue syndrome (CCFS) may be closely associated with a low motivation to learn induced by impaired neural reward processing. However, the extent to which reward processing is impaired in CCFS patients is unclear. The aim of the present functional magnetic resonance imaging (fMRI) study was to determine whether brain activity in regions related to reward sensitivity is impaired in CCFS patients. fMRI data were collected from 13 CCFS patients (mean age, 13.6 ± 1.0 years) and 13 healthy children

Watanabe Y(4).	0047, Japan			and adolescents (HCA) (mean age, 13.7 ± 1.3 years) performing a monetary reward task. Neural activity in high- and low-monetary-reward conditions was compared between CCFS and HCA groups. Severity of fatigue and the reward obtained from learning in daily life were evaluated by questionnaires. Activity of the putamen was lower in the CCFS group than in the HCA group in the low-reward condition, but not in the high-reward condition. Activity of the putamen in the low-reward condition in CCFS patients was negatively and positively correlated with severity of fatigue and the reward from learning in daily life, respectively. We previously revealed that motivation to learn was correlated with striatal activity, particularly the neural activity in the putamen. This suggests that in CCFS patients low putamen activity, associated with altered dopaminergic function, decreases reward sensitivity and lowers motivation to learn.
Mohamed HI(1), Mokarib HA(2), Saad ZM(3), Abd El Ghany WM(4).	(1)Faculty of Medicine, Gastroenterology and Endemic Medicine Department, Minya University, Minya, Egypt. halaibrahem@mu.edu.eg. (2)Faculty of Medicine, Gastroenterology and Endemic Medicine Department, Minya University, Minya, Egypt. medoo_9977@yahoo.com. (3)Faculty of Medicine, Gastroenterology and Endemic Medicine Department, Minya University, Minya, Egypt. saad_zienab@yahoo.com. (4)Faculty of Medicine, Gastroenterology and Endemic Medicine	The prevalence of functional dyspepsia using Rome III questionnaire among chronic hepatitis C patients.	260. BMC Gastroenterol. 2016 Mar 3;16:32.	BACKGROUND: Hepatitis C virus (HCV) is a common chronic infection that is widely associated with symptoms of fatigue and abdominal pain. The aim of the present study was to determine the prevalence of functional dyspepsia (FD) among patients with hepatitis C. METHODS: This study included 252 patients with chronic hepatitis C and 150 healthy volunteers. Clinical and laboratory data were recorded for every patient. All patients and controls were administered a questionnaire of FD according to Rome III criteria. RESULTS: The percentage of patients with FD was significantly higher in patients with chronic HCV than normal controls (65.9 % vs 28.7 %, respectively). In chronic HCV patients, post prandial distention syndrome (PDS) subtype was the predominant type (86.1 %). The percentage of patients with a high fibrosis score (F2-3) and raised ALT were significantly higher in patients with FD than in patients without FD ($P < 0.001$; $P < 0.04$; respectively). A multivariate regression analysis revealed a significant association between fibrosis score, BMI and FD CONCLUSION: FD is more prevalent in patients with chronic hepatitis C. Obese chronic HCV and those with higher fibrosis scores are more likely to have FD.

	Department, Minya University, Minya, Egypt. waelghany@mu.edu.eg.			
Morelli A(1), Vignozzi L, Maggi M.	(1)Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy.	Hypogonadotropic hypogonadism and metabolic syndrome: insights from the high-fat diet experimental rabbit animal model.	228. Minerva Endocrinol. 2016 Jun;41(2):240-9. Epub 2016 Apr 6.	The etiology of metabolic syndrome (MetS) is complex and involves the interplay between environmental, lifestyle and genetic determinants. MetS in men can be associated with a biochemical pattern of partial hypogonadotropic hypogonadism (HH). A similar pattern has been noted in both men and women with a variety of acute illnesses and chronic diseases, and there is ongoing debate regarding whether this phenomenon might adaptive (e.g. diverting resources from reproduction into survival), or maladaptive (e.g. anemia, sarcopenia, osteopenia and fatigue of androgen-deficiency amplify and widen the adverse consequences of the original disease-trigger). In women with hypothalamic amenorrhea (HA-HH secondary to chronic bioenergetic deficit from dietary restriction and/or intensive exercise), a genetic link to congenital HH (CHH) was recently established; women carrying monoallelic CHH gene mutations will typically not develop CHH, but are significantly more susceptible to HA. However, the male reproductive axis seems to be more resistant to similar environmental insults. In contrast, MetS-associated HH (mHH) is specifically a male phenomenon; the reproductive phenotype of females with MetS tending instead towards hyperandrogenism, rather than hypogonadism. The underlying pathogenic mechanisms responsible for mHH have not been clearly identified and, as yet, there has been no investigation of a potential role for CHH mutation carriage in its etiology. Over the decades, the use of either genetic- or diet-induced obesity and/or MetS animal models has greatly helped to illuminate the complex etiology of metabolic dysregulation, but the strong relationship between obesity/MetS and mHH in males has been largely neglected, with little or no information about the regulation of reproductive function by metabolic factors under conditions of bioenergetic excess. However, the pathogenic link between MetS and HH in males has been recently investigated in an animal model of high fat diet (HFD)-induced MetS, which perfectly recapitulates the human phenotype. Interesting insights derived by these studies have added novel information about the causative role played by hypothalamic alterations driven by metabolic disturbances in mHH. In particular, it appears that HFD-induced inflammatory injury at the hypothalamic level negatively affects GnRH neuron content, with the reduction of circulating gonadotropins and sex hormones being related to MetS severity.
Morita F(1), Hirai Y(1), Suzuki K(1), Uehara Y(1), Mitsuhashi K(1), Amano A(2),	(1)Department of General Medicine, Juntendo University Faculty of Medicine, Tokyo, Japan.	Infective endocarditis and Sjögren's syndrome diagnosed simultaneously.	20. IDCases. 2016 Nov 22;7:6-8. eCollection 2017.	Poor dentition and/or dental infection due to insufficient oral care are presumed to be risk factors for infective endocarditis (IE). We present a case of endocarditis caused by Granulicatella adiacens and Sjögren's syndrome (SS) with oral complications diagnosed simultaneously. A 67-year-old woman was admitted to our hospital with fever, general fatigue, arthralgia, and back pain. She was diagnosed with primary SS according to the

Naito T(1).	(2)Department of Cardiovascular Surgery, Juntendo University Faculty of Medicine, Tokyo, Japan.			criteria of the American-European Consensus Group. Transthoracic echocardiography carried out to examine her persistent fever revealed vegetation formation (14 × 5 mm) on the aortic valve and her blood cultures were positive for G. adiacens. According to modified Duke's criteria, she was also diagnosed with IE. She underwent aortic valve replacement and was administered ampicillin with gentamicin for 6 weeks following surgery. G. adiacens, which is formerly known as one of the nutritionally variant streptococci, is found as part of the normal microbiota of the oral cavity. The patient had chronic periodontitis associated with SS that likely predisposed to G. adiacens bacteremia and subsequent seeding of the aortic valve. Patients with SS may be at risk of IE because of the increased risk of bacteremia from oral complications such as dental caries or periodontal disease. An association between SS and IE has not yet been reported. Our case indicates that SS may be the underlying pathology in patients with IE due to an oral bacterium.
Morris G, Carvalho AF, Anderson G, Galecki P, Maes M(1).	(1)IMPACT Strategic Research Center, Barwon Health, Deakin University, Geelong, Vic, Australia. dr.michaelmaes@hotmail.com.	The Many Neuroprogressive Actions of Tryptophan Catabolites (TRYCATs) that may be Associated with the Pathophysiology of Neuro-Immune Disorders.	325. Curr Pharm Des. 2016;22(8):963-77.	Many, if not all, chronic medical, neurodegenerative and neuroprogressive illnesses are characterised by chronic immune activation, oxidative and nitrosative stress (O&NS) and systemic inflammation. These factors, notably elevated pro-inflammatory cytokines, activate indoleamine 2,3-dioxygenase (IDO) leading to an upregulated tryptophan catabolite (TRYCAT) pathway of tryptophan degradation in the periphery and in the brain. In such conditions the TRYCAT pathway becomes the predominant system for tryptophan degradation in all body compartments. In this paper we review the pathways whereby TRYCATs may play a role in neuro-inflammatory and neuroprogressive disease. Thus chronic activation of the TRYCAT pathway leads to the production of a range of neuroactive, neuroprotective and neurotoxic TRYCATs. Some TRYCATs such as quinolinic acid act as potent neurotoxins which inhibit ATP production by mitochondria, provoke increases in O&NS, disrupt neuron glial communication and blood brain barrier integrity, induce apoptosis of glial cells, directly damage neurons and function as a N-methyl D-aspartate (NMDA) receptor agonist. Other TRYCATs such as kynurenic acid function as antagonists of NMDA, α- amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid and kainate receptors and act to regulate levels of glutamate and dopamine. The neuroprotective functions of this TRYCAT are likely exercised via engagement with alpha7 nicotinic acetylcholine and aryl hydrocarbon receptors but the neuroprotective effects stemming from elevated kynurenic acid levels come at the price of severely compromised neurocognitive function and emotional processing. Other TRYCATS also possess neurotoxic or neuroprotective properties via pro-oxidant and antioxidant effects. Here we discuss the involvement of the abovementioned TRYCAT pathways in schizophrenia, Alzheimer's disease and chronic fatigue syndrome.
Morris G(1), Anderson G(2), Maes M(3,)(4,)(5,)(6).	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, Wales, SA152LW, UK. (2)CRC	Hypothalamic-Pituitary-Adrenal Hypofunction in Myalgic Encephalomyelitis (ME)/Chronic Fatigue	65. Mol Neurobiol. 2016 Oct 20.	There is evidence that immune-inflammatory and oxidative and nitrosative stress (O&NS) pathways play a role in the pathophysiology of myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS). There is also evidence that these neuroimmune diseases are accompanied by hypothalamic-pituitary-adrenal (HPA) axis hypoactivity as

	Scotland & London, Eccleston Square, London, UK. (3)IMPACT Strategic Research Centre, School of Medicine and Barwon Health, Deakin University, Geelong, VIC, Australia. dr.michaelmaes@hotmail.com. (4)Health Sciences Postgraduate Program, State University of Londrina, Londrina, Paraná, Brazil. dr.michaelmaes@hotmail.com. (5)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com. (6)Department of Psychiatry, Medical University of Plovdiv, Plovdiv, Bulgaria. dr.michaelmaes@hotmail.com.	Syndrome (CFS) as a Consequence of Activated Immune-Inflammatory and Oxidative and Nitrosative Pathways.		indicated by lowered baseline glucocorticoid levels. This paper aims to review the bidirectional communications between immune-inflammatory and O&NS pathways and HPA axis hypoactivity in ME/CFS, considering two possibilities: (a) Activation of immune-inflammatory pathways is secondary to HPA axis hypofunction via attenuated negative feedback mechanisms, or (b) chronic activated immune-inflammatory and O&NS pathways play a causative role in HPA axis hypoactivity. Electronic databases, i.e., PUBMED, Scopus, and Google Scholar, were used as sources for this narrative review by using keywords CFS, ME, cortisol, ACTH, CRH, HPA axis, glucocorticoid receptor, cytokines, immune, immunity, inflammation, and O&NS. Findings show that activation of immune-inflammatory and O&NS pathways in ME/CFS are probably not secondary to HPA axis hypoactivity and that activation of these pathways may underpin HPA axis hypofunction in ME/CFS. Mechanistic explanations comprise increased levels of tumor necrosis factor-α, T regulatory responses with elevated levels of interleukin-10 and transforming growth factor-β, elevated levels of nitric oxide, and viral/bacterial-mediated mechanisms. HPA axis hypoactivity in ME/CFS is most likely a consequence and not a cause of a wide variety of activated immune-inflammatory and O&NS pathways in that illness.
Morris G(1), Berk M, Carvalho AF, Caso JR, Sanz Y, Maes M.	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, SA152LW, Wales, United Kingdom. activatedmicroglia@gmail.com.	The role of microbiota and intestinal permeability in the pathophysiology of autoimmune and neuroimmune processes with an emphasis on Inflammatory Bowel	97. Curr Pharm Des. 2016 Sep 14.	BACKGROUND: In steady state conditions intestinal immune homeostasis is maintained by a sophisticated bidirectional dialogue between the microbiota and the intestinal immune system. This "cross talk" is enabled by the presence of highly adapted secretory cells, sampling cells and pattern recognition receptors in the gastric epithelium. METHODS: Herein we discuss the mechanisms involved in the breakdown of intestinal homeostasis and the development of systemic immune activation and neuroinflammation with a view to discussing the importance of these processes, in

		Disease Type 1 Diabetes and Chronic Fatigue Syndrome.		tandem with genetic and environmental factors, in the pathophysiology of (auto)immune diseases.Data is presented explaining how immune tolerance is maintained and how it may breakdown. CONCLUSIONS: The breakdown of immune homeostasis following the development of gut inflammation, caused for example by gut dysbiosis, and the consequent increased intestinal permeability, is increasingly considered to be the ultimate source of the systemic immune activation and T helper 17/T regulatory cell imbalances, and maybe neurological disturbances, seen in autoimmune diseases such as Type 1 diabetes and inflammatory bowel disease. Increased intestinal permeability and translocation of commensal antigens into the systemic circulation is also a likely cause of the severe fatigue and an almost bewildering range of neurocognitive, neuroimaging and overall symptom presentations seen in patients with a diagnosis of Chronic Fatigue Syndrome.
Morris G(1), Berk M(2,)(3,)(4,)(5), Galecki P(6), Walder K(7), Maes M(8,)(9,)(10,)(11).	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, SA152LW, Wales, UK. (2)IMPACT Strategic Research Centre, School of Medicine, Deakin University, P.O. Box 291, Geelong, 3220, Australia. (3)Orygen Youth Health Research Centre and the Centre of Youth Mental Health, Poplar Road 35, Parkville, 3052, Australia. (4)The Florey Institute for Neuroscience and Mental Health, University of Melbourne, Kenneth Myer Building, Royal Parade 30, Parkville, 3052, Australia. (5)Department of Psychiatry, University of Melbourne, Level 1 North, Main Block,	The Neuro-Immune Pathophysiology of Central and Peripheral Fatigue in Systemic Immune-Inflammatory and Neuro-Immune Diseases.	368. Mol Neurobiol. 2016 Mar;53(2):1195-219.	Many patients with systemic immune-inflammatory and neuro-inflammatory disorders, including depression, rheumatoid arthritis, systemic lupus erythematosus, Sjögren's disease, cancer, cardiovascular disorder, Parkinson's disease, multiple sclerosis, stroke, and chronic fatigue syndrome/myalgic encephalomyelitis, endure pathological levels of fatigue. The aim of this narrative review is to delineate the wide array of pathways that may underpin the incapacitating fatigue occurring in systemic and neuro-inflammatory disorders. A wide array of immune, inflammatory, oxidative and nitrosative stress (O&NS), bioenergetic, and neurophysiological abnormalities are involved in the etiopathology of these disease states and may underpin the incapacitating fatigue that accompanies these disorders. This range of abnormalities comprises: increased levels of pro-inflammatory cytokines, e.g., interleukin-1 (IL-1), IL-6, tumor necrosis factor (TNF) α and interferon (IFN) α; O&NS-induced muscle fatigue; activation of the Toll-Like Receptor Cycle through pathogen-associated (PAMPs) and damage-associated (DAMPs) molecular patterns, including heat shock proteins; altered glutaminergic and dopaminergic neurotransmission; mitochondrial dysfunctions; and O&NS-induced defects in the sodium-potassium pump. Fatigue is also associated with altered activities in specific brain regions and muscle pathology, such as reductions in maximum voluntary muscle force, downregulation of the mitochondrial biogenesis master gene peroxisome proliferator-activated receptor gamma coactivator 1-alpha, a shift to glycolysis and buildup of toxic metabolites within myocytes. As such, both mental and physical fatigue, which frequently accompany immune-inflammatory and neuro-inflammatory disorders, are the consequence of interactions between multiple systemic and central pathways.

	Royal Melbourne Hospital, Parkville, 3052, Australia. (6)Department of Adult Psychiatry, Medical University of Lodz, Lodz, Poland. (7)Metabolic Research Unit, Deakin University, Geelong, Australia. (8)IMPACT Strategic Research Centre, School of Medicine, Deakin University, P.O. Box 291, Geelong, 3220, Australia. dr.michaelmaes@hotmail.com. (9)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com. (10)Health Sciences Graduate Program, Health Sciences Center, State University of Londrina, Londrina, Brazil. dr.michaelmaes@hotmail.com. (11)Impact Strategic Research Center, Deakin University, Geelong, Australia. dr.michaelmaes@hotmail.com.			

Morris G(1), Berk M(2,)(3,)(4,)(5), Klein H(6), Walder K(7), Galecki P(8), Maes M(9,)(10,)(11,)(12,)(13).	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, SA152LW, Wales, UK. (2)IMPACT Strategic Research Centre, School of Medicine, Deakin University, P.O. Box 291, Geelong, 3220, Australia. (3)Orygen Youth Health Research Centre and the Centre of Youth Mental Health, Poplar Road 35, Parkville, 3052, Australia. (4)The Florey Institute for Neuroscience and Mental Health, University of Melbourne, Kenneth Myer Building, Royal Parade 30, Parkville, 3052, Australia. (5)Department of Psychiatry, Royal Melbourne Hospital, University of Melbourne, Level 1 North, Main Block, Parkville, 3052, Australia. (6)Department of Psychiatry, University of Groningen, UMCG, Groningen, The Netherlands. (7)Metabolic Research Unit, School of Medicine, Deakin	Nitrosative Stress, Hypernitrosylation, and Autoimmune Responses to Nitrosylated Proteins: New Pathways in Neuroprogressive Disorders Including Depression and Chronic Fatigue Syndrome.	155. Mol Neurobiol. 2016 Jun 23.	Nitric oxide plays an indispensable role in modulating cellular signaling and redox pathways. This role is mainly effected by the readily reversible nitrosylation of selective protein cysteine thiols. The reversibility and sophistication of this signaling system is enabled and regulated by a number of enzymes which form part of the thioredoxin, glutathione, and pyridoxine antioxidant systems. Increases in nitric oxide levels initially lead to a defensive increase in the number of nitrosylated proteins in an effort to preserve their function. However, in an environment of chronic oxidative and nitrosative stress (O&NS), nitrosylation of crucial cysteine groups within key enzymes of the thioredoxin, glutathione, and pyridoxine systems leads to their inactivation thereby disabling denitrosylation and transnitrosylation and subsequently a state described as "hypernitrosylation." This state leads to the development of pathology in multiple domains such as the inhibition of enzymes of the electron transport chain, decreased mitochondrial function, and altered conformation of proteins and amino acids leading to loss of immune tolerance and development of autoimmunity. Hypernitrosylation also leads to altered function or inactivation of proteins involved in the regulation of apoptosis, autophagy, proteomic degradation, transcription factor activity, immune-inflammatory pathways, energy production, and neural function and survival. Hypernitrosylation, as a consequence of chronically elevated O&NS and activated immune-inflammatory pathways, can explain many characteristic abnormalities observed in neuroprogressive disease including major depression and chronic fatigue syndrome/myalgic encephalomyelitis. In those disorders, increased bacterial translocation may drive hypernitrosylation and autoimmune responses against nitrosylated proteins.

	University, Waurn Ponds, Australia. (8)Department of Adult Psychiatry, Medical University of Lodz, Łódź, Poland. (9)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com. (10)Department of Psychiatry, Faculty of Medicine, State University of Londrina, Londrina, Brazil. dr.michaelmaes@hotmail.com. (11)Department of Psychiatry, Medical University Plovdiv, Plovdiv, Bulgaria. dr.michaelmaes@hotmail.com. (12)Revitalis, Waalre, The Netherlands. dr.michaelmaes@hotmail.com. (13)IMPACT Strategic Research Center, Barwon Health, Deakin University, Geelong, VIC, Australia. dr.michaelmaes@hotmail.com.			
Morris G(1), Berk M(2,)(3), Walder	(1)Tir Na Nog, Bryn Road seaside 87,	The Putative Role of Viruses, Bacteria, and	361. Mol Neurobiol. 2016 May;53(4):2550-71.	Patients who present with severe intractable apparently idiopathic fatigue accompanied by profound physical and or cognitive disability present a significant

K(4), Maes M(5,)(6).	Llanelli, SA15 2LW, Wales, UK. (2)IMPACT Strategic Research Centre, School of Medicine, Deakin University, Geelong, Australia. (3)Orygen, The National Centre of Excellence in Youth Mental Health, Department of Psychiatry and The Florey Institute of Neuroscience and Mental Health, The University of Melbourne, Parkville, Australia. (4)Centre for Molecular and Medical Research, School of Medicine, Deakin University, Geelong, Australia. (5)IMPACT Strategic Research Centre, School of Medicine, Deakin University, Geelong, Australia. dr.michaelmaes@hotmail.com. (6)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com.	Chronic Fungal Biotoxin Exposure in the Genesis of Intractable Fatigue Accompanied by Cognitive and Physical Disability.		therapeutic challenge. The effect of psychological counseling is limited, with significant but very slight improvements in psychometric measures of fatigue and disability but no improvement on scientific measures of physical impairment compared to controls. Similarly, exercise regimes either produce significant, but practically unimportant, benefit or provoke symptom exacerbation. Many such patients are afforded the exclusionary, non-specific diagnosis of chronic fatigue syndrome if rudimentary testing fails to discover the cause of their symptoms. More sophisticated investigations often reveal the presence of a range of pathogens capable of establishing life-long infections with sophisticated immune evasion strategies, including Parvoviruses, HHV6, variants of Epstein-Barr, Cytomegalovirus, Mycoplasma, and Borrelia burgdorferi. Other patients have a history of chronic fungal or other biotoxin exposure. Herein, we explain the epigenetic factors that may render such individuals susceptible to the chronic pathology induced by such agents, how such agents induce pathology, and, indeed, how such pathology can persist and even amplify even when infections have cleared or when biotoxin exposure has ceased. The presence of active, reactivated, or even latent Herpes virus could be a potential source of intractable fatigue accompanied by profound physical and or cognitive disability in some patients, and the same may be true of persistent Parvovirus B12 and mycoplasma infection. A history of chronic mold exposure is a feasible explanation for such symptoms, as is the presence of B. burgdorferi. The complex tropism, life cycles, genetic variability, and low titer of many of these pathogens makes their detection in blood a challenge. Examination of lymphoid tissue or CSF in such circumstances may be warranted.
Morris G(1), Walder K(2), Puri	(1)Tir Na Nog, Bryn Road seaside 87,	The Deleterious Effects of Oxidative and Nitrosative	351. Mol Neurobiol. 2016 Sep;53(7):4638-58.	Oxidative and nitrosative stress (O&NS) is causatively implicated in the pathogenesis of Alzheimer's and Parkinson's disease, multiple sclerosis, chronic fatigue syndrome,

BK(3), Berk M(4,)(5,)(6,)(7), Maes M(8,)(9,)(10).	Llanelli, SA152LW, Wales, UK. (2)Metabolic Research Unit, Deakin University, Geelong, Australia. (3)Department of Medicine, Hammersmith Hospital, Imperial College London, London, W12 0HS, UK. (4)Orygen, The National Centre of Excellence in Youth Mental Health and the Centre of Youth Mental Health, Poplar Road 35, Parkville, 3052, Australia. (5)The Florey Institute for Neuroscience and Mental Health, University of Melbourne, Kenneth Myer Building, Royal Parade 30, Parkville, 3052, Australia. (6)Department of Psychiatry, Royal Melbourne Hospital, University of Melbourne, Level 1 North, Main Block, Parkville, 3052, Australia. (7)IMPACT Strategic Research Center, School of Medicine, Deakin University, P.O. Box	Stress on Palmitoylation, Membrane Lipid Rafts and Lipid-Based Cellular Signalling: New Drug Targets in Neuroimmune Disorders.		schizophrenia and depression. Many of the consequences stemming from O&NS, including damage to proteins, lipids and DNA, are well known, whereas the effects of O&NS on lipoprotein-based cellular signalling involving palmitoylation and plasma membrane lipid rafts are less well documented. The aim of this narrative review is to discuss the mechanisms involved in lipid-based signalling, including palmitoylation, membrane/lipid raft (MLR) and n-3 polyunsaturated fatty acid (PUFA) functions, the effects of O&NS processes on these processes and their role in the abovementioned diseases. S-palmitoylation is a post-translational modification, which regulates protein trafficking and association with the plasma membrane, protein subcellular location and functions. Palmitoylation and MRLs play a key role in neuronal functions, including glutamatergic neurotransmission, and immune-inflammatory responses. Palmitoylation, MLRs and n-3 PUFAs are vulnerable to the corruptive effects of O&NS. Chronic O&NS inhibits palmitoylation and causes profound changes in lipid membrane composition, e.g. n-3 PUFA depletion, increased membrane permeability and reduced fluidity, which together lead to disorders in intracellular signal transduction, receptor dysfunction and increased neurotoxicity. Disruption of lipid-based signalling is a source of the neuroimmune disorders involved in the pathophysiology of the abovementioned diseases. n-3 PUFA supplementation is a rational therapeutic approach targeting disruptions in lipid-based signalling.

	291, Geelong, 3220, Australia. (8)IMPACT Strategic Research Center, School of Medicine, Deakin University, P.O. Box 291, Geelong, 3220, Australia. dr.michaelmaes@hotmail.com. (9)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com. (10)Health Sciences Graduate Program, Health Sciences Center, State University of Londrina, Londrina, Brazil. dr.michaelmaes@hotmail.com.			
Morris JA(1), Broughton SJ(2), Wessels Q(2).	(1)Department of Pathology, Royal Lancaster Infirmary, Lancaster LAI 4RP, UK. Electronic address: Jim.A.Morris@mbht.nhs.uk. (2)Faculty of Health and Medicine, Lancaster University, Lancaster LA1 4YQ, UK.	Microbes, molecular mimicry and molecules of mood and motivation.	296. Med Hypotheses. 2016 Feb;87:40-3.	The hypothesis proposed is that functional disorders, such as irritable bowel syndrome, chronic fatigue syndrome and anorexia nervosa are caused by auto-antibodies to neuronal proteins induced by molecular mimicry with microbial antigens. The age incidence of these conditions, the marked female excess, increase with economic and technological advance, precipitation by infection, and the paucity of histological changes are all consistent with the hypothesis. It can be tested directly using human sera to search for cross reaction with brain proteins in model systems such as Drosophila melanogaster. The conditions might be amenable to treatment using pooled immunoglobulin. Identification and elimination from the microbial flora of the bacteria that express the cross reacting antigens should be possible.
Morroy G(1), Keijmel SP(2,)(3,)(4), Delsing CE(5),	(1)Department of Infectious Diseases, Municipal Health Service Hart voor	Fatigue following Acute Q-Fever: A Systematic Literature Review.	185. PLoS One. 2016 May 25;11(5):e0155884.	BACKGROUND: Long-term fatigue with detrimental effects on daily functioning often occurs following acute Q-fever. Following the 2007-2010 Q-fever outbreak in the Netherlands with over 4000 notified cases, the emphasis on long-term consequences of Q-fever increased. The aim of this study was to provide an overview of all relevant

Bleijenberg G(4), Langendam M(6), Timen A(7), Bleeker-Rovers CP(2,)(3).	Brabant, 's-Hertogenbosch, the Netherlands. (2)Radboud Expertise Centre for Q fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical center, Nijmegen, the Netherlands. (3)Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical center, Nijmegen, the Netherlands. (4)Expert Centre for Chronic Fatigue, Radboud university medical center, Nijmegen, the Netherlands. (5)Department of Internal Medicine, Medisch Spectrum Twente, Enschede, the Netherlands. (6)Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Centre, Amsterdam, the Netherlands. (7)Centre for Infectious Disease Control, National Institute for Public			available literature, and to identify knowledge gaps regarding the definition, diagnosis, background, description, aetiology, prevention, therapy, and prognosis, of fatigue following acute Q-fever. DESIGN: A systematic review was conducted through searching Pubmed, Embase, and PsycInfo for relevant literature up to 26th May 2015. References of included articles were hand searched for additional documents, and included articles were quality assessed. RESULTS: Fifty-seven articles were included and four documents classified as grey literature. The quality of most studies was low. The studies suggest that although most patients recover from fatigue within 6-12 months after acute Q-fever, approximately 20% remain chronically fatigued. Several names are used indicating fatigue following acute Q-fever, of which Q-fever fatigue syndrome (QFS) is most customary. Although QFS is described to occur frequently in many countries, a uniform definition is lacking. The studies report major health and work-related consequences, and is frequently accompanied by nonspecific complaints. There is no consensus with regard to aetiology, prevention, treatment, and prognosis. CONCLUSIONS: Long-term fatigue following acute Q-fever, generally referred to as QFS, has major health-related consequences. However, information on aetiology, prevention, treatment, and prognosis of QFS is underrepresented in the international literature. In order to facilitate comparison of findings, and as platform for future studies, a uniform definition and diagnostic work-up and uniform measurement tools for QFS are proposed.

	Health and the Environment, Bilthoven, the Netherlands.			
Mueller T(1), Jerrentrup A(2), Bauer MJ(2), Fritsch HW(3), Schaefer JR(2).	(1)Center for undiagnosed and rare diseases, University clinic Marburg, Baldinger Str. 1, D-35043, Marburg, Germany. tobias.mueller@staff.uni-marburg.de. (2)Center for undiagnosed and rare diseases, University clinic Marburg, Baldinger Str. 1, D-35043, Marburg, Germany. (3)Information technology Department, University clinic Marburg, Baldinger Str. 1, D-35043, Marburg, Germany.	Characteristics of patients contacting a center for undiagnosed and rare diseases.	160. Orphanet J Rare Dis. 2016 Jun 21;11(1):81.	BACKGROUND: Little is known about the characteristics of patients seeking help from dedicated centers for undiagnosed and rare diseases. However, information about their demographics, symptoms, prior diagnoses and medical specialty is crucial to optimize these centers' processes and infrastructure. METHODS: Using a questionnaire, structured information from 522 adult patients contacting a center for undiagnosed and rare diseases was obtained. The information included basic sociodemographic data (age, gender, insurance status), previous hospital admissions, primary symptoms of complaint and previously determined diagnosis. RESULTS: The majority of patients completing the questionnaire were female, 300 (57 %) vs. 222 men (43 %). The median age was 52 years (range 18-92). More than half, 309 (59 %), of our patients had never been admitted to a university hospital. Common diagnoses included other soft tissue disorders, not classified elsewhere (ICD M79, n = 63, 15.3 %), somatoform disorders (ICD F45, n = 51, 12.3 %) and other polyneuropathies (ICD G62, n=36, 8.7 %). The most frequent symptoms were general weakness (n = 180, 36.6 %) followed by arthralgia (n = 124, 25.2 %) and abdominal discomfort (n = 113, 23.0 %). The majority of patients had either internal medicine (81.3 %) and/or neurologic (37.6 %) health problems. CONCLUSIONS: Pain-associated diagnoses and the typical "unexplained" medical conditions (chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome) are frequent among people contacting a center dedicated to undiagnosed diseases. The chief symptoms are mostly unspecific. An interdisciplinary organizational approach involving mainly internal medicine, neurology and psychiatry/psychosomatic care is needed.
Munford RS(1).	(1)Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD, USA munfordrs@niaid.nih.gov.	Endotoxemia-menace, marker, or mistake?	137. J Leukoc Biol. 2016 Oct;100(4):687-698. Epub 2016 Jul 14.	Endotoxemia is in its scientific ascendancy. Never has blood-borne, Gram-negative bacterial endotoxin (LPS) been invoked in the pathogenesis of so many diseases-not only as a trigger for septic shock, once its most cited role, but also as a contributor to atherosclerosis, obesity, chronic fatigue, metabolic syndrome, and many other conditions. Finding elevated plasma endotoxin levels has been essential supporting evidence for each of these links, yet the assays used to detect and quantitate endotoxin have important limitations. This article describes several assays for endotoxin in plasma, reviews what they do and do not measure, and discusses why LPS heterogeneity, LPS trafficking pathways, and host LPS inactivation mechanisms should be considered when interpreting endotoxin assay results.
Murdock KW(1), Wang XS(2), Shi	(1)Department of Psychology, Rice	The utility of patient-reported outcome	102. Qual Life Res. 2016 Sep 6.	PURPOSE: Debilitating fatigue is a core symptom of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS); however, the utility of patient-reported symptom outcome

Q(3), Cleeland CS(3), Fagundes CP(1,)(3), Vernon SD(4).	University, Houston, TX, USA. (2)Department of Symptom Research, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Unit 1450, Houston, TX, 77030, USA. xswang@mdanderson .org. (3)Department of Symptom Research, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Unit 1450, Houston, TX, 77030, USA. (4)Bateman Horne Center of Excellence, Salt Lake City, UT, USA.	measures among patients with myalgic encephalomyelitis/chronic fatigue syndrome.		measures of fatigue for ME/CFS patients is problematic due to ceiling effects and issues with reliability and validity. We sought to evaluate the performance of three patient-reported symptom measures in a sample of ME/CFS patients and matched controls. METHODS: Two hundred and forty ME/CFS patients and 88 age, sex, race, and zip code matched controls participated in the study. Participants completed the Multidimensional Fatigue Inventory-20, DePaul Symptom Questionnaire, and RAND SF-36. RESULTS: The general and physical fatigue subscales on Multidimensional Fatigue Inventory-20, as well as the role of physical health on the RAND SF-36, demonstrated questionable or unacceptable internal consistency and problematic ceiling effects. The DePaul Symptom Questionnaire demonstrated excellent internal reliability, and less than 5 % of participants were at the ceiling on each subscale. The post-exertional malaise subscale on the DePaul Symptom Questionnaire demonstrated excellent clinical utility as it was able to differentiate between ME/CFS patients and controls (OR 1.23, $p < .001$) and predicted ceiling effects on other patient-reported outcome subscales. A score of 20 on the post-exertional malaise subscale of the DePaul Symptom Questionnaire optimally differentiated between patients and controls. CONCLUSIONS: Significant ceiling effects and concerns with reliability and validity were observed among Multidimensional Fatigue Inventory-20 and RAND SF-36 subscales for ME/CFS patients. The DePaul Symptom Questionnaire addresses a number of concerns typically identified when using patient-reported outcome measures with ME/CFS patients; however, an improved multidimensional patient-reported outcome tool for measuring ME/CFS-related symptoms is warranted.
Narusyte J(1), Ropponen A(2), Alexanderson K(1), Svedberg P(1).	(1)Division of Insurance Medicine,Department of Clinical Neuroscience,Karolinska Institutet,Stockholm,Sweden. (2)Finnish Institute of Occupational Health,Helsinki,Finland.	Genetic and Environmental Influences on Disability Pension Due To Mental Diagnoses: Limited Importance of Major Depression, Generalized Anxiety, and Chronic Fatigue.	327. Twin Res Hum Genet. 2016 Feb;19(1):10-6.	BACKGROUND: Previous research indicates that liability to disability pension (DP) due to mental diagnoses is moderately influenced by genetic factors. This study investigates whether genetic contributions to the liability to DP due to mood and neurotic diagnoses overlap with the genetic influences on major depression (MD), generalized anxiety disorder (GAD), or chronic fatigue (CF). METHOD: A prospective cohort study including 9,985 female twins born in Sweden 1933-1958. The presence of MD, GAD, and CF was assessed by computer-assisted telephone interviews conducted in 1998-2002. Data on DP due to mood and neurotic diagnoses were obtained from nationwide registers for the years 1998-2010. Common genetic and environmental influences on the phenotypes were estimated by applying structural equation modeling. RESULTS: The prevalence of MD/GAD was 30%, CF 8%, and DP due to mood and neurotic diagnoses 3% in 2010. Genetic effects on MD/GAD explained 31% of the total genetic variation in DP, whereas genetic contributions in common with CF were small and not significant. The majority of the total non-shared environmental variance in DP (85%) was explained by the factors that were unique to DP. CONCLUSIONS: Large proportions of genetic and non-shared environmental influences in DP due to mood and neurotic diagnoses were not explained by the contributions from MD/GAD or CF. The results

				suggest that the process leading to DP is complex and influenced by factors other than those related to the disorder underlying DP.
Navaneetharaja N(1,)(2), Griffiths V(3), Wileman T(4,)(5), Carding SR(6,)(7).	(1)The Gut Health and Food Safety Research Programme, The Institute of Food Research, University of East Anglia, Norwich NR4 7UA, UK. navena.navaneetharaja@ifr.ac.uk. (2)Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK. navena.navaneetharaja@ifr.ac.uk. (3)Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK. v.griffiths@uea.ac.uk. (4)The Gut Health and Food Safety Research Programme, The Institute of Food Research, University of East Anglia, Norwich NR4 7UA, UK. t.wileman@uea.ac.uk. (5)Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK. t.wileman@uea.ac.uk. (6)The Gut Health and Food Safety Research Programme, The Institute of Food Research, University	A Role for the Intestinal Microbiota and Virome in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)?	171. J Clin Med. 2016 Jun 6;5(6). pii: E55.	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a heterogeneous disorder of significant societal impact that is proposed to involve both host and environmentally derived aetiologies that may be autoimmune in nature. Immune-related symptoms of at least moderate severity persisting for prolonged periods of time are common in ME/CFS patients and B cell depletion therapy is of significant therapeutic benefit. The origin of these symptoms and whether it is infectious or inflammatory in nature is not clear, with seeking evidence of acute or chronic virus infections contributing to the induction of autoimmune processes in ME/CFS being an area of recent interest. This article provides a comprehensive review of the current evidence supporting an infectious aetiology for ME/CFS leading us to propose the novel concept that the intestinal microbiota and in particular members of the virome are a source of the "infectious" trigger of the disease. Such an approach has the potential to identify disease biomarkers and influence therapeutics, providing much-needed approaches in preventing and managing a disease desperately in need of confronting.

	of East Anglia, Norwich NR4 7UA, UK. simon.carding@IFR.ac.uk. (7)Norwich Medical School, University of East Anglia, Norwich NR4 7TJ, UK. simon.carding@IFR.ac.uk.			
Naviaux RK(1,)(2,)(3,)(4), Naviaux JC(5,)(6), Li K(5,)(2), Bright AT(5,)(2), Alaynick WA(5,)(2), Wang L(5,)(2), Baxter A(7), Nathan N(7), Anderson W(7), Gordon E(7).	(1)The Mitochondrial and Metabolic Disease Center, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; rnaviaux@ucsd.edu. (2)Department of Medicine, University of California, San Diego School of Medicine, San Diego, CA 92103-8467. (3)Department of Pediatrics, University of California, San Diego School of Medicine, San Diego, CA 92103-8467. (4)Department of Pathology, University of California, San Diego School of Medicine, San Diego, CA 92103-8467. (5)The Mitochondrial and Metabolic Disease Center, University of California, San Diego	Reply to Vogt et al.: Metabolomics and chronic fatigue syndrome.	49. Proc Natl Acad Sci U S A. 2016 Nov 15;113(46):E7142-E7143. Epub 2016 Nov 3.	

	School of Medicine, San Diego, CA 92103-8467. (6)Department of Neurosciences, University of California, San Diego School of Medicine, San Diego, CA 92103-8467. (7)Gordon Medical Associates, Santa Rosa, CA 95403.			
Naviaux RK(1), Naviaux JC(2), Li K(3), Bright AT(3), Alaynick WA(3), Wang L(3), Baxter A(4), Nathan N(4), Anderson W(4), Gordon E(4).	(1)The Mitochondrial and Metabolic Disease Center, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; Department of Medicine, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; Department of Pediatrics, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; Department of Pathology, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; rnaviaux@ucsd.edu. (2)The Mitochondrial and Metabolic Disease Center, University of California, San Diego	Metabolic features of chronic fatigue syndrome.	109. Proc Natl Acad Sci U S A. 2016 Sep 13;113(37):E5472-80.	More than 2 million people in the United States have myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). We performed targeted, broad-spectrum metabolomics to gain insights into the biology of CFS. We studied a total of 84 subjects using these methods. Forty-five subjects (n = 22 men and 23 women) met diagnostic criteria for ME/CFS by Institute of Medicine, Canadian, and Fukuda criteria. Thirty-nine subjects (n = 18 men and 21 women) were age- and sex-matched normal controls. Males with CFS were 53 (±2.8) y old (mean ± SEM; range, 21-67 y). Females were 52 (±2.5) y old (range, 20-67 y). The Karnofsky performance scores were 62 (±3.2) for males and 54 (±3.3) for females. We targeted 612 metabolites in plasma from 63 biochemical pathways by hydrophilic interaction liquid chromatography, electrospray ionization, and tandem mass spectrometry in a single-injection method. Patients with CFS showed abnormalities in 20 metabolic pathways. Eighty percent of the diagnostic metabolites were decreased, consistent with a hypometabolic syndrome. Pathway abnormalities included sphingolipid, phospholipid, purine, cholesterol, microbiome, pyrroline-5-carboxylate, riboflavin, branch chain amino acid, peroxisomal, and mitochondrial metabolism. Area under the receiver operator characteristic curve analysis showed diagnostic accuracies of 94% [95% confidence interval (CI), 84-100%] in males using eight metabolites and 96% (95% CI, 86-100%) in females using 13 metabolites. Our data show that despite the heterogeneity of factors leading to CFS, the cellular metabolic response in patients was homogeneous, statistically robust, and chemically similar to the evolutionarily conserved persistence response to environmental stress known as dauer.

	School of Medicine, San Diego, CA 92103-8467; Department of Neurosciences, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; (3)The Mitochondrial and Metabolic Disease Center, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; Department of Medicine, University of California, San Diego School of Medicine, San Diego, CA 92103-8467; (4)Gordon Medical Associates, Santa Rosa, CA 95403.			
Nebgen DR(1), Rhodes HE, Hartman C, Munsell MF, Lu KH.	(1)Departments of Gynecologic Oncology and Reproductive Medicine and Biostatistics, the University of Texas MD Anderson Cancer Center, Houston, Texas.	Abnormal Uterine Bleeding as the Presenting Symptom of Hematologic Cancer.	144. Obstet Gynecol. 2016 Aug;128(2):357-63.	OBJECTIVE: To estimate the percentage of women with a hematologic cancer who present with abnormal uterine bleeding (AUB). METHODS: We performed a retrospective analysis of the records of women with hematologic malignancies treated at our institution from January 2002 through January 2016. Women with AUB as the chief presenting symptom were identified. RESULTS: Of the 10,682 women with hematologic malignancies, 38 had AUB as their chief presenting symptom. These women were young (median age 34 years), premenopausal, and otherwise healthy. The top four additional presenting symptoms were fatigue, dyspnea or shortness of breath, bruising or petechiae, and fever, with means (95% confidence interval) of 58% (41-74%), 42% (26-59%), 42% (26-59%), and 24% (11-40%), respectively. The complete blood count on initial presentation with AUB revealed that 33 (87%) women had anemia (mean hemoglobin level 8.6 g/dL) and 34 (89%) had thrombocytopenia (mean platelet count 81,000/microliter). Twelve (32%) women had neutropenia, eight (21%) women had normal white blood cell counts, and 18 (47%) women had leukocytosis. Thirty-three women (87%) were diagnosed with acute leukemia, one with myelodysplastic syndrome (3%) and four (11%) with chronic leukemia. CONCLUSION:

				We estimate the incidence of AUB as the chief presenting symptom is 3.6 cases per 1,000 women with hematologic cancer. These young, otherwise healthy women who present with acute, new-onset heavy menstrual bleeding in conjunction with thrombocytopenia or pancytopenia should be referred to hematology for evaluation of possible hematologic malignancy.
Neblett R(1), Hartzell MM(1), Mayer TG(2), Cohen H(3), Gatchel RJ(4).	(1)PRIDE Research Foundation, Dallas, Texas, U.S.A. (2)Department of Orthopedic Surgery, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, U.S.A. (3)Graduate School of Nursing, University of Texas at Arlington, Arlington, Texas, U.S.A. (4)Department of Psychology, University of Texas at Arlington, Arlington, Texas, U.S.A.	Establishing Clinically Relevant Severity Levels for the Central Sensitization Inventory	244. Pain Pract. 2016 Mar 15. .	OBJECTIVES: The aim of this study was to create and validate severity levels for the central sensitization inventory (CSI), a valid and reliable patient-reported outcome instrument designed to identify patients whose presenting symptoms may be related to a central sensitivity syndrome (CSS; eg, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome), with a proposed common etiology of central sensitization (CS). METHODS: Based on CSI score means and standard deviations from previously published subject samples, the following CSI severity levels were established: subclinical = 0 to 29; mild = 30 to 39; moderate = 40 to 49; severe = 50 to 59; and extreme = 60 to 100. The concurrent validity of the CSI severity levels was then confirmed in a separate chronic pain patient sample (58% with a CSS diagnosis and 42% without) by demonstrating associations between CSI scores and (1) the number of physician-diagnosed CSSs; (2) CSI score distributions in both CSS and non-CSS patient samples; (3) patient-reported history of CSSs; and (4) patient-reported psychosocial measures, which are known to be associated with CSSs. RESULTS: Compared to the non-CSS patient subsample, the score distribution of the CSS patient subsample was skewed toward the higher severity ranges. CSI mean scores moved into higher severity levels as the number of individual CSS diagnoses increased. Patients who scored in the extreme CSI severity level were more likely to report previous diagnoses of fibromyalgia, chronic fatigue syndrome, temporomandibular joint disorder, tension/migraine headaches, and anxiety or panic attacks ($P < 0.01$). CSI severity levels were also associated with patient-reported depressive symptoms, perceived disability, sleep disturbance, and pain intensity ($P \leq 0.02$). CONCLUSION: This study provides support for these CSI severity levels as a guideline for healthcare providers and researchers in interpreting CSI scores and evaluating treatment responsiveness.
Nes LS(1,)(2), Ehlers SL(1), Whipple MO(3), Vincent A(3).	(1)Department of Psychiatry and Psychology, Mayo Clinic, Rochester, Minnesota, USA. (2)Center for Shared Decision Making and Collaborative Care Research, Division of Medicine, Oslo University Hospital,	Self-Regulatory Fatigue: A Missing Link in Understanding Fibromyalgia and Other Chronic MultiSymptom Illnesses.	105. Pain Pract. 2016 Sep 2.	OBJECTIVE: Patients with chronic multisymptom illnesses such as fibromyalgia syndrome (FMS) are experiencing a multitude of physical and mental challenges. Facing such challenges may drain capacity to self-regulate, and research suggests patients with these illnesses may experience self-regulatory fatigue (SRF). This study sought to examine whether SRF can be associated with quality of life (QoL) in patients with FMS. METHODS: Patients (N = 258) diagnosed with FMS completed self-report measures related to demographics, SRF (Self-Regulatory Fatigue 18 [SRF-18]), anxiety (Generalized Anxiety Disorder questionnaire [GAD-7]), depression (Patient Health Questionnaire [PHQ-9]), physical fatigue (Multidimensional Fatigue Inventory [MFI]), symptoms related to FMS (Fibromyalgia Impact Questionnaire [FIQ]), and QoL (36-Item Short-Form Health Survey [SF-36]). RESULTS: Hierarchical regressions showed higher

	Oslo, Norway. (3)Division of General Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA.			SRF to be associated with lower QoL in terms of lower overall physical QoL, with subscales related to physical functioning, role limitations-physical, bodily pain, and general health (all P's > 0.001), as well as lower overall mental QoL, with subscales related to vitality, social functioning, role limitations-emotional, and mental health (all P's > 0.001). Including traditional predictors such as anxiety, depression, physical fatigue, and FMS-related symptoms as covariates in the analyses reduced the link between SRF and QoL somewhat, but the associations remained generally strong, particularly for SRF and mental QoL. CONCLUSION: This is the first study to show higher SRF relating to lower QoL for patients with FMS. Results suggest that SRF is distinct from anxiety, depression, and fatigue, and predicts QoL above and beyond these traditional factors in the area of chronic multisymptom illnesses such as FMS. SRF may be a "missing link" in understanding the complex nature of chronic multisymptom illnesses.
Newton JL(1), Finkelmeyer A(2), Petrides G(3), Frith J(1), Hodgson T(4), Maclachlan L(5), MacGowan G(1), Blamire AM(2).	(1)Institute of Cellular Medicine, Newcastle upon Tyne, UK; Newcastle University, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. (2)Institute of Cellular Medicine, Newcastle upon Tyne, UK; Newcastle Magnetic Resonance Centre, Newcastle upon Tyne, UK. (3)Newcastle University, Newcastle upon Tyne Hospitals NHS Foundation Trust , Newcastle upon Tyne , UK. (4)Newcastle Magnetic Resonance Centre , Newcastle upon Tyne , UK. (5)Institute of Cellular Medicine , Newcastle upon Tyne , UK.	Reduced cardiac volumes in chronic fatigue syndrome associate with plasma volume but not length of disease: a cohort study.	142. Open Heart. 2016 Jun 24;3(1):e000381.	OBJECTIVES: To explore potential mechanisms that underpin the cardiac abnormalities seen in chronic fatigue syndrome (CFS) using non-invasive cardiac impedance, red cell mass and plasma volume measurements. METHODS: Cardiac MR (MR) examinations were performed using 3 T Philips Intera Achieva scanner (Best, NL) in participants with CFS (Fukuda; n=47) and matched case-by-case controls. Total volume (TV), red cell volume (RCV) and plasma volume (PV) measurements were performed (41 CFS and 10 controls) using the indicator dilution technique using simultaneous 51-chromium labelling of red blood cells and 125-iodine labelling of serum albumin. RESULTS: The CFS group length of history (mean±SD) was 14±10 years. Patients with CFS had significantly reduced end-systolic and end-diastolic volumes together with reduced end-diastolic wall masses (all p<0.0001). Mean±SD RCV was 1565±443 mL with 26/41 (63%) having values below 95% of expected. PV was 2659±529 mL with 13/41 (32%) <95% expected. There were strong positive correlations between TV, RCV and PV and cardiac end-diastolic wall mass (all p<0.0001; r(2)=0.5). Increasing fatigue severity correlated negatively with lower PV (p=0.04; r(2)=0.2). There were no relationships between any MR or volume measurements and length of history, suggesting that deconditioning was unlikely to be the cause of these abnormalities. CONCLUSIONS: This study confirms an association between reduced cardiac volumes and blood volume in CFS. Lack of relationship between length of disease, cardiac and plasma volumes suggests findings are not secondary to deconditioning. The relationship between plasma volume and severity of fatigue symptoms suggests a potential therapeutic target in CFS.

Ng WF, Miller A, Bowman SJ, Price EJ, Kitas GD, Pease C, Emery P, Lanyon P, Hunter J, Gupta M, Giles I, Isenberg D, McLaren J, Regan M, Cooper A, Young-Min SA, McHugh N, Vadivelu S, Moots RJ, Coady D, MacKay K, Dasgupta B, Sutcliffe N, Bombardieri M, Pitzalis C, Griffiths B, Mitchell S, Miyamoto ST, Trenell M; UK Primary Sjögren's Syndrome Registry.		Physical activity but not sedentary activity is reduced in primary Sjögren's syndrome.	6. Rheumatol Int. 2016 Dec 24.	The aim of the study was to evaluate the levels of physical activity in individuals with primary Sjögren's syndrome (PSS) and its relationship to the clinical features of PSS. To this cross-sectional study, self-reported levels of physical activity from 273 PSS patients were measured using the International Physical Activity Questionnaire-short form (IPAQ-SF) and were compared with healthy controls matched for age, sex and body mass index. Fatigue and other clinical aspects of PSS including disease status, dryness, daytime sleepiness, dysautonomia, anxiety and depression were assessed using validated tools. Individuals with PSS had significantly reduced levels of physical activity [median (interquartile range, IQR) 1572 (594-3158) versus 3708 (1732-8255) metabolic equivalent of task (MET) × min/week, $p < 0.001$], but similar levels of sedentary activity [median (IQR) min 300 (135-375) versus 343 (223-433) (MET) × min/week, $p = 0.532$] compared to healthy individuals. Differences in physical activity between PSS and controls increased at moderate [median (IQR) 0 (0-480) versus 1560 (570-3900) MET × min/week, $p < 0.001$] and vigorous intensities [median (IQR) 0 (0-480) versus 480 (0-1920) MET × min/week, $p < 0.001$]. Correlation analysis revealed a significant association between physical activity and fatigue, orthostatic intolerance, depressive symptoms and quality of life. Sedentary activity did not correlate with fatigue. Stepwise linear regression analysis identified symptoms of depression and daytime sleepiness as independent predictors of levels of physical activity. Physical activity is reduced in people with PSS and is associated with symptoms of depression and daytime sleepiness. Sedentary activity is not increased in PSS. Clinical care teams should explore the clinical utility of targeting low levels of physical activity in PSS.
Nguyen T(1,)(2), Johnston S(1,)(2), Clarke L(1,)(2), Smith P(1), Staines D(1,)(2), Marshall-Gradisnik S(1,)(2).	(1) The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute, Gold Coast, QLD, Australia. (2)School of Medical Science, Griffith University, Gold Coast, QLD, Australia.	Impaired calcium mobilization in natural killer cells from chronic fatigue syndrome/myalgic encephalomyelitis patients is associated with transient receptor potential melastatin 3 ion channels.	74. Clin Exp Immunol. 2017 Feb;187(2):284-293.	Transient receptor potential melastatin subfamily 3 (TRPM3) ion channels play a role in calcium (Ca^{2+}) cell signalling. Reduced TRPM3 protein expression has been identified in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) patients. However, the significance of TRPM3 and association with intracellular Ca^{2+} mobilization has yet to be determined. Fifteen CFS/ME patients (mean age 48·82 ± 9·83 years) and 25 healthy controls (mean age 39·2 ± 12·12 years) were examined. Isolated natural killer (NK) cells were labelled with fluorescent antibodies to determine TRPM3, CD107a and CD69 receptors on CD56(dim) CD16(+) NK cells and CD56(bright) CD16(dim/-) NK cells. Ca^{2+} flux and NK cytotoxicity activity was measured under various stimulants, including pregnenolone sulphate (PregS), thapsigargin (TG), 2-aminoethoxydiphenyl borate (2APB) and ionomycin. Unstimulated CD56(bright) CD16(dim/-) NK cells showed significantly reduced TRPM3 receptors in CFS/ME compared with healthy controls (HC). Ca^{2+} flux showed no significant difference between groups. Moreover, PregS-stimulated CD56(bright) CD16(dim/-) NK cells showed a significant increase in Ca^{2+} flux in CFS/ME patients compared with HC. By comparison, unstimulated CD56(dim)

				CD16(+) NK cells showed no significant difference in both Ca(2+) flux and TRPM3 expression. PregS-stimulated CD56(dim) CD16(+) NK cells increased TRPM3 expression significantly in CFS/ME, but this was not associated with a significant increase in Ca(2+) flux. Furthermore, TG-stimulated CD56(dim) CD16(+) NK cells increased K562 cell lysis prior to PregS stimulation in CFS/ME patients compared with HC. Differential expression of TRPM3 and Ca(2+) flux between NK cell subtypes may provide evidence for their role in the pathomechanism involving NK cell cytotoxicity activity in CFS/ME.
Nguyen T(1,)(2), Staines D(3,)(4), Nilius B(5), Smith P(3), Marshall-Gradisnik S(3,)(4).	(1)The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute, Griffith University, Parklands Drive, Southport, Mailbox 68, Gold Coast, 4222, Australia. thao.nguyen2@griffithuni.edu.au. (2)School of Medical Science, Griffith University, Gold Coast, Australia. thao.nguyen2@griffithuni.edu.au. (3)The National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute, Griffith University, Parklands Drive, Southport, Mailbox 68, Gold Coast, 4222, Australia. (4)School of Medical Science, Griffith University, Gold Coast, Australia. (5)Department of Molecular Cell	Novel identification and characterisation of Transient receptor potential melastatin 3 ion channels on Natural Killer cells and B lymphocytes: effects on cell signalling in Chronic fatigue syndrome/Myalgic encephalomyelitis patients.	178. Biol Res. 2016 May 31;49(1):27.	BACKGROUND: Transient receptor potential melastatin 3 (TRPM3) cation channels are ubiquitously expressed by multiple cells and have an important regulatory role in calcium-dependent cell signalling to help maintain cellular homeostasis. TRPM3 protein expression has yet to be determined on Natural Killer (NK) cells and B lymphocytes. Multiple single nucleotide polymorphisms have been reported in TRPM3 genes from isolated peripheral blood mononuclear cells, NK and B cells in Chronic fatigue syndrome/Myalgic encephalomyelitis (CFS/ME) patients and have been proposed to correlate with illness presentation. The object of the study was to assess TRPM3 surface expression on NK and B lymphocytes from healthy controls, followed by a comparative investigation examining TRPM3 surface expression, and cytoplasmic and mitochondrial calcium influx in CD19(+) B cells, CD56(bright) and CD56(dim) cell populations from CFS/ME patients. RESULTS: TRPM3 cell surface expression was identified for NK and B lymphocytes in healthy controls (CD56(bright) TRPM3 35.72 % ± 7.37; CD56(dim) 5.74 % ± 2.00; B lymphocytes 2.05 % ± 0.19, respectively). There was a significant reduction of TRPM3 surface expression on CD19(+) B cells (1.56 ± 0.191) and CD56(bright) NK cells (17.37 % ± 5.34) in CFS/ME compared with healthy controls. Anti-CD21 and anti-IgM conjugated biotin was cross-linked with streptavidin,and subsequently treatment with thapsigargin. This showed a significant reduction in cytoplasmic calcium ion concentration in CD19(+) B lymphocytes. CD56(bright) NK cells also had a significant decrease in cytoplasmic calcium in the presence of 2-APB and thapsigargin in CFS/ME patients. CONCLUSIONS: The results from this preliminary investigation identify, for the first time, TRPM3 surface expression on both NK and B lymphocytes in healthy controls. We also report for the first time, significant reduction in TRPM3 cell surface expression in NK and B lymphocytes, as well as decreased intracellular calcium within specific conditions in CFS/ME patients. This warrants further examination of these pathways to elucidate whether TRPM3 and impaired calcium mobilisation has a role in CFS/ME.

	Biology, Laboratory of Ion Channel Research, KU Leuven University, 49 Herestraat, Leuven, B-3000, Belgium.			
Nguyen T(1), Johnston S, Chacko A, Gibson D, Cepon J, Smith P, Staines D, Marshall-Gradisnik S.	(1)School of Medical Science, Griffith University, Gold Coast, QLD, Australia.	Novel characterisation of mast cell phenotypes from peripheral blood mononuclear cells in chronic fatigue syndrome/myalgic encephalomyelitis patients.	149. Asian Pac J Allergy Immunol. 2016 Jun 30.	BACKGROUND: Mast cells (MCs) mediate inflammation through neuropeptides and cytokines, along with histamine and reactive oxygen species (ROS). Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is an illness characterized by an unexplained disabling fatigue with multiple physiological impairments as well as dysregulated cytokine profiles. OBJECTIVE: To determine mast cell phenotypes in isolated human PBMCs, in healthy controls and in CFS/ME patients. Second, determine receptor expression of RAGE and its ligand high mobility group box 1 protein (HMGB1). METHOD: Moderately severe CFS/ME patients (n=12, mean age 39.25±SD3.52 years), severe CFS/ME patients (n=6, mean age 43.00±SD4.02 years) and healthy controls (n=13, mean age 42.69±SD3.87 years) were included in this study. CFS/ME patients were classified according to the 2011 International Consensus Criteria. LSRFortessa X-20 Flow cytometry was used for the identification of phenotypic peripheral mast cell population in PBMCs using an exclusion marker Lin2 cocktail (anti-CD3, anti-CD14, anti-CD19, anti-CD20 and anti-CD56) and inclusion markers (CD117, CD34, FCεRI, chymase, HLA-DR and CD154) following comparative investigation. HMGB1 and soluble RAGE expression in plasma was measured by sandwich ELISA assay. RESULTS: There was a significant increase in CD117+CD34+FCεRI-chymase- mast cell populations in moderate and severe CFS/ME patients compared with healthy controls. There was a significant increase in CD40 ligand and MHC-II receptors on differentiated mast cell populations in the severe CFS/ME compared with healthy controls and moderate CFS/ME. There were no significant differences between groups for HMGB1 and sRAGE. CONCLUSIONS: This preliminary study investigates mast cell phenotypes from PBMCs in healthy controls. We report significant increase of naïve MCs in moderate and severe CFS/ME patients compared with healthy controls. Moreover, a significant increase in CD40 ligand and MHC-II receptors on differentiated mast cells in severe CFS/ME patients. Peripheral MCs may be present in CFS/ME pathology however, further investigation to determine their role is required.
Nijhof LN(1), Nijhof SL(2), Bleijenberg G(3), Stellato RK(4), Kimpen JL(5), Hulshoff Pol HE(6), van de Putte EM(7).	(1)Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, HP KE.04.133.1, Post box 85090, 3508 AB, Utrecht, The	The impact of chronic fatigue syndrome on cognitive functioning in adolescents.	348. Eur J Pediatr. 2016 Feb;175(2):245-52.	Chronic fatigue syndrome (CFS) is characterized by persistent fatigue and severe disability. Most adolescent patients report attention and concentration problems, with subsequent poor performance at school. This study investigated the impact of CFS on intellectual capacity by (1) assessing discrepancies between current intelligence quotient (IQ) and school level and (2) exploring differences in current IQ and pre-CFS school performance, compared with healthy individuals. Current data was cross-sectionally gathered and compared with retrospective pre-CFS school performance data. Fifty-nine CFS adolescents and 40 controls were evaluated on performance on

	Netherlands. L.N.Nijhof@umcutrecht.nl. (2)Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, HP KE.04.133.1, Post box 85090, 3508 AB, Utrecht, The Netherlands. S.L.Nijhof@umcutrecht.nl. (3)Expert Center Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. Gijs.Bleijenberg@radboudumc.nl. (4)Biostatistics, Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht, The Netherlands. R.K.Stellato@umcutrecht.nl. (5)Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, HP KE.04.133.1, Post box 85090, 3508 AB, Utrecht, The Netherlands. J.Kimpen@umcutrech			age-appropriate intelligence tests and school level. Current IQ scores of CFS adolescents were lower than expected on the basis of their school level. Furthermore, there was a difference in intelligence performance across time when current IQ scores were compared with pre-CFS cognitive achievement. Healthy controls did not show any discrepancies.CONCLUSION: According to their pre-CFS intelligence assessments, CFS patients started with appropriate secondary school levels at the age of 12. Our data suggest that CFS may be accompanied by a decline in general cognitive functioning. Given the critical age for intellectual development, we recommend a timely diagnosis followed by appropriate treatment of CFS in adolescents. WHAT IS KNOWN: Adolescent chronic fatigue syndrome (CFS) is a debilitating condition with major impact on social and intellectual development. Most patients report concentration problems, with subsequent poor performance at school. Little is known about the influence of CFS on intellectual performances. WHAT IS NEW: IQ scores of CFS adolescents are lower than the IQ scores of healthy peers with an equivalent school level. There is a decrease in intelligence performance across time when current IQ scores are compared with pre-CFS cognitive achievement. Healthy controls do not show any discrepancies between their current IQ, school level and previous cognitive functioning. This suggest that adolescent CFS may be accompanied by a decline in general cognitive functioning.

	t.nl. (6)Rudolf Magnus Institute of Neuroscience, Department of Psychiatry, University Medical Centre Utrecht, Utrecht, The Netherlands. H.E.Hulshoff@umcutrecht.nl. (7)Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, HP KE.04.133.1, Post box 85090, 3508 AB, Utrecht, The Netherlands. E.vandePutte@umcutrecht.nl.			
Nijs J(1,)(2,)(3), Malfliet A(1,)(2).	(1)Pain in Motion International Research Group, Vrije Universiteit Brussel, Brussel, Belgium. (2)Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium. (3)Department of Physical Medicine and Physiotherapy, University Hospital Brussels, Brussels, Belgium.	Rehabilitation for patients with myalgic encephalomyelitis/chronic fatigue syndrome: time to extent the boundaries of this field.	347. J Intern Med. 2016 Mar;279(3):265-7.	Comment on J Intern Med. 2016 Mar;279(3):268-82.

Nordin LE(1,)(2), Möller MC(3,)(4), Julin P(3,)(5), Bartfai A(3), Hashim F(2,)(6), Li TQ(1,)(2).	(1)Department of Diagnostic Medical Physics, Karolinska University Hospital Huddinge, Stockholm, Sweden. (2)Department of Clinical Science, Intervention and Technology, Division of Medical Imaging and Technology, Karolinska Institute, Stockholm, Sweden. (3)Department of Clinical Sciences, Danderyd Hospital, KIDS, Karolinska Institute, Solnavägen 1, 171 77 Solna, Sweden. (4)Centre for Clinical Research, Sörmland, Uppsala University, Uppsala, Sweden. (5)Neurological Rehabilitation Clinic, Stora Sköndal Foundation, Stockholm, Sweden. (6)Department of Radiology, Karolinska University Hospital, Stockholm, Sweden.	Post mTBI fatigue is associated with abnormal brain functional connectivity.	272. Sci Rep. 2016 Feb 16;6:21183.	This study set out to investigate the behavioral correlates of changes in resting-state functional connectivity before and after performing a 20 minute continuous psychomotor vigilance task (PVT) for patients with chronic post-concussion syndrome. Ten patients in chronic phase after mild traumatic brain injury (mTBI) with persisting symptoms of fatigue and ten matched healthy controls participated in the study. We assessed the participants' fatigue levels and conducted resting-state fMRI before and after a sustained PVT. We evaluated the changes in brain functional connectivity indices in relation to the subject's fatigue behavior using a quantitative data-driven analysis approach. We found that the PVT invoked significant mental fatigue and specific functional connectivity changes in mTBI patients. Furthermore, we found a significant linear correlation between self-reported fatigue and functional connectivity in the thalamus and middle frontal cortex. Our findings indicate that resting-state fMRI measurements may be a useful indicator of performance potential and a marker of fatigue level in the neural attentional system.
Norris T(1), Deere K(2), Tobias JH(2), Crawley E(3).	(1)Centre for Child and Adolescent Health, School of Social and Community Medicine, Bristol, United Kingdom.	Chronic Fatigue Syndrome and Chronic Widespread Pain in Adolescence: Population Birth Cohort Study.	36. J Pain. 2016 Nov 12. pii: S1526-5900(16)30308-X.	Although many studies have investigated the overlap between pain phenotypes and chronic fatigue syndrome (CFS) in adults, little is known about the relationship between these conditions in adolescents. The study's aim was therefore to identify whether a relationship exists between chronic widespread pain (CWP) and CFS in adolescents and investigate whether the two share common associations with a set of covariates. A questionnaire was administered to offspring of the Avon Longitudinal Study of Parents

	Electronic address: tom.norris@bristol.ac.uk. (2)Musculoskeletal Research Unit, School of Clinical Sciences, Bristol, United Kingdom. (3)Centre for Child and Adolescent Health, School of Social and Community Medicine, Bristol, United Kingdom.			and Children (ALSPAC) at age 17, asking about site, duration, and pain intensity, from which participants with CWP were identified. At the same research clinic, a computer-based Revised Clinical Interview Schedule was filled out, from which a classification of CFS was obtained. The relationship between selected covariates and CFS and CWP was investigated using a variety of logistic, ordinal logistic, and multinomial regressions. We identified 3,214 adolescents with complete data for all outcomes and covariates. There were 82 (2.6%) individuals classified as CFS and 145 (4.5%) as CWP. A classification of CFS resulted in an increased likelihood of having CWP (odds ratio = 3.87; 95% confidence interval, 2.05-7.31). Female adolescents were approximately twice as likely to have CFS or CWP, with multinomial regression revealing a greater sex effect for CWP compared with CFS. Those with exclusive CFS were more likely to report higher levels of pain and greater effect of pain compared with those without CFS, although associations attenuated to the null after adjustment for covariates, which did not occur in those with exclusive CWP. Multinomial regression revealed that relative to having neither CFS nor CWP, a 1-unit increase in the depression and anxiety scales increased the risk of having exclusive CFS and, to a greater extent, the risk of having comorbid CFS and CWP, but not exclusive CWP, which was only related to anxiety.PERSPECTIVE: In this cohort, 14.6% of adolescents with CFS have comorbid CWP. The likely greater proportion of more mild cases observed in this epidemiological study means that prevalence of overlap may be underestimated compared with those attending specialist services. Clinicians should be aware of the overlap between the 2 conditions and carefully consider treatment options offered.
Norris T(1), Hawton K(2), Hamilton-Shield J(2), Crawley E(3).	(1) School of Social & Community Medicine, University of Bristol, Bristol, UK. (2) NIHR Bristol Biomedical Research Unit in Nutrition and University of Bristol, Bristol, UK. (3)Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, Bristol, UK.	Obesity in adolescents with chronic fatigue syndrome: an observational study.	93. Arch Dis Child. 2017 Jan;102(1):35-39.	OBJECTIVE: Identify the prevalence of obesity in patients with chronic fatigue syndrome (CFS) compared with healthy adolescents, and those identified with CFS in a population cohort. DESIGN: Cross-sectional analysis of multiple imputed data. SETTING: Data from UK paediatric CFS/myalgic encephalomyelitis (CFS/ME) services compared with data collected at two time points in the Avon Longitudinal Study of Parents and Children (ALSPAC). PATIENTS: 1685 adolescents who attended a CFS/ME specialist service between 2004 and 2014 and 13 978 adolescents aged approximately 13 years and 16 years participating in the ALSPAC study. MAIN OUTCOME MEASURES: Body mass index (BMI) (kg/m(2)), sex-specific and age-specific BMI Z-scores (relative to the International Obesity Task Force cut-offs) and prevalence of obesity (%). RESULTS: Adolescents who had attended specialist CFS/ME services had a higher prevalence of obesity (age 13 years: 9.28%; age 16 years: 16.43%) compared with both adolescents classified as CFS/ME in ALSPAC (age 13 years: 3.72%; age 16 years: 5.46%) and those non-CFS in ALSPAC (age 13 years: 4.18%; age 16 years: 4.46%). The increased odds of obesity in those who attended specialist services (relative to non-CFS in ALSPAC) was apparent at both 13 years (OR: 2.31 (1.54 to 3.48)) and 16 years, with a greater likelihood observed at 16 years (OR: 4.07 (2.04 to 8.11)). CONCLUSIONS: We observed an increased prevalence of obesity in adolescents who were affected severely enough to be referred

				to a specialist CFS/ME service. Further longitudinal research is required in order to identify the temporal relationship between the two conditions.
O'Halloran KD(1), Lewis P(2), McDonald F(3).	(1)Department of Physiology, University College Cork, Cork, Ireland. Electronic address: k.ohalloran@ucc.ie. (2)Department of Physiology, University College Cork, Cork, Ireland; Institute and Policlinic for Occupational Medicine, Environmental Medicine and Preventative Research, University of Cologne, Germany. (3)Physiology, School of Medicine, University College Dublin, Dublin, Ireland; School of Clinical Sciences, Bristol University, Bristol, United Kingdom.	Sex, stress and sleep apnoea: Decreased susceptibility to upper airway muscle dysfunction following intermittent hypoxia in females.	30. Respir Physiol Neurobiol. 2016 Nov 21. pii: S1569-9048(16)30215-4.	Obstructive sleep apnoea syndrome (OSAS) is a devastating respiratory control disorder more common in men than women. The reasons for the sex difference in prevalence are multifactorial, but are partly attributable to protective effects of oestrogen. Indeed, OSAS prevalence increases in post-menopausal women. OSAS is characterized by repeated occlusions of the pharyngeal airway during sleep. Dysfunction of the upper airway muscles controlling airway calibre and collapsibility is implicated in the pathophysiology of OSAS, and sex differences in the neuro-mechanical control of upper airway patency are described. It is widely recognized that chronic intermittent hypoxia (CIH), a cardinal feature of OSAS due to recurrent apnoea, drives many of the morbid consequences characteristic of the disorder. In rodents, exposure to CIH-related redox stress causes upper airway muscle weakness and fatigue, associated with mitochondrial dysfunction. Of interest, in adults, there is female resilience to CIH-induced muscle dysfunction. Conversely, exposure to CIH in early life, results in upper airway muscle weakness equivalent between the two sexes at 3 and 6 weeks of age. Ovariectomy exacerbates the deleterious effects of exposure to CIH in adult female upper airway muscle, an effect partially restored by oestrogen replacement therapy. Intriguingly, female advantage intrinsic to upper airway muscle exists with evidence of substantially greater loss of performance in male muscle during acute exposure to severe hypoxic stress. Sex differences in upper airway muscle physiology may have relevance to human OSAS. The oestrogen-oestrogen receptor α axis represents a potential therapeutic target in OSAS, particularly in post-menopausal women.
O'Halloran KD(1).	(1)Department of Physiology, School of Medicine, University College Cork, Cork, Ireland. Electronic address: k.ohalloran@ucc.ie.	Chronic intermittent hypoxia creates the perfect storm with calamitous consequences for respiratory control.	335. Respir Physiol Neurobiol. 2016 Jun;226:63-7.	Obstructive sleep apnoea syndrome (OSAS) is a common respiratory disorder with devastating consequences for integrative body systems. A picture is emerging to illustrate wide-ranging deleterious consequences of disordered breathing during sleep for major homeostatic control systems, with considerable interest in cardiorespiratory and autonomic morbidity underpinning the development of hypertension. The vista is bleak when one also considers the link between OSAS and a host of other maladies. Exposure to chronic intermittent hypoxia (CIH), resulting from repeated obstructions of the pharyngeal airway, is a hallmark feature of OSAS that appears, in animal models, to drive the development and maintenance of several key morbidities. A growing body of evidence now points to aberrant respiratory plasticity at multiple levels following

				exposure to CIH. Herein, we review the experimental data revealing that CIH causes: respiratory muscle weakness and fatigue; impaired motor control of the upper airway; and, discordant respiratory rhythm and pattern generation. This multifaceted conspiracy creates the perfect storm with the potential to exacerbate OSAS-serving to establish an inescapable cycle of respiratory morbidity. Several pharmacological interventions in animal models appear wholly effective in preventing the calamitous consequences of CIH and may have application as adjunctive therapies in the treatment of OSAS.
Ohanian D(1), Brown A(1), Sunnquist M(1), Furst J(1), Nicholson L(1), Klebek L(1), Jason LA(1).	(1)DePaul University, Chicago, USA.	Identifying Key Symptoms Differentiating Myalgic Encephalomyelitis and Chronic Fatigue Syndrome from Multiple Sclerosis.	1. Neurology (ECronicon). 2016;4(2):41-45. Epub 2016 Dec 19.	It is unclear what key symptoms differentiate Myalgic Encephalomyelitis (ME) and Chronic Fatigue syndrome (CFS) from Multiple Sclerosis (MS). The current study compared self-report symptom data of patients with ME or CFS with those with MS. The self-report data is from the DePaul Symptom Questionnaire, and participants were recruited to take the questionnaire online. Data were analyzed using a machine learning technique called decision trees. Five symptoms best differentiated the groups. The best discriminating symptoms were from the immune domain (i.e., flu-like symptoms and tender lymph nodes), and the trees correctly categorized MS from ME or CFS 81.2% of the time, with those with ME or CFS having more severe symptoms. Our findings support the use of machine learning to further explore the unique nature of these different chronic diseases.
Olimulder MA(1), Galjee MA(1), Wagenaar LJ(1), van Es J(1), van der Palen J(2,)(3), Visser FC(4), Vermeulen RC(4), von Birgelen C(5,)(6).	(1)Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, The Netherlands. (2)Department of Epidemiology, Medisch Spectrum Twente, Enschede, The Netherlands. (3)Department of Research Methodology, Measurement & Data Analysis, University of Twente, Enschede, The Netherlands. (4)Centre for Chronic Fatigue Syndrome,	Chronic fatigue syndrome in women assessed with combined cardiac magnetic resonance imaging.	111. Neth Heart J. 2016 Dec;24(12):709-716.	OBJECTIVE: In chronic fatigue syndrome (CFS), only a few imaging and histopathological studies have previously assessed either cardiac dimensions/function or myocardial tissue, suggesting smaller left ventricular (LV) dimensions, LV wall motion abnormalities and occasionally viral persistence that may lead to cardiomyopathy. The present study with cardiac magnetic resonance (CMR) imaging is the first to use a contrast-enhanced approach to assess cardiac involvement, including tissue characterisation of the LV wall. METHODS: CMR measurements of 12 female CFS patients were compared with data of 36 age-matched, healthy female controls. With cine imaging, LV volumes, ejection fraction (EF), mass, and wall motion abnormalities were assessed. T2-weighted images were analysed for increased signal intensity, reflecting oedema (i. e. inflammation). In addition, the presence of contrast enhancement, reflecting fibrosis (i. e. myocardial damage), was analysed. RESULTS: When comparing CFS patients and healthy controls, LVEF (57.9 ± 4.3 % vs. 63.7 ± 3.7 %; $p < 0.01$), end-diastolic diameter (44 ± 3.7 mm vs. 49 ± 3.7 mm; $p < 0.01$), as well as body surface area corrected LV end-diastolic volume (77.5 ± 6.2 ml/m(2) vs. 86.0 ± 9.3 ml/m(2); $p < 0.01$), stroke volume (44.9 ± 4.5 ml/m(2) vs. 54.9 ± 6.3 ml/m(2); $p < 0.001$), and mass (39.8 ± 6.5 g/m(2) vs. 49.6 ± 7.1 g/m(2); $p = 0.02$) were significantly lower in patients. Wall motion abnormalities were observed in four patients and contrast enhancement (fibrosis) in three; none of the controls showed wall motion abnormalities or contrast enhancement. None of the patients or controls showed increased signal intensity on the T2-weighted images. CONCLUSION: In patients with CFS, CMR demonstrated lower LV dimensions and a mildly reduced LV

	Amsterdam, The Netherlands. (5)Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, The Netherlands. c.vonbirgelen@mst.nl. (6)Department of Health Technology and Services Research, MIRA-Institute for Biomedical Technology & Technical Medicine, University of Twente, Enschede, The Netherlands. c.vonbirgelen@mst.nl.			function. The presence of myocardial fibrosis in some CFS patients suggests that CMR assessment of cardiac involvement is warranted as part of the scientific exploration, which may imply serial non-invasive examinations.
Osterman JW(1).	(1)Montreal, Canada. johnwosterman@hotmail.com.	Comment on Detection of Mycotoxins in Patients with Chronic Fatigue Syndrome. Toxins 2013, 5, 605-617.	44. Toxins (Basel). 2016 Nov 7;8(11). pii: E322.	The paper by Brewer et al. entitled "Detection of Mycotoxins in Patients with Chronic Fatigue Syndrome.[..].
Ostojic SM(1,)(2), Stojanovic M(3), Drid P(4), Hoffman JR(5), Sekulic D(6,)(7), Zenic N(8).	(1)Faculty of Sport and Physical Education, University of Novi Sad, Novi Sad 21000, Serbia. sergej.ostojic@chess.edu.rs. (2)School of Medicine, University of Belgrade, Belgrade 11000, Serbia. sergej.ostojic@chess.edu.rs. (3)Faculty of Sport and Physical Education, University	Supplementation with Guanidinoacetic Acid in Women with Chronic Fatigue Syndrome	293. Nutrients. 2016 Jan 29;8(2):72. .	A variety of dietary interventions has been used in the management of chronic fatigue syndrome (CFS), yet no therapeutic modality has demonstrated conclusive positive results in terms of effectiveness. The main aim of this study was to evaluate the effects of orally administered guanidinoacetic acid (GAA) on multidimensional fatigue inventory (MFI), musculoskeletal soreness, health-related quality of life, exercise performance, screening laboratory studies, and the occurrence of adverse events in women with CFS. Twenty-one women (age 39.3 ± 8.8 years, weight 62.8 ± 8.5 kg, height 169.5 ± 5.8 cm) who fulfilled the 1994 Centers for Disease Control and Prevention criteria for CFS were randomized in a double-blind, cross-over design, from 1 September 2014 through 31 May 2015, to receive either GAA (2.4 grams per day) or placebo (cellulose) by oral administration for three months, with a two-month wash-out period. No effects of intervention were found for the primary efficacy outcome (MFI score for general fatigue), and musculoskeletal pain at rest and during activity. After three months of intervention, participants receiving GAA significantly increased

	of Novi Sad, Novi Sad 21000, Serbia. marko.stojanovic@chess.edu.rs. (4)Faculty of Sport and Physical Education, University of Novi Sad, Novi Sad 21000, Serbia. patrikdrid@gmail.com. (5)Department of Educational and Human Sciences, Burnett School of Biomedical Sciences, University of Central Florida, Orlando 32816, FL, USA. jay.hoffman@ucf.edu. (6)Faculty of Kinesiology, University of Split, Split 21000, Croatia. dado@kifst.hr. (7)Department of Health Care Studies, University of Split, Split 21000, Croatia. dado@kifst.hr. (8)Faculty of Kinesiology, University of Split, Split 21000, Croatia. natasa@kifst.hr.			muscular creatine levels compared with the placebo group (36.3% vs. 2.4%; $p < 0.01$). Furthermore, changes from baseline in muscular strength and aerobic power were significantly greater in the GAA group compared with placebo ($p < 0.05$). Results from this study indicated that supplemental GAA can positively affect creatine metabolism and work capacity in women with CFS, yet GAA had no effect on main clinical outcomes, such as general fatigue and musculoskeletal soreness.
Ostojic SM(1).	(1)Faculty of Sport and Physical Education, University of Novi Sad, Novi Sad 21000, Serbia School of Medicine, University of Belgrade,	Exercise-induced mitochondrial dysfunction: a myth or reality?	146. Clin Sci (Lond). 2016 Aug 1;130(16):1407-16.	Beneficial effects of physical activity on mitochondrial health are well substantiated in the scientific literature, with regular exercise improving mitochondrial quality and quantity in normal healthy population, and in cardiometabolic and neurodegenerative disorders and aging. However, several recent studies questioned this paradigm, suggesting that extremely heavy or exhaustive exercise fosters mitochondrial disturbances that could permanently damage its function in health and disease. Exercise-induced mitochondrial dysfunction (EIMD) might be a key proxy for negative

	Belgrade 11000, Serbia sergej.ostojic@chess.edu.rs).			outcomes of exhaustive exercise, being a pathophysiological substrate of heart abnormalities, chronic fatigue syndrome (CFS) or muscle degeneration. Here, we overview possible factors that mediate negative effects of exhaustive exercise on mitochondrial function and structure, and put forward alternative solutions for the management of EIMD.
Overman CL(1), Kool MB(2), Da Silva JA(3), Geenen R(2,)(4).	(1)Department of Clinical and Health Psychology, Utrecht University, PO Box 80.140, 3508 TC, Utrecht, The Netherlands. C.L.Overman@uu.nl. (2)Department of Clinical and Health Psychology, Utrecht University, PO Box 80.140, 3508 TC, Utrecht, The Netherlands. (3)Department of Rheumatology, Hospitais da Universidade de Coimbra, 3000-075, Coimbra, Portugal. (4)Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, PO Box 85.500, 3508 GA, Utrecht, The Netherlands.	The prevalence of severe fatigue in rheumatic diseases: an international study.	353. Clin Rheumatol. 2016 Feb;35(2):409-15.	Fatigue is a common, disabling, and difficult-to-manage problem in rheumatic diseases. Prevalence estimates of fatigue within rheumatic diseases vary considerably. Data on the prevalence of severe fatigue across multiple rheumatic diseases using a similar instrument is missing. Our aim was to provide an overview of the prevalence of severe fatigue across a broad range of rheumatic diseases and to examine its association with clinical and demographic variables. Online questionnaires were filled out by an international sample of 6120 patients (88 % female, mean age 47) encompassing 30 different rheumatic diseases. Fatigue was measured with the RAND(SF)-36 Vitality scale. A score of ≤35 was taken as representing severe fatigue (90 % sensitivity and 81 % specificity for chronic fatigue syndrome). Severe fatigue was present in 41 to 57 % of patients with a single inflammatory rheumatic disease such as rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, Sjögren's syndrome, psoriatic arthritis, and scleroderma. Severe fatigue was least prevalent in patients with osteoarthritis (35 %) and most prevalent in patients with fibromyalgia (82 %). In logistic regression analysis, severe fatigue was associated with having fibromyalgia, having multiple rheumatic diseases without fibromyalgia, younger age, lower education, and language (French: highest prevalence; Dutch: lowest prevalence). In conclusion, one out of every two patients with a rheumatic disease is severely fatigued. As severe fatigue is detrimental to the patient, the near environment, and society at large, unraveling the underlying mechanisms of fatigue and developing optimal treatment should be top priorities in rheumatologic research and practice.
Owe JF, Næss H, Gjerde IO, Bødtker JE, Tysnes OB.		[Investigation of suspected chronic fatigue syndrome / myalgic encephalomyelitis]. [Article in Norwegian]	227. Tidsskr Nor Laegeforen. 2016 Apr 5;136(6):510.	Erratum for Tidsskr Nor Laegeforen. 2016 Feb 9;136(3):227-32.
Owe JF(1), Næss	(1)Nevrologisk	Investigation of suspected	283. Tidsskr Nor	BACKGROUND: Chronic fatigue is a frequently occurring problem in both the primary

H(2), Gjerde IO(1), Bødtker JE(3), Tysnes OB(2).	avdeling Haukeland universitetssykehus. (2)Nevrologisk avdeling Haukeland universitetssykehus og Universitet i Bergen. (3)Klinikk for psykosomatisk medisin, Haukeland universitetssykehus.	chronic fatigue syndrome/myalgic encephalopathy. [Article in English, Norwegian]	Laegeforen. 2016 Feb 9;136(3):227-32. Erratum in Tidsskr Nor Laegeforen. 2016 Apr 5;136(6):510.	and specialist health services. The Department of Neurology at Haukeland University Hospital has established a standard assessment for patients referred with suspected CFS/ME. This study reports diagnoses and findings upon assessment, and considers the benefit of supplementary examinations. MATERIAL AND METHOD: Diagnoses and findings from examinations of 365 patients assessed for suspected CFS/ME are retrospectively reported. RESULTS: A total of 48 patients (13.2%) were diagnosed with CFS/ME, while a further 18 patients (4.9%) were diagnosed with post-infectious fatigue. Mental and behavioural disorders were diagnosed in 169 patients (46.3%), and these represented by far the largest group. Serious, but unrecognised somatic illness was discovered in two patients, while changes of uncertain significance were identified by MRI and lumbar puncture in a few patients. INTERPRETATION: Fatigue is a frequently occurring symptom in the population. Thorough somatic and psychiatric investigation is necessary before referral to the specialist health services. Mental disorders and reactions to life crises are common and important differential diagnoses for CFS/ME. Long waiting times in the specialist health services may result in delayed diagnosis for these patients.
Park SB(1), Kim KN, Sung E, Lee SY, Shin HC.	(1)Department of Family Practice and Community Health, Ajou University School of Medicine.	Human Placental Extract as a Subcutaneous Injection Is Effective in Chronic Fatigue Syndrome: A Multi-Center, Double-Blind, Randomized, Placebo-Controlled Study.	265. Biol Pharm Bull. 2016 May 1;39(5):674-9.	Chronic fatigue (CF) is a common reason for consulting a physician due to affecting quality of life, but only a few effective treatments are available. The aim of this study was to examine the effectiveness of subcutaneous injection of the human placental extract (HPE) on medically indescribable cases of CF and safety in a randomized, double-blind, placebo-controlled clinical trial. A total of 78 subjects with CF were randomly assigned to either a HPE group or a placebo group. Subjects in the HPE group were treated with HPE three times a week subcutaneously for 6 weeks, whereas those in the placebo group with normal saline. Then, the fatigue severity scale (FSS), visual analog scale (VAS) and multidimensional fatigue inventory (MFI) were measured in both CF group and chronic fatigue syndrome (CFS) and idiopathic chronic fatigue (ICF) subgroup. The FSS, VAS and MFI score at baseline were not different between the HPE and placebo group in total subjects with CF. In CFS group, the FSS (p=0.0242), VAS (p=0.0009) and MFI (p=0.0159) scores measured at the end of the study period decreased more in the HPE group than in the placebo group when compared with those at the baseline. There were no significant differences between the HPE group and placebo group in the mean change from baseline in FSS, VAS, and MFI in subjects with ICF during the study period. The subcutaneous injection of HPE was effective in the improvement of CFS.
Paulin J(1), Andersson L(2), Nordin S(1).	(1)Department of Psychology, Umeå University, Umeå, Sweden. (2)Department of Psychology, Umeå	Characteristics of hyperacusis in the general population.	110. Noise Health. 2016 Jul-Aug;18(83):178-84.	There is a need for better understanding of various characteristics in hyperacusis in the general population. The objectives of the present study were to investigate individuals in the general population with hyperacusis regarding demographics, lifestyle, perceived general health and hearing ability, hyperacusis-specific characteristics and behavior, and comorbidity. Using data from a large-scale population-based questionnaire study, we investigated individuals with physician-diagnosed (n = 66) and self-reported

	University, Umeå; Department of Occupational and Public Health Sciences, University of Gävle, Gävle, Sweden.			(n = 313) hyperacusis in comparison to individuals without hyperacusis (n = 2995). High age, female sex, and high education were associated with hyperacusis, and that trying to avoid sound sources, being able to affect the sound environment, and having sough medical attention were common reactions and behaviors. Posttraumatic stress disorder, chronic fatigue syndrome, generalized anxiety disorder, depression, exhaustion, fibromyalgia, irritable bowel syndrome, migraine, hearing impairment, tinnitus, and back/joint/muscle disorders were comorbid with hyperacusis. The results provide ground for future study of these characteristic features being risk factors for development of hyperacusis and/or consequences of hyperacusis.
Pavlik D(1), Agnew D, Stiles L, Ditoro R.	(1)Daniel Pavlik is an assistant professor in the Department of Medical Science at Arcadia University in Glenside, Pa., and practices in the ED at Our Lady of Lourdes Medical Center in Camden, N.J. Donna Agnew is an associate professor and director of the PA program at Salus University in Elkins Park, Pa., and practices internal medicine at Fountainville (Pa.) Medical Specialists. Lauren Stiles is the co-founder of Dysautonomia International, a nonprofit focused on advancing research on POTS and other autonomic disorders. Rachel Ditoro is an assistant professor in Arcadia University's Department of	Recognizing postural orthostatic tachycardia syndrome.	251. JAAPA. 2016 Apr;29(4):17-23.	This article describes the pathophysiology, clinical presentation, differential diagnosis, diagnosis, and management of postural orthostatic tachycardia syndrome (POTS), a potentially debilitating autonomic disorder that can have many causes and presentations. POTS can be mistaken for panic disorder, inappropriate sinus tachycardia, and chronic fatigue syndrome. Clinician suspicion for the syndrome is key to prompt patient diagnosis and treatment.

	Medical Science. The authors have disclosed no other potential conflicts of interest, financial or otherwise.			
Pendergrast T(1), Brown A(2), Sunnquist M(2), Jantke R(2), Newton JL(3), Strand EB(4), Jason LA(2).	(1)Center for Community Research, DePaul University, USA tpender1@depaul.edu . (2)Center for Community Research, DePaul University, USA. (3)Newcastle University, UK. (4)Oslo University Hospital, Norway.	Housebound versus nonhousebound patients with myalgic encephalomyelitis and chronic fatigue syndrome.	208. Chronic Illn. 2016 Dec;12(4):292-307. Epub 2016 Apr 28.	OBJECTIVES: The objective of this study was to examine individuals with myalgic encephalomyelitis and chronic fatigue syndrome who are confined to their homes due to severe symptomatology. The existing literature fails to address differences between this group, and less severe, nonhousebound patient populations. METHODS: Participants completed the DePaul Symptom Questionnaire, a measure of myalgic encephalomyelitis and chronic fatigue syndrome symptomology, and the SF-36, a measure of health impact on physical/mental functioning. ANOVAs and, where appropriate, MANCOVAS were used to compare housebound and nonhousebound patients with myalgic encephalomyelitis and chronic fatigue syndrome across areas of functioning, symptomatology, and illness onset characteristics. RESULTS: Findings indicated that the housebound group represented one quarter of the sample, and were significantly more impaired with regards to physical functioning, bodily pain, vitality, social functioning, fatigue, postexertional malaise, sleep, pain, neurocognitive, autonomic, neuroendocrine, and immune functioning compared to individuals who were not housebound. DISCUSSION: Findings indicated that housebound patients have more impairment on functional and symptom outcomes compared to those who were not housebound. Understanding the differences between housebound and not housebound groups holds implications for physicians and researchers as they develop interventions intended for patients who are most severely affected by this chronic illness. © The Author(s) 2016.
Penfold S(1), St Denis E(2), Mazhar MN(3).	(1) MD, Department of Psychiatry, Queen's University, Kingston, Ontario, Canada. (2) MSc, MD, Department of Psychiatry, Queen's University, Kingston, Ontario, Canada. (3)FRCPsych, FRCPC, DABPN, Department of Psychiatry, Queen's University, Kingston, Ontario, Canada.	The association between borderline personality disorder, fibromyalgia and chronic fatigue syndrome: systematic review.	81. BJPsych Open. 2016 Sep 2;2(4):275-279. eCollection 2016.	BACKGROUND: Overlap of aetiological factors and demographic characteristics with clinical observations of comorbidity has been documented in fibromyalgia syndrome, chronic fatigue syndrome (CFS) and borderline personality disorder (BPD). AIMS: The purpose of this study was to assess the association of BPD with fibromyalgia syndrome and CFS. The authors reviewed literature on the prevalence of BPD in patients with fibromyalgia or CFS and vice versa. METHODS: A search of five databases yielded six eligible studies. A hand search and contact with experts yielded two additional studies. We extracted information pertaining to study setting and design, demographic information, diagnostic criteria and prevalence. RESULTS: We did not identify any studies that specifically assessed the prevalence of fibromyalgia or CFS in patients with BPD. Three studies assessed the prevalence of BPD in fibromyalgia patients and reported prevalence of 1.0, 5.25 and 16.7%. Five studies assessed BPD in CFS patients and reported prevalence of 3.03, 1.8, 2.0, 6.5 and 17%. CONCLUSIONS: More research is required to clarify possible associations between BPD, fibromyalgia and CFS.

Penna F(1,)(2), Pin F(1,)(2), Ballarò R(1,)(2), Baccino FM(1), Costelli P(1,)(2).	(1)a Department of Clinical and Biological Sciences , University of Turin , Turin , Italy. (2)b Interuniversity Institute of Myology , Italy.	Novel investigational drugs mimicking exercise for the treatment of cachexia.	332. Expert Opin Investig Drugs. 2016;25(1):63-72.	INTRODUCTION: Cachexia is a syndrome characterized by body weight loss, muscle wasting and metabolic abnormalities, that frequently complicates the management of people affected by chronic diseases. No effective therapy is actually available, although several drugs are under clinical evaluation. Altered energy metabolism markedly contributes to the pathogenesis of cachexia; it can be improved by exercise, which is able to both induce anabolism and inhibit catabolism. AREAS COVERED: This review focuses on exercise mimetics and their potential inclusion in combined protocols to treat cachexia. The authors pay with particular reference to the cancer-associated cachexia. EXPERT OPINION: Even though exercise improves muscle phenotype, most patients retain sedentary habits which are quite difficult to disrupt. Moreover, they frequently present with chronic fatigue and comorbidities that reduce exercise tolerance. For these reasons, drugs mimicking exercise could be beneficial to those who are unable to comply with the practice of physical activity. Since some exercise mimetics may exert serious side effects, further investigations should focus on treatments which maintain their effectiveness on muscle phenotype while remaining tolerable at the same time.
Petty RD(1,)(2), McCarthy NE(3), Le Dieu R(2), Kerr JR(1,)(4).	(1)CFS Group, St George´s University of London, Cranmer Terrace, London, United Kingdom. (2)Centre for Haemato-Oncology, Bart's cancer institute, Queen Mary University of London, London, United Kingdom. (3)Centre for Immunobiology, The Blizzard institute, Queen Mary University of London, London, United Kingdom. (4)Grupo de Salud Publica, Escuela de Medicine y Ciencias de la Salud, Universidad del Rosario, Quinta de Mutis, Bogotá 111221,	MicroRNAs hsa-miR-99b, hsa-miR-330, hsa-miR-126 and hsa-miR-30c: Potential Diagnostic Biomarkers in Natural Killer (NK) Cells of Patients with Chronic Fatigue Syndrome (CFS)/ Myalgic Encephalomyelitis (ME).	252. PLoS One. 2016 Mar 11;11(3):e0150904.	BACKGROUND: Chronic Fatigue Syndrome (CFS/ME) is a complex multisystem disease of unknown aetiology which causes debilitating symptoms in up to 1% of the global population. Although a large cohort of genes have been shown to exhibit altered expression in CFS/ME patients, it is currently unknown whether microRNA (miRNA) molecules which regulate gene translation contribute to disease pathogenesis. We hypothesized that changes in microRNA expression in patient leukocytes contribute to CFS/ME pathology, and may therefore represent useful diagnostic biomarkers that can be detected in the peripheral blood of CFS/ME patients. METHODS: miRNA expression in peripheral blood mononuclear cells (PBMC) from CFS/ME patients and healthy controls was analysed using the Ambion Bioarray V1. miRNA demonstrating differential expression were validated by qRT-PCR and then replicated in fractionated blood leukocyte subsets from an independent patient cohort. The CFS/ME associated miRNA identified by these experiments were then transfected into primary NK cells and gene expression analyses conducted to identify their gene targets. RESULTS: Microarray analysis identified differential expression of 34 miRNA, all of which were up-regulated. Four of the 34 miRNA had confirmed expression changes by qRT-PCR. Fractionating PBMC samples by cell type from an independent patient cohort identified changes in miRNA expression in NK-cells, B-cells and monocytes with the most significant abnormalities occurring in NK cells. Transfecting primary NK cells with hsa-miR-99b or hsa-miR-330-3p, resulted in gene expression changes consistent with NK cell activation but diminished cytotoxicity, suggesting that defective NK cell function contributes to CFS/ME pathology. CONCLUSION: This study demonstrates altered microRNA expression in the peripheral blood mononuclear cells of CFS/ME patients, which are potential diagnostic biomarkers. The greatest degree of miRNA deregulation was

	Colombia.			identified in NK cells with targets consistent with cellular activation and altered effector function.
Pinxsterhuis I(1,)(2,)(3), Sandvik L(4), Strand EB(1), Bautz-Holter E(5), Sveen U(2,)(3,)(5).	(1)1 Division of Medicine, Oslo University Hospital, Oslo, Norway. (2)2 Department of Occupational Therapy, Prosthetics and Orthotics, Oslo, Norway. (3)3 Akershus University College of Applied Sciences, Oslo, Norway. (4)4 Center for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway. (5)5 Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Oslo, Norway.	Effectiveness of a group-based self-management program for people with chronic fatigue syndrome: a randomized controlled trial.	322. Clin Rehabil. 2017 Jan;31(1):93-103.	OBJECTIVE: To evaluate the effectiveness of a group-based self-management program for people with chronic fatigue syndrome. DESIGN: A randomized controlled trial. SETTING: Four mid-sized towns in southern Norway and two suburbs of Oslo. SUBJECTS: A total of 137 adults with chronic fatigue syndrome. INTERVENTION: A self-management program including eight biweekly meetings of 2.5 hours duration. The control group received usual care. MAIN MEASURES: Primary outcome measure: Medical Outcomes Study-Short Form-36 physical functioning subscale. SECONDARY OUTCOME MEASURES: Fatigue severity scale, self-efficacy scale, physical and mental component summary of the Short Form-36, and the illness cognition questionnaire (acceptance subscale). Assessments were performed at baseline, and at six-month and one-year follow-ups. RESULTS: At the six-month follow-up, a significant difference between the two groups was found concerning fatigue severity ($p = 0.039$) in favor of the control group, and concerning self-efficacy in favor of the intervention group ($p = 0.039$). These significant differences were not sustained at the one-year follow-up. No significant differences were found between the groups concerning physical functioning, acceptance, and health status at any of the measure points. The drop-out rate was 13.9% and the median number of sessions attended was seven (out of eight). CONCLUSIONS: The evaluated self-management program did not have any sustained effect, as compared with receiving usual care.
Plotnikoff G(1), Barber M(2).	(1)Senior Consultant for Minnesota Personalized Medicine in Minneapolis. gregory.plotnikoff@gmail.com. (2)Research Associate at the Integrative Medicine Institute in Portland, OR. msbarber@integrativemed.org.	Refractory Depression, Fatigue, Irritable Bowel Syndrome, and Chronic Pain: A Functional Medicine Case Report.	64. Perm J. 2016 Fall;20(4):104-107.	INTRODUCTION: Single-disorder or single-organ-system clinical practice guidelines are often of limited usefulness in guiding effective management of patients with chronic multidimensional signs and symptoms. The presence of multiple long-standing medical problems in a given patient despite intensive medical effort suggests that addressing systemic core imbalances could complement more narrowly focused approaches. CASE PRESENTATION: A 72-year-old man experiencing longstanding depression, fatigue, irritable bowel syndrome, and chronic pain in the context of additional refractory illnesses was assessed and treated, guided by a system-oriented approach to underlying core imbalances termed functional medicine. This patient was referred from a team of clinicians representing primary care, cardiology, gastroenterology, hematology, and psychology. Prior treatment had been unsuccessful in managing multiple chronic comorbidities. Diagnostic assessment included comprehensive stool and nutritional/metabolic laboratory testing. RESULTS: The blood-, urine-, or stool-based measurements of relevant markers for multiple systemic issues, including digestion/absorption, inflammation, oxidative stress, and methylation, identified previously unrecognized root causes of his constellation of symptoms. These functional

				measurements guided rational recommendations for dietary choices and supplementation. The patient experienced steady and significant improvement in his mental health, fatigue, chronic pain, and irritable bowel syndrome-as well as the unexpected resolution of his chronic idiopathic pancytopenia. CONCLUSION: The success in this case suggests that other patients with chronic, complex, and treatment-refractory illness may benefit from a system-oriented assessment of core imbalances guided by specialized nutritional/metabolic and digestive laboratory testing.
Priori R(1), Minniti A(1), Antonazzo B(1), Fusconi M(2), Valesini G(3), Curcio G(4).	(1)Department of Internal Medicine and Medical Specialties, Rheumatology Clinic, Sapienza University of Rome, Italy. (2)Department of Sensory Organs, Sapienza University of Rome, Italy. (3)Department of Internal Medicine and Medical Specialties, Rheumatology Clinic, Sapienza University of Rome, Italy. guido.valesini@uniroma1.it. (4)Department of Life, Health and Environmental Sciences, University of L'Aquila, Italy.	Sleep quality in patients with primary Sjögren's syndrome.	222. Clin Exp Rheumatol. 2016 May-Jun;34(3):373-9. Epub 2016 Apr 15.	OBJECTIVES: To assess the sleep quality in primary Sjögren's syndrome (pSS) patients and evaluate its relationship with the disease, quality of life and mood disorders. METHODS: The sleep quality of 29 pSS women and 29 matched controls was assessed by the Pittsburgh Sleep Quality Index (PSQI). Seven domains are grouped according to three factors: F1 perceived sleep quality (subjective sleep quality, sleep latency, use of sleeping medication), F2 sleep efficiency (sleep duration, habitual sleep efficiency) and F3 daily disturbances (sleep disturbances, daytime dysfunction). These domains are scored as a single factor of global sleep quality. The Short Form Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale and Hospital Anxiety and Depression Scale (HADS) were also administered. Disease activity and damage were evaluated with the EULAR Sjögren's syndrome disease activity index (ESSDAI), the Sjögren's Syndrome Disease Activity and Damage Indexes (SSDAI, SSDDI). RESULTS: The mean PSQI global score had higher pathological values (8.6±4.6) compared with controls (5.6±2.2) (p=0.002). F1 and F3 were significantly worse in cases (p=0.01, p=0.009). A negative correlation was found between SF-36 subscales and the global PSQI, F2 and F3. The anxiety HADS correlated with F2 and F3, while depression only with F3. No correlation with FACIT and disease indexes emerged. CONCLUSIONS: Using PSQI, an impaired sleep quality was demonstrated in pSS patients, especially with perceived quality and the daily disturbances. It is associated with a reduced quality of life but not with disease-related variables.
Ramos JA(1).	(1)From the Department of Anesthesiology, Division of Pain Medicine, University of Florida Health, Gainesville, Florida.	The Great Deceiver: A Case of Central Sensitization Presenting as Carcinoid Syndrome.	202. A A Case Rep. 2016 Jun 1;6(11):364-5.	Central sensitization defines a state of amplified sensory input within the nervous system across many organ systems; it overlaps syndromes as fibromyalgia, chronic fatigue, irritable bowel, and interstitial cystitis. Commonly, individuals will experience multiple syndromes during the course of their lifetime. A 62-year-old patient presented for evaluation of multiple medically unexplained symptoms postsurgically including chronic left chest wall and flank pain with concomitant diarrhea, abdominal pain, and facial flushing. After extensive multidisciplinary evaluations, he was diagnosed as having central sensitization in which the initial presentation mimicked carcinoid syndrome. He was subsequently treated with extensive multidisciplinary pain rehabilitation, and it did well.
Ramos S(1),	(1)Griffith Health	Regulatory T, natural killer	237. Asian Pac J Allergy	BACKGROUND: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME), and

Brenu E(1), Broadley S(2), Kwiatek R(3), Ng J(1), Nguyen T(1), Freeman S(1), Staines D(1), Marshall-Gradisnik S(1).	Institute - Griffith University, Gold Coast, QLD, Australia. (2)National Centre for Neuroimmunology and Emerging Diseases (NCNED) - Griffith University, Gold Coast, QLD, Australia. (3)Northern Adelaide Local Health Network, Adelaide, SA, Australia.	T and γδ T cells in multiple sclerosis and chronic fatigue syndrome/myalgic encephalomyelitis: a comparison.	Immunol. 2016 Dec;34(4):300-305.	Multiple Sclerosis (MS) may share some similarities in relation to reduced NK cell activity. It is likely that other cells such as regulatory T (Tregs), invariant Natural Killer T (iNKT) and gamma delta T (γδ T) cells may also be dysregulated in CFS/ME and MS. OBJECTIVE: To evaluate and compare specific immune regulatory cells of patients with CFS/ME, patients with MS and healthy controls. METHOD: Sixty three volunteers were included in this study: 24 were CFS/ME patients, 11 were MS patients and 27 were healthy controls. Blood samples were obtained from all participants for flow cytometry analysis of iNKT cells, Tregs and γδ T cell phenotypes. RESULTS: We observed a significant increase in Tregs in the CFS/ME group ($p \leq 0.05$) compared to the healthy control group. Total γδ and γδ2 T cells were significantly reduced in MS patients in comparison with the healthy control group. Conversely, CD4+iNKT percentage of iNKT, was significantly increased in the CFS/ME group compared with healthy controls and the double-negative iNKT percentage of iNKT significantly decreased compared with the healthy control group. CONCLUSIONS: This study has not identified any immunological disturbances that are common in both MS and CFS/ME patients. However, the differential expression of cell types between the conditions investigated suggests different pathways of disease. These differences need to be explored in further studies.
Rasouli O(1), Stensdotter AK(2), Van der Meer AL(3).	(1)Institute of Health Science, Faculty of Health and Social Sciences, Norwegian University of Science and Technology (NTNU), Trondheim, Norway; Department of Public Health and General Practice, Faculty of Medicine, Norwegian University of Science and Technology (NTNU), Trondheim, Norway. Electronic address: omid.rasouli@ntnu.no. (2)Institute of Health Science, Faculty of Health and Social Sciences, Norwegian University of Science	TauG-guidance of dynamic balance control during gait initiation in patients with chronic fatigue syndrome and fibromyalgia.	129. Clin Biomech (Bristol, Avon). 2016 Aug;37:147-52.	BACKGROUND: Impaired postural control has been reported in static conditions in chronic fatigue syndrome and fibromyalgia, but postural control in dynamic tasks have not yet been investigated. Thus, we investigated measurements from a force plate to evaluate dynamic balance control during gait initiation in patients with chronic fatigue syndrome and fibromyalgia compared to matched healthy controls. METHODS: Thirty female participants (10 per group) performed five trials of gait initiation. Center of pressure (CoP) trajectory of the initial weight shift onto the supporting foot in the mediolateral direction (CoPX) was analyzed using General Tau Theory. We investigated the hypothesis that tau of the CoPX motion-gap (τCoPx) is coupled onto an intrinsic tauG-guide (τG) by keeping the relation $\tau CoPx = K\tau G$, where K is a scaling factor that determines the relevant kinematics of a movement. FINDINGS: Mean K values were 0.57, 0.55, and 0.50 in fibromyalgia, chronic fatigue syndrome, and healthy controls, respectively. Both patient groups showed K values significantly higher than 0.50 ($P<0.05$), indicating that patients showed poorer dynamic balance control, CoPX colliding with the boundaries of the base of support ($K>0.5$). INTERPRETATION: The findings revealed a lower level of dynamic postural control in both fibromyalgia and chronic fatigue syndrome compared to controls.

	and Technology (NTNU), Trondheim, Norway. Electronic address: ann-katrin.stensdotter@ntnu.no. (3)Developmental Neuroscience Laboratory, Department of Psychology, Norwegian University of Science and Technology (NTNU), Trondheim, Norway. Electronic address: audrey.meer@svt.ntnu.no.			
Rasschaert M(1), Helsen S(2), Rolfo C(3), Van Brussel I(4), Ravelingien J(4), Peeters M(3,)(5).	(1)Department of Oncology, Multidisciplinary Oncological Center Antwerp, MOCA, University Hospital Antwerp, Wilrijkstraat 10, 2650, Edegem, Belgium. marika.rasschaert@uza.be. (2)Department of Ophtalmology, University Hospital Antwerp, Wilrijkstraat 10, 2650, Edegem, Belgium. (3)Department of Oncology, Multidisciplinary Oncological Center Antwerp, MOCA, University Hospital	Feasibility of an interactive electronic self-report tool for oral cancer therapy in an outpatient setting.	235. Support Care Cancer. 2016 Aug;24(8):3567-71.	BACKGROUND: The introduction of oral anti-cancer agents provides a convenient administration route for chronic cancer treatment to outpatients. Health information technology through web-based applications or other electronic tools can offer a platform to improve treatment compliance, symptom management, and patient-provider communication. PURPOSE: The purposes of this study were to test the feasibility and clinical utility of an electronic self-report device (RemeCoach) for patients or their caregivers and to register and prospectively evaluate the quality of data generated. PATIENTS AND METHODS: Patients using Teysuno® (S-1) for advanced gastrointestinal carcinoma used a pre-programmed device in order to register compliance to treatment and six clinical parameters. Real-time data were collected onto a central platform, which processed the data by an algorithm. This algorithm stratified the data into different grades based on the Common Terminology Criteria for Adverse Events (CTCAE v4.0). RESULTS: From December 2013 to March 2014, 11 patients (5 men, 6 women) were enrolled. Compliance to the device was high, six patients (55 %) registered timely intake of medication (demonstrating >95 % treatment compliance). Agreement between patients' and clinicians' reported toxicity was substantial for nausea, but discrepant for fatigue, hand-foot syndrome, and mucositis. CONCLUSION: The use of an interactive self-report tool is feasible, reliable, and acceptable to outpatients. The RemeCoach and the algorithm devised will be further developed as an interactive patient-reported outcome (PRO) system, to improve early detection of side effects in an outpatient setting. Further studies are needed to confirm these data and to explore the relationship between optimal patient support and

	Antwerp, Wilrijkstraat 10, 2650, Edegem, Belgium. (4)Remedus BVBA, Boomsesteenweg 44, 2630, Aartselaar, Belgium. (5)University of Antwerp, Prinsstraat 13, 2000, Antwerp, Belgium.			efficacy of treatment.
Reale M(1), Sánchez-Ramón S(2).	(1). (2)Dept. of Clinical Immunology and IdISSC, Hospital Clínico San Carlos, Madrid, Spain. ssramon@salud.madrid.org.	Lipids at the Cross-road of Autoimmunity in Multiple Sclerosis.	32. Curr Med Chem. 2016 Nov 22.	Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system (CNS) characterized by demyelination and neurodegeneration, driven by a Th17/Th1-immune response, which afflicts mainly young women. Although MS causes are not completely known, it is notorious that the disease is characterized by an extended focal degradation of the myelin sheath, with ulterior axon and neuronal damage. Lipid molecules play a main dual role in MS, both as target molecules of myelin destruction and as mediators of inflammation. Indeed, recent cumulative evidence suggests that abnormalities in the lipid-binding proteins of myelin and sphingolipid content that confer increased immunogenicity may underlie the autoimmune response against the myelin sheath. CNS is after all, the second organ richer on lipid content after adipose tissue. On the other hand, soluble factors called adipokines, secreted by adipose tissue, modulate inflammatory responses and contribute to metabolic dysfunction, which may be important in MS pathophysiology. Disability accumulation in MS patients is slow but persistent, often leading to a decreased mobility and physical activity, resulting in more weakness, fatigue and associated increased risk of the metabolic syndrome (MetS). In turn, MetS may trigger MS in susceptible individuals and is a worse prognostic factor. Here we review what are the facts linking lipids, MetS and MS, what we do not know yet, and what we should do to move this field forward.
Rimbaut S(1), Van Gutte C(1), Van Brabander L(1), Vanden Bossche L(1).	(1)a Department of Physical and Rehabilitation Medicine , University Hospital Ghent , De Pintelaan 185, Gent 9000 , Belgium.	Chronic fatigue syndrome - an update.	148. Acta Clin Belg. 2016 Jun 17:1-8.	BACKGROUND: Chronic fatigue syndrome is a widespread condition with a huge impact not only on a patient's life, but also on society as evidenced by substantial losses of productivity, informal costs, and medical expenses. The high prevalence rates (0.2-6.4%) and the low employment rates (27-41%) are responsible for the enormous burden imposed on society, with loss of productivity representing the highest cost. The objective of this review is to systematically review the recent literature on chronic fatigue syndrome/myalgic encephalomyelitis. METHODS: The published literature between 1 January 1990 and 1 April 2015 was searched using the MEDLINE, Cochrane Library, and Web of Sciences databases. The reference lists of the selected articles were screened for other relevant articles. RESULTS AND CONCLUSIONS: Despite extensive research, none of the proposed etiological factors have shown strong, reproducible

				scientific evidence. Over the years, the biopsychosocial model integrating many of the proposed hypotheses has been gaining popularity over the biomedical model, where the focus is on one physical cause. Since the etiological mechanism underlying chronic fatigue syndrome is currently unknown, disease-specific treatments do not exist. Various treatments have been investigated but only cognitive behavior therapy (CBT) and graded exercise therapy (GET) have shown moderate effectiveness.
Rimes KA(1), Ashcroft J(1), Bryan L(1), Chalder T(1).	(1)Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's College London.	Emotional suppression in chronic fatigue syndrome: Experimental study.	193. Health Psychol. 2016 Sep;35(9):979-86.	OBJECTIVE: Emotional processing differences in chronic fatigue syndrome (CFS) have been reported but have rarely been investigated experimentally. This study used self-report, observer ratings, and electrodermal responses to test hypotheses about emotion suppression and autonomic reactivity. METHODS: Eighty adults with CFS and 80 healthy controls (HC) watched a distressing film clip. Half of each group were instructed to suppress their emotions and half were told to express their feelings as they wished. Their reactions were filmed and rated by independent observers. Electrodermal activity (skin conductance response) was used as a measure of sympathetic nervous system arousal. RESULTS: CFS participants reported higher anxiety and sadness than the HC, both before and after the film. However, observers rated the CFS group as having lower emotional expression than HC in both emotional suppression and expression choice conditions. Beliefs about the unacceptability of negative emotions were associated with greater self-reported suppression. Electrodermal responses were greater in the CFS group than HC participants. Higher skin conductance responses were associated with larger posttask increases in fatigue in the CFS participants but not in the HC. CONCLUSIONS: CFS participants had lower observer-rated emotional expression than HC, despite greater distress and higher autonomic arousal. This may have implications for their ability to access social support at times of stress. As the degree of autonomic arousal was associated with short-term increases in fatigue in the CFS participants, this requires further investigation as a contributory factor for this condition. (PsycINFO Database Record
Roberts E(1), Wessely S(2), Chalder T(2), Chang CK(3), Hotopf M(2).	(1)Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, Weston Education Centre, London, UK. Electronic address: emmert.roberts@kcl.ac.uk. (2)Department of Psychological Medicine, Institute of	Mortality of people with chronic fatigue syndrome: a retrospective cohort study in England and Wales from the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Clinical Record Interactive Search (CRIS) Register.	275. Lancet. 2016 Apr 16;387(10028):1638-43.	BACKGROUND: Mortality associated with chronic fatigue syndrome is uncertain. We investigated mortality in individuals diagnosed with chronic fatigue syndrome in secondary and tertiary care using data from the South London and Maudsley NHS Foundation Trust Biomedical Research Centre (SLaM BRC) Clinical Record Interactive Search (CRIS) register. METHODS: We calculated standardised mortality ratios (SMRs) for all-cause, suicide-specific, and cancer-specific mortality for a 7-year observation period using the number of deaths observed in SLaM records compared with age-specific and sex-specific mortality statistics for England and Wales. Study participants were included if they had had contact with the chronic fatigue service (referral, discharge, or case note entry) and received a diagnosis of chronic fatigue syndrome. FINDINGS: We identified 2147 cases of chronic fatigue syndrome from CRIS and 17 deaths from Jan 1, 2007, to Dec 31, 2013. 1533 patients were women of whom 11 died, and 614 were men of whom six died. There was no significant difference in age-

	Psychiatry, Psychology and Neuroscience, King's College London, Weston Education Centre, London, UK. (3)Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, Denmark Hill, London, UK. Electronic address: chin-kuo.chang@kcl.ac.uk.			standardised and sex-standardised mortality ratios (SMRs) for all-cause mortality (SMR 1·14, 95% CI 0·65-1·85; p=0·67) or cancer-specific mortality (1·39, 0·60-2·73; p=0·45) in patients with chronic fatigue syndrome when compared with the general population in England and Wales. This remained the case when deaths from suicide were removed from the analysis. There was a significant increase in suicide-specific mortality (SMR 6·85, 95% CI 2·22-15·98; p=0·002). INTERPRETATION: We did not note increased all-cause mortality in people with chronic fatigue syndrome, but our findings show a substantial increase in mortality from suicide. This highlights the need for clinicians to be aware of the increased risk of completed suicide and to assess suicidality adequately in patients with chronic fatigue syndrome. FUNDING: National Institute for Health Research (NIHR) Biomedical Research Centre at South London and Maudsley NHS Foundation Trust and King's College London.
Robinson HC(1).	(1)Medical University of South Carolina Montgomery Center for Family Medicine, 155 Academy Ave, Greenwood, SC 29646.	Respiratory Conditions Update: Restrictive Lung Disease.	108. FP Essent. 2016 Sep;448:29-34.	Restrictive lung diseases are a heterogeneous group of conditions characterized by a restrictive pattern on spirometry and confirmed by a reduction in total lung volume. Patients with more severe symptoms may have a reduced diffusing capacity of the lung for carbon monoxide. Etiologies can be intrinsic with lung parenchymal involvement, as in interstitial lung diseases, or extrinsic to the lung, as in obesity and neuromuscular disorders. Idiopathic pulmonary fibrosis is a chronic progressive interstitial pneumonia with fibrosis for which treatment is primarily supportive with oxygen therapy, pulmonary rehabilitation, and management of comorbid conditions. Newer drugs for idiopathic pulmonary fibrosis, such as pirfenidone and nintedanib, can slow disease progression. Referral for evaluation for lung transplantation is recommended for appropriate patients. Obstructive sleep apnea and obesity hypoventilation syndrome increasingly are common health issues, with symptoms that can include snoring, daytime somnolence, difficulty concentrating, fatigue, witnessed apneas, and morning headaches. Serum bicarbonate may serve as a biomarker in screening for subclinical obesity hypoventilation syndrome. Preoperative evaluations should assess pulmonary risk in addition to cardiac risk with a thorough history, laboratory tests, and functional capacity assessments. Optimization of management may include weight loss, pulmonary rehabilitation, oxygen therapy, and respiratory support.
Robinson LJ(1,)(2), Durham J(3), Newton JL(4,)(5).	(1)Academic Psychiatry, Newcastle University, Newcastle upon Tyne, UK. (2)Northumberland Tyne and Wear NHS Foundation Trust,	A systematic review of the comorbidity between Temporomandibular Disorders and Chronic Fatigue Syndrome.	333. J Oral Rehabil. 2016 Apr;43(4):306-16.	The most common cause of chronic oro-facial pain is a group of disorders collectively termed temporomandibular disorders (TMDs). Chronic painful TMD is thought to be a 'central sensitivity syndrome' related to hypersensitivity of the nervous system, but the cause is unknown. A similar understanding is proposed for other unexplained conditions, including chronic fatigue syndrome (CFS). Exploring the comorbidity of the two conditions is a valuable first step in identifying potential common aetiological mechanisms or treatment targets.METHOD: Systematic literature review. Studies were

	Newcastle upon Tyne, UK. (3)Centre for Oral Health Research and Institute of Health & Society, Newcastle University, Newcastle upon Tyne, UK. (4)Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK. (5)Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.			included if they recruited community or control samples and identified how many reported having both TMD and CFS, or if they recruited a sample of patients with either TMD or CFS and measured the presence of the other condition. RESULTS: Six papers met inclusion criteria. In studies of patients with CFS (n = 3), 21-32% reported having TMD. In a sample of people with CFS and fibromyalgia, 50% reported having TMD. Studies in people with TMD (n = 3) reported 0-43% having CFS. Studies in samples recruited from oro-facial pain clinics (n = 2) reported a lower comorbidity with CFS (0-10%) than a study that recruited individuals from a TMD self-help organisation (43%). CONCLUSION: The review highlights the limited standard of evidence addressing the comorbidity between oro-facial pain and CFS. There is a valuable signal that the potential overlap in these two conditions could be high; however, studies employing more rigorous methodology including standardised clinical assessments rather than self-report of prior diagnosis are needed.
Roerink ME(1), Lenders JW(2,)(3), Schmits IC(4), Pistorius AM(5), Smit JW(2), Knoop H(4,)(6), van der Meer JW(2).	(1) Department of Internal Medicine, Radboud University Medical Centre, Nijmegen, the Netherlands. Megan.Roerink@radboudumc.nl. (2) Department of Internal Medicine, Radboud University Medical Centre, Nijmegen, the Netherlands. (3) Department of Internal Medicine III, University Hospital Carl Gustav Carus, Technical University of Dresden, Dresden, Germany. (4) Expert Centre for Chronic Fatigue, Radboud University Medical	Postural orthostatic tachycardia is not a useful diagnostic marker for chronic fatigue syndrome.	82. J Intern Med. 2016 Oct 2.	BACKGROUND: Postural orthostatic tachycardia syndrome (POTS) is considered a diagnostic marker for chronic fatigue syndrome (CFS). OBJECTIVES: The aims of this study were to (i) compare POTS prevalence in a CFS cohort with fatigued patients not meeting CFS criteria, and (ii) assess activity, impairment and response to cognitive behavioural therapy (CBT) in CFS patients with POTS (POTS-CFS) and without POTS (non-POTS-CFS). METHODS: Prospective cohort study at the Radboud University Medical Centre in the Netherlands. Between June 2013 and December 2014, 863 consecutive patients with persistent fatigue were screened. Patients underwent an active standing test, filled out questionnaires and wore an activity-sensing device for a period of 12 days. RESULTS: A total of 419 patients with CFS and 341 non-CFS fatigued patients were included in the study. POTS prevalence in adult patients with CFS was 5.7% vs. 6.9% in non-CFS adults (P = 0.54). In adolescents, prevalence rates were 18.2% and 17.4%, respectively (P = 0.93). Adult patients with POTS-CFS were younger (30 ± 12 vs. 40 ± 13 years, P = 0.001) and had a higher supine heart rate (71 ± 11 vs. 65 ± 9 beats per min, P = 0.009) compared with non-POTS-CFS patients. Severity and activity patterns did not differ between groups. In patients with CFS, criteria for Systemic Exertion Intolerance Disease (SEID) were met in 76% of adults and 67% of adolescents. In these patients with CFS fulfilling the SEID criteria, the prevalence of POTS was not different from that in the overall CFS population. POTS-CFS adolescents had less clinically significant improvement after CBT than non-POTS-CFS adolescents (58% vs. 88%, P = 0.017). CONCLUSION: In adults with CFS, the prevalence of POTS was low, was not different from the rate in non-CFS fatigued patients and was not related to disease severity or treatment outcome. In POTS-CFS adolescents, CBT was less successful than in non-POTS-CFS patients. The evaluation of POTS appears to be of limited value for the

	Centre, Nijmegen, the Netherlands. (5) Centre for Molecular and Biomolecular Informatics, Radboud University Medical Centre, Nijmegen, the Netherlands. (6)Department of Medical Psychology, Academic Medical Centre (AMC), University of Amsterdam, Amsterdam, the Netherlands.			diagnosis of CFS.
Rogers DC(1), Dittner AJ(2), Rimes KA(3), Chalder T(4).	(1)King's College London, King's Health Partners, (formerly Behavioural and Developmental Psychiatry Clinical Academic Group, Maudsley Adult ADHD Service, South London and Maudsley NHS Foundation Trust), London, UK. (2)King's College London, King's Health Partners, Psychological Medicine Clinical Academic Group, Chronic Fatigue Research and Treatment Unit (formerly Behavioural and Developmental Psychiatry Clinical Academic Group,	Fatigue in an adult attention deficit hyperactivity disorder population: A trans-diagnostic approach	22. Br J Clin Psychol. 2016 Dec 5.	OBJECTIVES: Trans-diagnostic approaches suggest that key cognitive and behavioural processes maintain symptoms across a wide range of mental health disorders. Fatigue is a common clinical feature of attention deficit hyperactivity disorder (ADHD) in adulthood; however, empirical data supporting its prevalence are lacking. This study aimed to collate outcomes from outpatient services to (1) investigate the prevalence of fatigue in adults with ADHD, (2) examine symptoms of ADHD in adults with chronic fatigue syndrome (CFS), and (3) consider secondary clinical characteristics common to both disorder groups. METHODS: Measures of self-reported fatigue were compared across groups of adults with ADHD (N = 243), CFS (N = 86), and healthy controls (HC) (N = 211) using a between-subjects cross-sectional design. Groups were also compared on secondary clinical measures of functional impairment, mood, anxiety, sleep, self-efficacy, and their beliefs about the acceptability of expressing emotions. RESULTS: The ADHD group were significantly more fatigued than HC with 62% meeting criteria for fatigue caseness. ADHD symptoms were significantly greater in the CFS group than in HC. ADHD and CFS groups did not differ significantly on measures of functional impairment, mood, and self-efficacy. No significant differences were detected on measures of anxiety when items relating to physical restlessness were removed from the analysis. CONCLUSIONS: Adults with ADHD experience greater fatigue than HC. Adults with CFS and ADHD share many trans-diagnostic clinical characteristics, including difficulties with low mood, anxiety, and reduced self-efficacy, which impact upon their overall functioning. Further research is required to investigate extraneous factors mediating fatigue severity in these clinical groups. PRACTITIONER POINTS: Fatigue is a common clinical feature of attention deficit hyperactivity disorder (ADHD) in adulthood. Evidence-based interventions for chronic fatigue syndrome could be adapted to

	Maudsley Adult ADHD Service), South London and Maudsley NHS Foundation Trust, London, UK. (3)Department of Psychology, Institute of Psychiatry, Psychology and Neuroscience, King's Health Partners, King's College London, UK. (4)Department of Psychological Medicine, King's College London, Weston Education Centre, London, UK.			address fatigue in ADHD in adults.
Roomruangwong C(1), Kanchanatawan B(1), Sirivichayakul S(2), Mahieu B(3), Nowak G(4,)(5), Maes M(6,)(7,)(8,)(9,)(10).	(1)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. (2)Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. (3)Laboratory of Biochemistry, Antwerp Hospital Network, Antwerp, Belgium. (4)Laboratory of Trace Elements Neurobiology, Institute of Pharmacology PAS,	Lower Serum Zinc and Higher CRP Strongly Predict Prenatal Depression and Physio-somatic Symptoms, Which All Together Predict Postnatal Depressive Symptoms.	290. Mol Neurobiol. 2016 Feb 5.	Pregnancy and delivery are associated with activation of immune-inflammatory pathways which may prime parturients to develop postnatal depression. There are, however, few data on the associations between immune-inflammatory pathways and prenatal depression and physio-somatic symptoms. This study examined the associations between serum zinc, C-reactive protein (CRP), and haptoglobin at the end of term and prenatal physio-somatic symptoms (fatigue, back pain, muscle pain, dyspepsia, obstipation) and prenatal and postnatal depressive and anxiety symptoms as measured using the Edinburgh Postnatal Depression Scale (EPDS), Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HAMD), and Spielberger's State Anxiety Inventory (STAI). Zinc and haptoglobin were significantly lower and CRP increased at the end of term as compared with non-pregnant women. Prenatal depression was predicted by lower zinc and lifetime history of depression, anxiety, and premenstrual tension syndrome (PMS). The latter histories were also significantly and inversely related to lower zinc. The severity of prenatal EDPS, HAMD, BDI, STAI, and physio-somatic symptoms was predicted by fatigue in the first and second trimesters, a positive life history of depression, anxiety, and PMS, and lower zinc and higher CRP. Postnatal depressive symptoms are predicted by prenatal depression, physio-somatic symptoms, zinc and CRP. Prenatal depressive and physio-somatic symptoms have an immune-inflammatory pathophysiology, while postnatal depressive symptoms are highly predicted by prenatal immune activation, prenatal depression, and a lifetime history of depression and PMS. Previous episodes of depression, anxiety disorders, and PMS may prime pregnant females to develop prenatal and postnatal depressive

	Krakow, Poland. (5)Department of Pharmacobiology, Jagiellonian University Medical College, Krakow, Poland. (6)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com. (7)Department of Psychiatry, Medical University Plovdiv, Plovdiv, Bulgaria. dr.michaelmaes@hotmail.com. (8)Department of Psychiatry, Faculty of Medicine, State University of Londrina, Londrina, Brazil. dr.michaelmaes@hotmail.com. (9)Revitalis Clinic, Waalre, Netherlands. dr.michaelmaes@hotmail.com. (10)IMPACT Strategic Research Center, Barwon Health, Deakin University, Geelong, VIC, Australia. dr.michaelmaes@hotmail.com.			symptoms via activated immune pathways.
Roversi S(1), Fabbri LM(1), Sin	(1)1 Department of Metabolic Medicine,	Chronic Obstructive Pulmonary Disease and	106. Am J Respir Crit Care Med. 2016 Dec	Chronic obstructive pulmonary disease (COPD) is a global health issue with high social and economic costs. Concomitant chronic cardiac disorders are frequent in patients

DD(2), Hawkins NM(3), Agustí A(4).	University of Modena and Reggio Emilia and Sant'Agostino Estense Hospital, Modena, Italy. (2)2 Division of Respirology and. (3)3 Division of Cardiology, Department of Medicine, Centre for Heart Lung Innovation, University of British Columbia, Vancouver, British Columbia, Canada; and. (4)4 Thorax Institute, Hospital Clinic in Barcelona, University of Barcelona, Barcelona, Spain.	Cardiac Diseases. An Urgent Need for Integrated Care.	1;194(11):1319-1336.	with COPD, likely owing to shared risk factors (e.g., aging, cigarette smoke, inactivity, persistent low-grade pulmonary and systemic inflammation) and add to the overall morbidity and mortality of patients with COPD. The prevalence and incidence of cardiac comorbidities are higher in patients with COPD than in matched control subjects, although estimates of prevalence vary widely. Furthermore, cardiac diseases contribute to disease severity in patients with COPD, being a common cause of hospitalization and a frequent cause of death. The differential diagnosis may be challenging, especially in older and smoking subjects complaining of unspecific symptoms, such as dyspnea and fatigue. The therapeutic management of patients with cardiac and pulmonary comorbidities may be similarly challenging: bronchodilators may have cardiac side effects, and, vice versa, some cardiac medications should be used with caution in patients with lung disease. The aim of this review is to summarize the evidence of the relationship between COPD and the three most frequent and important cardiac comorbidities in patients with COPD: ischemic heart disease, heart failure, and atrial fibrillation. We have chosen a practical approach, first summarizing relevant epidemiological and clinical data, then discussing the diagnostic and screening procedures, and finally evaluating the impact of lung-heart comorbidities on the therapeutic management of patients with COPD and heart diseases.
Rowe PC(1), Fontaine KR(2), Lauver M(1), Jasion SE(1), Marden CL(1), Moni M(1), Thompson CB(3), Violand RL(4).	(1)Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States of America. (2)Department of Health Behavior, University of Alabama at Birmingham School of Public Health, Birmingham, Alabama, United States of America. (3)Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore,	Neuromuscular Strain Increases Symptom Intensity in Chronic Fatigue Syndrome.	136. PLoS One. 2016 Jul 18;11(7):e0159386.	Chronic fatigue syndrome (CFS) is a complex, multisystem disorder that can be disabling. CFS symptoms can be provoked by increased physical or cognitive activity, and by orthostatic stress. In preliminary work, we noted that CFS symptoms also could be provoked by application of longitudinal neural and soft tissue strain to the limbs and spine of affected individuals. In this study we measured the responses to a straight leg raise neuromuscular strain maneuver in individuals with CFS and healthy controls. We randomly assigned 60 individuals with CFS and 20 healthy controls to either a 15 minute period of passive supine straight leg raise (true neuromuscular strain) or a sham straight leg raise. The primary outcome measure was the symptom intensity difference between the scores during and 24 hours after the study maneuver compared to baseline. Fatigue, body pain, lightheadedness, concentration difficulties, and headache scores were measured individually on a 0-10 scale, and summed to create a composite symptom score. Compared to individuals with CFS in the sham strain group, those with CFS in the true strain group reported significantly increased body pain (P = 0.04) and concentration difficulties (P = 0.02) as well as increased composite symptom scores (all P = 0.03) during the maneuver. After 24 hours, the symptom intensity differences were significantly greater for the CFS true strain group for the individual symptom of lightheadedness (P = 0.001) and for the composite symptom score (P = 0.005). During and 24 hours after the exposure to the true strain maneuver, those with CFS had significantly higher individual and composite symptom intensity changes compared to

	Maryland, United States of America. (4)Rick Violand, PT LLC, Ellicott City, Maryland, United States of America.			the healthy controls. We conclude that a longitudinal strain applied to the nerves and soft tissues of the lower limb is capable of increasing symptom intensity in individuals with CFS for up to 24 hours. These findings support our preliminary observations that increased mechanical sensitivity may be a contributor to the provocation of symptoms in this disorder.
Rowe PC(1), Marden CL(1), Jasion SE(1), Cranston EM(1,)(2), Flaherty MA(1,)(2), Kelly KJ(3).	(1)Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD, USA. (2)University of Maryland School of Medicine, Baltimore, MD, USA. (3)Pediatric Specialty Care, Willow Grove, PA, USA.	Cow's milk protein intolerance in adolescents and young adults with chronic fatigue syndrome.	196. Acta Paediatr. 2016 Sep;105(9):e412-8.	AIM: To examine the prevalence, clinical features and influence on illness severity of cow's milk protein intolerance in young people with chronic fatigue syndrome. METHODS: In a two-year prospective study of 55 adolescents and young adults with chronic fatigue syndrome, we defined intolerance to milk protein if subjects reported (i) no evidence of immediate or anaphylactic reactions to milk, (ii) at least 2 of the following 3 chronic symptoms: gastroesophageal reflux, early satiety and epigastric/abdominal pain, (iii) improvement in upper gastrointestinal symptoms on a milk protein elimination diet and (iv) at least 2 recurrences of upper gastrointestinal symptoms >two hours following open re-exposure to milk protein. Subjects completed three quality of life surveys at baseline and at six months. RESULTS: The mean (SD) age of the 55 participants was 16.5 (2.1) years. Seventeen (31%; 95% CI, 19-43%) met study criteria for cow's milk protein intolerance. Compared to milk-tolerant subjects, milk-sensitive participants had significantly worse health-related quality of life at baseline but not at six months (after institution of the milk-free diet). CONCLUSION: Cow's milk protein intolerance is a common problem in young people with chronic fatigue syndrome and is a treatable contributor to their symptoms.
Russek LN(1,)(2), LaShomb EA(3), Ware AM(4), Wesner SM(5), Westcott V(6).	(1)Clarkson University, Potsdam, NY, USA. (2)Canton-Potsdam Hospital, Potsdam, NY, USA. (3)Highland Nursing Home and Rehab, Massena, NY, USA. (4)Ladacin Network, Wanamassa, NJ, USA. (5)Rehabresources at Syracuse Homes Association, Oswego, NY, USA. (6)Walton Rehabilitation Hospital, Augusta, GA, USA.	United States Physical Therapists' Knowledge About Joint Hypermobility Syndrome Compared with Fibromyalgia and Rheumatoid Arthritis.	369. Physiother Res Int. 2016 Mar;21(1):22-35.	BACKGROUND: Joint hypermobility syndrome (JHS) is one of the most common inherited connective tissue disorders. It causes significant pain and disability for all age groups, ranging from developmental delay among children to widespread chronic pain in adults. Experts in JHS assert that the condition is under-recognized and poorly managed. PURPOSE: The aim of this study was to assess US physical therapists' knowledge about JHS compared with other causes of widespread pain and activity limitations: fibromyalgia, juvenile rheumatoid arthritis and adult rheumatoid arthritis. METHODS: Cross-sectional, Internet-based survey of randomly selected members of the American Physical Therapy Association and descriptive statistics were used to explore physical therapists' knowledge about JHS, fibromyalgia, juvenile rheumatoid arthritis and adult rheumatoid arthritis, and chi square was used to compare knowledge about the different conditions. RESULTS: The response rate was 15.5% (496). Although 36% recognized the Beighton Scale for assessing joint hypermobility, only 26.8% of respondents were familiar with the Brighton Criteria for diagnosing JHS. Few respondents (11-19%) realized that JHS has extra-articular features such as anxiety disorder, fatigue, headache, delayed motor development, easy bruising and sleep disturbance. Physical therapists working in environments most likely to see patients with JHS underestimated the likely prevalence in their patient population.

				CONCLUSIONS: The results suggest that many physical therapists in the United States are not familiar with the diagnostic criteria, prevalence or common clinical presentation of JHS.
Russell C(1), Kyle SD(2), Wearden AJ(3).	(1)School of Psychological Sciences, University of Manchester, UK. Electronic address: Charlotte.Russell@rlbuht.nhs.uk. (2)Sleep and Circadian Neuroscience Institute (SCNi), Nuffield Department of Clinical Neurosciences, University of Oxford, UK. (3)School of Psychological Sciences, University of Manchester, UK.	Do evidence based interventions for chronic fatigue syndrome improve sleep? A systematic review and narrative synthesis.	116. Sleep Med Rev. 2016 May 13. pii: S1087-0792(16)30012-0.	Cognitive behavioural therapy (CBT) and graded exercise therapy (GET) are recommended evidence based treatments for chronic fatigue syndrome (CFS), with research supporting their effectiveness in reducing fatigue and functional impairment. However, little research has focussed on the effect of these treatments on sleep, despite high reported sleep disturbance in CFS. Using a narrative synthesis approach, we aimed to 1) systematically identify and summarise the current evidence for the effectiveness of CBT and GET in improving sleep; 2) consider factors influencing treatment effectiveness, including incorporation of sleep management techniques; and 3) consider the appropriateness of sleep outcome measures used within evaluations. Studies evaluating CBT and/or GET for CFS, and including a sleep outcome were eligible for inclusion. Eight studies were identified. We found that GET interventions can improve sleep but this effect is inconsistent across studies. For CBT the evidence is limited with only one of two evaluations demonstrating sleep-related improvements. We conclude from existing research that we know little about the effects of including sleep management components within CBT and GET interventions. We suggest that future research should explore the effectiveness of sleep components within interventions, and sleep specific interventions, using comprehensive outcome measures that fully capture the range of sleep difficulties experienced in CFS.
Russell C(1), Wearden AJ(1), Fairclough G(2), Emsley RA(3), Kyle SD(4).	(1)School of Psychological Sciences, University of Manchester, United Kingdom. (2)Department of Clinical Health Psychology, Salford Royal NHS Foundation Trust, United Kingdom. (3)Centre for Biostatistics, Institute of Population Health, University of Manchester, United Kingdom. (4)Sleep and Circadian Neuroscience Institute (SCNi), Nuffield	Subjective but Not Actigraphy-Defined Sleep Predicts Next-Day Fatigue in Chronic Fatigue Syndrome: A Prospective Daily Diary Study	316. Sleep. 2016 Apr 1;39(4):937-44. .	STUDY OBJECTIVES: This study aimed to (1) examine the relationship between subjective and actigraphy-defined sleep, and next-day fatigue in chronic fatigue syndrome (CFS); and (2) investigate the potential mediating role of negative mood on this relationship. We also sought to examine the effect of presleep arousal on perceptions of sleep. METHODS: Twenty-seven adults meeting the Oxford criteria for CFS and self-identifying as experiencing sleep difficulties were recruited to take part in a prospective daily diary study, enabling symptom capture in real time over a 6-day period. A paper diary was used to record nightly subjective sleep and presleep arousal. Mood and fatigue symptoms were rated four times each day. Actigraphy was employed to provide objective estimations of sleep duration and continuity. RESULTS: Multilevel modelling revealed that subjective sleep variables, namely sleep quality, efficiency, and perceiving sleep to be unrefreshing, predicted following-day fatigue levels, with poorer subjective sleep related to increased fatigue. Lower subjective sleep efficiency and perceiving sleep as unrefreshing predicted reduced variance in fatigue across the following day. Negative mood on waking partially mediated these relationships. Increased presleep cognitive and somatic arousal predicted self-reported poor sleep. Actigraphy-defined sleep, however, was not found to predict following-day fatigue. CONCLUSIONS: For the first time we show that nightly subjective sleep predicts next-day fatigue in CFS and identify important factors driving this relationship. Our data

	Department of Clinical Neurosciences, Sir William Dunn School of Pathology, University of Oxford, United Kingdom.			suggest that sleep specific interventions, targeting presleep arousal, perceptions of sleep and negative mood on waking, may improve fatigue in CFS.
Russell L(1), Broderick G(2,)(3,)(4), Taylor R(5), Fernandes H(1), Harvey J(6,)(7), Barnes Z(6,)(7,)(8), Smylie A(1), Collado F(7), Balbin EG(6), Katz BZ(9), Klimas NG(7,)(8), Fletcher MA(7,)(8).	(1)Department of Medicine, University of Alberta, Edmonton, AB, Canada. (2)Department of Medicine, University of Alberta, Edmonton, AB, Canada. gbroderick@nova.edu. (3)Miami Veterans Affairs Medical Center, Miami, FL, USA. gbroderick@nova.edu. (4)Institute for Neuro-immune Medicine, Nova Southeastern University, Suite 3440 University Park Plaza, 3424 South University Drive, Fort Lauderdale, FL, 33328, USA. gbroderick@nova.edu. (5)Department of Occupational Therapy, University of Illinois at Chicago, Chicago, IL, USA. (6)Department of Medicine, University of Miami, Miami, FL, USA. (7)Miami Veterans	Illness progression in chronic fatigue syndrome: a shifting immune baseline.	255. BMC Immunol. 2016 Mar 10;17:3.	BACKGROUND: Validation of biomarkers for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) across data sets has proven disappointing. As immune signature may be affected by many factors, our objective was to explore the shift in discriminatory cytokines across ME/CFS subjects separated by duration of illness. METHODS: Cytokine expression collected at rest across multiple studies for female ME/CFS subjects (i) 18 years or younger, ill for 2 years or less (n = 18), (ii) 18-50 years of age, ill for 7 years (n = 22), and (iii) age 50 years or older (n = 28), ill for 11 years on average. Control subjects were matched for age and body mass index (BMI). Data describing the levels of 16 cytokines using a chemiluminescent assay was used to support the identification of separate linear classification models for each subgroup. In order to isolate the effects of duration of illness alone, cytokines that changed significantly with age in the healthy control subjects were excluded a priori. RESULTS: Optimal selection of cytokines in each group resulted in subsets of IL-1α, 6, 8, 15 and TNFα. Common to any 2 of 3 groups were IL-1α, 6 and 8. Setting these 3 markers as a triple screen and adjusting their contribution according to illness duration sub-groups produced ME/CFS classification accuracies of 75-88 %. The contribution of IL-1α, higher in recently ill adolescent ME/CFS subjects was progressively less important with duration. While high levels of IL-8 screened positive for ME/CFS in the recently afflicted, the opposite was true for subjects ill for more than 2 years. Similarly, while low levels of IL-6 suggested early ME/CFS, the reverse was true in subjects over 18 years of age ill for more than 2 years. CONCLUSIONS: These preliminary results suggest that IL-1α, 6 and 8 adjusted for illness duration may serve as robust biomarkers, independent of age, in screening for ME/CFS.

	Affairs Medical Center, Miami, FL, USA. (8)Institute for Neuro-immune Medicine, Nova Southeastern University, Suite 3440 University Park Plaza, 3424 South University Drive, Fort Lauderdale, FL, 33328, USA. (9)Division of Infectious Diseases, Ann & Robert H Lurie Children's Hospital of Chicago, Chicago, IL, USA.			
Rutherford G(1), Manning P(1), Newton JL(2).	(1)Institute of Cellular Medicine, Newcastle University, Newcastle NE2 4HH, UK. (2)Institute of Cellular Medicine, Newcastle University, Newcastle NE2 4HH, UK; Newcastle Hospitals NHS Foundation Trust, UK NIHR Biomedical Research Centre in Ageing and Age Related Disease, Newcastle University, Newcastle NE2 4HH, UK.	Understanding Muscle Dysfunction in Chronic Fatigue Syndrome.	241. J Aging Res. 2016;2016:2497348	Introduction. Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a debilitating disorder of unknown aetiology, characterised by severe disabling fatigue in the absence of alternative diagnosis. Historically, there has been a tendency to draw psychological explanations for the origin of fatigue; however, this model is at odds with findings that fatigue and accompanying symptoms may be explained by central and peripheral pathophysiological mechanisms, including effects of the immune, oxidative, mitochondrial, and neuronal pathways. For example, patient descriptions of their fatigue regularly cite difficulty in maintaining muscle activity due to perceived lack of energy. This narrative review examined the literature for evidence of biochemical dysfunction in CFS/ME at the skeletal muscle level. Methods. Literature was examined following searches of PUB MED, MEDLINE, and Google Scholar, using key words such as CFS/ME, immune, autoimmune, mitochondria, muscle, and acidosis. Results. Studies show evidence for skeletal muscle biochemical abnormality in CFS/ME patients, particularly in relation to bioenergetic dysfunction. Discussion. Bioenergetic muscle dysfunction is evident in CFS/ME, with a tendency towards an overutilisation of the lactate dehydrogenase pathway following low-level exercise, in addition to slowed acid clearance after exercise. Potentially, these abnormalities may lead to the perception of severe fatigue in CFS/ME.
Ryckeghem H(1,)(2), Delesie L(1,)(3), Tobback E(1,)(3), Lievens S(4), Vogelaers	(1)Department of General Internal Medicine, Ghent University Hospital, Ghent, Belgium.	Exploring the potential role of the Advanced Nurse Practitioner within a care path for patients with Chronic Fatigue	7. J Adv Nurs. 2016 Dec 21.	AIMS: To explore the experiences and expectations of patients with Chronic Fatigue Syndrome and general practitioners in order to develop the potential role of an Advanced Nurse Practitioner at the diagnostic care path of abnormal fatigue developed for regional transmural implementation in the Belgian provinces of East and West Flanders. BACKGROUND: Patients with Chronic Fatigue Syndrome experience an

D(1,)(3,)(5), Mariman A(1,)(3,)(5).	(2)Department of endocrinology and diabetology, Onze-Lieve-Vrouw Ziekenhuis, Aalst, Belgium. (3)Centre for Neurophysiologic Monitoring, Ghent University Hospital, Ghent, Belgium. (4)General and Applied Psychology, Faculty of Psychology and Educational Sciences, Ghent University, Ghent, Belgium. (5)Department of Internal Medicine, Faculty of Medicine and Health Sciences, University of Ghent, Belgium.	Syndrome.		incapacitating chronic fatigue that is present for at least six months. Since many uncertainties exist about the causes and progression of the disease, patients have to cope with disbelief and scepticism. Access to health care may be hampered, which could lead to inappropriate treatments and guidance. Design Qualitative design. METHODS: Individual semi-structured interviews were conducted with patients with Chronic Fatigue Syndrome and general practitioners in Belgium. Data were collected over 9 months in 2014-2015. All interviews were audio recorded and transcribed for qualitative analysis using open explorative thematic coding. RESULTS: Fifteen patients and fifteen general practitioners were interviewed. Three themes were identified: mixed feelings with the diagnosis, lack of one central intermediator and insufficient coordination. Participants stressed the need for education, knowledge and an intermediator to provide relevant information at the right time and to build up a trust relationship. CONCLUSION: This qualitative exploration underscores some clear deficiencies in the guidance of patients suffering from Chronic Fatigue Syndrome and abnormal fatigue. An Advanced Nurse Practitioner as a central intermediator in the transmural care of these patients could promote interdisciplinary/multidisciplinary collaboration and effective communication, provide education and ensure a structured and coordinated approach.
Sakudo A(1).	(1)Laboratory of Biometabolic Chemistry, School of Health Sciences, Faculty of Medicine, University of The Ryukyus, Nishihara, Okinawa 903‐0215, Japan.	Potential use of visible and near-infrared spectroscopy for the analysis and diagnosis of chronic fatigue syndrome (Review).	135. Mol Med Rep. 2016 Sep;14(3):1875-9.	At present, chronic fatigue syndrome (CFS) is diagnosed on the basis of clinical symptoms. Although various psychological, endocrinological and immunological abnormalities of patients with CFS have been reported, no clear consensus exists regarding the symptoms for this disorder. Thus, an objective diagnostic method for CFS is urgently required. The present study investigated the diagnosis and analysis of CFS using visible and near‐infrared (Vis‐NIR) spectroscopy. Previous studies have demonstrated the potential of Vis-NIR spectroscopy for diagnosing CFS by analyzing either serum samples as an invasive approach or thumbs as a non‐invasive approach. Analysis of the Vis‐NIR spectra of blood and thumbs suggested that factors absorbing in this spectral region are altered in patients with CFS compared with healthy individuals. These findings are likely to facilitate the search for biomarkers associated with CFS and to increase our understanding of the pathophysiology of the disorder. The current review aimed to outline the latest studies and discuss the future perspectives for CFS made possible by Vis-NIR spectroscopy.
Salehi H(1), Salehi M(2), Roghanian R(3), Bozari M(3),	(1)Department of Infectious Diseases, Faculty of Medicine,	Comparison of serological and molecular test for diagnosis of infectious	164. Adv Biomed Res. 2016 May 30;5:95.	BACKGROUND: Epstein-Bar virus (EBV) is the main etiology of infectious mononucleosis (IM) syndrome that is characterized by fever, sore throat, and lymph adenopathy. Since, this virus could be associated with a number of malignancies, some hematologic

Taleifard S(3), Salehi MM(4), Salehi M(4).	Isfahan University of Medical Sciences, Isfahan, Iran. (2)Student Research Center, Faculty of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran. (3)Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran. (4)Student Research Center, Faculty of Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran.	mononucleosis.		disorders, and chronic fatigue syndrome, identification of IM is very important. The aim of study was to evaluate the specificity, as well as sensitivity of the two different methods that is, serology versus molecular diagnosis that are currently used for diagnosis of IM. MATERIALS AND METHODS: In this study, during a period of 3.5 years, 100 suspected patients as case group and 100 healthy individuals as a control group were studied. Fifty samples in each group were tested by polymerase chain reaction (PCR) and all the samples including case group and control group were carried out by enzyme-linked immunosorbent assay (ELISA). RESULTS: In 76% of patients and in 20% of the healthy individuals, samples were detected EBV DNA by PCR. On the other hand, 68.5% of the samples belong to the case group and 46% in the control group showed positivity by ELISA. CONCLUSION: By comparing the two methods, since PCR is very expensive and time consuming, and the percentages of difference ranges are narrow, ELISA could be applied as a first, easiest, and preliminary diagnostic test for IM. In addition, this test could be applied in various phases of the disease with a higher sensitivity comparing to PCR. Although PCR is routinely used for diagnosis of various infectious agents, it is considered as an expensive test and merely could be used after 1-2 weeks from the onset of the illness.
Sambataro D(1,)(2), Sambataro G(2), Dal Bosco Y(1), Polosa R(1).	(1)a Department of Clinical and Experimental Medicine, Teaching Hospital Policlinico 'G. Rodolico' , University of Catania , Catania , Italy. (2)b Outpatient Clinic of Rheumatology accredited to National Health System , 'Artroreuma srl' , Mascalucia , Italy.	Present and future of biologic drugs in primary Sjögren's syndrome.	100. Expert Opin Biol Ther. 2017 Jan;17(1):63-75. Epub 2016 Sep 20.	INTRODUCTION: Primary Sjögren's (pSS) syndrome is a chronic, autoimmune, and systemic disease characterized by xerostomia, xerophthalmia, muscle pain and fatigue. The disease may be complicated by a systemic involvement, such as a pulmonary fibrosis or the development of lymphoma which severely worsens the prognosis. Actually, there are no recommendations for the management of pSS. However, recent advances in the understanding of its pathogenesis have uncovered some pathways that have potential as therapeutic targets. Areas covered: In this review, the authors present the biologic drugs potentially valuable to the treatment of pSS in light of its physiopathology with a 'bird's eye' view of future prospects. The authors took into account relevant studies published from 2004 to 2016. Expert opinion: Biological treatment in pSS is a promising opportunity to potentially control disease activity and prevent its complication. Currently, inhibition of B-cell and IL-17 pathways seem to be the most promising avenues. New achievements in the knowledge of pSS pathophysiology are necessary in order to try to simultaneously predict the predominant pathogenic pathway, the kind of patients at major risk to develop a more severe disease, and the appropriate biological therapy to use.
Sandler CX(1,)(2), Hamilton BA(1), Horsfield SL(1), Bennett BK(2), Vollmer-Conna U(3), Tzarimas C(1), Lloyd	(1)Fatigue Clinic, Lifestyle Clinic, School of Medical Sciences, University of New South Wales, Sydney, New South Wales, Australia. (2)National	Outcomes and predictors of response from an optimised, multidisciplinary intervention for chronic fatigue states.	99. Intern Med J. 2016 Dec;46(12):1421-1429.	BACKGROUND: Medically unexplained chronic fatigue states are prevalent and challenging to manage. Cognitive behavioural therapy (CBT) and graded exercise therapy (GET) are effective in clinical trials. The evaluation of delivery in a standard healthcare setting is rare. An integrated treatment programme with individualised allocation of resources to patients' needs was developed and implemented through an academic outpatient clinic. It was hypothesised that the programme would result in similar responses to those observed in the clinical trials. AIM: To evaluate the outcomes

AR(1,)(2,)(4).	Centre for Cancer Survivorship, University of New South Wales, Sydney, New South Wales, Australia. (3)Department of Human Behaviour, School of Psychiatry, University of New South Wales, Sydney, New South Wales, Australia. (4)Inflammation and Infection Research Centre, School of Medical Sciences, University of New South Wales, Sydney, New South Wales, Australia.			of an integrated, 12-week CBT and GET programme delivered by exercise physiologists and clinical psychologists. METHODS: Consecutive eligible patients (n = 264) who met the diagnostic criteria for chronic fatigue syndrome or post-cancer fatigue were evaluated with self-report measures of fatigue, functional capacity and mood disturbance at baseline, end-of-treatment (12 weeks) and follow-up (24 weeks). A semi-structured interview recording the same parameters was conducted pre- and post-treatment by an independent clinician. Primary outcome was analysed by repeated measures analysis of variance and predictors of response were analysed by logistic regression. RESULTS: The intervention produced sustained improvements in symptom severity and functional capacity. A substantial minority of patients (35%) gained significant improvement, with male gender and higher pain scores at baseline predicting non-response. A small minority of patients (3%) worsened. CONCLUSION: The manualised protocol of integrated CBT and GET was successfully implemented, confirming the generally positive findings of clinical trials. Assessment and treatment protocols are available for dissemination to allow standardised management. The beneficial effects described here provide the basis for ongoing studies to optimise the intervention further and better identify those most likely to respond.
Sandler CX(1), Lloyd AR, Barry BK.	(1)1Fatigue Clinic, Lifestyle Clinic, School of Medical Sciences, University of New South Wales, Sydney, NSW, AUSTRALIA; 2Inflammation and Infection Research Centre, School of Medical Sciences, University of New South Wales, Sydney, NSW, AUSTRALIA; and 3Neuroscience Research Australia, University of New South Wales, Sydney, AUSTRALIA.	Fatigue Exacerbation by Interval or Continuous Exercise in Chronic Fatigue Syndrome.	194. Med Sci Sports Exerc. 2016 Oct;48(10):1875-85.	PURPOSE: The objective of this study is to determine whether the typical exacerbation of symptoms in patients with chronic fatigue syndrome (CFS) after a bout of exercise differs between high-intensity interval training (HIIT) or continuous (CONT) aerobic exercise of the same duration and mechanical work. METHODS: Participants with specialist-diagnosed CFS performed two 20-min bouts of cycling in a randomized crossover study. The bouts were either moderate-intensity continuous (70% age-predicted HR maximum) or high-intensity interval exercise, separated by at least 2 wk. Self-report questionnaires capturing fatigue, the related symptoms, and actigraphy were collected across 2 d before and 4 d after the exercise. Comparisons between exercise bouts were made using paired sample t-tests. RESULTS: Fourteen moderately affected participants who were unable to work, but not bed bound, completed the study (nine female, 32 ± 10 yr, 67 ± 11 kg). Mechanical work was matched successfully between the exercise bouts (HIIT, 83,037, vs CONT, 83,348 J, P = 0.84). Mean HR (HIIT, 76% ± 5%, vs CONT, 73% ± 6% age-predicted HR maximum, P < 0.05) and RPE (6-20) in the legs (HIIT, 15.4 ± 1.4, vs CONT, 13.2 ± 1.2, P < 0.001) were higher for the interval compared with continuous exercise. Mean fatigue scores (0-10) were similar before each exercise challenge (HIIT, 4.5 ± 1.8, vs CONT, 4.1 ± 1.7, P = 0.43). Participants reported an increase in fatigue scores after both challenges (mean difference: HIIT, 1.0 ± 1.3, P < 0.01; CONT, 1.5 ± 0.7, P < 0.001), but these exacerbations in fatigue were not

				statistically or clinically different (P = 0.20). CONCLUSIONS: High-intensity interval exercise did not exacerbate fatigue any more than continuous exercise of comparable workload. This finding supports evaluation of HIIT in graded exercise therapy interventions for patients with CFS.
Sarvaiya K(1), Goswami S(2).	(1)Department of Pharmacology, L.M. College of Pharmacy, Ahmedabad, 380009 Gujarat, India. Electronic address: Sarvaiyakuldeep5393 @gmail.com. (2)Department of Pharmacology, L.M. College of Pharmacy, Ahmedabad, 380009 Gujarat, India.	Investigation of the effects of vanilloids in chronic fatigue syndrome.	61. Brain Res Bull. 2016 Oct;127:187-194.	AIM OF THE STUDY: To assess the effectiveness of TRPV1 modulators in animal model of Chronic fatigue syndrome (CFS). To assess central and peripheral behavioral activity of TRPV1 modulators. MATERIAL AND METHODS: CFS was induced by forcing the rats to swim for 10min for 21 consecutive days. The rats were treated with capsaicin (TRPV1 agonist, 2.5mg/kg) and n-tert-butylcyclohexanol (TRPV1 antagonist, 10mg/kg) for 21days 30min before the exposure to stress procedure. The behavioral consequence of CFS was measured in terms of immobility time, grip strength, locomotor activity, and anxiety level using Rota rod, Actophotometer, and Elevated plus maze model respectively. The other parameters include Plasma corticosterone, adrenal gland and spleen weight, complete blood count, blood urea niterogen (BUN), Lactate dehydrogenase (LDH), Lipid peroxidation, catalase and reduced glutathione (GSH). RESULTS AND DISCUSSION: TRPV1 modulators reversed ($p<0.05$) the increase in immobility period, anxiety, spleen weight, BUN and LDH levels, and MDA levels along with decrease in grip strength, locomotor activity, plasma corticosterone, adrenal gland weight, catalase, and GSH. There was also significant increase in total WBC count when compared with the disease control group. The reversal was attributed to modulation of HPA axis, oxidative stress, anaerobic respiration product, muscle degradation product. CONCLUSION: The present study reveals the effectiveness of n-tert-butylcyclohexanol and capsaicin against chronic fatigue syndrome. The mechanism of action can be attributed to inhibition of TRPV1 channel and thereby modulating pain perception, neuroendocrine function, oxidative stress and immune function.
Saugstad OD.		Re: Kronisk utmattelsessyndrom/myalgisk encefalopati--sykdomsmekanismer, diagnostikk og behandling. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2016 Feb 9;136(3):205. Comment on Tidsskr Nor Laegeforen. 2015 Dec 15;135(23-24):2172-5.	
Saury JM(1).	(1)ME/CFS Rehabilitation Unit, Rehabilitation Clinic, Danderyd University Hospital, SE-18288 Stockholm, Sweden. Electronic address: jean-michel.saury@ds.se.	The role of the hippocampus in the pathogenesis of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).	303. Med Hypotheses. 2016 Jan;86:30-8.	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a severe acquired illness characterized by a profound sensation of fatigue, not ameliorated by rest and resulting in a substantial decrease in the amount and quality of occupational, social and recreational activities. Despite intense research, the aetiology and pathogenesis of ME/CFS is still unknown and no conclusive biological markers have been found. As a consequence, an accepted curative treatment is still lacking and rehabilitation programmes are not very effective, as few patients recover. Increased knowledge of the mechanisms leading to the emergence and maintenance of the illness is called for. In this study, I will put forth an alternative hypothesis to explain some of the

				pathologies associated with ME/CFS, by concentrating on one of the major strategic organs of the brain, the hippocampus. I will show that the ME/CFS triggering factors also impact the hippocampus, leading to neurocognitive deficits and disturbances in the regulation of the stress system and pain perception. These deficits lead to a substantial decrease in activity and to sleep disorders, which, in turn, impact the hippocampus and initiate a vicious circle of increased disability.
Schaffner AK(1).	(1)School of European Culture and Languages, University of Kent, Canterbury, CT2 7NF, UK. A.K.Schaffner@kent.ac.uk.	Exhaustion and the Pathologization of Modernity.	372. J Med Humanit. 2016 Sep;37(3):327-41.	This essay analyses six case studies of theories of exhaustion-related conditions from the early eighteenth century to the present day. It explores the ways in which George Cheyne, George Beard, Richard von Krafft-Ebing, Sigmund Freud, Alain Ehrenberg and Jonathan Crary use medical ideas about exhaustion as a starting point for more wide-ranging cultural critiques related to specific social and technological transformations. In these accounts, physical and psychological symptoms are associated with particular external developments, which are thus not just construed as pathology-generators but also pathologized. The essay challenges some of the persistently repeated claims about exhaustion and its unhappy relationship with modernity.
Scheper MC(1,)(2), Pacey V(3,)(4), Rombaut L(5), Adams RD(6), Tofts L(3,)(7), Calders P(8), Nicholson LL(3,)(9), Engelbert RH(1,)(2).	(1)ACHIEVE, Center for Applied Research, Faculty of Health, University of Applied Sciences Amsterdam, Amsterdam, The Netherlands. (2)Department of Rehabilitation, Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands. (3)Kids Rehab, The Children's Hospital at Westmead, Sydney, Australia. (4)Department of Health Professions, Macquarie University, Sydney, Australia. (5)Center for Medical Genetics, Ghent University Hospital,	Generalized Hyperalgesia in children and adults diagnosed with Hypermobility Syndrome and Ehlers-Danlos Syndrome Hypermobility type: A discriminative analysis.	127. Arthritis Care Res (Hoboken). 2016 Aug 2.	INTRODUCTION: Lowered pressure pain thresholds have been demonstrated in adults with Ehlers-Danlos Hypermobility type(EDS-HT), however it remains unclear if these findings are also present in children. Therefore, the objectives of the study were to: (1)determine if generalized hyperalgesia is present in Hypermobility syndrome (HMS)/EDS-HT children, (2)explore potential differences in pressure pain thresholds between HMS/EDS-HT children and adults, and (3)determine the discriminative value of generalized hyperalgesia. METHODS: Patients classified in one of three groups: HMS/EDS-HT, hypermobile (Beighton score ≥4/9) and healthy controls. Descriptive data of age, gender, body mass index, Beighton score, skin laxity and medication usage were collected. Generalized hyperalgesia was quantified by the averaged pressure pain thresholds collected from 12 locations. The following confounders were collected: pain locations/intensity, fatigue, psychological distress. Comparisons between HMS/EDS-HT children and normative values, between children and adults with HMS/EDS-HT, corrected confounders, were analysed with MANCOVA. The discriminative value of generalized hyperalgesia employed in order to differentiate between HMS/EDS-HT, hypermobile and controls was quantified with logistic regression. RESULTS: Significantly lower pressure pain thresholds were found in children with HMS/EDS-HT compared to normative values (range: -22.0% to -59.0%, p=<.05). When applying a threshold of 30.8 N/cm(2) for males and 29.0 N/cm(2) for females, the presence of generalized hyperalgesia discriminated between individuals with HMS/EDS-HT, hypermobile and healthy controls (odds ratio=6.0). CONCLUSION: Children and adults with HMS/EDS-HT are characterized by hypermobility, chronic pain, as well as generalized hyperalgesia. The presence of generalized hyperalgesia may indicate involvement of the central nervous system in the development of chronic pain. This article is protected by

	Ghent, Belgium. (6)Discipline of Physiotherapy, University of Sydney, Sydney, Australia. (7)Discipline of Paediatrics and Child Health, University of Sydney, Sydney, Australia. (8)Department of Rehabilitation Sciences and Physiotherapy, Ghent University Ghent, Belgium. (9)Discipline of Biomedical Sciences, University of Sydney, Sydney, Australia.			
Scherber RM(1,)(2), Kosiorek HE(3), Senyak Z(4), Dueck AC(3), Clark MM(5), Boxer MA(6), Geyer HL(1), McCallister A(4), Cotter M(4), Van Husen B(7), Harrison CN(8,)(9), Mesa RA(1).	(1)Division of Hematology and Medical Oncology, Mayo Clinic, Scottsdale, Arizona. (2)Department of Hematology and Oncology, Oregon Health and Science University, Portland, Oregon. (3)Division of Biostatistics, Mayo Clinic, Scottsdale, Arizona. (4)MPN Forum, MPN Research Foundation, Chicago, Illinois. (5)Department of Psychiatry and Psychology, Mayo Clinic, Rochester,	Comprehensively understanding fatigue in patients with myeloproliferative neoplasms.	323. Cancer. 2016 Feb 1;122(3):477-85.	BACKGROUND: Patients with myeloproliferative neoplasms (MPNs) experience a high persistence, prevalence, and severity of fatigue. There is currently only limited information regarding factors that contribute to fatigue in patients with MPNs. METHODS: A 70-item, Internet-based survey regarding fatigue was developed by MPN investigators and patients/advocates and hosted by the Mayo Clinic Survey Research Center. RESULTS: Fatigue was found to be prevalent and severe among international survey respondents (1788 respondents). Higher body mass index (P<.001), current use of alcohol (P<.001), and current tobacco use (P = .0025) were found to be significantly associated with greater fatigue. Moderate/severe fatigue was present more frequently in those individuals who did not exercise compared with those who reported exercising at least once per week (P<.001). Medical comorbidities found to be significantly associated with greater fatigue included restless leg syndrome (P = .006), diabetes mellitus (P = .045), fibromyalgia (P < 0.001), chronic fatigue syndrome (P = .006), and chronic kidney disease (P = .02). Current use of antidepressants (P<.001), antihistamines (P = .0276), antianxiety medications (P = .0357), and prescription pain medications (P<.001) were found to be associated with worsened fatigue. Nearly 25% of respondents scored > 2 on the Patient Health Questionnaire, indicating a high probability of depression. Higher Brief Fatigue Inventory score, Myeloproliferative Neoplasm Total Symptom Score, and individual symptom items were all associated with a higher likelihood of depressive symptoms (P<.0001). CONCLUSIONS: The

	Minnesota. (6)Arizona Oncology, Tucson, Arizona. (7)MPN Research Foundation, Chicago, Illinois. (8)Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom. (9)MPN Voice, London, United Kingdom.			management of fatigue should be multifactorial, with a comprehensive assessment and treatment plan to address all modifiable fatigue etiologies. Patients with MPNs likely have a higher prevalence of mood disturbances compared with the general population, suggesting the need to assess and intervene in this domain.
Schlauch KA(1), Khaiboullina SF(2,)(3), De Meirleir KL(2), Rawat S(2), Petereit J(1), Rizvanov AA(3), Blatt N(3), Mijatovic T(4), Kulick D(5), Palotás A(3,)(6), Lombardi VC(1,)(2).	(1)Department of Biochemistry and Molecular Biology, University of Nevada, Reno, NV, USA. (2)Nevada Center for Biomedical Research, University of Nevada, Reno, NV, USA. (3)Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan, Russian Federation. (4)R.E.D Laboratories, Zellik, Belgium. (5)Mayo Clinic, Scottsdale, AZ, USA. (6)Asklepios-Med (private medical practice and research center), Szeged, Hungary.	Genome-wide association analysis identifies genetic variations in subjects with myalgic encephalomyelitis/chronic fatigue syndrome.	286. Transl Psychiatry. 2016 Feb 9;6:e730.	Myalgic encephalomyelitis, also known as chronic fatigue syndrome or ME/CFS, is a multifactorial and debilitating disease that has an impact on over 4 million people in the United States alone. The pathogenesis of ME/CFS remains largely unknown; however, a genetic predisposition has been suggested. In the present study, we used a DNA single-nucleotide polymorphism (SNP) chip representing over 906,600 known SNPs to analyze DNA from ME/CFS subjects and healthy controls. To the best of our knowledge, this study represents the most comprehensive genome-wide association study (GWAS) of an ME/CFS cohort conducted to date. Here 442 SNPs were identified as candidates for association with ME/CFS (adjusted P-value<0.05). Whereas the majority of these SNPs are represented in non-coding regions of the genome, 12 SNPs were identified in the coding region of their respective gene. Among these, two candidate SNPs resulted in missense substitutions, one in a pattern recognition receptor and the other in an uncharacterized coiled-coil domain-containing protein. We also identified five SNPs that cluster in the non-coding regions of T-cell receptor loci. Further examination of these polymorphisms may help identify contributing factors to the pathophysiology of ME/CFS, as well as categorize potential targets for medical intervention strategies.
Schmaling KB(1), Betterton KL(2).	(1)Department of Psychology, Washington State University, 14204 NE	Neurocognitive complaints and functional status among patients with chronic fatigue	337. Qual Life Res. 2016 May;25(5):1257-63.	PURPOSE: The purpose of this study was to conduct a longitudinal examination of cognitive complaints and functional status in patients with chronic fatigue syndrome (CFS) alone and those who also had fibromyalgia (CFS/FM). METHODS: A total of 93 patients from a tertiary care fatigue clinic were evaluated on four occasions, each 6

	Salmon Creek Avenue, Vancouver, WA, 98686, USA. karen.schmaling@wsu.edu. (2)Department of Psychology, Washington State University, 14204 NE Salmon Creek Avenue, Vancouver, WA, 98686, USA.	syndrome and fibromyalgia.		months apart. Each evaluation included a tender point assessment, and self-reported functional status and cognitive complaints. RESULTS: Patients with CFS/FM reported significantly worse physical functioning, more bodily pain, and more cognitive difficulties (visuo-perceptual ability and verbal memory) than patients with CFS alone. Over time, bodily pain decreased only for participants with CFS alone. Verbal memory problems were associated with more bodily pain for both patient groups, whereas visuo-perceptual problems were associated with worse functional status for patients with CFS alone. CONCLUSIONS: This study adds to the literature on functional status, longitudinal course, and cognitive difficulties among patients with CFS and those with CFS and FM. The results suggest that patients with CFS/FM are more disabled, have more cognitive complaints, and improve more slowly over time than patients with CFS alone. Specific cognitive difficulties are related to worse functional status, which supports the addition of cognitive difficulties to the FM case criteria.
Schneck AS(1,)(2), Anty R(3,)(2), Tran A(3,)(2), Hastier A(3), Amor IB(1), Gugenheim J(1,)(2), Iannelli A(1,)(2), Piche T(4,)(5).	(1)Service de Chirurgie Digestive et Transplantation Hépatique, Hôpital Archet 2, Pôle Digestif, CHU Nice, Université de Nice Sophia-Antipolis, Nice, France. (2)INSERM, U1065, Team 8 "Hepatic complications in obesity", C3M, Nice, France. (3)Service d'Hépato-Gastroentérologie et de Cancérologie Digestive, Hôpital Archet 2, Pôle Digestif, CHU de Nice, Université de Nice Sophia-Antipolis, Nice, France. (4)Service d'Hépato-Gastroentérologie et de Cancérologie Digestive, Hôpital	Increased Prevalence of Irritable Bowel Syndrome in a Cohort of French Morbidly Obese Patients Candidate for Bariatric Surgery.	340. Obes Surg. 2016 Jul;26(7):1525-30.	BACKGROUND: Only a few recent reports have suggested a correlation between obesity and irritable bowel syndrome (IBS). We aimed to determine the prevalence and severity of IBS in a prospective cohort of obese patients undergoing bariatric surgery in Nice Hospital (France). METHODS: One hundred obese patients were included prospectively before bariatric surgery. A diagnosis of IBS and each subtype was performed according to Rome-III criteria using a Bristol scale for stool consistency. Patients provided information on IBS-related comorbidities, including chronic fatigue, migraine, lower back pain, gastroesophageal reflux disease (GERD), genitourinary problems, and dyspepsia. Patients completed questionnaires to assess the severity of IBS, GERD, psychological factors (anxiety, depression), fatigue, and quality of life. RESULTS: Thirty patients fulfilled the Rome-III criteria for IBS. There was no difference in age, gender, or BMI between obese patients with or without IBS. Obese patients with IBS reported a significantly higher prevalence of GERD, migraines, lower back pain, genitourinary problems, chronic fatigue, and dyspepsia. Obese patients with IBS had significant higher scores of fatigue, anxiety, depression, and poorer quality of life. Obese patients that had both IBS and GERD had significantly higher IBS severity scores than those without GERD. In a logistic regression model including BMI, anxiety, depression, gender, and GERD score, only anxiety was significantly and independently associated with IBS. CONCLUSIONS: Thirty percent of obese patients had IBS: its severity was not correlated with BMI. However, anxiety was independently associated with IBS, suggesting that psychological factors are key features of IBS, whatever the presence of obesity.

	Archet 2, Pôle Digestif, CHU de Nice, Université de Nice Sophia-Antipolis, Nice, France. piche.t@chu-nice.fr. (5)Service d'Immunologie, Pôle Biologie, EA 6302 Tolérance Immunitaire, Hôpital Archet 1 Université de Nice Sophia-Antipolis, Nice, France. piche.t@chu-nice.fr.			
Schrepf A(1), O'Donnell MA(2), Luo Y(3), Bradley CS(4), Kreder KJ(3), Lutgendorf SK(5).	(1)Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, MI. (2)Department of Obstetrics and Gynecology, University of Iowa, Iowa City, IA. (3)Department of Urology, University of Iowa, Iowa City, IA. (4)Department of Obstetrics and Gynecology, University of Iowa, Iowa City, IA; Department of Urology, University of Iowa, Iowa City, IA. (5)Department of Obstetrics and Gynecology, University of Iowa, Iowa City, IA; Department of	Inflammation and Symptom Change in Interstitial Cystitis or Bladder Pain Syndrome: A Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network Study.	310. Urology. 2016 Apr;90:56-61.	OBJECTIVE: To explore inflammatory factors that influence symptom changes in interstitial cystitis or bladder pain syndrome (IC or BPS). This longitudinal, prospective study examined the association of inflammation elicited by Toll-like receptor (TLR) stimulation in peripheral blood mononuclear cells (PBMCs) and diurnal cortisol rhythms with changes in painful and urinary symptoms of IC or BPS and symptom flares over a 48-week period. MATERIALS AND METHODS: Participants were 24 women meeting criteria for IC or BPS who supplied blood for isolation of PBMCs and 3 days of salivary cortisol samples prior to a baseline visit. Participants completed the Genitourinary Pain Index (pain and urinary subscales) and reported symptom flares every 2 weeks for 48 weeks. Mixed effects longitudinal and regression models were used to determine if inflammatory variables were associated with the changes in IC or BPS symptoms (time × variable interactions), and the probability of a symptom flare. RESULTS: Elevated TLR-4 inflammation (P = .031) and elevated TLR-2 inflammation (P = .045) from PBMCs, and flattened diurnal cortisol slope (P = .012) were each associated with less improvement in genitourinary pain over time. Additionally, elevated TLR-4 inflammation was associated with less improvement in urinary symptoms (P = .018), whereas TLR-2 inflammation and cortisol slopes were not (both P > .16). In contrast, no inflammatory measure was associated with an increased likelihood of reporting a symptom flare (all P > .25). CONCLUSION: TLR-mediated inflammation and diurnal cortisol slope may be useful as markers of symptom changes in IC or BPS.

	Urology, University of Iowa, Iowa City, IA; Department of Psychological and Brain Science, University of Iowa, Iowa City, IA. Electronic address: Susan-lutgendorf@uiowa.edu.			
Sen MS(1), Sahoo S(2), Aggarwal S(3), Singh SM(4).	(1)Associate Professor, Department of Psychiatry, Post graduate Institute of Medical Education and Research, Chandigarh, 160012, India. Electronic address: mahadevsinghsen@gmail.com. (2)Associate Professor, Department of Psychiatry, Post graduate Institute of Medical Education and Research, Chandigarh, 160012, India. Electronic address: swapnajit.same@gmail.com. (3)Associate Professor, Department of Psychiatry, Post graduate Institute of Medical Education and Research,	Systemic exercise intolerance disease: What's in a name?	119. Asian J Psychiatr. 2016 Aug;22:157-8.	The syndrome characterized primarily by chronic, disabling fatigue without adequate explanation has been of interest to patients, clinicians and researchers. Chronic fatigue syndrome (CFS) is a widely used term for this condition in scientific and lay literature but is not acceptable to many patients because of perceived stigma due to implied psychological causation. CFS has recently been replaced by systemic exercise intolerance disease (SEID) by the Institute of medicine with the objectives of providing and disseminating evidence-based criteria and to provide a more acceptable name for this condition. Simultaneously, changes have taken place in DSM-5 with regards to this condition. Mental health professionals need to be aware of this change in the interests of patient care. The need to replace CFS with SEID and the nosological changes also indicate an inability to do away with the Descartian mind-body dualism despite efforts to the contrary and a need to debate the failure of the bio-psycho-social model to 'mainstream' and destigmatize psychiatry.

	Chandigarh, 160012, India. Electronic address: shivaliaggarwal88@gmail.com. (4)Associate Professor, Department of Psychiatry, Post graduate Institute of Medical Education and Research, Chandigarh, 160012, India. Electronic address: shubhmohan@gmail.com.			
Shan ZY(1), Kwiatek R(2), Burnet R(3), Del Fante P(4), Staines DR(5), Marshall-Gradisnik SM(5), Barnden LR(5).	(1)National Centre for Neuroimmunology and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, Australia. z.shan@griffith.edu.au. (2)Division of Medical Subspecialities, Lyell McEwin Hospital, Elizabeth Vale, SA, Australia. (3)Endocrinology department, Royal Adelaide Hospital, Adelaide, Australia. (4)Healthfirst Network, Woodville, Australia. (5)National Centre for Neuroimmunology	Progressive brain changes in patients with chronic fatigue syndrome: A longitudinal MRI study.	210. J Magn Reson Imaging. 2016 Nov;44(5):1301-1311.	PURPOSE: To examine progressive brain changes associated with chronic fatigue syndrome (CFS). MATERIALS AND METHODS: We investigated progressive brain changes with longitudinal MRI in 15 CFS and 10 normal controls (NCs) scanned twice 6 years apart on the same 1.5 Tesla (T) scanner. MR images yielded gray matter (GM) volumes, white matter (WM) volumes, and T1- and T2-weighted signal intensities (T1w and T2w). Each participant was characterized with Bell disability scores, and somatic and neurological symptom scores. We tested for differences in longitudinal changes between CFS and NC groups, inter group differences between pooled CFS and pooled NC populations, and correlations between MRI and symptom scores using voxel based morphometry. The analysis methodologies were first optimized using simulated atrophy. RESULTS: We found a significant decrease in WM volumes in the left inferior fronto-occipital fasciculus (IFOF) in CFS while in NCs it was unchanged (family wise error adjusted cluster level P value, PFWE < 0.05). This longitudinal finding was consolidated by the group comparisons which detected significantly decreased regional WM volumes in adjacent regions (PFWE < 0.05) and decreased GM and blood volumes in contralateral regions (PFWE < 0.05). Moreover, the regional GM and WM volumes and T2w in those areas showed significant correlations with CFS symptom scores (PFWE < 0.05). CONCLUSION: The results suggested that CFS is associated with IFOF WM deficits which continue to deteriorate at an abnormal rate. J. Magn. Reson. Imaging 2016;44:1301-1311.

	and Emerging Diseases, Menzies Health Institute Queensland, Griffith University, Southport, Australia.			
Shephard RJ(1).	(1)Faculty of Kinesiology and Physical Education, University of Toronto, Toronto, Ontario.	Exercise and the Athlete With Infectious Mononucleosis.	153. Clin J Sport Med. 2016 Jun 22.	OBJECTIVE: To determine appropriate management of the active individual with infectious mononucleosis (IM), including issues of diagnosis, the determination of splenomegaly, and other measures of disease status, the relationship of the disease to chronic fatigue syndrome (CFS), and the risks of exercise at various points in the disease process. DATA SOURCES: An Ovid/MEDLINE search (January 1996-June 2015) was widely supplemented by "similar articles" found in Ovid/MEDLINE and PubMed, reference lists, and personal files. MAIN RESULTS: Clinical diagnoses of IM are unreliable. Traditional laboratory indicators (lymphocytosis, abnormal lymphocytes, and a heterophile-positive slide test) can be supplemented by more sensitive and more specific but also more costly Epstein-Barr antigen determinations. Clinical estimates of splenomegaly are fallible. Laboratory determinations, commonly by 2D ultrasonography, must take account of methodology, the formulae used in calculations and the individual's body size. The SD of normal values matches the typical increase of size in IM, but repeat measurements can help to monitor regression of the disease. The main risks to the athlete are spontaneous splenic rupture (seen in 0.1%-0.5% of patients and signaled by acute abdominal pain) and progression to chronic fatigue, best avoided by 3 to 4 weeks of restricted activity followed by graded reconditioning. A full recovery of athletic performance is usual with 2 to 3 months of conservative management. CONCLUSIONS: Infectious mononucleosis is a common issue for young athletes. But given accurate diagnosis and the avoidance of splenic rupture and progression to CFS through a few weeks of restricted activity, long-term risks to the health of athletes are few.
Shrivastava K(1), Naidu G(2), Gupta M(1), Singh N(1).	(1)Senior Lecturer, Department of Oral Medicine and Radiology, Rishiraj College of Dental Sciences & Research Centre , Bhopal, Madhya Pradesh, India . (2)Reader, Oral Medicine and Radiology, Peoples Dental Academy ,	Fibrofascitis - An Enigma for the Dentist: A Case Report.	191. J Clin Diagn Res. 2016 Apr;10(4):ZD04-5.	Fibromyalgia is a chronic syndrome that causes widespread musculoskeletal pain and stiffness throughout the connective tissues that support and move the bones and joints. Pain and localized tender points occur in the muscles, particularly those that support the neck, spine, shoulders, and hips. Moreover the disorder includes fatigue, depression, sleep disturbances and constipation. A combination of treatments including medications, patient education, physical therapy and counseling are usually recommended. Here, we present a case report of fibromyalgia and the treatment given to the patient, a combination of dental and orthopedic treatment.

	Bhopal, Madhya Pradesh, India .			
Shu Q(1,)(2), Wang H(1,)(2), Litscher D(3), Wu S(1,)(2), Chen L(1,)(2), Gaischek I(3), Wang L(3), He W(1,)(2), Zhou H(1,)(2), Litscher G(1,)(2,)(3), Liang F(1,)(2).	(1)Acupuncture &Moxibustion Institute, Hubei University of Chinese Medicine, Wuhan (430061), China. (2)Hubei Provincial Collaborative Innovation Center of Preventive Treatment by Acupuncture &Moxibustion, Wuhan (430061), China. (3)TCM Research Center Graz, Research Unit for Complementary and Integrative Laser Medicine, Research Unit of Biomedical Engineering in Anesthesia and Intensive Care Medicine, Medical University of Graz, Graz (8036), Austria.	Acupuncture and Moxibustion have Different Effects on Fatigue by Regulating the Autonomic Nervous System: A Pilot Controlled Clinical Trial.	29. Sci Rep. 2016 Nov 25;6:37846.	In order to investigate the different effects of acupuncture and moxibustion on chronic fatigue syndrome (CFS) and alterations in the autonomic nervous system by measuring heart rate variability (HRV). Forty-five participants were recruited and randomly divided into 3 groups using a randomization schedule. The control group (CG, n = 15) and the acupuncture group (AG, n = 15) were treated by manipulation acupuncture, and the moxibustion group (MG, n = 15) was treated by indirect moxibustion. Primary outcomes were the scores of the Fatigue Assessment Instrument (FAI). Secondary outcomes were the HRV parameters which can reflect activity of the autonomic nervous system. This trial considered both instantaneous changes and long-term effectiveness. FAI scores decreased after the 4th and 10th treatments in the 3 groups. The decrease in FAI in the MG was greater than that in the AG. Acupuncture was more effective in instantaneous changes of HRV and moxibustion in long-term aspects. Both acupuncture and moxibustion improved fatigue in CFS patients, but moxibustion was more effective. The possible mechanism of the intervention may be through activation of the vagus nerve. Moxibustion was more effective than acupuncture in long-term treatment of CFS.
Sibelli A(1), Chalder T(2), Everitt H(3), Workman P(1), Windgassen S(4), Moss-Morris R(1).	(1)Health Psychology Section,Department of Psychology,Institute of Psychiatry, Psychology and Neuroscience,King's College London,5th Floor Bermondsey Wing,Guy's Hospital Campus,London Bridge,London SE1 9RT,UK.	A systematic review with meta-analysis of the role of anxiety and depression in irritable bowel syndrome onset.	58. Psychol Med. 2016 Nov;46(15):3065-3080. Epub 2016 Sep 8.	BACKGROUND: It is well established that people with irritable bowel syndrome (IBS) have higher levels of anxiety and depression compared with controls. However, the role of these as risk factors is less clearly established. The aims of this systematic review were to investigate: (1) whether anxiety and/or depression predict IBS onset; (2) the size of the relative risk (RR) of anxiety versus depression in IBS onset. Subgroup analyses explored if methodological factors affected the overall findings. METHOD: Prospective cohort or case-control studies were included if they: (1) focused on the development of IBS in population-based or gastroenteritis cohorts; (2) explored the effects of anxiety and/or depression at baseline as predictors of IBS onset at a future point. In all, 11 studies were included of which eight recruited participants with a gastrointestinal infection. Meta-analyses were conducted. RESULTS: The risk of developing IBS was double for anxiety cases at baseline compared with those who were

	(2)Department of Psychological Medicine,Institute of Psychiatry, Psychology and Neuroscience,King's College London,Weston Education Centre,Cutcombe Road,London SE5 9RJ,UK. (3)Primary Care and Population Sciences,Faculty of Medicine,University of Southampton,Aldermoor Health Centre,Aldermoor Close,Southampton SO16 5ST,UK. (4)Department of Psychological Medicine,Institute of Psychiatry, Psychology and Neuroscience,King's College London,Chronic Fatigue Research and Treatment Unit,Mapother House,De Crespigny Park,Denmark Hill,London SE5 8AZ,UK.			not [RR 2.38, 95% confidence interval (CI) 1.58-3.60]. Similar results were found for depression (RR 2.06, 95% CI 1.44-2.96). Anxiety and depression seemed to play a stronger role in IBS onset in individuals with a gastrointestinal infection although this could be attributed to other differences in methodology, such as use of diagnostic interviews rather than self-report. CONCLUSIONS: The findings suggest that self-reported anxiety and depression provide a twofold risk for IBS onset. There is less support for the role of anxiety or depressive disorder diagnosed using clinical interview. These findings may have implications for the development of interventions focused on IBS prevention and treatment.
Singh S(1), Stafford P(2), Schlauch KA(3,)(4), Tillett RR(4), Gollery	(1)Nevada Center for Biomedical Research, 1664 N Virginia St. MS 0552, Reno, NV, 89557-0552, USA.	Humoral Immunity Profiling of Subjects with Myalgic Encephalomyelitis Using a Random Peptide Microarray Differentiates	13. Mol Neurobiol. 2016 Dec 15.	Myalgic encephalomyelitis (ME) is a complex, heterogeneous illness of unknown etiology. The search for biomarkers that can delineate cases from controls is one of the most active areas of ME research; however, little progress has been made in achieving this goal. In contrast to identifying biomarkers that are directly involved in the pathological process, an immunosignature identifies antibodies raised to proteins

M(5), Johnston SA(2), Khaiboullina SF(1,)(6), De Meirleir KL(1), Rawat S(1), Mijatovic T(7), Subramanian K(1), Palotás A(8,)(9), Lombardi VC(10,)(11).	(2)The Biodesign Institute Center for Innovations in Medicine at Arizona State University, Tempe, AZ, USA. (3)Department of Biochemistry and Molecular Biology, University of Nevada, Reno, NV, USA. (4)Nevada INBRE Bioinformatics Core, University of Nevada, Reno, NV, USA. (5)Tahoe Bioinformatics, Incline Village, Reno, NV, USA. (6)Kazan Federal University, Kazan, Russian Federation. (7)R.E.D. Laboratories, Zellik, Belgium. (8)Kazan Federal University, Kazan, Russian Federation. palotas@asklepios-med.eu. (9)Asklepios-Med (private medical practice and research center), Kossuth Lajos sgt. 23, Szeged, 6722, Hungary. palotas@asklepios-med.eu. (10)Nevada Center for Biomedical Research, 1664 N Virginia St. MS 0552, Reno, NV, 89557-0552, USA.	Cases from Controls with High Specificity and Sensitivity.		expressed during, and potentially involved in, the pathological process. Although these proteins might be unknown, it is possible to detect antibodies that react to these proteins using random peptide arrays. In the present study, we probe a custom 125,000 random 12-mer peptide microarray with sera from 21 ME cases and 21 controls from the USA and Europe and used these data to develop a diagnostic signature. We further used these peptide sequences to potentially uncover the naturally occurring candidate antigens to which these antibodies may specifically react with in vivo. Our analysis revealed a subset of 25 peptides that distinguished cases and controls with high specificity and sensitivity. Additionally, Basic Local Alignment Search Tool (BLAST) searches suggest that these peptides primarily represent human self-antigens and endogenous retroviral sequences and, to a minor extent, viral and bacterial pathogens.

	vclombardi@nvcbr.org. (11)Department of Pharmacology, University of Nevada, Reno, School of Medicine, Reno, NV, USA. vclombardi@nvcbr.org.			
Singh Sen M(1), Sahoo S(2), Aggarwal S(3), Singh SM(4).	(1)Department of Psychiatry, Post Graduate Institute of Medical Education & Research, Chandigarh, India. Electronic address: mahadevsinghsen@gmail.com.	Reply to: Myalgic Encephalomyelitis, chronic fatigue syndrome or systemic exercise intolerance disease: What's in a name?	19. Asian J Psychiatr. 2016 Dec;24:69-70.	
Sivak S, Nosal V, Bittsansky M, Dluha J, Dobrota D, Kurca E.		Type and occurrence of serious complications in patients after mild traumatic brain injury.	302. Bratisl Lek Listy. 2016;117(1):22-5.	Traumatic brain injury (TBI) remains a major public health and socio-economic problem, and 70-90% of all TBIs are classified as mild. Mild TBIs and concussions are mostly considered to be non-serious conditions with symptoms subsiding within a few days or weeks. However in 10-15% of patients, the symptoms persist one year after concussion and mostly include headache, fatigue, irritability, and cognitive problems (e.g. memory, concentration). These persisting symptoms negatively influence patient daily activities as postconcussion syndrome (PCS). Second-impact syndrome (SIS) is a very rare but usually fatal condition and occurs when repeated brain injuries lead to a catastrophic diffuse brain swelling. There is no scientific evidence on the incidence and risk of SIS. Chronic traumatic encephalopathy (CTE) is a progressive degenerative disease of the brain found in patients with a history of repetitive brain trauma. CTE presents with behavioural, cognitive, and motor symptoms. The literature to date lacks prospective epidemiological studies of the incidence of CTE. In recent medical literature, there is a description of 110 athletes with postmortem diagnosis of CTE (Tab. 1, Ref. 37).
Slyepchenko A(1), Maes M, Jacka FN, Köhler CA, Barichello T, McIntyre RS, Berk M, Grande I, Foster JA, Vieta E, Carvalho AF.	(1)McMaster Integrative Neuroscience Discovery and Study (MiNDS), McMaster University, Hamilton, Ont., Canada.	Gut Microbiota, Bacterial Translocation, and Interactions with Diet: Pathophysiological Links between Major Depressive Disorder and Non-Communicable Medical Comorbidities.	31. Psychother Psychosom. 2017;86(1):31-46. Epub 2016 Nov 25.	BACKGROUND: Persistent low-grade immune-inflammatory processes, oxidative and nitrosative stress (O&NS), and hypothalamic-pituitary-adrenal axis activation are integral to the pathophysiology of major depressive disorder (MDD). The microbiome, intestinal compositional changes, and resultant bacterial translocation add a new element to the bidirectional interactions of the gut-brain axis; new evidence implicates these pathways in the patho-aetiology of MDD. In addition, abnormalities in the gut-brain axis are associated with several chronic non-communicable disorders, which frequently co-occur in individuals with MDD, including but not limited to irritable bowel

				syndrome (IBS), chronic fatigue syndrome (CFS), obesity, and type 2 diabetes mellitus (T2DM). METHODS: We searched the PubMed/MEDLINE database up until May 1, 2016 for studies which investigated intestinal dysbiosis and bacterial translocation (the 'leaky gut') in the pathophysiology of MDD and co-occurring somatic comorbidities with an emphasis on IBS, CFS, obesity, and T2DM. RESULTS: The composition of the gut microbiota is influenced by several genetic and environmental factors (e.g. diet). Several lines of evidence indicate that gut-microbiota-diet interactions play a significant pathophysiological role in MDD and related medical comorbidities. Gut dysbiosis and the leaky gut may influence several pathways implicated in the biology of MDD, including but not limited to immune activation, O&NS, and neuroplasticity cascades. However, methodological inconsistencies and limitations limit comparisons across studies. CONCLUSIONS: Intestinal dysbiosis and the leaky gut may constitute a key pathophysiological link between MDD and its medical comorbidities. This emerging literature opens relevant preventative and therapeutic perspectives.
Speer LM(1), Mushkbar S(1), Erbele T(1).	(1)University of Toledo College of Medicine and Life Sciences, Toledo, OH, USA.	Chronic Pelvic Pain in Women.	261. Am Fam Physician. 2016 Mar 1;93(5):380-7.	Chronic pelvic pain in women is defined as persistent, noncyclic pain perceived to be in structures related to the pelvis and lasting more than six months. Often no specific etiology can be identified, and it can be conceptualized as a chronic regional pain syndrome or functional somatic pain syndrome. It is typically associated with other functional somatic pain syndromes (e.g., irritable bowel syndrome, nonspecific chronic fatigue syndrome) and mental health disorders (e.g., posttraumatic stress disorder, depression). Diagnosis is based on findings from the history and physical examination. Pelvic ultrasonography is indicated to rule out anatomic abnormalities. Referral for diagnostic evaluation of endometriosis by laparoscopy is usually indicated in severe cases. Curative treatment is elusive, and evidence-based therapies are limited. Patient engagement in a biopsychosocial approach is recommended, with treatment of any identifiable disease process such as endometriosis, interstitial cystitis/painful bladder syndrome, and comorbid depression. Potentially beneficial medications include depot medroxyprogesterone, gabapentin, nonsteroidal anti-inflammatory drugs, and gonadotropin-releasing hormone agonists with add-back hormone therapy. Pelvic floor physical therapy may be helpful. Behavioral therapy is an integral part of treatment. In select cases, neuromodulation of sacral nerves may be appropriate. Hysterectomy may be considered as a last resort if pain seems to be of uterine origin, although significant improvement occurs in only about one-half of cases. Chronic pelvic pain should be managed with a collaborative, patient-centered approach.
Stadje R(1), Dornieden K(2), Baum E(2), Becker A(2), Biroga T(2), Bösner S(2),	(1)Department of General Practice/Family Medicine, University of Marburg, Karl-von-Frisch-Str. 4, 35043,	The differential diagnosis of tiredness: a systematic review.	67. BMC Fam Pract. 2016 Oct 20;17(1):147.	BACKGROUND: Tiredness is one of the most frequent complaints in primary care. Although often self-limiting and frequently associated with psychosocial stress, patients but also their physicians are often uncertain regarding a serious cause and appropriate diagnostic work-up. We conducted a systematic review and meta-analysis of studies reporting on differential diagnosis of fatigue in primary care. METHODS: MEDLINE, EMBASE and conference abstracts were searched for primary care based studies of

Haasenritter J(2), Keunecke C(2), Viniol A(2), Donner-Banzhoff N(2).	Marburg, Germany. Rebekka.Stadje@t-online.de. (2)Department of General Practice/Family Medicine, University of Marburg, Karl-von-Frisch-Str. 4, 35043, Marburg, Germany.			patients presenting with tiredness. Twenty-six studies were included. We report on anaemia, malignancy, serious organic disease, depression and the chronic fatigue syndrome (CFS) as causes of tiredness as presenting complaint. RESULTS: We found considerable heterogeneity of estimates which was reduced by limiting our analysis to high quality studies. Prevalences were as follows-anaemia: 2.8 % (CI (confidence interval) 1.6-4.8 %); malignancy: 0.6 % (CI 0.3-1.3 %); serious somatic disease: 4.3 % (CI 2.7-6.7 %); depression 18.5 % (CI 16.2-21.0 %). Pooling was not appropriate for CFS. In studies with control groups of patients without the symptom of tiredness, prevalence of somatic disease was identical to those complaining of tiredness. Depression, however, was more frequent among those with tiredness. CONCLUSIONS: Serious somatic disease is rare in patients complaining of tiredness. Since prevalence is similar in patients without tiredness, the association may not be causal. Extensive investigations are only warranted in case of specific findings from the history or clinical examination. Instead, attention should focus on depression and psychosocial problems.
Sukocheva OA(1,)(2), Manavis J(3), Kok TW(4), Turra M(5), Izzo A(6), Blumbergs P(3), Marmion BP(1,)(5).	(1)Q Fever Research Group (1993-2009), Hanson Institute, Adelaide, South Australia. (2)School of Health Sciences, Flinders University, Bedford Park, South Australia. (3)Centre for Neurological Diseases, SA Pathology, Adelaide, South Australia. (4)School of Biological Sciences, University of Adelaide, Adelaide, South Australia. tuckweng.kok@adelaide.edu.au. (5)Microbiology and Infectious Diseases Laboratory, SA Pathology, Adelaide, South Australia. (6)Colorado State University, Colorado,	Coxiella burnetii dormancy in a fatal ten-year multisystem dysfunctional illness: case report	220. BMC Infect Dis. 2016 Apr 18;16:165. .	BACKGROUND: In a previous study of a Q fever outbreak in Birmingham, our group identified a non-infective complex of Coxiella burnetii (C.b.) antigens able to survive in the host and provoked aberrant humoral and cell-mediated immunity responses. The study led to recognition of a possible pathogenic link between C.b. infection and subsequent long-term post Q fever fatigue syndrome (QFS). This report presents an unusually severe case of C.b. antigen and DNA detection in post-mortem specimens from a patient with QFS. CASE PRESENTATION: We report a 19-year old female patient who became ill with an acute unexplained febrile encephalitis-like illness, followed by increasingly severe multisystem dysfunction and death 10 years later. During life, extensive clinical and laboratory investigations from different disciplinary stand points failed to deliver a definitive identification of a cause. Given the history of susceptibility to infection from birth, acute fever and the diagnosis of "post viral syndrome", tests for infective agents were done starting with C.b. and Legionella pneumophila. The patient had previously visited farms a number of times. Comprehensive neuropathological assessment at the time of autopsy had not revealed gross or microscopic abnormalities. The aim was to extend detailed studies with the post-mortem samples and identify possible factors driving severe disturbance of homeostasis and organ dysfunction exhibited by the course of the patient's ten-year illness. Immunohistochemistry for C.b. antigen and PCR for DNA were tested on paraffin embedded blocks of autopsy tissues from brain, spleen, liver, lymph nodes (LN), bone marrow (BM), heart and lung. Standard H&E staining of brain sections was unrevealing. Immuno-staining analysis for astrocyte cytoskeleton proteins using glial fibrillary acidic protein (GFAP) antibodies showed a reactive morphology. Coxiella antigens were demonstrated in GFAP immuno-positive grey and white matter astrocytes, spleen, liver, heart, BM and LN. PCR analysis (COM1/IS1111 genes) confirmed the presence of C.b. DNA in heart, lung, spleen, liver & LN, but not in brain or BM. CONCLUSION: The study revealed the persistence of C. b.

	USA.			cell components in various organs, including astrocytes of the brain, in a post-infection QFS. The possible mechanisms and molecular adaptations for this alternative C.b. life style are discussed.
Sun Y(1), Zhang ZX(2), Liu X(1).	(1)Department of Pharmacology, School of Pharmacy, Second Military Medical University, Shanghai, China. (2)Department of Chinese Medicine, Yueyang Hospital, Shanghai, China.	Orosomucoid (ORM) as a Potential Biomarker for the Diagnosis of Chronic Fatigue Syndrome (CFS).	295. CNS Neurosci Ther. 2016 Mar;22(3):251-2.	
Sutar R(1), Yadav S(1), Desai G(1).	(1)a Department of Psychiatry , National Institute of Mental Health and Neurosciences , Bangalore , India.	Yoga intervention and functional pain syndromes: a selective review.	166. Int Rev Psychiatry. 2016 Jun;28(3):316-22.	The definition of functional pain syndromes is varied across literature. No effort has been made to see all functional pain disorder groups under broad nomenclature which would exclude conditions for which pathophysiology is strongly known. Since these disorders are commonly treated with alternative treatment modalities and impose significant burden on health utilization, an effort to look into studies on yoga-based interventions on 'functional pain syndromes' (FPS) was made. This study defined FPS as 'Chronic relapsing remitting pain conditions, the origin of which is difficult to trace with no definite physical pathology on clinical suspicion or available laboratory measures and are valid based on subjective pain reporting, associated distress and socio-occupational dysfunction'. Chronic headache, neck pain, back pain, fibromyalgia, pelvic pain, Irritable Bowel Syndrome, Chronic Fatigue Syndrome, and somatoform pain disorders were included for this review. The review found four meta-analyses on the selected topic both indicating modest efficacy and benefit of yoga in these disorders. Future efforts should be directed to do a large meta-analysis of functional pain syndromes.
Taw LB, Henry E.		Acupuncture and Trigger Point Injections for Fibromyalgia: East-West Medicine Case Report.	309. Altern Ther Health Med. 2016 Jan-Feb;22(1):58-61.	Fibromyalgia is a clinical syndrome characterized by chronic widespread pain that is often accompanied by ≥1 concomitant symptoms (eg, fatigue, poor sleep, cognitive alterations, and mood disturbances). In 2005, an estimated 5 million people in the United States suffered from fibromyalgia, and its growing effect on health-related quality of life is substantial. An increasingly popular hypothesis proposes that noxious, peripheral sensory input might contribute to the initiation and perpetuation of the diffuse pain seen in patients with fibromyalgia. That theory has led to the evaluation of multiple interventions to stimulate distal areas as a means to modulate the peripheral and central nervous systems. It has been the authors' experiences that the combination of trigger point injections and acupuncture provides improved clinical outcomes. In the current article, the authors present a case report of a patient with fibromyalgia who was successfully treated with an integrative approach that combined acupuncture with trigger point injections.

Taylor AK(1), Loades M(2), Brigden AL(1), Collin SM(1), Crawley E(3).	(1)Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, UK. (2)Department of Psychology, University of Bath, UK. (3)Centre for Child and Adolescent Health, School of Social and Community Medicine, University of Bristol, UK Esther.crawley@bristol.ac.uk.	'It's personal to me': A qualitative study of depression in young people with CFS/ME.	70. Clin Child Psychol Psychiatry. 2016 Oct 14. pii: 1359104516672507.	BACKGROUND: Paediatric chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) has a prevalence of 0.4-2.4% and is defined as 'generalised disabling fatigue persisting after routine tests and investigations have failed to identify an obvious underlying cause'. One-third of young people with CFS/ME have probable depression. Little is known about why depression develops, the relationship between depression and CFS/ME, or what treatment might be helpful. METHODS: We conducted nine semi-structured interviews with young people with CFS/ME (aged 13-17 years, 8/9 female) and probable depression, covering perceived causes of depression, the relationship between CFS/ME and depression, and treatment strategies. RESULTS: Most thought CFS/ME caused depression. Many discussed a cyclical relationship: low mood made CFS/ME worse. A sense of loss was common. CFS/ME restricted activities participants valued and changed systemic structures, causing depression. There was no single helpful treatment approach. Individualised approaches using combinations of cognitive behavioural therapy (CBT), medication, activity management and other strategies were described. CONCLUSION: This study suggests that depression may be secondary to CFS/ME in young people because of the impact of CFS/ME on quality of life. Clinicians treating young people with CFS/ME need to consider strategies to prevent development of depression, and research is needed into approaches that are effective in treating CFS/ME with co-morbid depression.
Thomas LV(1), Jenkins G(2), Belton J(3), Clements S(4), Jacob C(5), Johnson N(6), Joy D(7), Low J(8), Munson E(9), Sheppard J(10).	(1)Science Director, Yakult UK Limited, South Ruislip, UK. (2)GP, Whiteladies Health Centre, Bristol, UK. (3)Operational & Strategic Director, Cuckoo Lane Surgery, Hanwell, UK. (4)Education Lead & Associate Trainer, Hertfordshire Community NHS Trust, Welwyn Garden City, UK. (5)Practice Nurse in Centric Health and vice-Chair Irish Practice Nurse Association, Newbridge, Republic of Ireland. (6)Assistant	Nutritional advice for community patients: insights from a panel discussion.	259. Br J Community Nurs. 2016 Mar;21(3):130-7.	This article describes the conclusions of an expert panel that discussed four case studies; these were examples of patients typically encountered by nurses working in the community. The panel considered the nutritional and lifestyle advice that could be given by nurses relating to conditions such as irritable bowel syndrome (IBS), depression, chronic fatigue syndrome, vulnerability to common infections, elderly care, recurrent urinary tract infection, antibiotic use, and risk of type 2 diabetes. A general conclusion was the importance of motivational interviewing techniques in achieving full understanding of patients' concerns and to determine the best health strategy. As well as specific guidance appropriate for each disorder, a range of information sources for both health professionals and patients are listed in the paper. The panel noted that, although general nutritional advice can be given by nurses working at GP surgeries and in the community, patients should always be referred to registered dietitians or nutritionists if significant dietary changes are considered.

	Science Manager, Yakult UK Limited, South Ruislip, UK. (7)Senior Science Officer, Yakult Ireland, Dublin, Republic of Ireland. (8)Consultant Registered Dietitian, JL Nutrition Clinic, Sevenoaks, Kent, UK. (9)Senior Lecturer, University of South Wales, Pontypridd, Wales, UK. (10)Science Officer, Yakult UK Limited, South Ruislip, UK.			
Thorkelson G(1), Bielefeldt K, Szigethy E.	(1)*Department of Psychiatry, University of Pittsburgh, Pittsburgh, Pennsylvania; and †Division of Gastroenterology, University of Pittsburgh, Pittsburgh, Pennsylvania.	Empirically Supported Use of Psychiatric Medications in Adolescents and Adults with IBD	197. Inflamm Bowel Dis. 2016 Jun;22(6):1509-22. .	BACKGROUND: The use of psychotropic medications, particularly antidepressants, is common in patients with inflammatory bowel disease (IBD) in spite of a lack of their robust efficacy in this population. This review provides an overview of the use trends of different classes of antidepressant and anti-anxiety medication and their effects on mood, nervous system function, gastrointestinal physiology and immunity drawing from the literature available in the general population, other medical conditions, and when available, patients with IBD. It also covers the evidence base for the actions, efficacy, and potential complications of antidepressants organized by different classes. METHODS: We conducted a PubMed search of articles relating the different drug classes probed to the terms above in different populations of interest. All types of articles were accepted including case reports and series, open and randomized trials, reviews, and expert opinion. We also examined the reference lists of the publications found. RESULTS: Selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) are the most commonly prescribed agents for anxiety and depression in patients with IBD, though their efficacy for these conditions in the general population are mild to moderate at best. SSRIs are generally well tolerated, though at higher doses, they, like most antidepressant classes, can be associated with activation, serotonergic syndrome, and increased suicidal ideation. TCAs have many more serious side effects but have some shown efficacy for functional GI symptoms. A newer class, the serotonin noradrenergic reuptake inhibitors (SNRIs), can be effective for refractory depression, anxiety and chronic pain syndromes with a side effect profile similar to both SSRIs and more mild manifestations of TCAs. Mirtazapine has moderate efficacy for depression if sedation and weight gain side effects are tolerated and some small

				support for use in nausea and vomiting. Bupropion targets dopamine and noradrenaline reuptake and has moderate efficacy for depression, and some small support for use in fatigue and smoking cessation. Buspirone has an indication for generalized anxiety disorder though studies show only a minimal benefit. It has some growing evidence for use in functional dyspepsia. Most of these agents have physiological effects on the brain, immune system, and gastrointestinal tract (with the exception of bupropion) hence their therapeutic and side effects manifested in these systems. CONCLUSION: Antidepressant medications are frequently prescribed for depression, anxiety disorders, and chronic pain syndromes, but overall support for their efficacy is modest at best. Psychological interventions have growing support for having much more robust effects without the side effects of antidepressants and should be considered first-line treatment or at least an adjunct to psychotropic medications for these conditions.
Tobback E(1,)(2), Hanoulle I(1), Mariman A(1,)(2), Delesie L(1,)(2), Pevernagie D(3,)(4), Vogelaers D(1,)(2,)(4).	(1)a Department of General Internal Medicine , University Hospital Ghent , Ghent , Belgium. (2)b Department of General Internal Medicine, Centre for Neurophysiologic Monitoring , University Hospital Ghent , Ghent , Belgium. (3)c Sleep Medicine Centre, Kempenhaeghe Foundation , Heeze , The Netherlands. (4)d Faculty of Medicine and Health Sciences, Department of Internal Medicine , University of Ghent , Ghent , Belgium.	Factors determining fatigue in the chronic fatigue syndrome: a path analysis.	203. Acta Clin Belg. 2016 May 3:1-6.	OBJECTIVES: To explore the interrelationship of different dimensions (fatigue, neuroticism, sleep quality, global mental and physical health) in patients with chronic fatigue syndrome (CFS). METHODS: Patients meeting the Fukuda criteria of CFS filled out two independent fatigue scales (Fatigue Questionnaire, FQ and Checklist Individual Strength, CIS), NEO-Five Factor Inventory (NEO-FFI), Pittsburgh Sleep Quality Index (PSQI) and Medical Outcomes Study 36-item Short Form Health Survey (SF36). Exploratory and confirmatory path analyses were performed. RESULTS: Out of 226 eligible patients, 167 subjects were included (mean age 39.13 years, SD 10.14, 92% female). In a first exploratory path analysis, using FQ for assessment of fatigue, night-time PSQI sleep quality had a direct effect on SF36 physical quality of life (PQoL) and no effect on FQ fatigue. This was confirmed by a subsequent path analysis with CIS fatigue and by confirmatory path analyses in 81 patients. These unexpected results raised the question whether FQ or CIS fatigue sufficiently operationalizes fatigue in CFS patients. CONCLUSIONS: Poor sleep quality seems to directly impact on mental quality of life (MQoL) and PQoL without mediation of fatigue assessed with FQ and CIS. A more cohesive framework needs to be developed with more comprehensive clinical tools for the different dimensions in the construct of CFS.
Torrell H(1), Alonso Y(2), Garrabou G(3), Mulet D(2),	(1)Centre for Omic Sciences, Centre Tecnològic de Nutrició i Salut. Universitat	Mitochondrial dysfunction in a family with psychosis and chronic fatigue syndrome.	12. Mitochondrion. 2016 Oct 27. pii: S1567-7249(16)30221-5.	Mitochondrial impairment is hypothesized to be involved in chronic fatigue syndrome (CFS) and schizophrenia. We performed a clinical, genetic and functional mitochondrial study in a family consisting of a female presenting schizophrenia in addition to CFS symptoms and her mother and older sister, both presenting with CFS. The three family

Catalán M(3), Valiente-Pallejà A(2), Carreño-Gago L(4), García-Arumí E(4), Montaña E(1), Vilella E(1), Martorell L(5).	Rovira i Virgili. Reus, Catalonia, Spain. Electronic address: lourdes.martorell@urv.cat.			members showed higher blood lactate levels, higher mitochondrial mass, lower mtDNA content and overall lower mitochondrial enzymatic activities and lower oxygen consumption capacities than healthy women. This family presented mtDNA depletion; however, no mutation was identified neither in the mtDNA nor in the nuclear genes related with mtDNA depletion, even though C16179A and T16519A variants should be further studied.
Twisk F(1).	(1)Research, ME-de-patiënten Foundation, Limmen, 1906HB, Netherlands. Electronic address: frank.twisk@hetnet.nl.	PACE: CBT and GET are not rehabilitative therapies.	305. Lancet Psychiatry. 2016 Feb;3(2):e6.	Comment in Lancet Psychiatry. 2016 Feb;3(2):e8-9.
Twisk FN(1).	(1)ME-de-patiënten Foundation, Zonnedauw 15, 1906 HB Limmen, The Netherlands. Electronic address: frank.twisk@hetnet.nl.	Myalgic Encephalomyelitis, chronic fatigue syndrome or systemic exercise intolerance disease: What's in a name?	15. Asian J Psychiatr. 2016 Oct;23:70.	
Twisk FN(1).	(1)ME-de-patiënten Foundation, Zonnedauw 15, 1906 HB Limmen, The Netherlands. frank.twisk@hetnet.nl.	Replacing Myalgic Encephalomyelitis and Chronic Fatigue Syndrome with Systemic Exercise Intolerance Disease Is Not the Way forward.	282. Diagnostics (Basel). 2016 Feb 5;6(1). pii: E10.	Myalgic encephalomyelitis (ME), described in the medical literature since 1938, is characterized by distinctive muscular symptoms, neurological symptoms, and signs of circulatory impairment. The only mandatory feature of chronic fatigue syndrome (CFS), introduced in 1988 and redefined in 1994, is chronic fatigue, which should be accompanied by at least four or more out of eight "additional" symptoms. The use of the abstract, polythetic criteria of CFS, which define a heterogeneous patient population, and self-report has hampered both scientific progress and accurate diagnosis. To resolve the "diagnostic impasse" the Institute of Medicine proposes that a new clinical entity, systemic exercise intolerance disease (SEID), should replace the clinical entities ME and CFS. However, adopting SEID and its defining symptoms, does not resolve methodological and diagnostic issues. Firstly, a new diagnostic entity cannot replace two distinct, partially overlapping, clinical entities such as ME and CFS. Secondly, due to the nature of the diagnostic criteria, the employment of self-report, and the lack of criteria to exclude patients with other conditions, the SEID criteria seem to select an even more heterogeneous patient population, causing additional diagnostic confusion. This article discusses methodological and diagnostic issues related to SEID and proposes a methodological solution for the current "diagnostic impasse".

Ulvestad E.		[Re: Chronic fatigue syndrome/myalgic encephalo-myelitis--pathophysiology, diagnosis and treatment]. [Article in Norwegian]	300. Tidsskr Nor Laegeforen. 2016 Jan 26;136(2):105.	Comment on Tidsskr Nor Laegeforen. 2015 Oct 20;135(19):1756-9. Tidsskr Nor Laegeforen. 2015 Dec 15;135(23-24):2172-5.
Underhill RA.		Myalgic encephalomyelitis, chronic fatigue syndrome: An infectious disease.	330. Med Hypotheses. 2015 Dec;85(6):765-73. Epub 2016 Oct 19.	The etiology of myalgic encephalomyelitis also known as chronic fatigue syndrome or ME/CFS has not been established. Controversies exist over whether it is an organic disease or a psychological disorder and even the existence of ME/CFS as a disease entity is sometimes denied. Suggested causal hypotheses have included psychosomatic disorders, infectious agents, immune dysfunctions, autoimmunity, metabolic disturbances, toxins and inherited genetic factors. Clinical, immunological and epidemiological evidence supports the hypothesis that: ME/CFS is an infectious disease; the causal pathogen persists in patients; the pathogen can be transmitted by casual contact; host factors determine susceptibility to the illness; and there is a population of healthy carriers, who may be able to shed the pathogen. ME/CFS is endemic globally as sporadic cases and occasional cluster outbreaks (epidemics). Cluster outbreaks imply an infectious agent. An abrupt flu-like onset resembling an infectious illness occurs in outbreak patients and many sporadic patients. Immune responses in sporadic patients resemble immune responses in other infectious diseases. Contagion is shown by finding secondary cases in outbreaks, and suggested by a higher prevalence of ME/CFS in sporadic patients' genetically unrelated close contacts (spouses/partners) than the community. Abortive cases, sub-clinical cases, and carrier state individuals were found in outbreaks. The chronic phase of ME/CFS does not appear to be particularly infective. Some healthy patient-contacts show immune responses similar to patients' immune responses, suggesting exposure to the same antigen (a pathogen). The chronicity of symptoms and of immune system changes and the occurrence of secondary cases suggest persistence of a causal pathogen. Risk factors which predispose to developing ME/CFS are: a close family member with ME/CFS; inherited genetic factors; female gender; age; rest/activity; previous exposure to stress or toxins; various infectious diseases preceding the onset of ME/CFS; and occupational exposure of health care professionals. The hypothesis implies that ME/CFS patients should not donate blood or tissue and usual precautions should be taken when handling patients' blood and tissue. No known pathogen has been shown to cause ME/CFS. Confirmation of the hypothesis requires identification of a causal pathogen. Research should focus on a search for unknown and known pathogens. Finding a causal pathogen could assist with diagnosis; help find a biomarker; enable the development of anti-microbial treatments; suggest preventive measures; explain pathophysiological findings; and reassure patients about the validity of their symptoms.
Unger ER, Lin JS,		CDC Grand Rounds:	4. MMWR Morb Mortal	Chronic fatigue syndrome (CFS) is a complex and serious illness that is often

Brimmer DJ, Lapp CW, Komaroff AL, Nath A, Laird S, Iskander J.		Chronic Fatigue Syndrome - Advancing Research and Clinical Education.	Wkly Rep. 2016 Dec 30;65(5051):1434-1438.	misunderstood. Experts have noted that the terminology "chronic fatigue syndrome" can trivialize this illness and stigmatize persons who experience its symptoms (1). The name was coined by a group of clinicians convened by CDC in the late 1980s to develop a research case definition for the illness, which, at the time, was called chronic Epstein-Barr virus syndrome. The name CFS was suggested because of the characteristic persistent fatigue experienced by all those affected and the evidence that acute or reactivated Epstein-Barr virus infection was not associated with many cases (2). However, the fatigue in this illness is striking and quite distinct from the common fatigue everyone experiences. A variety of other names have been used, including myalgic encephalomyelitis (ME), ME/CFS, chronic fatigue immune dysfunction, and most recently, systemic exertion intolerance disease (3). The lack of agreement about nomenclature need not be an impediment for advancing critically needed research and education. The term ME/CFS will be used in this article.
Unger ER(1), Lin JM(1), Tian H(1), Gurbaxani BM(1), Boneva RS(1), Jones JF(1).	(1)Division of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infections, Centers for Disease Control and Prevention, 1600 Clifton Road, MS G41, Atlanta, GA 30329 USA.	Methods of applying the 1994 case definition of chronic fatigue syndrome - impact on classification and observed illness characteristics.	250. Popul Health Metr. 2016 Mar 12;14:5.	BACKGROUND: Multiple case definitions are in use to identify chronic fatigue syndrome (CFS). Even when using the same definition, methods used to apply definitional criteria may affect results. The Centers for Disease Control and Prevention (CDC) conducted two population-based studies estimating CFS prevalence using the 1994 case definition; one relied on direct questions for criteria of fatigue, functional impairment and symptoms (1997 Wichita; Method 1), and the other used subscale score thresholds of standardized questionnaires for criteria (2004 Georgia; Method 2). Compared to previous reports the 2004 CFS prevalence estimate was higher, raising questions about whether changes in the method of operationalizing affected this and illness characteristics. METHODS: The follow-up of the Georgia cohort allowed direct comparison of both methods of applying the 1994 case definition. Of 1961 participants (53 % of eligible) who completed the detailed telephone interview, 919 (47 %) were eligible for and 751 (81 %) underwent clinical evaluation including medical/psychiatric evaluations. Data from the 499 individuals with complete data and without exclusionary conditions was available for this analysis. RESULTS: A total of 86 participants were classified as CFS by one or both methods; 44 cases identified by both methods, 15 only identified by Method 1, and 27 only identified by Method 2 (Kappa 0.63; 95 % confidence interval [CI]: 0.53, 0.73 and concordance 91.59 %). The CFS group identified by both methods were more fatigued, had worse functioning, and more symptoms than those identified by only one method. Moderate to severe depression was noted in only one individual who was classified as CFS by both methods. When comparing the CFS groups identified by only one method, those only identified by Method 2 were either similar to or more severely affected in fatigue, function, and symptoms than those only identified by Method 1. CONCLUSIONS: The two methods demonstrated substantial concordance. While Method 2 classified more participants as CFS, there was no indication that they were less severely ill or more depressed. The classification differences do not fully explain the prevalence increase noted in the 2004

				Georgia study. Use of standardized instruments for the major CFS domains provides advantages for disease stratification and comparing CFS patients to other illnesses.
Vaillant J(1), Revillet P(2), Sevenier AM(3), Juvin R(3).	(1) Université de Grenoble Alpes, laboratoire AGEIS, Grenoble, France. Electronic address: JVaillant@chu-grenoble.fr. (2) CHU de Grenoble Alpes, école de kinésithérapie, Grenoble, France. (3)CHU de Grenoble Alpes, clinique de rhumatologie, Grenoble, France.	Impact of fatigue on postural control in quiet standing in fibromyalgia.	88. Ann Phys Rehabil Med. 2016 Sep;59S:e124-e125.	OBJECTIVE: Fibromyalgia fatigue was described as an overwhelming feeling of tiredness that is not relieved by sleep or rest and is often not in proportion to the effort realized. In fibromyalgia syndrome (FMS), the fatigue has an important functional impact, often limiting the activities of daily living, can induce a state of deconditioning, and causing disturbance of locomotion, whose reasons are not fully understood. The aims of this study was to evaluate the postural performance in quite standing of FMS patients, and to compare them to a control group, and to assess the influence on the posture of a fatigue induced by a short walk. MATERIAL/PATIENTS AND METHODS: Were included: 11 fibromyalgia patients in fibromyalgia groupe (FMG) and 12 healthy subjects appaired in control group (CG). Foot center of pressure (CP) displacements on a task-force platform under two conditions: eyes opened - i.e. vision and eyes closed - i.e. no-vision, before and after a six-minutes walk test (6MWT) were recorded. RESULTS: The results showed that subjects with fibromyalgia have a surface displacement of center of pressure more important than healthy subjects. Therefore, before 6MWT, in "No-vision" condition, CP displacement was 200.05±145.31mm(2) (m±SD) in CG vs 397.03±242.82mm(2) in FMG (P<0.05). In "Vision" condition CP displacement were respectively 139.08±61.78mm (2) vs 237.70±136.41mm(2) (P=0.06). The deterioration was more significant in FMG after the 6MWT, only in "No-vision" condition (P<0.05). DISCUSSION-CONCLUSION: FMG had postural impaired performance compared to healthy subjects, especially in the absence of compensation with visual input. This might be explained by sensory changes induced by chronic painful condition affecting muscles. In addition, the disturbance of postural performance is more important after 6MWT (unlike CG), highlighting the state of fragility of subjects and the risk of falls in fatigue condition. We conclude that the compensation by the vision is important. The walk test induced fatigue property and a possible decrease in sensitivity of proprioceptive system. Thus, this study demonstrates lower postural performance in patients with fibromyalgia and a higher sensitivity to fatigue, but other explanatory factors are to be found, such as the influence of pain.
van Dam A(1).	(1)GGZ WNB Mental Health Institute, Research and InnovationHalsteren, Netherlands; Tranzo Scientific Center for Care and Welfare, Tilburg UniversityTilburg, Netherlands.	Subgroup Analysis in Burnout: Relations Between Fatigue, Anxiety, and Depression.	278. Front Psychol. 2016 Feb 4;7:90.	Several authors have suggested that burned out patients do not form a homogeneous group and that subgroups should be considered. The identification of these subgroups may contribute to a better understanding of the burnout construct and lead to more specific therapeutic interventions. Subgroup analysis may also help clarify whether burnout is a distinct entity and whether subgroups of burnout overlap with other disorders such as depression and chronic fatigue syndrome. In a group of 113 clinically diagnosed burned out patients, levels of fatigue, depression, and anxiety were assessed. In order to identify possible subgroups, we performed a two-step cluster analysis. The analysis revealed two clusters that differed from one another in terms of symptom severity on the three aforementioned measures. Depression appeared to be

				the strongest predictor of group membership. These results are considered in the light of the scientific debate on whether burnout can be distinguished from depression and whether burnout subtyping is useful. Finally, implications for clinical practice and future research are discussed.
Van Der Gucht A(1), Aoun Sebaiti M(2), Guedj E(3), Aouizerate J(2), Yara S(4), Gherardi R(2), Evangelista E(2), Chalaye J(2), Cottereau AS(2), Verger A(5), Bachoud-Levi AC(2), Itti E(2), Authier FJ(2).	(1)CHU Henri Mondr, France. (2)CHU Henri Mondor. (3)CHU Timone Marseille, France. (4)sabrina.yara@hmn.aphp.fr. (5)CHU Nancy.	Brain FDG-PET metabolic abnormalities in patients with long-lasting macrophagic myofasciitis.	66. J Nucl Med. 2016 Oct 20. pii: jnumed.114.151878.	PURPOSE: Macrophagic myofasciitis (MMF) is an emerging condition with specific muscle lesions characterized by an abnormal long-term persistence of aluminum hydroxide particles within macrophages at the site of previous immunization. Patients present with diffuse arthromyalgias, chronic fatigue, and cognitive dysfunction. The aim of this study was to characterize brain FDG-PET metabolic abnormalities in MMF patients, and the relation with cognitive dysfunction. METHODS: FDG-PET brain imaging and a comprehensive battery of neuropsychological tests were performed in 100 consecutive MMF patients (mean age, 45.9 ± 11.8 y; women, 74%) followed in our Reference Center for Rare Neuromuscular Diseases. Images were analyzed using statistical parametric mapping (SPM12). Using ANCOVA analysis, all FDG-PET brain images of MMF patients were compared to a reference population of 44 healthy subjects matched for age (mean age, 45.4 ± 16 y; P = 0.87) and gender (women, 73%; P = 0.88). All results were collected at a P-value < 0.005 at the voxel level, for clusters k ≥ 200 voxels (corrected for cluster volume) with adjustment for age and gender. The neuropsychological assessment identified four categories of patients with: (i) no significant cognitive impairment (n = 42); (ii) frontal sub-cortical (FSC) dysfunction (n = 29); (iii) papezian dysfunction (n = 22); and (iv) callosal disconnection (n = 7). RESULTS: In comparison with healthy subjects, ANCOVA analysis of the whole population of patients with MMF exhibited a pattern of hypometabolism (p<0.001) involving occipital lobes, temporal lobes, limbic system, cerebellum and frontoparietal cortices. The subgroup of patients with FSC dysfunction exhibited larger extents of involved area (35223 voxels vs. 13680 voxels in the subgroup with papezian dysfunction and 5453 voxels in patients without cognitive impairment). Not significant result was obtained in the last subgroup due to its small population size. CONCLUSION: Our study identified in MMF patients a peculiar patterm of a cerebral glucose hypometabolism mostly marked in MMF patients with FSC dysfunction. This characteristic pattern could reprensent a diagnostic biomarker of MMF in patients with chronic fatigue syndrome and cognitive dysfunction.
van der Schaaf ME(1), De Lange FP(2), Schmits IC(3), Geurts DE(4), Roelofs K(3), van der Meer JW(5), Toni I(3), Knoop H(6).	(1)Expert Centre for Chronic Fatigue, Nijmegen; Donders Institute for Brain, Cognition, and Behaviour, Centre for Neuroimaging, Radboud University	Prefrontal Structure Varies as Function of Pain Symptoms in Chronic Fatigue Syndrome.	48. Biol Psychiatry. 2016 Aug 31. pii: S0006-3223(16)32737-8.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by severe fatigue persisting for ≥6 months and leading to considerable impairment in daily functioning. Neuroimaging studies of patients with CFS have revealed alterations in prefrontal brain morphology. However, it remains to be determined whether these alterations are specific for fatigue or whether they relate to other common CFS symptoms (e.g., chronic pain, lower psychomotor speed, and reduced physical activity). METHODS: We used magnetic resonance imaging to quantify gray matter volume (GMV) and the N-acetylaspartate and N-acetylaspartylglutamate/creatine ratio (NAA/Cr) in a group of 89

	Nijmegen, Nijmegen. Electronic address: marieke.vandershcaaf@donders.ru.nl. (2)Donders Institute for Brain, Cognition, and Behaviour, Centre for Neuroimaging, Radboud University Nijmegen, Nijmegen. (3)Expert Centre for Chronic Fatigue, Nijmegen. (4)Department of Psychiatry, Radboud University Medical Center, Nijmegen; Donders Institute for Brain, Cognition, and Behaviour, Centre for Neuroimaging, Radboud University Nijmegen, Nijmegen; Adult Personality Disorder Service, South London and Maudsley National Health Service Foundation Trust, London, United Kingdom. (5)Department of Internal Medicine, Nijmegen. (6)Expert Centre for Chronic Fatigue, Nijmegen; Department of Medical Psychology, Academic Medical Centre, University of			women with CFS. Building on previous reports, we tested whether GMV and NAA/Cr in the dorsolateral prefrontal cortex are associated with fatigue severity, pain, psychomotor speed, and physical activity, while controlling for depressive symptoms. We also considered GMV and NAA/Cr differences between patients with CFS and 26 sex-, age-, and education-matched healthy controls. RESULTS: The presence of pain symptoms was the main predictor of both GMV and NAA/Cr in the left dorsolateral prefrontal cortex of patients with CFS. More pain was associated with reduced GMVs and NAA/Cr, over and above the effects of fatigue, depressive symptoms, physical activity, and psychomotor speed. In contrast to previous reports and despite a large representative sample, global GMV did not differ between the CFS and healthy control groups. CONCLUSIONS: CFS, as diagnosed by Centers for Disease Control and Prevention criteria, is not a clinical entity reliably associated with reduced GMV. Individual variation in the presence of pain, rather than fatigue, is associated with neuronal alterations in the dorsolateral prefrontal cortex of patients with CFS.

	Amsterdam, Amsterdam, The Netherlands.			
van Dijk EH(1), Dijkman G(1), Biermasz NR(2), van Haalen FM(2), Pereira AM(2), Boon CJ(1).	(1)Department of Ophthalmology, Leiden University Medical Center, Leiden - The Netherlands. (2)Department of Medicine, Division of Endocrinology, and Center for Endocrine Tumors, Leiden University Medical Center, Leiden - The Netherlands.	Chronic central serous chorioretinopathy as a presenting symptom of Cushing syndrome.	206. Eur J Ophthalmol. 2016 Aug 4;26(5):442-8.	PURPOSE: To describe 4 patients who were diagnosed with chronic central serous chorioretinopathy (cCSC), which appeared to be the presenting symptom of Cushing syndrome (CS). METHODS: In this retrospective review of charts, all patients received extensive ophthalmologic examination and endocrinologic analyses. RESULTS: A 56-year-old man and a 49-year-old woman were treated because of bilaterally active, therapy-resistant cCSC. The clinical sign indicative for CS leading to referral to the endocrinologist was muscle weakness in the man and plethora in the woman. In a 37-year-old woman with known diabetes mellitus and central obesity, bilateral cCSC was diagnosed before CS screening. Another 49-year-old woman was treated for unilateral cCSC for 4 years. Complaints of fatigue, muscle weakness, central adiposity, and skin atrophy led to referral and a CS diagnosis due to bilateral macronodular adrenal hyperplasia. In all patients, CS surgery resulted in complete resolution of subretinal fluid. During postsurgical follow-up, no reactivation of cCSC was observed. CONCLUSIONS: Chronic CSC can be the principal manifestation of relatively mildly symptomatic and unrecognized CS. In patients with cCSC, ophthalmologists should have a high index of suspicion for clinical signs of CS that warrant endocrinologic analysis. Cushing syndrome surgery can stop active subretinal fluid leakage in cCSC.
Veauthier C(1), Hasselmann H(2), Gold SM(3), Paul F(4).	(1)Interdisciplinary Center for Sleep Medicine, Charité - Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany ; NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany. (2)NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany ;	The Berlin Treatment Algorithm: recommendations for tailored innovative therapeutic strategies for multiple sclerosis-related fatigue.	25. EPMA J. 2016 Nov 24;7:25. eCollection 2016.	More than 80% of multiple sclerosis (MS) patients suffer from fatigue. Despite this, there are few therapeutic options and evidence-based pharmacological treatments are lacking. The associated societal burden is substantial (MS fatigue is a major reason for part-time employment or early retirement), and at least one out of four MS patients view fatigue as the most burdensome symptom of their disease. The mechanisms underlying MS-related fatigue are poorly understood, and objective criteria for distinguishing and evaluating levels of fatigue and tiredness have not yet been developed. A further complication is that both symptoms may also be unspecific indicators of many other diseases (including depression, sleep disorders, anemia, renal failure, liver diseases, chronic obstructive pulmonary disease, drug side effects, recent MS relapses, infections, nocturia, cancer, thyroid hypofunction, lack of physical exercise). This paper reviews current treatment options of MS-related fatigue in order to establish an individualized therapeutic strategy that factors in existing comorbid disorders. To ensure that such a strategy can also be easily and widely implemented, a comprehensive approach is needed, which ideally takes into account all other possible causes and which is moreover cost efficient. Using a diagnostic interview, depressive disorders, sleep disorders and side effects of the medication should be identified and addressed. All MS patients suffering from fatigue should fill out the Modified Fatigue Impact Scale, Epworth Sleepiness Scale, the Beck Depression Inventory (or a similar depression scale), and the Pittsburgh Sleep Quality Index (or the Insomnia Severity

	Department of Psychiatry and Psychotherapy, Charité - Universitätsmedizin Berlin, Hindenburgdamm 30, 12203 Berlin, Germany. (3)Department of Psychiatry and Psychotherapy, Charité - Universitätsmedizin Berlin, Hindenburgdamm 30, 12203 Berlin, Germany ; Institute of Neuroimmunology and Multiple Sclerosis (INIMS), Center for Molecular Neurobiology (ZMNH), University Medical Center Hamburg-Eppendorf, 20251 Hamburg, Germany. (4)NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin, Germany ; Clinical and Experimental Multiple Sclerosis Research Center, Department of Neurology, Charité - Universitätsmedizin Berlin, 10117 Berlin,			Index). In some patients, polygraphic or polysomnographic investigations should be performed. The treatment of underlying sleep disorders, drug therapy with alfacalcidol or fampridine, exercise therapy, and cognitive behavioral therapy-based interventions may be effective against MS-related fatigue. The objectives of this article are to identify the reasons for fatigue in patients suffering from multiple sclerosis and to introduce individually tailored treatment approaches. Moreover, this paper focuses on current knowledge about MS-related fatigue in relation to brain atrophy and lesions, cognition, disease course, and other findings in an attempt to identify future research directions.

	Germany ; Experimental and Clinical Research Center, Max Delbrück Center for Molecular Medicine and Charité - Universitätsmedizin Berlin, Berlin, Germany.			
Velleman S(1), Collin SM(2), Beasant L(2), Crawley E(2).	(1)Paediatric CFS/ME Service, Royal National Hospital for Rheumatic Diseases NHS Foundation Trust, UK sophie.velleman@rnhrd.nhs.uk. (2)Centre for Child and Adolescent Health, University of Bristol, UK.	Psychological wellbeing and quality-of-life among siblings of paediatric CFS/ME patients: A mixed-methods study.	55. Clin Child Psychol Psychiatry. 2016 Oct;21(4):618-633. Epub 2015 Sep 22.	Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is a disabling condition known to have a negative impact on all aspects of a child's life. However, little is understood about the impact of CFS/ME on siblings. A total of 34 siblings completed questionnaires measuring depression (Hospital Anxiety and Depression Scale (HADS)), anxiety (HADS and Spence Children's Anxiety Scale (SCAS)) and European Quality-of-life-Youth (EQ-5D-Y). These scores were compared with scores from normative samples. Siblings had higher levels of anxiety on the SCAS than adolescents of the same age recruited from a normative sample; however, depression and quality-of-life were similar. Interviews were undertaken with nine siblings of children with CFS/ME who returned questionnaires. Interview data were analysed using a framework approach to thematic analysis. Siblings identified restrictions on family life, 'not knowing' and lack of communication as negative impacts on their family, and change of role/focus, emotional reactions and social stigma as negative impacts on themselves. They also described positive communication, social support and extra activities as protective factors. Paediatric services should be aware of the impact of CFS/ME on the siblings of children with CFS/ME, understand the importance of assessing paediatric CFS/ME patients within the context of their family and consider providing information for siblings about CFS/ME.
Velvin G(1,)(2), Bathen T(3), Rand-Hendriksen S(3,)(4), Geirdal AØ(5).	(1)TRS National Resource Centre for Rare Disorders, Sunnaas Rehabilitation Hospital, 1450, Nesoddtangen, Norway. gry.velvin@sunnaas.no. (2)Department of Social Work, Child Welfare and Social Policy, Faculty of	Satisfaction with life in adults with Marfan syndrome (MFS): associations with health-related consequences of MFS, pain, fatigue, and demographic factors.	314. Qual Life Res. 2016 Jul;25(7):1779-90.	PURPOSE: The objective with this study was to explore satisfaction with life (SWL) among adults with Marfan syndrome (MFS) compared to the general Norwegian population and other patient groups and further to examine the associations between SWL and demographic factors, contact with social and health services, MFS-related health problems, chronic pain, and fatigue. METHODS: This is a cross-sectional study with postal questionnaire, including the Satisfaction with Life Scale (SWLS), questions on demographic factors, health-related aspects of MFS, and validated instruments measuring chronic pain (Standardized Nordic Questionnaire) and fatigue (Fatigue Severity Scale). One hundred and seventeen adults with MFS were invited to participate, and 73 (62 %) participated. RESULTS: The SWLS mean score in adults with MFS was significantly lower than that reported for the general Norwegian population, but similar to or higher than that reported for other patient groups. Only fatigue, aortic dissection, and having regular contact with psychologist showed significant unique

	Social Sciences, Oslo and Akershus University College of Applied Sciences, Oslo, Norway. gry.velvin@sunnaas.no. (3)TRS National Resource Centre for Rare Disorders, Sunnaas Rehabilitation Hospital, 1450, Nesoddtangen, Norway. (4)Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Oslo, Norway. (5)Department of Social Work, Child Welfare and Social Policy, Faculty of Social Sciences, Oslo and Akershus University College of Applied Sciences, Oslo, Norway.			contribution to the SWLS score in the hierarchical multiple linear analyses. The total variance explained by the model was 45.2 % $p \leq 0.000$, confirming that the combination of independent variables significantly predicted SWLS. CONCLUSIONS: The results reflect that MFS influences people's SWL and that particularly severe fatigue, aortic dissection, and psychological aspects are associated with lower SWL. This is important to take into account in the clinical work with people with MFS. Further investigation is needed, especially on larger sample groups. Studies with combination of qualitative and quantitative approaches are recommended to obtain more comprehensive and accurate knowledge about the consequences of MFS on satisfaction with life.
Vogt H(1), Ulvestad E(2), Wyller VB(3).	(1)General Practice Research Unit, Department of Public Health and General Practice, Norwegian University of Science and Technology, 8905 Trondheim, Norway; henrik.vogt@ntnu.no. (2)Department of Microbiology, Haukeland University Hospital, 5021 Bergen,	Metabolic features of chronic fatigue syndrome revisited.	50. Proc Natl Acad Sci U S A. 2016 Nov 15;113(46):E7140-E7141. Epub 2016 Nov 3.	

	Norway. (3)Department of Pediatrics and Adolescent Medicine, Akershus University Hospital, 1478 Lørenskog, Norway.			
Vos-Vromans DC(1), Huijnen IP(2), Rijnders LJ(3), Winkens B(4), Knottnerus JA(5), Smeets RJ(2).	(1)Revant Rehabilitation Centre Breda, Brabantlaan 1, 4817 JW Breda, The Netherlands. Electronic address: d.vos@revant.nl. (2)Department of Rehabilitation Medicine, Research School CAPHRI Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands; Department of Rehabilitation Medicine, Academic Hospital Maastricht, P.O. Box 5800, 6202 ZA Maastricht, The Netherlands; Adelante Centre of Expertise in Rehabilitation and Audiology, P.O. Box 88, 6430 AB Hoensbroek, The Netherlands. (3)Revant Rehabilitation Centre Breda, Brabantlaan 1, 4817 JW Breda, The Netherlands.	Treatment expectations influence the outcome of multidisciplinary rehabilitation treatment in patients with CFS.	236. J Psychosom Res. 2016 Apr;83:40-5.	OBJECTIVE: To improve the effectiveness of treatment in patients with chronic fatigue syndrome it is worthwhile studying factors influencing outcomes. The aims of this study were (1) to assess the association of expectancy and credibility on treatment outcomes, and (2) to identify baseline variables associated with treatment expectancy and credibility. METHODS: 122 patients were included in a randomized controlled trial of whom 60 received cognitive behavioural therapy (CBT) and 62 multidisciplinary rehabilitation treatment (MRT). Expectancy and credibility were measured with the credibility and expectancy questionnaire. Outcomes of treatment, fatigue, and quality of life (QoL), were measured at baseline and post-treatment. Multiple linear regressions were performed to analyse associations. RESULTS: In explaining fatigue and the physical component of the QoL, the effect of expectancy was significant for MRT, whereas in CBT no such associations were found. The main effect of expectancy on the mental component of QoL was not significant. For credibility, the overall effect on fatigue and the physical component of QoL was not significant. In explaining the mental component of QoL, the interaction between treatment and credibility was significant. However, the effects within each group were not significant. In the regression model with expectancy as dependent variable, only treatment centre appeared significantly associated. In explaining credibility, treatment centre, treatment allocation and depression contributed significantly. CONCLUSIONS: For clinical practice it seems important to check the expectations of the patient, since expectations influence the outcome after MRT.

	(4)Department of Methodology and Statistics, Research School CAPHRI, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands. (5)Department of General Practice, Research School CAPHRI, Maastricht University, P.O. Box 616, 6200 MD Maastricht, The Netherlands.			
Vos-Vromans DC(1), Smeets RJ(2,)(3,)(4), Huijnen IP(2,)(3,)(4), Köke AJ(4), Hitters WM(5), Rijnders LJ(1), Pont M(6), Winkens B(7), Knottnerus JA(8).	(1)Revant Rehabilitation Centre Breda, Breda, The Netherlands.	Multidisciplinary rehabilitation treatment versus cognitive behavioural therapy for patients with chronic fatigue syndrome: a randomized controlled trial.	352. J Intern Med. 2016 Mar;279(3):268-82.	OBJECTIVES: The aim of this trial was to evaluate the difference in treatment effect, at 26 and 52 weeks after the start of treatment, between cognitive behavioural therapy (CBT) and multidisciplinary rehabilitation treatment (MRT) for patients with chronic fatigue syndrome (CFS). DESIGN: Multicentre, randomized controlled trial of patients with CFS. Participants were randomly assigned to MRT or CBT. SETTING: Four rehabilitation centres in the Netherlands. SUBJECTS: A total of 122 patients participated in the trial. MAIN OUTCOME MEASURES: Primary outcomes were fatigue measured by the fatigue subscale of the Checklist Individual Strength and health-related quality of life measured by the Short-Form 36. Outcomes were assessed prior to treatment and at 26 and 52 weeks after treatment initiation. RESULTS: A total of 114 participants completed the assessment at 26 weeks, and 112 completed the assessment at 52 weeks. MRT was significantly more effective than CBT in reducing fatigue at 52 weeks. The estimated difference in fatigue between the two treatments was -3.02 [95% confidence interval (CI) -8.07 to 2.03; P = 0.24] at 26 weeks and -5.69 (95% CI -10.62 to -0.76; P = 0.02) at 52 weeks. Patients showed an improvement in quality of life over time, but between-group differences were not significant. CONCLUSION: This study provides evidence that MRT is more effective in reducing long-term fatigue severity than CBT in patients with CFS. Although implementation in comparable populations can be recommended based on clinical effectiveness, it is advisable to analyse the cost-effectiveness and replicate these findings in another multicentre trial.
Vugts MA(1), Joosen MC, van Bergen AH, Vrijhoef HJ.	(1)Tranzo Scientific Center for Care and Welfare, Tilburg School of Social and	Feasibility of Applied Gaming During Interdisciplinary Rehabilitation for Patients	232. JMIR Serious Games. 2016 Apr 1;4(1):e2.	BACKGROUND: Applied gaming holds potential as a convenient and engaging means for the delivery of behavioral interventions. For developing and evaluating feasible computer-based interventions, policy makers and designers rely on limited knowledge about what causes variation in usage. OBJECTIVE: In this study, we looked closely at

	Behavioral Sciences, Tilburg University, Tilburg, Netherlands. m.a.p.vugts@tilburguniversity.edu.	With Complex Chronic Pain and Fatigue Complaints: A Mixed-Methods Study.		why and by whom an applied game (LAKA) is demanded and whether it is feasible (with respect to acceptability, demand, practicality, implementation, and efficacy) and devised a complementary intervention during an interdisciplinary rehabilitation program (IRP) for patients with complex chronic pain and fatigue complaints. METHODS: A mixed-methods design was used. Quantitative process analyses and assessments of feasibility were carried out with patients of a Dutch rehabilitation center who received access to LAKA without professional support during a 16-week interdisciplinary outpatient program. The quantitative data included records of routinely collected baseline variables (t0), additional surveys to measure technology acceptance before (t1) and after 8 weeks of access to LAKA (t2), and automatic log files of usage behavior (frequency, length, and progress). Subsequently, semistructured interviews were held with purposively selected patients. Interview codes triangulated and illustrated explanations of usage and supplemented quantitative findings on other feasibility domains. RESULTS: Of the 410 eligible patients who started an IRP during the study period, 116 patients participated in additional data collections (108 with problematic fatigue and 47 with moderate or severe pain). Qualitative data verified that hedonic motivation was the most important factor for behavioral intentions to use LAKA (P<.001). Moreover, quotes illustrated a positive association between usage intentions (t1) and baseline level (t0) coping by active engagement (Spearman ρ=0.25; P=.008) and why patients who often respond by seeking social support were represented in a group of 71 patients who accessed the game (P=.034). The median behavioral intention to use LAKA was moderately positive and declined over time. Twenty patients played the game from start to finish. Behavioral change content was recognized and seen as potentially helpful by interview respondents who exposed themselves to the content of LAKA. CONCLUSIONS: Variation in the demand for applied gaming is generally explained by perceived enjoyment and effort and by individual differences in coping resources. An applied game can be offered as a feasible complementary intervention for more patients with complex chronic pain or fatigue complaints by embedding and delivering in alignment with patient experiences. Feasibility, effectiveness, and cost-effectiveness can be evaluated in a full-scale evaluation. New observations elicit areas of further research on the usage of computer-based interventions.
Wadman M.		For chronic fatigue syndrome, a 'shifting tide' at NIH.	35. Science. 2016 Nov 11;354(6313):691-692.	
Walitt B(1), Ceko M, Gracely JL, Gracely RH.	(1)National Center for Complementary and Integrative Health, National Institutes of Health, 10 Center	Neuroimaging of Central Sensitivity Syndromes: Key Insights from the Scientific Literature.	315. Curr Rheumatol Rev. 2016;12(1):55-87.	Central sensitivity syndromes are characterized by distressing symptoms, such as pain and fatigue, in the absence of clinically obvious pathology. The scientific underpinnings of these disorders are not currently known. Modern neuroimaging techniques promise new insights into mechanisms mediating these postulated syndromes. We review the results of neuroimaging applied to five central sensitivity syndromes: fibromyalgia,

	Drive, Bethesda, MD 20814, USA. Brian.walitt@nih.gov.			chronic fatigue syndrome, irritable bowel syndrome, temporomandibular joint disorder, and vulvodynia syndrome. Neuroimaging studies of basal metabolism, anatomic constitution, molecular constituents, evoked neural activity, and treatment effect are compared across all of these syndromes. Evoked sensory paradigms reveal sensory augmentation to both painful and nonpainful stimulation. This is a transformative observation for these syndromes, which were historically considered to be completely of hysterical or feigned in origin. However, whether sensory augmentation represents the cause of these syndromes, a predisposing factor, an endophenotype, or an epiphenomenon cannot be discerned from the current literature. Further, the result from cross-sectional neuroimaging studies of basal activity, anatomy, and molecular constituency are extremely heterogeneous within and between the syndromes. A defining neuroimaging "signature" cannot be discerned for any of the particular syndromes or for an over-arching central sensitization mechanism common to all of the syndromes. Several issues confound initial attempts to meaningfully measure treatment effects in these syndromes. At this time, the existence of "central sensitivity syndromes" is based more soundly on clinical and epidemiological evidence. A coherent picture of a "central sensitization" mechanism that bridges across all of these syndromes does not emerge from the existing scientific evidence.
Wallis A(1), Butt H(2), Ball M(1), Lewis DP(3), Bruck D(1).	(1)a Psychology Department , Victoria University , Victoria , Australia. (2)b Bioscreen (Aust) Pty Ltd , Victoria , Australia. (3)c CFS Discovery Clinic , Donvale , Victoria , Australia.	Support for the microgenderome invites enquiry into sex differences.	53. Gut Microbes. 2016 Nov 3:1-7.	The microgenderome defines the interaction between microbiota, sex hormones and the immune system. Our recent research inferred support for the microgenderome by showing sex differences in microbiota-symptom associations in a clinical sample of patients with myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS). This addendum expands upon the sex-specific pattern of associations that were observed. Interpretations are hypothesized in relation to genera versus species-level analyses and D-lactate theory. Evidence of sex-differences invites future research to consider sex comparisons in microbial function even when microbial abundance is statistically similar. Pairing assessment of clinical symptoms with microbial culture, DNA sequencing and metabolomics methods will help advance our current understandings of the role of the microbiome in health and disease.
Wallis A(1), Butt H(2), Ball M(1), Lewis DP(3), Bruck D(1).	(1)Psychology Department, Victoria University, Victoria, Australia. (2)Bioscreen (Aust) Pty Ltd, Victoria, Australia. (3)CFS Discovery Clinic, Donvale, Victoria, Australia.	Support for the Microgenderome: Associations in a Human Clinical Population.	312. Sci Rep. 2016 Jan 13;6:19171.	The 'microgenderome' provides a paradigm shift that highlights the role of sex differences in the host-microbiota interaction relevant for autoimmune and neuro-immune conditions. Analysis of cross-sectional self-report and faecal microbial data from 274 patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) suggests that commensal gut microorganisms may play both protective and deleterious roles in symptom expression. Results revealed significant sex-specific interactions between Firmicutes (Clostridium, Streptococcus, Lactobacillus and Enterococcus) and ME/CFS symptoms (including neurological, immune and mood symptoms), regardless of compositional similarity in microbial levels across the sexes. Extending animal studies, we provide support for the microgenderome in a human clinical population. Applied and mechanistic research needs to consider sex-interactions when examining

				the composition and function of human microbiota.
Watanabe A(1), Satoh K(2), Maniwa T(2), Matsumoto K(2).	(1)Division of Clinical Genetics, Nippon Medical School Hospital, Tokyo 113-8603, Japan. (2)Department of Biosignaling and Radioisotope Experiment, Interdisciplinary Center for Science Research, Organization for Research, Shimane University, Izumo, Shimane 693-8501, Japan.	Proteomic analysis for the identification of serum diagnostic markers for joint hypermobility syndrome.	317. Int J Mol Med. 2016 Feb;37(2):461-7.	Joint hypermobility syndrome (JHS) (also termed Ehlers-Danlos syndrome, hypermobility type) is a heritable connective tissue disorder which is characterized by generalized joint hypermobility, chronic pain, dizziness, fatigue, and minor skin changes. However, it has yet to be determined in patients with JHS whether specific genetic factors are involved in the risk of developing the disorder. Therefore, interventions have been limited to symptomatic treatments, and biomarkers for diagnosis and therapy have not yet been identified. In the present study, to identify potential serum biomarkers for JHS, we examined proteins with differential levels in sera from patients with JHS and in sera from control individuals using isobaric tags for relative and absolute quantitation (iTRAQ) labeling in combination with nano LC-MALDI-TOF/TOF-MS/MS followed by ProteinPilot analysis. In the sera of patients with JHS, a total of 106 proteins with differential levels were identified, and they were further narrowed down to 6 proteins ($p<0.05$, patient vs. control). Of the 6 proteins, proteins involved in the complement system including complement C1r subcomponent (C1R), vitronectin (VTN), complement component C9 (C9), and C4b-binding protein alpha chain (C4BPA) were identified as increased proteins in sera from patients with JHS compared with those in sera from controls. We confirmed increased levels of C1R and VTN in sera from patients with JHS by western blot analyses. The results indicate the possibility of a locally occurring inflammatory process in patients with JHS.
White PD(1), Chalder T(2), Sharpe M(3).	(1)Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine, Queen Mary University of London, London, UK. (2)Academic Department of Psychological Medicine, King's College London, Weston Education Centre, London, UK. (3)Department of Psychiatry, Psychological Medicine Research, University of Oxford,	Comment on: 'Reports of recovery in chronic fatigue syndrome may present less than meets the eye'.	306. Evid Based Ment Health. 2016 Feb;19(1):32. Comment on Evid Based Ment Health. 2014 Aug;17(3):95.	

	Oxford, UK.			
Williams AM(1), Christopher G(2), Jenkinson E(2).	(1)University of the West of England, UK Ashley.Williams4@nhs.net. (2)University of the West of England, UK.	The psychological impact of dependency in adults with chronic fatigue syndrome/myalgic encephalomyelitis: A qualitative exploration.	218. J Health Psychol. 2016 Apr 19. pii: 1359105316643376.	Chronic fatigue syndrome/myalgic encephalomyelitis can limit functional capacity, producing various degrees of disability and psychological distress. Semi-structured interviews explored the experiences of adults with chronic fatigue syndrome/myalgic encephalomyelitis being physically dependent on other people for help in daily life, and whether physical dependency affects their psychological well-being. Thematic analysis generated six themes: loss of independence and self-identity, an invisible illness, anxieties of today and the future, catch-22, internalised anger, and acceptance of the condition. The findings provide insight into the psychological impact of dependency. Implications for intervention include better education relating to chronic fatigue syndrome/myalgic encephalomyelitis for family members, carers, and friends; ways to communicate their needs to others who may not understand chronic fatigue syndrome/myalgic encephalomyelitis; and awareness that acceptance of the condition could improve psychological well-being.
Williams MV(1,)(2), Cox B(3), Ariza ME(4,)(5).	(1) Department of Cancer Biology and Genetics, Wexner Medical Center, Ohio State University, Columbus, OH 43210, USA. Williams.70@osu.edu. (2)Institute for Behavioral Medicine Research, Ohio State University, Columbus, OH 43210, USA. Williams.70@osu.edu.	Herpesviruses dUTPases: A New Family of Pathogen-Associated Molecular Pattern (PAMP) Proteins with Implications for Human Disease.	3. Pathogens. 2016 Dec 28;6(1). pii: E2.	The human herpesviruses are ubiquitous viruses and have a prevalence of over 90% in the adult population. Following a primary infection they establish latency and can be reactivated over a person's lifetime. While it is well accepted that human herpesviruses are implicated in numerous diseases ranging from dermatological and autoimmune disease to cancer, the role of lytic proteins in the pathophysiology of herpesvirus-associated diseases remains largely understudies. Only recently have we begun to appreciate the importance of lytic proteins produced during reactivation of the virus, in particular the deoxyuridine triphosphate nucleotidohydrolases (dUTPase), as key modulators of the host innate and adaptive immune responses. In this review, we provide evidence from animal and human studies of the Epstein-Barr virus as a prototype, supporting the notion that herpesviruses dUTPases are a family of proteins with unique immunoregulatory functions that can alter the inflammatory microenvironment and thus exacerbate the immune pathology of herpesvirus-related diseases including myalgic encephalomyelitis/chronic fatigue syndrome, autoimmune diseases, and cancer.

	(3)Institute for Behavioral Medicine Research, Ohio State University, Columbus, OH 43210, USA. Brandon.Cox@osumc.edu. (4)Department of Cancer Biology and Genetics, Wexner Medical Center, Ohio State University, Columbus, OH 43210, USA. maria.ariza@osumc.edu. (5)Institute for Behavioral Medicine Research, Ohio State University, Columbus, OH 43210, USA. maria.ariza@osumc.edu.			
Worm-Smeitink M(1), Nikolaus	(1)Expert Centre for Chronic Fatigue,	Cognitive behaviour therapy for chronic	139. J Psychosom Res. 2016 Aug;87:43-9.	OBJECTIVE: Cognitive behaviour therapy (CBT) reduces fatigue and disability in chronic fatigue syndrome (CFS). However, outcomes vary between studies, possibly because of

S(1), Goldsmith K(2), Wiborg J(1), Ali S(3), Knoop H(4), Chalder T(5).	Radboud University Medical Center, Reinier Postlaan 4 (916), 6525GC Nijmegen, The Netherlands. (2)Biostatistics Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, 16 De Crespigny Park, London SE5 8AF, United Kingdom. (3)Chronic Fatigue Research and Treatment Unit, South London and Maudsley NHS Foundation Trust, Mapother House, Maudsley Hospital, Denmark Hill, London SE5 8AZ, United Kingdom. (4)Expert Centre for Chronic Fatigue, Radboud University Medical Center, Reinier Postlaan 4 (916), 6525GC Nijmegen, The Netherlands; Department of Medical Psychology, Academic Medical Centre (AMC), University of Amsterdam, Amsterdam, The Netherlands.	fatigue syndrome: Differences in treatment outcome between a tertiary treatment centre in the United Kingdom and the Netherlands.		differences in patient characteristics, treatment protocols, diagnostic criteria and outcome measures. The objective was to compare outcomes after CBT in tertiary treatment centres in the Netherlands (NL) and the United Kingdom (UK), using different treatment protocols but identical outcome measures, while controlling for differences in patient characteristics and diagnostic criteria. METHODS: Consecutively referred CFS patients who received CBT were included (NL: n=293, UK: n=163). Uncontrolled effect sizes for improvement in fatigue (Chalder Fatigue Questionnaire), physical functioning (SF-36 physical functioning subscale) and social functioning (Work and Social Adjustment Scale) were compared. Multiple regression analysis was used to examine whether patient differences explained outcome differences between centres. RESULTS: Effect sizes differed between centres for fatigue (Cohen's D NL=1.74, 95% CI=1.52-1.95; UK=0.99, CI=0.73-1.25), physical functioning (NL=0.99, CI=0.81-1.18; UK=0.33, CI=0.08-0.58) and social functioning (NL=1.47, CI=1.26-1.69; UK=0.61, CI=0.35-0.86). Patients in the UK had worse physical functioning at baseline and there were minor demographic differences. These could not explain differences in centre outcome. CONCLUSION: Effectiveness of CBT differed between treatment centres. Differences in treatment protocols may explain this and should be investigated to help further improve outcomes.

	Electronic address: hans.knoop@amc.uva.nl. (5)Department of Psychological Medicine, King's College London, Weston Education Centre, Cutcombe Road, London SE5 9RJ, United Kingdom; Chronic Fatigue Research and Treatment Unit, South London and Maudsley NHS Foundation Trust, Mapother House, Maudsley Hospital, Denmark Hill, London SE5 8AZ, United Kingdom.			
Wortinger LA(1,)(2), Endestad T(2), Melinder AM(3), Øie MG(2,)(4), Sevenius A(2), Bruun Wyller V(1).	(1)Department of Pediatrics, Akershus University Hospital, Nordbyhagen, Norway. (2)Department of Psychology, University of Oslo, Oslo, Norway. (3)Cognitive Developmental Research Unit, Department of Psychology, University of Oslo, Oslo, Norway. (4)Research Department, Innlandet Hospital Trust, Lillehammer, Norway.	Aberrant Resting-State Functional Connectivity in the Salience Network of Adolescent Chronic Fatigue Syndrome.	138. PLoS One. 2016 Jul 14;11(7):e0159351.	Neural network investigations are currently absent in adolescent chronic fatigue syndrome (CFS). In this study, we examine whether the core intrinsic connectivity networks (ICNs) are altered in adolescent CFS patients. Eighteen adolescent patients with CFS and 18 aged matched healthy adolescent control subjects underwent resting-state functional magnetic resonance imaging (rfMRI). Data was analyzed using dual-regression independent components analysis, which is a data-driven approach for the identification of independent brain networks. Intrinsic connectivity was evaluated in the default mode network (DMN), salience network (SN), and central executive network (CEN). Associations between network characteristics and symptoms of CFS were also explored. Adolescent CFS patients displayed a significant decrease in SN functional connectivity to the right posterior insula compared to healthy comparison participants, which was related to fatigue symptoms. Additionally, there was an association between pain intensity and SN functional connectivity to the left middle insula and caudate that differed between adolescent patients and healthy comparison participants. Our findings of insula dysfunction and its association with fatigue severity and pain intensity in adolescent CFS demonstrate an aberration of the salience network which might play a role in CFS pathophysiology.
Wortinger	(1)a Department of	Emotional conflict	95. J Clin Exp	INTRODUCTION: Studies of neurocognition suggest that abnormalities in cognitive

LA(1,)(2), Endestad T(2), Melinder AM(3), Øie MG(2,)(4), Sulheim D(5,)(6), Fagermoen E(7), Wyller VB(1).	Pediatrics , Akershus University Hospital , Nordbyhagen , Norway. (2)b Department of Psychology , University of Oslo , Oslo , Norway. (3)c Cognitive Developmental Research Unit, Department of Psychology , University of Oslo , Oslo , Norway. (4)d Research Department , Innlandet Hospital Trust , Lillehammer , Norway. (5)e Department of Pediatrics , Oslo University Hospital , Oslo , Norway. (6)f Department of Pediatrics , Innlandet Hospital Trust , Lillehammer , Norway. (7)g Department of Anesthesiology and Critical Care , Oslo University Hospital , Oslo , Norway.	processing in adolescent chronic fatigue syndrome: A pilot study using functional magnetic resonance imaging.	Neuropsychol. 2016 Sep 20:1-14.	control contribute to the pathophysiology of chronic fatigue syndrome (CFS) in adolescents, yet these abnormalities remain poorly understood at the neurobiological level. Reports indicate that adolescents with CFS are significantly impaired in conflict processing, a primary element of cognitive control. METHOD: In this study, we examine whether emotional conflict processing is altered on behavioral and neural levels in adolescents with CFS and a healthy comparison group. Fifteen adolescent patients with CFS and 24 healthy adolescent participants underwent functional magnetic resonance imaging (fMRI) while performing an emotional conflict task that involved categorizing facial affect while ignoring overlaid affect labeled words. RESULTS: Adolescent CFS patients were less able to engage the left amygdala and left midposterior insula (mpINS) in response to conflict than the healthy comparison group. An association between accuracy interference and conflict-related reactivity in the amygdala was observed in CFS patients. A relationship between response time interference and conflict-related reactivity in the mpINS was also reported. Neural responses in the amygdala and mpINS were specific to fatigue severity. CONCLUSIONS: These data demonstrate that adolescent CFS patients displayed deficits in emotional conflict processing. Our results suggest abnormalities in affective and cognitive functioning of the salience network, which might underlie the pathophysiology of adolescent CFS.
Wu T(1), Qi X(1), Su Y(2), Teng J(1), Xu X(1).	(1)Internal Medicine-Neurology, Shandong Provincial Traditional Chinese Medical Hospital, Jinan, People's Republic of China. (2)School of Mathematic and	Electroencephalogram characteristics in patients with chronic fatigue syndrome.	279. Neuropsychiatr Dis Treat. 2016 Jan 28;12:241-9.	OBJECTIVE: To explore the electroencephalogram (EEG) characteristics in patients with chronic fatigue syndrome (CFS) using brain electrical activity mapping (BEAM) and EEG nonlinear dynamical analysis. METHODS: Forty-seven outpatients were selected over a 3-month period and divided into an observation group (24 outpatients) and a control group (23 outpatients) by using the non-probability sampling method. All the patients were given a routine EEG. The BEAM and the correlation dimension changes were analyzed to characterize the EEG features. RESULTS: 1) BEAM results indicated that the energy values of δ, θ, and α1 waves significantly increased in the observation group,

	Quantitative Economics, Shandong University of Finance and Economics, Jinan, People's Republic of China.			compared with the control group (P<0.05, P<0.01, respectively), which suggests that the brain electrical activities in CFS patients were significantly reduced and stayed in an inhibitory state; 2) the increase of δ, θ, and α1 energy values in the right frontal and left occipital regions was more significant than other encephalic regions in CFS patients, indicating the region-specific encephalic distribution; 3) the correlation dimension in the observation group was significantly lower than the control group, suggesting decreased EEG complexity in CFS patients. CONCLUSION: The spontaneous brain electrical activities in CFS patients were significantly reduced. The abnormal changes in the cerebral functions were localized at the right frontal and left occipital regions in CFS patients.
Wyller VB(1,)(2), Vitelli V(3), Sulheim D(4,)(5), Fagermoen E(6,)(7), Winger A(8), Godang K(9), Bollerslev J(9).	(1)Division of Medicine and Laboratory Sciences, Medical Faculty, University of Oslo, Oslo, Norway. brwylle@online.no. (2)Department of Paediatrics, Akershus University Hospital, Nordbyhagen, 1478, Lørenskog, Norway. brwylle@online.no. (3)Department of Biostatistics, Institute of Basic Medical Sciences, Oslo Centre for Biostatistics and Epidemiology, University of Oslo, Oslo, Norway. (4)Department of Paediatrics, Oslo University Hospital, Oslo, Norway. (5)Department of Paediatrics, Lillehammer County Hospital, Lillehammer, Norway. (6)Institute of	Altered neuroendocrine control and association to clinical symptoms in adolescent chronic fatigue syndrome: a cross-sectional study.	201. J Transl Med. 2016 May 5;14(1):121.	BACKGROUND: Chronic fatigue syndrome (CFS) is a common and disabling disorder, and a major threat against adolescent health. The pathophysiology is unknown, but alteration of neuroendocrine control systems might be a central element, resulting in attenuation of the hypothalamus-pituitary-adrenalin (HPA) axis and enhancement of the sympathetic/adrenal medulla (SAM) system. This study explored differences in neuroendocrine control mechanisms between adolescent CFS patients and healthy controls, and whether characteristics of the control mechanisms are associated with important clinical variables within the CFS group. METHODS: CFS patients 12-18 years of age were recruited nation-wide to a single referral center as part of the NorCAPITAL project. A broad case definition of CFS was applied. A comparable group of healthy controls were recruited from local schools. A total of nine hormones were assayed and subjected to network analyses using the ARACNE algorithm. Symptoms were charted by a questionnaire, and daily physical activity was recorded by an accelerometer. RESULTS: A total of 120 CFS patients and 68 healthy controls were included. CFS patients had significantly higher levels of plasma norepinephrine, plasma epinephrine and plasma FT4, and significantly lower levels of urine cortisol/creatinine ratio. Subgrouping according to other case definitions as well as adjusting for confounding factors did not alter the results. Multivariate linear regression models as well as network analyses revealed different interrelations between hormones of the HPA axis, the SAM system, and the thyroid system in CFS patients and healthy controls. Also, single hormone degree centrality was associated with clinical markers within the CFS group. CONCLUSION: This study reveals different interrelation between hormones of the HPA axis, the SAM system, and the thyroid system in CFS patients and healthy controls, and an association between hormone control characteristics and important clinical variables in the CFS group. These results add to the growing insight of CFS disease mechanisms. Trial registration Clinical Trials NCT01040429.

	Clinical Medicine, Medical Faculty, University of Oslo, Oslo, Norway. (7)Department of Anesthesiology and Critical Care, Oslo University Hospital, Oslo, Norway. (8)Institute of Nursing Sciences, Oslo and Akershus University College of Applied Sciences, Oslo, Norway. (9)Section of Specialized Endocrinology, Department of Endocrinology, Oslo University Hospital Rikshospitalet, Oslo, Norway.			
Xiao LY, Liu WA, Wu QM, Wang LY, Zhou KM, Ye HM, Fu L.		[Influence of Herbal-cake-separated Moxibustion on Contents of 5-HT, DA and NE in Hypothalamus in Rats with Functional Dyspepsia of Liver Stagnation and Spleen Deficiency Syndrome]. [Article in Chinese]	Zhen Ci Yan Jiu. 2016 Feb;41(1):60-4.	OBJECTIVE: To observe the influence of herbal cake-separated moxibustion on the contents of 5-hydroxy tryptamine (5-HT), dopamine (DA) and norepinephrine (NE) in the hypothalamus in rats with functional dyspepsia (FD) of syndrome of liver stagnation and spleen deficiency, so as to explore its mechanism underlying improvement of FD. METHODS: Sixty SD rats were randomly divided into 6 groups: control, model, herbal cake-separated moxibustion, moxa-cone moxibustion, Xiaoyaosan (decoction for relieving liver stagnation) and Domperidon, with 10 rats in each group. The FD model was established by applying chronic restraint stress + excessive fatigue + irregular food + tail clipping+ shaking for 21 consecutive days. Moxibustion (herbal cake-separated or moxa-cone) was applied to bilateral "Ganshu" (BL 18), "Pishu" (BL 20) and "Weishu" (BL 21), or "Zhangmen"(LR 13), "Qimen" (LR 14) and "Zhongwan" (CV 12) for 30 min, once daily for 14 d. For rats of the two medication groups, Xiaoyaosan [1 mL (2 g)/100 g] and Domperidone [1 mL (0.3 g)/100 g] were administrated by gavage, respectively. The contents of 5-HT, DA and NE in the hypothalamus tissue were detected by high performance liquid Phrnm.tnrnh, RESULTS: The gastric empty rate was obviously lower in the model group than in the control group (P<0. 01). After the treatment, the gastric empty rate in the herbal cake-separated moxibustion, moxa-cone moxibustion, Xiaoyaosan and Domperidone groups were significantly increased in comparison with

				the model group (P<0. 01) , but there were no significant differences among the four treatment groups (P > 0.05). Compared to the control group, the contents of 5-HT, DA and NE in the hypothalamus were markedly decreased in the model group (P < 0.01), while compared to the model group, the contents of hypothalamic 5- HT, DA and NE contents were significantly up-regulated in both the herbal cake-separated moxibustion and Xiaoyaosan groups (P < 0.01), rather than in the moxa-cone moxibustion and Domperidone groups (P > 0.05). No significant differences were found between the herbal cake-separated moxibustion and Xioayaosan groups in increasing hypothalamic 5-HT, DA and NE levels (P > 0.05). CONCLUSION: Herbal cake-separated moxibustion can promote the gastric empty rate in FD rats, which may be associated with its effects in inhibiting stress induced decrease of hypothalamic 5-HT, DA and NE levels.
Yadlapati S(1), Efthimiou P(2).	(1)a Associate chief, Rheumatology Division, New York Methodist Hospital , Brooklyn , NY , USA. (2)b Rheumatology Division, New York Methodist Hospital, Associate Professor of Clinical Medicine and Rheumatology, Weill Cornell Medical College , New York , NY , USA.	Impact of IL-1 inhibition on fatigue associated with autoinflammatory syndromes.	358. Mod Rheumatol. 2016;26(1):3-8.	Cryopyrin-associated periodic syndromes (CAPS) is a rare group of autoinflammatory disorders that includes familial cold autoinflammatory syndrome or FCAS, Muckle-wells syndrome or MWS, and neonatal-onset multisystem inflammatory disease or NOMID. CAPS is caused by a mutation in the NOD-like receptor family, pyrin domain containing 3 (NLRP3) gene. This ultimately leads to increased production of interleukin (IL)-1β. IL-1β is a biologically active member of the IL-1 family. It is not only a pro-inflammatory cytokine responsible for features such as fever, rash, and arthritis, but is also a major mediator in the central pathways of fatigue. Fatigue is a major component of CAPS and is associated with severely compromised quality of life. In clinical studies, fatigue was measured using functional assessment of chronic illness therapy-fatigue or FACIT-F and short form-36 or SF-36, physical component score instruments. These questionnaires can also be used to monitor improvement of fatigue following initiation of therapy. IL-1 inhibitors block the IL-1 signaling cascade, thereby preventing systemic inflammation in CAPS. The decrease in systemic inflammation is accompanied by improvement in fatigue.
Yamano E(1), Sugimoto M(2), Hirayama A(2), Kume S(3), Yamato M(3), Jin G(3), Tajima S(3,)(4), Goda N(5), Iwai K(6), Fukuda S(1,)(7), Yamaguti K(1,)(8), Kuratsune H(7,)(8), Soga T(2), Watanabe Y(1,)(9), Kataoka	(1) Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan. (2) Institute for Advanced Biosciences, Keio University, 246-2 Mizukami Kakuganji, Tsuruoka Yamagata 997-0052, Japan. (3) Cellular Function	Index markers of chronic fatigue syndrome with dysfunction of TCA and urea cycles	75. Sci Rep. 2016 Oct 11;6:34990. .	Chronic fatigue syndrome (CFS) is a persistent and unexplained pathological state characterized by exertional and severely debilitating fatigue, with/without infectious or neuropsychiatric symptoms, lasting at least 6 consecutive months. Its pathogenesis remains incompletely understood. Here, we performed comprehensive metabolomic analyses of 133 plasma samples obtained from CFS patients and healthy controls to establish an objective diagnosis of CFS. CFS patients exhibited significant differences in intermediate metabolite concentrations in the tricarboxylic acid (TCA) and urea cycles. The combination of ornithine/citrulline and pyruvate/isocitrate ratios discriminated CFS patients from healthy controls, yielding area under the receiver operating characteristic curve values of 0.801 (95% confidential interval [CI]: 0.711-0.890, P < 0.0001) and 0.750 (95% CI: 0.584-0.916, P = 0.0069) for training (n = 93) and validation (n = 40) datasets, respectively. These findings provide compelling evidence that a clinical diagnostic tool could be developed for CFS based on the ratios of metabolites in plasma.

Y(1,)(3).	Imaging Team, Division of Bio-function Dynamics Imaging, RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-minamimachi, Chuo-ku, Kobe, Hyogo 650-0047, Japan. (4) Hyogo Children's Sleep and Development Medical Research Center, Hyogo Rehabilitation Centre Central Hospital, 1070 Akebono-cho, Nishi-ku, Kobe, Hyogo 651-2181, Japan. (5) Department of Life Science and Medical Bio-Science, School of Advanced Science and Engineering, Waseda University, 2-2 Wakamatsu-cho, Shinjuku-ku, Tokyo 162-8480, Japan. (6) Department of Molecular and Cellular Physiology, Graduate School of Medicine, Kyoto University, Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan. (7) Department of Health Science, Kansai University of Welfare Sciences, 3-11-1			

	Asahigaoka, Kashihara, Osaka 582-0026, Japan. (8) Department of Endocrinology, Metabolism and Molecular Medicine, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan. (9)Pathophysiological and Health Science Team, RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-minamimachi, Chuo-ku, Kobe, Hyogo 650-0047, Japan.			
Yazmalar L(1), Deveci Ö(2), Batmaz İ(1), İpek D(2), Çelepkolu T(3), Alpaycı M(4), Hattapoğlu E(1), Akdeniz D(1), Sarıyıldız MA(1).	(1)Departments of Physical Medicine and Rehabilitation, Dicle University, Diyarbakır, Turkey. (2)Departments of Infectious Disease and Clinical Microbiology, Dicle University, Diyarbakır, Turkey. (3)Departments of Family Physician, Faculty of Medicine, Dicle University, Diyarbakır, Turkey. (4)Department of Physical Medicine and Rehabilitation, Faculty	Fibromyalgia incidence among patients with hepatitis B infection.	359. Int J Rheum Dis. 2016 Jul;19(7):637-43.	AIM: The purpose of our investigation was to evaluate the incidence of fibromyalgia syndrome (FMS) and identify FMS-related clinical symptoms in hepatitis B virus (HBV) patients. METHODS: One hundred and eighteen HBV surface antigen (HbsAg)-positive patients (40 with chronic active hepatitis B, 40 hepatitis B carriers and 38, all of whom had been antiretroviral-treated for at least 3 months) were included in this study. In addition, 60 age- and gender-matched HbsAg-negative healthy controls were included in the study. RESULTS: There was no significant difference in age, gender or body mass index (BMI) between the two groups ($P > 0.05$). Serum aspartate aminotransferase and alanine aminotransferase levels were significantly higher in HBV patients relative to the control group ($P < 0.05$). The incidence of FMS, widespread body pain, fatigue, sleep disturbance, anxiety, morning stiffness, arthralgia was significantly greater among HBV patients relative to the control group. Additionally, the mean tender point counts and the visual analog scale values were significantly higher among the HBV patients ($P < 0.05$). CONCLUSIONS: The results of the present study demonstrate that FMS incidence is greater among HBV patients relative to control subjects. However, there were no differences in FMS incidence among the subgroups of HBV diagnoses.

	of Medicine, Yüzüncüyıl University, Van, Turkey.			
Yi T(1), Qi L(2), Li J(1), Le JJ(1), Shao L(1), Du X(1), Dong JC(1).	(1)Department of Integrative Medicine, Huashan Hospital, Fudan University, Shanghai, China; College of Integrated Traditional Chinese and Western Medicine, Fudan University, Shanghai, China. (2)E-institute of Shanghai Municipal Education Committee, Shanghai University of Traditional Chinese Medicine, Shanghai, China.	Moxibustion upregulates hippocampal progranulin expression.	188. Neural Regen Res. 2016 Apr;11(4):610-6.	In China, moxibustion is reported to be useful and has few side effects for chronic fatigue syndrome, but its mechanisms are largely unknown. More recently, the focus has been on the wealth of information supporting stress as a factor in chronic fatigue syndrome, and largely concerns dysregulation in the stress-related hypothalamic-pituitary-adrenal axis. In the present study, we aimed to determine the effect of moxibustion on behavioral symptoms in chronic fatigue syndrome rats and examine possible mechanisms. Rats were subjected to a combination of chronic restraint stress and forced swimming to induce chronic fatigue syndrome. The acupoints Guanyuan (CV4) and Zusanli (ST36, bilateral) were simultaneously administered moxibustion. Untreated chronic fatigue syndrome rats and normal rats were used as controls. Results from the forced swimming test, open field test, tail suspension test, real-time PCR, enzyme-linked immunosorbent assay, and western blot assay showed that moxibustion treatment decreased mRNA expression of corticotropin-releasing hormone in the hypothalamus, and adrenocorticotropic hormone and corticosterone levels in plasma, and markedly increased progranulin mRNA and protein expression in the hippocampus. These findings suggest that moxibustion may relieve the behavioral symptoms of chronic fatigue syndrome, at least in part, by modulating the hypothalamic-pituitary-adrenal axis and upregulating hippocampal progranulin.
Zabotti A(1), Della Siega P, Picco L, Quartuccio L, Bassetti M, De Vita S.	(1)Department of Medical and Biological Sciences, Rheumatology Clinic, Santa Maria della Misericordia University-Hospital, Udine. zabottialen@gmail.com.	Gitelman syndrome disclosed by calcium pyrophosphate deposition disease: early diagnosis by ultrasonographic study.	157. Reumatismo. 2016 Jun 23;68(1):53-5.	Gitelman's syndrome is a rare autosomal-recessive tubular disorder characterized by hypomagnesemia and hypocalciuria associated to hypokalemia. The clinical spectrum is wide and usually characterized by chronic fatigue, cramps, muscle weakness and paresthesiae. We describe a case of a 43 year-old male patient with early onset of knee arthritis and no other symptoms. Ultrasound revealed diffuse and confluent hyperechoic deposits in cartilage, fibrocartilage of the menisci and synovium and calcium pyrophosphate crystals were observed in the synovial fluid of the knee. The concomitant presence of hypomagnesemia, hypocalciuria and hypokalemia made clear the diagnosis of Gitelman's syndrome associated with chondrocalcinosis.
Zhang ZT(1), Du XM(1), Ma XJ(1), Zong Y(1), Chen JK(1), Yu CL(2), Liu YG(1), Chen YC(1), Zhao LJ(3), Lu GC(4).	(1)Department of Health Toxicology, College of Tropical Medicine and Public Health, Second Military Medical University, Shanghai, 200433, China. (2)Laboratory Animal	Activation of the NLRP3 inflammasome in lipopolysaccharide-induced mouse fatigue and its relevance to chronic fatigue syndrome.	229. J Neuroinflammation. 2016 Apr 5;13(1):71.	BACKGROUND: The NLRP3 inflammasome (NOD-like receptor family, pyrin domain containing 3) is an intracellular protein complex that plays an important role in innate immune sensing. Its activation leads to the maturation of caspase-1 and regulates the cleavage of interleukin (IL)-1β and IL-18. Various studies have shown that activation of the immune system plays a pivotal role in the development of fatigue. However, the mechanisms underlying the association between immune activation and fatigue remained elusive, and few reports have described the involvement of NLRP3 inflammasome activation in fatigue. METHODS: We established a mouse fatigue model with lipopolysaccharide (LPS, 3 mg/kg) challenge combined with swim stress. Both

	Center, Second Military Medical University, Shanghai, 200433, China. (3)Department of Respiratory Medicine, Changhai Hospital, Second Military Medical University, Shanghai, 200433, China. zlj6583@163.com. (4)Department of Health Toxicology, College of Tropical Medicine and Public Health, Second Military Medical University, Shanghai, 200433, China. newdrug@smmu.edu.cn.			behavioural and biochemical parameters were measured to illustrate the characteristics of this model. We also assessed NLRP3 inflammasome activation in the mouse diencephalon, which is the brain region that has been suggested to be responsible for fatigue sensation. To further identify the role of NLRP3 inflammasome activation in the pathogenesis of chronic fatigue syndrome (CFS), NLRP3 KO mice were also subjected to LPS treatment and swim stress, and the same parameters were evaluated. RESULTS: Mice challenged with LPS and subjected to the swim stress test showed decreased locomotor activity, decreased fall-off time in a rota-rod test and increased serum levels of IL-1β and IL-6 compared with untreated mice. Serum levels of lactic acid and malondialdehyde (MDA) were not significantly altered in the treated mice. We demonstrated increased NLRP3 expression, IL-1β production and caspase-1 activation in the diencephalons of the treated mice. In NLRP3 KO mice, we found remarkably increased locomotor activity with longer fall-off times and decreased serum IL-1β levels compared with those of wild-type (WT) mice after LPS challenge and the swim stress test. IL-1β levels in the diencephalon were also significantly decreased in the NLRP3 KO mice. By contrast, IL-6 levels were not significantly altered. CONCLUSIONS: These findings suggest that LPS-induced fatigue is an IL-1β-dependent process and that the NLRP3/caspase-1 pathway is involved in the mechanisms of LPS-induced fatigue behaviours. NLRP3/caspase-1 inhibition may be a promising therapy for fatigue treatment.
Zinn ML(1), Zinn MA(2), Jason LA(2).	(1)Department of Community Psychology, Center for Community Research, DePaul University, Chicago, IL, 60614, USA. mzinn1@depaul.edu. (2)Department of Community Psychology, Center for Community Research, DePaul University, Chicago, IL, 60614, USA.	Intrinsic Functional Hypoconnectivity in Core Neurocognitive Networks Suggests Central Nervous System Pathology in Patients with Myalgic Encephalomyelitis: A Pilot Study.	280. Appl Psychophysiol Biofeedback. 2016 Sep;41(3):283-300.	Exact low resolution electromagnetic tomography (eLORETA) was recorded from nineteen EEG channels in nine patients with myalgic encephalomyelitis (ME) and 9 healthy controls to assess current source density and functional connectivity, a physiological measure of similarity between pairs of distributed regions of interest, between groups. Current source density and functional connectivity were measured using eLORETA software. We found significantly decreased eLORETA source analysis oscillations in the occipital, parietal, posterior cingulate, and posterior temporal lobes in Alpha and Alpha-2. For connectivity analysis, we assessed functional connectivity within Menon triple network model of neuropathology. We found support for all three networks of the triple network model, namely the central executive network (CEN), salience network (SN), and the default mode network (DMN) indicating hypo-connectivity in the Delta, Alpha, and Alpha-2 frequency bands in patients with ME compared to controls. In addition to the current source density resting state dysfunction in the occipital, parietal, posterior temporal and posterior cingulate, the disrupted connectivity of the CEN, SN, and DMN appears to be involved in cognitive impairment for patients with ME. This research suggests that disruptions in these regions and networks could be a neurobiological feature of the disorder, representing underlying neural dysfunction.

2015				
Authors	Author address	Title	Publication	Abstract
[No authors listed]		Increased expression of activation antigens on CD8+ T lymphocytes in Myalgic Encephalomyelitis/chronic fatigue syndrome: inverse associations with lowered CD19+ expression and CD4+/CD8+ ratio, but no	Neuro Endocrinol Lett. 2015 Nov 28;36(5):439-446. [Epub ahead of print]	BACKGROUND: There is now evidence that specific subgroups of patients with Myalgic Encephalomyelitis / chronic fatigue syndrome (ME/CFS) suffer from a neuro-psychiatric-immune disorder. This study was carried out to delineate the expression of the activation markers CD38 and human leukocyte antigen (HLA) DR on CD4+ and CD8+ peripheral blood lymphocytes in ME/CFS. METHODS: Proportions and absolute numbers of peripheral lymphocytes expressing CD3+, CD19+, CD4+, CD8+, CD38+ and HLA-DR+ were measured in ME/CFS (n=139), chronic fatigue (CF, n=65) and normal controls (n=40). RESULTS: The proportions of CD3+, CD8+, CD8+CD38+ and CD8+HLA-DR+ were significantly higher in ME/CFS patients than controls, while CD38+,

		associations with (auto)immune.		CD8+CD38+, CD8+HLA-DR+ and CD38+HLA-DR+ were significantly higher in ME/CFS than CF. The percentage of CD19+ cells and the CD4+/CD8+ ratio were significantly lower in ME/CFS and CF than in controls. There were highly significant inverse correlations between the increased expression of CD38+, especially that of CD8+CD38+, and the lowered CD4+/CD8+ ratio and CD19+ expression. There were no significant associations between the flow cytometric results and severity or duration of illness and peripheral blood biomarkers of oxidative and nitrosative stress (O&NS, i.e. IgM responses to O&N modified epitopes), leaky gut (IgM or IgA responses to LPS of gut commensal bacteria), cytokines (interleukin-1, tumor necrosis factor-α), neopterin, lysozyme and autoimmune responses to serotonin. CONCLUSIONS: The results support that a) increased CD38 and HLA-DR expression on CD8+ T cells are biomarkers of ME/CFS; b) increased CD38 antigen expression may contribute to suppression of the CD4+/CD8+ ratio and CD19+ expression; c) there are different immune subgroups of ME/CFS patients, e.g. increased CD8+ activation marker expression versus inflammation or O&NS processes; and d) viral infections or reactivation may play a role in a some ME/CFS patients.
[No authors listed]		Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness.	Mil Med. 2015 Jul;180(7):721-3. doi: 10.7205/MILMED-D-15-00085.	
[No authors listed]		What's in a name? Systemic exertion intolerance disease.	Lancet. 2015 Feb 21;385(9969):663. doi: 10.1016/S0140-6736(15)60270-7. Epub 2015 Feb 20.	
[No authors listed]		US panel proposes new name and diagnostic criteria for chronic fatigue syndrome.	BMJ. 2015 Feb 16;350:h932. doi: 10.1136/bmj.h932.	
Committee on the Diagnostic Criteria for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome; Board on the Health of Select Populations; Institute of		Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness.	Washington (DC): National Academies Press (US); 2015 Feb.	Myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS) are serious, debilitating conditions that affect millions of people in the United States and around the world. ME/CFS can cause significant impairment and disability. Despite substantial efforts by researchers to better understand ME/CFS, there is no known cause or effective treatment. Diagnosing the disease remains a challenge, and patients often struggle with their illness for years before an identification is made. Some health care providers have been skeptical about the serious physiological — rather than psychological — nature of the illness. Once diagnosed, patients often complain of receiving hostility from their health care provider as well as being subjected to treatment strategies that exacerbate their symptoms. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome proposes new diagnostic clinical criteria

Medicine. Washington (DC): National Academies Press (US); 2015 Feb. The National Academies Collection: Reports funded by National Institutes of Health.				for ME/CFS and a new term for the illness — systemic exertion intolerance disease (SEID). According to this report, the term myalgic encephalomyelitis does not accurately describe this illness, and the term chronic fatigue syndrome can result in trivialization and stigmatization for patients afflicted with this illness. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome stresses that SEID is a medical — not a psychiatric or psychological — illness. This report lists the major symptoms of SEID and recommends a diagnostic process.One of the report's most important conclusions is that a thorough history, physical examination, and targeted work-up are necessary and often sufficient for diagnosis. The new criteria will allow a large percentage of undiagnosed patients to receive an accurate diagnosis and appropriate care. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome will be a valuable resource to promote the prompt diagnosis of patients with this complex, multisystem, and often devastating disorder; enhance public understanding; and provide a firm foundation for future improvements in diagnosis and treatment.
Acker H(1), Schmidt-Rathjens C(2), Acker T(3), Fandrey J(4), Ehleben W(5).	(1)Forschungsinstitut für Notfallmedizin und Gesundheit, Dortmund, Germany; Institute für Physiologie, Universität Duisburg-Essen, Essen, Germany. Electronic address: helmut.acker@uni-due.de.	Acupuncture-brain interactions as hypothesized by mood scale recordings.	Med Hypotheses. 2015 Sep;85(3):371-9. doi: 10.1016/j.mehy.2015.05.013. Epub 2015 May 22.	Mood expressions encompassing positive scales like "activity, elation, contemplation, calmness" and negative scales like "anger, excitement, depression, fatigue" were applied for introducing a new tool to assess the effects of acupuncture on brain structures. Traditional acupuncture points defined in the literature for their effects on task negative and task positive brain structures were applied to chronic disease patients supposed to have dominant negative mood scales. Burn-out syndrome (n=10) and female chronic pain patients (n=22) showed a significant improvement on positive mood scales and a decline in negative mood scales after 10 acupuncture sessions. We observed a direct effect of acupuncture on brain structures in 5 burn-out syndrome patients showing an immediate, fast suppression of unusual slow high amplitude EEG waves in response to acupuncture needle rotation. These EEG waves described here for the first time in awake patients disappeared after 10 sessions but gradually returned after 1-1.5 years without acupuncture. This was accompanied with deterioration of positive mood scales and a return to negative mood scales. Both male (n=16) and female chronic pain patients reported a significant decrease of pain intensity after 10 sessions. Female patients only, however, showed a linear correlation between initial pain intensity and pain relief as well as a linear correlation between changes in pain intensity and mood scales accompanied by a drop of their heart rate during the acupuncture sessions. We hypothesized that mood scale recordings are a sensitive and specific new tool to reveal individual acupuncture-brain interaction.
Aerenhouts D(1,)(2), Ickmans K(3,)(4,)(5), Clarys P(1), Zinzen E(2),	(1)a Department of Human Biometry and Biomechanics , and. (2)b Department of	Sleep characteristics, exercise capacity and physical activity in patients with chronic	Disabil Rehabil. 2015;37(22):2044-50. doi: 10.3109/09638288.2014.993093. Epub 2014 Dec 16.	PURPOSE: Unrefreshing sleep and lowered physical activity are commonly observed in chronic fatigue syndrome (CFS) patients, but how they might influence each other remains unexplored. Therefore, this study simultaneously examined the exercise capacity, sleep characteristics and physical activity in CFS patients. METHODS: Handgrip

Meersdom G(6), Lambrecht L(7), Nijs J(3,)(4,)(5).	Movement Education and Sports Training , Vrije Universiteit Brussel , Brussels , Belgium .	fatigue syndrome.		strength and cycle exercise capacity were assessed in 42 female CFS patients and 24 inactive control subjects. During four consecutive days and nights, energy expenditure, activity and sleep-wake pattern were objectively registered using a Sensewear Armband. RESULTS: Exercise capacity was significantly lower in CFS patients. In both groups VO2peak correlated with the time subjects were physically active. In CFS patients only, VO2peak correlated negatively with sleeping during the day whilst physical activity level and energy expenditure correlated negatively with sleep latency and lying awake at night. CONCLUSIONS: In the present study, CFS patients with higher VO2peak tend to sleep less over day. Occupation in physical activities was negatively associated with sleep latency and lying awake at night. Increased physical activity potentially has beneficial effects on sleep quality in CFS. However, a close monitoring of the effects of increasing physical activity is essential to avoid negative effects on the health status of patients. IMPLICATIONS FOR REHABILITATION: Female patients with chronic fatigue syndrome (CFS) have normal sleep latency and sleep efficiency, but sleep more and spent more time in bed as compared to healthy inactive women. Female CFS patients have lower exercise capacity, and a lower physical activity level as compared to healthy inactive women. CFS patients appear to be more sensitive for sleep quality (sleep latency and lying awake at night), which is associated with a low physical activity level.
Ajamian M(1), Cooperstock M(2), Wormser GP(3), Vernon SD(4), Alaedini A(5).	(1)Department of Medicine, Columbia University Medical Center, New York, NY, USA. aa819@columbia.edu.	Anti-neural antibody response in patients with post-treatment Lyme disease symptoms versus those with myalgic encephalomyelitis/chronic fatigue syndrome.	Brain Behav Immun. 2015 Aug;48:354-5. doi: 10.1016/j.bbi.2015.04.006 . Epub 2015 Apr 10.	
Alijotas-Reig J(1).	(1)Systemic Autoimmune Disease Unit, Department of Internal Medicine I, Vall d'Hebron UniversityHospital, Barcelona, Spain Faculty of Medicine, Universitat Autonoma, Barcelona, Spain 16297jar@comb.es jalijotas@vhebron.net .	Human adjuvant-related syndrome or autoimmune/inflammatory syndrome induced by adjuvants. Where have we come from? Where are we going? A proposal for new diagnostic criteria.	Lupus. 2015 Sep;24(10):1012-8. doi: 10.1177/0961203315579092. Epub 2015 Mar 25.	In 1964, Miyoshi reported a series of patients with diverse symptoms after receiving treatment with silicone or paraffin fillers. Miyoshi named this condition 'human adjuvant disease'. Since then, the literature has been flooded with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines, infection or other adjuvants such as silicone and other biomaterials. A new term - autoimmune/inflammatory syndrome induced by adjuvants--has recently been coined for a process that includes several clinical features previously described by Miyoshi plus other clinical and laboratory parameters related to exposure to diverse external stimuli. Disorders such as siliconosis, Gulf War syndrome, macrophagic myofasciitis syndrome, sick building syndrome and post-vaccination syndrome have been included in autoimmune/inflammatory syndrome induced by adjuvants. Disorders such as Spanish toxic oil syndrome and Ardystil syndrome could also be included. Furthermore, biomaterials other than silicone should also be considered as triggering factors for these adjuvant-related syndromes. New diagnostic criteria in this field have been

				proposed. Nevertheless, many of these criteria are too subjective, leading to some patients being diagnosed with chronic fatigue syndrome or other 'central sensitization syndromes'. Diagnostic criteria based only on objective clinical and laboratory data to be further discussed and validated are proposed herein.
Antcliff D(1), Campbell M(2), Woby S(3), Keeley P(4).	(1)D. Antcliff, PhD, BSc(Hons), MCSP, Physiotherapy Department, The Pennine Acute Hospitals NHS Trust, North Manchester General Hospital, Manchester, M8 5RB, United Kingdom	Assessing the Psychometric Properties of an Activity Pacing Questionnaire for Chronic Pain and Fatigue.	Phys Ther. 2015 Sep;95(9):1274-86. doi: 10.2522/ptj.20140405. Epub 2015 Apr 23.	BACKGROUND: Therapists frequently advise the use of activity pacing as a coping strategy to manage long-term conditions (eg, chronic low back pain, chronic widespread pain, chronic fatigue syndrome/myalgic encephalomyelitis). However, activity pacing has not been clearly operationalized, and there is a paucity of empirical evidence regarding pacing. This paucity of evidence may be partly due to the absence of a widely used pacing scale. To address the limitations of existing pacing scales, the 38-item Activity Pacing Questionnaire (APQ-38) was previously developed using the Delphi technique. OBJECTIVE: The aims of this study were: (1) to explore the psychometric properties of the APQ-38, (2) to identify underlying pacing themes, and (3) to assess the reliability and validity of the scale. DESIGN: This was a cross-sectional questionnaire study. METHODS: Three hundred eleven adult patients with chronic pain or fatigue participated, of whom 69 completed the test-retest analysis. Data obtained for the APQ-38 were analyzed using exploratory factor analysis, internal and test-retest reliability, and validity against 2 existing pacing subscales and validated measures of pain, fatigue, anxiety, depression, avoidance, and mental and physical function. RESULTS: Following factor analysis, 12 items were removed from the APQ-38, and 5 themes of pacing were identified in the resulting 26-item Activity Pacing Questionnaire (APQ-26): activity adjustment, activity consistency, activity progression, activity planning, and activity acceptance. These themes demonstrated satisfactory internal consistency (Cronbach α=.72-.92), test-retest reliability (intraclass correlation coefficient=.50-.78, P≤.001), and construct validity. Activity adjustment, activity progression, and activity acceptance correlated with worsened symptoms; activity consistency correlated with improved symptoms; and activity planning correlated with both improved and worsened symptoms. LIMITATIONS: Data were collected from self-report questionnaires only. CONCLUSIONS: Developed to be widely used across a heterogeneous group of patients with chronic pain or fatigue, the APQ-26 is multifaceted and demonstrates reliability and validity. Further study will explore the effects of pacing on patients' symptoms to guide therapists toward advising pacing themes with empirical benefits.
Antcliff D(1), Keeley P(2), Campbell M(3), Woby S(4),	The Pennine Acute Hospitals NHS Trust, Physiotherapy Department, Nr	Exploring patients' opinions of activity pacing and a new activity pacing questionnaire for chronic	Physiotherapy. 2015 Aug 19. pii: S0031-9406(15)03811-0. doi: 10.1016/j.physio.2015.08.	OBJECTIVE: Despite the frequent recommendation of activity pacing as a coping strategy for patients with chronic pain and/or fatigue, pacing is interpreted in different ways and there is an absence of a widely accepted pacing scale. We have developed a new Activity Pacing Questionnaire (APQ). The aims of this study were to explore

McGowan L(5).	Manchester General Hospital, Manchester	pain and/or fatigue: a qualitative study.	001. [Epub ahead of print]	patients' views and beliefs about the concept of pacing, together with the acceptability of the APQ. DESIGN: Qualitative pragmatic study using semi-structured telephone interviews. Data were analysed using Framework analysis. PARTICIPANTS: 16 adult patients attending secondary care physiotherapy out-patient departments were recruited via purposive sampling. Diagnoses included chronic low back pain, chronic widespread pain, fibromyalgia and chronic fatigue syndrome/myalgic encephalomyelitis. FINDINGS: Pacing emerged as a multifaceted concept from participants' descriptions. The implementation of pacing was influenced by participants' age, the presence of co-morbidities and participants' emotions. The APQ was found to be generally acceptable in comparison to two existing pacing subscales. Participants undertook activities using quota/symptom-contingent approaches. Four behavioural typologies emerged: Task avoidance, Task persistence, Task fluctuation (boom-bust) and Task modification (activity pacing). CONCLUSIONS: The APQ appears to be easy to complete, and acceptable to patients who are attending physiotherapy for the management of long-term conditions. It emerged that individual patients implemented different pacing facets to varying degrees, and that different behavioural typologies were apparent. The relationships between behavioural typologies and facets of pacing warrant further investigation to facilitate the development of effective tailored pacing interventions.
Argento AC(1), Wolfe CR, Wahidi MM, Shofer SL, Mahmood K.	(1)1 Interventional Pulmonology, Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, Emory University, Atlanta, Georgia	Bronchomediastinal fistula caused by endobronchial aspergilloma.	Ann Am Thorac Soc. 2015 Jan;12(1):91-5. doi: 10.1513/AnnalsATS.201406-247BC.	RATIONALE: Endobronchial aspergilloma is a rare condition affecting immunocompromised patients. We present three cases resulting in airway fistulae. CASE PRESENTATIONS: A 68-year-old male with orthotopic heart transplantation presented with fatigue, cough, and dyspnea. A computerized tomography (CT) scan of the chest and bronchoscopy revealed an endobronchial right mainstem mass and airway fistula to the mediastinum. The mass was debrided and biopsy showed Aspergillus fumigatus. He was treated with antifungals and recovered. A 52-year-old male with acquired immunodeficiency syndrome presented with cough, dyspnea, and hypoxemia. Chest CT showed a bronchus intermedius mass and fistula to the mediastinum. Bronchoscopy revealed a necrotic endobronchial mass and pseudomembranes and confirmed the presence of a fistula. The mass was resected bronchoscopically and Aspergillus fumigatus was isolated. He was treated with antifungals and the fistula healed. A 63-year-old male with chronic lymphoid leukemia was admitted for dyspnea, cough, weakness, and dysphagia. Chest CT and bronchoscopy showed a mass causing obstruction of the subglottic trachea and a fistula to the mediastinum. Biopsy showed Aspergillus fumigatus and he was treated with antifungals. The sinus healed but the patient died of leukemia. MAIN RESULTS: Risk factors for airway aspergilloma include immune deficiency, mucosal damage, and ischemia. We report airway fistula formation as a complication of this infection, which has not been previously emphasized. CONCLUSIONS: Endobronchial aspergillomas may form fistulae to the mediastinum. Aggressive treatment with antifungals and

				bronchoscopic interventions are required.
Arnold LM(1), Blom TJ(2), Welge JA(2), Mariutto E(3), Heller A(3).	(1)Women's Health Research Program, Department of Psychiatry and Behavioral Neuroscience, University of Cincinnati College of Medicine, Cincinnati, OH. Electronic address: Lesley.Arnold@uc.edu .	A randomized, placebo-controlled, double-blinded trial of duloxetine in the treatment of general fatigue in patients with chronic fatigue syndrome.	Psychosomatics. 2015 May-Jun;56(3):242-53. doi: 10.1016/j.psym.2014.12.003. Epub 2014 Dec 16.	OBJECTIVE: To assess the efficacy and safety of duloxetine in patients with chronic fatigue syndrome. METHODS: A 12-week, randomized, double-blind study was designed to compare duloxetine 60-120 mg/d (n = 30) with placebo (n = 30) for efficacy and safety in the treatment of patients with chronic fatigue syndrome. The primary outcome measure was the Multidimensional Fatigue Inventory general fatigue subscale (range: 4-20, with higher scores indicating greater fatigue). Secondary measures were the remaining Multidimensional Fatigue Inventory subscales, Brief Pain Inventory, Medical Outcomes Study Short Form-36, Hospital Anxiety and Depression Scale, Centers for Disease Control and Prevention Symptom Inventory, Patient Global Impression of Improvement, and Clinical Global Impression of Severity. The primary analysis of efficacy for continuous variables was a longitudinal analysis of the intent-to-treat sample, with treatment-by-time interaction as the measure of effect. RESULTS: The improvement in the Multidimensional Fatigue Inventory general fatigue scores for the duloxetine group was not significantly greater than for the placebo group (P = 0.23; estimated difference between groups at week 12 = -1.0 [95% CI: -2.8, 0.7]). The duloxetine group was significantly superior to the placebo group on the Multidimensional Fatigue Inventory mental fatigue score, Brief Pain Inventory average pain severity and interference scores, Short Form-36 bodily pain domain, and Clinical Global Impression of Severity score. Duloxetine was generally well tolerated. CONCLUSION: The primary efficacy measure of general fatigue did not significantly improve with duloxetine when compared with placebo. Significant improvement in secondary measures of mental fatigue, pain, and global measure of severity suggests that duloxetine may be efficacious for some chronic fatigue syndrome symptom domains, but larger controlled trials are needed to confirm these results.
Asprusten TT(1), Fagermoen E, Sulheim D, Skovlund E, Sørensen Ø, Mollnes TE, Wyller VB.	(1)Division of Medicine and Laboratory Sciences, Medical Faculty, University of Oslo, Oslo, Norway.	Study findings challenge the content validity of the Canadian Consensus Criteria for adolescent chronic fatigue syndrome.	Acta Paediatr. 2015 May;104(5):498-503. doi: 10.1111/apa.12950. Epub 2015 Mar 23.	AIM: The 2003 Canadian Consensus Criteria for chronic fatigue syndrome (CFS) are often assumed to suggest low-grade systemic inflammation, but have never been formally validated. This study explored the content validity of the Criteria in a sample of adolescents with CFS selected according to a wide case definition. METHODS: A total of 120 patients with CFS with a mean age of 15.4 years (range 12-18 years) included in the NorCAPITAL project were post hoc subgrouped according to the Canadian Consensus Criteria. Those who satisfied the criteria (Criteria positive) and those who did not (Criteria negative) were compared across a wide range of disease markers and markers of prognosis. RESULTS: A total of 46 patients were classified as Criteria positive, 69 were classified as Criteria negative, and five could not be classified. All disease markers were equal across the two groups, except the digit span backward test of cognitive function, which showed poorer performance in the Criteria-positive group. Also, the prognosis over a 30-week period was equal between the groups. CONCLUSION: This study questions the content validity of the Canadian Consensus Criteria, as few differences were found between adolescent patients with CFS who did and did not

				satisfy the Criteria.
Attard L(1), Bonvicini F(2), Gelsomino F(3), Manfredi R(1), Cascavilla A(1), Viale P(1), Varani S(3), Gallinella G(4).	(1)University of Bologna, Department of Medicine and Surgery, Division of Infectious Diseases, S.Orsola-Malpighi Hospital, Bologna, Italy. giorgio.gallinella@unibo.it.	Paradoxical response to intravenous immunoglobulin in a case of Parvovirus B19-associated chronic fatigue syndrome.	J Clin Virol. 2015 Jan;62:54-7. doi: 10.1016/j.jcv.2014.11.021. Epub 2014 Nov 22.	We describe a case of chronic fatigue syndrome (CFS) associated to Parvovirus B19 infection where administration of intravenous immunoglobulins (IVIG), previously reported as effective, induced a paradoxical clinical response and increased viral replication. The indication of IVIG administration in the treatment of Parvovirus B19-associated CFS should be carefully reconsidered.
Baday M(1), Calamak S(1), Durmus NG(2,)(3), Davis RW(2,)(3,)(4), Steinmetz LM(3,)(4), Demirci U(1).	(1)Canary Center at Stanford for Cancer Early Detection, Radiology Department, School of Medicine, Stanford University, CA, 94304, USA.	Integrating Cell Phone Imaging with Magnetic Levitation (i-LEV) for Label-Free Blood Analysis at the Point-of-Living.	Small. 2015 Nov 2. doi: 10.1002/smll.201501845. [Epub ahead of print]	There is an emerging need for portable, robust, inexpensive, and easy-to-use disease diagnosis and prognosis monitoring platforms to share health information at the point-of-living, including clinical and home settings. Recent advances in digital health technologies have improved early diagnosis, drug treatment, and personalized medicine. Smartphones with high-resolution cameras and high data processing power enable intriguing biomedical applications when integrated with diagnostic devices. Further, these devices have immense potential to contribute to public health in resource-limited settings where there is a particular need for portable, rapid, label-free, easy-to-use, and affordable biomedical devices to diagnose and continuously monitor patients for precision medicine, especially those suffering from rare diseases, such as sickle cell anemia, thalassemia, and chronic fatigue syndrome. Here, a magnetic levitation-based diagnosis system is presented in which different cell types (i.e., white and red blood cells) are levitated in a magnetic gradient and separated due to their unique densities. Moreover, an easy-to-use, smartphone incorporated levitation system for cell analysis is introduced. Using our portable imaging magnetic levitation (i-LEV) system, it is shown that white and red blood cells can be identified and cell numbers can be quantified without using any labels. In addition, cells levitated in i-LEV can be distinguished at single-cell resolution, potentially enabling diagnosis and monitoring, as well as clinical and research applications.
Baj A(1), Colombo M(1), Headley JL(2), McFarlane JR(3), Liethof MA(4), Toniolo A(5).	(1)Laboratory of Clinical Microbiology, University of Insubria Medical School, Viale Borri 57, 21100 Varese, Italy. antonio.toniolo@uninsubria.it.	Post-poliomyelitis syndrome as a possible viral disease.	Int J Infect Dis. 2015 Jun;35:107-16. doi: 10.1016/j.ijid.2015.04.018. Epub 2015 May 1.	This review summarizes current concepts on post-polio syndrome (PPS), a condition that may arise in polio survivors after partial or complete functional recovery followed by a prolonged interval of stable neurological function. PPS affects 15-20 million people worldwide. Epidemiological data are reported, together with the pathogenic pathways that possibly lead to the progressive degeneration and loss of neuromuscular motor units. As a consequence of PPS, polio survivors experience new weakness, generalized fatigue, atrophy of previously unaffected muscles, and a physical decline that may culminate in the loss of independent life. Emphasis is given to the possible pathogenic role of persistent poliovirus infection and chronic inflammation. These factors could contribute to the neurological and physical decline in polio survivors. A perspective is

				then given on novel anti-poliovirus compounds and monoclonal antibodies that have been developed to contribute to the final phases of polio eradication. These agents could also be useful for the treatment or prevention of PPS. Some of these compounds/antibodies are in early clinical development. Finally, current clinical trials for PPS are reported. In this area, the intravenous infusion of normal human immunoglobulins appears both feasible and promising.
Band R(1), Wearden A(1), Barrowclough C(1).	School of Psychological Sciences & Manchester Centre for Health Psychology, University of Manchester.	Patient Outcomes in Association With Significant Other Responses to Chronic Fatigue Syndrome: A Systematic Review of the Literature.	Clin Psychol (New York). 2015 Mar;22(1):29-46. Epub 2015 Mar 14.	Social processes have been suggested as important in the maintenance of chronic fatigue syndrome (also known as myalgic encephalomyelitis; CFS/ME), but the specific role of close interpersonal relationships remains unclear. We reviewed 14 articles investigating significant other responses to close others with CFS/ME and the relationships between these responses and patient outcomes. Significant other beliefs attributing patient responsibility for the onset and ongoing symptoms of CFS/ME were associated with increased patient distress. Increased symptom severity, disability, and distress were also associated with both solicitous and negative significant other responses. Specific aspects of dyadic relationship quality, including high Expressed Emotion, were identified as important. We propose extending current theoretical models of CFS/ME to include two potential perpetuating interpersonal processes; the evidence reviewed suggests that the development of significant other-focused interventions may also be beneficial.
Band R(1,)(2), Barrowclough C(1), Emsley R(3), Machin M(4), Wearden AJ(1).	School of Psychological Sciences & Manchester Centre for Health Psychology, University of Manchester, UK.	Significant other behavioural responses and patient chronic fatigue syndrome symptom fluctuations in the context of daily life: An experience sampling study.	Br J Health Psychol. 2015 Dec 24. doi: 10.1111/bjhp.12179. [Epub ahead of print]	OBJECTIVE: Significant other responses to patients' symptoms are important for patient illness outcomes in chronic fatigue syndrome (CFS/ME); negative responses have been associated with increased patient depression, whilst increased disability and fatigue have been associated with solicitous significant other responses. The current study aimed to examine the relationship between significant other responses and patient outcomes within the context of daily life. DESIGN: Experience Sampling Methodology (ESM). METHOD: Twenty-three patients with CFS/ME and their significant others were recruited from specialist CFS/ME services. Sixty momentary assessments, delivered using individual San Francisco Android Smartphones, were conducted over a period of 6 days. All participants reported on affect, dyadic contact, and significant other responses to the patient. Patients reported on symptom severity, disability, and activity management strategies. RESULTS: Negative significant other responses were associated with increased patient symptom severity and distress reported at the same momentary assessment; there was evidence of a potentially mediating role of concurrent distress on symptom severity. Patient-perceived solicitous responses were associated with reduced patient activity and disability reported at the same momentary assessment. Lagged analyses indicate that momentary associations between significant other responses and patient outcomes are largely transitory; significant other responses were not associated with any of the patient outcomes at the subsequent assessment. CONCLUSION: The results indicate that significant other responses are important influences on the day-to-day experience of CFS/ME. Further research examining patient

				outcomes in association with specific significant other behavioural responses is warranted and future interventions that target such significant other behaviours may be beneficial. Statement of contribution What is already known on this subject? The existing literature has identified that significant other responses are important with respect to patient outcomes in CFS/ME. In particular, when examined cross-sectionally and longitudinally, negative and solicitous significant other responses are associated with poorer illness outcomes. This study is the first to examine the momentary associations between negative and solicitous responses, as reported by the patient and significant other, and patient-reported outcomes. An ESM paradigm was used to assess these temporal relationships within the context of participants' daily life. What does this study add? Negative responses were associated with increased momentary patient distress and symptoms. Perceived solicitousness was associated with activity limitation but less perceived disability. The impact of significant other responses on patient outcomes was found to be transitory.
Barbour AG(1).	(1)Departments of Medicine and Microbiology & Molecular Genetics, University of California, Irvine.	"Lyme": Chronic Fatigue Syndrome by Another Name?	Clin Infect Dis. 2016 Jan 1;62(1):134-5. doi: 10.1093/cid/civ699. Epub 2015 Aug 12.	
Barnden LR(1), Crouch B, Kwiatek R, Burnet R, Del Fante P.	(1)Department of Nuclear Medicine, The Queen Elizabeth Hospital, Woodville, SA, Australia; School of Chemistry and Physics, University of Adelaide, Adelaide, SA, Australia; National Centre for NeuroImmunology and Emerging Diseases, Griffith University, Gold Coast, Qld, Australia.	Evidence in chronic fatigue syndrome for severity-dependent upregulation of prefrontal myelination that is independent of anxiety and depression.	NMR Biomed. 2015 Mar;28(3):404-13. doi: 10.1002/nbm.3261.	White matter (WM) involvement in chronic fatigue syndrome (CFS) was assessed using voxel-based regressions of brain MRI against CFS severity scores and CFS duration in 25 subjects with CFS and 25 normal controls (NCs). As well as voxel-based morphometry, a novel voxel-based quantitative analysis of T1 - and T2 -weighted spin-echo (T1w and T2w) MRI signal level was performed. Severity scores included the Bell CFS disability scale and scores based on the 10 most common CFS symptoms. Hospital Anxiety and Depression Scale (HADS) depression and anxiety scores were included as nuisance covariates. By relaxing the threshold for cluster formation, we showed that the T1w signal is elevated with increasing CFS severity in the ventrolateral thalamus, internal capsule and prefrontal WM. Earlier reports of WM volume losses and neuroinflammation in the midbrain, together with the upregulated prefrontal myelination suggested here, are consistent with the midbrain changes being associated with impaired nerve conduction which stimulates a plastic response on the cortical side of the thalamic relay in the same circuits. The T2w signal versus CFS duration and comparison of T2w signal in the CFS group with the NC group revealed changes in the right middle temporal lobe WM, where impaired communication can affect cognitive function. Adjustment for depression markedly strengthened cluster statistics and increased cluster size in both T1w severity regressions, but adjustment for anxiety less so. Thus, depression and anxiety are statistical confounders here, meaning that they

				contribute variance to the T1w signal in prefrontal WM but this does not correlate with the co-located variance from CFS severity. MRI regressions with depression itself only detected associations with WM volume, also located in prefrontal WM. We propose that impaired reciprocal brain-body and brain-brain communication through the midbrain provokes peripheral and central responses which contribute to CFS symptoms. Although anxiety, depression and CFS may share biological features, the present evidence indicates that CFS is a distinct disorder.
Bauer AE(1), Olivas S(2), Cooper M(3), Hornstra H(4), Keim P(5), Pearson T(6), Johnson AJ(7,)(8).	(1)Department of Comparative Pathobiology, College of Veterinary Medicine, Purdue University, West Lafayette, IN, USA. bauer20@purdue.edu.	Estimated herd prevalence and sequence types of Coxiella burnetii in bulk tank milk samples from commercial dairies in Indiana.	BMC Vet Res. 2015 Aug 7;11:186. doi: 10.1186/s12917-015-0517-3.	BACKGROUND: Coxiella burnetii is the etiologic agent of Q fever, a zoonotic disease causing influenza-like illness, pregnancy loss, cardiovascular disease and chronic fatigue syndrome in people. C. burnetii is considered to be enzootic in ruminants, but clinical signs of infection do not always manifest. National studies have documented the presence of C. burnetii in dairy herds in Indiana. This represents an opportunity to better characterize the distribution and prevalence of C. burnetii infection at the state scale, allowing evaluation of the need for surveillance and response planning to occur at this level. A cross-sectional study was conducted to estimate the herd prevalence of C. burnetii in commercial cattle dairies in Indiana and characterize the strains of C. burnetii within these dairies. RESULTS: Bulk tank milk samples were collected between June and August of 2011 by the Indiana State Board of Animal Health (ISBOAH). A total of 316 of these samples were tested for the IS1111 transposon of C. burnetii using quantitative real time polymerase chain reaction (PCR). Single nucleotide polymorphism (SNP) genotyping was used to identify the multispacer sequence genotypes (ST) present in samples where the IS1111 transposon was identified. The geographic distribution of dairies testing positive for C. burnetii DNA and the identified STs were also evaluated. The estimated overall herd prevalence for C. burnetii DNA was 61.1 % (95 % CI 55.6-66.3 %). The highest estimated regional prevalence was 70.2 % in the Central region of Indiana. An ST was identifiable in 74 of the positive 178 samples (41.6 %) and none of the 10 negative samples tested. Of these samples, 71 (95.9 %) were identified as ST20, 2 (2.7 %) as ST8 and a combination of ST20 and ST8 was identified in a single sample. CONCLUSIONS: C. burnetii is present in dairy herds throughout Indiana. Indiana follows national trends with ST20 most commonly identified. The presence of multiple STs in a single bulk tank sample indicates that multiple strains of C. burnetii can circulate within a herd. This supports potential transmission of C. burnetii between goats and cattle, presenting the potential for a switch in the dominant genotype found in a given species.
Baumann FT(1), Hallek M(2), Meyer J(1), Galvão DA(3), Bloch W(1), Elter T(2).	(1)Abteilung Molekulare und Zelluläre Sportmedizin, Institut für Kreislaufforschung und Sportmedizin,	[Evidence and recommendations for oncologic clinical exercise - a personalized treatment concept for cancer patients].[Article in	Dtsch Med Wochenschr. 2015 Sep;140(19):1457-61. doi: 10.1055/s-0041-104465. Epub 2015 Sep 24.	Oncological treatments can lead to acute and chronic cancer related toxicities. In recent years, a large number of clinical studies have reported positive effects of exercise to the bio-psycho-social regeneration of cancer patients. However, very few evidence-based programs have been implemented into practice with little opportunity for cancer patients to engage in such programs. Reviews and RCT studies on exercise and cancer are showing that specific exercise programs have a positive impact on fatigue

	Deutsche Sporthochschule Köln. (2)Klinik I für Innere Medizin der Universitätsklinik zu Köln. (3)Edith Cowan University Health and Wellness Institute, Joondalup, WA, Australia.	German]		syndrome, urinary incontinence, lymphedema, polyneuropathy, arthralgia, and androgen deprivation related toxicities. With the increasing evidence for exercise oncology interventions, recommendations arising from clinical trials should be translated into clinical practice and this should be viewed as an important next step in this fast moving field of exercise oncology. For that the personalized treatment concept "Oncologic clinical exercise" (OTT) was developed.
Bağdatlı AO(1), Donmez A(2), Eröksüz R(3), Bahadır G(4), Turan M(5), Erdoğan N(3).	(1)Optimed Medical Center, Department of Physical Therapy and Rehabilitation, Salih Omurtak Caddesi No. 58, Çorlu, Tekirdağ, Turkey.	Does addition of 'mud-pack and hot pool treatment' to patient education make a difference in fibromyalgia patients? A randomized controlled single blind study.	Int J Biometeorol. 2015 Dec;59(12):1905-11. doi: 10.1007/s00484-015-0997-7. Epub 2015 Apr 28.	The aim of this randomized controlled single-blind study is to explore whether addition of mud-pack and hot pool treatments to patient education make a significant difference in short and mild term outcomes of the patients with fibromyalgia. Seventy women with fibromyalgia syndrome were randomly assigned to either balneotherapy with mud-pack and hot pool treatments (35) or control (35) groups. After randomization, five patients from balneotherapy group and five patients from control group were dropped out from the study with different excuses. All patients had 6-h patient education programme about fibromyalgia syndrome and were given a home exercise programme. The patients in balneotherapy group had heated pool treatment at 38 °C for 20 min a day, and mud-pack treatment afterwards on back region at 45 °C. Balneotherapy was applied on weekdays for 2 weeks. All patients continued to take their medical treatment. An investigator who was blinded to the intervention assessed all the patients before and after the treatment, at the first and the third months of follow-up. Outcome measures were FIQ, BDI and both patient's and physician's global assessments. Balneotherapy group was significantly better than control group at after the treatment and at the end of the first month follow-up assessments in terms of patient's and physician's global assessment, total FIQ score, and pain intensity, fatigue, non-refreshed awaking, stiffness, anxiety and depression subscales of FIQ. No significant difference was found between the groups in terms of BDI scores. It is concluded that patient education combined with 2 weeks balneotherapy application has more beneficial effects in patients with fibromyalgia syndrome as compared to patient education alone.
Belcaro G(1), Cornelli U, Luzzi R, Ledda A, Cacchio M, Saggino A, Cesarone MR, Dugall M,	(1)Irvine3 Circulation/Vascular Labs, Chieti‑Pescara University, Pescara, Italy, Irvine3 Circulaion Sciences Network.	Robuvit® (Quercus robur extract) supplementation in subjects with chronic fatigue syndrome and increased oxidative stress. A pilot registry study.	J Neurosurg Sci. 2015 Jun;59(2):105-17. Epub 2014 Nov 14.	AIM: The aim of this registry study was to evaluate the effects of supplementation with Robuvit® (French Quercus robur extract) capsules in subjects with Chronic Fatigue Syndrome (CFS) associated with an increased oxidative stress. Robuvit is a wood extract from Quercus robur (Horphag Research) used to improve liver dysfunction and chronic fatigue. After excluding any disease, subjects observed a defined management plan to improve CFS. Signs/symptoms had been present for more than 6 months in association with an increase in oxidative stress (measured as plasma free radicals). Blood tests

Feragalli B, Hu S, Pellegrini L, Ippolito E.				were within normal values. METHODS: The registry study included 38 CFS subjects and 42 comparable controls. There were no dropouts in the 4 weeks of follow-up; the subjects were evaluated for a further period of 6 months. The management plan included: improved/increased sleep; reduction/abolition in smoking and alcohol or any other agent that may have affected them; control of diet, increase in dietary proteins; good hydration; rest (1/2-1 h/day) and exercise (at least 30 min/day); planned relaxation time; increased time in open spaces. In the Robuvit® supplementation group 300 mg/day of Robuvit® was used. RESULTS: Symptoms improved in both groups with a significantly more important improvement in the supplement group (P<0.05). The single items in the Multidimensional Assessment of Fatigue (MAF) questionnaire were statistically better improved (P<0.05) in the supplement group. A parallel improvement in oxidative stress was observed in the supplemented subjects. In the follow up, at 6 months no organic disease was discovered or disease markers found. CONCLUSION: This preliminary registry indicates that supplementation with Robuvit® improves CFS in otherwise healthy subjects with no presence of clinical disease or risk conditions. The effects of Robuvit® in CFS may be partially mediated by a clear reduction of plasma free radicals and oxidative stress.
Bested AC, Marshall LM.		Review of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: an evidence-based approach to diagnosis and management by clinicians.	Rev Environ Health. 2015 Dec 1;30(4):223-49. doi: 10.1515/reveh-2015-0026.	This review was written from the viewpoint of the treating clinician to educate health care professionals and the public about Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). It includes: the clinical definition of ME/CFS with emphasis on how to diagnose ME/CFS; the etiology, pathophysiology, management approach, long-term prognosis and economic cost of ME/CFS. After reading this review, you will be better able to diagnose and treat your patients with ME/CFS using the tools and information provided. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a complex, chronic medical condition characterized by symptom clusters that include: pathological fatigue and malaise that is worse after exertion, cognitive dysfunction, immune dysfunction, unrefreshing sleep, pain, autonomic dysfunction, neuroendocrine and immune symptoms. ME/CFS is common, often severely disabling and costly. The Institute of Medicine (IOM) reviewed the ME/CFS literature and estimates that between 836,000 and 2.5 million Americans have ME/CFS at a cost of between 17 and 24 billion dollars annually in the US. The IOM suggested a new name for ME/CFS and called it Systemic Exertion Intolerance Disease (SEID). SEID's diagnostic criteria are less specific and do not exclude psychiatric disorders in the criteria. The 2010 Canadian Community Health Survey discovered that 29% of patients with ME/CFS had unmet health care needs and 20% had food insecurity - lack of access to sufficient healthy foods. ME/CFS can be severely disabling and cause patients to be bedridden. Yet most patients (80%) struggle to get a diagnosis because doctors have not been taught how to diagnose or treat ME/CFS in medical schools or in their post-graduate educational training. Consequently, the patients with ME/CFS suffer. They are not diagnosed with ME/CFS and are not treated accordingly. Instead of compassionate care from their

				doctors, they are often ridiculed by the very people from whom they seek help. The precise etiology of ME/CFS remains unknown, but recent advances and research discoveries are beginning to shed light on the enigma of this disease including the following contributors: infectious, genetic, immune, cognitive including sleep, metabolic and biochemical abnormalities. Management of patients with ME/CFS is supportive symptomatic treatment with a patient centered care approach that begins with the symptoms that are most troublesome for the patient. Pacing of activities with strategic rest periods is, in our opinion, the most important coping strategy patients can learn to better manage their illness and stop their post-exertional fatigue and malaise. Pacing allows patients to regain the ability to plan activities and begin to make slow incremental improvements in functionality.
Bhattacharjee M(1), Rajeevan MS(2), Sillanpää MJ(3).	(1)School of Mathematics and Statistics, University of Hyderabad, Hyderabad, 500046, India. mbsm@uohyd.ernet.in.	Prediction of complex human diseases from pathway-focused candidate markers by joint estimation of marker effects: case of chronic fatigue syndrome.	Hum Genomics. 2015 Jun 11;9:8. doi: 10.1186/s40246-015-0030-6.	BACKGROUND: The current practice of using only a few strongly associated genetic markers in regression models results in generally low power in prediction or accounting for heritability of complex human traits. PURPOSE: We illustrate here a Bayesian joint estimation of single nucleotide polymorphism (SNP) effects principle to improve prediction of phenotype status from pathway-focused sets of SNPs. Chronic fatigue syndrome (CFS), a complex disease of unknown etiology with no laboratory methods for diagnosis, was chosen to demonstrate the power of this Bayesian method. For CFS, such a genetic predictive model in combination with clinical evidence might lead to an earlier diagnosis than one based solely on clinical findings. METHODS: One of our goals is to model disease status using Bayesian statistics which perform variable selection and parameter estimation simultaneously and which can induce the sparseness and smoothness of the SNP effects. Smoothness of the SNP effects is obtained by explicit modeling of the covariance structure of the SNP effects. RESULTS: The Bayesian model achieved perfect goodness of fit when tested within the sampled data. Tenfold cross-validation resulted in 80% accuracy, one of the best so far for CFS in comparison to previous prediction models. Model reduction aspects were investigated in a computationally feasible manner. Additionally, genetic variation estimates provided by the model identified specific genetic markers for their biological role in the disease pathophysiology. CONCLUSIONS: This proof-of-principle study provides a powerful approach combining Bayesian methods, SNPs representing multiple pathways and rigorous case ascertainment for accurate genetic risk prediction modeling of complex diseases like CFS and other chronic diseases.
Binkiewicz-Glińska A(1), Bakuła S(1), Tomczak H(2), Landowski J(3), Ruckemann-Dziurdzińska K(4),	(1)Katedra Rehabilitacji GUMed w Gdańsku.	Fibromyalgia Syndrome - a multidisciplinary approach.	Psychiatr Pol. 2015;49(4):801-810. doi: 10.12740/psychiatriapolska.pl/online-first/4.	According to American College of Rheumatology fibromyalgia syndrome (FMS) is a common health problem characterized by widespread pain and tenderness. The pain and tenderness, although chronic, present a tendency to fluctuate both in intensity and location around the body. Patients with FMS experience fatigue and often have sleep disorders. It is estimated that FMS affects two to four percent of the general population. It is most common in women, though it can also occur in men. FMS most often first occur in the middle adulthood, but it can start as early as in the teen years or

Zaborowska-Sapeta K(5), Kowalski I(5), Kiebzak W(6).				in the old age. The causes of FMS are unclear. Various infectious agents have recently been linked with the development of FMS. Some genes are potentially linked with an increased risk of developing FMS and some other health problems, which are common comorbidities to FMS. It is the genes that determine individual sensitivity and reaction to pain, quality of the antinociceptive system and complex biochemistry of pain sensation. Diagnosis and therapy may be complex and require cooperation of many special- ists. Rheumatologists often make the diagnosis and differentiate FMS with other disorders from the rheumatoid group. FMS patients may also require help from the Psychiatric Clinic (Out-Patients Clinic) due to accompanying mental problems. As the pharmacological treatment options are limited and only complex therapy gives relatively good results, the treatment plan should include elements of physical therapy.
Blazquez A(1), Ruiz E, Aliste L, García-Quintana A, Alegre J.	(1)a Unit of CFS and Fibromyalgia, Vall Hebron Hospital, Internal Medicine , Barcelona , Spain.	The effect of fatigue and fibromyalgia on sexual dysfunction in women with chronic fatigue syndrome.	J Sex Marital Ther. 2015;41(1):1-10. doi: 10.1080/0092623X.2013.864370. Epub 2014 Mar 11.	Sexual dysfunction in patients with chronic fatigue syndrome is attracting growing interest but, to date, few studies have analyzed it. For this reason, the authors evaluated sexual dysfunction in women with chronic fatigue syndrome (using the Golombok Rust Inventory of Sexual Satisfaction) and explore correlations with fatigue and other symptoms. Sexual dysfunction was greater in patients with chronic fatigue syndrome (n = 615) with a higher number of cognitive, neurological, and neurovegetative symptoms, concomitant fibromyalgia, Sjögren's syndrome, or myofascial pain syndrome, and more intense fatigue (p <.05).
Bloot L(1), Heins MJ, Donders R, Bleijenberg G, Knoop H.	(1)*Expert Centre for Chronic Fatigue †Department for Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands.	The Process of Change in Pain During Cognitive-Behavior Therapy for Chronic Fatigue Syndrome.	Clin J Pain. 2015 Oct;31(10):914-21. doi: 10.1097/AJP.0000000000000191.	BACKGROUND: Cognitive-behavior therapy (CBT) leads to a reduction of fatigue and pain in chronic fatigue syndrome. The processes underlying the reduction in pain have not been investigated. Recently, it was shown that increased self-efficacy, decreased focusing on symptoms, increased physical functioning, and a change in beliefs about activity contribute to the decrease in fatigue. OBJECTIVES: The present study has 2 objectives: (1) to determine the relationship between the reduction of fatigue and pain during CBT; (2) test to what extent the model for change in fatigue is applicable to the reduction in pain. MATERIALS AND METHODS: One hundred forty-two patients meeting United States centers for Disease Control and Prevention criteria for chronic fatigue syndrome, currently reporting pain, and starting CBT were included. A cross-lagged analysis was performed to study the causal direction of change between pain and fatigue. Pain and process variables were assessed before therapy, 3 times during CBT, and after therapy. Actual physical activity was also assessed. The model was tested with multiple regression analyses. RESULTS: The direction of change between pain and fatigue could not be determined. An increase in physical functioning and decrease in focusing on symptoms explained 4% to 14% of the change in pain. CONCLUSIONS: Pain and fatigue most probably decrease simultaneously during CBT. Pain reduction can partly be explained by a reduction of symptom focusing and increased physical functioning. Additional, yet unknown cognitive-behavioral factors also play a role in the reduction of pain.
Blundell S(1), Ray	(1)Centre for	Chronic fatigue syndrome	Brain Behav Immun. 2015	There has been much interest in the role of the immune system in the pathophysiology

KK(2), Buckland M(3), White PD(4).	Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine, Queen Mary University of London, United Kingdom. (2)East London Foundation NHS Trust, London, United Kingdom. (3)Barts Health Trust, London, United Kingdom. (4)Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine, Queen Mary University of London, United Kingdom. Electronic address: p.d.white@qmul.ac.uk.	and circulating cytokines: A systematic review.	Nov;50:186-95. doi: 10.1016/j.bbi.2015.07.004. Epub 2015 Jul 3.	of chronic fatigue syndrome (CFS), as CFS may develop following an infection and cytokines are known to induce acute sickness behaviour, with similar symptoms to CFS. Using the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analyses) guidelines, a search was conducted on PubMed, Web of Science, Embase and PsycINFO, for CFS related-terms in combination with cytokine-related terms. Cases had to meet established criteria for CFS and be compared with healthy controls. Papers retrieved were assessed for both inclusionary criteria and quality. 38 papers met the inclusionary criteria. The quality of the studies varied. 77 serum or plasma cytokines were measured without immune stimulation. Cases of CFS had significantly elevated concentrations of transforming growth factor-beta (TGF-β) in five out of eight (63%) studies. No other cytokines were present in abnormal concentrations in the majority of studies, although insufficient data were available for some cytokines. Following physical exercise there were no differences in circulating cytokine levels between cases and controls and exercise made no difference to already elevated TGF-β concentrations. The finding of elevated TGF-β concentration, at biologically relevant levels, needs further exploration, but circulating cytokines do not seem to explain the core characteristic of post-exertional fatigue.
Boissoneault J(1), Letzen J(1), Lai S(2), O'Shea A(1), Craggs J(1), Robinson M(1), Staud R(3).	(1)Department of Clinical and Health Psychology, University of Florida. (2)Department of Radiation Oncology, and Human Imaging Core of Clinical and Translational Science Institute, University of Florida. (3)Department of Medicine, University	Abnormal resting state functional connectivity in patients with chronic fatigue syndrome: An arterial spin-labeling fMRI study.	Magn Reson Imaging. 2015 Dec 17. pii: S0730-725X(15)00303-3. doi: 10.1016/j.mri.2015.12.008. [Epub ahead of print]	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a debilitating disorder characterized by severe fatigue and neurocognitive dysfunction. Recent work from our laboratory and others utilizing arterial spin labeling functional magnetic resonance imaging (ASL) indicated that ME/CFS patients have lower resting state regional cerebral blood flow (rCBF) in several brain areas associated with memory, cognitive, affective, and motor function. This hypoperfusion may underlie ME/CFS pathogenesis and may result in alterations of functional relationships between brain regions. The current report used ASL to compare functional connectivity of regions implicated in ME/CFS between patients and healthy controls (HC). METHODS: Participants were 17 ME/CFS patients (Mage=48.88years, SD=12) fulfilling the 1994 CDC criteria and 17 age/sex matched HC (Mage=49.82years, SD=11.32). All participants underwent T1-weighted structural MRI as well as a 6-min pseudo-continuous arterial spin labeling (pCASL) sequence, which quantifies CBF by magnetically labeling blood as

	of Florida. Electronic address: staudr@ufl.edu.			it enters the brain. Imaging data were preprocessed using SPM 12 and ASL tbx, and seed-to-voxel functional connectivity analysis was conducted using the CONN toolbox. All effects noted below are significant at p<0.05 with cluster-wise FDR correction for multiple comparisons. RESULTS: ME/CFS patients demonstrated greater functional connectivity relative to HC in bilateral superior frontal gyrus, ACC, precuneus, and right angular gyrus to regions including precuneus, right postcentral gyrus, supplementary motor area, posterior cingulate gyrus, and thalamus. In contrast, HC patients had greater functional connectivity than ME/CFS in ACC, left parahippocampal gyrus, and bilateral pallidum to regions including right insula, right precentral gyrus, and hippocampus. Connectivity of the left parahippocampal gyrus correlated strongly with overall clinical fatigue of ME/CFS patients. CONCLUSION: This is the first ASL based connectivity analysis of patients with ME/CFS. Our results demonstrate altered functional connectivity of several regions associated with cognitive, affective, memory, and higher cognitive function in ME/CFS patients. Connectivity to memory related brain areas (para-hippocampal gyrus) was correlated with clinical fatigue ratings, providing supporting evidence that brain network abnormalities may contribute to ME/CFS pathogenesis.
Boles RG(1), Zaki EA(2), Kerr JR(3), Das K(2), Biswas S(2), Gardner A(4).	(1)Division of Medical Genetics and the Saban Research Institute, Children's Hospital Los Angeles, CA USA; Department of Pediatrics, Keck School of Medicine at the University of Southern California, Los Angeles, CA USA. Electronic address: richard.boles@courtagen.com.	Increased prevalence of two mitochondrial DNA polymorphisms in functional disease: Are we describing different parts of an energy-depleted elephant?	Mitochondrion. 2015 Jul;23:1-6. doi: 10.1016/j.mito.2015.04.005. Epub 2015 Apr 29.	About 20% of the population suffers from "functional syndromes". Since these syndromes overlap greatly in terms of co-morbidity, pathophysiology (including aberrant autonomic activity) and treatment responses, common predisposing genetic factors have been postulated. We had previously showed that two common mitochondrial DNA (mtDNA) polymorphisms at positions 16519 and 3010 are statistically associated with the functional syndromes of migraine, cyclic vomiting syndrome and non-specific abdominal pain. Herein, among individuals with mtDNA haplogroup H (HgH), the presence of these two mtDNA polymorphisms were ascertained in additional functional syndromes: chronic fatigue syndrome, complex regional pain syndrome, sudden infant death syndrome, and major depressive disorder. Polymorphic prevalence rates were compared between disease and control groups, and within each disease group in participants with and without specific clinical findings. In all four conditions, one or both of the polymorphisms was significantly associated with the respective condition and/or co-morbid functional symptomatology. Thus, we conclude that these two mtDNA polymorphisms likely modify risk for the development of multiple functional syndromes, likely constituting a proportion of the postulated common genetic factor, at least among individuals with HgH. Pathophysiology likely involves broad effects on the autonomic nervous system.
Boneva RS(1), Lin JM, Unger ER.	(1)From the Centers for Disease Control and Prevention, Atlanta, GA.	Early menopause and other gynecologic risk indicators for chronic fatigue syndrome in women.	Menopause. 2015 Aug;22(8):826-34. doi: 10.1097/GME.0000000000000411.	OBJECTIVE: This study aims to examine whether gynecologic conditions are associated with chronic fatigue syndrome (CFS). METHODS: This study includes a subset of 157 women from a population-based case-control study in Georgia, United States, conducted in 2004-2009. Gynecologic history was collected using a self-administered questionnaire. Crude odds ratios (ORs) with 95% CIs and ORs adjusted for body mass

				index and other covariates, where relevant, were estimated for gynecologic conditions between 84 CFS cases and 73 healthy controls. RESULTS: Cases and controls were of similar age. Women with CFS reported significantly more gynecologic conditions and surgical operations than controls: menopause status (61.9% vs 37.0%; OR, 2.37; 95% CI, 1.21-4.66), earlier mean age at menopause onset (37.6 vs 48.6 y; adjusted OR, 1.22; 95% CI, 1.09-1.36), excessive menstrual bleeding (73.8% vs 42.5%; adjusted OR, 3.33; 95% CI, 1.66-6.70), bleeding between periods (48.8% vs 23.3%; adjusted OR, 3.31; 95% CI, 1.60-6.86), endometriosis (29.8% vs 12.3%; adjusted OR, 3.67; 95% CI, 1.53-8.84), use of noncontraceptive hormonal preparations (57.1% vs 26.0%; adjusted OR, 2.95; 95% CI, 1.36-6.38), nonmenstrual pelvic pain (26.2% vs 2.7%; adjusted OR, 11.98; 95% CI, 2.57-55.81), and gynecologic surgical operation (65.5% vs 31.5%; adjusted OR, 3.33; 95% CI, 1.66-6.67), especially hysterectomy (54.8% vs 19.2%; adjusted OR, 3.23; 95% CI, 1.46-7.17). Hysterectomy and oophorectomy occurred at a significantly younger mean age in the CFS group than in controls and occurred before CFS onset in 71% of women with records of date of surgical operation and date of CFS onset. CONCLUSIONS: Menstrual abnormalities, endometriosis, pelvic pain, hysterectomy, and early/surgical menopause are all associated with CFS. Clinicians should be aware of the association between common gynecologic problems and CFS in women. Further work is warranted to determine whether these conditions contribute to the development and/or perpetuation of CFS in some women.
Boomershine CS(1).	(1)Medical Director, Boomershine Wellness Centers, PLC, 1195 Old Hickory Blvd, Suite 102, Brentwood, TN 37027, USA. fibromd@comcast.net.	Fibromyalgia: the prototypical central sensitivity syndrome.	Curr Rheumatol Rev. 2015;11(2):131-45.	Fibromyalgia syndrome (FM), the most common central sensitivity syndrome (CSS) affecting over 5% of the population, is a disorder of chronic widespread pain accompanied by numerous other symptoms that causes significant functional impairment. The core FM symptom domains can be recalled using the FIBRO mnemonic and include Fatigue and Fog (cognitive dysfunction), Insomnia (difficulties with all aspects of sleep including initiation, maintenance and restorative), Blues (depression and anxiety), Rigidity (stiffness in muscles and joints) and Ow! (widespread pain and tenderness). While typically presenting in middle-aged women, FM can affect both sexes at any age. FM is a syndrome of abnormal central pain processing and increased central sensitivity caused by neurobiological changes that cause dysregulation of mechanisms that normally regulate pain sensation. There are currently three different methods for diagnosing FM; the 1990, 2010 and modified 2010 American College of Rheumatology (ACR) criteria. While disabling, FM symptoms can be managed with a regimen of pharmacologic and nonpharmacologic treatments. Medication types with benefit in treating FM include anticonvulsants, antidepressants, anti-inflammatories, muscle relaxers, tramadol, and stimulants. Beneficial nonpharmacologic therapies include aerobic and resistance exercise, stretching, cognitive behavioral therapy, and education. Effective management requires formulation of an individualized regimen since patients differ widely in symptoms and treatments they find beneficial. Such an individualized regimen should be based on a systematic assessment of problematic

				symptoms conducted at baseline and each follow-up with treatments modified over time. While challenging, FM symptoms can be effectively managed and patients can lead full, productive lives.
Borchers AT(1), Gershwin ME(2).	(1)Division of Rheumatology, Allergy and Clinical Immunology, University of California at Davis School of Medicine, 451 Health Sciences Drive, Suite 6510, Davis, CA, 95616, USA.	Fibromyalgia: A Critical and Comprehensive Review.	Clin Rev Allergy Immunol. 2015 Oct;49(2):100-51. doi: 10.1007/s12016-015-8509-4.	Fibromyalgia is a disorder that is part of a spectrum of syndromes that lack precise classification. It is often considered as part of the global overview of functional somatic syndromes that are otherwise medically unexplained or part of a somatization disorder. Patients with fibromyalgia share symptoms with other functional somatic problems, including issues of myalgias, arthralgias, fatigue and sleep disturbances. Indeed, there is often diagnostic and classification overlap for the case definitions of a variety of somatization disorders. Fibromyalgia, however, is a critically important syndrome for physicians and scientists to be aware of. Patients should be taken very seriously and provided optimal care. Although inflammatory, infectious, and autoimmune disorders have all been ascribed to be etiological events in the development of fibromyalgia, there is very little data to support such a thesis. Many of these disorders are associated with depression and anxiety and may even be part of what has been sometimes called affected spectrum disorders. There is no evidence that physical trauma, i.e., automobile accidents, is associated with the development or exacerbation of fibromyalgia. Treatment should be placed on education, patient support, physical therapy, nutrition, and exercise, including the use of drugs that are approved for the treatment of fibromyalgia. Treatment should not include opiates and patients should not become poly pharmacies in which the treatment itself can lead to significant morbidities. Patients with fibromyalgia are living and not dying of this disorder and positive outlooks and family support are key elements in the management of patients.
Bourke J(1).	(1)Centre for Psychiatry at The Wolfson Institute for Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, UK.	Fibromyalgia and chronic fatigue syndrome: management issues.	Adv Psychosom Med. 2015;34:78-91. doi: 10.1159/000369087. Epub 2015 Mar 30.	Fibromyalgia and chronic fatigue syndrome represent two of the most commonly encountered functional somatic syndromes in clinical practice. Both have been contentious diagnoses in the past, and this diagnostic dispute has resulted in a therapeutic nihilism that has been of great detriment to their management and to alleviation of the intense suffering and disability that they have caused their innumerable sufferers. A new age has dawned in terms of a better understanding of these syndromes' physiology and improved approaches to their management. Here, the diagnosis and management of these closely related disorders are discussed, with particular reference to the recent empirical evidence that has come to light as a consequence of neurophysiological insights and robustly designed randomised clinical trials. Much work remains to be done in this vein, but we are better placed to facilitate recovery from these disorders than we have been previously. Whilst remission should always be a goal, complete symptom resolution is not the norm, but 'moderate' improvements are certainly attainable with appropriate management.
Brinth LS(1), Pors K(1), Theibel AC(1), Mehlsen	(1)Coordinating Research Centre, Frederiksberg	Orthostatic intolerance and postural tachycardia syndrome as suspected	Vaccine. 2015 May 21;33(22):2602-5. doi: 10.1016/j.vaccine.2015.03	BACKGROUND: Infections with human papilloma virus (HPV) can result in cervical, oropharyngeal, anal, and penile cancer and vaccination programs have been launched in many countries as a preventive measure. We report the characteristics of a number

J(2).	Hospital, Nordre Fasanvej 57, 2000 Frederiksberg, Denmark.	adverse effects of vaccination against human papilloma virus.	.098. Epub 2015 Apr 14.	of patients with a syndrome of orthostatic intolerance, headache, fatigue, cognitive dysfunction, and neuropathic pain starting in close relation to HPV vaccination. METHODS: Patients were referred for orthostatic intolerance following HPV vaccination. Symptoms of autonomic dysfunction were quantified by standardised questionnaire. The diagnosis of postural orthostatic tachycardia syndrome (POTS) rested on finding a sustained heart rate increment of >30 min(-1) (>40 min(-1) in adolescents) or to levels >120 min(-1) during orthostatic challenge. RESULTS: 35 women aged 23.3 ± 7.1 years participated. Twenty-five had a high level of physical activity before vaccination and irregular periods were reported by all patients not on treatment with oral contraception. Serum bilirubin was below the lower detection limit in 17 patients. Twenty-one of the referred patients fulfilled the criteria for a diagnosis of POTS (60%, 95%CI 43-77%). All patients had orthostatic intolerance, 94% nausea, 82% chronic headache, 82% fatigue, 77% cognitive dysfunction, 72% segmental dystonia, 68% neuropathic pain. CONCLUSIONS: In a population referred for symptoms of orthostatic intolerance and other symptoms consistent with autonomic dysfunction that began in close temporal association with a quadrivalent HPV vaccination, we identified a 60% prevalence of POTS. Further work is urgently needed to elucidate the potential for a causal link between the vaccine and circulatory abnormalities and to establish targeted treatment options for the affected patients.
Brown AE(1), Jones DE(2), Walker M(2), Newton JL(3).	(1)Institute of Cellular Medicine, William Leech Building, Medical School, Newcastle University, Newcastle upon Tyne, United Kingdom. .	Abnormalities of AMPK activation and glucose uptake in cultured skeletal muscle cells from individuals with chronic fatigue syndrome.	PLoS One. 2015 Apr 2;10(4):e0122982. doi: 10.1371/journal.pone.0122982. eCollection 2015.	BACKGROUND: Post exertional muscle fatigue is a key feature in Chronic Fatigue Syndrome (CFS). Abnormalities of skeletal muscle function have been identified in some but not all patients with CFS. To try to limit potential confounders that might contribute to this clinical heterogeneity, we developed a novel in vitro system that allows comparison of AMP kinase (AMPK) activation and metabolic responses to exercise in cultured skeletal muscle cells from CFS patients and control subjects. METHODS: Skeletal muscle cell cultures were established from 10 subjects with CFS and 7 age-matched controls, subjected to electrical pulse stimulation (EPS) for up to 24h and examined for changes associated with exercise. RESULTS: In the basal state, CFS cultures showed increased myogenin expression but decreased IL6 secretion during differentiation compared with control cultures. Control cultures subjected to 16 h EPS showed a significant increase in both AMPK phosphorylation and glucose uptake compared with unstimulated cells. In contrast, CFS cultures showed no increase in AMPK phosphorylation or glucose uptake after 16 h EPS. However, glucose uptake remained responsive to insulin in the CFS cells pointing to an exercise-related defect. IL6 secretion in response to EPS was significantly reduced in CFS compared with control cultures at all time points measured. CONCLUSION: EPS is an effective model for eliciting muscle contraction and the metabolic changes associated with exercise in cultured skeletal muscle cells. We found four main differences in cultured skeletal muscle cells from subjects with CFS; increased myogenin expression in the basal state, impaired activation of AMPK, impaired stimulation of glucose uptake and diminished

				release of IL6. The retention of these differences in cultured muscle cells from CFS subjects points to a genetic/epigenetic mechanism, and provides a system to identify novel therapeutic targets.
Brown H(1), Cartwright R(2).	(1)School of Medicine and Public Health, University of Wisconsin, Madison, WI, USA.	Re: The Relationship Between Irritable Bowel Syndrome, Functional Dyspepsia, Chronic Fatigue and Overactive Bladder Syndrome: A Controlled Study 6 Years After Acute Gastrointestinal Infection.	Eur Urol. 2015 Dec;68(6):1099-100. doi: 10.1016/j.eururo.2015.08.048.	
Burfeind KG(1), Michaelis KA(1), Marks DL(2).	(1)Papé Family Pediatric Research Institute, Oregon Health & Science University, Portland, OR, USA; MD/PhD Program, Oregon Health & Science University, Portland, OR, USA.	The central role of hypothalamic inflammation in the acute illness response and cachexia.	Semin Cell Dev Biol. 2015 Nov 3. pii: S1084-9521(15)00245-1. doi: 10.1016/j.semcdb.2015.10.038. [Epub ahead of print]	When challenged with a variety of inflammatory threats, multiple systems across the body undergo physiological responses to promote defense and survival. The constellation of fever, anorexia, and fatigue is known as the acute illness response, and represents an adaptive behavioral and physiological reaction to stimuli such as infection. On the other end of the spectrum, cachexia is a deadly and clinically challenging syndrome involving anorexia, fatigue, and muscle wasting. Both of these processes are governed by inflammatory mediators including cytokines, chemokines, and immune cells. Though the effects of cachexia can be partially explained by direct effects of disease processes on wasting tissues, a growing body of evidence shows the central nervous system (CNS) also plays an essential mechanistic role in cachexia. In the context of inflammatory stress, the hypothalamus integrates signals from peripheral systems, which it translates into neuroendocrine perturbations, altered neuronal signaling, and global metabolic derangements. Therefore, we will discuss how hypothalamic inflammation is an essential driver of both the acute illness response and cachexia, and why this organ is uniquely equipped to generate and maintain chronic inflammation. First, we will focus on the role of the hypothalamus in acute responses to dietary and infectious stimuli. Next, we will discuss the role of cytokines in driving homeostatic disequilibrium, resulting in muscle wasting, anorexia, and weight loss. Finally, we will address mechanisms and mediators of chronic hypothalamic inflammation, including endothelial cells, chemokines, and peripheral leukocytes.
Calandre EP(1), Rico-Villademoros F, Slim M.	(1)Universidad de Granada, Instituto de Neurociencias , Granada, 18012 , Spain +0034 958246291 ; +0034 958246187 ; calandre@gmail.com.	An update on pharmacotherapy for the treatment of fibromyalgia.	Expert Opin Pharmacother. 2015 Jun;16(9):1347-68. doi: 10.1517/14656566.2015.1047343.	INTRODUCTION: Fibromyalgia is a syndrome characterized by chronic generalized pain in addition to different symptoms such as fatigue, sleep disturbances, stiffness, cognitive impairment, and psychological distress. Multidisciplinary treatment combining pharmacological and nonpharmacological therapies is advised. AREAS COVERED: Publications describing randomized controlled trials and long-term extension studies evaluating drug treatment for fibromyalgia were searched in PubMed and Scopus and included in this review. EXPERT OPINION: Different drugs are recommended for the treatment of fibromyalgia by different published guidelines,

				although only three of them have been approved for this indication by the US FDA, and none have been approved by the European Medicines Agency. According to the available evidence, pregabalin, duloxetine and milnacipran should be the drugs of choice for the treatment of this disease, followed by amitriptyline and cyclobenzaprine. Other drugs with at least one positive clinical trial include some selective serotonin reuptake inhibitors, moclobemide, pirlindole, gabapentin, tramadol, tropisetron, sodium oxybate and nabilone. None of the currently available drugs are fully effective against the whole spectrum of fibromyalgia symptoms, namely pain, fatigue, sleep disturbances and depression, among the most relevant symptoms. Combination therapy is an option that needs to be more thoroughly investigated in clinical trials.
Calvo N(1), Sáez-Francàs N(1), Valero S(2), Alegre J(3), Casas M(1).	(1)Departamento de Psiquiatría. Hospital Universitari Vall d’Hebron. CIBERSAM. Universitat Autònoma de Barcelona	Comorbid personality disorders in chronic fatigue syndrome patients: a marker of psychopathological severity.	Actas Esp Psiquiatr. 2015 Mar-Apr;43(2):58-65. Epub 2015 Mar 1.	INTRODUCTION: This study was designed to evaluate the presence of personality disorders (PDs) in Chronic Fatigue Syndrome (CFS) patients and to determine their influence on the severity of the associated psychopathology. METHODS: 132 CFS patients were assessed using SCID-I, Personality Diagnostic Questionnaire-4+ (PDQ-4+) with its Clinical Significance Scale, and Fatigue Impact Scale. The Beck Depression Inventory, Buss-Durkee Hostility Inventory and the State-Trait Anxiety Inventory were also administered. RESULTS: 48.5% patients presented PDs, being the most frequent the Obsessive-Compulsive and Avoidant ones. Patients with PDs had more depressive symptoms. Irritability, resentment, suspicion and guilt were the symptoms related with PDQ-4+ total score. CONCLUSIONS: According to these results, PDs may be frequent in CFS patients. This comorbidity is associated with a complex clinical profile, secondary to more severe psychiatric symptoms.
Camargo RG(1), Quintas Teixeira Ribeiro H(2), Geraldo MV(3), Matos-Neto E(2), Neves RX(2), Carlos Carnevali L Jr(2), Donatto FF(2), Alcântara PS(4), Ottoch JP(4), Seelaender M(1).	(1)Cancer Metabolism Research Group, Institute of Biomedical Sciences, University of São Paulo, Avenida Professor Lineu Prestes 1524, Cidade Universitária, 05508-000 São Paulo, SP, Brazil ; NAPmiR-miRNA Research Group, University of São Paulo, Avenida Professor Lineu Prestes 1524, Cidade Universitária, 05508-000 São Paulo, SP, Brazil.	Cancer Cachexia and MicroRNAs.	Mediators Inflamm. 2015;2015:367561. doi: 10.1155/2015/367561. Epub 2015 Oct 4.	Cancer cachexia is a paraneoplastic syndrome compromising quality of life and survival, mainly characterized by involuntary weight loss, fatigue, and systemic inflammation. The syndrome is described as a result of tumor-host interactions characterized by an inflammatory response by the host to the presence of the tumor. Indeed, systemic inflammation is considered a pivotal feature in cachexia progression and maintenance. Cytokines are intimately related to chronic systemic inflammation and the mechanisms underlying the release of these factors are not totally elucidated, the etiology of cachexia being still not fully understood. Therefore, the understanding of cachexia-related mechanisms, as well as the establishment of markers for the syndrome, is very relevant. MicroRNAs (miRNAs) are a class of noncoding RNAs interfering with gene regulation. Different miRNA expression profiles are associated with different diseases and inflammatory processes. miRNAs modulate adipose and skeletal muscle tissue metabolism in cancer cachexia and also tumor and tissue derived inflammation. Therefore, we propose a possible role for miRNAs in the modulation of the host inflammatory response during cachexia. Moreover, the establishment of a robust body of evidence in regard to miRNAs and the mechanisms underlying cachexia is mandatory, and shall contribute to the improvement of its diagnosis and treatment.

Capelli E(1), Lorusso L(2), Ghitti M(1), Venturini L(3), Cusa C(4), Ricevuti G(5).	(1)Immunology and Genetic Analysis Laboratory, Department of Earth and Environmental Sciences, University of Pavia, Pavia, Italy.	Chronic fatigue syndrome: Features of a population of patients from northern Italy.	Int J Immunopathol Pharmacol. 2015 Mar;28(1):53-9. doi: 10.1177/0394632015572074.	In this study we analyzed the clinical features of a population of Italian patients with chronic fatigue syndrome (CFS) diagnosed according to the CDC-1994 criteria. The aim was to investigate CFS patients and their relatives, in order to search for events related to the onset of the disease and to identify correlations with other diseases. The analysis was carried out by examining medical records belonging to 82 patients suffering from the syndrome. The documentation was collected between 2008 and 2011 and provided by the non-profit Italian organization AMCFS (Associazione Malati di CFS). The influence of gender on the age of onset and association with potential risk factors were investigated in patients and in their relatives. From the results a significant correlation between the age of onset and autoimmunity was observed.
Carey EJ(1), Ali AH(1), Lindor KD(2).	(1)Division of Gastroenterology and Hepatology, Mayo Clinic, Phoenix, AZ, USA. (2)Division of Gastroenterology and Hepatology, Mayo Clinic, Phoenix, AZ, USA; Arizona State University, College of Health Solutions, Phoenix, AZ, USA. Electronic address: Keith.lindor@asu.edu.	Primary biliary cirrhosis.	Lancet. 2015 Oct 17;386(10003):1565-75. doi: 10.1016/S0140-6736(15)00154-3. Epub 2015 Sep 11.	Primary biliary cirrhosis is a chronic cholestatic liver disease characterised by destruction of small intrahepatic bile ducts, leading to fibrosis and potential cirrhosis through resulting complications. The serological hallmark of primary biliary cirrhosis is the antimitochondrial antibody, a highly disease-specific antibody identified in about 95% of patients with primary biliary cirrhosis. These patients usually have fatigue and pruritus, both of which occur independently of disease severity. The typical course of primary biliary cirrhosis has changed substantially with the introduöction of ursodeoxycholic acid (UDCA). Several randomised placebo-controlled studies have shown that UDCA improves transplant-free survival in primary biliary cirrhosis. However, about 40% of patients do not have a biochemical response to UDCA and would benefit from new therapies. Liver transplantation is a life-saving surgery with excellent outcomes for those with decompensated cirrhosis. Meanwhile, research on nuclear receptor hormones has led to the development of exciting new potential treatments. This Seminar will review the current understanding of the epidemiology, pathogenesis, and natural history of primary biliary cirrhosis, discuss management of the disease and its sequelae, and introduce research on new therapeutic options.
Carod-Artal FJ(1,)(2).	(1)a 1 Neurology Department, Raigmore hospital, Old Perth road, IV2 3UJ, Inverness, UK. (2)b 2 Health Sciences Faculty, Universitat Internacional de Catalunya (UIC), Barcelona, Spain.	Post-Ebolavirus disease syndrome: what do we know?	Expert Rev Anti Infect Ther. 2015 Oct;13(10):1185-7. doi: 10.1586/14787210.2015.1079128. Epub 2015 Aug 13.	As the current Zaire ebolavirus disease outbreak in West Africa fades, the health problems of the more than 16,500 survivors have come to light. A wide range of mental and physical symptoms may occur during the convalescence stage. Reported symptoms of "post-Ebolavirus disease syndrome" (PEVDS) include chronic joint and muscle pain, fatigue, anorexia, hearing loss, blurred vision, headache, sleep disturbances, low mood and short-term memory problems. PEVDS has been associated with a decrease in functionality and difficulties to return to work. Further studies are needed to fully categorize the clinical spectrum of PEVDS. Diagnostic criteria and surrogate markers for the early diagnosis of PEVDS, and implementation of specialized health services to treat and follow-up survivors are also needed.
Carod-Artal FJ(1).	(1)Neurology Department, Raigmore hospital, Old Perth road, IV2 3UJ,	Post-Ebolavirus disease syndrome: What do we know?	Expert Rev Anti Infect Ther. 2015 Aug 13:1-3. [Epub ahead of print]	As the current Zaire ebolavirus disease outbreak in West Africa fades, the health problems of the more than 16,500 survivors have come to light. A wide range of mental and physical symptoms may occur during the convalescence stage. Reported symptoms of "post-Ebolavirus disease syndrome" (PEVDS) include chronic joint and muscle pain,

	Inverness, UK.			fatigue, anorexia, hearing loss, blurred vision, headache, sleep disturbances, low mood and short-term memory problems. PEVDS has been associated with a decrease in functionality and difficulties to return to work. Further studies are needed to fully categorize the clinical spectrum of PEVDS. Diagnostic criteria and surrogate markers for the early diagnosis of PEVDS, and implementation of specialized health services to treat and follow-up survivors are also needed.
Castelein B(1), Cools A(2), Bostyn E(2), Delemarre J(2), Lemahieu T(2), Cagnie B(2).	(1)Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University Hospital, Ghent, Belgium. Electronic address: Birgit.Castelein@ugent.be. (2)Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University Hospital, Ghent, Belgium.	Analysis of scapular muscle EMG activity in patients with idiopathic neck pain: a systematic review.	J Electromyogr Kinesiol. 2015 Apr;25(2):371-86. doi: 10.1016/j.jelekin.2015.01.006. Epub 2015 Jan 31.	It is proposed that altered scapular muscle function can contribute to abnormal loading of the cervical spine. However, it is not clear if patients with idiopathic neck pain show altered activity of the scapular muscles. The aim of this paper was to systematically review the literature regarding the differences or similarities in scapular muscle activity, measured by electromyography (= EMG), between patients with chronic idiopathic neck pain compared to pain-free controls. Case-control (neck pain/healthy) studies investigating scapular muscle EMG activity (amplitude, timing and fatigue parameters) were searched in Pubmed and Web of Science. 25 articles were included in the systematic review. During rest and activities below shoulder height, no clear differences in mean Upper Trapezius (= UT) EMG activity exist between patients with idiopathic neck pain and a healthy control group. During overhead activities, no conclusion for scapular EMG amplitude can be drawn as a large variation of results were reported. Adaptation strategies during overhead tasks are not the same between studies. Only one study investigated timing of the scapular muscles and found a delayed onset and shorter duration of the SA during elevation in patients with idiopathic neck pain. For scapular muscle fatigue, no definite conclusions can be made as a wide variation and conflicting results are reported. Further high quality EMG research on scapular muscles (broader than the UT) is necessary to understand/draw conclusions on how scapular muscles react in the presence of idiopathic neck pain.
Castori M.		Ehlers-Danlos syndrome(s) mimicking child abuse: Is there an impact on clinical practice?	Am J Med Genet C Semin Med Genet. 2015 Oct 9. doi: 10.1002/ajmg.c.31460. [Epub ahead of print]	Ehlers-Danlos syndrome is a heterogeneous group of heritable connective tissue disorders characterized by increased fragility of various non-ossified tissues. It is usually ascertained due to abnormal skin texture, scarring complications, vascular fragility, or chronic symptoms, such as fatigue and musculoskeletal pain. Sometimes, Ehlers-Danlos syndrome remains undetected until the patient, usually in the pediatric age, shows extensive or severe mucocutaneous injuries after only minor traumas. In this scenario, the misdiagnosis of Ehlers-Danlos syndrome with child abuse is a possibility, as occasionally reported in the literature. Recently, more attention was posed by lay people between the possible association of Ehlers-Danlos syndrome and bone fragility. Literature and personal experience show a strong association between Ehlers-Danlos syndrome, generalized joint hypermobility and reduced bone mass density in older children and adults, especially fertile women. The existence of a true increased risk of fracture in Ehlers-Danlos syndrome is still a matter of debate in children and adults with little and conflicting evidence. In case of suspected child abuse, Ehlers-Danlos syndrome is certainly on the differential for bruising, especially in EDS types with

				marked cutaneous and capillary involvement. In suspected child abuse cases, careful examination of the index case and her/his extended family is routine, as well as exclusion of other disorders such as osteogenesis imperfecta. The hypothesis of Ehlers-Danlos syndrome as an alternative explanation for infantile fractures remains speculative. © 2015 Wiley Periodicals, Inc.
Castro-Marrero J(1), Cordero MD, Segundo MJ, Sáez-Francàs N, Calvo N, Román-Malo L, Aliste L, Fernández de Sevilla T, Alegre J.	(1)1 CFS Clinical Unit, Vall d'Hebron Research Institute, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona , Barcelona, Spain .	Does oral coenzyme Q10 plus NADH supplementation improve fatigue and biochemical parameters in chronic fatigue syndrome?	Antioxid Redox Signal. 2015 Mar 10;22(8):679-85. doi: 10.1089/ars.2014.6181. Epub 2014 Dec 18.	Chronic fatigue syndrome (CFS) is a chronic and extremely debilitating illness characterized by prolonged fatigue and multiple symptoms with unknown cause, diagnostic test, or universally effective treatment. Inflammation, oxidative stress, mitochondrial dysfunction, and CoQ10 deficiency have been well documented in CFS. We conducted an 8-week, randomized, double-blind placebo-controlled trial to evaluate the benefits of oral CoQ10 (200 mg/day) plus NADH (20 mg/day) supplementation on fatigue and biochemical parameters in 73 Spanish CFS patients. This study was registered in ClinicalTrials.gov (NCT02063126). A significant improvement of fatigue showing a reduction in fatigue impact scale total score ($p<0.05$) was reported in treated group versus placebo. In addition, a recovery of the biochemical parameters was also reported. NAD+/NADH ($p<0.001$), CoQ10 ($p<0.05$), ATP ($p<0.05$), and citrate synthase ($p<0.05$) were significantly higher, and lipoperoxides ($p<0.05$) were significantly lower in blood mononuclear cells of the treated group. These observations lead to the hypothesis that the oral CoQ10 plus NADH supplementation could confer potential therapeutic benefits on fatigue and biochemical parameters in CFS. Larger sample trials are warranted to confirm these findings.
Castro-Marrero J(1), Sáez-Francàs N(2), Segundo MJ(3), Calvo N(4), Faro M(5), Aliste L(5), Fernández de Sevilla T(5), Alegre J(5).	(1)CFS Clinical Unit, Vall d'Hebron University Hospital Research Institute, Universitat Autònoma de Barcelona, 08035, Barcelona, Spain. Electronic address: jesus.castro@vhir.org.	Effect of coenzyme Q10 plus nicotinamide adenine dinucleotide supplementation on maximum heart rate after exercise testing in chronic fatigue syndrome - A randomized, controlled, double-blind trial.	Clin Nutr. 2015 Jul 17. pii: S0261-5614(15)00189-2. doi: 10.1016/j.clnu.2015.07.010. [Epub ahead of print]	BACKGROUND & AIMS: Chronic Fatigue Syndrome (CFS) is a complex condition, characterized by severe disabling fatigue with no known cause, no established diagnostic tests, and no universally effective treatment. Several studies have proposed symptomatic treatment with coenzyme Q10 (CoQ10) and nicotinamide adenine dinucleotide (NADH) supplementation. The primary endpoint was to assess the effect of CoQ10 plus NADH supplementation on age-predicted maximum heart rate (max HR) during a cycle ergometer test. Secondary measures included fatigue, pain and sleep. METHODS: A proof-of-concept, 8-week, randomized, controlled, double-blind trial was conducted in 80 CFS patients assigned to receive either CoQ10 plus NADH supplementation or matching placebo twice daily. Maximum HR was evaluated at baseline and at end of the run-in period using an exercise test. Fatigue, pain and sleep were evaluated at baseline, and then reassessed at 4- and 8-weeks through self-reported questionnaires. RESULTS: The CoQ10 plus NADH group showed a significant reduction in max HR during a cycle ergometer test at week 8 versus baseline ($P = 0.022$). Perception of fatigue also showed a decrease through all follow-up visits in active group versus placebo ($P = 0.03$). However, pain and sleep did not improve in the active group. Coenzyme Q10 plus NADH was generally safe and well tolerated. CONCLUSIONS: Our results suggest that CoQ10 plus NADH supplementation for 8

				weeks is safe and potentially effective in reducing max HR during a cycle ergometer test and also on fatigue in CFS. Further additional larger controlled trials are needed to confirm these findings. Clinical trial registrationThis trial was registered at clinicaltrials.gov as NCT02063126.
Cerdá-Olmedo G(1), Mena-Durán AV(2), Monsalve V(2), Oltra E(3).	(1)Facultad de Medicina, Universidad Católica de Valencia "San Vicente Mártir", Valencia, Spain; Cátedra Umivale en innovación e investigación en patologías del trabajo, Valencia, Spain.	Identification of a microRNA signature for the diagnosis of fibromyalgia.	PLoS One. 2015 Mar 24;10(3):e0121903. doi: 10.1371/journal.pone.0121903. eCollection 2015.	BACKGROUND: Diagnosis of fibromyalgia (FM), a chronic musculoskeletal pain syndrome characterized by generalized body pain, hyperalgesia and other functional and emotional comorbidities, is a challenging process hindered by symptom heterogeneity and clinical overlap with other disorders. No objective diagnostic method exists at present. The aim of this study was to identify changes in miRNA expression profiles (miRNome) of these patients for the development of a quantitative diagnostic method of FM. In addition, knowledge of FM patient miRNomes should lead to a deeper understanding of the etiology and/or symptom severity of this complex disease. METHODS: Genome-wide expression profiling of miRNAs was assessed in Peripheral Blood Mononuclear Cells (PBMCs) of FM patients (N=11) and population-age-matched controls (N=10) using human v16-miRbase 3D-Gene microarrays (Toray Industries, Japan). Selected miRNAs from the screen were further validated by RT-qPCR. Participating patients were long term sufferers (over 10 years) diagnosed by more than one specialist under 1990 American College of Rheumatology criteria. RESULTS: Microarray analysis of FM patient PBMCs evidenced a marked downregulation of hsa-miR223-3p, hsa-miR451a, hsa-miR338-3p, hsa-miR143-3p, hsa-miR145-5p and hsa-miR-21-5p (4-fold or more). All but the mildest inhibited miRNA, hsa-miR-21-5p, were validated by RT-qPCR. Globally, 20% of the miRNAs analyzed (233/1212) showed downregulation of at least 2-fold in patients. This might indicate a general de-regulation of the miRNA synthetic pathway in FM. No significant correlations between miRNA inhibition and FM cardinal symptoms could be identified. However, the patient with the lowest score for mental fatigue coincided with the mildest inhibition in four of the five miRNAs associated with the FM-group. CONCLUSIONS: We propose a signature of five strikingly downregulated miRNAs (hsa-miR223-3p, hsa-miR451a, hsa-miR338-3p, hsa-miR143-3p and hsa-miR145-5p) to be used as biomarkers of FM. Validation in larger study groups is required before the results can be transferred to the clinic.
Chalder T(1), Goldsmith KA(2), White PD(3), Sharpe M(4), Pickles AR(2).	(1)Academic Department of Psychological Medicine, King's College London, Weston Education Centre, London, UK.	Rehabilitative therapies for chronic fatigue syndrome: a secondary mediation analysis of the PACE trial.	Lancet Psychiatry. 2015 Feb;2(2):141-52. doi: 10.1016/S2215-0366(14)00069-8. Epub 2015 Jan 28.	BACKGROUND: Cognitive behaviour therapy (CBT) added to specialist medical care (SMC), or graded exercise therapy (GET) added to SMC, are more effective in reducing fatigue and improving physical function than both adaptive pacing therapy (APT) plus SMC and SMC alone for chronic fatigue syndrome. We investigate putative treatment mechanisms. METHODS: We did a planned secondary mediation analysis of the PACE trial comparing SMC alone or SMC plus APT with SMC plus CBT and SMC plus GET for patients with chronic fatigue syndrome. 641 participants were recruited from six

	Electronic address: trudie.chalder@kcl.ac.uk.			specialist chronic fatigue syndrome clinics in the UK National Health Service between March 18, 2005, and Nov 28, 2008. We assessed mediation using the product of coefficients method with the 12 week measure of the mediators and the 52 week measure of the outcomes. The primary outcomes were fatigue measured by the Chalder fatigue scale and physical function measured by the physical function subscale of the SF-36. We included confounder covariates and used treatment by mediator interaction terms to examine differences in mediator-outcome relations by treatment group. FINDINGS: The largest mediated effect for both CBT and GET and both primary outcomes was through fear avoidance beliefs with an effect of larger magnitude for GET (standardised effects ×10, CBT vs APT, fatigue -1.22, 95% CI -0.52 to -1.97, physical function 1.54, 0.86 to 2.31; GET vs APT, fatigue -1.86, -0.80 to -2.89, physical function 2.35, 1.35 to 3.39). Increase in exercise tolerance (6 min walk distance) was a potent mediator of the effect of GET (vs APT, fatigue -1.37, 95% CI -0.76 to -2.21, physical function 1.90, 1.10 to 2.91), but not CBT. INTERPRETATION: Our main finding was that fear avoidance beliefs were the strongest mediator for both CBT and GET. Changes in both beliefs and behaviour mediated the effects of both CBT and GET, but more so for GET. The results support a treatment model in which both beliefs and behaviour play a part in perpetuating fatigue and disability in chronic fatigue syndrome. FUNDING: UK Medical Research Council, Department of Health for England, Scottish Chief Scientist Office, Department for Work and Pensions, National Institute for Health Research (NIHR), NIHR Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust, and Institute of Psychiatry, Psychology, and Neuroscience, King's College London.
Chao CH(1), Chen HJ(2,)(3), Wang HY(4,)(5), Li TC(6,)(7), Kao CH(8,)(9).	(1)Division of Chest Medicine, Department of Internal Medicine, Chang Bing Show Chwan Memorial Hospital, Changhua, Taiwan.	Increased risk of organic erectile dysfunction in patients with chronic fatigue syndrome: a nationwide population-based cohort study.	Andrology. 2015 Jul;3(4):666-71. doi: 10.1111/andr.12052.	Chronic fatigue syndrome (CFS) is a complex disorder characterized by profound and persistent fatigue and several comorbidities. CFS was previously reported to be associated with female sexual dysfunction. We propose that CFS might also be associated with organic erectile dysfunction (organic ED). We conducted a retrospective cohort study by using data from the National Health Insurance (NHI) Research Database. We identified 2156 male patients who were newly diagnosed with CFS between January 1, 2003 and December 31, 2006. After excluding those younger than 20 years and prevalent cases, 1976 patients were subjected to analysis, and 7904 people served as healthy controls. All study subjects were followed up from the index date to the date of organic ED diagnosis, withdrawal from the NHI program, or the end of 2011. Compared with the non-CFS cohort, the incidence density rate of organic ED was 1.88-fold higher than that in the CFS cohort (3.23 vs. 1.73 per 1000 person-years) with an adjusted hazard ratio (HR) of 1.88 (95% CI = 1.26-2.81) when adjusting for sex and comorbidities. The combined impacts of patients with CFS and cardiovascular disease (CVD), diabetes mellitus (DM), chronic kidney disease (CKD), depression, and anxiety showed a significant by joint association with organic ED risk compared with patients with no CFS and no counterpart comorbidity. The greatest magnitude of

				adjusted HR of ED for CFS was observed in individuals without any comorbidity (3.87, 1.95-7.66). The incidence of organic ED is higher among males aged 40 years and over for both CFS and non-CFS cohorts. As the number of comorbidity increases, the incidence of organic ED increases in males without CFS. Higher incidence of organic ED was observed in males with CVD, DM, CKD, depression, or anxiety for both CFS and non-CFS cohorts.
Check JH.		Sympathomimetic amines are a safe, highly effective therapy for several female chronic disorders that do not respond well to conventional therapy.	Clin Exp Obstet Gynecol. 2015;42(3):267-78.	PURPOSE: To evaluate the efficacy of sympathomimetic amine therapy for women with chronic disorders including, but not limited to, pelvic pain. MATERIALS AND METHODS: Dextroamphetamine sulfate 15-mg extended release capsules were given to women with a variety of treatment refractory conditions including, but not limited to, pelvic pain. The dosage could be increased to 60 mg depending on tolerance to the medication and degree of improvement of the condition. RESULTS: A very high percentage showed marked amelioration of their symptoms despite previous failure with medical or surgical therapy. CONCLUSIONS: The human species, especially women, seem to be more prone to certain specific tissue permeability defects and diminished sympathetic tone, which compounds the problem, since the sympathetic nervous system controls permeability. Thus, besides pelvic pain and interstitial cystitis, dextroamphetamine sulfate, which seems to restore sympathetic tone possibly by increasing dopamine secretion to the nerve fiber, provides gratifying relief to a variety of chronic disorders. These other disorders include: severe headaches, inflammatory bowel disease, gastrointestinal motility disorders, fibromyalgia, and other musculoskeletal pain, chronic fatigue syndrome, and urticaria.
Chelimsky G(1), Kovacic K(1), Nugent M(2), Mueller A(1), Simpson P(2), Chelimsky TC(3).	(1)Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Center for Pediatric Neurogastroenterology, Motility, and Autonomic Disorders, Medical College of Wisconsin, Milwaukee, WI.	Comorbid Conditions Do Not Differ in Children and Young Adults with Functional Disorders with or without Postural Tachycardia Syndrome.	J Pediatr. 2015 Jul;167(1):120-4. doi: 10.1016/j.jpeds.2015.03.039. Epub 2015 Apr 25.	OBJECTIVE: To determine if several multisystem comorbid conditions occur more frequently in subjects with tilt-table defined postural tachycardia syndrome (POTS) compared with those without. STUDY DESIGN: Retrospective chart review of 67 subjects aged 6-24 years, referred to a tertiary care neurogastroenterology and autonomic disorders clinic for a constellation of functional gastrointestinal, chronic pain, and autonomic complaints. All patients underwent formal autonomic testing, Beighton scores assessment for joint hypermobility (0-9), and fibromyalgia tender points (0-18) (43 subjects). RESULTS: Twenty-five subjects (37%) met tilt table criteria for POTS. The median age of 16 years (range, 12-24 years) in the POTS group differed from 15 years (range, 6-21 years) in the no-POTS group (P = .03). Comorbidities including chronic fatigue, sleep disturbances, dizziness, syncope, migraines, functional gastrointestinal disorders, chronic nausea, fibromyalgia, and joint hypermobility did not differ between groups. All subjects with fibromyalgia by tender point-examination had a Beighton score ≥ 4 (P = .002). CONCLUSIONS: Comorbid conditions are equally prevalent in children and young adults with and without tilt-table defined POTS, suggesting that POTS itself is not a cause of the other comorbidities. Instead, POTS likely reflects another comorbid condition in children with functional disorders. Dizziness and syncope, classically associated with POTS, are not predictive of a

				diagnosis of POTS by tilt table, a test that is still required for formal diagnosis. These results suggest a paradigm shift in the concept of POTS as the physiological basis of many functional symptoms.
Chen Y(1), Liu W(2), Zhang L(1), Yan M(3), Zeng Y(4).	(1)School of Computer, Guangdong University of Technology, Guangzhou, China.	Hybrid facial image feature extraction and recognition for non-invasive chronic fatigue syndrome diagnosis.	Comput Biol Med. 2015 Sep;64:30-9. doi: 10.1016/j.compbiomed.2015.06.005. Epub 2015 Jun 15.	Due to an absence of reliable biochemical markers, the diagnosis of chronic fatigue syndrome (CFS) mainly relies on the clinical symptoms, and the experience and skill of the doctors currently. To improve objectivity and reduce work intensity, a hybrid facial feature is proposed. First, several kinds of appearance features are identified in different facial regions according to clinical observations of traditional Chinese medicine experts, including vertical striped wrinkles on the forehead, puffiness of the lower eyelid, the skin colour of the cheeks, nose and lips, and the shape of the mouth corner. Afterwards, such features are extracted and systematically combined to form a hybrid feature. We divide the face into several regions based on twelve active appearance model (AAM) feature points, and ten straight lines across them. Then, Gabor wavelet filtering, CIELab color components, threshold-based segmentation and curve fitting are applied to extract features, and Gabor features are reduced by a manifold preserving projection method. Finally, an AdaBoost based score level fusion of multi-modal features is performed after classification of each feature. Despite that the subjects involved in this trial are exclusively Chinese, the method achieves an average accuracy of 89.04% on the training set and 88.32% on the testing set based on the K-fold cross-validation. In addition, the method also possesses desirable sensitivity and specificity on CFS prediction.
Chi A(1), Kang C(2), Zhang Y(3), Tang L(2), Guo H(2), Li H(2), Zhang K(2).	(1)Laboratory of Nutrition and Hygiene, Shaanxi Normal University, Xi'an 710062, China. Electronic address: chimu@snnu.edu.cn. (2)Laboratory of Nutrition and Hygiene, Shaanxi Normal University, Xi'an 710062, China. (3)Department of Pharmacology, University of California, Irvine, CA 92697, USA.	Immunomodulating and antioxidant effects of polysaccharide conjugates from the fruits of Ziziphus Jujube on Chronic Fatigue Syndrome rats.	Carbohydr Polym. 2015 May 20;122:189-96. doi: 10.1016/j.carbpol.2014.12.082. Epub 2015 Jan 14.	To detect the treatment effect of the fruits of Ziziphus Jujube in Chronic Fatigue Syndrome (CFS). Jujube polysaccharide conjugates (JPC) were isolated from the fruits of Z. Jujube. General physicochemical properties of JPC were analyzed. A four-week rats CFS model was established and JPC were orally administrated, the behavior experiments were conducted after CFS. The activities of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and the levels of malondialdehyde (MDA) in serum were elevated and T lymphocyte proliferation, CD4(+)/CD8(+) ratio and natural killer (NK) cells activity were analyzed. JPC markedly improved behaviors of CFS rats, also decreased MDA levels in serum, and elevated T lymphocyte proliferation, CD4(+)/CD8(+) ratio and natural killer (NK) cells activities. This suggests that JPC can improve the immune system and antioxidant activity of CFS rats and might be regarded as a biological response modifier.
Christensen SS(1), Frostholm L(1),	(1)The Research Clinic for Functional	Changes in illness perceptions mediated the	J Psychosom Res. 2015 Apr;78(4):363-70. doi:	OBJECTIVE: Although there is substantial evidence that cognitive behavioural therapy alleviates symptoms in functional somatic syndromes, the mechanisms of change are

Ørnbøl E(1), Schröder A(2).	Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 44, Aarhus C, Denmark. (2)The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 44, Aarhus C, Denmark. Electronic address: andreas.schroeder@aarhus.rm.dk.	effect of cognitive behavioural therapy in severe functional somatic syndromes.	10.1016/j.jpsychores.2014.12.005. Epub 2014 Dec 13.	less investigated. This study examined whether changes in illness perceptions mediated the effect of cognitive behavioural therapy. METHODS: We analysed additional data from a randomised controlled trial comparing completers of cognitive behavioural group therapy (46 patients) to an enhanced usual care group (66 patients). Proposed mediators (illness perceptions) and primary (physical health) and secondary (somatic symptoms and illness worry) outcomes were assessed by means of questionnaires at referral, baseline, end of treatment, and 10 and 16 months after randomisation. Multiple mediation analysis determined whether (1) changes in specific illness perceptions during treatment mediated the effect of cognitive behavioural therapy (primary analysis), and (2) whether changes in illness perceptions during the whole trial period were associated with improved outcome (secondary analysis). RESULTS: Improvements in illness perceptions during treatment partially mediated the effect of cognitive behavioural therapy on physical health one year after treatment (sum of indirect effects 1.556, BCa 95% CI (0.006; 3.620)). Improving perceived control was particularly important. Changes in illness perceptions from baseline to 16 months after randomisation were associated with clinically meaningful improvements in physical health, somatic symptoms and illness worry during the same period. CONCLUSION: Our results suggest that changing patients' illness perceptions is an important process in cognitive behavioural therapy for functional somatic syndromes. Challenging patients' own understanding of their illness may hence be a key element of successful treatment.
Chu L, Bateman L, Davenport T, Stein E, Stevens S.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):887. doi: 10.7326/L15-5174.	
Clayton EW(1).	(1)Center for Biomedical Ethics and Society, Vanderbilt University, Nashville, Tennessee.	Beyond myalgic encephalomyelitis/chronic fatigue syndrome: an IOM report on redefining an illness.	JAMA. 2015 Mar 17;313(11):1101-2. doi: 10.1001/jama.2015.1346.	
Clayton EW(1).	(1)Vanderbilt University Medical Center, Nashville, Tennessee.	Redefining Myalgic Encephalomyelitis/Chronic Fatigue Syndrome--Reply.	JAMA. 2015 Jul 7;314(1):85-6. doi: 10.1001/jama.2015.5760.	
Cleare AJ(1), Reid S, Chalder T, Hotopf M, Wessely S.	(1)King's College London, Institute of Psychiatry, Psychology and Neuroscience, Centre for Affective	Chronic fatigue syndrome.	BMJ Clin Evid. 2015 Sep 28;2015. pii: 1101.	INTRODUCTION: Chronic fatigue syndrome affects between 0.006% and 3% of the population depending on the criteria of definition used, with women being at higher risk than men. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of selected treatments for chronic fatigue syndrome? We searched: Medline, Embase, The

	Disorders, Department of Psychological Medicine, London, UK.			Cochrane Library, and other important databases up to November 2013 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). RESULTS: At this update, searching of electronic databases retrieved 169 studies. After deduplication and removal of conference abstracts, 86 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 71 studies and the further review of 15 full publications. Of the 15 full articles evaluated, two systematic reviews, one RCT, and one further follow-up report of an RCT were added at this update. We performed a GRADE evaluation for 23 PICO combinations. CONCLUSIONS: In this systematic overview, we categorised the effectiveness of four interventions based on information relating to the effectiveness and safety of antidepressants, cognitive behavioural therapy, corticosteroids, and graded exercise therapy.
Collin SM(1), Nuevo R(1), van de Putte EM(2), Nijhof SL(2), Crawley E(1).	(1)Centre for Child & Adolescent Health, School of Social and Community Medicine, University of Bristol, Bristol, UK. (2)Department of Paediatrics, Wilhelmina Children's Hospital, University Medical Centre, Utrecht, The Netherlands.	Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) is different in children compared to in adults: a study of UK and Dutch clinical cohorts.	BMJ Open. 2015 Oct 28;5(10):e008830. doi: 10.1136/bmjopen-2015-008830.	OBJECTIVE: To investigate differences between young children, adolescents and adults with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). STUDY DESIGN: Comparison of clinical cohorts from 8 paediatric and 27 adult CFS/ME services in the UK and a paediatric randomised controlled trial from the Netherlands. Outcome measures include: fatigue (the UK-Chalder Fatigue Scale); Disability (the UK-SF-36 physical function subscale; the Netherlands-CHQ-CF87); school attendance, pain, anxiety and depression (the UK-Hospital Anxiety & Depression Scale, Spence Children's Anxiety Scale; the Netherlands-Spielberger State-Trait Anxiety Inventory for Children, Children's Depression Inventory); symptoms; time-to-assessment; and body mass index. We used multinomial regression to compare younger (aged <12 years) and older (aged 12-18 years) children with adults, and logistic regression to compare UK and Dutch adolescents. RESULTS: Younger children had a more equal gender balance compared to adolescents and adults. Adults had more disability and fatigue, and had been ill for longer. Younger children were less likely to have cognitive symptoms (OR 0.18 (95% CI 0.13 to 0.25)) and more likely to present with a sore throat (OR 1.42 (1.07 to 1.90). Adolescents were more likely to have headaches (81.1%, OR 1.56 (1.36% to 1.80%)) and less likely to have tender lymph nodes, palpitations, dizziness, general malaise and pain, compared to adults. Adolescents were more likely to have comorbid depression (OR 1.51 (1.33 to 1.72)) and less likely to have anxiety (OR 0.46 (0.41 to 0.53)) compared to adults. CONCLUSIONS: Paediatricians need to recognise that children with CFS/ME present differently from adults. Whether these differences reflect an underlying aetiopathology requires further investigation. TRIAL REGISTRATION NUMBERS: FITNET trial registration numbers are ISRCTN59878666 and NCT00893438. This paper includes secondary (post-results) analysis of data from this trial, but are unrelated to trial outcomes.
Collin SM(1), Tilling K(2), Joinson C(3),	(1)School of Social and Community Medicine, University	Maternal and childhood psychological factors predict chronic disabling	J Adolesc Health. 2015 Feb;56(2):181-7. doi: 10.1016/j.jadohealth.2014	PURPOSE: To investigate whether premorbid maternal and childhood psychological problems are risk factors for chronic disabling fatigue at age 13 years among children in the Avon Longitudinal Study of Parents and Children birth cohort. METHODS: Chronic

Rimes KA(4), Pearson RM(2), Hughes RA(2), Sterne JA(2), Crawley E(3).	of Bristol, Bristol, United Kingdom; Centre for Child and Adolescent Health, University of Bristol, Bristol, United Kingdom. Electronic address: simon.collin@bristol.ac.uk.	fatigue at age 13 years.	.09.002. Epub 2014 Nov 18.	disabling fatigue was defined as fatigue of at least 3-month, and up to 5-year, duration that prevented school attendance or hobbies/sport/leisure activities, and for which other causes were not identified. Maternal psychological factors were symptoms of anxiety and depression assessed up to eight times between pregnancy and age 6 years. We investigated critical periods for maternal effects and effects of paternal depression at three time points. Child psychological factors included internalizing and externalizing problems and upsetting life events occurring at age 7-8 years. RESULTS: Of 5,657 children, 110 (1.9%) had chronic disabling fatigue at age 13 years. Maternal anxiety (adjusted odds ratio [AOR], 1.19; 95% confidence interval [CI], 1.09-1.31 per episode), maternal depression (AOR, 1.24; CI, 1.11-1.39 per episode), child psychological problems (AOR, 1.19; CI, 1.00-1.41 per problem), and upsetting events (AOR, 1.22; CI, .99-1.58 per event) were associated with chronic disabling fatigue. Associations of child psychological problems and upsetting events were attenuated (AOR, 1.12; CI, .93-1.33 per problem; AOR, 1.19; CI, .94-1.52 per event) after further adjusting for maternal anxiety and depression. CONCLUSIONS: Pediatricians need to be aware that children whose mothers experience anxiety and/or depression between pregnancy and child's age 6 years have an increased risk of developing chronic disabling fatigue in early adolescence. Conversely, clinicians need to be alert to fatigue in children whose mothers have longstanding anxiety and depression. These findings suggest the importance of family-based approaches to treatment.
Coplan J(1), Singh D, Gopinath S, Mathew SJ, Bulbena A.	(1)From the Division of Neuropsychopharmacology, Dept. of Psychiatry and Behavioral Sciences, State University of New York Downstate Medical Center, Brooklyn, NY (JC, SG); the Dept. of Psychiatry, Winthrop University Hospital, Mineola, NY (DS); the Michael E. Debakey VA Medical Center, Houston, TX (SJM); the Menninger Dept. of Psychiatry and Behavioral Sciences,	A Novel Anxiety and Affective Spectrum Disorder of Mind and Body-The ALPIM (Anxiety-Laxity-Pain-Immune-Mood) Syndrome: A Preliminary Report.	J Neuropsychiatry Clin Neurosci. 2015;27(2):93-103. doi: 10.1176/appi.neuropsych.14060132.	The authors describe a spectrum disorder comprising a core anxiety (A) disorder and four domains: joint laxity (L), chronic pain syndromes (P), immune disorders (I), and mood disorders (M)-dubbed the ALPIM syndrome. This study examined 76 consecutive outpatients with an anxiety disorder plus at least one somatic condition from three domains. More than 80% of the patients had panic attacks, fibromyalgia, and major depressive episodes. Associations were found between joint laxity and bipolar III, headache with bipolar II, and bipolar II with chronic fatigue syndrome. Significant relationships were demonstrated within and between domains, validating ALPIM as a syndrome.

	Baylor College of Medicine, Houston, TX (SJM); and the Institut de Neuropsiquiatria i Addiccions, Hospital del Mar, Parc de Salut Mar, Barcelona, Spain (AB).			
Cornea MI(1), Levrat E(2), Pugin P(3), Betticher DC(4).	(1)Hôpital Cantonal Fribourg, Chemin des Pensionnats 2, 1708, Fribourg, Switzerland. Mihaela.Precup@h-fr.ch. (2)Hôpital Cantonal Fribourg, Chemin des Pensionnats 2, 1708, Fribourg, Switzerland. Emmanuel.Levrat@h-fr.ch. (3)Hôpital Cantonal Fribourg, Chemin des Pensionnats 2, 1708, Fribourg, Switzerland. Paul.Pugin@h-fr.ch. (4)Hôpital Cantonal Fribourg, Chemin des Pensionnats 2, 1708, Fribourg, Switzerland. Daniel.Betticher@h-fr.ch.	BCR-ABL1- positive chronic myeloid leukemia with erythrocytosis presenting as polycythemia vera: a case report.	J Med Case Rep. 2015 Apr 8;9:30. doi: 10.1186/1752-1947-9-30.	INTRODUCTION: The World Health Organization classification of chronic myeloproliferative disease encompasses eight entities of bone marrow neoplasms, among them Breakpoint cluster region-Abelson murine leukemia viral oncogene homolog 1-positive chronic myeloid leukemia and polycythemia vera. Polycythemia vera requires, in the majority of cases (95%), the negativity of Breakpoint cluster region-Abelson murine leukemia viral oncogene homolog 1 rearrangement and the presence of the Janus kinase 2 mutation. We report a case of erythrocytosis as the primary manifestation of a chronic myeloid leukemia, with the presence of the Philadelphia chromosome and the Breakpoint cluster region-Abelson murine leukemia viral oncogene homolog 1 fusion gene, and in the absence of any Janus kinase 2 mutation. CASE PRESENTATION: A 68-year-old Caucasian woman, with a history of cigarette consumption and obstructive sleep apnoea syndrome (undergoing continuous positive airway pressure treatment) had presented to our institution with fatigue and a hemoglobin level of 18.6g/L, with slight leukocytosis at 16G/L, and no other anomalies on her complete blood cell count. Examination of her arterial blood gases found only a slight hypoxemia; erythropoietin and ferritin levels were very low and could not explain a secondary erythrocytosis. Further analyses revealed the absence of any Janus kinase 2 mutation, thus excluding polycythemia vera. Taken together with a high vitamin B12 level, we conducted a Breakpoint cluster region-Abelson murine leukemia viral oncogene homolog 1 gene analysis and bone marrow cytogenetic analysis, both of which returned positive, leading to the diagnosis of chronic myeloid leukemia. CONCLUSIONS: To date, this case is the first description of a Breakpoint cluster region-Abelson murine leukemia viral oncogene homolog 1-positive chronic myeloid leukemia, presenting with erythrocytosis as the initial manifestation, and mimicking a Janus kinase 2 V617F-negative polycythemia vera. Her impressive response to imatinib therapy underscores the importance of not missing this diagnosis.
Couch Y(1), Xie Q(1), Lundberg L(2), Sharp T(1), Anthony DC(1).	(1)Department of Pharmacology, Mansfield Road, Oxford, OX1 3QT, United Kingdom. (2)Department of	A Model of Post-Infection Fatigue Is Associated with Increased TNF and 5-HT2A Receptor Expression in Mice.	PLoS One. 2015 Jul 6;10(7):e0130643. doi: 10.1371/journal.pone.0130643. eCollection 2015.	It is well documented that serotonin (5-HT) plays an important role in psychiatric illness. For example, myalgic encephalomyelitis (ME/CFS), which is often provoked by infection, is a disabling illness with an unknown aetiology and diagnosis is based on symptom-specific criteria. However, 5-HT2A receptor expression and peripheral cytokines are known to be upregulated in ME. We sought to examine the relationship between the 5-HT system and cytokine expression following systemic bacterial

	Pharmacology, Mansfield Road, Oxford, OX1 3QT, United Kingdom; Public Health England, Centre for Radiation, Chemical and Environmental Hazards, Chilton, Didcot, Oxford OX11 0RQ, United Kingdom.			endotoxin challenge (LPS, 0.5 mg/kg i.p.), at a time when the acute sickness behaviours have largely resolved. At 24 hours post-injection mice exhibit no overt changes in locomotor behaviour, but do show increased immobility in a forced swim test, as well as decreased sucrose preference and reduced marble burying activity, indicating a depressive-like state. While peripheral IDO activity was increased after LPS challenge, central activity levels remained stable and there was no change in total brain 5-HT levels or 5-HIAA/5-HT. However, within the brain, levels of TNF and 5-HT2A receptor mRNA within various regions increased significantly. This increase in receptor expression is reflected by an increase in the functional response of the 5-HT2A receptor to agonist, DOI. These data suggest that regulation of fatigue and depressive-like moods after episodes of systemic inflammation may be regulated by changes in 5-HT receptor expression, rather than by levels of enzyme activity or cytokine expression in the CNS.
Courtney R.		Harms and benefits associated with exercise therapy for CFS/ME.	Disabil Rehabil. 2015;37(5):465. doi: 10.3109/09638288.2014.952453. Epub 2014 Aug 19.	Comment on Disabil Rehabil. 2014;36(5):387-94.
Courtois I(1), Cools F(2), Calsius J(3).	(1)Reval Research Center, University Hasselt, Faculty Medicine and Life Science, Belgium. Electronic address: imke.courtois@uhasselt.be. (2)Belgian Center for Evidence-Based Medicine, Belgian Branch of the Dutch Cochrane Center (CEBAM), Belgium. Electronic address: filip.cools@uzbrussel.be. (3)Reval Research Center, University Hasselt, Faculty Medicine and Life Science, Belgium. Electronic address: joeri.calsius@uhasselt	Effectiveness of body awareness interventions in fibromyalgia and chronic fatigue syndrome: a systematic review and meta-analysis.	J Bodyw Mov Ther. 2015 Jan;19(1):35-56. doi: 10.1016/j.jbmt.2014.04.003. Epub 2014 Apr 18.	OBJECTIVES: Patients with long-lasting pain problems often complain of lack of confidence and trust in their body. Through physical experiences and reflections they can develop a more positive body- and self-experience. Body awareness has been suggested as an approach for treating patients with chronic pain and other psychosomatic conditions. The aim of this systematic review is to assess the effectiveness of body awareness interventions (BAI) in fibromyalgia (FM) and chronic fatigue syndrome (CFS). METHODS: Two independent readers conducted a search on Medline, Cochrane Central, PsycINFO, Web of knowledge, PEDro and Cinahl for randomized controlled trials. RESULTS: We identified and screened 7.107 records of which 29 articles met the inclusion criteria. Overall, there is evidence that BAI has positive effects on the Fibromyalgia Impact Questionnaire (FIQ) (MD -5.55; CI -8.71 to -2.40), pain (SMD -0.39, CI -0.75 to -0.02), depression (SMD -0.23, CI -0.39 to -0.06), anxiety (SMD -0.23, CI -0.44 to -0.02) and Health Related Quality of Life (HRQoL) (SMD 0.62, CI 0.35-0.90) when compared with control conditions. The overall heterogeneity is very strong for FIQ (I(2) 92%) and pain (I(2) 97%), which cannot be explained by differences in control condition or type of BAI (hands-on/hands-off). The overall heterogeneity for anxiety, depression and HRQoL ranges from low to moderate (I(2) 0%-37%). CONCLUSIONS: Body awareness seems to play an important role in anxiety, depression and HRQoL. Still, interpretations have to be done carefully since the lack of high quality studies.

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Craig C(1).	(1)Private Practice, Queens, NY, United States. Electronic address: info@drcourtneycraig.com.	Mitoprotective dietary approaches for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Caloric restriction, fasting, and ketogenic diets.	Med Hypotheses. 2015 Nov;85(5):690-3. doi: 10.1016/j.mehy.2015.08.013. Epub 2015 Aug 21.	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome is an idiopathic illness characterized by debilitating fatigue and neuro-immune abnormalities. A growing body of evidence proposes mitochondrial dysfunction as a central perpetrator of the illness due to activation of immune-inflammatory pathways that burden the mitochondria. Under a model of mitochondrial dysfunction, this paper explores dietary strategies that are mitoprotective. Studied for decades, the cellular mechanisms of ketogenic diets, fasting, and caloric restriction now reveal mitochondria-specific mechanisms which could play a role in symptom reduction in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Future research should examine the physiological effects of these dietary strategies in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.
Crichton A(1), Knight S(2), Oakley E(3), Babl FE(3), Anderson V(4).	(1)Victorian Pediatric Rehabilitation Service, Monash Children's, Melbourne, Australia; Murdoch Childrens Research Institute, Melbourne, Australia; School of Psychological Sciences and ali.crichton@mcri.edu.au.	Fatigue in child chronic health conditions: a systematic review of assessment instruments.	Pediatrics. 2015 Apr;135(4):e1015-31. doi: 10.1542/peds.2014-2440. Epub 2015 Mar 23.	BACKGROUND AND OBJECTIVE: Fatigue is common in chronic health conditions in childhood, associated with decreased quality of life and functioning, yet there are limited data to compare assessment instruments across conditions and childhood development. Our objective was to describe fatigue assessment instruments used in children with chronic health conditions and critically appraise the evidence for the measurement properties of identified instruments. METHODS: Data sources included Medline, Cumulative Index to Nursing and Allied Health Literature, and PsycINFO (using the EBSCOhost platform). Study selection included quantitative assessment of fatigue in children with health conditions. Data extraction was as follows: (1) study design, participant and fatigue instruments, (2) measurement properties of fatigue instruments, (3) methodological quality of included studies, and (4) synthesis of the quality of evidence across studies for the measurement properties of fatigue instruments. RESULTS: Twenty fatigue assessment instruments were identified (12 child reports, 7 parent reports, 1 staff report), used in 89 studies. Fatigue was assessed in over 14 health conditions, most commonly in children with cancer and chronic fatigue syndrome. Evidence for the measurement properties of instruments varied, and overall quality was low. Two fatigue instruments demonstrated strong measurement properties for use in children with diverse health conditions and children with cancer. CONCLUSIONS: The review is limited to children younger than 18 years and results are specific to health conditions described, limiting generalizability of findings to other populations. Evidence for the measurement properties of fatigue instruments varied according to the population in which instruments were used and informant. Further evidence is required for assessment of fatigue in younger children, and children with particular health conditions.
Crowhurst G(1).		The BJN Award: recognising the role of unpaid nurses.	Br J Nurs. 2015 Aug 13-Sep 19;24(15):768. doi: 10.12968/bjon.2015.24.15.768.	
Cullen T(1),	(1)Cardiff School of	The relationship between	Cytokine. 2015	IL-6 plays a mechanistic role in conditions such as metabolic syndrome, chronic fatigue

Thomas AW(2), Webb R(2), Hughes MG(3).	Sport, Cardiff Metropolitan University, Cardiff CF23 6XD, UK. Electronic address: tcullen@cardiffmet.ac.uk. (2)Cardiff School of Health Sciences, Cardiff Metropolitan University, Cardiff CF5 2YB, UK. (3)Cardiff School of Sport, Cardiff Metropolitan University, Cardiff CF23 6XD, UK.	interleukin-6 in saliva, venous and capillary plasma, at rest and in response to exercise.	Feb;71(2):397-400. doi: 10.1016/j.cyto.2014.10.011. Epub 2014 Nov 15.	syndrome and clinical depression and also plays a major role in inflammatory and immune responses to exercise. The purpose of this study was to investigate the levels of resting and post exercise IL-6 when measured in venous plasma, saliva and capillary plasma. Five male and five females completed 2 separate exercise trials, both of which involved standardized exercise sessions on a cycle ergometer. Venous blood and saliva samples were taken immediately before and after Trial A, venous and capillary blood samples were taken immediately before and after Trial B. IL-6 values were obtained using a high-sensitivity enzyme-linked immunosorbent assay (ELISA). In Trial A venous plasma IL-6 increased significantly from 0.4±0.14pg/ml to 0.99±0.29pg/ml ($P<0.01$) while there was no increase in salivary IL-6. Venous plasma and salivary IL-6 responses were not correlated at rest, post exercise or when expressed as an exercise induced change. In Trial B venous and capillary plasma IL-6 increased significantly (venous: 0.22±0.18 to 0.74±0.28pg/ml ($P\leqslant0.01$); capillary: 0.37±0.22 to 1.08±0.30pg/ml ($P<0.01$). Venous and capillary plasma responses did not correlate at rest ($r=0.59$, $P=0.07$) but did correlate post exercise ($r=0.79$, $P\geqslant0.001$) and when expressed as an exercise induced change ($r=0.71$, $P=0.02$). Saliva does not appear to reflect systemic IL-6 responses, either at rest or in response to exercise. Conversely, capillary plasma responses are reflective of systemic IL-6 responses to exercise.
Czarnecka AM(1), Oborska S, Rzepecki P, Szczylik C.	(1)Department of Oncology with Laboratory of Molecular Oncology, Military Institute of Medicine, Warsaw, Poland.	Development of chronic myeloid leukaemia in patients treated with anti-VEGF therapies for clear cell renal cell cancer.	Future Oncol. 2015;11(1):17-26. doi: 10.2217/fon.14.135.	Tyrosine kinase inhibitors are novel therapies targeting specific cellular signalling pathways. Sunitinib and sorafenib primarily block tyrosine kinase receptors involved in the progression of many tumours, including clear cell renal cell cancer (ccRCC). Although developed to target selected receptors, it is becoming apparent that they inhibit other kinases; this may result in the development of unexpected side effects. This is potentially dangerous as kinases on noncancerous cells are also inhibited. TKI off-target effects contributing to cardiotoxicity, hypothyroidism, hypertension, fatigue, hair depigmentation, hand-foot syndrome and gastrointestinal perforation have been described. We report three patients (3/412) treated with sunitinib and sorafenib who developed chronic myeloid leukaemia (CML) during treatment for ccRCC, proposing a molecular mechanism of tyrosine kinase inhibitors action on bone marrow cells that might be co-responsible for CML development.
d'Alessandro A, Niglio T, Desogus A, d'Alessandro A, Mandolesi D.		New acoustic wave therapy improves quality of life in patients with multiple sclerosis and chronic cerebrospinal venous insufficiency.	Ann Ital Chir. 2015 Jul-Aug;86(4):336-9.	A Multiple Sclerosis patient with chronic cerebrospinal venous insufficiency (CCSVI) treated by acoustic waves, modulated in frequency and power of the Dreno-MAM® device, showed a progressive improvement in motor coordination, resistance to work, muscular power and rigidity, and distal microcirculation. Life quality, chronic fatigue, and clinical severity questionnaires EDSS show marked improvements with a follow-up of two years. We suggest that the method could be also used in the chronic fatigue syndrome and other neurological diseases such as Parkinson or Meniere syndrome. Analyses on statistically robust samples are in progress to validate such impressive result obtained by this nonpharmacological and non-invasive treatment.KEY WORDS: Acoustic waves, Chronic cerebrospinal venous insufficiency, Multiple sclerosis.

Daenen L(1), Varkey E, Kellmann M, Nijs J.	(1)*Department of Neurology, Faculty of Medicine, University of Antwerp (UA) †Pain in Motion Research Group, Departments of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel (VUB), Belgium ‡Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden §Faculty of Sport Science, Ruhr-University Bochum, Bochum, Germany ‖Schools of Human Movement Studies and of Psychology, The University of Queensland, Brisbane, Qld, Australia.	Exercise, not to exercise, or how to exercise in patients with chronic pain? Applying science to practice.	Clin J Pain. 2015 Feb;31(2):108-14. doi: 10.1097/AJP.0000000000000099.	BACKGROUND: Exercise is an effective treatment strategy in various chronic musculoskeletal pain disorders, including chronic neck pain, osteoarthritis, headache, fibromyalgia and chronic low back pain. Although exercise can benefit those with chronic pain (CP), some patients (eg, those with fibromyalgia, myalgic encephalomyelitis/chronic fatigue syndrome and chronic whiplash associated disorders) encounter exercise as a pain inducing stimulus and report symptom flares due to exercise. OBJECTIVES: This paper focuses on the clinical benefits and detrimental effects of exercise in patients with CP. It summarizes the positive and negative effects of exercise therapy in migraine and tension-type headache and provides an overview of the scientific evidence of dysfunctional endogenous analgesia during exercise in patients with certain types of CP. Further, the paper explains the relationship between exercise and recovery highlighting the need to address recovery strategies as well as exercise regimes in the rehabilitation of these patients. The characteristics, demands and strategies of adequate recovery to compensate stress from exercise and return to homeostatic balance will be described. METHODS: narrative review. RESULTS: Exercise is shown to be effective in the treatment of chronic tension-type headache and migraine. Aerobic exercise is the best option in migraine prophylaxis, whereas specific neck and shoulder exercises is a better choice in treating chronic tension-type headache. Besides the consensus that exercise therapy is beneficial in the treatment of CP, the lack of endogenous analgesia in some CP disorders should not be ignored. Clinicians should account for this when treating CP patients. Furthermore, optimizing the balance between exercise and recovery is of crucial merit in order to avoid stress-related detrimental effects and achieve optimal functioning in patients with CP. CONCLUSION: Exercise therapy has found to be beneficial in CP, but it should be appropriately and individually tailored with emphasis on prevention of symptom flares and applying adequate recovery strategies.
Dahan H(1), Shir Y, Velly A, Allison P.	(1)Division of Oral Health and Society, Faculty of Dentistry, McGill University, Montreal, QC, H3A 1G1, Canada, haissam.dahan@mail.mcgill.ca.	Specific and number of comorbidities are associated with increased levels of temporomandibular pain intensity and duration.	J Headache Pain. 2015;16:528. doi: 10.1186/s10194-015-0528-2. Epub 2015 May 20.	BACKGROUND: Temporomandibular pain disorder (TMD) is a common pain condition in the face. People with TMD report multiple pain comorbidities. The presence of fibromyalgia and migraine in people with TMD is associated with an increase in TMD pain intensity and duration. However, data on the relationship between increasing number of pain comorbidities and TMD pain are rare. The aims of this study were: firstly to evaluate the extent to which increasing number of comorbidities is associated with increasing TMD pain intensity and duration; and secondly to evaluate the extent to which the presence of specific comorbidities is associated with increasing TMD pain intensity and duration. METHODS: The sample included 180 people seeking TMD treatment at Boston and Montreal clinics. TMD was diagnosed using the Research Diagnostic Criteria for TMD. A Numerical Pain Rating Scale assessed TMD pain intensity and participants provided their TMD pain duration in a study questionnaire. The

				comorbidities of migraine, chronic fatigue syndrome, irritable bowel syndrome, interstitial cystitis and restless leg syndrome were diagnosed by 5 validated diagnostic questionnaires. The associations were analyzed by linear regression, controlling for confounders. RESULTS: There was a positive association between the number of comorbidities present and TMD pain intensity ($p < 0.01$) and between the number of comorbidities present and TMD pain duration ($p < 0.01$). Also, the presence of migraine was positively associated with TMD pain intensity ($p < 0.01$) and the presence of chronic fatigue syndrome was positively associated with TMD pain intensity ($p < 0.05$) and with TMD pain duration ($p < 0.01$). When TMD patients were separated into groups, these associations did not change for the myofascial pain group, whereas in the non-myofascial pain group, the relationship between number of comorbidities and TMD pain duration was the only one still present. CONCLUSION: This study shows that the number of comorbidities is positively associated with TMD pain duration and intensity. The presence of specific conditions, such as migraine and chronic fatigue syndrome, is associated with an increase in TMD intensity and duration.
Dai T(1), Tang T.	(1)Department of Gastrointestinal, The First Hospital of Jilin University, Changchun 130021, China. tangtongyu@163.com.	[Research progress of fecal microbiota transplantation].[Article in Chinese]	Zhonghua Wei Chang Wai Ke Za Zhi. 2015 Jul;18(7):733-7.	Intestinal microbial ecosystem is the most complex and the largest micro-ecosystem of the mammals. The use of antibiotics can lead to a lot of major changes of the flora, making the intestinal flora damaged and impacted, even developing Clostridium difficile infection. Fecal microbiota transplantation (FMT) as a special organ transplant therapy, which can rebuild the intestinal flora, has raised the clinical concerns. It has been used in the refractory Clostridium difficile, inflammatory bowel disease, irritable bowel syndrome, chronic fatigue syndrome, and some non-intestinal diseases related to the metabolic disorders. But this method of treatment has not become a normal treatment, and many clinicians and patients can not accept it. This paper reviews relevant literature in terms of origin, indications, mechanism, production process, current situation and future research, and provide a reference for the clinical application of the treatment of fecal microbiota transplantation.
Das SS(1), Bhattacharya S(2), Bhartia S(2).	(1)Department of Transfusion Medicine, Apollo Gleneagles Hospitals, Kolkata, West Bengal, India. (2)Department of Hematology, Apollo Gleneagles Hospitals, Kolkata, West Bengal, India.	Clinical and serological characterization of cold agglutinin syndrome in a Tertiary Care Hospital in Eastern India.	Asian J Transfus Sci. 2015 Jul-Dec;9(2):173-6. doi: 10.4103/0973-6247.154258.	BACKGROUND AND AIM: Cold agglutinin syndrome (CAS) primary or secondary represents approximately 16-32% of autoimmune hemolytic anemia cases. Most patients present with mild, chronic hemolytic anemia with exacerbation of the condition in the cold environment. Red cell transfusions are only indicated when there is a life-threatening anemia causing crisis. We studied the clinical and serological characterization of CAS with the aim that the information gained from this study would help in proper diagnosis and management of these patients. MATERIALS AND METHODS: The prospective study included nine patients who were admitted with severe anemia. Detailed work-up were conducted to establish the diagnosis, severity of in vivo hemolysis and transfusion management. RESULTS: All patients presented with pallor, weakness, fatigue and painful fingers and toes with exacerbation of symptoms in winter months. Secondary CAS was observed in three patients suffering from malignant lymphoma. Red cells of all patients were coated with complements (C3) more

				specifically C3d. In one patient suffering from malignant lymphoma, the cold autoagglutinin titer was as high as 4096. Autoantibody in seven patients was specific to "I" antigen and one to "i" antigen. CONCLUSIONS: We conclude that detailed clinical and serological characterization is needed to diagnose and manage CAS. Whereas avoidance of cold exposure is the primary therapy, but no critical patient should be denied blood transfusion due to serological complications. All transfusion services should follow the correct protocol to maximize blood safety in CAS.
De Luca C(1), Gugliandolo A(2), Calabrò C(2), Currò M(2), Ientile R(2), Raskovic D(3), Korkina L(4), Caccamo D(2).	(1)Centre of Innovative Biotechnological Investigations (Cibi-Nanolab), 197 Vernadskogo Prospekt, Moscow 119571, Russia ; Active Longevity Clinic "Institut Krasoty na Arbate", 8 Maly Nikolopeskovsky lane, Moscow 119002, Russia.	Role of polymorphisms of inducible nitric oxide synthase and endothelial nitric oxide synthase in idiopathic environmental intolerances.	Mediators Inflamm. 2015;2015:245308. doi: 10.1155/2015/245308. Epub 2015 Mar 24.	Oxidative stress and inflammation play a pathogenetic role in idiopathic environmental intolerances (IEI), namely, multiple chemical sensitivity (MCS), fibromyalgia (FM), and chronic fatigue syndrome (CFS). Given the reported association of nitric oxide synthase (NOS) gene polymorphisms with inflammatory disorders, we aimed to investigate the distribution of NOS2A -2.5 kb (CCTTT) n as well as Ser608Leu and NOS3 -786T>C variants and their correlation with nitrite/nitrate levels, in a study cohort including 170 MCS, 108 suspected MCS (SMCS), 89 FM/CFS, and 196 healthy subjects. Patients and controls had similar distributions of NOS2A Ser608Leu and NOS3 -786T>C polymorphisms. Interestingly, the NOS3 -786TT genotype was associated with increased nitrite/nitrate levels only in IEI patients. We also found that the NOS2A -2.5 kb (CCTTT)11 allele represents a genetic determinant for FM/CFS, and the (CCTTT)16 allele discriminates MCS from SMCS patients. Instead, the (CCTTT)8 allele reduces by three-, six-, and tenfold, respectively, the risk for MCS, SMCS, and FM/CFS. Moreover, a short number of (CCTTT) repeats is associated with higher concentrations of nitrites/nitrates. Here, we first demonstrate that NOS3 -786T>C variant affects nitrite/nitrate levels in IEI patients and that screening for NOS2A -2.5 kb (CCTTT) n polymorphism may be useful for differential diagnosis of various IEI.
Delano-Wood L(1,)(2,)(3), Bangen KJ(4,)(5), Sorg SF(4,)(6,)(5), Clark AL(7), Schiehser DM(4,)(6,)(5), Luc N(4,)(6), Bondi MW(4,)(5), Werhane M(7), Kim RT(4,)(6), Bigler ED(8,)(9).	(1)Veterans Affairs San Diego Healthcare System (116B), 3350 La Jolla Village Drive, San Diego, CA, 92161, USA. ldelano@ucsd.edu.	Brainstem white matter integrity is related to loss of consciousness and postconcussive symptomatology in veterans with chronic mild to moderate traumatic brain injury.	Brain Imaging Behav. 2015 Sep;9(3):500-12. doi: 10.1007/s11682-015-9432-2.	We investigated associations between DTI indices of three brainstem white matter tracts, traumatic brain injury (TBI) injury characteristics, and postconcussive symptomatology (PCS) in a well-characterized sample of veterans with history of mild to moderate TBI (mTBI). 58 military veterans (mTBI: n = 38, mean age = 33.2, mean time since injury = 90.9 months; military controls [MC]; n = 20; mean age = 29.4) were administered 3T DTI scans as well as a comprehensive neuropsychiatric evaluation including evaluation of TBI injury characteristics and PCS symptoms (e.g., negative mood, dizziness, balance and coordination difficulties). Tractography was employed by seeding ROIs along 3 brainstem white matter tracts (i.e., medial lemniscus-central tegmentum tract [ML-CTT]; corticospinal tracts [CST], and pontine tegmentum [PT]), and mean DTI values were derived from fractional anisotropic (FA) maps. Results showed that there were no significant difference in FA between the MC and TBI groups across the 3 regions of interest; however, among the TBI group, CST FA was significantly negatively associated with LOC duration. Additionally, lower FA of certain tracts-most especially the PT-was significantly associated with increased PCS symptoms (i.e., more severe vestibular symptoms, poorer physical functioning, and greater levels of fatigue),

				even after adjusting for PTSD symptoms. Our findings show that, in our sample of veterans with mTBI, tractography-based DTI indices of brainstem white matter tracts of interest are related to the presence and severity of PCS symptoms. Findings are promising as they show linkages between brainstem white matter integrity and injury severity (LOC), and they raise the possibility that the pontine tegmentum in particular may be a useful marker of PCS symptoms. Collectively, these data point to important neurobiological substrates of the chronic and complex constellation of symptoms following the 'signature injury' of our combat-exposed veterans.
Dell'Osso L(1), Bazzichi L(2), Baroni S(1), Falaschi V(1), Conversano C(1), Carmassi C(1), Marazziti D(1).	(1)Section of Psychiatry, Department of Clinical and Experimental Medicine, University of Pisa, Italy. (2)Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy.	The inflammatory hypothesis of mood spectrum broadened to fibromyalgia and chronic fatigue syndrome.	Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl 88):S109-16. Epub 2015 Mar 18.	OBJECTIVES: The present paper aimed at reviewing literature data on the inflammatory hypothesis of mood spectrum, as well as the overlapping features with some chronic rheumatologic disorders, in particular fibromyalgia and chronic fatigue syndrome. METHODS: A literature search was carried out for English papers published in the years 2000-2014, while using the following words: mood spectrum, depression, bipolar disorders, fibromyalgia, chronic fatigue syndrome, neurotransmitters, inflammation, neuroinflammation, cytokines. RESULTS: Overlapping features were highlighted between mood spectrum, fibromyalgia and chronic fatigue syndrome suggesting common underlying mechanisms at pathophysiological level involving both central nervous and the immune systems. CONCLUSIONS: Taken together, the literature would suggest that the borders between different medical domains should be reconsidered in the light of common processes linking them.
DePalma RG. In: Kobeissy FH, editor.		Combat TBI: History, Epidemiology, and Injury Modes().	Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects. Boca Raton (FL): CRC Press/Taylor & Francis; 2015. Chapter 2. Frontiers in Neuroengineering.	Although types and modes of combat injury have changed over the centuries as weapons of war evolved, details about combat traumatic brain injury (TBI) date from the earliest accounts of warfare. This chapter provides a brief historical overview of combat TBI resulting from primitive blunt and penetrating head injuries to current blast-related injuries. Updated numbers of TBI events and injuring mechanisms will be considered. Brain injury causes loss or alteration of consciousness, prograde and retrograde amnesia, and immediate physical and neurological effects ranging from mild to severe. These injuries, in certain cases, cause varying chronic physical, cognitive, and behavioral issues. The most common form of brain injury, acute mild TBI or concussion (mTBI/concussion), has multiple definitions derived from various sources. Vasterling et al. have provided a useful summary of these iterations (Vasterling, 2012). The operative definition selected for this review includes loss or alteration consciousness for up to 30 minutes at the time of injury, a confused or disoriented state lasting less than 24 hours, memory loss lasting less than 24 hours, and normal structural brain imaging on computed tomographic scanning. Glasgow Coma Scale scores of 13–15 characterize acute mTBI, whereas lower Glasgow Coma Scale scores, 9–12, designate acute moderate TBI. Glasgow Coma Scale scores of 3–8 designate acute severe TBI (Teasdale and Jennett, 1974). Current combat or military TBI/concussions most frequently are classified as mild. Although recovery from mTBI/concussion is said to be the norm, in about 15% (estimates range from 10%–25%) of cases, physical disabilities and

				symptoms persist beyond three months to become a chronic condition, also known as postconcussion syndrome (Vasterling, 2012). Chronic sequelae of postconcussion syndrome include headache, insomnia, fatigue, sensory, balance, and other neurologic defects as well as cognitive and emotional disorders. Symptoms can be subtle and variable in severity and frequency over time; mTBI and concussion are often used clinically as synonyms. This chapter focuses on mTBI/concussion as a combat injury. Diagnosis of posttraumatic stress disorder (PTSD), first accepted as a formal diagnosis in 1980 (Horowitz et al., 1980), and other mental illness including depression are reportedly more common in combatants as compared with nondeployed service members during current ongoing military operations (Blakely, 2013). The methods used to obtain estimates affect data concerning numbers of cases of TBI, PTSD, and other mental disorders. Individuals usually are reported only once as a case within a category; data can be presented as the number of diagnoses (prevalence), rate of new diagnoses in a population (incidence), or total number of cases in a population. The total number of diagnoses changes in relation to population size, which for military conditions increases over time with continued combat activities (Blakely, 2013). This chapter uses numbers available from public sources for the Department of Defense (DOD) and updated data through 2013 from the tracking tool used by the Department of Veterans Affairs (VA). PTSD results from exposure to a traumatic event with risk of serious injury or bodily harm to self or others and a response to that event involving intense fear, horror, or helplessness. Symptoms include reexperiencing of the traumatic event, including nightmares and distressing recollections, avoidance of stimuli associated with the trauma with diminished responsiveness and loss of interest in activities, and hyperarousal including irritability, anger, hypervigilance, insomnia, and concentration difficulties. Cognitive and behavioral symptoms of PTSD and depression overlap with those of mTBI; mTBI sustained during the stress of battle is believed to predispose to or accentuate PTSD (Bryant, 2011; Vasterling, 2012). Historical narratives reveal connections or associations between past and current relationships (Rabins, 2013). Vignettes from past and present conflicts yield insights into the causes and sequelae of combat injuries affecting the brain. Currently, blast injuries predominate among combatants in Operations Enduring Freedom, Iraqi Freedom, and New Dawn (OEF/OIF/OND). Recognition of the importance of mTBI and PTSD relates to enhanced surveillance and clinical guidelines initiated by the DOD and the VA (Management of Concussion/mTBI Working Group 2009). Incidence and prevalence data from both sources provide ongoing estimates of the numbers of service members affected by TBI; the frequency of this particular injury has become a matter of increasing concern. Although the long-term effects of brain damage caused by differing modes of head injury seem to appear identical in the long term (Belanger et al., 2009), recent observations suggest that differing modes of combat injury—for example, blunt as compared with blast injuries—result in differing vestibular-ocular and spinal reflexes

				(Hoffer et al., 2009) and neural activation responses (Fischer et al., 2013). Behavioral disorders appear to be more common with blast as opposed to blunt injury (Mendez et al., 2013). Repeated injuries, particularly sports-related, have become a public health concern because of their long-term consequences (Jordan, 2013). These emerging observations are important for assessing treatments, outcomes, and disability determinations.
Dobryakova E(1), Genova HM(2), DeLuca J(3), Wylie GR(4).	(1)Traumatic Brain Injury Laboratory, Kessler Foundation , West Orange, NJ , USA ; Department of Physical Medicine and Rehabilitation, Rutgers - New Jersey Medical School , Newark, NJ , USA.	The dopamine imbalance hypothesis of fatigue in multiple sclerosis and other neurological disorders.	Front Neurol. 2015 Mar 12;6:52. doi: 10.3389/fneur.2015.00052. eCollection 2015.	Fatigue is one of the most pervasive symptoms of multiple sclerosis (MS), and has engendered hundreds of investigations on the topic. While there is a growing literature using various methods to study fatigue, a unified theory of fatigue in MS is yet to emerge. In the current review, we synthesize findings from neuroimaging, pharmacological, neuropsychological, and immunological studies of fatigue in MS, which point to a specific hypothesis of fatigue in MS: the dopamine imbalance hypothesis. The communication between the striatum and prefrontal cortex is reliant on dopamine, a modulatory neurotransmitter. Neuroimaging findings suggest that fatigue results from the disruption of communication between these regions. Supporting the dopamine imbalance hypothesis, structural and functional neuroimaging studies show abnormalities in the frontal and striatal regions that are heavily innervated by dopamine neurons. Further, dopaminergic psychostimulant medication has been shown to alleviate fatigue in individuals with traumatic brain injury, chronic fatigue syndrome, and in cancer patients, also indicating that dopamine might play an important role in fatigue perception. This paper reviews the structural and functional neuroimaging evidence as well as pharmacological studies that suggest that dopamine plays a critical role in the phenomenon of fatigue. We conclude with how specific aspects of the dopamine imbalance hypothesis can be tested in future research.
Dong Y(1,)(2), Li Y(3,)(4,)(5), Sun Y(6), Mao J(7), Yao F(8), Tian Y(9), Wang L(10), Li L(11), Li S(12,)(13,)(14), Li J(15,)(16,)(17).	(1)Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing, 100700, China. docsxx@163.com. Province, Zhengzhou, Henan,	Bufei Jianpi granules improve skeletal muscle and mitochondrial dysfunction in rats with chronic obstructive pulmonary disease.	BMC Complement Altern Med. 2015 Mar 10;15:51. doi: 10.1186/s12906-015-0559-x.	BACKGROUND: Bufei Jianpi granules has been confirmed effective in improving pulmonary function, alleviating acute exacerbations, improving six-minute walk distance and quality of life, and benefited in 12-month follow-up in chronic obstructive pulmonary disease (COPD) patients with syndrome of lung-spleen qi deficiency. Skeletal muscle dysfunction (SMD), an important extrapulmonary complication, occurs in the very initiation of COPD and is closely related to morbidity and mortality. To evaluate the efficacy of Bufei Jianpi granules on SMD, we observed skeletal muscular function and histomorphology, mitochondrial morphormetry and proteins in COPD rats induced by cigarette-smoke and Klebsiella pneumoniae. METHODS: Seventy-two Sprague-Dawley rats were randomized into Control + Saline, Control + Bufei Jianpi, Control + Aminophylline, COPD + Saline, COPD + Bufei Jianpi and COPD + Aminophylline groups. From week 9 to 20, rats were administrated intragastricly by normal saline, Bufei Jianpi granules and aminophylline, respectively. Muscular tension and fatigue index of intercostal muscle, quadriceps, biceps and soleus were detected by using electrophysiological technology. Pathological and ultrastructural changes and

				expressions of mitochondrial Bcl-2 nineteen-kilodalton interacting protein 3 (Bnip3) and cytoplasm cytochrome C (Cyto C) in the four skeletal muscles were observed by using optical and electron microscope and western blotting. RESULTS: There was no statistical difference among the control rats treated with saline, Bufei Jianpi granules or aminophylline in above-mentioned parameters. Muscular tension, mitochondria volume density (Vv) and compared membrane surface (δm) of the four muscles were significantly lower in COPD + Saline group compared to Control + Saline group, while fatigue index, mitochondria surface area (δ), Bnip3 and Cyto C were higher ($P < 0.05$). COPD rats showed more morphological changes in muscle tissues than controls, such as atrophy, degeneration, necrosis and matrix hyperplasia. Utrastructurally, mitochondria populations decreased significantly in the four muscles, and were shrunken and even cavitation changed. The up-mentioned parameters were improved in Bufei Jianpi group ($P < 0.05$) in the four muscles. CONCLUSIONS: Bufei Jianpi granules can improve skeletal muscle function via improving mitochondria population and function, reducing apoptotic factors such as Bnip3 and Cyto C, and is more effective than aminophylline.
Dryden MS(1), Saeed K(1), Ogborn S(2), Swales P(2).	(1)Department of Microbiology,Royal Hampshire County Hospital,Winchester,UK. (2)Department of Medicine,Royal Hampshire County Hospital,Winchester,UK.	Lyme borreliosis in southern United Kingdom and a case for a new syndrome, chronic arthropod-borne neuropathy.	Epidemiol Infect. 2015 Feb;143(3):561-72. doi: 10.1017/S0950268814001071. Epub 2014 May 9.	This series of serologically confirmed Lyme disease is the largest reported in the UK and represents 508 patients who presented to one hospital in the South of England between 1992 and 2012. The mean rate of borreliosis throughout this period was 9·8/100,000 population, much higher than the reported national rate of 1·7/100,000. The actual rate increased each year until 2009 when it levelled off. Patients clinically presented with rash (71%), neurological symptoms (16%, of whom half had VII cranial nerve palsies), arthropathy (8%), pyrexia (5%), cardiac abnormalities (1%) or other manifestations (<1%). Twenty percent of patients had additional non-specific symptoms of fatigue, myalgia, and cognitive changes. Serological diagnosis was with a two-tiered system of ELISA and immunoblot. There was a marked seasonal presentation in the summer months and in the first and sixth decades of life. A third of patients gave a clear history of a tick bite. The median interval between tick bite and clinical symptoms was 15 days [interquartile range (IQR) 9-28 days], with a further interval of 14 days to clinical diagnosis/treatment (IQR 2-31 days). Most cases were acquired locally and only 5% abroad. Patients responded to standard antibiotic therapy and recurrence or persistence was extremely rare. A second group of patients, not included in the clinical case series, were those who believed they had Lyme disease based on a probable tick bite but were seronegative by currently available validated tests and presented with subjective symptoms. This condition is often labelled chronic Lyme disease. These patients have a different disease from Lyme disease and therefore an alternative name, chronic arthropod-borne neuropathy (CAN), and case definition for this condition is proposed. We suggest that this chronic condition needs to be distinguished from Lyme disease, as calling the chronic illness 'Lyme disease' causes confusion to patients and physicians. We recommend research initiatives to investigate the aetiology, diagnosis and therapy of CAN.

Durham J, McDonald C, Hutchinson L, Newton JL.		Painful temporomandibular disorders are common in patients with postural orthostatic tachycardia syndrome and impact significantly upon quality of life.	J Oral Facial Pain Headache. 2015 Spring;29(2):152-7. doi: 10.11607/ofph.1396.	AIMS: To explore the point prevalence of painful temporomandibular disorders (TMD) in a well-characterized clinical cohort of postural orthostatic tachycardia syndrome (PoTS) sufferers and to understand the functional and physiologic impact of this comorbidity on the patient. METHODS: Patients with PoTS were retrospectively recruited from a previous study conducted in a UK hospital setting. Data had previously been collected on several parameters, including sociodemographic, physiologic, and functional. The participants were mailed a highly sensitive (99%) and specific (97%) self-report screening instrument for painful TMD. Simple descriptive statistics with Fisher Exact and Kruskal-Wallis tests were used to examine the data and draw inferences from it. RESULTS: A total of 36 individuals responded (69% response rate). Just under half (47%) of the sample screened positive for painful TMD. There was no significant difference between the screening result for TMD or previously reported headaches or joint pain ($P < .05$). Chronic fatigue syndrome (CFS) was diagnosed by the Fukuda Criteria in 44% of the total sample and in 56% of those with painful TMD. There were no significant differences in physiologic parameters in CFS and TMD. TMD caused a significant decrease in quality of life as measured by the Patient-Reported Outcomes Measurement Information System, Health Assessment Questionnaire ($P < .05$). CONCLUSION: TMD are common in patients with PoTS. They have a significant, additional impact on patients' quality of life and should therefore be screened for at an early stage in PoTS.
Dziadkowiak E(1), Sebastian A(2), Wiland P(2), Waliszewska-Prosół M(1), Wieczorek M(3), Zagrajek M(1), Ejma M(1).	(1)a Department of Neurology , Wrocław Medical University , Poland. (2)b Department of Rheumatology , Wrocław Medical University , Poland. (3)c Department of Geography and Regional Development , University of Wrocław , Poland.	Endogenous event-related potentials in patients with primary Sjögren's syndrome without central nervous system involvement.	Scand J Rheumatol. 2015 Nov;44(6):487-94. doi: 10.3109/03009742.2015.1032345. Epub 2015 Aug 14.	OBJECTIVES: Endogenous cognitive event-related potentials (CERPs) reflect higher-level processing of sensory information and can be used to evaluate cognitive functions. The aim of this paper was to determine whether there are any abnormalities in the electrophysiological parameters of CERPs in patients with primary Sjögren's syndrome (pSS) but without symptoms of central nervous system (CNS) involvement or mental disorder. The analysis of CERP parameters was then correlated with the clinical status of the patients and with some of the immunological parameters in the patient group. METHOD: Thirty consecutive patients with pSS (29 females, one male) were included in the study. All the patients underwent CERP examination. RESULTS: There was a significant prolongation of the latency of P300 and N200 potentials in patients with pSS. Abnormalities in electrophysiological parameters of CERPs correlated with the duration of the disease, salivary gland abnormalities, and elevated erythrocyte sedimentation rate (ESR) values. Patients with coexisting chronic fatigue syndrome (CFS) had larger P300 amplitudes. There were no statistically significant changes in the electrophysiological parameters of CERPs in patients with pSS dependent on the presence of peripheral nervous system (PNS) lesions, skin changes, arthritis, abnormalities in white blood cells and the immune system or the levels of blood lipids. CONCLUSIONS: The results of the study suggest the presence of a minor cognitive dysfunction in patients with pSS without symptoms of CNS involvement or mental disorder. Cognitive dysfunction correlated with the disease duration time and the

				severity of inflammatory changes (salivary gland abnormalities and inflammatory markers in the blood). Further and larger longitudinal studies are necessary for confirmation of this correlation.
Eccles JA(1), Owens AP(2), Mathias CJ(2), Umeda S(3), Critchley HD(4).	(1)Psychiatry, Brighton and Sussex Medical School Brighton, UK ; Sussex Partnership National Health Service Foundation Trust Brighton, UK.	Neurovisceral phenotypes in the expression of psychiatric symptoms.	Front Neurosci. 2015 Feb 10;9:4. doi: 10.3389/fnins.2015.00004 . eCollection 2015.	This review explores the proposal that vulnerability to psychological symptoms, particularly anxiety, originates in constitutional differences in the control of bodily state, exemplified by a set of conditions that include Joint Hypermobility, Postural Tachycardia Syndrome and Vasovagal Syncope. Research is revealing how brain-body mechanisms underlie individual differences in psychophysiological reactivity that can be important for predicting, stratifying and treating individuals with anxiety disorders and related conditions. One common constitutional difference is Joint Hypermobility, in which there is an increased range of joint movement as a result of a variant of collagen. Joint hypermobility is over-represented in people with anxiety, mood and neurodevelopmental disorders. It is also linked to stress-sensitive medical conditions such as irritable bowel syndrome, chronic fatigue syndrome and fibromyalgia. Structural differences in "emotional" brain regions are reported in hypermobile individuals, and many people with joint hypermobility manifest autonomic abnormalities, typically Postural Tachycardia Syndrome. Enhanced heart rate reactivity during postural change and as recently recognized factors causing vasodilatation (as noted post-prandially, post-exertion and with heat) is characteristic of Postural Tachycardia Syndrome, and there is a phenomenological overlap with anxiety disorders, which may be partially accounted for by exaggerated neural reactivity within ventromedial prefrontal cortex. People who experience Vasovagal Syncope, a heritable tendency to fainting induced by emotional challenges (and needle/blood phobia), are also more vulnerable to anxiety disorders. Neuroimaging implicates brainstem differences in vulnerability to faints, yet the structural integrity of the caudate nucleus appears important for the control of fainting frequency in relation to parasympathetic tone and anxiety. Together there is clinical and neuroanatomical evidence to show that common constitutional differences affecting autonomic responsivity are linked to psychiatric symptoms, notably anxiety.
Efrati S(1), Golan H(2), Bechor Y(3), Faran Y(4), Daphna-Tekoah S(5), Sekler G(6), Fishlev G(7), Ablin JN(8), Bergan J(7), Volkov O(2), Friedman M(7), Ben-Jacob E(9),	(1)Research and Development Unit, Assaf Harofeh Medical Center, Zerifin, Israel; The Institute of Hyperbaric Medicine, Assaf Harofeh Medical Center, Zerifin, Israel; Sackler School of Medicine, Tel-Aviv University, Tel-Aviv,	Hyperbaric oxygen therapy can diminish fibromyalgia syndrome--prospective clinical trial.	PLoS One. 2015 May 26;10(5):e0127012. doi: 10.1371/journal.pone.0127012. eCollection 2015.	BACKGROUND: Fibromyalgia Syndrome (FMS) is a persistent and debilitating disorder estimated to impair the quality of life of 2-4% of the population, with 9:1 female-to-male incidence ratio. FMS is an important representative example of central nervous system sensitization and is associated with abnormal brain activity. Key symptoms include chronic widespread pain, allodynia and diffuse tenderness, along with fatigue and sleep disturbance. The syndrome is still elusive and refractory. The goal of this study was to evaluate the effect of hyperbaric oxygen therapy (HBOT) on symptoms and brain activity in FMS. METHODS AND FINDINGS: A prospective, active control, crossover clinical trial. Patients were randomly assigned to treated and crossover groups: The treated group patients were evaluated at baseline and after HBOT. Patients in the crossover-control group were evaluated three times: baseline, after a control

Buskila D(10).	Israel; Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel.			period of no treatment, and after HBOT. Evaluations consisted of physical examination, including tender point count and pain threshold, extensive evaluation of quality of life, and single photon emission computed tomography (SPECT) imaging for evaluation of brain activity. The HBOT protocol comprised 40 sessions, 5 days/week, 90 minutes, 100% oxygen at 2ATA. Sixty female patients were included, aged 21-67 years and diagnosed with FMS at least 2 years earlier. HBOT in both groups led to significant amelioration of all FMS symptoms, with significant improvement in life quality. Analysis of SPECT imaging revealed rectification of the abnormal brain activity: decrease of the hyperactivity mainly in the posterior region and elevation of the reduced activity mainly in frontal areas. No improvement in any of the parameters was observed following the control period. CONCLUSIONS: The study provides evidence that HBOT can improve the symptoms and life quality of FMS patients. Moreover, it shows that HBOT can induce neuroplasticity and significantly rectify abnormal brain activity in pain related areas of FMS patients. TRIAL REGISTRATION: ClinicalTrials.gov NCT01827683.
[Article in English, Norwegian]	Egeland T, Angelsen A, Haug R, Henriksen JO, Lea TE, Saugstad OD.	What exactly is myalgic encephalomyelitis?	Tidsskr Nor Laegeforen. 2015 Oct 20;135(19):1756-9. doi: 10.4045/tidsskr.15.0089. eCollection 2015.	Comment in Tidsskr Nor Laegeforen. 2015 Dec 1;135(22):2021.
Eidi H(1,)(2), David MO(3), Crépeaux G(4), Henry L(5), Joshi V(6), Berger MH(7), Sennour M(8), Cadusseau J(9,)(10), Gherardi RK(11), Curmi PA(12).	(1)Institut National de la Santé et de la Recherche Médicale (INSERM) - UMR 1204, Université Evry-Val d'Essonne, Laboratoire Structure-Activité des Biomolécules Normales et Pathologiques, Evry, France. housam.eidi@gmail.com. josette.cadusseau@inserm.fr.	Fluorescent nanodiamonds as a relevant tag for the assessment of alum adjuvant particle biodisposition.	BMC Med. 2015 Jun 17;13:144. doi: 10.1186/s12916-015-0388-2.	BACKGROUND: Aluminum oxyhydroxide (alum) is a crystalline compound widely used as an immunologic adjuvant of vaccines. Concerns linked to alum particles have emerged following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion in patients with myalgic encephalomyelitis, revealing an unexpectedly long-lasting biopersistence of alum within immune cells and a fundamental misconception of its biodisposition. Evidence that aluminum-coated particles phagocytozed in the injected muscle and its draining lymph nodes can disseminate within phagocytes throughout the body and slowly accumulate in the brain further suggested that alum safety should be evaluated in the long term. However, lack of specific staining makes difficult the assessment of low quantities of bona fide alum adjuvant particles in tissues. METHODS: We explored the feasibility of using fluorescent functionalized nanodiamonds (mfNDs) as a permanent label of alum (Alhydrogel(®)). mfNDs have a specific and perfectly photostable fluorescence based on the presence within the diamond lattice of nitrogen-vacancy centers (NV centers). As the NV center does not bleach, it allows the microspectrometric detection of mfNDs at very low levels and in the long-term. We thus developed fluorescent nanodiamonds functionalized by hyperbranched polyglycerol (mfNDs) allowing good coupling and stability of alum:mfNDs (AluDia) complexes. Specificities of AluDia complexes were comparable to the whole reference vaccine (anti-hepatitis B vaccine) in terms of particle size and zeta potential. RESULTS: In vivo, AluDia injection was followed by prompt phagocytosis and AluDia particles remained easily detectable by the specific signal of the fND particles in

				the injected muscle, draining lymph nodes, spleen, liver and brain. In vitro, mfNDs had low toxicity on THP-1 cells and AluDia showed cell toxicity similar to alum alone. Expectedly, AluDia elicited autophagy, and allowed highly specific detection of small amounts of alum in autophagosomes. CONCLUSIONS: The fluorescent nanodiamond technology is able to overcome the limitations of previously used organic fluorophores, thus appearing as a choice methodology for studying distribution, persistence and long-term neurotoxicity of alum adjuvants and beyond of other types of nanoparticles.
Engen DJ(1), McAllister SJ(2), Whipple MO(2), Cha SS(3), Dion LJ(2), Vincent A(2), Bauer BA(2), Wahner-Roedler DL(4).	(1)Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, Minnesota 55905, USA.	Effects of transdermal magnesium chloride on quality of life for patients with fibromyalgia: a feasibility study.	J Integr Med. 2015 Sep;13(5):306-13. doi: 10.1016/S2095-4964(15)60195-9.	BACKGROUND: Fibromyalgia is a syndrome characterized by chronic pain, fatigue, depression, and sleep disturbances. Its primary cause is unclear. Several studies have reported decreased intracellular magnesium levels in patients with fibromyalgia and have found negative correlation between magnesium levels and fibromyalgia symptoms. OBJECTIVE: To gather preliminary data on whether transdermal magnesium can improve quality of life for women who have fibromyalgia. DESIGN, SETTING, PARTICIPANTS AND INTERVENTIONS: This is a patient questionnaires and survey in a fibromyalgia clinic at a tertiary medical center. Forty female patients with the diagnosis of fibromyalgia were enrolled. Each participant was provided a spray bottle containing a transdermal magnesium chloride solution and asked to apply 4 sprays per limb twice daily for 4 weeks. Participants were asked to complete the Revised Fibromyalgia Impact Questionnaire, SF-36v2 Health Survey, and a quality-of-life analog scale at baseline, week 2, and week 4. MAIN OUTCOME MEASURE: Questionnaire and survey scores, evaluated through intent-to-treat and per-protocol analyses. RESULTS: Twenty-four patients completed the study (mean [SD] age, 57.2 [7.6] years; white, 95%; mean body mass index, 31.3 kg/m2). With intention-to-treat analysis, Revised Fibromyalgia Impact Questionnaire subscale and total scores were significantly improved at week 2 and week 4 (total score, P=0.001). Per-protocol analysis results were similar: all subscales of the Revised Fibromyalgia Impact Questionnaire were significantly improved at week 2 and week 4 (total score, P=0.001). CONCLUSION: This pilot study suggests that transdermal magnesium chloride applied on upper and lower limbs may be beneficial to patients with fibromyalgia. TRIAL REGISTRATION: ClinicalTrials.gov.Identifier NCT01968772.
Eriksson EM(1), Andrén KI(1), Kurlberg GK(1), Eriksson HT(1).	(1)Elsa Maria Eriksson, Kristina Ingrid Andrén, Göran Karl Kurlberg, Henry Ture Eriksson, Department of Functional Gastroenterology,	Aspects of the non-pharmacological treatment of irritable bowel syndrome.	World J Gastroenterol. 2015 Oct 28;21(40):11439-49. doi: 10.3748/wjg.v21.i40.11439.	Irritable bowel syndrome (IBS) is one of the most commonly diagnosed gastrointestinal conditions. It represents a significant healthcare burden and remains a clinical challenge. Over the years IBS has been described from a variety of different perspectives; from a strict illness of the gastrointestinal tract (medical model) to a more complex multi-symptomatic disorder of the brain-gut axis (biopsychosocial/psychosomatic model). In this article we present aspects of the pathophysiology and the non-pharmacological treatment of IBS based on current knowledge. Effects of conditioned stress and/or traumatic influences on the emotional

	Pavilion 2, Sahlgrenska University Hospital/Östra, SE-416 78 Göteborg, Sweden.			system (top-down) as well as effects on the intestine through stressors, infection, inflammation, food and dysbiosis (bottom-up) can affect brain-gut communication and result in dysregulation of the autonomic nervous system (ANS), playing an important role in the pathophysiology of IBS. Conditioned stress together with dysregulation of the autonomic nervous system and the emotional system may involve reactions in which the distress inside the body is not recognized due to low body awareness. This may explain why patients have difficulty identifying their symptoms despite dysfunction in muscle tension, movement patterns, and posture and biochemical functions in addition to gastrointestinal symptoms. IBS shares many features with other idiopathic conditions, such as fibromyalgia, chronic fatigue syndrome and somatoform disorders. The key to effective treatment is a thorough examination, including a gastroenterological examination to exclude other diseases along with an assessment of body awareness by a body-mind therapist. The literature suggests that early interdisciplinary diagnostic co-operation between gastroenterologists and body-mind therapists is necessary. Re-establishing balance in the ANS is an important component of IBS treatment. This article discusses the current knowledge of body-mind treatment, addressing the topic from a practical point of view.
Evans M(1), Jason LA(2).	(1)Center for Community Research, DePaul University, Chicago, IL, USA mevans24@depaul.edu. (2)Center for Community Research, DePaul University, Chicago, IL, USA.	Effects of Time Frame on the Recall Reliability of CFS Symptoms.	Eval Health Prof. 2015 Sep;38(3):367-81. doi: 10.1177/0163278713497014. Epub 2013 Sep 23.	This study serves as an investigation of the reliability of symptom data as reported by individuals with chronic fatigue syndrome (CFS), across three recall time frames (the past week, the past month, and the past 6 months), and at two assessment points (with 1 week in between each assessment). Multilevel model analyses were used to determine the optimal recall time frame, in terms of test -retest reliability, for each of the Fukuda et al. (1994) case defining symptoms. Results suggested that the optimal time frame for reliably reporting CFS symptoms was six months for sore throat, lymph node pain, muscle pain, post-exertional malaise, headaches, memory/concentration difficulties, and unrefreshing sleep. For joint pain, the optimal time frame was one month. Researchers who are interested in the assessment of CFS symptoms need to take recall time frame into account, especially when the intended goal is to standardize and improve the methods used to reliably and accurately diagnose this complex illness.
Evans M(1), Barry M, Im Y, Brown A, Jason LA.	(1)a Center for Community Research, DePaul University , Chicago , Illinois , USA.	An investigation of symptoms predating CFS onset.	J Prev Interv Community. 2015;43(1):54-61. doi: 10.1080/10852352.2014.973240.	The Fukuda et al. (1994) criteria for chronic fatigue syndrome (CFS) specifies that a symptom can only be included within a diagnosis if it is experienced concurrently or following the onset of fatigue. In order to investigate this issue, participants provided information on persisting symptoms (lasting greater than six months) and whether those symptoms occurred prior to, concurrently, or following the onset of their fatigue. More symptoms were experienced after the fatigue onset than prior to the fatigue onset; however, a considerable number of participants reported experiencing persisting symptoms prior to the onset of CFS. Particularly, rates of hay fever and asthma were higher prior to the illness. Investigating symptoms prior to the onset of the illness might provide investigators with ways to better understand the etiology of this illness.
Eyskens JB(1),	(1)Department of	Reduced gait automaticity	J Rehabil Res Dev.	Patients with chronic fatigue syndrome (CFS) report difficulties walking for a prolonged

Nijs J, Wouters K, Moorkens G.	Internal Medicine, Antwerp University Hospital, Antwerp, Belgium;	in female patients with chronic fatigue syndrome: Case-control study.	2015;52(7):805-14. doi: 10.1682/JRRD.2014.11.0293.	period of time. This study compares gait automaticity between women with CFS and nondisabled controls. The "stops walking with eyes closed with secondary cognitive task" test is based on the classic "stops walking while talking" test but compares walking with eyes closed while performing a secondary cognitive task in a female CFS population (n = 34) and in female nondisabled controls (n = 38). When initiating gate, 23.5% of patients with CFS looked toward the ground compared with only 2.6% of nondisabled controls. After 7 m, subjects were asked to close their eyes, and after another 7 m, they were asked, "How much is 100 minus 7?" Of the patients with CFS, 55.9% stopped walking compared with 5.3% of nondisabled controls. Less automated walking was observed in patients with CFS than in nondisabled controls ($p < 0.001$). The test-retest reliability is moderate for global stopping. This simple test observed reduced gait automaticity in patients with CFS for the first time. Dual tasking could be helpful to address the functional limitations found in this particular study.
Eyskens JB(1), Nijs J, D'Août K, Sand A, Wouters K, Moorkens G.	(1)Department of Internal Medicine, Antwerp University Hospital, Belgium;	Timed loaded standing in female chronic fatigue syndrome compared with other populations.	J Rehabil Res Dev. 2015;52(1):21-9. doi: 10.1682/JRRD.2014.03.0086.	Patients with chronic fatigue syndrome (CFS), like patients with osteoporosis, have similar difficulties in standing and sitting. The aim of the study was to compare combined trunk and arm endurance between women with CFS (n = 72), women with osteoporosis (n = 30), nondisabled women (n = 55), and women from non-industrialized countries (n = 58) using the timed loaded standing (TLS) test. TLS measures how long a person can hold a 1 kg dumbbell in each hand in front of him/her with straight arms. TLS was higher in the industrialized nondisabled population than in the non-industrialized study population ($p < 0.001$) and in patients with osteoporosis ($p = 0.002$). TLS was lower in patients with CFS than in nondisabled controls ($p < 0.001$). After adjustment for age, body height, and weight, combined trunk and arm endurance was even lower in CFS than in osteoporotic patients more than 25 yr old ($p < 0.001$). In CFS, TLS was lower compared in the non-industrialized group ($p = 0.02$). Since only women were studied, external validity of the results is limited to adult female patients with CFS. TLS revealed a specific biomechanical weakness in CFS patients that can be taken into account from the onset of a rehabilitation program. We propose that influencing the quality, rather than the quantity, of movement could be used in the rehabilitation.
Fagermoen E(1,)(2), Sulheim D(3,)(4), Winger A(5), Andersen AM(6), Gjerstad J(7,)(8), Godang K(9), Rowe PC(10), Saul JP(11), Skovlund E(12,)(13), Wyller	(1)Institute of Clinical Medicine, Medical Faculty, University of Oslo, P.O.Box 1171, Blindern, 0318, Oslo, Norway. feef@online.no.	Effects of low-dose clonidine on cardiovascular and autonomic variables in adolescents with chronic fatigue: a randomized controlled trial.	BMC Pediatr. 2015 Sep 10;15:117. doi: 10.1186/s12887-015-0428-2.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is a common and disabling condition in adolescence with few treatment options. A central feature of CFS is orthostatic intolerance and abnormal autonomic cardiovascular control characterized by sympathetic predominance. We hypothesized that symptoms as well as the underlying pathophysiology might improve by treatment with the alpha2A-adrenoceptor agonist clonidine. METHODS: A total of 176 adolescent CFS patients (12-18 years) were assessed for eligibility at a single referral center recruiting nation-wide. Patients were randomized 1:1 by a computer system and started treatment with clonidine capsules (25 μg or 50 μg twice daily, respectively, for body weight below/above 35 kg) or placebo capsules for 9 weeks. Double-blinding was provided. Data were collected from

VB(14,)(15).				March 2010 until October 2012 as part of The Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial (NorCAPITAL). Effect of clonidine intervention was assessed by general linear models in intention-to-treat analyses, including baseline values as covariates in the model. RESULTS: A total of 120 patients (clonidine group n = 60, placebo group n = 60) were enrolled and started treatment. There were 14 drop-outs (5 in the clonidine group, 9 in the placebo group) during the intervention period. At 8 weeks, the clonidine group had lower plasma norepinephrine (difference = 205 pmol/L, p = 0.05) and urine norepinephrine/creatinine ratio (difference = 3.9 nmol/mmol, p = 0.002). During supine rest, the clonidine group had higher heart rate variability in the low-frequency range (LF-HRV, absolute units) (ratio = 1.4, p = 0.007) as well as higher standard deviation of all RR-intervals (SDNN) (difference = 12.0 ms, p = 0.05); during 20° head-up tilt there were no statistical differences in any cardiovascular variable. Symptoms of orthostatic intolerance did not change during the intervention period. CONCLUSIONS: Low-dose clonidine reduces catecholamine levels in adolescent CFS, but the effects on autonomic cardiovascular control are sparse. Clonidine does not improve symptoms of orthostatic intolerance. TRIAL REGISTRATION: Clinical Trials ID: NCT01040429, date of registration 12/28/2009.
Falconi D, Tattoli F, Brunetti C, De Prisco O, Gherzi M, Marazzi F, Marengo M, Serra I, Tamagnone M, Formica M.		[Rhabdomyolysis from gabapentin: a case report].[Article in Italian]	G Ital Nefrol. 2015 Mar-Apr;32(2). pii: gin/32.2.37.	Gabapentin (GBP) is a drug with different indications.Is not metabolized and is excreted by the kidney. The common side effects are: arthralgia, myalgia, fatigue, dizziness and ataxia. Rhabdomyolysis is an extremely rare side effect. This latter, that can be caused by trauma, strenuous exercise, infections, drugs and toxins, is a syndrome characterized by loss of skeletal muscle resulting in the release of myocyte components in the circulation. Following a case of rhabdomyolysis caused by GBP in patient with chronic renal failure (CRF). A 65-year-old diabetic men, in peritoneal dialysis (PD), affected by ischemic and hypokinetic cardiomyopathy, sensorimotor neuropathy. The patient reported: weakness, diffuse myalgias, hypotension. He had been taking GBP for three days, after the failure of therapies with tricyclic antidepressants, opioids and NSAIDs. Laboratory tests confirmed the increase of the indices of muscle necrosis.The immediate withdrawal of the drug in association with CAPD dialysis treatment, led to improvement of the clinical and biochemical parameters. During the last 10 years, 3 cases of rhabdomyolysis referred to the assumption of GBP have been reported. The use of PD for treatment of acute renal failure, has been significantly reduced over the years. The effectiveness of the purification method is much lower than the one with the continuous extracorporeal treatments. In conclusion, GBP may be associated with rhabdomyolysis. Since GBP toxicity in CRF patients is often overlooked, a better awareness of this phenomenon and a thorough follow-up of laboratory tests to detect any possible early adverse reaction is suggested.
Falk Hvidberg M(1), Brinth	(1)Danish Center for Healthcare	The Health-Related Quality of Life for Patients	PLoS One. 2015 Jul 6;10(7):e0132421. doi:	INTRODUCTION: Myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) is a common, severe condition affecting 0.2 to 0.4 per cent of the population. Even so, no

LS(2), Olesen AV(1), Petersen KD(1), Ehlers L(1).	Improvements, Aalborg University, Aalborg, Denmark. (2)Coordinating Research-unit, Frederiksberg Hospital, Frederiksberg, Denmark.	with Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS).	10.1371/journal.pone.0132421. eCollection 2015.	recent international EQ-5D based health-related quality of life (HRQoL) estimates exist for ME/CFS patients. The main purpose of this study was to estimate HRQoL scores using the EQ-5D-3L with Danish time trade-off tariffs. Secondary, the aims were to explore whether the results are not influenced by other conditions using regression, to compare the estimates to 20 other conditions and finally to present ME/CFS patient characteristics for use in clinical practice. MATERIAL AND METHODS: All members of the Danish ME/CFS Patient Association in 2013 (n=319) were asked to fill out a questionnaire including the EQ-5D-3L. From these, 105 ME/CFS patients were identified and gave valid responses. Unadjusted EQ-5D-3L means were calculated and compared to the population mean as well as to the mean of 20 other conditions. Furthermore, adjusted estimates were calculated using ordinary least squares (OLS) regression, adjusting for gender, age, education, and co-morbidity of 18 self-reported conditions. Data from the North Denmark Health Profile 2010 was used as population reference in the regression analysis (n=23,392). RESULTS: The unadjusted EQ-5D-3L mean of ME/CFS was 0.47 [0.41-0.53] compared to a population mean of 0.85 [0.84-0.86]. The OLS regression estimated a disutility of -0.29 [-0.21;-0.34] for ME/CFS patients in this study. The characteristics of ME/CFS patients are different from the population with respect to gender, relationship, employment etc. CONCLUSION: The EQ-5D-3L-based HRQoL of ME/CFS is significantly lower than the population mean and the lowest of all the compared conditions. The adjusted analysis confirms that poor HRQoL of ME/CFS is distinctly different from and not a proxy of the other included conditions. However, further studies are needed to exclude the possible selection bias of the current study.
Fallon N(1), Li X(2), Chiu Y(3), Nurmikko T(4), Stancak A(2).	(1)Department Psychological Sciences, Institute of Psychology, Health, and Society, University of Liverpool, E-mail: nickfal@liverpool.ac.uk. (2)Dept Psychological Sciences, Institute of Psychology, Health, and Society, University of Liverpool, (3)Wirral University Teaching Hospital NHS Foundation Trust, Wirral, UK. (4)Pain Research Institute,	Altered cortical processing of observed pain in patients with fibromyalgia syndrome.	J Pain. 2015 Aug;16(8):717-26. doi: 10.1016/j.jpain.2015.04.008. Epub 2015 May 12.	Fibromyalgia syndrome (FMS) is characterized by widespread chronic pain, fatigue, sleep disorders, and cognitive-emotional disturbance. Patients with FMS exhibit increased sensitivity to experimental pain and pain-related cues, as well as deficits in emotional regulation. The present study investigated the spatiotemporal patterns of brain activations for observed pain in 19 patients with FMS and 18 age-matched, healthy control individuals using event-related potential analysis. Patients with FMS attributed greater pain and unpleasantness to pain pictures, relative to healthy control participants. An augmented late positive potential (LPP) component (>500 milliseconds) was found in patients viewing both pain and nonpain pictures, and this amplitude difference in the LPP covaried with perceived unpleasantness of pictures. Mid-latency potentials (250-450 milliseconds) demonstrated similar amplitude increases of positive potentials in the FMS patient group. By contrast, the short-latency positive potential (140 milliseconds) was reduced in patients with FMS relative to healthy control participants. Results suggest amplitude increases to mid- to long-latency cortical activations in patients with FMS, which are known to reflect emotional control and motivational salience of stimuli.PERSPECTIVE: Patients with FMS demonstrate increased activations associated with pain and nonpain pictures. The findings suggest that even innocuous, everyday visual stimuli with somatic connotations may challenge

	Institute of Ageing and Chronic Disease, University of Liverpool,; The Walton Centre NHS Foundation Trust, Liverpool, U.K			the emotional state of patients with FMS. Our study points toward the importance of cognitive-emotional therapeutic approaches for the treatment of FMS.
Farmer MA(1), Huang L(1), Martucci K(2), Yang CC(3), Maravilla KR(4), Harris RE(5), Clauw DJ(5), Mackey S(2), Ellingson BM(6), Mayer EA(6), Schaeffer AJ(7), Apkarian AV(8); MAPP Research Network.	(1)Department of Physiology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.	Brain White Matter Abnormalities in Female Interstitial Cystitis/Bladder Pain Syndrome: A MAPP Network Neuroimaging Study.	J Urol. 2015 Jul;194(1):118-26. doi: 10.1016/j.juro.2015.02.082. Epub 2015 Feb 21.	PURPOSE: Several chronic pain conditions may be distinguished by condition specific brain anatomical and functional abnormalities on imaging, which are suggestive of underlying disease processes. We present what is to our knowledge the first characterization of interstitial cystitis/bladder pain syndrome associated white matter (axonal) abnormalities based on multicenter neuroimaging from the MAPP Research Network. MATERIALS AND METHODS: We assessed 34 women with interstitial cystitis/bladder pain syndrome and 32 healthy controls using questionnaires on pain, mood and daily function. White matter microstructure was evaluated by diffusion tensor imaging to model directional water flow along axons or fractional anisotropy. Regions correlating with clinical parameters were further examined for gender and syndrome dependence. RESULTS: Women with interstitial cystitis/bladder pain syndrome showed numerous white matter abnormalities that correlated with pain severity, urinary symptoms and impaired quality of life. Interstitial cystitis/bladder pain syndrome was characterized by decreased fractional anisotropy in aspects of the right anterior thalamic radiation, the left forceps major and the right longitudinal fasciculus. Increased fractional anisotropy was detected in the right superior and bilateral inferior longitudinal fasciculi. CONCLUSIONS: To our knowledge we report the first characterization of brain white matter abnormalities in women with interstitial cystitis/bladder pain syndrome. Regional decreases and increases in white matter integrity across multiple axonal tracts were associated with symptom severity. Given that white matter abnormalities closely correlated with hallmark symptoms of interstitial cystitis/bladder pain syndrome, including bladder pain and urinary symptoms, brain anatomical alterations suggest that there are neuropathological contributions to chronic urological pelvic pain.
Faro M(1), Sàez-Francás N(2), Castro-Marrero J(2), Aliste L(2), Fernández de Sevilla T(2), Alegre J(2).	(1)EAP CAP Terrassa Nord, Consorci Sanitari de Terrassa, Barcelona, España. Electronic address: 34174mfc@comb.cat. (2)Unidad de Fatiga Crónica, Servicio de Medicina Interna,	Gender differences in chronic fatigue syndrome.	Reumatol Clin. 2015 Jul 16. pii: S1699-258X(15)00081-9. doi: 10.1016/j.reuma.2015.05.007. [Epub ahead of print]	BACKGROUND AND OBJECTIVES: Chronic fatigue syndrome (CFS) is a chronic condition that predominantly affects women. To date, there are few epidemiologic studies on CFS in men. The objective of the study was to assess whether there are gender-related differences in CFS, and to define a clinical phenotype in men. PATIENTS AND METHODS: A prospective, cross-sectional cohort study was conducted including CFS patients at the time of diagnosis. Sociodemographic data, clinical variables, comorbid phenomena, fatigue, pain, anxiety/depression, and health quality of life, were assessed in the CFS population. A comparative study was also conducted between genders. RESULTS: The study included 1309 CFS patients, of which 119 (9.1%) were men. The mean age and

	Hospital Universitario Vall d'Hebron, Barcelona, España.			symptoms onset were lower in men than women. The subjects included 30% single men vs. 15% single women, and 32% of men had specialist work vs. 20% of women. The most common triggering factor was an infection. Widespread pain, muscle spasms, dizziness, sexual dysfunction, Raynaud's phenomenon, morning stiffness, migratory arthralgias, drug and metals allergy, and facial oedema were less frequent in men. Fibromyalgia was present in 29% of men vs. 58% in women. The scores on physical function, physical role, and overall physical health of the SF-36 were higher in men. The sensory and affective dimensions of pain were lower in men. CONCLUSIONS: The clinical phenotype of the men with CFS was young, single, skilled worker, and infection as the main triggering agent. Men had less pain and less muscle and immune symptoms, fewer comorbid phenomena, and a better quality of life.
Fasano A(1), Sapone A(2), Zevallos V(3), Schuppan D(4).	(1)Mucosal Immunology and Biology Research Center and Center for Celiac Research, Massachusetts General Hospital for Children, Harvard Medical School, Boston, Massachusetts. Electronic address: afasano@mgh.harvard.edu.	Nonceliac gluten sensitivity.	Gastroenterology. 2015 May;148(6):1195-204. doi: 10.1053/j.gastro.2014.12.049. Epub 2015 Jan 9.	During the past decade there has been an impressive increase in popularity of the gluten-free diet (GFD)-now the most trendy alimentary habit in the United States and other countries. According to recent surveys, as many as 100 million Americans will consume gluten-free products within a year. Operating under the concept that the GFD benefits only individuals with celiac disease, health care professionals have struggled to separate the wheat from the chaff; there are claims that eliminating gluten from the diet increases health and helps with weight loss, or even that gluten can be harmful to every human being. However, apart from unfounded trends, a disorder related to ingestion of gluten or gluten-containing cereals, namely nonceliac gluten sensitivity (NCGS), has resurfaced in the literature, fueling a debate on the appropriateness of the GFD for people without celiac disease. Although there is clearly a fad component to the popularity of the GFD, there is also undisputable and increasing evidence for NCGS. However, we require a better understanding of the clinical presentation of NCGS, as well as its pathogenesis, epidemiology, management, and role in conditions such as irritable bowel syndrome, chronic fatigue, and autoimmunity. Before we can begin to identify and manage NCGS, there must be agreement on the nomenclature and definition of the disorder based on proper peer-reviewed scientific information. We review the most recent findings on NCGS and outline directions to dissipate some of the confusion related to this disorder.
Fernie BA(1,)(2), Maher-Edwards L(3), Murphy G(4), Nikčević AV(5), Spada MM(6).	(1)Department of Psychology, King's College London, London, UK. (2)CASCAID, South London & Maudsley NHS Foundation Trust, London, UK. (3)Chelsea and Westminster NHS	The Metacognitions about Symptoms Control Scale: Development and Concurrent Validity.	Clin Psychol Psychother. 2015 Sep-Oct;22(5):443-9. doi: 10.1002/cpp.1906. Epub 2014 Jun 4.	OBJECTIVE: This paper presents the development and preliminary validation of a self-report instrument designed to measure metacognitions pertaining to symptoms control in the form of the following: (1) symptoms focusing and (2) symptoms conceptual thinking. METHODS: A total of 124 patients (95 female and 29 male) presenting with chronic fatigue syndrome (CFS) contributed data to the study to test the structure and psychometric properties of the Metacognitions about Symptoms Control Scale (MaSCS). RESULTS: A principal components factor analysis indicated that a two-factor solution best fitted the data. The factors were labelled positive and negative metacognitions about symptoms control. Further analyses revealed that both factors had good internal consistency. Correlation analyses established preliminary concurrent validity, indicating

	Foundation Trust, London, UK. (4)Fatigue Service, Royal Free London NHS Foundation Trust, London, UK. (5)Faculty of Arts and Social Sciences, Kingston University, London, UK. (6)Department of Psychology, Faculty of Arts and Human Sciences, London South Bank University, London, UK.			that both positive and negative metacognitions about symptoms control were significantly associated with levels of fatigue in CFS. Regression analysis revealed that positive and negative metacognitions about symptoms control significantly predicted fatigue severity when controlling for anxiety and depression. CONCLUSIONS: The newly developed instrument may help future research that examines the role of metacognitions in CFS, as well as aiding clinical assessment and case formulation. KEY PRACTITIONER MESSAGE: The MaSCS is a useful first instrument to assess metacognitions in CFS. The MaSCS may help to deepen our understanding of symptoms control (symptoms focusing and conceptual thinking about symptoms) in the experience of CFS symptoms. Assessing and conceptualizing symptoms control through the MaSCS may aid treatment of CFS.
Fernie BA(1), Murphy G(2), Wells A(3), Nikčević AV(4), Spada MM(5).	(1)King's College London,Institute of Psychiatry,Psychology and Neuroscience, and Cascaid,South London and Maudsley NHS Foundation Trust,UK. (2)Royal Free Hampstead NHS Foundation Trust,London,UK. (3)University of Manchester,UK. (4)Kingston University,Kingston upon Thames,UK. (5)London South Bank University,UK.	Treatment Outcome and Metacognitive Change in CBT and GET for Chronic Fatigue Syndrome.	Behav Cogn Psychother. 2015 Apr 21:1-13. [Epub ahead of print]	BACKGROUND: Studies have reported that Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) are effective treatments for Chronic Fatigue Syndrome (CFS). METHOD: One hundred and seventy-one patients undertook a course of either CBT (n = 116) or GET (n = 55) and were assessed on a variety of self-report measures at pre- and posttreatment and follow-up. AIMS: In this paper we present analyses on treatment outcomes for CBT and GET in routine clinical practice and evaluate whether changes on subscales of the Metacognitions Questionnaire-30 (MCQ-30) predict fatigue severity independently of changes in other covariates, and across the two treatment modalities. RESULTS: Both CBT and GET were equally effective at decreasing fatigue, anxiety, and depression, and at increasing physical functioning. Changes on the subscales of the MCQ-30 were also found to have a significant effect on fatigue severity independently of changes in other covariates and across treatment modalities. CONCLUSION: The findings from the current study suggest that CFS treatment protocols for CBT and GET, based on those from the PACE trial, achieve similar to poorer outcomes in routine clinical practice as in a RCT.
Fink P(1), Schröder A(1).	(1)Research Clinic for Functional Disorders, Aarhus University Hospital, Aarhus, Denmark.	Redefining Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	JAMA. 2015 Jul 7;314(1):85. doi: 10.1001/jama.2015.5731.	Comment in JAMA. 2015 Jul 7;314(1):85-6.
Fleming KC(1), Volcheck MM(2).	(1)Assistant Professor of Medicine, College	Central sensitization syndrome and the initial	Rambam Maimonides Med J. 2015 Apr	In both primary care and consultative practices, patients presenting with fibromyalgia (FM) often have other medically unexplained somatic symptoms and are ultimately

	of Medicine; Division of General Internal Medicine, Section of Complementary and Integrative Medicine, and Fibromyalgia and Chronic Fatigue Clinic, Mayo Clinic, Rochester, Minnesota, USA; (2)Nursing in Fibromyalgia/Pain Rehabilitation Center, Mayo Clinic, Rochester, Minnesota, USA.	evaluation of a patient with fibromyalgia: a review.	29;6(2):e0020. doi: 10.5041/RMMJ.10204. eCollection 2015.	diagnosed as having central sensitization (CS). Central sensitization encompasses many disorders where the central nervous system amplifies sensory input across many organ systems and results in myriad symptoms. A pragmatic approach to evaluate FM and related symptoms, including a focused review of medical records, interviewing techniques, and observations, is offered here, giving valuable tools for identifying and addressing the most relevant symptoms. At the time of the clinical evaluation, early consideration of CS may improve the efficiency of the visit, reduce excessive testing, and help in discerning between typical and atypical cases so as to avoid an inaccurate diagnosis. Discussion of pain and neurophysiology and sensitization often proves helpful.
Floege J(1).	(1)Division of Nephrology and Clinical Immunology, RWTH University of Aachen, Pauwelsstr. 30, 52057, Aachen, Germany, juergen.floege@rwth-aachen.de.	Magnesium in CKD: more than a calcification inhibitor?	J Nephrol. 2015 Jun;28(3):269-77. doi: 10.1007/s40620-014-0140-6. Epub 2014 Sep 17.	Magnesium fulfils important roles in multiple physiological processes. Accordingly, a tight regulation of magnesium homeostasis is essential. Dysregulated magnesium serum levels, in particular hypomagnesaemia, are common in patients with chronic kidney disease (CKD) and have been associated with poor clinical outcomes. In cell culture studies as well as in clinical situations magnesium levels were associated with vascular calcification, cardiovascular disease and altered bone-mineral metabolism. Magnesium has also been linked to diseases such as metabolic syndrome, diabetes, hypertension, fatigue and depression, all of which are common in CKD. The present review summarizes and discusses the latest clinical data on the impact of magnesium and possible effects of higher levels on the health status of patients with CKD, including an outlook on the use of magnesium-based phosphate-binding agents in this context.
Fluge Ø(1), Risa K(1), Lunde S(1), Alme K(1), Rekeland IG(1), Sapkota D(2), Kristoffersen EK(3), Sørland K(1), Bruland O(4), Dahl O(5), Mella O(5).	(1)Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway.	B-Lymphocyte Depletion in Myalgic Encephalopathy/ Chronic Fatigue Syndrome. An Open-Label Phase II Study with Rituximab Maintenance Treatment.	PLoS One. 2015 Jul 1;10(7):e0129898. doi: 10.1371/journal.pone.0129898. eCollection 2015.	BACKGROUND: Myalgic Encephalopathy/Chronic Fatigue Syndrome (ME/CFS) is a disease of unknown etiology. We previously reported a pilot case series followed by a small, randomized, placebo-controlled phase II study, suggesting that B-cell depletion using the monoclonal anti-CD20 antibody rituximab can yield clinical benefit in ME/CFS. METHODS: In this single-center, open-label, one-armed phase II study (NCT01156909), 29 patients were included for treatment with rituximab (500 mg/m2) two infusions two weeks apart, followed by maintenance rituximab infusions after 3, 6, 10 and 15 months, and with follow-up for 36 months. FINDINGS: Major or moderate responses, predefined as lasting improvements in self-reported Fatigue score, were detected in 18 out of 29 patients (intention to treat). Clinically significant responses were seen in 18 out of 28 patients (64%) receiving rituximab maintenance treatment. For these 18 patients, the mean response durations within the 156 weeks study period were 105 weeks in 14 major responders, and 69 weeks in four moderate responders. At end of follow-up (36 months), 11 out of 18 responding patients were still in ongoing clinical remission. For

				major responders, the mean lag time from first rituximab infusion until start of clinical response was 23 weeks (range 8-66). Among the nine patients from the placebo group in the previous randomized study with no significant improvement during 12 months follow-up after saline infusions, six achieved a clinical response before 12 months after rituximab maintenance infusions in the present study. Two patients had an allergic reaction to rituximab and two had an episode of uncomplicated late-onset neutropenia. Eight patients experienced one or more transient symptom flares after rituximab infusions. There was no unexpected toxicity. CONCLUSION: In a subgroup of ME/CFS patients, prolonged B-cell depletion with rituximab maintenance infusions was associated with sustained clinical responses. The observed patterns of delayed responses and relapse after B-cell depletion and regeneration, a three times higher disease prevalence in women than in men, and a previously demonstrated increase in B-cell lymphoma risk for elderly ME/CFS patients, suggest that ME/CFS may be a variant of an autoimmune disease. TRIAL REGISTRATION: ClinicalTrials.gov NCT01156909.
Fontana J(1), Wenz R(2), Groden C(2), Schmieder K(3), Wenz H(2).	(1)Department of Neurosurgery, Ruhr-University Bochum, Bochum, Germany. Electronic address: johann.fontana@kk-bochum.de. (2)Department of Neuroradiology, University Medicine Mannheim, Medical Faculty Mannheim of the University of Heidelberg, Heidelberg, Germany. (3)Department of Neurosurgery, Ruhr-University Bochum, Bochum, Germany.	The Preinterventional Psychiatric History as a Major Predictor for a Reduced Quality of Life After Treatment of Unruptured Intracranial Aneurysms.	World Neurosurg. 2015 Nov;84(5):1215-22. doi: 10.1016/j.wneu.2015.06.047. Epub 2015 Jul 2.	BACKGROUND: A significantly increased rate of positive preinterventional psychiatric histories in the unruptured aneurysm collective was demonstrated previously. The current study was designed to analyze the influence of the preinterventional psychiatric status on the outcome after treatment of unruptured intracranial aneurysms. METHODS: Patients treated due to meningioma World Health Organization °I and unruptured intracranial aneurysms in 2 German neurosurgical centers between 2007 and 2013 were screened for exclusion criteria including malignant/chronic diseases, recurrence of the tumor/aneurysm, and neurologic deficits among others. The preinterventional psychiatric histories and the rates of postinterventional headaches, sleeping disorders, symptoms of chronic fatigue syndrome, and quality of life (QOL) were determined by questionnaires that were mailed to the patients in a printed version. RESULTS: A total of 58 M patients and 45 iA patients who met the inclusion criteria returned the questionnaires; 10 M (17.2%) and 17 iA patients (37.8%) had a positive psychiatric history. The overall Incidental aneurysm collective demonstrated significantly lower overall QOL scores (P = 0.003) and significant greater rates of chronic fatigue syndrome (P = 0.009) compared with the M collective. After we excluded all patients with positive pre-interventional psychiatric histories, those differences were no longer reproducible. Subjectively, the patients did not realize any significant changes in their QOL after successful aneurysm treatment. CONCLUSIONS: The results of the current study demonstrate the importance of taking the preinterventional psychiatric history into considerations when evaluating the outcome after unruptured aneurysm treatment. The unfavorable outcome of the aneurysm group seems to be caused by factors that are not related the aneurysm diagnosis or treatment itself.
Frangoulidis D(1), Fischer SF(2).	(1)Institut für Mikrobiologie der Bundeswehr,	[Q fever].[Article in German]	Dtsch Med Wochenschr. 2015 Aug;140(16):1206-8. doi: 10.1055/s-0041-	The article summarizes some important recently identified findings about the Coxiella burnetii disease, Q fever. Beside new diagnostic parameters for follow-up issues, the importance of a timely identification of chronic Q fever and the peculiarities of the post

	München. (2)Landesgesundheitsamt Baden-Württemberg, Stuttgart.		103640. Epub 2015 Aug 11.	Q fever fatigue syndrome are depicted.
Furquim BD(1), Flamengui LM(2), Conti PC(3).	(1)University of São Paulo. (2)School of Dentistry, USP, Bauru. (3)Department of Prosthesis, School of Dentistry, USP, Bauru.	TMD and chronic pain: a current view.	Dental Press J Orthod. 2015 Jan-Feb;20(1):127-33. doi: 10.1590/2176-9451.20.1.127-133.sar.	This review aims at presenting a current view on the physiopathologic mechanisms associated with temporomandibular disorders (TMDs). While joint pain is characterized by a well-defined inflammatory process mediated by tumor necrosis factor-α and interleukin, chronic muscle pain presents with enigmatic physiopathologic mechanisms, being considered a functional pain syndrome similar to fibromyalgia, irritable bowel syndrome, interstitial cystitis and chronic fatigue syndrome. Central sensitization is the common factor unifying these conditions, and may be influenced by the autonomic nervous system and genetic polymorphisms. Thus, TMDs symptoms should be understood as a complex response which might get worse or improve depending on an individual's adaptation.
Gambuzza ME(1), Salmeri FM, Soraci L, Soraci G, Sofo V, Marino S, Bramanti P.	(1)Ministry of Health, Territorial Office of Messina, Messina, Italy. gambuzza2002@yahoo.it.	The Role of Toll-Like Receptors in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: A New Promising Therapeutic Approach?	CNS Neurol Disord Drug Targets. 2015;14(7):903-14.	Perturbations in immune processes play an important role in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), a multifactorial disorder mainly characterized by severe and prolonged fatigue and tipically affecting a variety of bodily systems including the immune system. Recent reports have shown that CFS/ME is an inflammatory disorder may be associated with autoimmune responses, mainly characterized by reduced functional activity of most immune cells, including neutrophils, natural killer cells, monocytes/macrophage and dendritic cells, together with dysregulations in cytokine levels, responsible for changes in the adaptive immune system. Interactions between gut microorganisms and host immune function have been shown to contribute to aberrant inflammation in CFS/ME patients. Commensal and/or pathogen-associated molecular patterns detected by Toll-like receptors (TLRs) expressed on intestinal epithelial cells appear to trigger inflammatory signaling cascade leading to neuroinflammation and neurodegeneration. This paper examines the role of TLR-mediated innate immunity in CFS/ME with evaluation of the current literature, also discussing about innovative therapeutic approaches represented by immunomodulators TLR-targeting.
Ganiats TG.		Redefining the chronic fatigue syndrome.	Ann Intern Med. 2015 May 5;162(9):653-4. doi: 10.7326/M15-0357.	
García-Leiva JM(1), Carrasco JL, Slim M, Calandre EP.	(1)Instituto de Neurociencias "Federico Olóriz", Universidad de	Celiac symptoms in patients with fibromyalgia: a cross-sectional study.	Rheumatol Int. 2015 Mar;35(3):561-7. doi: 10.1007/s00296-014-3110-3. Epub 2014 Aug	Fibromyalgia is a chronic pain syndrome associated with numerous somatic symptoms including gastrointestinal manifestations of nonspecific nature. Celiac disease and nongluten sensitivity frequently evolve in adults with gastrointestinal and extraintestinal symptoms similar to those found among patients with fibromyalgia. The

	Granada, Avenida de Madrid, 11, 18012, Granada, Spain.		15.	objective of the present study was to evaluate the presence of celiac-type symptoms among patients with fibromyalgia in comparison with healthy subjects and with those experienced by adult celiac patients and subjects with gluten sensitivity. A list of typical celiac-type symptoms was developed, comparing the frequency of presentation of these symptoms between patients with fibromyalgia (N = 178) and healthy subjects (N = 131), in addition to those of celiac patients and gluten-sensitive patients reported in the literature. The frequency of presentation of every celiac-type symptom, excepting anemia, was significantly higher among patients with fibromyalgia compared to controls ($p < 0.0001$). Regarding the existing data in the literature, the prevalence of fatigue, depression, cognitive symptoms and cutaneous lesions predominated among patients with fibromyalgia, whereas the prevalence of gastrointestinal symptoms was higher among patients with fibromyalgia compared to gluten-sensitive patients and was similar among patients with fibromyalgia and celiac disease patient. The symptomatological similarity of both pathologies, especially gastrointestinal symptoms, suggests that at least a subgroup of patients with fibromyalgia could experience subclinical celiac disease or nonceliac gluten intolerance.
García-Álvarez L(1), Pérez-Matute P(1), Blanco JR(1), Ibarra V(1), Oteo JA(2).	(1)Infectious Diseases Department, Hospital San Pedro-Center for Biomedical Research of La Rioja (CIBIR), Logroño, La Rioja, Spain. (2)Infectious Diseases Department, Hospital San Pedro-Center for Biomedical Research of La Rioja (CIBIR), Logroño, La Rioja, Spain. Electronic address: jaoteo@riojasalud.es.	High prevalence of asymptomatic carriers of Tropheryma whipplei in different populations from the North of Spain.	Enferm Infecc Microbiol Clin. 2015 Nov 13. pii: S0213-005X(15)00343-2. doi: 10.1016/j.eimc.2015.09.006. [Epub ahead of print]	INTRODUCTION: Tropheryma whipplei is the causative agent of Whipple disease. T. whipplei has also been detected in asymptomatic carriers with a very different prevalence. To date, in Spain, there are no data regarding the prevalence of T. whipplei in a healthy population or in HIV-positive patients, or in chronic fatigue syndrome (CFS). Therefore, the aim of this work was to assess the prevalence of T. whipplei in stools in those populations. METHODS: Stools from 21 HIV-negative subjects, 65 HIV-infected, and 12 CFS patients were analysed using real time-PCR. HIV-negative and positive subjects were divided into two groups, depending on the presence/absence of metabolic syndrome (MS). Positive samples were sequenced. RESULTS: The prevalence of T. whipplei was 25.51% in 98 stool samples analysed. Prevalence in HIV-positive patients was significantly higher than in HIV-negative (33.8% vs. 9.09%, p=0.008). Prevalence in the control group with no associated diseases was 20%, whereas no positive samples were observed in HIV-negative patients with MS, or in those diagnosed with CFS. The prevalence observed in HIV-positive patients without MS was 30.35%, and with MS it was 55.5%. The number of positive samples varies depending on the primers used, although no statistically significant differences were observed. CONCLUSIONS: There is a high prevalence of asymptomatic carriers of T. whipplei among healthy and in HIV-infected people from Spain. The role of T. whipplei in HIV patients with MS is unclear, but the prevalence is higher than in other populations.
Gardani M(1), Morfiri E(2), Thomson A(3), O'Neill B(4), McMillan TM(5).	(1)Institute of Health and Wellbeing, University of Glasgow, Glasgow, United Kingdom. Electronic	Evaluation of Sleep Disorders in Patients With Severe Traumatic Brain Injury During Rehabilitation.	Arch Phys Med Rehabil. 2015 Sep;96(9):1691-7.e3. doi: 10.1016/j.apmr.2015.05.006. Epub 2015 May 21.	OBJECTIVE: To explore the presence and types of sleep disorders in chronic patients with severe traumatic brain injury (TBI) undergoing inpatient rehabilitation using formal diagnostic criteria based on the International Classification of Sleep Disorders, 2nd edition. DESIGN: Cross-sectional study. SETTING: Inpatient brain injury rehabilitation units. PARTICIPANTS: Chronic inpatients with severe TBI (N=30) were evaluated during

	address: maria.gardani@glasgow.ac.uk.			rehabilitation. INTERVENTIONS: Not applicable. MAIN OUTCOME MEASURES: Participants wore an actiwatch for 7 days and completed self-report measures on sleep, mood, fatigue, pain, and daytime sleepiness. RESULTS: Twenty participants (67%) had a sleep-wake cycle disturbance, of which 15 (50%) met diagnostic criteria for a sleep disorder. Diagnosed sleep disorders in the sample were insomnia (26.7%), posttraumatic hypersomnia (6.7%), delayed sleep phase syndrome (10%), irregular sleep-wake pattern disorder (3.3%), and periodic limb movement disorder (3.3%). Sleep quality was estimated by senior clinical staff as interfering with rehabilitation in 36.6% of the sample. Poor sleep quality was associated with greater anxiety, fatigue, and daytime sleepiness. CONCLUSIONS: Consistent with previous studies, the present study showed high levels of sleep-wake cycle disturbances in patients with severe TBI undergoing rehabilitation, which were associated with anxiety, fatigue, and daytime sleepiness. These findings highlight the importance of assessing and treating sleep problems in patients with TBI undergoing rehabilitation.
Garland EM(1), Celedonio JE, Raj SR.	(1)Autonomic Dysfunction Center, Vanderbilt University School of Medicine, Nashville, TN, USA, Emily.garland@vanderbilt.edu.	Postural Tachycardia Syndrome: Beyond Orthostatic Intolerance.	Curr Neurol Neurosci Rep. 2015 Sep;15(9):60. doi: 10.1007/s11910-015-0583-8.	Postural tachycardia syndrome (POTS) is a form of chronic orthostatic intolerance for which the hallmark physiological trait is an excessive increase in heart rate with assumption of upright posture. The orthostatic tachycardia occurs in the absence of orthostatic hypotension and is associated with a >6-month history of symptoms that are relieved by recumbence. The heart rate abnormality and orthostatic symptoms should not be caused by medications that impair autonomic regulation or by debilitating disorders that can cause tachycardia. POTS is a "final common pathway" for a number of overlapping pathophysiologies, including an autonomic neuropathy in the lower body, hypovolemia, elevated sympathetic tone, mast cell activation, deconditioning, and autoantibodies. Not only may patients be affected by more than one of these pathophysiologies but also the phenotype of POTS has similarities to a number of other disorders, e.g., chronic fatigue syndrome, Ehlers-Danlos syndrome, vasovagal syncope, and inappropriate sinus tachycardia. POTS can be treated with a combination of non-pharmacological approaches, a structured exercise training program, and often some pharmacological support.
Gay CW(1), Robinson ME(1), Lai S(2), O'Shea A(1), Craggs JG(1), Price DD(3), Staud R(4).	(1)1 Department of Clinical & Health Psychology, University of Florida College of Medicine , Gainesville, Florida. (2)2 Department of Radiation Oncology & Neurology, University of Florida College of Medicine , Gainesville,	Abnormal Resting-State Functional Connectivity in Patients with Chronic Fatigue Syndrome: Results of Seed and Data-Driven Analyses.	Brain Connect. 2015 Nov 10. [Epub ahead of print]	Although altered resting-state functional connectivity (FC) is a characteristic of many chronic pain conditions, it has not yet been evaluated in patients with chronic fatigue. Our objective was to investigate the association between fatigue and altered resting-state FC in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Thirty-six female subjects, 19 ME/CFS and 17 healthy controls, completed a fatigue inventory before undergoing functional magnetic resonance imaging. Two methods, (1) data driven and (2) model based, were used to estimate and compare the intraregional FC between both groups during the resting state (RS). The first approach using independent component analysis was applied to investigate five RS networks: the default mode network, salience network (SN), left frontoparietal networks (LFPN) and right frontoparietal networks, and the sensory motor network (SMN). The second

	Florida. (3)3 Department of Maxillo-Facial Surgery, University of Florida College of Medicine , Gainesville, Florida. (4)4 Department of Medicine, University of Florida College of Medicine , Gainesville, Florida.			approach used a priori selected seed regions demonstrating abnormal regional cerebral blood flow (rCBF) in ME/CFS patients at rest. In ME/CFS patients, Method-1 identified decreased intrinsic connectivity among regions within the LFPN. Furthermore, the FC of the left anterior midcingulate with the SMN and the connectivity of the left posterior cingulate cortex with the SN were significantly decreased. For Method-2, five distinct clusters within the right parahippocampus and occipital lobes, demonstrating significant rCBF reductions in ME/CFS patients, were used as seeds. The parahippocampal seed and three occipital lobe seeds showed altered FC with other brain regions. The degree of abnormal connectivity correlated with the level of self-reported fatigue. Our results confirm altered RS FC in patients with ME/CFS, which was significantly correlated with the severity of their chronic fatigue.
Gewin V.		Medical research: Subject to reflection.	Nature. 2015 May 28;521(7553):551-3.	
Gheitasi H(1), Kostov B(2), Solans R(3), Fraile G(4), Suárez-Cuervo C(5), Casanovas A(6), Rascón FJ(7), Qanneta R(8), Pérez-Alvarez R(9), Ripoll M(10), Akasbi M(11), Pinilla B(12), Bosch JA(3), Nava-Mateos J(4), Díaz-López B(5), Morera-Morales ML(6), Retamozo S(1), Ramos-Casals M(1), Brito-Zerón P(13); SS Study Group, Autoimmune Diseases Study Group (GEAS), Spanish Society of Internal	(1)Sjögren Syndrome Research Group (AGAUR), Laboratory of Autoimmune Diseases Josep Font, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Department of Autoimmune Diseases, ICMiD, Hospital Clínic, Barcelona, Spain. Electronic address: mbrito@clinic.ub.es.	How are we treating our systemic patients with primary Sjögren syndrome? Analysis of 1120 patients.	Int Immunopharmacol. 2015 Aug;27(2):194-9. doi: 10.1016/j.intimp.2015.03.027. Epub 2015 Apr 18.	OBJECTIVE: To describe how systemic disease is treated in a large cohort of Spanish patients with primary Sjögren syndrome (pSS) in daily practice, focusing on the adequacy of therapies for the level of systemic activity measured by ESSDAI score. PATIENTS AND METHODS: By December 2014, our database included 1120 consecutive patients who fulfilled the 2002 classification criteria for SS. Therapeutic schedules were classified into 4 categories: no systemic therapies, hydroxychloroquine (HCQ) and/or low dose glucocorticoids (GCS) (<20mg/day), high dose GCS (>20mg/day) and use of second-line therapies (immunosuppressive agents, intravenous immunoglobulins [IVIG] and/or rituximab [RTX]). RESULTS: There were 1048 (94%) women and 72 (6%) men , with a mean age at diagnosis of 54 years. The main drug-based therapeutic approaches for systemic pSS during follow-up were HCQ in 282 (25%) patients, GCS in 475 (42%, at doses >20mg/day in 255-23%), immunosuppressive agents in 148 (13%), IVIG in 25 (2%) and RTX in 35 (3%) patients. HCQ was associated with a lower risk of death (adjusted HR of 0.57, 95% 0.34-0.95). We classified 16 (7%) of the 255 patients treated with >20mg GCS and 21/148 (14%) treated with immunosuppressive agents as patients inadequately treated, mainly associated with articular involvement of low/moderate activity. CONCLUSION: The management of pSS should be organ-specific, using low dose GCS in patients with moderate systemic activity, limiting the use of high dose GCS and second-line therapies to refractory or potentially severe scenarios. The use of systemic therapies for dryness, chronic pain or fatigue is not warranted.

Medicine (SEMI).				
Gherardi RK(1), Eidi H(1), Crépeaux G(1), Authier FJ(1), Cadusseau J(1).	(1)Faculté de Médecine and Faculté des Sciences et Technologie, INSERM U955 Team 10, Université Paris Est-Créteil , Créteil , France.	Biopersistence and brain translocation of aluminum adjuvants of vaccines.	Front Neurol. 2015 Feb 5;6:4. doi: 10.3389/fneur.2015.00004. eCollection 2015.	Aluminum oxyhydroxide (alum) is a crystalline compound widely used as an immunological adjuvant of vaccines. Concerns linked to the use of alum particles emerged following recognition of their causative role in the so-called macrophagic myofasciitis (MMF) lesion detected in patients with myalgic encephalomyelitis/chronic fatigue/syndrome. MMF revealed an unexpectedly long-lasting biopersistence of alum within immune cells in presumably susceptible individuals, stressing the previous fundamental misconception of its biodisposition. We previously showed that poorly biodegradable aluminum-coated particles injected into muscle are promptly phagocytosed in muscle and the draining lymph nodes, and can disseminate within phagocytic cells throughout the body and slowly accumulate in brain. This strongly suggests that long-term adjuvant biopersistence within phagocytic cells is a prerequisite for slow brain translocation and delayed neurotoxicity. The understanding of basic mechanisms of particle biopersistence and brain translocation represents a major health challenge, since it could help to define susceptibility factors to develop chronic neurotoxic damage. Biopersistence of alum may be linked to its lysosome-destabilizing effect, which is likely due to direct crystal-induced rupture of phagolysosomal membranes. Macrophages that continuously perceive foreign particles in their cytosol will likely reiterate, with variable interindividual efficiency, a dedicated form of autophagy (xenophagy) until they dispose of alien materials. Successful compartmentalization of particles within double membrane autophagosomes and subsequent fusion with repaired and re-acidified lysosomes will expose alum to lysosomal acidic pH, the sole factor that can solubilize alum particles. Brain translocation of alum particles is linked to a Trojan horse mechanism previously described for infectious particles (HIV, HCV), that obeys to CCL2, signaling the major inflammatory monocyte chemoattractant.
Gladwell PW(1).	(1)North Bristol NHS Trust, Southmead Hospital , Bristol , UK.	Author's comments in response to letters by Tom Kindlon, Anna Sheridan and Robert Courtney.	Disabil Rehabil. 2015;37(5):468-9. doi: 10.3109/09638288.2014.1002581. Epub 2015 Jan 19.	Comment on Disabil Rehabil. 2015;37(5):465. Disabil Rehabil. 2015;37(5):464. Disabil Rehabil. 2014;36(5):387-94. Disabil Rehabil. 2015;37(5):466-7.
Goel AK(1), Talwar D(1), Jain SK(1).	(1)Department of Respiratory, Sleep, Allergy, and Critical Care Medicine, Metro Centre for Respiratory Diseases, Metro Group of Hospitals, Noida, Uttar Pradesh,	Evaluation of short-term use of nocturnal nasal continuous positive airway pressure for a clinical profile and exercise capacity in adult patients with obstructive sleep apnea-hypopnea	Lung India. 2015 May-Jun;32(3):225-32. doi: 10.4103/0970-2113.156226.	BACKGROUND AND AIM: The obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common chronic respiratory disease, characterized by repetitive complete or partial collapse of the upper airway during sleep. The clinical spectrum extends between stoppage of breathing, snoring, daytime somnolence, and fatigue, to serious cardiovascular disease, stroke, metabolic syndrome, increased morbidity, and mortality. We aim to evaluate the short-term use of nasal continuous positive airway pressure (nCPAP) therapy for the clinical profile and exercise capacity of patients with OSAHS. PATIENT SELECTION: Twenty patients diagnosed with moderate-to-severe

	India.	syndrome.		OSAHS were enrolled in the study (study group - 15; clinically and PSG-matched control group - 5). MATERIALS AND METHODS: Each patient was clinically evaluated for sleep-related symptoms, and also assessed with spirometry, the six-minute walk test (6MWT), and a symptom-limited incremental cardiopulmonary exercise test (CPET). The study group patients were administered nCPAP therapy for eight hours each night for four weeks, while the control group patients were just observed. They were re-assessed after four weeks and the data were statistically analyzed between the two groups. RESULTS: The study group patients showed a significant (P- < 0.05) improvement in the OSAHS symptoms-the Epworth sleepiness score, six-minute walk distance; duration of exercise, power output, peak oxygen uptake, anaerobic threshold, diastolic blood pressure, dyspnea, and fatigue-in comparison with the control group patients. The improvement in exercise capacity following nCPAP therapy was attributed to the relief of disabling the OSAHS symptoms and improved cardiovascular, ventilator, and musculoskeletal functions. CONCLUSION: All OSAHS patients must be treated with nCPAP.
Goldsmith LP(1,)(2,)(3), Dunn G(1,)(2), Bentall RP(4), Lewis SW(2,)(5), Wearden AJ(2,)(6).	(1)Centre for Biostatistics, Institute of Population Health, University of Manchester, Manchester, United Kingdom. (2)Manchester Academic Health Science Centre, Manchester, United Kingdom. (3)School of Health and Human Sciences, University of Huddersfield, Huddersfield, United Kingdom. (4)Institute of Psychology, Health and Society, University of Liverpool, Liverpool, United Kingdom. (5)Institute of Brain, Behaviour and Mental Health, University of	Therapist Effects and the Impact of Early Therapeutic Alliance on Symptomatic Outcome in Chronic Fatigue Syndrome.	PLoS One. 2015 Dec 14;10(12):e0144623. doi: 10.1371/journal.pone.0144623. eCollection 2015.	Few studies have examined therapist effects and therapeutic alliance (TA) in treatments for chronic fatigue syndrome (CFS). Therapist effects are the differences in outcomes achieved by different therapists. TA is the quality of the bond and level of agreement regarding the goals and tasks of therapy. Prior research suffers the methodological problem that the allocation of therapist was not randomized, meaning therapist effects may be confounded with selection effects. We used data from a randomized controlled treatment trial of 296 people with CFS. The trial compared pragmatic rehabilitation (PR), a nurse led, home based self-help treatment, a counselling-based treatment called supportive listening (SL), with general practitioner treatment as usual. Therapist allocation was randomized. Primary outcome measures, fatigue and physical functioning were assessed blind to treatment allocation. TA was measured in the PR and SL arms. Regression models allowing for interactions were used to examine relationships between (i) therapist and therapeutic alliance, and (ii) therapist and average treatment effect (the difference in mean outcomes between different treatment conditions). We found no therapist effects. We found no relationship between TA and the average treatment effect of a therapist. One therapist formed stronger alliances when delivering PR compared to when delivering SL (effect size 0.76, SE 0.33, 95% CI 0.11 to 1.41). In these therapies for CFS, TA does not influence symptomatic outcome. The lack of significant therapist effects on outcome may result from the trial's rigorous quality control, or random therapist allocation, eliminating selection effects. Further research is needed.TRIAL REGISTRATION: ISRCTN74156610.

	Manchester, Manchester, United Kingdom. (6)School of Psychological Sciences and Manchester Centre for Health Psychology, University of Manchester, Manchester, United Kingdom.			
Gonthier A, Favrat B.		[Chronic fatigue syndrome].[Article in French]	Rev Med Suisse. 2015 Nov 25;11(496):2236, 2238-42.	Chronic fatigue syndrome (CFS) is a debilitating disorder, characterized by a severe, persistant and unexplained fatigue, which can be associated with diffuse pain, sleep difficulties, neurocognitive and neurovegetative troubles. Its prevalence has been estimated between 0.3 and 0.9%. Though its physiopathology remains controversial, evidence is growing that dysimmunity, oxidative stress and mitochondrial dysfunction are involved in its pathogeny. No medication has demonstrated specifc efficacy in the CFS. The management of CFS involves limiting unnecessary investigations, promoting graded exercice therapy, and providing empathic counselling in order to prevent negative thoughts.
Gorman GS(1), Elson JL(2), Newman J(3), Payne B(4), McFarland R(3), Newton JL(5), Turnbull DM(3).	(1)Wellcome Trust Centre for Mitochondrial Research, Institute for Ageing and Health, Newcastle University, Newcastle upon Tyne NE2 4HH, UK; Institute of Ageing and Health and NIHR Biomedical Research Centre for Ageing, Newcastle University, Newcastle upon Tyne NE4 5PL, UK. Electronic address: grainne.gorman@ncl.ac.uk.	Perceived fatigue is highly prevalent and debilitating in patients with mitochondrial disease.	Neuromuscul Disord. 2015 Jul;25(7):563-6. doi: 10.1016/j.nmd.2015.03.001. Epub 2015 Apr 23.	Perceived fatigue is a prominent symptom in patients with mitochondrial disease but to date its prevalence, impact and aetiology are poorly understood. Our aim was to determine the prevalence and assess for comorbidities associated with clinically relevant fatigue in patients with mitochondrial disease. A cross-sectional postal survey of patients with mitochondrial disease was undertaken using a validated self-completion, patient-reported outcome measures (response rate: 60%; n = 132). The prevalence and perceived functional impact of experienced fatigue were assessed using the Fatigue Impact Scale. Other putative biological mechanisms were evaluated using the Hospital Anxiety Depression scale and Epworth sleepiness scale. Data were compared with those for healthy control subjects and patients with Myalgic Encephalopathy/Chronic Fatigue Syndrome matched for age and gender. Sixty-two per cent of patients with mitochondrial disease reported excessive symptomatic fatigue (Fatigue Impact Scale ≥ 40); whilst 32% reported severe, functionally limiting fatigue symptoms (Fatigue Impact Scale ≥ 80) comparable to perceived fatigue in patients with Myalgic Encephalopathy/Chronic Fatigue Syndrome. Fatigue is common and often severe in patients with mitochondrial disease irrespective of age, gender or genotype. Future evaluation of causal factors in mitochondrial disease-associated fatigue is warranted with the potential to guide future treatment modalities.
Gotts ZM(1), Newton JL(2,)(3), Ellis JG(1), Deary	(1)Faculty of Health and Life Sciences, Northumbria	The experience of sleep in chronic fatigue syndrome: A qualitative interview	Br J Health Psychol. 2016 Feb;21(1):71-92. doi: 10.1111/bjhp.12136. Epub	OBJECTIVES: Sleep disturbances are common in chronic fatigue syndrome (CFS), and one of the key symptom complaints, yet it has been neglected by previous qualitative research. The aim was to explore the specific role of sleep in patients' experience of

V(1).	University, Newcastle-Upon-Tyne, UK. (2)Institute of Cellular Medicine, Medical School, Newcastle University & Newcastle Hospitals NHS Foundation Trust, UK. (3)UK NIHR Biomedical Research Centre in Ageing, Newcastle-Upon-Tyne, UK.	study with patients.	2015 Feb 26.	their illness. DESIGN: A qualitative semi-structured interview format facilitated a detailed and open exploration of sleep, and the extent to which its management and problems were linked to the lived experience of CFS. METHODS: Eleven semi-structured interviews were conducted with individuals with CFS. Data were transcribed verbatim and analysed thematically, to explore and describe patients' experience of their sleep, and its impact on their condition. RESULTS: Sleep emerged as a key aspect of the illness experience, and its management and effect on daytime functioning was a central pre-occupation for all 11 participants; all of them saw sleep as playing a critical role in their illness through either maintaining or exacerbating existing symptoms. Exploration of individual experiences presented three overarching themes: (1) sleep pattern variability over illness course and from day to day; (2) effect of sleep on daytime functioning; and (3) attempts at coping and sleep management. CONCLUSIONS: Each patient with CFS has a unique experience of sleep. Despite the differing narratives regarding the role of sleep in CFS, all participants held the belief that sleep is a vital process for health and well-being which has had a direct bearing on the course and progression of their CFS. Also, every participant regarded their sleep as in some way 'broken' and in need of management/repair. Patients' insights demonstrate sleep-specific influences on their CFS, and the impact of disturbed sleep should be a consideration for clinical and research work. Statement of contribution What is already known on this subject? Sleep disturbances are common in CFS, and one of the key symptom complaints, yet it has been neglected by previous qualitative research. Ontology of CFS is a matter of dispute, with models ranging from the biological to the psychological competing to explain symptomatology in this illness. A qualitative study has the potential to add some clarity to the debate by making the patients' lived experience of the condition, and their own understanding of it, the focus of research. What this study adds? Coping and attempts at managing sleep problems in CFS adds to the 'illness burden' experienced by patients. Disturbed sleep is universally seen by patients with CFS as impacting on other daytime symptoms. Broken sleep may contribute to a biopsychosocial cycle that serves to maintain this illness.
Gotts ZM(1), Ellis JG(1), Deary V(1), Barclay N(1), Newton JL(2).	(1)Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, United Kingdom. (2)Institute of Cellular Medicine, Medical School, Newcastle University & Newcastle Hospitals NHS Foundation Trust	The association between daytime napping and cognitive functioning in chronic fatigue syndrome.	PLoS One. 2015 Jan 9;10(1):e0117136. doi: 10.1371/journal.pone.0117136. eCollection 2015.	OBJECTIVES: The precise relationship between sleep and physical and mental functioning in chronic fatigue syndrome (CFS) has not been examined directly, nor has the impact of daytime napping. This study aimed to examine self-reported sleep in patients with CFS and explore whether sleep quality and daytime napping, specific patient characteristics (gender, illness length) and levels of anxiety and depression, predicted daytime fatigue severity, levels of daytime sleepiness and cognitive functioning, all key dimensions of the illness experience. METHODS: 118 adults meeting the 1994 CDC case criteria for CFS completed a standardised sleep diary over 14 days. Momentary functional assessments of fatigue, sleepiness, cognition and mood were completed by patients as part of usual care. Levels of daytime functioning and disability were quantified using symptom assessment tools, measuring fatigue (Chalder Fatigue

	and UK NIHR Biomedical Research Centre in Ageing, Newcastle-upon-Tyne, United Kingdom.			Scale), sleepiness (Epworth Sleepiness Scale), cognitive functioning (Trail Making Test, Cognitive Failures Questionnaire), and mood (Hospital Anxiety and Depression Scale). RESULTS: Hierarchical Regressions demonstrated that a shorter time since diagnosis, higher depression and longer wake time after sleep onset predicted 23.4% of the variance in fatigue severity (p <.001). Being male, higher depression and more afternoon naps predicted 25.6% of the variance in objective cognitive dysfunction (p <.001). Higher anxiety and depression and morning napping predicted 32.2% of the variance in subjective cognitive dysfunction (p <.001). When patients were classified into groups of mild and moderate sleepiness, those with longer daytime naps, those who mainly napped in the afternoon, and those with higher levels of anxiety, were more likely to be in the moderately sleepy group. CONCLUSIONS: Napping, particularly in the afternoon is associated with poorer cognitive functioning and more daytime sleepiness in CFS. These findings have clinical implications for symptom management strategies.
Goulart R(1), Pessoa C(2), Junior IL(3).	(1)Programa de Pós-Graduação Interdisciplinar em Ciências da Saúde, Universidade Federal de São Paulo, Santos, SP, Brasil. Electronic address: rubens_goulart@yahoo.com. (2)Serviço de Reabilitação e Fisioterapia, Prefeitura Municipal de Santos, Santos, SP, Brasil. (3)Departamento de Ciências do Movimento Humano, Universidade Federal de São Paulo, Santos, SP, Brasil.	[Psychological aspects of juvenile fibromyalgia syndrome: a literature review].[Article in Portuguese]	Rev Bras Reumatol. 2015 Sep 14. pii: S0482-5004(15)00123-0. doi: 10.1016/j.rbr.2015.07.008. [Epub ahead of print]	Juvenile fibromyalgia syndrome (JFMS) is a non-inflammatory chronic pain condition that occurs mainly in girls aged nine to 15 years. JFMS is characterized by constant widespread pain in different parts of the body, poor sleep quality, daytime sleepiness and an altered mood. Concomitant psychological and organic factors result in a diminished capacity to cope with pain. The quality of life of individuals with chronic pain and their caregivers is severely restricted and the occurrence of symptoms of anxiety and depression is common in this population. The aim of the present study was to perform a systematic review of the literature on psychosocial factors related to JFMS. The findings reveal differences in opinion between patients and family members regarding the effect of the condition, as mothers tend to classify JFMS as more severe than the patients themselves. Individuals with JFMS seem to share the same personality traits and there seems to be a type of family environment that is favorable to the occurrence of this condition. Psychological and functional aspects should be treated with methods that can help patients and family members alter their coping strategies regarding day-to-day problems, attenuate the dysfunctional consequences of pain and fatigue and diminish the risk of catastrophizing that individuals submitted to constant pain develop in relation to their surrounding environment.
Green CR, Cowan P, Elk R, O'Neil KM, Rasmussen AL.	The National Institutes of Health (NIH) Pathways to Prevention Workshop:	National Institutes of Health Pathways to Prevention Workshop: Advancing the Research	Ann Intern Med. 2015 Jun 16;162(12):860-5. doi: 10.7326/M15-0338.	

	Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome was cosponsored by the NIH Office of Disease Prevention and the Trans-NIH Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Research Working Group. A multidisciplinary working group developed the agenda, and an Evidence-based Practice Center prepared an evidence report through a contract with the Agency for Healthcare Research and Quality to facilitate the discussion. During the 1.5-day workshop, invited experts discussed the body of evidence and attendees had the opportunity to comment during open discussions. After weighing evidence from the evidence report, expert presentations, and public comments, an unbiased,	on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.		

	independent panel prepared a draft report that identified research gaps and future research priorities. The report was posted on the NIH Office of Disease Prevention Web site for 4 weeks for public comment.			
Grossman S(1), Tagliavini LB.	(1)Sheila Grossman, PhD, APRN, FNP-BC, FAAN, is a Professor, Coordinator of Family Nurse Practitioner Program & Director, Evaluation, Faculty Scholarship & Mentoring, Fairfield University School of Nursing, Fairfield, Connecticut. Lynda B. Tagliavini, MSN, CPNP, is a Pediatric Nurse Practitioner, Pediatric & Adolescent Medicine, 2207 Boston Rd., Wilbraham, Massachusetts.	Managing Sjogren's Syndrome.	Home Healthc Now. 2015 Oct;33(9):487-92. doi: 10.1097/NHH.0000000000000295.	There are approximately 4 million Americans diagnosed with Sjogren's Syndrome. This article discusses the epidemiology, pathophysiology, diagnostics, and implications for home care clinicians who may encounter patients with this syndrome. Chronic pain is discussed as well as interventions to manage symptoms such fatigue, dry eyes mouth and skin.
Guenther S(1), Loebel M(1), Mooslechner AA(1), Knops M(2), Hanitsch LG(1), Grabowski P(1), Wittke K(1), Meisel C(3), Unterwalder	(1)Institute of Medical Immunology, Charité Universitätsmedizin Berlin, Berlin, Germany.	Frequent IgG subclass and mannose binding lectin deficiency in patients with chronic fatigue syndrome.	Hum Immunol. 2015 Oct;76(10):729-35. doi: 10.1016/j.humimm.2015.09.028. Epub 2015 Sep 30.	Chronic fatigue syndrome (CFS) is a severe disease characterized by various symptoms of immune dysfunction. CFS onset is typically with an infection and many patients suffer from frequently recurrent viral or bacterial infections. Immunoglobulin and mannose binding lectin (MBL) deficiency are frequent causes for increased susceptibility to infections. In this study we retrospectively analysed 300 patients with CFS for immunoglobulin and MBL levels, and B-cell subset frequencies. 25% of the CFS patients had decreased serum levels of at least one antibody class or subclass with IgG3 and IgG4 subclass deficiencies as most common phenotypes. However, we found elevated immunoglobulin levels with an excess of IgM and IgG2 in particular in another

N(3), Volk HD(4), Scheibenbogen C(5).				25% of patients. No major alteration in numbers of B cells and B-cell subsets was seen. Deficiency of MBL was found in 15% of the CFS patients in contrast to 6% in a historical control group. In a 2nd cohort of 168 patients similar frequencies of IgG subclass and MBL deficiency were found. Thus, humoral immune defects are frequent in CFS patients and are associated with infections of the respiratory tract.
Guillamó E(1), Barbany JR, Blazquez A, Delicado MC, Ventura-Farré JL, Javierre C.	(1)Department of Physiological Sciences II, Exercise Physiology Unit, School of Medicine, University of Barcelona, Barcelona, Spain - eguillamo@gencat.cat	Physical effects of a reconditioning programme in a group of chronic fatigue syndrome patients.	J Sports Med Phys Fitness. 2015 Feb 18. [Epub ahead of print]	AIM: Physical exercise can be part of treatment in patients with chronic fatigue syndrome (CFS), where the aim would be to improve strength and endurance through increasing physical exercise (intensity and time) without aggravating symptomatology. The present study examines the effectiveness of a reconditioning programme (focusing on strength, endurance, balance and propioception) for achieving maximum functional capacity according to the clinical status of CFS patients. METHODS: Sixty-eight patients with CFS were randomly assigned to two groups: a control group (CG) comprising 22 patients and an active group (AG) of 46 patients, the latter being invited to take part in a functional reconditioning programme based on 12 weeks of laboratory training followed by a further 12-week home training period. Functional assessments were as follows: before (I) and after (II) the laboratory training and after (III) the home training. RESULTS: In the AG, 22 patients (67%) completed the intervention (laboratory) stage and 20 finished the whole protocol (61%). Patients in the AG showed improved static and dynamic balance, as well as significantly greater maximum strength ($F=7.059$, $p<0.05$). Differences in resistance strength were also observed, with the AG showing a 19.9% improvement between functional assessments I and II ($p=0.04$). We don't found changes in the CG. CONCLUSION: A physical exercise programme of this kind might offer CFS patients the opportunity to improve their strength, balance and quality of life, there being only a very small risk of relapse and none of the adverse effects of other treatments.
Gupta AA(1), Mhaske SA(2), Ahmad MA(3), Yuwanati MB(1), Prabhu S(3), Pardhe N(4).	(1)Reader, Department of Oral Pathology & Microbiology, People's Dental academy , Bhopal, India . (2)Professor & Head, Department of Oral Pathology & Microbiology, People's Dental academy , Bhopal, India . (3)Post-Graduate Student, Department of Oral Pathology &	Ergonomic Microscope: Need of the Hour.	J Clin Diagn Res. 2015 May;9(5):ZC62-5. doi: 10.7860/JCDR/2015/11742.5952. Epub 2015 May 1.	BACKGROUND: Prolonged use of conventional microscope develops musculo-skeletal injuries like chronic pain syndrome, including shoulder, neck, back aches & fatigue. Since the problems go unnoticed, the injuries can lead to some serious permanent damages. This further leads to a compromise in the health and welfare of the person and the institute. Hence, an understanding about the ergonomics is the need of the hour in this postmodern era. Inspite of few studies and surveys about ergonomics, there is still a steep rise in the musculoskeletal disorders. AIM OF THE STUDY: The aim of our study was to gauge the general awareness of pathologists, microbiologists and oral pathologists towards ergonomics in their profession. MATERIALS AND METHODS: A cross-sectional survey based study was de-signed, which included a questionnaire. The questionnaire included multiple choice questions with four alternatives. Professionals (pathologists, microbiologists and oral pathologists) were included in the survey. Teaching faculty (Professors, Associate Professors and Lecturers) and Post graduate students formed the study group. RESULTS AND OBSERVATIONS: The response to the questionnaire was 100%. Less than 50% of oral pathologists were aware of the

	Microbiology, People's Dental academy , Bhopal, India . (4)Professor & Head, Department of Oral Pathology & Microbiology, NIMS Dental College , Jaipur, India .			importance of ergonomics in their profession. The most common site affected was neck and back. One of the drastic observations was that, Oral Pathologists suffered from a combination of problems affecting neck, back, eyes, headache, shoulders, arms and wrists. CONCLUSION: Increase in our understanding regarding ergonomic-ally designed microscopes can increase our efficiency and in turn improve our general well-being. With improvements in ergonomics, professionals would be able to modify and optimize their working conditions. Certain guidelines need to be followed by the profes-sionals to reduce chances of musculoskeletal disorders.
Hackett KL(1,)(2), Lambson RL(3), Strassheim V(1), Gotts Z(4), Deary V(1,)(5), Newton JL(1,)(3).	1)CRESTA Fatigue Clinic, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.	A concept mapping study evaluating the UK's first NHS generic fatigue clinic.	Health Expect. 2015 Sep 1. doi: 10.1111/hex.12405. [Epub ahead of print]	IMPORTANCE: Fatigue is a significant and debilitating symptom affecting 25% of the population. It occurs in those with a range of chronic diseases, can be idiopathic and in 0.2-0.4% of the UK population occurs in combination with other symptoms that together constitute chronic fatigue syndrome (CFS). Until recently, NHS clinical services only focussed upon CFS and excluded the majority of fatigued patients who did not meet the CFS diagnostic criteria. The CRESTA Fatigue interdisciplinary clinic was established in 2013 in response to this unmet need. OBJECTIVE: To identify the service needs of the heterogeneous group of patients accessing the CRESTA Fatigue Clinic, to prioritize these needs, to determine whether each is being met and to plan targeted service enhancements. DESIGN: Using a group concept mapping approach, we objectively identified the shared understanding of service users accessing this novel clinic. SETTING: NHS Clinics for Research & Service in Themed Assessment (CRESTA) Fatigue Clinic, Newcastle Upon Tyne, UK. PARTICIPANTS: Patients (n = 30) and referrers (n = 10) to the CRESTA Fatigue Clinic contributed towards a statement generation exercise to identify ways the clinic could support service users to improve their quality of life. Patients (n = 46) participated in the sorting and rating task where resulting statements were sorted into groups similar in meaning and rated for 'importance' and 'current success'. MAIN OUTCOME AND MEASURE: We mapped the needs of patients attending the CRESTA Fatigue Clinic and identified which high-priority needs were being successfully met and which were not. RESULTS: Multidimensional scaling and hierarchical cluster analysis depicted the following eight themed clusters from the data which related to various service-user requirements: 'clinic ethos', 'communication', 'support to self-manage', 'peer support', 'allied health services', 'telemedicine', 'written information' and 'service operation'. Service improvement targets were identified within value bivariate plots of the statements. CONCLUSION AND RELEVANCE: Service development concepts were grouped into thematic clusters and prioritized for both importance and current success. The resulting concept maps depict where the CRESTA Fatigue Clinic successfully addresses issues which matter to patients and highlights

				areas for service enhancement. Unmet needs of patients have been identified in a rigorous service evaluation, and these are currently being addressed in collaboration with a service-user group.
Hackett KL(1), Deane KH(2), Strassheim V(3), Deary V(4), Rapley T(5), Newton JL(3), Ng WF(6).	(1)Musculoskeletal Research Group, Institute of Cellular Medicine & NIHR Biomedical Research Centre for Ageing and Chronic Diseases, Newcastle University Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne. fai.ng@ncl.ac.uk.	A systematic review of non-pharmacological interventions for primary Sjögren's syndrome.	Rheumatology (Oxford). 2015 Nov;54(11):2025-32. doi: 10.1093/rheumatology/kev227. Epub 2015 Jun 30.	OBJECTIVE: To evaluate the effects of non-pharmacological interventions for primary SS (pSS) on outcomes falling within the World Health Organization International Classification of Functioning Disability and Health domains. METHODS: We searched the following databases from inception to September 2014: Cochrane Database of Systematic Reviews; Medline; Embase; PsychINFO; CINAHL; and clinical trials registers. We included randomized controlled trials of any non-pharmacological intervention. Two authors independently reviewed titles and abstracts against the inclusion/exclusion criteria and independently assessed trial quality and extracted data. RESULTS: A total of 1463 studies were identified, from which 17 full text articles were screened and 5 studies were included in the review; a total of 130 participants were randomized. The included studies investigated the effectiveness of an oral lubricating device for dry mouth, acupuncture for dry mouth, lacrimal punctum plugs for dry eyes and psychodynamic group therapy for coping with symptoms. Overall, the studies were of low quality and at high risk of bias. Although one study showed punctum plugs to improve dry eyes, the sample size was relatively small. CONCLUSION: Further high-quality studies to evaluate non-pharmacological interventions for PSS are needed.
Hall DL(1), Antoni MH(2), Lattie EG(1), Jutagir DR(1), Czaja SJ(3), Perdomo D(3), Lechner SC(4), Stagl JM(5), Bouchard LC(1), Gudenkauf LM(1), Traeger L(5), Fletcher M(6), Klimas NG(6).	(1)Department of Psychology, University of Miami. (2)Department of Psychology, University of Miami ; Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine ; Department of Psychiatry and Behavioral Sciences, University of Miami. (3)Department of Psychiatry and Behavioral Sciences, University of Miami. (4)Sylvester Comprehensive	Perceived Fatigue Interference and Depressed Mood: Comparison of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis Patients with Fatigued Breast Cancer Survivors.	Fatigue. 2015;3(3):142-155.	OBJECTIVE: Persistent fatigue and depressive symptoms are both highly prevalent among patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) as well as breast cancer survivors. This study aimed to assess and directly compare perceptions of fatigue as highly interfering in one's daily functioning in both patient populations to better understand their relationships with depressed mood. METHODS: Participants were 95 female CFS/ME patients and 67 females who were approximately 5 years post-treatment for stage 0-III breast cancer presenting with clinically elevated fatigue severity. Self-report measures were obtained on participants' fatigue-related interference in daily functioning and fatigue severity as well as depressed mood. Hierarchical regression was used to test effects controlling for relevant demographic, psychosocial, and medical covariates. RESULTS: CFS/ME patients endorsed greater depressed mood and fatigue interference than did fatigued breast cancer survivors, p's<.001. These factors were significantly positively correlated among CFS/ME patients (β=.36, p<.001), but not the fatigued breast cancer survivors (β=.18, p=.19). CONCLUSIONS: CFS/ME patients reported elevated fatigue symptoms and depression relative to fatigued breast cancer survivors. In the former group, greater depressed mood was highly and significantly associated with greater fatigue-related inference in daily activities. Potential targets for cognitive behavioral interventions are discussed.

	Cancer Center, University of Miami Miller School of Medicine. (5)Department of Psychiatry, Massachusetts General Hospital/Harvard Medical School. (6)Institute for Neuro Immune Medicine, Nova Southeastern University.			
Hampson JP(1), Zick SM(2), Khabir T(2), Wright BD(2), Harris RE(1).	(1)Chronic Pain and Fatigue Research Center, Department of Anesthesiology, University of Michigan, Ann Arbor, MI 48106, USA. (2)Department of Family Medicine, University of Michigan, Ann Arbor, MI, USA.	Altered resting brain connectivity in persistent cancer related fatigue.	Neuroimage Clin. 2015 May 7;8:305-13. doi: 10.1016/j.nicl.2015.04.022. eCollection 2015.	There is an estimated 3 million women in the US living as breast cancer survivors and persistent cancer related fatigue (PCRF) disrupts the lives of an estimated 30% of these women. PCRF is associated with decreased quality of life, decreased sleep quality, impaired cognition and depression. The mechanisms of cancer related fatigue are not well understood; however, preliminary findings indicate dysfunctional activity in the brain as a potential factor. Here we investigate the relationship between PCRF on intrinsic resting state connectivity in this population. Twenty-three age matched breast cancer survivors (15 fatigued and 8 non-fatigued) who completed all cancer-related treatments at least 12 weeks prior to the study, were recruited to undergo functional connectivity magnetic resonance imaging (fcMRI). Intrinsic resting state networks were examined with both seed based and independent component analysis methods. Comparisons of brain connectivity patterns between groups as well as correlations with self-reported fatigue symptoms were performed. Fatigued patients displayed greater left inferior parietal lobule to superior frontal gyrus connectivity as compared to non-fatigued patients ($P < 0.05$ FDR corrected). This enhanced connectivity was associated with increased physical fatigue ($P = 0.04$, $r = 0.52$) and poor sleep quality ($P = 0.04$, $r = 0.52$) in the fatigued group. In contrast greater connectivity in the non-fatigued group was found between the right precuneus to the periaqueductal gray as well as the left IPL to subgenual cortex ($P < 0.05$ FDR corrected). Mental fatigue scores were associated with greater default mode network (DMN) connectivity to the superior frontal gyrus ($P = 0.05$ FDR corrected) among fatigued subjects ($r = 0.82$) and less connectivity in the non-fatigued group ($r = -0.88$). These findings indicate that there is enhanced intrinsic DMN connectivity to the frontal gyrus in breast cancer survivors with persistent fatigue. As the DMN is a network involved in self-referential thinking we speculate that enhanced connectivity between the DMN and the frontal gyrus may be related to mental fatigue and poor sleep quality. In contrast, enhanced connectivity

				between the DMN and regions in the subgenual cingulate and brainstem may serve a protective function in the non-fatigued group.
Haney E, Smith ME, McDonagh M, Pappas M, Daeges M, Wasson N, Nelson HD.		Diagnostic Methods for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop.	Ann Intern Med. 2015 Jun 16;162(12):834-40. doi: 10.7326/M15-0443.	BACKGROUND: The diagnosis of myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) is based on clinical criteria, yet there has been no consensus regarding which set of criteria best identifies patients with the condition. The Institute of Medicine has recently proposed a new case definition and diagnostic algorithm. PURPOSE: To review methods to diagnose ME/CFS in adults and identify research gaps and needs for future research. DATA SOURCES: MEDLINE, PsycINFO, and Cochrane databases (January 1988 to September 2014); clinical trial registries; and reference lists. STUDY SELECTION: English-language studies describing methods of diagnosis of ME/CFS and their accuracy. DATA EXTRACTION: Data on participants, study design, analysis, follow-up, and results were extracted and confirmed. Study quality was dual-rated by using prespecified criteria, and discrepancies were resolved through consensus. DATA SYNTHESIS: Forty-four studies met inclusion criteria. Eight case definitions have been used to define ME/CFS; a ninth, recently proposed by the Institute of Medicine, includes principal elements of previous definitions. Patients meeting criteria for ME represent a more symptomatic subset of the broader ME/CFS population. Scales rating self-reported symptoms differentiate patients with ME/CFS from healthy controls under study conditions but have not been evaluated in clinically undiagnosed patients to determine validity and generalizability. LIMITATIONS: Studies were heterogeneous and were limited by size, number, applicability, and methodological quality. Most methods were tested in highly selected patient populations. CONCLUSION: Nine sets of clinical criteria are available to define ME/CFS, yet none of the current diagnostic methods have been adequately tested to identify patients with ME/CFS when diagnostic uncertainty exists. More definitive studies in broader populations are needed to address these research gaps.
Hardcastle SL(1), Brenu EW(2), Johnston S(3), Nguyen T(4), Huth T(5), Ramos S(6), Staines D(7), Marshall-Gradisnik S(8).	(1)National Centre for Neuroimmunology and Emerging Diseases, 9.22, G40 Griffith Health Institute, School of Medical Science, Griffith University, Parklands Drive, Gold Coast, QLD, 4222, Australia. sharni.hardcastle@hotmail.com	Longitudinal analysis of immune abnormalities in varying severities of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis patients.	J Transl Med. 2015 Sep 14;13:299. doi: 10.1186/s12967-015-0653-3.	BACKGROUND: Research has identified immunological abnormalities in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME), a heterogeneous illness with an unknown cause and absence of diagnostic test. There have been no CFS/ME studies examining innate and adaptive immune cells longitudinally in patients with varying severities. This is the first study to investigate immune cells over 6 months while also examining CFS/ME patients of varying symptom severity. METHODS: Participants were grouped into 18 healthy controls, 12 moderate and 12 severe CFS/ME patients and flow cytometry was used to examine cell parameters at 0 and 6 months. RESULTS: Over time, iNKT CD62L expression significantly increased in moderate CFS/ME patients and CD56(bright) NK receptors differed in severe CFS/ME. Naïve CD8(+)T cells, CD8(-)CD4(-) and CD56(-)CD16(-) iNKT phenotypes, γδ2T cells and effector memory subsets were significantly increased in severe CFS/ME patients at 6 months. Severe CFS/ME patients were significantly reduced in CD56(bright)CD16(dim) NKG2D, CD56(dim)CD16(-) KIR2DL2/DL3, CD94(-)CD11a(-) γδ1T cells and CD62L(+)CD11a(-) γδ1T cells at 6 months.

				CONCLUSIONS: Severe CFS/ME patients differed from controls and moderate CFS/ME patients over time and expressed significant alterations in iNKT cell phenotypes, CD8(+)T cell markers, NK cell receptors and γδT cells at 6 months. This highlights the importance of further assessing these potential immune biomarkers longitudinally in both moderate and severe CFS/ME patients.
Hardcastle SL(1), Brenu EW(2), Johnston S(3), Nguyen T(4), Huth T(5), Wong N(6), Ramos S(7), Staines D(8), Marshall-Gradisnik S(9).	(1)National Centre for Neuroimmunology and Emerging Diseases, Griffith Health Centre, School of Medical Science, Griffith University, Gold Coast, QLD, Australia. sharni.hardcastle@hotmail.com	Characterisation of cell functions and receptors in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME).	BMC Immunol. 2015 Jun 2;16:35. doi: 10.1186/s12865-015-0101-4.	BACKGROUND: Abnormal immune function is often an underlying component of illness pathophysiology and symptom presentation. Functional and phenotypic immune-related alterations may play a role in the obscure pathomechanism of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). The objective of this study was to investigate the functional ability of innate and adaptive immune cells in moderate and severe CFS/ME patients. The 1994 Fukuda criteria for CFS/ME were used to define CFS/ME patients. CFS/ME participants were grouped based on illness severity with 15 moderately affected (moderate) and 12 severely affected (severe) CFS/ME patients who were age and sex matched with 18 healthy controls. Flow cytometric protocols were used for immunological analysis of dendritic cells, monocytes and neutrophil function as well as measures of lytic proteins and T, natural killer (NK) and B cell receptors. RESULTS: CFS/ME patients exhibited alterations in NK receptors and adhesion markers and receptors on CD4(+)T and CD8(+)T cells. Moderate CFS/ME patients had increased CD8(+) CD45RA effector memory T cells, SLAM expression on NK cells, KIR2DL5(+) on CD4(+)T cells and BTLA4(+) on CD4(+)T central memory cells. Moderate CFS/ME patients also had reduced CD8(+)T central memory LFA-1, total CD8(+)T KLRG1, naïve CD4(+)T KLRG1 and CD56(dim)CD16(-) NK cell CD2(+) and CD18(+)CD2(+). Severe CFS/ME patients had increased CD18(+)CD11c(-) in the CD56(dim)CD16(-) NK cell phenotype and reduced NKp46 in CD56(bright)CD16(dim) NK cells. CONCLUSIONS: This research accentuated the presence of immunological abnormalities in CFS/ME and highlighted the importance of assessing functional parameters of both innate and adaptive immune systems in the illness.
Hardcastle SL(1), Brenu EW(1), Johnston S(1), Nguyen T(1), Huth T(1), Ramos S(1), Staines D(1), Marshall-Gradisnik S(1).	(1)National Centre for Neuroimmunology and Emerging Diseases, 9.22, G40 Griffith Health Institute, School of Medical Science, Griffith University, Parklands Drive, 4222, Gold Coast, QLD, Australia.	Serum Immune Proteins in Moderate and Severe Chronic Fatigue Syndrome/Myalgic Encephalomyelitis Patients.	Int J Med Sci. 2015 Sep 5;12(10):764-72. doi: 10.7150/ijms.12399. eCollection 2015.	Immunological dysregulation is present in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME), with recent studies also highlighting the importance of examining symptom severity. This research addressed this relationship between CFS/ME severity subgroups, assessing serum immunoglobulins and serum cytokines in severe and moderate CFS/ME patients. Participants included healthy controls (n= 22), moderately (n = 22) and severely (n=19) affected CFS/ME patients. The 1994 Fukuda Criteria defined CFS/ME and severity scales confirmed mobile and housebound CFS/ME patients as moderate and severe respectively. IL-1β was significantly reduced in severe compared with moderate CFS/ME patients. IL-6 was significantly decreased in moderate CFS/ME patients compared with healthy controls and severe CFS/ME patients. RANTES was significantly increased in moderate CFS/ME patients compared to severe CFS/ME patients. Serum IL-7 and IL-8 were significantly higher in the severe CFS/ME group compared with healthy controls and moderate CFS/ME patients. IFN-γ

				was significantly increased in severe CFS/ME patients compared with moderately affected patients. This was the first study to show cytokine variation in moderate and severe CFS/ME patients, with significant differences shown between CFS/ME symptom severity groups. This research suggests that distinguishing severity subgroups in CFS/ME research settings may allow for a more stringent analysis of the heterogeneous and otherwise inconsistent illness.
Hausotter W.		[Medical certification of chronic fatigue syndrome].[Article in German]	Versicherungsmedizin. 2015 Mar 1;67(1):13-8.	Chronic fatigue or chronic fatigue syndrome (CFS) is not a new disease, yet in recent years it has become increasingly important as an evaluation problem. It coincides with the well-known clinical picture of neurasthenia, shows extensive overlap with symptoms of depression and, finally, to the current concept of "burnout". Regarding the etiology there is fierce controversy between the representatives of a somatic and a psychological etiology. As reviewers you will be guided by the assessment criteria for somatoform disorders, especially because objectified findings are lacking. CFS can be independently encoded as neurological diagnosis G 93.3 according to ICD-10, although never objectified neurological deficits were detected, as well as neurasthenia F 48.0 or accompanying physical symptoms as somatization disorder F 45.0.
Hayer SD(1), Rabago DP(2), Amaza IP(1), Kille T(3), Coe CL(4), Zgierska A(1), Zakletskaia L(1), Mundt MP(1), Krahn D(5), Obasi CN(1), Molander RC(5).	(1)1100 Delaplaine Court, Madison, WI 53715, Department of Family Medicine, School of Medicine and Public Health, University of Wisconsin-Madison, United States.	Effectiveness of nasal irrigation for chronic rhinosinusitis and fatigue in patients with Gulf War illness: protocol for a randomized controlled trial.	Contemp Clin Trials. 2015 Mar;41:219-26. doi: 10.1016/j.cct.2015.01.008 . Epub 2015 Jan 24.	INTRODUCTION: Gulf War Illness (GWI) affects 1 in 7 returned Persian Gulf War veterans. Quality-of-life impact is large; there is no cure. Chronic sinus symptoms and fatigue are common. Nasal irrigation with saline (NI-S) or xylitol (NI-X) improve sinus symptoms and fatigue in the general population. This trial will assess the effect of NI-S and NI-X on sinus and fatigue symptoms, economic outcomes and pro-inflammatory milieu among participants with GWI. METHODS: 75 participants (age 35 to 65 years, 25 in each of three arms) with GWI will be recruited from the Veteran's Administration and the community. They will use routine care for sinus symptoms and fatigue and be randomized to continued usual care alone or additional therapy with NI-S or NI-X. Participants will be able to adjust specific elements of the NI procedure. The primary outcome (Sinonasal Outcome Test, SNOT-20) and other self-reported assessments will occur at baseline, 8 and 26 weeks; lab assessment of pro-inflammatory cellular and cytokine profiles will occur at baseline and 26 weeks. Other outcomes will include fatigue-specific and overall health-related quality of life, pro-inflammatory cellular and cytokine profiles, cost-effectiveness and participant satisfaction. RESULTS: Baseline demographic and clinical data from the first 10 participants show effective participant recruitment, enrollment, randomization, retention and data collection. CONCLUSION: Early study conduct suggests that our participant-oriented approach will yield high rates of participant adherence and data capture, facilitating robust analysis. Results of this study will clarify the value of NI for chronic sinus symptoms and fatigue among patients with GWI. CLINICAL TRIAL REGISTRATION: clinicaltrials.gov identifier

				NCT01700725.
Higgins N(1), Pickard J(2), Lever A(3).	(1)Department of Radiology, Addenbrooke's Hospital, Cambridge, United Kingdom. (2)Department of Neurosurgery, Addenbrooke's Hospital, Cambridge, United Kingdom. (3)Department of Infectious diseases, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom.	Borderline Intracranial Hypertension Manifesting as Chronic Fatigue Syndrome Treated by Venous Sinus Stenting.	J Neurol Surg Rep. 2015 Nov;76(2):e244-7. doi: 10.1055/s-0035-1564060. Epub 2015 Sep 14.	Chronic fatigue syndrome and cases of idiopathic intracranial hypertension without signs of raised intracranial pressure can be impossible to distinguish without direct measurement of intracranial pressure. Moreover, lumbar puncture, the usual method of measuring intracranial pressure, can produce a similar respite from symptoms in patients with chronic fatigue as it does in idiopathic intracranial hypertension. This suggests a connection between them, with chronic fatigue syndrome representing a forme fruste variant of idiopathic intracranial hypertension. If this were the case, then treatments available for idiopathic intracranial hypertension might be appropriate for chronic fatigue. We describe a 49-year-old woman with a long and debilitating history of chronic fatigue syndrome who was targeted for investigation of intracranial pressure because of headache, then diagnosed with borderline idiopathic intracranial hypertension after lumbar puncture and cerebrospinal fluid drainage. Further investigation showed narrowings at the anterior ends of the transverse sinuses, typical of those seen in idiopathic intracranial hypertension and associated with pressure gradients. Stenting of both transverse sinuses brought about a life-changing remission of symptoms with no regression in 2 years of follow-up. This result invites study of an alternative approach to the investigation and management of chronic fatigue.
Hornig M(1), Gottschalk G(2), Peterson DL(2), Knox KK(3), Schultz AF(4), Eddy ML(4), Che X(4), Lipkin WI(5).	(1)1] Center for Infection and Immunity, Columbia University Mailman School of Public Health, New York, NY, USA	Cytokine network analysis of cerebrospinal fluid in myalgic encephalomyelitis/chronic fatigue syndrome.	Mol Psychiatry. 2015 Mar 31. doi: 10.1038/mp.2015.29. [Epub ahead of print]	Myalgic encephalomyelitis/chronic fatigue syndrome is an unexplained debilitating disorder that is frequently associated with cognitive and motor dysfunction. We analyzed cerebrospinal fluid from 32 cases, 40 subjects with multiple sclerosis and 19 normal subjects frequency-matched for age and sex using a 51-plex cytokine assay. Group-specific differences were found for the majority of analytes with an increase in cases of CCL11 (eotaxin), a chemokine involved in eosinophil recruitment. Network analysis revealed an inverse relationship between interleukin 1 receptor antagonist and colony-stimulating factor 1, colony-stimulating factor 2 and interleukin 17F, without effects on interleukin 1α or interleukin 1β, suggesting a disturbance in interleukin 1 signaling. Our results indicate a markedly disturbed immune signature in the cerebrospinal fluid of cases that is consistent with immune activation in the central nervous system, and a shift toward an allergic or T helper type-2 pattern associated with autoimmunity.Molecular Psychiatry advance online publication, 31 March 2015; doi:10.1038/mp.2015.29.
Hornig M(1), Montoya JG(2), Klimas NG(3), Levine S(4), Felsenstein D(5), Bateman L(6), Peterson DL(7), Gottschalk CG(7),	(1)Center for Infection and Immunity, Columbia University Mailman School of Public Health, New York, NY 10032, USA	Distinct plasma immune signatures in ME/CFS are present early in the course of illness.	Sci Adv. 2015 Feb;1(1). pii: e1400121.	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is an unexplained incapacitating illness that may affect up to 4 million people in the United States alone. There are no validated laboratory tests for diagnosis or management despite global efforts to find biomarkers of disease. We considered the possibility that inability to identify such biomarkers reflected variations in diagnostic criteria and laboratory methods as well as the timing of sample collection during the course of the illness. Accordingly, we leveraged two large, multicenter cohort studies of ME/CFS to assess the relationship of immune signatures with diagnosis, illness duration, and other clinical

Schultz AF(8), Che X(8), Eddy ML(8), Komaroff AL(9), Lipkin WI(10).				variables. Controls were frequency-matched on key variables known to affect immune status, including season of sampling and geographic site, in addition to age and sex. We report here distinct alterations in plasma immune signatures early in the course of ME/CFS (n = 52) relative to healthy controls (n = 348) that are not present in subjects with longer duration of illness (n = 246). Analyses based on disease duration revealed that early ME/CFS cases had a prominent activation of both pro- and anti-inflammatory cytokines as well as dissociation of intercytokine regulatory networks. We found a stronger correlation of cytokine alterations with illness duration than with measures of illness severity, suggesting that the immunopathology of ME/CFS is not static. These findings have critical implications for discovery of interventional strategies and early diagnosis of ME/CFS.
Hosman A, Westermann CJ, Snijder R, Disch F, Mummery CL, Mager JJ.		Follow-up of Thalidomide treatment in patients with Hereditary Haemorrhagic Telangiectasia.	Rhinology. 2015 Dec;53(4):340-4. doi: 10.4193/Rhin14.289.	BACKGROUND: Patients with a hereditary vascular disorder called Rendu-Osler-Weber syndrome (Hereditary Haemorrhagic Telangiectasia, HHT) haemorrhage easily due to weak-walled vessels. Haemorrhage in lungs or brain can be fatal but patients suffer most from chronic and prolonged nosebleeds (epistaxis), the frequency and intensity of which increases with age. Several years ago, it was discovered serendipitously that the drug Thalidomide had beneficial effects on the disease symptoms in several of a small group of HHT patients: epistaxis and the incidence of anaemia were reduced and patients required fewer blood transfusions. In addition, they reported a better quality of life. However, Thalidomide has significant negative side effects, including neuropathy and fatigue. METHODS: We followed up all HHT patients in the Netherlands who had been taking Thalidomide at the time the original study was completed to find out (i) how many had continued taking Thalidomide and for how long (ii) the nature and severity of any side-effects and (iii) whether side-effects had influenced their decision to continue taking Thalidomide. RESULTS: Only a minority of patients had continued taking the drug despite its beneficial effects on their symptoms and that the side effects were the primary reason to stop. CONCLUSION: Despite symptom reduction, alternative treatments are still necessary for epistaxis in HHT patients and a large-scale clinical trial is not justified although incidental use in the most severely affected patients can be considered.
Huang CY(1), Chung SD, Kao LT, Lin HC, Wang LH.	(1)Department of Urology, National Taiwan University Hospital, College of Medicine National Taiwan University, Taipei, Taiwan.	Statin Use Is Associated with Bladder Pain Syndrome/Interstitial Cystitis: A Population-Based Case-Control Study.	Urol Int. 2015;95(2):227-32. doi: 10.1159/000431185. Epub 2015 Jul 16.	INTRODUCTION: Statin may induce epithelial dysfunction of the bladder urothelium. Epithelial dysfunction was proposed as one of the major potential etiologies for bladder pain syndrome/interstitial cystitis (BPS/IC). In this study, we examined the association between statin use and BPS/IC using a population-based study. SUBJECTS AND METHODS: This case-control study used the Taiwan Longitudinal Health Insurance Database. In total, 815 female subjects with BPS/IC and 4075 randomly selected female controls were included. We used a conditional logistic regression to compute the odds ratio (OR) for having previously used statins between cases and controls. RESULTS: A conditional logistic regression analysis showed that the OR of prior statin users for cases was 1.52 (95% confidence interval (CI): 1.19-1.94) compared to controls after

				adjusting for diabetes, hypertension, coronary heart disease, obesity, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraines, sicca syndrome, allergies, endometriosis, and asthma. Furthermore, adjusted ORs of regular and irregular statin use for cases were 1.58 (95% CI: 1.20-2.08) and 1.53 (95% CI: 1.02-2.31), respectively, compared to controls. CONCLUSION: We concluded that there was an association between statin use and BPS/IC.
Huang H(1), Hohler AD(2).	(1)Department of Neurology, Boston University Medical Campus, 72 East Concord St, A-302, Boston, MA, 02118, USA. hhuang@bu.edu. (2)Department of Neurology, Boston University Medical Campus, 72 East Concord St, A-302, Boston, MA, 02118, USA.	The Dermatological Manifestations of Postural Tachycardia Syndrome: A Review with Illustrated Cases.	Am J Clin Dermatol. 2015 Oct;16(5):425-30. doi: 10.1007/s40257-015-0144-6.	Postural tachycardia syndrome (POTS) is a syndrome of excessive tachycardia with orthostatic challenge, and relief of such symptoms with recumbence. There are several proposed subtypes of the syndrome, each with unique pathophysiology. Numerous symptoms such as excessive tachycardia, lightheadedness, blurry vision, weakness, fatigue, palpitations, chest pain, and tremulousness are associated with orthostatic intolerance. Other co-morbid conditions associated with POTS are not clearly attributable to orthostatic intolerance. These include chronic headache, fibromyalgia, functional gastrointestinal or bladder disorders, cognitive impairment, and sleep disturbances. Dermatological manifestations of POTS are also common and wide ranging, from livedo reticularis to Raynaud's phenomenon, from cutaneous flushing to erythromelalgia. Here, we provide three illustrative cases of POTS with dermatological manifestations. We discuss the potential pathophysiology underlying such dermatological manifestations, and how such mechanisms could in turn help guide development of management.
Huang YH(1), Chen HC(2,)(3), Huang KW(4,)(5,)(6), Chen PC(7,)(8), Hu CJ(9,)(10), Tsai CP(11,)(12), Tam KW(13,)(14,)(15,)(16,)(17,)(18), Kuan YC(19,)(20,)(21,)(22).	(1)Department of Neurology, Taipei Medical University-Shuang Ho Hospital, New Taipei City, Taiwan. hyh0103@gmail.com.	Intravenous immunoglobulin for postpolio syndrome: a systematic review and meta-analysis.	BMC Neurol. 2015 Mar 22;15:39. doi: 10.1186/s12883-015-0301-9.	BACKGROUND: Postpolio syndrome (PPS) is characterized by progressive disabilities that develop decades after prior paralytic poliomyelitis. Because chronic inflammation may be the process underlying the development of PPS, immunomodulatory management, such as intravenous immunoglobulin (IVIg) administration, may be beneficial. METHODS: We performed a systematic review and meta-analysis of published randomized controlled trials (RCTs) and prospective studies that evaluated the efficacy of IVIg in managing PPS. Electronic databases, including PubMed, EMBASE, CINAHL, and the Cochrane Central Register of Controlled Trials, were searched for articles on PPS published before December 2014. The primary outcomes were pain severity, fatigue scores, and muscle strength. The secondary outcomes were physical performance, quality of life (QoL), and cytokine expression levels. RESULTS: We identified 3 RCTs involving 241 patients and 5 prospective studies involving 267 patients. The meta-analysis of pain severity (weighted mean difference [WMD] = -1.02, 95% confidence interval [CI] = -2.51 to 0.47), fatigue scores (WMD = 0.28, 95% CI -0.56 to 1.12), and muscle strength revealed no significant differences between the IVIg and the placebo group. Regarding QoL, the RCTs yielded controversial outcomes, with improvement in only certain domains of the Short Form 36 (SF-36). Moreover, one prospective study reported significant improvement on SF-36, particularly in patients aged younger than 65 years, those with paresis of the lower limbs, and high pain

				intensity. CONCLUSION: The present review indicated that IVIg is unlikely to produce significant improvements in pain, fatigue, or muscle strength. Thus, routinely administering IVIg to patients with PPS is not recommended based on RCTs. However, a potential effect in younger patients with lower limbs weakness and intense pain requires confirmation from further well-structured trials.
Iacob E(1), Light AR(2), Donaldson GW(1), Okifuji A(1), Hughen RW(2), White AT(3), Light KC(2).	(1)Department of Anesthesiology Pain Research Center, University of Utah, Salt Lake City, UT. (2)Department of Anesthesiology, University of Utah, Salt Lake City, UT. (3)Department of Exercise and Sport Science, University of Utah, USA, Salt Lake City, UT.	Gene expression factor analysis to differentiate pathways linked to fibromyalgia, chronic fatigue syndrome, and depression in a diverse patient sample.	Arthritis Care Res (Hoboken). 2015 Jun 19. doi: 10.1002/acr.22639. [Epub ahead of print]	OBJECTIVE: To determine if independent candidate genes can be grouped into meaningful biological factors and if these factors are associated with the diagnosis of chronic fatigue syndrome (CFS) and fibromyalgia (FMS) while controlling for co-morbid depression, sex, and age. METHODS: We included leukocyte mRNA gene expression from a total of 261 individuals including healthy controls (n=61), patients with FMS only (n=15), CFS only (n=33), co-morbid CFS and FMS (n=79), and medication-resistant (n=42) or medication-responsive (n=31) depression. We used Exploratory Factor Analysis (EFA) on 34 candidate genes to determine factor scores and regression analysis to examine if these factors were associated with specific diagnoses. RESULTS: EFA resulted in four independent factors with minimal overlap of genes between factors explaining 51% of the variance. We labeled these factors by function as: 1) Purinergic and cellular modulators; 2) Neuronal growth and immune function; 3) Nociception and stress mediators; 4) Energy and mitochondrial function. Regression analysis predicting these biological factors using FMS, CFS, depression severity, age, and sex revealed that greater expression in Factors 1 and 3 was positively associated with CFS and negatively associated with depression severity (QIDS score), but not associated with FMS. CONCLUSION: Expression of candidate genes can be grouped into meaningful clusters, and CFS and depression are associated with the same 2 clusters but in opposite directions when controlling for co-morbid FMS. Given high co-morbid disease and interrelationships between biomarkers, EFA may help determine patient subgroups in this population based on gene expression.
Ickmans K(1), Meeus M(2), De Kooning M(3), Lambrecht L(4), Pattyn N(5), Nijs J(6).	(1)Pain in Motion Research Group (www.paininmotion.be). (2)1Pain in Motion Research Group (www.paininmotion.be); Rehabilitation Sciences and Physiotherapy, Faculty of Medicine & Health Sciences, Ghent University, Ghent, Belgium;	Associations Between Cognitive Performance and Pain in Chronic Fatigue Syndrome: Comorbidity with Fibromyalgia Does Matter.	Pain Physician. 2015 Sep-Oct;18(5):E841-52.	BACKGROUND: In addition to the frequently reported pain complaints, performance-based cognitive capabilities in patients with chronic fatigue syndrome (CFS) with and without comorbid fibromyalgia (FM) are significantly worse than those of healthy controls. In various chronic pain populations, cognitive impairments are known to be related to pain severity. However, to the best of our knowledge, the association between cognitive performance and experimental pain measurements has never been examined in CFS patients. OBJECTIVES: This study aimed to examine the association between cognitive performance and self-reported as well as experimental pain measurements in CFS patients with and without FM. STUDY DESIGN: Observational study. SETTING: The present study took place at the Vrije Universiteit Brussel and the University of Antwerp. METHODS: Forty-eight (18 CFS-only and 30 CFS+FM) patients and 30 healthy controls were studied. Participants first completed 3 performance-based cognitive tests designed to assess selective and sustained attention, cognitive inhibition, and working memory capacity. Seven days later, experimental pain

				measurements (pressure pain thresholds [PPT], temporal summation [TS], and conditioned pain modulation [CPM]) took place and participants were asked to fill out 3 questionnaires to assess self-reported pain, fatigue, and depressive symptoms. RESULTS: In the CFS+FM group, the capacity of pain inhibition was significantly associated with cognitive inhibition. Self-reported pain was significantly associated with simple reaction time in CFS-only patients. The CFS+FM but not the CFS-only group showed a significantly lower PPT and enhanced TS compared with controls. LIMITATIONS: The cross-sectional nature of this study does not allow for inferences of causation. CONCLUSIONS: The results underline disease heterogeneity in CFS by indicating that a measure of endogenous pain inhibition might be a significant predictor of cognitive functioning in CFS patients with FM, while self-reported pain appears more appropriate to predict cognitive functioning in CFS patients without FM.
Ikeda S(1).	(1)Department of Medicine (Neurology and Rheumatology), Shinshu University School of Medicine.	[Neurologic Complications in HPV Vaccination].[Article in Japanese]	Brain Nerve. 2015 Jul;67(7):835-43. doi: 10.11477/mf.1416200222.	A relatively high incidence of chronic limb pain, frequently complicated by violent, tremulous involuntary movements, has been noted in Japanese girls following human papillomavirus vaccination. The average incubation period after the first dose of the vaccine was 5.47 ± 5.00 months. Frequent manifestations included headaches, general fatigue, coldness of the feet, limb pain, and weakness. The skin temperature of the girls with limb symptoms was slightly lower in the fingers and moderately lower in the toes. Digital plethysmograms revealed a reduced peak of the waves, especially in the toes. Limb symptoms of the affected girls were compatible with the diagnostic criteria for complex regional pain syndrome. The Schellong test identified a significant number of patients with orthostatic hypotension and a few with postural orthostatic tachycardia syndrome. Electron-microscopic examinations of the intradermal nerves showed an abnormal pathology in the unmyelinated fibers in two of the three girls examined. The symptoms observed in this study can be explained by abnormal peripheral sympathetic responses. The most common previous diagnosis in the patients was psychosomatic disease. Recently, delayed manifestation of cognitive dysfunction in the post-vaccinated girls has attracted attention. The symptoms include memory loss and difficulty in reading textbooks and/or calculation.
Inui T(1), Kubo K(2), Kuchiike D(3), Uto Y(4), Nishikata T(5), Sakamoto N(6), Mette M(7).	(1)Department of Life System, Institute of Technology and Science, Graduate School, Tokushima University, Tokushima, Japan Saisei Mirai Cell Processing Center, Osaka, Japan Inui Immunotherapy Clinic, Osaka, Japan	Oral Colostrum Macrophage-activating Factor for Serious Infection and Chronic Fatigue Syndrome: Three Case Reports.	Anticancer Res. 2015 Aug;35(8):4545-9.	BACKGROUND: Gc protein-derived macrophage-activating factor (GcMAF) immunotherapy has been steadily advancing over the last two decades. Oral colostrum macrophage-activating factor (MAF) produced from bovine colostrum has shown high macrophage phagocytic activity. GcMAF-based immunotherapy has a wide application for use in treating many diseases via macrophage activation or for use as supportive therapy. RESULTS: Three case studies demonstrate that oral colostrum MAF can be used for serious infection and chronic fatigue syndrome (CFS) without adverse effects. CONCLUSION: We demonstrate that colostrum MAF shows promising clinical results in patients with infectious diseases and for symptoms of fatigue, which is common in many chronic diseases.

	contact@saisei-mirai.or.jp.			
[Article in English, Spanish]	Isasi C(1), Tejerina E(2), Fernandez-Puga N(3), Serrano-Vela JI(4).	Fibromyalgia and chronic fatigue syndrome caused by non-celiac gluten sensitivity.	Reumatol Clin. 2015 Jan-Feb;11(1):56-7. doi: 10.1016/j.reuma.2014.06.005. Epub 2014 Jul 19.	(1)Servicio de Reumatología, Hospital Puerta de Hierro, Majadahonda, Madrid, España. Electronic address: carlosmaria.isasi@salud.madrid.org. (2)Servicio de Anatomía Patológica, Hospital Puerta de Hierro, Majadahonda, Madrid, España. (3)Servicio de Aparato Digestivo, Hospital Puerta de Hierro, Majadahonda, Madrid, España. (4)Asociación de celíacos y sensibles al gluten de Madrid, Madrid, España.
Isasi Zaragozá C(1).	(1)Servicio de Reumatología, Hospital Puerta de Hierro, Majadahonda, España. Electronic address: cisasi.hpth@salud.madrid.org.	Chronic fatigue syndrome and non-celiac gluten sensitivity. Association or cause?	Reumatol Clin. 2015 May-Jun;11(3):184. doi: 10.1016/j.reuma.2014.10.010. Epub 2014 Dec 10.	Comment on Reumatol Clin. 2014 Mar-Apr;10(2):132-3.
Jakez-Ocampo J(1), Atisha-Fregoso Y, Llorente L.	(1)From the *Department of Immunology and Rheumatology and †Medical Direction, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico.	Refractory primary Sjögren syndrome successfully treated with bortezomib.	J Clin Rheumatol. 2015 Jan;21(1):31-2. doi: 10.1097/RHU.0000000000000210.	Primary Sjögren syndrome (PSS) is a chronic autoimmune disease characterized by sicca complex and various systemic manifestations. Although it is well accepted to use corticosteroids for the treatment of systemic manifestations, there is scarce information available regarding the use of targeted therapy for refractory cases. We describe a case of a severe PSS patient refractory to conventional treatment with a response to bortezomib, a proteasome inhibitor commonly used for the treatment of multiple myeloma. Bortezomib administration resulted in a notable improvement of the general symptoms, particularly fatigue, and a decrease in serum globulin levels as well as in serum viscosity. Hyperglobulinemic purpura disappeared, and prednisone tapering succeeded. Because of chronicity, no clinical changes were observed in sicca symptoms. As far as we know, this is the first report on the use of bortezomib in a refractory case of PSS.
James K(1,)(2), Al-Ali S(2,)(3), Tarn J(2), Cockell SJ(4), Gillespie CS(5), Hindmarsh V(6), Locke J(2), Mitchell S(6), Lendrem D(2), Bowman S(7), Price E(8), Pease CT(9), Emery P(9), Lanyon P(10), Hunter JA(11),	(1)Interdisciplinary Computing and Complex BioSystems Research Group, Newcastle University, Newcastle upon Tyne, United Kingdom.	A Transcriptional Signature of Fatigue Derived from Patients with Primary Sjögren's Syndrome.	PLoS One. 2015 Dec 22;10(12):e0143970. doi: 10.1371/journal.pone.0143970. eCollection 2015.	BACKGROUND: Fatigue is a debilitating condition with a significant impact on patients' quality of life. Fatigue is frequently reported by patients suffering from primary Sjögren's Syndrome (pSS), a chronic autoimmune condition characterised by dryness of the eyes and the mouth. However, although fatigue is common in pSS, it does not manifest in all sufferers, providing an excellent model with which to explore the potential underpinning biological mechanisms. METHODS: Whole blood samples from 133 fully-phenotyped pSS patients stratified for the presence of fatigue, collected by the UK primary Sjögren's Syndrome Registry, were used for whole genome microarray. The resulting data were analysed both on a gene by gene basis and using pre-defined groups of genes. Finally, gene set enrichment analysis (GSEA) was used as a feature selection technique for input into a support vector machine (SVM) classifier. Classification was assessed using area under curve (AUC) of receiver operator characteristic and standard error of Wilcoxon statistic, SE(W). RESULTS: Although no

Gupta M(11), Bombardieri M(12), Sutcliffe N(12), Pitzalis C(12), McLaren J(13), Cooper A(14,)(15), Regan M(16), Giles I(17), Isenberg D(17), Saravanan V(18), Coady D(19), Dasgupta B(20), McHugh N(21), Young-Min S(15), Moots R(22), Gendi N(23), Akil M(24), Griffiths B(6); UK Primary Sjögren's Syndrome registry, Wipat A(1), Newton J(6,)(25), Jones DE(2), Isaacs J(2,)(26), Hallinan J(1,)(27), Ng WF(2,)(26).				genes were individually found to be associated with fatigue, 19 metabolic pathways were enriched in the high fatigue patient group using GSEA. Analysis revealed that these enrichments arose from the presence of a subset of 55 genes. A radial kernel SVM classifier with this subset of genes as input displayed significantly improved performance over classifiers using all pathway genes as input. The classifiers had AUCs of 0.866 (SE(W) 0.002) and 0.525 (SE(W) 0.006), respectively. CONCLUSIONS: Systematic analysis of gene expression data from pSS patients discordant for fatigue identified 55 genes which are predictive of fatigue level using SVM classification. This list represents the first step in understanding the underlying pathophysiological mechanisms of fatigue in patients with pSS.
Janse A(1), Worm-Smeitink M(2), Bussel-Lagarde J(3), Bleijenberg G(4), Nikolaus S(5), Knoop H(6).	(1)Expert Centre for Chronic Fatigue, Radboud university medical center, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. Anthonie.Janse@radboudumc.nl.	Testing the efficacy of web-based cognitive behavioural therapy for adult patients with chronic fatigue syndrome (CBIT): study protocol for a randomized controlled trial.	BMC Neurol. 2015 Aug 12;15:137. doi: 10.1186/s12883-015-0392-3.	BACKGROUND: Cognitive behavioural therapy (CBT) is an effective treatment for fatigue and disabilities in patients with chronic fatigue syndrome (CFS). However, treatment capacity is limited. Providing web-based CBT and tailoring the amount of contact with the therapist to the individual needs of the patient may increase the efficiency of the intervention. Web-based CBT for adolescents with CFS has proven to be effective in reducing fatigue and increasing school attendance. In the proposed study the efficacy of a web-based CBT intervention for adult patients with CFS will be explored. Two different formats of web-based CBT will be tested. In the first format named protocol driven feedback, patients report on their progress and receive feedback from a therapist according to a preset schedule. In the second format named support on demand, feedback and support of the therapist is only given when patients ask for it. The primary objective of the study is to determine the efficacy of a web-based CBT intervention on fatigue severity. METHOD/DESIGN: A randomized clinical

				trial will be conducted. Two-hundred-forty adults who have been diagnosed with CFS according to the US Centers for Disease Control and Prevention (CDC) consensus criteria will be recruited and randomized to one of three conditions: web-based CBT with protocol driven feedback, web-based CBT with support on demand, or wait list. Feedback will be delivered by therapists specialized in CBT for CFS. Each of the web-based CBT interventions will be compared to a wait list condition with respect to its effect on the primary outcome measure; fatigue severity. Secondary outcome measures are level of disability, physical functioning, psychological distress, and the proportion of patients with clinical significant improvement in fatigue severity. Outcomes will be assessed at baseline and six months post randomization. The web-based CBT formats will be compared with respect to the time therapists need to deliver the intervention. DISCUSSION: As far as we know this is the first randomized controlled trial (RCT) that evaluates the efficacy of a web-based CBT intervention for adult patients with CFS. TRIAL REGISTRATION: NTR4013.
Janssens KA(1), Zijlema WL, Joustra ML, Rosmalen JG.	(1)From the Interdisciplinary Center Psychopathology and Emotion Regulation (Janssens, Joustra, Rosmalen) and Department of Epidemiology (Zijlema), University Medical Center Groningen, University of Groningen.	Mood and Anxiety Disorders in Chronic Fatigue Syndrome, Fibromyalgia, and Irritable Bowel Syndrome: Results From the LifeLines Cohort Study.	Psychosom Med. 2015 May;77(4):449-57. doi: 10.1097/PSY.0000000000000161.	OBJECTIVE: Functional somatic syndromes (FSSs) have often been linked to psychopathology. The aim of the current study was to compare prevalence rates of psychiatric disorders among individuals with chronic fatigue syndrome (CFS), fibromyalgia (FM), and irritable bowel syndrome (IBS). METHODS: This study was conducted in 94,516 participants (mean [standard deviation] age = 44.6 [12.5] years, 58.7% women) of the general-population cohort LifeLines. FSSs were assessed by self-reports. Mood disorders (i.e., major depressive disorder and dysthymia) and anxiety disorders (i.e., generalized anxiety disorder, social phobia, panic disorder with/without agoraphobia, and agoraphobia) were assessed by means of the Mini International Neuropsychiatric Interview. Risks on psychiatric disorders were compared for individuals with CFS, FM, and IBS by using logistic regression analyses adjusted for age and sex. RESULTS: Prevalence rates of CFS, FM, and IBS were 1.3%, 3.0%, and 9.7%, respectively. Individuals with CFS, FM, and IBS had significantly more mood (odds ratios [ORs] = 1.72-5.42) and anxiety disorders (ORs = 1.52-3.96) than did individuals without FSSs, but prevalence rates were low (1.6%-28.6%). Individuals with CFS more often had mood (ORs = 2.00-4.08) and anxiety disorders (ORs = 1.63-2.32) than did individuals with FM and IBS. Major depressive disorder was more common in FM than in IBS (OR = 1.58, 95% confidence interval = 1.24-2.01), whereas these groups did not differ on dysthymia or anxiety disorders. CONCLUSIONS: Mood and anxiety disorders are more prevalent in individuals with FSSs, and particularly CFS, than in individuals without FSSs. However, most individuals with FSSs do not have mood or anxiety disorders.
Jason LA(1), Sunnquist M(1), Brown A(1), Newton JL(2), Strand EB(3),	(1)DePaul University. (2)Newcastle University. (3)Oslo University Hospital. (4)Solve ME/CFS	Chronic Fatigue Syndrome versus Systemic Exertion Intolerance Disease.	Fatigue. 2015 Jul;3(3):127-141.	BACKGROUND: The Institute of Medicine has recommended a change in the name and criteria for Chronic Fatigue Syndrome (CFS), renaming the illness Systemic Exertion Intolerance Disease (SEID). The new SEID case definition requires substantial reductions or impairments in the ability to engage in pre-illness activities, unrefreshing sleep, post-exertional malaise, and either cognitive impairment or orthostatic intolerance.

Vernon SD(4).	Initiative.			PURPOSE: In the current study, samples were generated through several different methods and were used to compare this new case definition to previous case definitions for CFS, Myalgic Encephalomyelitis (ME-ICC), Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), as well as a case definition developed through empirical methods. METHODS: We used a cross-sectional design with samples from tertiary care settings, a biobank sample, and other forums. 796 patients from the US, Great Britain, and Norway completed the DePaul Symptom Questionnaire. RESULTS: Findings indicated that the SEID criteria identified 88% of participants in the samples analyzed, which is comparable to the 92% that met the Fukuda criteria. The SEID case definition was compared to a four item empiric criteria, and findings indicated that the four item empiric criteria identified a smaller, more functionally limited and symptomatic group of patients. CONCLUSION: The recently developed SEID criteria appears to identify a group comparable in size to the Fukuda et al. criteria, but a larger group of patients than the Canadian ME/CFS and ME criteria, and selects more patients who have less impairment and fewer symptoms than a four item empiric criteria.
Jason LA, Zinn ML, Zinn MA(1).	(1)Center for Community Research, DePaul University, 990 W. Fullerton Ave., Chicago, Illinois, 60614-3504 United States.	Myalgic Encephalomyelitis: Symptoms and Biomarkers.	Curr Neuropharmacol. 2015;13(5):701-34.	Myalgic Encephalomyelitis (ME) continues to cause significant morbidity worldwide with an estimated one million cases in the United States. Hurdles to establishing consensus to achieve accurate evaluation of patients with ME continue, fueled by poor agreement about case definitions, slow progress in development of standardized diagnostic approaches, and issues surrounding research priorities. Because there are other medical problems, such as early MS and Parkinson's Disease, which have some similar clinical presentations, it is critical to accurately diagnose ME to make a differential diagnosis. In this article, we explore and summarize advances in the physiological and neurological approaches to understanding, diagnosing, and treating ME. We identify key areas and approaches to elucidate the core and secondary symptom clusters in ME so as to provide some practical suggestions in evaluation of ME for clinicians and researchers. This review, therefore, represents a synthesis of key discussions in the literature, and has important implications for a better understanding of ME, its biological markers, and diagnostic criteria. There is a clear need for more longitudinal studies in this area with larger data sets, which correct for multiple testing.
Jason LA, Sunnquist M, Brown A, McManimen S, Furst J.		Reflections on the Institute of Medicine's systemic exertion intolerance disease.	Pol Arch Med Wewn. 2015;125(7-8):576-81.	The Institute of Medicine (IOM) in the United States has recently proposed that the term systemic exertion intolerance disease (SEID) replace chronic fatigue syndrome. In addition, the IOM proposed a new case definition for SEID, which includes substantial reductions or impairments in the ability to engage in pre‐illness activities, unrefreshing sleep, postexertional malaise, and either cognitive impairment or orthostatic intolerance. Unfortunately, these recommendations for a name change were not vetted with patient and professional audiences, and the new criteria were not evaluated with data sets of patients and controls. A recent poll suggests that the majority of patients reject this new name. In addition, studies have found that

				prevalence rates will dramatically increase with the new criteria, particularly due to the ambiguity revolving around exclusionary illnesses. Findings suggest that the new criteria select more patients who have less impairment and fewer symptoms than several other criteria. The implications of these findings are discussed in the current review.
Jason LA(1), Kot B(1), Sunnquist M(1), Brown A(1), Evans M(1), Jantke R(1), Williams Y(1), Furst J(1), Vernon SD(2).	(1)DePaul University. (2)Solve ME/CFS Initiative.	Chronic Fatigue Syndrome and Myalgic Encephalomyelitis: Toward An Empirical Case Definition.	Health Psychol Behav Med. 2015;3(1):82-93.	Current case definitions of Myalgic Encephalomyelitis (ME) and chronic fatigue syndrome (CFS) have been based on consensus methods, but empirical methods could be used to identify core symptoms and thereby improve the reliability. In the present study, several methods (i.e., continuous scores of symptoms, theoretically and empirically derived cut off scores of symptoms) were used to identify core symptoms best differentiating patients from controls. In addition, data mining with decision trees was conducted. Our study found a small number of core symptoms that have good sensitivity and specificity, and these included fatigue, post-exertional malaise, a neurocognitive symptom, and unrefreshing sleep. Outcomes from these analyses suggest that using empirically selected symptoms can help guide the creation of a more reliable case definition.
Jason LA(1), Evans M, Brown A, Sunnquist M, Newton JL.	(1)a Center for Community Research, DePaul University , Chicago , Illinois , USA.	Chronic fatigue syndrome versus sudden onset myalgic encephalomyelitis.	J Prev Interv Community. 2015;43(1):62-77. doi: 10.1080/10852352.2014.973233.	A revised sudden onset case definition for Myalgic Encephalomyelitis (ME) has been developed (Jason, Damrongvachiraphan, et al., 2012) based on past case definitions. In a prior study, Jason, Brown, and colleagues (2012) compared patients recruited using the 1994 case definition of chronic fatigue syndrome (CFS) to contrast those meeting criteria for the revised ME criteria. They found that this revised ME case definition identified patients with more functional impairments and physical, mental, and cognitive problems than those meeting the CFS criteria. The study by Jason, Brown, et al. (2012) only selected individuals who first met the CFS criteria, and it only relied on one Chicago-based data set. The current study replicated this comparison with two distinct data sets with different case ascertainment methods. Results indicate that the ME criteria identified a group of patients with more functional disabilities as well as more severe post-exertional malaise symptoms.
Jason LA(1), Evans M, So S, Scott J, Brown A.	(1)a Center for Community Research, DePaul University , Chicago , Illinois , USA.	Problems in defining post-exertional malaise.	J Prev Interv Community. 2015;43(1):20-31. doi: 10.1080/10852352.2014.973239.	Post-exertional malaise (PEM) is a cardinal symptom of the illnesses referred to as Myalgic Encephalomyelitis (ME), Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS), and chronic fatigue syndrome (CFS). PEM is reported to occur in many of these patients, and with several criteria (e.g., ME and ME/CFS), this symptom is mandatory (Carruthers et al., 2003 , 2011). In the present study, 32 participants diagnosed with CFS (Fukuda et al., 1994) were examined on their responses to self-report items that were developed to capture the characteristics and patterns of PEM. As shown in the results, the slight differences in wording for various items may affect whether one is determined to have PEM according to currently used self-report criteria to assess CFS. Better understanding of how this symptom is assessed might help improve the diagnostic reliability and validity of ME, ME/CFS, and CFS.
Johanson L.		The Gluten-Free Frenzy:	Medsurg Nurs. 2015 Jul-	Although the gluten-free diet has been recognized as therapeutic for individuals

		Fad or Fitting?	Aug;24(4):213-7.	suffering from celiac disease, it has been promoted recently for other indications, such as autism, chronic fatigue syn- drome, and irritable bowel syndrome, or simply as a healthy dietary choice for anyone. The basics of the gluten-free diet are explored, with evidence-based indications and nursing implications when patients choose gluten-free.
Joustra ML(1), Janssens KA(2), Bültmann U(3), Rosmalen JG(1).	(1)University of Groningen, University Medical Center Groningen, Interdisciplinary Center Psychopathology and Emotion Regulation, The Netherlands. (2)University of Groningen, University Medical Center Groningen, Interdisciplinary Center Psychopathology and Emotion Regulation, The Netherlands. Electronic address: k.a.m.janssens@umcg .nl. (3)University of Groningen, University Medical Center Groningen, Department of Health Sciences, Community and Occupational Medicine, The Netherlands.	Functional limitations in functional somatic syndromes and well-defined medical diseases. Results from the general population cohort LifeLines.	J Psychosom Res. 2015 Aug;79(2):94-9. doi: 10.1016/j.jpsychores.2015 .05.004. Epub 2015 May 16.	OBJECTIVE: Functional somatic syndromes (FSS), defined as physical syndromes without known underlying organic pathology, are sometimes regarded as less serious conditions than well-defined medical diseases (MD). The aims of this study were to evaluate functional limitations in FSS, and to compare the results to MD patients with the same core symptoms. METHODS: This study was performed in 89,585 participants (age: 44.4±12.4 years, 58.5% female) of the general-population cohort LifeLines. Quality of Life (QoL) and work participation were examined as indicators of functional limitations. QoL was assessed with two summary scales of the RAND-36: the physical component summary (PCS) and the mental component summary (MCS). Work participation was assessed with a self-reported questionnaire. QoL and work participation were compared between FSS and MD patients, using Chi-squared tests and ANCOVA-analyses, adjusted for age, sex, educational level, and mental disorders. RESULTS: Of the participants, 11.0% (n=9861) reported a FSS, and 2.7% (n=2395) reported a MD. Total QoL, PCS and MCS were significantly lower in all separate FSS and MD compared to controls (P≤.001). Clinically relevant differences in QoL were found between chronic fatigue syndrome and multiple sclerosis patients, and between fibromyalgia syndrome and rheumatoid arthritis patients. Compared to controls, FSS and MD patients reported a comparably reduced working percentage, increased sick absence, early retirement due to health-related reasons, and disability percentage (P≤.001). CONCLUSION: Functional limitations in FSS patients are common, and as severe as those in patients with MD when looking at QoL and work participation, emphasizing that FSS are serious health conditions.
Kairys AE(1), Schmidt-Wilcke T(2), Puiu T(1), Ichesco E(3), Labus JS(4), Martucci K(5), Farmer MA(6),	(1)Department of Anesthesiology, and the Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, Michigan.	Increased brain gray matter in the primary somatosensory cortex is associated with increased pain and mood disturbance in patients with interstitial	J Urol. 2015 Jan;193(1):131-7. doi: 10.1016/j.juro.2014.08.04 2. Epub 2014 Aug 14.	PURPOSE: Interstitial cystitis is a highly prevalent pain condition estimated to affect 3% to 6% of women in the United States. Emerging data suggest there are central neurobiological components to the etiology of this disease. We report the first brain structural imaging findings from the MAPP network with data on more than 300 participants. MATERIALS AND METHODS: We used voxel based morphometry to determine whether human patients with chronic interstitial cystitis display changes in brain morphology compared to healthy controls. A total of 33 female patients with

Ness TJ(7), Deutsch G(7), Mayer EA(4), Mackey S(5), Apkarian AV(6), Maravilla K(8), Clauw DJ(1), Harris RE(1).		cystitis/painful bladder syndrome.		interstitial cystitis without comorbidities and 33 age and gender matched controls taken from the larger sample underwent structural magnetic resonance imaging at 5 MAPP sites across the United States. RESULTS: Compared to controls, females with interstitial cystitis displayed significant increased gray matter volume in several regions of the brain including the right primary somatosensory cortex, the superior parietal lobule bilaterally and the right supplementary motor area. Gray matter volume in the right primary somatosensory cortex was associated with greater pain, mood (anxiety) and urological symptoms. We explored these correlations in a linear regression model, and found independent effects of these 3 measures on primary somatosensory cortex gray matter volume, namely clinical pain (McGill pain sensory total), a measure of urgency and anxiety (HADS). CONCLUSIONS: These data support the notion that changes in somatosensory gray matter may have an important role in pain sensitivity as well as affective and sensory aspects of interstitial cystitis. Further studies are needed to confirm the generalizability of these findings to other pain conditions.
Kaiser JD(1).	(1)Department of Medicine, University of California San Francisco Medical School San Francisco, CA, USA ; Medical Director, K-PAX Pharmaceuticals, Inc. Mill Valley, CA, USA.	A prospective, proof-of-concept investigation of KPAX002 in chronic fatigue syndrome.	Int J Clin Exp Med. 2015 Jul 15;8(7):11064-74. eCollection 2015.	Stimulant drugs and various micronutrient interventions have previously been studied in chronic fatigue syndrome (CFS) but they have never been studied in combination. This proof of concept investigation seeks to examine the clinical effects and safety profile of KPAX002 (a combination of methylphenidate hydrochloride and mitochondrial support nutrients) in patients with CFS. Fifteen patients diagnosed with CFS by 1994 Fukuda criteria were recruited and treated with KPAX002 to explore a potential synergistic effect of this combination. Fatigue and concentration disturbance symptoms were measured at baseline, 4 weeks, and 12 weeks using two clinically validated tools: Checklist Individual Strength (CIS) and Visual Analog Scale (VAS). The primary outcome objective was a decrease in the total CIS score of ≥25% in at least 50% of the subjects. The mean total CIS score decreased by 36.4 points (34%) at 12 weeks ($P<0.0001$), corresponding to a ≥25% decrease in 87% of the participants. Treatment with KPAX002 was well tolerated and significantly improved fatigue and concentration disturbance symptoms in greater than 50% of patients with CFS. These results were statistically significant. This combination treatment is worthy of additional investigation.
Kallestad H(1), Jacobsen HB(2), Landrø NI(3), Borchgrevink PC(2), Stiles TC(4).	(1)Norwegian University of Science and Technology, Department of Neuroscience, Trondheim, Norway; St. Olav's University Hospital, Department of Østmarka, Trondheim, Norway.	The role of insomnia in the treatment of chronic fatigue.	J Psychosom Res. 2015 May;78(5):427-32. doi: 10.1016/j.jpsychores.2014.11.022. Epub 2014 Dec 5.	BACKGROUND: The definition of Chronic Fatigue Syndrome (CFS) overlaps with definitions of insomnia, but there is limited knowledge about the role of insomnia in the treatment of chronic fatigue. AIMS: To test if improvement of insomnia during treatment of chronic fatigue was associated with improved outcomes on 1) fatigue and 2) cortisol recovery span during a standardized stress exposure. METHODS: Patients (n = 122) with chronic fatigue received a 3.5-week inpatient return-to-work rehabilitation program based on Acceptance and Commitment Therapy, and had been on paid sick leave>8 weeks due their condition. A physician and a psychologist examined the patients, assessed medication use, and SCID-I diagnoses. Patients completed self-report questionnaires measuring fatigue, pain, depression, anxiety, and insomnia before and

	Electronic address: havard.kallestad@ntnu.no.			after treatment. A subgroup (n = 25) also completed the Trier Social Stress Test for Groups (TSST-G) before and after treatment. Seven cortisol samples were collected during each test and cortisol spans for the TSST-G were calculated. RESULTS: A hierarchical regression analysis in nine steps showed that insomnia improvement predicted improvement in fatigue, independently of age, gender, improvement in pain intensity, depression and anxiety. A second hierarchical regression analysis showed that improvement in insomnia significantly predicted the cortisol recovery span after the TSST-G independently of improvement in fatigue. CONCLUSION: Improvement in insomnia severity had a significant impact on both improvement in fatigue and the ability to recover from a stressful situation. Insomnia severity may be a maintaining factor in chronic fatigue and specifically targeting this in treatment could increase treatment response.
Keech A(1), Sandler CX(2), Vollmer-Conna U(3), Cvejic E(3), Lloyd AR(4), Barry BK(5).	(1)School of Medical Sciences, University of New South Wales, Sydney, Australia. Electronic address: andrew.keech@unsw.edu.au. (2)School of Medical Sciences, University of New South Wales, Sydney, Australia. (3)School of Psychiatry, University of New South Wales, Sydney, Australia. (4)Inflammation and Infection Research Centre, School of Medical Sciences, University of New South Wales, Sydney, Australia. (5)School of Medical Sciences, University of New South Wales, Sydney, Australia; Neuroscience Research Australia, Sydney, Australia.	Capturing the post-exertional exacerbation of fatigue following physical and cognitive challenge in patients with chronic fatigue syndrome.	J Psychosom Res. 2015 Dec;79(6):537-49. doi: 10.1016/j.jpsychores.2015.08.008. Epub 2015 Sep 2.	OBJECTIVE: To design and validate an instrument to capture the characteristic post-exertional exacerbation of fatigue in patients with chronic fatigue syndrome (CFS). METHODS: Firstly, patients with CFS (N=19) participated in five focus group discussions to jointly explore the nature of fatigue and dynamic changes after activity, and inform development of a self-report instrument - the Fatigue and Energy Scale (FES). The psychometric properties of the FES were then examined in two case-control challenge studies: a physically-demanding challenge (moderate-intensity aerobic exercise; N=10 patients), and a cognitively-demanding challenge (simulated driving; N=11 patients). Finally, ecological validity was evaluated by recording in association with tasks of daily living (N=9). RESULTS: Common descriptors for fatigue included 'exhaustion', 'tiredness', 'drained of energy', 'heaviness in the limbs', and 'foggy in the head'. Based on the qualitative data, fatigue was conceptualised as consisting of 'physical' and 'cognitive' dimensions. Analysis of the psychometric properties of the FES showed good sensitivity to the changing symptoms during a post-exertional exacerbation of fatigue following both physical exercise and driving simulation challenges, as well as tasks of daily living. CONCLUSION: The 'fatigue' experienced by patients with CFS covers both physical and cognitive components. The FES captured the phenomenon of a post-exertional exacerbation of fatigue commonly reported by patients with CFS. The characteristics of the symptom response to physical and cognitive challenges were similar. Both the FES and the challenge paradigms offer key tools to reliably investigate biological correlates of the dynamic changes in fatigue.

Keijmel SP(1), Saxe J(2), van der Meer JW(3), Nikolaus S(4), Netea MG(5), Bleijenberg G(6), Bleeker-Rovers CP(7), Knoop H(8).	(1)Radboud Expertise Centre for Q fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical center, Nijmegen, The Netherlands; Department of Internal Medicine, Division of Infectious Diseases, Radboud university medical center, Nijmegen, The Netherlands; Expert Centre for Chronic Fatigue, Radboud university medical center, Nijmegen, The Netherlands. Electronic address: Stephan.Keijmel@radboudumc.nl.	A comparison of patients with Q fever fatigue syndrome and patients with chronic fatigue syndrome with a focus on inflammatory markers and possible fatigue perpetuating cognitions and behaviour.	J Psychosom Res. 2015 Oct;79(4):295-302. doi: 10.1016/j.jpsychores.2015.07.005. Epub 2015 Jul 17.	OBJECTIVE: Comparison of Q fever fatigue syndrome (QFS) and chronic fatigue syndrome (CFS) patients, with a focus on markers of inflammation and fatigue-related cognitive-behavioural variables. METHODS: Data from two independent prospective studies on QFS (n=117) and CFS (n=173), respectively, were pooled and analyzed. RESULTS: QFS patients were less often female, had a higher BMI, and had less often received treatment for depression before the onset of symptoms. After controlling for symptom duration and correcting for differences in diagnostic criteria for QFS and CFS with respect to the level of impairment and the presence of additional symptoms, differences in the proportion of females and BMI remained significant. After correction, QFS patients were also significantly older. In all analyses QFS patients were as fatigued and distressed as CFS patients, but reported less additional symptoms. QFS patients had stronger somatic attributions, and higher levels of physical activity. No differences were found with regard to inflammatory markers and in other fatigue-related cognitive-behavioural variables. The relationship between cognitive-behavioural variables and fatigue, previously established in CFS, could not be confirmed in QFS patients with the exception of the negative relationship between physical activity and fatigue. CONCLUSION: Differences and similarities between QFS and CFS patients were found. Although the relationship between perpetuating factors and fatigue previously established in CFS could not be confirmed in QFS patients, the considerable overlap in fatigue-related cognitive-behavioural variables and the relationship found between physical activity and fatigue may suggest that behavioural interventions could reduce fatigue severity in QFS patients.
Kempke S(1), Claes S(1).	(1)University of Leuven, Leuven, Belgium.	Perfectionism and stress reactivity in patients with chronic fatigue syndrome.	Psychoneuroendocrinology. 2015 Nov;61:59. doi: 10.1016/j.psyneuen.2015.07.551. Epub 2015 Aug 8.	
Kempke S(1), Luyten P(2), De Coninck S(3), Van Houdenhove B(4), Mayes LC(5), Claes S(4).	(1)Faculty of Psychology and Educational Sciences, University of Leuven, Leuven, Belgium. Electronic address: stefan.kempke@ppw.kuleuven.be. (2)Faculty of Psychology and Educational Sciences,	Effects of early childhood trauma on hypothalamic-pituitary-adrenal (HPA) axis function in patients with Chronic Fatigue Syndrome.	Psychoneuroendocrinology. 2015 Feb;52:14-21. doi: 10.1016/j.psyneuen.2014.10.027. Epub 2014 Nov 8.	BACKGROUND: There is a paucity of studies that have investigated the assumption that early childhood trauma is associated with hypothalamic-pituitary-adrenal (HPA) axis dysfunction in Chronic Fatigue Syndrome (CFS). The current study is the first to simultaneously investigate relationships among early childhood trauma, cortisol activity, and cortisol stress reactivity to psychosocial stress in a sample of well-screened CFS patients. We also examined whether self-critical perfectionism (SCP) plays a mediating role in the potential relationship between early trauma and neurobiological stress responses. METHODS: A total of 40 female patients diagnosed with CFS were asked to provide morning saliva cortisol samples (after awakening, 30min later, and 1h later) for seven consecutive days as a measure of cortisol activity. In addition, patients were exposed to the Trier Social Stress Test, a well-validated stress test, to investigate

	University of Leuven, Leuven, Belgium; Research Department of Clinical, Educational and Health Psychology, University College London, London, UK. (3)Biological Psychology, Faculty of Psychology and Educational Sciences, Vrije Universiteit Brussel, Brussels, Belgium. (4)Department of Psychiatry, University Hospitals Leuven, University of Leuven, Leuven, Belgium. (5)Yale Child Study Center, Yale Medical School, Yale University, New Haven, USA.			the relationship between early childhood trauma and cortisol stress reactivity. Before the start of the study, patients completed the Childhood Trauma Questionnaire-Short form (CTQ-SF) as a measure of early childhood trauma (i.e. sexual, physical and emotional traumatic experiences). SCP was measured with the Depressive Experiences Questionnaire (DEQ). Data were analyzed by calculating several indices of cortisol secretion (i.e. Cortisol Awakening Response and Area Under the Curve). RESULTS: There was no association between early childhood trauma and cortisol as measured over the 7-day period. However, emotional neglect was significantly negatively related to cortisol reactivity in the TSST. SCP did not significantly mediate this association. CONCLUSION: Findings of this study suggest that emotional neglect is associated with blunted HPA axis reactivity, congruent with the assumption that CFS may reflect loss of adaptability of the neuroendocrine stress response system in at least a subgroup of patients.
Kempke S, Luyten P, Mayes LC, Van Houdenhove B, Claes S.		Self-Critical Perfectionism Predicts Lower Cortisol Response to Experimental Stress in Patients With Chronic Fatigue Syndrome.	Health Psychol. 2015 Dec 21. [Epub ahead of print]	OBJECTIVE: Previous studies have suggested that self-critical perfectionism (SCP) may play a role in the development and maintenance of Chronic Fatigue Syndrome (CFS). In this study we investigated whether SCP is related to a hypofunction of the hypothalamic-pituitary-adrenal (HPA) axis, which has been shown to be a key factor in the pathophysiology of CFS. METHOD: We conducted a quasi-experimental study to examine the association between SCP (as measured with the Depressive Experiences Questionnaire) and stress reactivity in a sample of 41 female CFS patients. Participants were exposed to the Trier Social Stress Test (TSST). Both subjective stress and salivary cortisol levels were measured until 90 min after the TSST. We also examined the relationship between stress reactivity and illness characteristics (i.e., duration and severity of symptoms). RESULTS: The results showed that SCP was associated with increased subjective stress reactivity, but with decreased HPA-axis reactivity as indicated by a blunted cortisol response to the TSST. Furthermore, we found an inverse relationship between cortisol reactivity and symptom severity. There was no relationship between cortisol reactivity and illness duration. CONCLUSION: Our findings

				suggest that SCP is associated with loss of resilience of the neurobiological stress response system in CFS. (PsycINFO Database Record
Khaiboullina SF(1), DeMeirleir KL(2), Rawat S(2), Berk GS(2), Gaynor-Berk RS(3), Mijatovic T(4), Blatt N(5), Rizvanov AA(5), Young SG(3), Lombardi VC(6).	(1)Department of Biochemistry and Molecular Biology, University of Nevada School of Medicine, Reno, NV, USA; WPI, Reno, NV, USA.	Cytokine expression provides clues to the pathophysiology of Gulf War illness and myalgic encephalomyelitis.	Cytokine. 2015 Mar;72(1):1-8. doi: 10.1016/j.cyto.2014.11.019. Epub 2014 Dec 13.	Gulf War illness (GWI) is a chronic disease of unknown etiology characterized by persistent symptoms such as cognitive impairment, unexplained fatigue, pervasive pain, headaches, and gastrointestinal abnormalities. Current reports suggest that as many as 200,000 veterans who served in the 1990-1991 Persian Gulf War were afflicted. Several potential triggers of GWI have been proposed including chemical exposure, toxins, vaccines, and unknown infectious agents. However, a definitive cause of GWI has not been identified and a specific biological marker that can consistently delineate the disease has not been defined. Myalgic encephalomyelitis (ME) is a disease with similar and overlapping symptomology, and subjects diagnosed with GWI typically fit the diagnostic criteria for ME. For these reasons, GWI is often considered a subgroup of ME. To explore this possibility and identify immune parameters that may help to understand GWI pathophysiology, we measured 77 serum cytokines in subjects with GWI and compared these data to that of subjects with ME as well as healthy controls. Our analysis identified a group of cytokines that identified ME and GWI cases with sensitivities of 92.5% and 64.9%, respectively. The five most significant cytokines in decreasing order of importance were IL-7, IL-4, TNF-α, IL-13, and IL-17F. When delineating GWI and ME cases from healthy controls, the observed specificity was only 33.3%, suggesting that with respect to cytokine expression, GWI cases resemble control subjects to a greater extent than ME cases across a number of parameters. These results imply that serum cytokines are representative of ME pathology to a greater extent than GWI and further suggest that the two diseases have distinct immune profiles despite their overlapping symptomology.
Khundadze M(1), Mkheidze R(1), Geladze N(1), Bakhtadze S(1), Khachapuridze N(1).	(1)Tbilisi State Medical University, Department of Child Neurology, Department of Neuroscience, Georgia.	THE CAUSES AND SYMPTOMS OF SOMATOFORM DISORDERS IN CHILDREN (REVIEW).	Georgian Med News. 2015 Sep;(246):59-65.	The causes of somatoform disorders in children and adolescents and clinical description of various syndromes like hypochondric impairment, non epileptic paroxysmal disorders, chronic fatigue syndrome, trauma and headache are presented in this review. The modern epidemiological evidences of mentioned conditions are also considered which indicate on progressive increase of these diseases for recent 20 years. We have also discussed the standardized methods of prevention, differential diagnosis and treatment of somatoform diseases.
Kim BH(1), Namkoong K(1), Kim JJ(1), Lee S(2), Yoon KJ(3), Choi M(2), Jung YC(4).	(1)Department of Psychiatry, Yonsei University College of Medicine, Seoul 120-752, South Korea; Institute of Behavioral Science in Medicine, Yonsei University College of Medicine,	Altered resting-state functional connectivity in women with chronic fatigue syndrome.	Psychiatry Res. 2015 Dec 30;234(3):292-7. doi: 10.1016/j.pscychresns.2015.10.014. Epub 2015 Oct 23.	The biological underpinnings of the psychological factors characterizing chronic fatigue syndrome (CFS) have not been extensively studied. Our aim was to evaluate alterations of resting-state functional connectivity in CFS patients. Participants comprised 18 women with CFS and 18 age-matched female healthy controls who were recruited from the local community. Structural and functional magnetic resonance images were acquired during a 6-min passive-viewing block scan. Posterior cingulate cortex seeded resting-state functional connectivity was evaluated, and correlation analyses of connectivity strength were performed. Graph theory analysis of 90 nodes of the brain was conducted to compare the global and local efficiency of connectivity networks in

	Seoul 120-752, South Korea. (2)Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul 120-752, South Korea. (3)Gangnam St. Peter's Hospital, Seoul 135-270, South Korea. (4)Department of Psychiatry, Yonsei University College of Medicine, Seoul 120-752, South Korea; Institute of Behavioral Science in Medicine, Yonsei University College of Medicine, Seoul 120-752, South Korea. Electronic address: eugenejung@yuhs.ac.			CFS patients with that in healthy controls. The posterior cingulate cortex in CFS patients showed increased resting-state functional connectivity with the dorsal and rostral anterior cingulate cortex. Connectivity strength of the posterior cingulate cortex to the dorsal anterior cingulate cortex significantly correlated with the Chalder Fatigue Scale score, while the Beck Depression Inventory (BDI) score was controlled. Connectivity strength to the rostral anterior cingulate cortex significantly correlated with the Chalder Fatigue Scale score. Global efficiency of the posterior cingulate cortex was significantly lower in CFS patients, while local efficiency showed no difference from findings in healthy controls. The findings suggest that CFS patients show inefficient increments in resting-state functional connectivity that are linked to the psychological factors observed in the syndrome.
Kim JE(1), Seo BK(2), Choi JB(3), Kim HJ(4), Kim TH(5,)(6), Lee MH(7), Kang KW(8), Kim JH(9), Shin KM(10), Lee S(11,)(12), Jung SY(13), Kim AR(14), Shin MS(15), Jung HJ(16), Park HJ(17), Kim SP(18), Baek YH(19), Hong KE(20,)(21), Choi SM(22).	(1)Acupuncture, Moxibustion & Meridian Research Group, Korea Institute of Oriental Medicine, Daejeon, South Korea. eujuki@gmail.com.	Acupuncture for chronic fatigue syndrome and idiopathic chronic fatigue: a multicenter, nonblinded, randomized controlled trial.	Trials. 2015 Jul 26;16:314. doi: 10.1186/s13063-015-0857-0.	BACKGROUND: The causes of chronic fatigue syndrome (CFS) and idiopathic chronic fatigue (ICF) are not clearly known, and there are no definitive treatments for them. Therefore, patients with CFS and ICF are interested in Oriental medicine or complementary and alternative medicine. For this reason, the effectiveness of complementary and alternative treatments should be verified. We investigated the effectiveness of two forms of acupuncture added to usual care for CFS and ICF compared to usual care alone. METHODS: A three-arm parallel, non-blinded, randomized controlled trial was performed in four hospitals. We divided 150 participants into treatment and control groups at the same ratio. The treatment groups (Group A, body acupuncture; Group B, Sa-am acupuncture) received 10 sessions for 4 weeks. The control group (Group C) continued usual care alone. The primary outcome was the Fatigue Severity Scale (FSS) at 5 weeks after randomization. Secondary outcomes were the FSS at 13 weeks and a short form of the Stress Response Inventory (SRI), the Beck Depression Inventory (BDI), the Numeric Rating Scale (NRS), and the EuroQol-5 Dimension (EQ-5D) at 5 and 13 weeks. RESULTS: Group A showed significantly lower FSS scores than Group C at 5 weeks (P = 0.023). SRI scores were significantly lower in the treatment groups than in the control group at 5 (Group A, P =

				0.032; B, P <0.001) and 13 weeks (Group A, P = 0.037; B, P <0.001). Group B showed significantly lower BDI scores than Group C at 13 weeks (P = 0.007). NRS scores from the treatment groups were significantly reduced compared to control at 5 (Group A and B, P <0.001) and 13 weeks (Group A, P = 0.011; B, P = 0.002). CONCLUSIONS: Body acupuncture for 4 weeks in addition to usual care may help improve fatigue in CFS and ICF patients. TRIAL REGISTRATION: Clinical Research Information Service (CRIS) KCT0000508; Registered on 12 August 2012.
Kindlon T(1), Baldwin A(2).	(1)Irish ME/CFS Association, Dublin, Ireland. (2)Bristol, UK.	Response to: reports of recovery in chronic fatigue syndrome may present less than meets the eye.	Evid Based Ment Health. 2015 May;18(2):e5. doi: 10.1136/eb-2014-101961. Epub 2014 Sep 19.	Comment on Evid Based Ment Health. 2014 Aug;17(3):95.
Kindlon T, Shepherd C.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):887-8. doi: 10.7326/L15-5175.	
Kindlon T(1).	(1)Irish ME/CFS Association , Dublin , Ireland.	Elements of rehabilitative strategies associated with negative outcomes in CFS/ME: the need for further investigations.	Disabil Rehabil. 2015;37(5):466-7. doi: 10.3109/09638288.2014.952456. Epub 2014 Aug 19.	Comment in Disabil Rehabil. 2015;37(5):468-9.
Kirby SB.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):885-6. doi: 10.7326/L15-5172.	
Klemenc-Ketiš Z(1,)(2,)(3), Kersnik J(4,)(5).	(1)Department of Family Medicine, Medical School, University of Maribor, Maribor, Slovenia. zalika.klemenc-ketis@uni-mb.si. (2)Department of Family Medicine, Medical School, University of Ljubljana, Ljubljana, Slovenia. zalika.klemenc-ketis@uni-mb.si. (3), Kersnikova 1, 3320, Velenje, Slovenia. zalika.klemenc-	Focus points in prevention actions against legal substances' abuse.	Wien Klin Wochenschr. 2015 Dec;127 Suppl 5:241-6. doi: 10.1007/s00508-015-0706-x. Epub 2015 Mar 19.	AIM: To determine the factors associated with alcohol and tobacco abuse in Slovenian general population. MATERIAL AND METHODS: We performed an observational cross-sectional study in a representative sample of 1002 Slovenian inhabitants in June 2011. It was performed using a method of computer-assisted telephone interview. The telephone interview consisted of questions about the prevalence and duration of preselected health-related symptoms in the past month, questions about the presence of chronic diseases, question about the presence of current smoking, EQ-5D questionnaire and AUDIT-C questionnaire. RESULTS: Risky drinking was found in 103 (14.3 %) of the sample and smoking was found in 226 (22.6 %) of the sample. Men reported risky drinking more often when compared with women (17.7 vs. 10.5 %, P = 0.007). Multivariate analysis showed that male sex, current tobacco smoking, lower education level, self-reported presence of anxiety/depression and self-reported presence of muscle pain and excessive fatigue in the past month were independently associated with risky drinking and that male sex, lower education and income, the presence of chronic disease, self-reported problems in daily activities, risky drinking, self-reported troubles in sleeping and restless leg syndrome were independently associated with current tobacco smoking. CONCLUSION: Risky alcohol drinking and smoking are still major public health problems in Slovenia and are associated with

	ketis@uni-mb.si. (4)Department of Family Medicine, Medical School, University of Maribor, Maribor, Slovenia. (5)Department of Family Medicine, Medical School, University of Ljubljana, Ljubljana, Slovenia.			known demographic risk factors but also with some symptoms of somatoform disorders. These findings should be incorporated into the guidelines for family physicians as the important focus points for screening and intervening against legal substances' abuse in their patients.
Kloeffler GD.		Women of valor: post-traumatic stress disorder in the dental practice.	J Calif Dent Assoc. 2015 Jan;43(1):21-8.	Dental professionals can intervene in head, neck and facial pain found in female patients who suffer from post-traumatic stress disorder (PTSD). There are three theories for why women are predisposed to pain: hormonal differences, nervous system rewiring and sympathetic issues. This article includes case studies of three patients who are representative of these theories. A rapid, nonintrusive intervention will also be described.
Knoop H(1), Wiborg J(2).	(1)Expert Centre for Chronic Fatigue, Radboud University Medical Center, 6500 HB Nijmegen, Netherlands. Electronic address: hans.knoop@radboudumc.nl. (2)Expert Centre for Chronic Fatigue, Radboud University Medical Center, 6500 HB Nijmegen, Netherlands.	What makes a difference in chronic fatigue syndrome?	Lancet Psychiatry. 2015 Feb;2(2):113-4. doi: 10.1016/S2215-0366(14)00145-X. Epub 2015 Jan 28.	Comment on Lancet Psychiatry. 2015 Feb;2(2):141-52.
Komaroff AL.		Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Real Illness.	Ann Intern Med. 2015 Jun 16;162(12):871-2. doi: 10.7326/M15-0647.	
Kos D(1), van Eupen I(2), Meirte J(3), Van	(1)Daphne Kos, PhD, OT, is Assistant Professor,	Activity Pacing Self-Management in Chronic Fatigue Syndrome: A	Am J Occup Ther. 2015 Sep-Oct;69(5):6905290020.	OBJECTIVE: To evaluate the effectiveness of an activity pacing self-management (APSM) intervention in improving performance of daily life activities in women with chronic fatigue syndrome (CFS). METHOD: A total of 33 women with CFS (age 41.1±11.2 yr)

Cauwenbergh D(4), Moorkens G(5), Meeus M(6), Nijs J(7).	Department of Rehabilitation Sciences, Neuromotor Research Group, KU Leuven-University of Leuven, Belgium; Lecturer, Division of Occupational Therapy, Department of Health and Social Care, Artesis Plantijn University College, Antwerp, Belgium; and Member, Pain in Motion Research Group, Brussels, Belgium; daphne.kos@faber.kuleuven.be	Randomized Controlled Trial.	doi: 10.5014/ajot.2015.016287.	were randomly allocated to APSM (experimental group; n=16) or relaxation (control group; n=17). Main outcome measures included the Canadian Occupational Performance Measure (COPM; primary) and Checklist Individual Strength (CIS). RESULTS: COPM scores changed significantly over time in both groups (p=.03). The change in Satisfaction scores showed a significant difference in favor only of APSM (effect size=0.74 [0.11, 1.4]). CIS scores decreased significantly in the experimental group only (p<.01). CONCLUSION: APSM was found to be feasible and effective in optimizing participation in desired daily life activities in women with CFS. Replication in a larger sample with long-term follow-up is required.
Krieger JN(1), Stephens AJ(2), Landis JR(2), Clemens JQ(3), Kreder K(4), Lai HH(5), Afari N(6), Rodríguez L(7), Schaeffer A(8), Mackey S(9), Andriole GL(5), Williams DA(3); MAPP Research Network.		Relationship between chronic nonurological associated somatic syndromes and symptom severity in urological chronic pelvic pain syndromes: baseline evaluation of the MAPP study.	J Urol. 2015 Apr;193(4):1254-62. doi: 10.1016/j.juro.2014.10.086. Epub 2014 Oct 22.	PURPOSE: We used MAPP data to identify participants with urological chronic pelvic pain syndromes only or a chronic functional nonurological associated somatic syndrome in addition to urological chronic pelvic pain syndromes. We characterized these 2 subgroups and explored them using 3 criteria, including 1) MAPP eligibility criteria, 2) self-reported medical history or 3) RICE criteria. MATERIALS AND METHODS: Self-reported cross-sectional data were collected on men and women with urological chronic pelvic pain syndromes, including predominant symptoms, symptom duration and severity, nonurological associated somatic syndrome symptoms and psychosocial factors. RESULTS: Of 424 participants with urological chronic pelvic pain syndromes 162 (38%) had a nonurological associated somatic syndrome, including irritable bowel syndrome in 93 (22%), fibromyalgia in 15 (4%), chronic fatigue syndrome in 13 (3%) and multiple syndromes in 41 (10%). Of 233 females 103 (44%) had a nonurological associated somatic syndrome compared to 59 of 191 males (31%) (p = 0.006). Participants with a nonurological associated somatic syndrome had more severe urological symptoms and more frequent depression and anxiety. Of 424 participants 228 (54%) met RICE criteria. Of 228 RICE positive participants 108 (47%) had a nonurological associated somatic syndrome compared to 54 of 203 RICE negative patients (28%) with a nonurological associated somatic syndrome (p < 0.001). CONCLUSIONS: Nonurological associated somatic syndromes represent important clinical characteristics of urological chronic pelvic pain syndromes. Participants with a nonurological associated somatic syndrome have more severe symptoms, longer

				duration and higher rates of depression and anxiety. RICE positive patients are more likely to have a nonurological associated somatic syndrome and more severe symptoms. Because nonurological associated somatic syndromes are more common in women, future studies must account for this potential confounding factor in urological chronic pelvic pain syndromes.
Krzeczkowska A(1), Karatzias T, Dickson A.	(1)a School of Life, Sport and Social Sciences , Edinburgh Napier University , Edinburgh , UK.	Pain in people with chronic fatigue syndrome/myalgic encephalomyelitis: the role of traumatic stress and coping strategies.	Psychol Health Med. 2015;20(2):210-6. doi: 10.1080/13548506.2014.951370. Epub 2014 Sep 2.	Pain is a significant problem for many people with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME). This exploratory study investigated the extent to which severity of pain was related to coping strategies and post-traumatic symptomatology in people with CFS/ME. Participants comprised 27 individuals with CFS/ME and 27 healthy controls. All participants completed the CFS/ME Symptom Questionnaire, the brief pain inventory, the impact of event scale-revised and the brief-COPE. It was found that CFS/ME participants present with significantly more post-traumatic stress symptoms and report significantly less emotion focused strategies and problem focused coping strategies compared with healthy controls. Severity of pain in the CFS/ME subgroup was not associated with traumatic symptomatology, although those with severe pain reported less use of self-distraction, positive re-framing and acceptance than those with mild pain. Our results suggest that the enhancement of certain coping strategies (facilitated by psychological interventions such as acceptance and commitment therapy) may be beneficial in alleviating pain in people with CFS/ME.
Kuemmerle-Deschner JB(1).	(1)Division of Pediatric Rheumatology, Department of Pediatrics, University Children's Hospital Tuebingen, Hoppe-Seyler-Strasse 1, 72076, Tuebingen, Germany, kuemmerle.deschner@uni-tuebingen.de.	CAPS--pathogenesis, presentation and treatment of an autoinflammatory disease.	Semin Immunopathol. 2015 Jul;37(4):377-85. doi: 10.1007/s00281-015-0491-7. Epub 2015 May 12.	The cryopyrin-associated periodic syndrome (CAPS) is a severity spectrum of rare diseases. CAPS comprises the three conditions previously described as familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disorder (NOMID), also known as chronic infantile neurologic, cutaneous, and articular (CINCA) syndrome. The clinical phenotype of CAPS is characterized by systemic inflammation. General symptoms are fatigue and fever. Local manifestations affect multiple tissues such as skin, joints, muscles, eyes, and the central nervous system. Distinct clinical features are characteristic for each subphenotype. In FCAS, these are cold-induced urticaria and fever, in MWS systemic amyloidosis and hearing loss and in NOMID/CINCA central nervous system inflammation and bone deformities. CAPS is caused by single heterozygous germline or somatic gain of function mutations in the NLRP3 gene encoding the protein cryopyrin. Cryopyrin nucleates an NLRP3 inflammasome, which regulates the activation and cleavage of caspase-1 that cleaves the pro-inflammatory cytokines, IL-1β and IL-18. IL-1β plays the key role in the induction of inflammation in CAPS. This has been confirmed by the application of IL-1 blocking agents, which lead not only to a rapid and sustained reversal of daily symptoms but also to some extent of long-term disease sequelae. To prevent CAPS-induced organ damage, early diagnosis and swift initiation of effective treatment are mandatory.

Kutch JJ(1), Yani MS(1), Asavasopon S(2), Kirages DJ(1), Rana M(1), Cosand L(3), Labus JS(4), Kilpatrick LA(4), Ashe-McNalley C(4), Farmer MA(5), Johnson KA(6), Ness TJ(7), Deutsch G(7), Harris RE(8), Apkarian AV(5), Clauw DJ(8), Mackey SC(6), Mullins C(9), Mayer EA(4).	(1)Division of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA, USA.	Altered resting state neuromotor connectivity in men with chronic prostatitis/chronic pelvic pain syndrome: A MAPP: Research Network Neuroimaging Study.	Neuroimage Clin. 2015 Jun 5;8:493-502. doi: 10.1016/j.nicl.2015.05.013. eCollection 2015.	Brain network activity associated with altered motor control in individuals with chronic pain is not well understood. Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) is a debilitating condition in which previous studies have revealed altered resting pelvic floor muscle activity in men with CP/CPPS compared to healthy controls. We hypothesized that the brain networks controlling pelvic floor muscles would also show altered resting state function in men with CP/CPPS. Here we describe the results of the first test of this hypothesis focusing on the motor cortical regions, termed pelvic-motor, that can directly activate pelvic floor muscles. A group of men with CP/CPPS (N = 28), as well as group of age-matched healthy male controls (N = 27), had resting state functional magnetic resonance imaging scans as part of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Research Network study. Brain maps of the functional connectivity of pelvic-motor were compared between groups. A significant group difference was observed in the functional connectivity between pelvic-motor and the right posterior insula. The effect size of this group difference was among the largest effect sizes in functional connectivity between all pairs of 165 anatomically-defined subregions of the brain. Interestingly, many of the atlas region pairs with large effect sizes also involved other subregions of the insular cortices. We conclude that functional connectivity between motor cortex and the posterior insula may be among the most important markers of altered brain function in men with CP/CPPS, and may represent changes in the integration of viscerosensory and motor processing.
Lai HH(1), Krieger JN(2), Pontari MA(3), Buchwald D(4), Hou X(5), Landis JR(5); MAPP Research Network.	(1)Division of Urologic Surgery, Department of Surgery and Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri. Electronic address: laih@wudosis.wustl.edu. (2)Department of Urology, School of Medicine, University of Washington, Seattle, Washington. (3)Department of Urology, Temple University School of	Painful Bladder Filling and Painful Urgency are Distinct Characteristics in Men and Women with Urological Chronic Pelvic Pain Syndromes: A MAPP Research Network Study.	J Urol. 2015 Dec;194(6):1634-41. doi: 10.1016/j.juro.2015.05.105. Epub 2015 Jul 17.	PURPOSE: We describe bladder associated symptoms in patients with urological chronic pelvic pain syndromes. We correlated these symptoms with urological, nonurological, psychosocial and quality of life measures. MATERIALS AND METHODS: Study participants included 233 women and 191 men with interstitial cystitis/bladder pain syndrome or chronic prostatitis/chronic pelvic pain syndrome in a multicenter study. They completed a battery of measures, including items asking whether pain worsened with bladder filling (painful filling) or whether the urge to urinate was due to pain, pressure or discomfort (painful urgency). Participants were categorized into 3 groups, including group 1-painful filling and painful urgency (both), 2-painful filling or painful urgency (either) and 3-no painful filling or painful urgency (neither). RESULTS: Of the men 75% and of the women 88% were categorized as both or either. These bladder characteristics were associated with more severe urological symptoms (increased pain, frequency and urgency), a higher somatic symptom burden, depression and worse quality of life (3-group trend test each $p < 0.01$). A gradient effect was observed across the groups (both > either > neither). Compared to those in the neither group men categorized as both or either reported more frequent urological chronic pelvic pain syndrome symptom flares, catastrophizing and irritable bowel syndrome, and women categorized as both or either were more likely to have a negative affect and chronic

	Medicine, Philadelphia, Pennsylvania. (4)Department of Epidemiology, School of Public Health, University of Washington, Seattle, Washington; Department of Medicine, University of Washington, Seattle, Washington. (5)Department of Biostatistics and Epidemiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania.			fatigue syndrome. CONCLUSIONS: Men and women with bladder symptoms characterized as painful filling or painful urgency had more severe urological symptoms, more generalized symptoms and worse quality of life than participants who reported neither characteristic, suggesting that these symptom characteristics might represent important subsets of patients with urological chronic pelvic pain syndromes.
Lai JS(1), Beaumont JL(1), Diaz J(2), Khan S(2), Cella D(1).	(1)Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, Illinois. (2)Novartis Pharma AG, Basel, Switzerland.	Validation of a short questionnaire to measure symptoms and functional limitations associated with hand-foot syndrome and mucositis in patients with metastatic renal cell carcinoma.	Cancer. 2016 Jan 15;122(2):287-95. doi: 10.1002/cncr.29655. Epub 2015 Oct 12.	BACKGROUND: Hand-foot syndrome and mucositis/stomatitis are frequent adverse events (AEs) of treatment with tyrosine kinase inhibitors in cancer therapy. Quality-of-life instruments that measure the functional consequences of these AEs are needed to assess the impact of therapeutic interventions and to guide patient care. The Hand-Foot and Mucositis Symptom and Impact Questionnaire (HAMSIQ [formerly the Supplementary Quality of Life Questionnaire]) was used in the COMPARZ trial (Pazopanib vs Sunitinib in the Treatment of Locally Advanced and/or Metastatic Renal Cell Carcinoma [national clinical trial no. NCT00720941]) and the PISCES study (Patient Preference Study of Pazopanib vs Sunitinib in Advanced or Metastatic Kidney Cancer [clinicaltrials.gov NCT01064310]) to assess mouth/throat and hand/foot soreness symptoms and subsequent limitations in patients receiving pazopanib or sunitinib for metastatic renal cell carcinoma. The objective of the current analysis was to validate the HAMSIQ using data from the PISCES study. METHODS: The HAMSIQ was administered in the PISCES study at baseline and every 2 weeks over two 10-week periods to patients who were receiving pazopanib or sunitinib. Data from the first 10-week period were used to assess the feasibility, validity, and responsiveness of the HAMSIQ. RESULTS: In total, ≥85% of 169 patients completed the HAMSIQ (excluding the item concerning days off work). Correlations among items within the same limitation

				subscale generally were high (Cronbach α ≥ .80). HAMSIQ limitation scores differentiated patients according to their baseline performance status and severity of soreness. Small-to-moderate correlations were observed for the symptoms/limitation scores and for changes from baseline scores between the HAMSIQ and the Functional Assessment of Chronic Illness Therapy fatigue survey. The HAMSIQ demonstrated responsiveness to changes in clinical status and the development of hand-foot syndrome AEs over time. CONCLUSIONS: The HAMSIQ is a feasible, valid, reliable, and responsive instrument for assessing the impact of hand-foot syndrome and mucositis in patients receiving tyrosine kinase inhibitors. Cancer 2016;122:287-295. © 2015 American Cancer Society.
Lanasa MC(1), Andritsos L(2), Brown JR(3), Gabrilove J(4), Caligaris-Cappio F(5), Ghia P(5), Larson RA(6), Kipps TJ(7), Leblond V(8), Milligan DW(9), Janssens A(10), Johnson AJ(2), Heerema NA(2), Bühler A(11), Stilgenbauer S(11), Devin J(12), Hallek M(13), Byrd JC(14), Grever MR(2).	(1)Duke University Medical Center, Durham, NC, United States.	Final results of EFC6663: a multicenter, international, phase 2 study of alvocidib for patients with fludarabine-refractory chronic lymphocytic leukemia.	Leuk Res. 2015 May;39(5):495-500. doi: 10.1016/j.leukres.2015.02.001. Epub 2015 Feb 7.	Early phase studies of alvocidib showed activity in relapsed CLL including patients with high risk genomic features and those refractory to fludarabine. A multi-center, international, phase II study of alvocidib in fludarabine refractory CLL was undertaken to validate these early results. Patients with fludarabine refractory CLL or prolymphocytic leukemia arising from CLL were treated with single agent alvocidib. The primary outcome measure was overall response rate, with secondary outcomes including survival, toxicity, and response duration. One hundred and sixty five patients were enrolled and 159 patients were treated. The median age was 61 years, the median number of prior therapies was 4, and 96% of patients were fludarabine refractory. The investigator-assessed overall response rate was 25%; the majority of responses were partial. Response rates were lower among patients with del(17p) (14%), but equivalent in patients with del(11q) or bulky lymphadenopathy. Median progression free and overall survival were 7.6 and 14.6 months, respectively. Tumor lysis occurred in 39 patients (25%), and 13 received hemodialysis. Diarrhea, fatigue, and hematologic toxicities were common. Alvocidib has clinical activity in patients with advanced, fludarabine refractory CLL. Future studies should focus on discovery of biomarkers of clinical response and tumor lysis, and enhanced supportive care measures.
Landi A(1), Broadhurst D(2), Vernon SD(3), Tyrrell DL(4), Houghton M(5).	(1)Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, Canada. Electronic address: landi@ualberta.ca. (2)Department of Medicine, Katz Group Centre for Pharmacy	Reductions in circulating levels of IL-16, IL-7 and VEGF-A in myalgic encephalomyelitis/chronic fatigue syndrome.	Cytokine. 2016 Feb;78:27-36. doi: 10.1016/j.cyto.2015.11.018. Epub 2015 Nov 28.	Recently, differences in the levels of various chemokines and cytokines were reported in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) as compared with controls. Moreover, the analyte profile differed between chronic ME/CFS patients of long duration versus patients with disease of less than 3years. In the current study, we measured the plasma levels of 34 cytokines, chemokines and growth factors in 100 chronic ME/CFS patients of long duration and in 79 gender and age-matched controls. We observed highly significant reductions in the concentration of circulating interleukin (IL)-16, IL-7, and Vascular Endothelial Growth Factor A (VEGF-A) in ME/CFS patients. All three biomarkers were significantly correlated in a multivariate cluster analysis. In addition, we identified significant reductions in the concentrations of fractalkine (CX3CL1) and monokine-induced-by-IFN-γ (MIG; CXCL9)

	& Health, University of Alberta, Edmonton, AB T6G 2E1, Canada. (3)Bateman Horne Center, 1002 E. South Temple, Suite 408, Salt Lake City, UT 84102, USA. (4)Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, Canada. (5)Li Ka Shing Institute of Virology, Department of Medical Microbiology and Immunology, Canada. Electronic address: michael.houghton@ualberta.ca.			along with increases in the concentrations of eotaxin 2 (CCL24) in ME/CFS patients. Our data recapitulates previous data from another USA ME/CFS cohort in which circulating levels of IL-7 were reduced. Also, a reduced level of VEGF-A was reported previously in sera of patients with Gulf War Illness as well as in cerebral spinal fluid samples from a different cohort of USA ME/CFS patients. To our knowledge, we are the first to test for levels of IL-16 in ME/CFS patients. In combination with previous data, our work suggests that the clustered reduction of IL-7, IL-16 and VEGF-A may have physiological relevance to ME/CFS disease. This profile is ME/CFS-specific since measurement of the same analytes present in chronic infectious and autoimmune liver diseases, where persistent fatigue is also a major symptom, failed to demonstrate the same changes. Further studies of other ME/CFS and overlapping disease cohorts are warranted in future.
Landry BW(1), Fischer PR(2), Driscoll SW(3), Koch KM(4), Harbeck-Weber C(5), Mack KJ(6), Wilder RT(7), Bauer BA(8), Brandenburg JE(9).	(1)Department of Physical Medicine and Rehabilitation, Mayo Clinic, 200 First St SW, Rochester, MN 55905(∗). Electronic address: landry.bradford@mayo.edu.	Managing Chronic Pain in Children and Adolescents: A Clinical Review.	PM R. 2015 Nov;7(11 Suppl):S295-315. doi: 10.1016/j.pmrj.2015.09.006.	Chronic pain in children and adolescents can be difficult for a single provider to manage in a busy clinical setting. Part of this difficulty is that pediatric chronic pain not only impacts the child but also the families of these children. In this review article, we discuss etiology and pathophysiology of chronic pain, along with variables that impact the severity of chronic pain and functional loss. We review diagnosis and management of selected chronic pain conditions in pediatric patients, including headache, low back pain, hypermobility, chronic fatigue, postural orthostatic tachycardia syndrome, abdominal pain, fibromyalgia, and complex regional pain syndrome. For each condition, we create a road map that contains therapy prescriptions, exercise recommendations, and variables that may influence pain severity. Potential medications for these pain conditions and associated symptoms are reviewed. A multidisciplinary approach for managing children with these conditions, including pediatric pain rehabilitation programs, is emphasized. Lastly, we discuss psychological factors and interventions for pediatric chronic pain and potential complementary and alternative natural products and interventions.
Larun L(1), Odgaard-Jensen J, Price JR,	(1)Primary Health Care Unit, Norwegian Knowledge Centre for	An abridged version of the Cochrane review of exercise therapy for	Eur J Phys Rehabil Med. 2015 Sep 16. [Epub ahead of print]	Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME) is estimated to affect between 2 in 1000 and 2 in 100 adults depending on how diagnostic criteria are applied. Patients with CFS have long-lasting fatigue in addition to symptoms

Brurberg KG.	the Health Services, Oslo, Norway.	chronic fatigue syndrome.		including muscle pain, concentration and sleep problems. These symptoms cause significant disability and distress to the people affected. This review is an update of a previous Cochrane review (2004) that showed that exercise therapy was a promising treatment for adults with CFS. The aim of this systematic review was to determine the effects of exercise therapy for patients with CFS. We searched electronic databases, including SPORTDiscus, up to May 2014 using a comprehensive list of free-text terms for CFS and exercise. Randomised clinical trials from all health care settings with participants over 18 years with a primary diagnosis of CFS, able to attend an outpatient clinic for exercise therapy, were included. We have included eight randomised clinical studies that reported data from 1518 participants. Seven studies used aerobic exercise such as walking, swimming, or cycling and one study used non-aerobic exercise. The exercise therapies lasted between 12 and 26 weeks. Meta-analysis was done when appropriate. Exercise therapy was more effective at reducing fatigue than "passive" treatments or no treatment at end of treatment. Exercise therapy also had a positive effect on people's daily physical functioning, sleep quality and self-rated overall health. Nearly twice as many patients reported improvement self- rated overall health after exercise therapy (40 per 100) compared to standard treatment (22 per 100). The evidence was too sparse and/or of too low quality to conclude if exercise therapy has an effect on pain, quality of life, anxiety or depression. Exercise therapy was not found to worsen symptoms for people with CFS, while serious side effects were rare in all exercise and comparison groups.
Larun L(1), Brurberg KG, Odgaard-Jensen J, Price JR.	(1)Primary Health Care Unit, Norwegian Knowledge Centre for the Health Services, PO Box 7004, St Olav's plass, Oslo, Norway, N-0130. Lillebeth.Larun@kunnskapssenteret.no	Exercise therapy for chronic fatigue syndrome.	Cochrane Database Syst Rev. 2015 Feb 10;2:CD003200. doi: 10.1002/14651858.CD003200.pub3.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterised by persistent, medically unexplained fatigue, as well as symptoms such as musculoskeletal pain, sleep disturbance, headaches and impaired concentration and short-term memory. CFS presents as a common, debilitating and serious health problem. Treatment may include physical interventions, such as exercise therapy, which was last reviewed in 2004. OBJECTIVES: The objective of this review was to determine the effects of exercise therapy (ET) for patients with CFS as compared with any other intervention or control.• Exercise therapy versus 'passive control' (e.g. treatment as usual, waiting-list control, relaxation, flexibility).• Exercise therapy versus other active treatment (e.g. cognitive-behavioural therapy (CBT), cognitive treatment, supportive therapy, pacing, pharmacological therapy such as antidepressants).• Exercise therapy in combination with other specified treatment strategies versus other specified treatment strategies (e.g. exercise combined with pharmacological treatment vs pharmacological treatment alone). SEARCH METHODS: We searched The Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (CCDANCTR), the Cochrane Central Register of Controlled Trials (CENTRAL) and SPORTDiscus up to May 2014 using a comprehensive list of free-text terms for CFS and exercise. We located unpublished or ongoing trials through the World Health Organization (WHO) International Clinical Trials Registry Platform (to May 2014). We screened reference lists of retrieved articles and

				contacted experts in the field for additional studies SELECTION CRITERIA: Randomised controlled trials involving adults with a primary diagnosis of CFS who were able to participate in exercise therapy. Studies had to compare exercise therapy with passive control, psychological therapies, adaptive pacing therapy or pharmacological therapy. DATA COLLECTION AND ANALYSIS: Two review authors independently performed study selection, risk of bias assessments and data extraction. We combined continuous measures of outcomes using mean differences (MDs) and standardised mean differences (SMDs). We combined serious adverse reactions and drop-outs using risk ratios (RRs). We calculated an overall effect size with 95% confidence intervals (CIs) for each outcome. MAIN RESULTS: We have included eight randomised controlled studies and have reported data from 1518 participants in this review. Three studies diagnosed individuals with CFS using the 1994 criteria of the Centers for Disease Control and Prevention (CDC); five used the Oxford criteria. Exercise therapy lasted from 12 to 26 weeks. Seven studies used variations of aerobic exercise therapy such as walking, swimming, cycling or dancing provided at mixed levels in terms of intensity of the aerobic exercise from very low to quite rigorous, whilst one study used anaerobic exercise. Control groups consisted of passive control (eight studies; e.g. treatment as usual, relaxation, flexibility) or CBT (two studies), cognitive therapy (one study), supportive listening (one study), pacing (one study), pharmacological treatment (one study) and combination treatment (one study). Risk of bias varied across studies, but within each study, little variation was found in the risk of bias across our primary and secondary outcome measures.Investigators compared exercise therapy with 'passive' control in eight trials, which enrolled 971 participants. Seven studies consistently showed a reduction in fatigue following exercise therapy at end of treatment, even though the fatigue scales used different scoring systems: an 11-item scale with a scoring system of 0 to 11 points (MD -6.06, 95% CI -6.95 to -5.17; one study, 148 participants; low-quality evidence); the same 11-item scale with a scoring system of 0 to 33 points (MD -2.82, 95% CI -4.07 to -1.57; three studies, 540 participants; moderate-quality evidence); and a 14-item scale with a scoring system of 0 to 42 points (MD -6.80, 95% CI -10.31 to -3.28; three studies, 152 participants; moderate-quality evidence). Serious adverse reactions were rare in both groups (RR 0.99, 95% CI 0.14 to 6.97; one study, 319 participants; moderate-quality evidence), but sparse data made it impossible for review authors to draw conclusions. Study authors reported a positive effect of exercise therapy at end of treatment with respect to sleep (MD -1.49, 95% CI -2.95 to -0.02; two studies, 323 participants), physical functioning (MD 13.10, 95% CI 1.98 to 24.22; five studies, 725 participants) and self-perceived changes in overall health (RR 1.83, 95% CI 1.39 to 2.40; four studies, 489 participants). It was not possible for review authors to draw conclusions regarding the remaining outcomes.Investigators compared exercise therapy with CBT in two trials (351 participants). One trial (298 participants) reported little or no difference in fatigue at end of treatment between the

				two groups using an 11-item scale with a scoring system of 0 to 33 points (MD 0.20, 95% CI -1.49 to 1.89). Both studies measured differences in fatigue at follow-up, but neither found differences between the two groups using an 11-item fatigue scale with a scoring system of 0 to 33 points (MD 0.30, 95% CI -1.45 to 2.05) and a nine-item Fatigue Severity Scale with a scoring system of 1 to 7 points (MD 0.40, 95% CI -0.34 to 1.14). Serious adverse reactions were rare in both groups (RR 0.67, 95% CI 0.11 to 3.96). We observed little or no difference in physical functioning, depression, anxiety and sleep, and we were not able to draw any conclusions with regard to pain, self-perceived changes in overall health, use of health service resources and drop-out rate.With regard to other comparisons, one study (320 participants) suggested a general benefit of exercise over adaptive pacing, and another study (183 participants) a benefit of exercise over supportive listening. The available evidence was too sparse to draw conclusions about the effect of pharmaceutical interventions. AUTHORS' CONCLUSIONS: Patients with CFS may generally benefit and feel less fatigued following exercise therapy, and no evidence suggests that exercise therapy may worsen outcomes. A positive effect with respect to sleep, physical function and self-perceived general health has been observed, but no conclusions for the outcomes of pain, quality of life, anxiety, depression, drop-out rate and health service resources were possible. The effectiveness of exercise therapy seems greater than that of pacing but similar to that of CBT. Randomised trials with low risk of bias are needed to investigate the type, duration and intensity of the most beneficial exercise intervention.
Laskowski RA, Creed JA, Raghupathi R		Pathophysiology of Mild TBI: Implications for Altered Signaling Pathways.	In: Kobeissy FH, editor. Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects. Boca Raton (FL): CRC Press/Taylor & Francis; 2015. Chapter 4. Frontiers in Neuroengineering.	Concussions and mild traumatic brain injury (TBI) represent a substantial portion of the annual incidence of TBI aided by the increased reporting of concussions in youth sports, and the increased exposure of soldiers to blast injuries in the war theater. The pathophysiology of concussions and mild TBI consist predominantly of axonal injury at the cellular level and working memory deficits at the behavioral level. Importantly, studies in humans and in animals are making it clear that concussions and mild TBI are not merely a milder form of moderate-severe TBI but represent a separate disease/injury state. Therefore, acute and chronic treatment strategies, both behavioral and pharmacological, need to be implemented based on thorough pre-clinical assessment. The review in this chapter focuses on two under-studied components of the pathophysiology of mild TBI—the role of the c-Jun N-terminal kinase pathway in axonal injury, and the role of the dopaminergic system in working memory deficits. The growing awareness of the incidence of concussion in contact sports, coupled with the emergence of blast-related injuries in combat fighting, has heightened the urgency to understand the underlying mechanisms of mild brain trauma and devise potential therapeutic interventions. TBI in general, and mild TBI in particular, is considered a “silent epidemic” because many of the acute and enduring alterations in cognitive, motor, and somatosensory functions may not be readily apparent to external observers. Moderate to severe TBI is a major cause of injury-induced death and

				disability with an annual incidence of approximately 500 in 100,000 people affected in the United States (Sosin et al., 1989; Kraus and McArthur, 1996; Rutland-Brown et al., 2006). However, approximately 80% of all TBI cases are categorized as mild head injuries (Bazarian et al., 2005; Langlois et al., 2006). It is important to note that these approximations are underestimates because they do not account for incidents of TBI in which the person does not seek medical care (Faul et al., 2010). Recent estimates to correct for this underreporting have placed the annual incidence at approximately 3.8 million (Bazarian et al., 2005; Ropper and Gorson, 2007; Halstead and Walter, 2010). The Glasgow Coma Scale (GCS) score, which measures level of consciousness, has been the primary clinical tool for assessing initial brain injury severity in mild (GCS 13–15), moderate (GCS 9–12), or severe (GCS < 8) cases (Teasdale and Jennett, 1974). Although this scoring system serves as a reliable predictor of patient survival (Steyerberg et al., 2008), particularly in the acute phase of trauma and for those patients with more severe head injury (Saatman et al., 2008), it does not necessarily reflect the underlying cerebral pathology because different structural abnormalities can produce a similar clinical picture. Concussions are a frequent occurrence in contact sports such as football, hockey, lacrosse, and soccer, and increasing evidence suggests that athletes may sustain multiple concussions throughout their career (Bakhos et al., 2010; Bazarian et al., 2005; Grady, 2010; McCrory et al., 2009). Another significant population is soldiers suffering from blast-related injuries, with one in six soldiers returning from combat deployment in Iraq meeting the criteria for concussion (Wilk et al., 2010). Gender factors may also play a role in the epidemiology of concussion. Comparisons of similar sports have yielded the observation that females have nearly twice the rate of concussion compared with males (Dick, 2009; Lincoln et al., 2011). It is important to note that concussed high school males and females self-report different symptoms, with females more often complaining of drowsiness and noise sensitivity, whereas males complain of cognitive deficits and amnesia (Frommer et al., 2011). Furthermore, females also have a higher postconcussion symptom score 3 months postinjury (Bazarian et al., 2010). Two primary complications of concussion are the postconcussion syndrome and second impact syndrome. The postconcussion syndrome is the persistence of concussion-induced symptomatology for greater than 3 months postinjury, presumably because of both neurophysiological and neuropathological processes secondary to the initial concussion (Silverberg and Iverson, 2011). Second impact syndrome is a condition in which a second head impact is sustained during a “vulnerable period” before the complete symptomatic resolution of the initial impact leading to profound engorgement, massive edema, and increased intracranial pressure within minutes of the impact and resulting in brain herniation, followed by coma and death (Cantu, 1998; Field et al., 2003). It is believed that this vulnerable period is the duration of an injury-induced failure of cerebral blood flow autoregulation (Lam et al., 1997), which can leave the patient highly vulnerable to drastic fluxes and extremes of

				blood pressure. Second impact syndrome has a morbidity rate of 100% and a mortality rate of 50%, and it is important to note that as of 2001, all reported cases of second impact syndrome had occurred in athletes younger than 20 years of age (McCrory, 2001). Neurobehavioral symptoms, which often correlate with severity of the TBI, vary in type and duration and are manifested as somatic and/or neuropsychiatric symptoms (reviewed in Riggio and Wong, 2009). Somatic symptoms refer to the physical changes associated with TBI and include headache, dizziness/nausea, fatigue or lethargy, and changes in sleep pattern. Headache is the most commonly reported somatic symptom after mild TBI and is considered acute if resolved within 2 months or chronic if headaches persist for longer than 2 months. Dizziness is another commonly reported symptom of TBI and generally resolves within 2 months but may continue in patients with moderate or severe TBI. Another particularly debilitating symptom is fatigue, likely due to difficulty in initiating or maintaining sleep. Neuropsychiatric sequelae after TBI comprise cognitive deficits and behavioral disorders and are identified in almost all TBI patients for up to 3 months, with a small percentage exhibiting persistent (months—years) symptoms. Cognitive deficits are characterized by impaired attention, memory, and/or executive function and may cause the patient to become irritable, anxious, or depressed. Cognitive deficits in cases of mild TBI generally resolve within days and do not have to be associated with loss of consciousness and posttraumatic amnesia. Behavioral manifestations after TBI include personality changes, depression, and anxiety. Personality changes describe aggression, impulsivity, irritability, emotional lability, and apathy. Major depression is one of the most frequently reported behavioral sequelae of TBI, accounting for approximately 25% to 40% of cases of moderate-to-severe TBI (Riggio and Wong, 2009). Collectively, these observations underscore the need to develop age-, sex-, and injury severity—appropriate animal models of mild TBI and concussions. The following review describes the current state of knowledge of the pathophysiology of mild TBI/concussions, with particular attention to axonal injury and cognitive deficits.
Lau CI(1), Lin CC(2), Chen WH(3), Wang HC(4), Kao CH(5).	(1)Department of Neurology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan; Division of Clinical Neurology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; College of Medicine, Fu-Jen	Increased risk of chronic fatigue syndrome in patients with migraine: A retrospective cohort study.	J Psychosom Res. 2015 Dec;79(6):514-8. doi: 10.1016/j.jpsychores.2015.10.005. Epub 2015 Oct 20.	

	Catholic University, Taipei, Taiwan.Author information:			
LeBlanc TW(1), Nipp RD(2), Rushing CN(3), Samsa GP(3), Locke SC(3), Kamal AH(4), Cella DF(5), Abernethy AP(6).	(1)Duke Cancer Institute, Duke University School of Medicine, Durham, North Carolina, USA; Center for Learning Health Care, Duke Clinical Research Institute, Durham, North Carolina, USA; Division of Hematologic Malignancies and Cellular Therapy, Department of Medicine, Duke University School of Medicine, Durham, North Carolina, USA. amy.abernethy@duke.edu.	Correlation between the international consensus definition of the Cancer Anorexia-Cachexia Syndrome (CACS) and patient-centered outcomes in advanced non-small cell lung cancer.	J Pain Symptom Manage. 2015 Apr;49(4):680-9. doi: 10.1016/j.jpainsymman.2014.09.008. Epub 2014 Nov 4.	CONTEXT: The cancer anorexia-cachexia syndrome (CACS) is common in patients with advanced solid tumors and is associated with adverse outcomes including poor quality of life (QOL), impaired functioning, and shortened survival. OBJECTIVES: To apply the recently posed weight-based international consensus CACS definition to a population of patients with advanced non-small cell lung cancer (NSCLC) and explore its impact on patient-reported outcomes. METHODS: Ninety-nine patients participated in up to four study visits over a six-month period. Longitudinal assessments included measures of physical function, QOL, and other clinical variables such as weight and survival. RESULTS: Patients meeting the consensus CACS criteria at Visit 1 had a significantly shorter median survival (239.5 vs. 446 days; hazard ratio, 2.06, $P < 0.05$). Physical function was worse in the CACS group (mean Karnofsky Performance Status score 68 vs. 77, Eastern Cooperative Oncology Group Performance Status score 1.8 vs. 1.3, $P < 0.05$ for both), as was QOL (Functional Assessment of Cancer Therapy-General [FACT-G] Lung Cancer subscale of 17.2 vs. 19.9, Anorexia/Cachexia subscale of 31.4 vs. 37.9, $P < 0.05$ for both). Differences in the FACT-G and the Functional Assessment of Chronic Illness Therapy-Fatigue subscale approached but did not reach statistical significance. Longitudinally, all measures of physical function and QOL worsened regardless of CACS status, but the rate of decline was more rapid in the CACS group. CONCLUSION: The weight-based component of the recently proposed international consensus CACS definition is useful in identifying patients with advanced NSCLC who are likely to have significantly inferior survival and who will develop more precipitous declines in physical function and QOL. This definition may be useful for clinical screening purposes and identify patients with high palliative care needs.
Leblebici B(1), Özelsancak R(2), Yılmaz EE(1), Doruk P(1).	(1)Department of Physical Medicine and Rehabilitation, Baskent University Faculty of Medicine, Adana Medical and Research Center, Adana, Turkey. (2)Department of Nephrology, Baskent University Faculty of Medicine, Adana Medical and Research Center, Adana,	Fibromyalgia syndrome in Turkish hemodialysis patients.	Hemodial Int. 2015 Jul 22. doi: 10.1111/hdi.12332. [Epub ahead of print]	The aim of our study was to evaluate the frequency of fibromyalgia syndrome (FMS) in hemodialysis (HD) patients and to assess whether this syndrome is associated with gender, age, duration of HD, or various laboratory parameters. This study was composed of 221 chronic HD patients (99 females and 122 males), and we recorded each participant's age, gender, causes of kidney failure, HD duration, education level, and symptoms related to FMS, which was diagnosed according to the 2010 American College of Rheumatology criteria. We documented the laboratory parameters for all patients. In addition, patients with FMS filled out the Fibromyalgia Impact Questionnaire. Twenty-two patients met the diagnostic criteria for FMS (9%), and there were no statistically significant differences related to age, gender, or HD duration between FMS and non-FMS groups ($P > 0.05$). In addition, the education levels were lower in patients diagnosed with FMS ($P < 0.05$), and there were statistically significant differences related to sleep disturbance, fatigue, and cognitive symptoms between the two groups ($P < 0.05$) as well. However, their laboratory parameters were similar

	Turkey.			(P > 0.05). There was a higher prevalence of FMS in HD patients than in the general population. Sleep disturbances, fatigue, education level, and cognitive symptoms were associated with FMS, but there was no correlation between the laboratory parameters and this condition.
Lee JH(1), Kim JE, Jang YJ, Lee CC, Lim TG, Jung SK, Lee E, Lim SS, Heo YS, Seo SG, Son JE, Kim JR, Lee CY, Lee HJ, Lee KW.	(1)WCU Biomodulation Major, Department of Agricultural Biotechnology and Center for Food and Bioconvergence, Seoul National University, Seoul, Republic of Korea; Advanced Institutes of Convergence Technology, Seoul National University, Suwon, Republic of Korea.	Dehydroglyasperin C suppresses TPA-induced cell transformation through direct inhibition of MKK4 and PI3K.	Mol Carcinog. 2015 Mar 18. doi: 10.1002/mc.22302. [Epub ahead of print]	Bioactive natural compounds from plant-derived sources have received substantial interest due to their potential therapeutic and preventive effects toward various human diseases. Licorice (Glycyrrhiza), a frequently-used component in traditional oriental medicines, has been incorporated into recipes not only to enhance taste, but also to treat various conditions including inflammation, chronic fatigue syndrome, and even cancer. Dehydroglyasperin C (DGC) is a major isoflavone found in the root of licorice. In the present study, we investigated the cancer chemopreventive effect of DGC and the underlying molecular mechanisms involved, by analyzing its effects on 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced neoplastic cell transformation and cyclooxygenase (COX)-2 expression in JB6 P+ mouse epidermal cells. DGC treatment attenuated TPA-induced activator protein-1 (AP-1) and nuclear factor-κB (NF-κB) transcriptional activation, two major regulators of TPA-induced cell transformation, and COX-2 expression. TPA-induced phosphorylation of p38, JNK1/2 and Akt was also suppressed by DGC. Kinase assay data revealed that DGC inhibited the kinase activity of MKK4 and PI3K and this outcome was due to direct physical binding with DGC. Notably, DGC bound directly to MKK4 and PI3K in an ATP-competitive manner. Taken together, these results suggest that DGC exhibits cancer chemopreventive potential via its inhibitory effect on TPA-induced neoplastic cell transformation and COX-2 modulation through regulation of the MKK4 and PI3K pathways. © 2015 Wiley Periodicals, Inc.
Lee JH(1), Kim SK(2), Ko SJ(2), Lee SH(3), Lee JH(4), Kim MJ(2), Han G(2), Kim J(2), Chung SY(2), Lee BJ(2), Park JW(2).	(1)1 Kyung Hee Medical Center , Seoul, Republic of Korea. (2)2 College of Korean Medicine, Kyung Hee University , Seoul, Republic of Korea. (3)3 Music Therapy Center, Kyung Hee University Hospital at Gangdong , Seoul, Republic of Korea. (4)4 Korea Institute of Oriental Medicine , Daejeon, Republic of Korea.	The Effect of Oriental Medicine Music Therapy on Idiopathic Chronic Fatigue.	J Altern Complement Med. 2015 Jul;21(7):422-9. doi: 10.1089/acm.2014.0271. Epub 2015 May 26.	OBJECTIVE: Idiopathic chronic fatigue (ICF), defined as medically unexplained chronic fatigue, is common these days. To date, there is no definite cure for ICF, and alternative therapies are being investigated. Oriental medicine music therapy (OMMT), a novel music therapy that occurs through an active behavioral process, has been applied to various chronic diseases, including ICF. In the present study, we aimed to evaluate the effect of OMMT on ICF. DESIGN: Randomized controlled trial of OMMT compared with the waitlist control (6 sessions each) during a 2-week period. PARTICIPANTS: Thirty participants who had had ICF for at least 6 months before the experiments were recruited. OUTCOME MEASURES: We evaluated fatigue severity scale (FSS), visual analog scale (VAS) for overall fatigue, revised Chalder fatigue scale (RCFS), World Health Organization quality of life scale abbreviated version (WHOQOL-BREF), Buzhongyiqi-Tang questionnaire (BZTQ), and salivary cortisol level at baseline (week 0) and at the end of the study (week 2) in the two groups. RESULTS: FSS, VAS, and RCFS scores were significantly lower, and WHOQOL-BREF scores were significantly higher in the OMMT group than in the waitlist group (p=0.006, p=0.004, p=0.002, and p=0.002, respectively). In contrast, salivary cortisol level and BZTQ scores were not significantly different between the OMMT group and the waitlist group. CONCLUSIONS: The present study

				suggests that OMMT may be an alternative treatment for ICF. Based on this result, further studies including possible mechanisms are needed.
Lengert N(1), Drossel B(2).	(1)Institute for Condensed Matter Physics, Technische Universität Darmstadt, Hochschulstr. 6, 64289 Darmstadt, Germany. Electronic address: nicor@fkp.tu-darmstadt.de. (2)Institute for Condensed Matter Physics, Technische Universität Darmstadt, Hochschulstr. 6, 64289 Darmstadt, Germany.	In silico analysis of exercise intolerance in myalgic encephalomyelitis/chronic fatigue syndrome.	Biophys Chem. 2015 Jul;202:21-31. doi: 10.1016/j.bpc.2015.03.009. Epub 2015 Apr 4.	Post-exertional malaise is commonly observed in patients with myalgic encephalomyelitis/chronic fatigue syndrome, but its mechanism is not yet well understood. A reduced capacity for mitochondrial ATP synthesis is associated with the pathogenesis of CFS and is suspected to be a major contribution to exercise intolerance in CFS patients. To demonstrate the connection between a reduced mitochondrial capacity and exercise intolerance, we present a model which simulates metabolite dynamics in skeletal muscles during exercise and recovery. CFS simulations exhibit critically low levels of ATP, where an increased rate of cell death would be expected. To stabilize the energy supply at low ATP concentrations the total adenine nucleotide pool is reduced substantially causing a prolonged recovery time even without consideration of other factors, such as immunological dysregulations and oxidative stress. Repeated exercises worsen this situation considerably. Furthermore, CFS simulations exhibited an increased acidosis and lactate accumulation consistent with experimental observations.
Leombruni P(1), Miniotti M(1), Colonna F(1), Sica C(1), Castelli L(2), Bruzzone M(3), Parisi S(3), Fusaro E(3), Sarzi-Puttini P(4), Atzeni F(5), Torta RG(1).	(1)Rita Levi Montalcini Department of Neuroscience, University of Turin, Turin, Italy. (2)Department of Psychology, University of Turin, Turin, Italy. (3)Rheumatology Department, Azienda Ospedaliera Città della Salute e della Scienza di Torino, Turin, Italy. (4)Rheumatology Unit, L. Sacco University Hospital, Milan, Italy. (5)IRCCS Galeazzi Orthopaedic Institute, Milan, Italy.	A randomised controlled trial comparing duloxetine and acetyl L-carnitine in fibromyalgic patients: preliminary data.	Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl 88):S82-5. Epub 2015 Mar 18.	OBJECTIVES: Fibromyalgia syndrome (FMS) is a chronic disorder characterised by widespread musculoskeletal pain, troubled sleep, disturbed mood, and fatigue. Recently published reviews have demonstrated that it is influenced by various psychological aspects, and antidepressants are now considered the treatment of choice for most patients. The aim of this randomised controlled trial was to compare the effects of duloxetine and acetyl L-carnitine on pain, depression, anxiety and well-being in FMS patients. METHODS: Sixty-five female outpatients with FMS diagnosed by a rheumatologist were recruited between January 2011 and May 2012, and randomised to receive duloxetine 60 mg/day or acetyl L-carnitine 1500 mg/day (500 mg t.i.d.). Drug efficacy and side effects were assessed by the same psychiatrist at baseline, and four and 12 weeks later. RESULTS: Both drugs led to a general clinical improvement, with positive effects on pain and depressive symptoms; but neither induced a significant improvement in anxiety. Both drugs had a positive effect on the physical component of the quality of life, but only duloxetine improved the psychological component. CONCLUSIONS: Although they need to be confirmed by further studies, these preliminary findings confirm the efficacy of duloxetine, and suggest that acetyl L-carnitine is also efficacious in improving depressive symptoms, pain, and the quality of life of FMS patients.
Leong PK(1), Wong HS(1), Chen J(1), Ko	(1)Division of Life Science, The Hong Kong University of	Yang/Qi invigoration: an herbal therapy for chronic fatigue syndrome with	Evid Based Complement Alternat Med. 2015;2015:945901. doi:	According to traditional Chinese medicine (TCM) theory, Yang and Qi are driving forces of biological activities in the human body. Based on the crucial role of the mitochondrion in energy metabolism, we propose an extended view of Yang and Qi in

KM(1).	Science & Technology, Clear Water Bay, Hong Kong.	yang deficiency?	10.1155/2015/945901. Epub 2015 Feb 11.	the context of mitochondrion-driven cellular and body function. It is of interest that the clinical manifestations of Yang/Qi deficiencies in TCM resemble those of chronic fatigue syndrome in Western medicine, which is pathologically associated with mitochondrial dysfunction. By virtue of their ability to enhance mitochondrial function and its regulation, Yang- and Qi-invigorating tonic herbs, such as Cistanches Herba and Schisandrae Fructus, may therefore prove to be beneficial in the treatment of chronic fatigue syndrome with Yang deficiency.
Li DQ(1), Li ZC(2), Dai ZY(3).	(1)Department of Integrated Internal Medicine, The First Affiliated Hospital, College of Medicine, Zhejiang University Hangzhou 310003, Zhejiang, China. (2)Department of Neurology, Tongde Hospital of Zhejiang Province Hangzhou, China. (3)Department of Preventive Medicine, Xiaoying Street Community Health Center Hangzhou, China.	Selective serotonin reuptake inhibitor combined with dengzhanshengmai capsule improves the fatigue symptoms: a 12-week open-label pilot study.	Int J Clin Exp Med. 2015 Jul 15;8(7):11811-7. eCollection 2015.	OBJECTIVE: This study was to assess the efficacy and safety of selective serotonin reuptake inhibitor (SSRI) plus Dengzhanshengmai capsule in patients with chronic fatigue syndrome (CFS). METHODS: SSRI at a moderate dose plus Dengzhanshengmai (n = 134) with SSRI alone (n = 134) were compared for the efficacy and safety in the treatment of CFS. The therapeutic efficacy and safety were evaluated. RESULTS: As compared to monotherapy group, the efficacy in combined therapy group was better and characterized by the improvement of general fatigue (0.8±0.6 vs. 1.3±0.7), physical fatigue (0.6±0.3 vs. 1.0±0.4) and reduced activity (1.0±0.5 vs. 1.3±0.6) since the 2nd week (P<0.01) and in reduced motivation (2.1±0.8 vs. 2.4±1.0) since the 8th week (P<0.01) and the improvement continued thereafter. The mental fatigue score and HAD score were comparable between two groups (P>0.05). No significant difference was found in the drop-out rate between SSRI group (15.7%) and SSRI plus Dengzhanshengmai group (18.0%). The reasons for drop out were adverse events (7.5% vs. 9.7%), requests of the patients or career requirement (3.7% vs. 4.5%), loss to follow-up and others (2.2% vs. 3.0%) and lack of efficacy (2.2% vs. 0.7%). Although the patients in combined therapy group experienced a higher rate of hypertension than (5.8% vs. 1.5%), no significant difference was observed (P = 0.08). CONCLUSION: SSRI combined with Dengzhanshengmai capsule may significantly improve the general fatigue, physical fatigue, reduced activity and reduced motivation of CFS patients as compared to monotherapy with SSRI. Furthermore, this combined therapy is safe and tolerable.
Li J(1), Chan JS(2), Chow AY(3), Yuen LP(4), Chan CL(2).	(1)Renmin University of China, 59 Zhongguancun Street, 1007 Block D, Huixian Building, Haidian, Beijing 100872, China.	From Body to Mind and Spirit: Qigong Exercise for Bereaved Persons with Chronic Fatigue Syndrome-Like Illness.	Evid Based Complement Alternat Med. 2015;2015:631410. doi: 10.1155/2015/631410. Epub 2015 Oct 4.	Bereavement may bring negative impacts on the mind, body, and spiritual well-being of grieving persons. Some bereaved persons with chronic fatigue syndrome- (CFS-) illness experience a dual burden of distress. This study investigated the effects of bereavement on CFS-like illness by comparing bereaved and nonbereaved participants. It also adopted a random group design to investigate the effectiveness of Qigong on improving the well-being of bereaved participants. The Qigong intervention comprised 10 group sessions delivered twice a week for 5 weeks and home-practice for at least three times a week lasting 15-30 minutes each. The participants' fatigue, anxiety, and depression, quality of life (QoL), and spiritual well-being were measured at baseline and 3 months after treatment. The bereaved participants experienced significantly greater mental fatigue (16.09 versus 14.44, p = 0.017) and lower physical QoL (34.02 versus 37.17, p = 0.011) than their nonbereaved counterparts. After 3 months, the mental fatigue (-8 versus -4, p = 0.010) and physical fatigue (-10 versus -5, p = 0.007)

				experienced by intervention group had declined significantly, and improvements on their spirituality (14 versus -2, p = 0.013) and psychological QoL (8.91 versus 0.69, p = 0.002) scores exceeded those of the control group.
Lian OS(1), Nettleton S(2).	(1)University of Tromsø-The Arctic University of Norway, Tromsø, Norway olaug.lian@uit.no. (2)University of Tromsø-The Arctic University of Norway, Tromsø, Norway University of York, York, United Kingdom.	"United We Stand": Framing Myalgic Encephalomyelitis in a Virtual Symbolic Community.	Qual Health Res. 2015 Oct;25(10):1383-94. doi: 10.1177/1049732314562893. Epub 2014 Dec 8.	In this article, we report on a study that seeks to explore how the contested chronic condition myalgic encephalomyelitis (ME), one of the current medical diagnoses for medically unexplained long-term exhaustion, is negotiated within the context of Norwegian internet sites. From an analysis of discussions on 14 internet forums sustained by and for people living with ME, we seek to understand how their online activity sustains a virtual symbolic community (VSC). After exploring the content on these sites, we identified four discursive domains, or fields of conversation, that are demarcated by a discursive frame, or norms, values, and goals that define and reinforce the boundaries of the community. Interpreting discursive domains and their discursive frame provides insight not only to the culture of the ME VSC but also to its role in an international social health movement, including its potential for becoming politically influential.
Lian OS(1), Hansen AH(2).	(1)University of Tromsø - The Arctic University of Norway, Norway olaug.lian@uit.no. (2)University of Tromsø - The Arctic University of Norway, Norway; University Hospital of North Norway, Norway.	Factors facilitating patient satisfaction among women with medically unexplained long-term fatigue: A relational perspective.	Health (London). 2015 May 14. pii: 1363459315583158. [Epub ahead of print]	Bodily conditions that are difficult to identify, explain and treat with the aid of medical knowledge and technology appear to be particularly challenging to medical encounters. Patients are often dissatisfied with the help they receive, and they often experience that their medical needs are not met. To explore factors facilitating patient satisfaction among patients with a medically unexplained condition, we ask: what is the importance of individual versus relational factors in facilitating patient satisfaction in clinical encounters between general practitioners (GPs) and women with medically unexplained long-term fatigue? We approach this question through a statistical analysis of survey data collected from a net sample of 431 women recruited through a patient organisation for people suffering from myalgic encephalomyelitis in 2013. Participants were asked about their experiences with general practitioners in the Norwegian national health system in two different phases: shortly after illness onset, and current regular general practitioner last 12 months. The questions evolved around themes concerning shared understanding and decision making, being taken seriously, being paid due respect and being treated as an equal partner. Through descriptive statistics and multivariable logistic regression analyses, we explored how their experiences were related to individual and relational factors, respectively. Free-text comments from the questionnaires were used while interpreting the results. The analysis illuminates that relational aspects in medical encounters between GPs and ME patients, especially continuity, congruence in doctor-patient views and being seen by a specialist, are important catalysts of patient satisfaction. The probability of being satisfied with the initial investigation was more than six times higher in women who were referred to specialists, compared to those who were not. We conclude that continuity of care and experiences of being in a partnership that operates on a common ground - a shared understanding of the patient's illness - foster patient satisfaction among women with

				medically unexplained long-term fatigue.
Lian OS(1), Bondevik H(2).	(1)Department of Community Medicine, University of Tromsø - The Arctic University of Norway, Norway. (2)Institute of Health and Society, University of Oslo, Norway.	Medical constructions of long-term exhaustion, past and present.	Sociol Health Illn. 2015 Jul;37(6):920-35. doi: 10.1111/1467-9566.12249. Epub 2015 Apr 24.	Culture and history affect the ways in which medical knowledge is shaped, sustained and changed. The less knowledge we have, the larger the space for the cultural imprint becomes. Based on these assumptions, we ask: how have medical constructions of long-term exhaustion changed over time, and how are changing constructions related to societal change? To discuss these questions we conducted a comparative study of medical texts from two historical periods: 1860-1930 and 1970-2013. Our data are limited to two diagnoses: neurasthenia and encephalomyelitis. After comparing the two periods by identifying diverging and converging aspects, we interpreted observed continuities and interruptions in relation to historical developments. We found that in the medical literature, long-term exhaustion became transformed from a somatic ailment bred by modern civilisation to a self-inflicted psychiatric ailment. At the same time, it changed from being a male-connoted high-status condition to a female-connoted low-status condition. We interpret these changes as contingent upon culturally available modes of interpretations. Medical knowledge thereby becomes infused with cultural norms and values which give them a distinct cultural bias. The historical controversies surrounding this medically contested condition neatly display the socially contingent factors that govern the social construction of medical knowledge.
Liu Z(1), Guo W(2).	(1)Department of Biostatistics, Indiana University, Schools of Public Health and Medicine, Indianapolis, IN, 46202, U.S.A. (2)Department of Biostatistics & Epidemiology, University of Pennsylvania, School of Medicine, Philadelphia, 19104, PA, U.S.A.	Modeling diurnal hormone profiles by hierarchical state space models.	Stat Med. 2015 Oct 30;34(24):3223-34. doi: 10.1002/sim.6579. Epub 2015 Jul 7.	Adrenocorticotropic hormone (ACTH) diurnal patterns contain both smooth circadian rhythms and pulsatile activities. How to evaluate and compare them between different groups is a challenging statistical task. In particular, we are interested in testing (1) whether the smooth ACTH circadian rhythms in chronic fatigue syndrome and fibromyalgia patients differ from those in healthy controls and (2) whether the patterns of pulsatile activities are different. In this paper, a hierarchical state space model is proposed to extract these signals from noisy observations. The smooth circadian rhythms shared by a group of subjects are modeled by periodic smoothing splines. The subject level pulsatile activities are modeled by autoregressive processes. A functional random effect is adopted at the pair level to account for the matched pair design. Parameters are estimated by maximizing the marginal likelihood. Signals are extracted as posterior means. Computationally efficient Kalman filter algorithms are adopted for implementation. Application of the proposed model reveals that the smooth circadian rhythms are similar in the two groups but the pulsatile activities in patients are weaker than those in the healthy controls.
Lloyd AR(1), Meer JW(2).	(1)Inflammation and Infection Research Centre, University of New South Wales, Sydney 2052, Australia a.lloyd@unsw.edu.au.	The long wait for a breakthrough in chronic fatigue syndrome.	BMJ. 2015 May 5;350:h2087. doi: 10.1136/bmj.h2087.	

	(2)Department of Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands.			
Loades M(1).	(1)Department of Psychology, University of Bath, Bath, UK.	The Cognitive Behavioral Treatment of Depression and Low Self-Esteem in the Context of Pediatric Chronic Fatigue Syndrome (CFS/ME): A Case Study.	J Child Adolesc Psychiatr Nurs. 2015 Nov;28(4):165-74. doi: 10.1111/jcap.12125. Epub 2015 Oct 16.	PROBLEM: Up to one in three young people with chronic fatigue syndrome (CFS/ME) also has depressive symptoms. It is not known how best to treat young people with this comorbidity. METHOD: This case report seeks to describe and discuss the use of a cognitive behavioral approach for depression and low self-esteem in a 16-year-old girl with CFS/ME. FINDINGS/CONCLUSION: Therapy was effective in remediating the young person's mood difficulties, but appeared to exacerbate their CFS/ME symptoms. Therefore, it is crucial that CFS/ME and mood treatments are designed and trialed to ensure a complementary approach. Good communication and joint working between involved professionals is also important, and ideally, treatments for mood and for CFS/ME would be provided by the same team to facilitate this.
Loebel M(1), Grabowski P(2), Heidecke H(3), Bauer S(2), Hanitsch LG(2), Wittke K(2), Meisel C(4), Reinke P(5), Volk HD(6), Fluge Ø(7), Mella O(8), Scheibenbogen C(6).	(1)Institute for Medical Immunology, Charité University Medicine Berlin, Campus Virchow, Berlin, Germany. Electronic address: madlen.loebel@charite.de.	Antibodies to β adrenergic and muscarinic cholinergic receptors in patients with Chronic Fatigue Syndrome.	Brain Behav Immun. 2015 Sep 21. pii: S0889-1591(15)30020-9. doi: 10.1016/j.bbi.2015.09.013. [Epub ahead of print]	Infection-triggered disease onset, chronic immune activation and autonomic dysregulation in CFS point to an autoimmune disease directed against neurotransmitter receptors. Autoantibodies against G-protein coupled receptors were shown to play a pathogenic role in several autoimmune diseases. Here, serum samples from a patient cohort from Berlin (n=268) and from Bergen with pre- and post-treatment samples from 25 patients treated within the KTS-2 rituximab trial were analysed for IgG against human α and β adrenergic, muscarinic (M) 1-5 acetylcholine, dopamine, serotonin, angiotensin, and endothelin receptors by ELISA and compared to a healthy control cohort (n=108). Antibodies against β2, M3 and M4 receptors were significantly elevated in CFS patients compared to controls. In contrast, levels of antibodies against α adrenergic, dopamine, serotonin, angiotensin, and endothelin receptors were not different between patients and controls. A high correlation was found between levels of autoantibodies and elevated IgG1-3 subclasses, but not with IgG4. Further patients with high β2 antibodies had significantly more frequently activated HLA-DR+ T cells and more frequently thyreoperoxidase and anti-nuclear antibodies. In patients receiving rituximab maintenance treatment achieving prolonged B-cell depletion, elevated β2 and M4 receptor autoantibodies significantly declined in clinical responder, but not in non-responder. We provide evidence that 29.5% of patients with CFS had elevated antibodies against one or more M acetylcholine and β adrenergic receptors which are potential biomarkers for response to B-cell depleting therapy. The association of autoantibodies with immune markers suggests that they activate B and T cells expressing β adrenergic and M acetylcholine receptors. Dysregulation of acetylcholine and adrenergic signalling could also explain various clinical symptoms of CFS.
Loganovsky K(1),	(1)State Institution	Workers on	World J Biol Psychiatry.	OBJECTIVES: The present study aimed at assessing bioelectric activity and cognitive

Perchuk I, Marazziti D.	"National Research Center for Radiation Medicine of the National Academy of Medical Sciences of Ukraine" , Kyiv , Ukraine.	transformation of the shelter object of the Chernobyl nuclear power plant into an ecologically-safe system show qEEG abnormalities and cognitive dysfunctions: A follow-up study.	2015 May 23:1-8. [Epub ahead of print]	functions in the workers on the conversion project of the "Shelter" object (SO) of the Chernobyl nuclear power plant into an environmentally safe system. METHODS: A total of 196 men were included and examined before (t0) and after (t1) working on the SO in the period 2004-2008. They underwent a qEEG and a battery of neuropsychological and psychiatric assessments. RESULTS: At t1, the organized type of qEEG shifted towards the disorganized one. An increase of spectral δ-power in the left frontotemporal area, of θ- and α-power in the left temporal area, with redistribution of α-activity to the front and reduction of dominant frequency in the left temporal area, were registered. Further, neurocognitive tests revealed the presence of mild cognitive disorders at t1. Interestingly, those subjects previously exposed to radiation with no consequences, were more resistant to these detrimental effects. CONCLUSIONS: Taken together, the disturbances observed may be considered as cognitive symptoms of a chronic fatigue syndrome resulting from the exposure to ionizing radiation. Simple and non-invasive assessments, such as those performed by us, may be helpful to detect early brain changes caused by the presence of radiological risk factors.
Lukkahatai N(1), Walitt B(2), Espina A(3), Wang D(3), Saligan LN(4).	(1)School of Nursing, University of Nevada, Las Vegas, NV, USA National Institute of Nursing Research (NINR), National Institutes of Health (NIH), Bethesda, MD, USA. (2)National Institute of Nursing Research (NINR), National Institutes of Health (NIH), Bethesda, MD, USA Section of Rheumatology, Washington Hospital Center, Washington, DC, USA. (3)National Institute of Nursing Research (NINR), National Institutes of Health (NIH),	Comparing Genomic Profiles of Women With and Without Fibromyalgia.	Biol Res Nurs. 2015 Jul;17(4):373-83. doi: 10.1177/1099800415589785. Epub 2015 May 26.	BACKGROUND: Fibromyalgia syndrome (FMS), a chronic musculoskeletal condition characterized by diffuse pain, fatigue, sleep impairment, and cognitive dysfunction, is associated with significant functional disability. Its underlying biological mechanisms are unknown. This study investigated differentially expressed genes between women with FMS and healthy volunteers. METHODS: Women who met the 1990 or 2010 American College of Rheumatology fibromyalgia criteria were compared to age- and race-matched pain-free healthy women. Peripheral blood samples were collected, and a full genome microarray gene expression analysis was performed. One-way analysis of variance was used to identify differentially expressed genes using the filtering criterion of 1% false discovery rate. Analysis of canonical pathways associated with these genes was performed. Confirmatory quantitative real-time polymerase chain reaction and enzyme-linked immunosorbent assay verified microarray results. Independent t-tests compared gene and protein expression between groups. RESULT: Participants were 54 women with FMS and 25 controls. Expression arrays from a subset of women with FMS ($n = 29$) and controls ($n = 20$) showed upregulation of 12 genes (>1.8-fold change, $p < .05$) in the FMS sample. Differentially expressed genes were related to B-cell development, primary immunodeficiency signaling, and mitotic roles of polo-like kinase. CENPK and HSP90AA1 were the most differentially expressed genes ($p < .01$). CONCLUSION: Activity of interrelated pathways related to immune response, and homeostasis appears to be relevant to the experience of FMS. Replication and exploration of the relationship between gene expression and symptom severity will help determine clinical relevance of these findings.

	Bethesda, MD, USA. (4)National Institute of Nursing Research (NINR), National Institutes of Health (NIH), Bethesda, MD, USA saliganl@mail.nih.gov.			
Löbel M(1), Mooslechner AA(2), Bauer S(3), Günther S(4), Letsch A(5), Hanitsch LG(6), Grabowski P(7), Meisel C(8,)(9), Volk HD(10,)(11), Scheibenbogen C(12,)(13).	(1)Institute for Medical Immunology, Charité-Universitätsmedizin Berlin, Campus Virchow, Augustenburger Platz 1/Südstraße 2, 13353, Berlin, Germany. madlen.loebel@charite.de.	Polymorphism in COMT is associated with IgG3 subclass level and susceptibility to infection in patients with chronic fatigue syndrome.	J Transl Med. 2015 Aug 14;13:264. doi: 10.1186/s12967-015-0628-4.	BACKGROUND: Chronic fatigue syndrome (CFS) is considered as a neuroimmunological disease but the etiology and pathophysiology is poorly understood. Patients suffer from sustained exhaustion, cognitive impairment and an increased sensitivity to pain and sensory stimuli. A subset of patients has frequent respiratory tract infections (RRTI). Dysregulation of the sympathetic nervous system and an association with genetic variations in the catechol-O-methyltransferase (COMT) and glucocorticoid receptor genes influencing sympathetic and glucocorticoid metabolism were reported in CFS. Here, we analyzed the prevalence of SNPs of COMT and glucocorticoid receptor-associated genes in CFS patients and correlated them to immunoglobulin levels and susceptibility to RRTI. METHODS: We analyzed blood cells of 74 CFS patients and 76 healthy controls for polymorphisms in COMT, FKBP5 and CRHR1 by allelic discrimination PCR. Serum immunoglobulins were determined by immunoturbidimetric technique, cortisol levels by ECLIA. RESULTS: Contrary to previous reports, we found no difference between CFS patients and healthy controls in the prevalence of SNPs for COMT, FKBP5 and CRHR1. In patients with the Met/Met variant of COMT rs4680 we observed enhanced cortisol levels providing evidence for its functional relevance. Both enhanced IgE and diminished IgG3 levels and an increased susceptibility to RRTI were observed in CFS patients with the Met/Met variant. Such an association was not observed in 68 non-CFS patients with RRTI. CONCLUSION: Our results indicate a relationship of COMT polymorphism rs4680 with immune dysregulation in CFS providing a potential link for the association between stress and infection susceptibility in CFS.
Lüthi U.		["Discriminated against, ignored and psychologized"].[Article in German]	Krankenpfl Soins Infirm. 2015;108(5):12-3.	
Lüthi U.		[Solidarity is what is needed].[Article in German]	Krankenpfl Soins Infirm. 2015;108(5):1.	
M'saad S(1), Yangui I(2), Feki W(2), Abid N(2),	(1)Service de pneumo-allergologie, CHU Hédi Chaker,	[The syndrome of increased upper airways resistance: What are the	Rev Mal Respir. 2015 Dec;32(10):1002-15. doi: 10.1016/j.rmr.2015.08.00	The upper airway resistance syndrome "UARS" is a poorly defined entity, often described as a moderate variant of the obstructive sleep apnea syndrome. It is associated with respiratory effort-related arousal, absence of obstructive sleep apnea,

Bahloul N(2), Marouen F(2), Chakroun A(3), Kammoun S(2).	3029 Sfax, Tunisie. Electronic address: msaadsameh@yahoo.fr. (2)Service de pneumo-allergologie, CHU Hédi Chaker, 3029 Sfax, Tunisie. (3)Service d'oto-rhino-laryngologie, CHU Habib Bourguiba, 3029 Sfax, Tunisie.	clinical features and diagnostic procedures?].	1. Epub 2015 Oct 30.	and absence of significant desaturation. It is a relatively common condition that predominantly affects non-obese young adults, with no predominance in either sex. The degree of upper airway collapsibility during sleep of patients with UARS is intermediate between that of normal subjects and that of patients with mild-to-moderate sleep apnea syndrome. Craniofacial and palatal abnormalities are often noted. Patients frequently complain of a functional somatic syndrome, especially daytime sleepiness and chronic fatigue. Polysomnography with esophageal pressure measurements remains the gold standard diagnostic test. The absence of any neurological abnormality gives UARS a good prognosis and it is potentially reversible if treated early. However, some studies suggest that untreated UARS has an increased risk of arterial hypertension. It can also evolve into obstructive sleep apnea.
Maes M(1).	(1)IMPACT Strategic Research Center, Barwon Health, Deakin University, Geelong, Vic, Australia.	A new case definition of Neuro-Inflammatory and Oxidative Fatigue (NIOF), a neuroprogressive disorder, formerly known as chronic fatigue syndrome or Myalgic Encephalomyelitis: results of multivariate pattern recognition methods and external validation by neuro-immune biomarkers.	Neuro Endocrinol Lett. 2015 Sep 12;36(4):320-329. [Epub ahead of print]	BACKGROUND: Chronic fatigue syndrome (CFS) or Myalgic Encephalomyelitis (ME) is characterized by neuro-psychiatric (e.g. depression, irritability, sleep disorders, autonomic symptoms and neurocognitive defects) and physio-somatic (fatigue, a flu-like malaise, hyperalgesia, irritable bowel, muscle pain and tension) symptoms. New ME/CFS case definitions based on consensus criteria among experts are largely inadequate, e.g. those of the US Institute of Medicine . OBJECTIVES: The aim of the present study was to delineate a new case definition of ME/CFS based on pattern recognition methods and using neuro-immune, inflammatory, oxidative and nitrosative stress (neuro-IO&NS) biomarkers as external validating criteria. METHODS: We measured the 12-item Fibromyalgia and Chronic Fatigue Syndrome Rating (FF) Scale in 196 subjects with CFS (CDC criteria) and 83 with chronic fatigue. The "Neuro-IO&NS" biomarkers were: IgM / IgA responses against LPS of gut commensal bacteria (leaky gut), IgM responses to O&NS modified neoepitopes, autoimmunity to serotonin, plasma interleukin-1 (IL-1) and serum neopterin. RESULTS: Cluster analysis showed the presence of two well-separated clusters with highly significant differences in symptoms and biomarkers. The cluster with higher scores on all FF items was externally validated against all IO&NS biomarkers and therefore this diagnostic group was labeled "Neuro-IO&NS Fatigue" or "Neuro-Inflammatory and Oxidative Fatigue" (NIOF). An algorithm was constructed which defined NIOF as chronic fatigue and 4 or more of the following 6 symptoms: muscle tension, memory disturbances, sleep disorders, irritable bowel, headache or a flu-like malaise. There was a significant overlap between NIOF and CFS although NIOF criteria were much more restrictive. Factor analysis showed two factors, the first a fatigue-hyperalgesia (fibromyalgic complaints) and the second a fatigue-depression factor.
Magnus P(1), Gunnes N(2), Tveito K(3), Bakken IJ(2), Ghaderi S(2),	(1)Norwegian Institute of Public Health, 4404 Nydalen, 0403 Oslo, Norway. Electronic address:	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is associated with pandemic influenza	Vaccine. 2015 Nov 17;33(46):6173-7. doi: 10.1016/j.vaccine.2015.10.018. Epub 2015 Oct 17.	BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is associated to infections and it has been suggested that vaccination can trigger the disease. However, little is known about the specific association between clinically manifest influenza/influenza vaccine and CFS/ME. As part of a registry surveillance of adverse effects after mass vaccination in Norway during the 2009 influenza A (H1N1)

Stoltenberg C(2), Hornig M(4), Lipkin WI(4), Trogstad L(2), Håberg SE(2).	per.magnus@fhi.no. (2)Norwegian Institute of Public Health, 4404 Nydalen, 0403 Oslo, Norway. (3)Journal of the Norwegian Medical Association, Oslo, Norway. (4)Center for Infection and Immunity, Columbia University, NY, NY, USA.	infection, but not with an adjuvanted pandemic influenza vaccine.		pandemic, we had the opportunity to estimate and contrast the risk of CFS/ME after infection and vaccination. METHODS: Using the unique personal identification number assigned to everybody who is registered as resident in Norway, we followed the complete Norwegian population as of October 1, 2009, through national registries of vaccination, communicable diseases, primary health, and specialist health care until December 31, 2012. Hazard ratios (HRs) of CFS/ME, as diagnosed in the specialist health care services (diagnostic code G93.3 in the International Classification of Diseases, Version 10), after influenza infection and/or vaccination were estimated using Cox proportional-hazards regression. RESULTS: The incidence rate of CFS/ME was 2.08 per 100,000 person-months at risk. The adjusted HR of CFS/ME after pandemic vaccination was 0.97 (95% confidence interval [CI]: 0.91-1.04), while it was 2.04 (95% CI: 1.78-2.33) after being diagnosed with influenza infection during the peak pandemic period. CONCLUSIONS: Pandemic influenza A (H1N1) infection was associated with a more than two-fold increased risk of CFS/ME. We found no indication of increased risk of CFS/ME after vaccination. Our findings are consistent with a model whereby symptomatic infection, rather than antigenic stimulation may trigger CFS/ME.
Marks MR(1), Huws JC(2), Whitehead L(1).	(1)Betsi Cadwaladr University Health Board, UK. (2)Bangor University, UK j.huws@bangor.ac.uk.	Working with uncertainty: A grounded theory study of health-care professionals' experiences of working with children and adolescents with chronic fatigue syndrome.	J Health Psychol. 2015 May 8. pii: 1359105315583367. [Epub ahead of print]	This grounded theory study explores conceptualisations of chronic fatigue syndrome/myalgic encephalomyelitis from semi-structured interviews with 10 health-care professionals working with children and adolescents. The findings suggest that a lack of a clear empirical understanding of chronic fatigue syndrome/myalgic encephalomyelitis leads to 'working with uncertainty', whereby health-care professionals utilise previous experiences to make sense of the condition and inform their clinical practice. How health-care professionals make sense of chronic fatigue syndrome/myalgic encephalomyelitis may influence the labels given to young people and the interventions they receive. The findings provide insight into a currently understudied area, and highlight potential avenues for further research and clinical practice.
Maroti D(1), Westerberg AF, Saury JM, Bileviciute-Ljungar I.	(1)ME/CFS-Rehabilitation, Department of Rehabilitation Medicine, Karolinska Institutet Danderyd University Hospital, Stockholm, Sweden.	Computerized training improves verbal working memory in patients with myalgic encephalomyelitis/chronic fatigue syndrome: A pilot study.	J Rehabil Med. 2015 Aug 18;47(7):665-8. doi: 10.2340/16501977-1976.	OBJECTIVE: Patients with myalgic encephalomyelitis/chronic fatigue syndrome experience cognitive difficulties. The aim of this study was to evaluate the effect of computerized training on working memory in this syndrome. DESIGN: Non-randomized (quasi-experimental) study with no-treatment control group and non-equivalent dependent variable design in a myalgic encephalomyelitis/chronic fatigue syndrome-cohort. SUBJECTS: Patients with myalgic encephalomyelitis/chronic fatigue syndrome who participated in a 6-month outpatient rehabilitation programme were included in the study. Eleven patients who showed signs of working memory deficit were recruited for additional memory training and 12 patients with no working memory deficit served as controls. METHODS: Cognitive training with computerized working memory tasks of increasing difficulty was performed 30-45 min/day, 5 days/week over a 5-week period. Short-term and working memory tests (Digit Span - forward, backward, total) were used as primary outcome measures. Nine of the 11 patients were able to complete the

				training. RESULTS: Cognitive training increased working memory (p = 0.003) and general attention (p = 0.004) to the mean level. Short-term memory was also improved, but the difference was not statistically significant (p = 0.052) vs prior training. The control group did not show any significant improvement in primary outcome measures. CONCLUSION: Cognitive training may be a new treatment for patients with myalgic encephalomyelitis/chronic fatigue syndrome.
Marques MM(1), De Gucht V(2), Gouveia MJ(3), Leal I(3), Maes S(2).	(1)Health and Medical Psychology Unit, Leiden University, The Netherlands; Research I&D Psychology and Health Unit (UIPES), ISPA-University Institute, Lisbon, Portugal; Interdisciplinary Centre for the Study of Human Performance (CIPER), Faculty of Human Kinetics, University of Lisbon, Portugal. Electronic address: mmarques@ispa.pt. (2)Health and Medical Psychology Unit, Leiden University, The Netherlands. (3)Research I&D Psychology and Health Unit (UIPES), ISPA-University Institute, Lisbon, Portugal.	Differential effects of behavioral interventions with a graded physical activity component in patients suffering from Chronic Fatigue (Syndrome): An updated systematic review and meta-analysis.	Clin Psychol Rev. 2015 Aug;40:123-37. doi: 10.1016/j.cpr.2015.05.009 . Epub 2015 Jun 4.	An updated systematic review and meta-analysis was conducted to (1) evaluate the effects of behavioral and psychological interventions containing a graded physical activity component upon fatigue severity, physical functioning, physical activity and psychological distress, and to (2) examine potential moderator effects of trial characteristics (type of control, setting, provider, length of treatment, psychological component, flexibility in physical activity, and minimal face to face patient-provider contact). Pertinent content of selected studies was extracted and rated on a scale of methodological quality. Sixteen randomized controlled trials (N=2004) were included in the meta-analyses. Significant small to medium effect sizes (Hedge's g=0.25 to g=0.66) were found for all outcomes at post-treatment (M=5.2months) and follow-up (M=11.7months), with the exception of physical activity at post-treatment (g=0.11). The largest effects were found for fatigue severity (g=0.61 to g=0.66). Subgroup analyses revealed that minimal contact interventions had additional beneficial effects upon fatigue (g=0.96) and depression (g=0.85). Interventions provided by psychologists-psychotherapists and interventions conducted in secondary-tertiary settings also resulted in more beneficial effects on fatigue. We found some indication of publication bias. The small number of studies and variability between them are limitations of this study. Future research should explore additional moderating effects in order to improve the effectiveness of interventions.
Martínez-Lavín M(1), Martínez-Martínez LA(2), Reyes-Loyola P(2).	(1)Departamento de Reumatología, Instituto Nacional de Cardiología Ignacio Chávez, Juan Badiano 1, 14080, Mexico City, Mexico.	HPV vaccination syndrome. A questionnaire-based study.	Clin Rheumatol. 2015 Nov;34(11):1981-3. doi: 10.1007/s10067-015-3070-3. Epub 2015 Sep 10.	Isolated cases and small series have described the development of complex regional pain syndrome, postural orthostatic tachycardia, and fibromyalgia after human papillomavirus (HPV) vaccination. These illnesses are difficult to diagnose and have overlapping clinical features. Small fiber neuropathy and dysautonomia may play a major role in the pathogenesis of these entities. We used the following validated questionnaires to appraise the chronic illness that might appear after HPV vaccination: The 2010 American College of Rheumatology Fibromyalgia Diagnostic Criteria,

	drmartinezlavin@gmail.com. (2)Departamento de Reumatología, Instituto Nacional de Cardiología Ignacio Chávez, Juan Badiano 1, 14080, Mexico City, Mexico.			COMPASS 31 dysautonomia questionnaire, and S-LANSS neuropathic pain form. These questionnaires and a "present illness" survey were e-mailed to persons who had the onset of a chronic ailment soon after HPV vaccination. Forty-five filled questionnaires from individuals living in 13 different countries were collected in a month's period. Mean (±SD) age at vaccination time was 14 ± 5 years. Twenty-nine percent of the cases had immediate (within 24 h) post-vaccination illness onset. The most common presenting complaints were musculoskeletal pain (66 %), fatigue (57 %), headache (57 %), dizziness/vertigo (43 %), and paresthesias/allodynia (36 %). Fifty-three percent of affected individuals fulfill the fibromyalgia criteria. COMPASS-31 score was 43 ± 21, implying advanced autonomic dysfunction. Eighty-three percent of the patients who had ongoing pain displayed S-LANSS values >12, suggesting a neuropathic component in their pain experience. After a mean period of 4.2 ± 2.5 years post-vaccination, 93 % of patients continue to have incapacitating symptoms and remain unable to attend school or work. In conclusion, a disabling syndrome of chronic neuropathic pain, fatigue, and autonomic dysfunction may appear after HPV vaccination.
Martínez-Lavín M(1).	(1)Rheumatology Department, Instituto Nacional de Cardiología Ignacio Chávez, Juan Badiano 1, 14080, Mexico City, Mexico, drmartinezlavin@gmail.com.	Hypothesis: Human papillomavirus vaccination syndrome--small fiber neuropathy and dysautonomia could be its underlying pathogenesis.	Clin Rheumatol. 2015 Jul;34(7):1165-9. doi: 10.1007/s10067-015-2969-z. Epub 2015 May 20.	Vaccination has been one of the most effective public health measures in the history of medicine. However, seemingly inexplicit adverse reactions have been described after the injection of the newer vaccines vs. human papillomavirus (HPV). The symptoms more often reported are chronic pain with paresthesias, headaches, fatigue, and orthostatic intolerance. Adverse reactions appear to be more frequent after HPV vaccination when compared to other type of immunizations. Different isolated cases and small series have described the development of complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), and fibromyalgia after HPV vaccination. These are illnesses often difficult to diagnose that have overlapping clinical features. Sympathetic nervous system dysfunction seems to play a major role in the pathogenesis of these syndromes. Also, small fiber neuropathy has been recently recognized in CRPS, POTS, and fibromyalgia. This article forwards the hypothesis that small fiber neuropathy and dysautonomia could be the common underlying pathogenesis to the group of rare, but severe reactions that follow HPV vaccination. Clinicians should be aware of the possible association between HPV vaccination and the development of these difficult to diagnose painful dysautonomic syndromes.
Masi AT(1), Vincent A.	(1)Department of Medicine, University of Illinois College of Medicine at Peoria, One Illini Drive, Box 1649, Peoria, Illinois 61656. amasi@uic.edu.	A historical and clinical perspective endorsing person-centered management of fibromyalgia syndrome.	Curr Rheumatol Rev. 2015;11(2):86-95.	Fibromyalgia or fibromyalgia syndrome (FMS) is a complex chronic pain disorder of unknown causation frequently associated with debilitating fatigue, unrefreshing sleep, cognitive and affective symptoms. A fibromyalgia-type suffering was possibly described in the Book of Job. Analogous symptomatic conditions have been medically recognized since the early 1900s, when initially labeled as "fibrositis". Since the early 1980s, FMS has evolved and differentiated after its characterization in a controlled study. Since then, research has focused on multiple aspects of this disorder, including characterization and management of symptoms, psychophysiology, neuroendocrine-immune pathophysiology, including central sensitization mechanisms. The complex and

				multifaceted nature of FMS lends itself better to a holistic (integrative medicine) or biopsychosocial approach than the more specific bioscientific pathways typical for a pathologically-defined disease. A person-centered approach to evaluation and care more effectively addresses and encompasses the biopsychosocial aspects of this disorder than traditional bioscientific clinical methods. This review outlines a holistic multi-modal, patientcentered approach to evaluation and care as a framework for primary clinic settings. Future directions in research, diagnosis, and management of fibromyalgia patients should incorporate revised person-centered and other qualitative models of care for critical comparison to current conventional concepts and clinical practice. The more comprehensive personcentered services need to be compared to the current standardized practice in terms of their cost-effective outcomes, patient satisfaction, physician gratification, and practical logistics of providing long-term follow up and management.
Matthees A.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):886-7. doi: 10.7326/L15-5173.	
Matthees A(1).	(1), P.O. Box 6483, East Perth, WA, 6892, Australia, alem.matthees@gmail.com.	Assessment of recovery status in chronic fatigue syndrome using normative data.	Qual Life Res. 2015 Apr;24(4):905-7. doi: 10.1007/s11136-014-0819-0. Epub 2014 Oct 11.	INTRODUCTION: Adamowicz et al. have reviewed criteria previously employed to define recovery in chronic fatigue syndrome (CFS). They suggested such criteria have generally lacked stringency and consistency between studies and recommended future research should require "normalization of symptoms and functioning". METHODS: Options regarding how "normalization of symptoms and functioning" might be operationalized for CFS cohorts are explored. RESULTS: A diagnosis of CFS excludes many chronic disabling illnesses present in the general population, and CFS cohorts can almost exclusively consist of people of working age; therefore, it is suggested that thresholds for recovery should not be based on population samples which include a significant proportion of sick, disabled or elderly individuals. It is highlighted how a widely used measure in CFS research, the SF-36 physical function subscale, is not normally distributed. This is discussed in relation to how recovery was defined for a large intervention trial, the PACE trial, using a method that assumes a normal distribution. Summary data on population samples are also given, and alternative methods to assess recovery are proposed. CONCLUSIONS: The "normalization of symptoms and function" holds promise as a means of defining recovery from CFS at the current time. However, care is required regarding how such requirements are operationalized, otherwise recovery rates may be overstated, and perpetuate the confusion and controversy noted by Adamowicz et al.
McCarthy M(1).		US panel proposes new name and diagnostic criteria for chronic fatigue syndrome.	BMJ. 2015 Feb 10;350:h775. doi: 10.1136/bmj.h775.	Erratum in BMJ. 2015;350:h932.

McInnis OA(1), McQuaid RJ, Bombay A, Matheson K, Anisman H.	(1)Department of Neuroscience, Carleton University , Ottawa, ON , Canada .	Finding benefit in stressful uncertain circumstances: relations to social support and stigma among women with unexplained illnesses.	Stress. 2015;18(2):169-77. doi: 10.3109/10253890.2014.1001975. Epub 2015 Jan 23.	Living with a chronic illness can be challenging, but the ability to derive benefits and grow from this experience may enhance well-being. However, the possibility of obtaining such benefits may be dependent on the levels of stigmatization and lack of social support experienced by an individual as a result of the illness. Chronic fatigue syndrome (CFS) and fibromyalgia are chronic conditions that remain largely unexplained and those with these conditions must often contend with stigma and skepticism from others. Individuals with CFS/fibromyalgia often display stress-related biological alterations and the experience of stressful life events has been associated with illness development. The present study demonstrated that women with CFS/fibromyalgia (n = 40) as well as community participants who were depressed/anxious (n = 37), reported higher stigma levels than healthy women (n = 33). Moreover, women with CFS/fibromyalgia and those with depression/anxiety also reported greater levels of stigma than women with a chronic yet more widely accepted condition (n = 35; rheumatoid arthritis, osteoarthritis and multiple sclerosis). Secrecy related to stigma among those with CFS/fibromyalgia declined with increased social support, but this was not apparent among those with other chronic conditions. In addition, posttraumatic growth was lower among women with CFS/fibromyalgia compared to those with other chronic conditions. Qualitative analysis examining both negative impacts and positive changes stemming from illness experience revealed many similarities between women with CFS/fibromyalgia and those with other chronic conditions, including elevated appreciation for life, personal growth and compassion for others. However, women with CFS/fibromyalgia tended to report less positive change regarding interpersonal relationships compared to women with other chronic conditions. In general, unexplained illnesses were also accompanied by stigmatization which might ultimately contribute to women's lower ability to derive positive growth from their illness experience.
Meeus M(1), Nijs J(2), Vanderheiden T(3), Baert I(4), Descheemaeker F(5), Struyf F(4).	(1)Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium Pain in Motion Research Group, Belgium mira.meeus@ugent.be.	The effect of relaxation therapy on autonomic functioning, symptoms and daily functioning, in patients with chronic fatigue syndrome or fibromyalgia: a systematic review.	Clin Rehabil. 2015 Mar;29(3):221-33. doi: 10.1177/0269215514542635. Epub 2014 Sep 8.	OBJECTIVE: To establish the effects of relaxation therapy on autonomic function, pain, fatigue and daily functioning in patients with chronic fatigue syndrome or fibromyalgia. METHOD: A systematic literature study was performed. Using specific keywords related to fibromyalgia or chronic fatigue syndrome and relaxation therapy, the electronic databases PubMed and Web of Science were searched. Included articles were assessed for their risk of bias and relevant information regarding relaxation was extracted. The review was conducted and reported according to the PRISMA-statement. RESULTS: Thirteen randomized clinical trials of sufficient quality were included, resulting in a total of 650 fibromyalgia patients (11 studies) and 88 chronic fatigue syndrome patients (3 studies). None of the studies reported effects on autonomic function. Six studies reported the effect of guided imagery on pain and daily functioning in fibromyalgia. The acute effect of a single session of guided imagery was studied in two studies and seems beneficial for pain relief. For other relaxation techniques (eg. muscle relaxation, autogenic training) no conclusive evidence was found for the effect on pain and

				functioning in fibromyalgia patients comparison to multimodal treatment programs. For fatigue a multimodal approach seemed better than relaxation, as shown in the sole three studies on chronic fatigue syndrome patients. CONCLUSION: There is moderate evidence for the acute effect of guided imagery on pain, although the content of the visualization is a matter of debate. Other relaxation formats and the effects on functionality and autonomic function require further study.
Meeus M(1), Hermans L, Ickmans K, Struyf F, Van Cauwenbergh D, Bronckaerts L, De Clerck LS, Moorken G, Hans G, Grosemans S, Nijs J.	(1)Departments of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium; Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium; Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium; "Pain in Motion" Research Group.	Endogenous pain modulation in response to exercise in patients with rheumatoid arthritis, patients with chronic fatigue syndrome and comorbid fibromyalgia, and healthy controls: a double-blind randomized controlled trial.	Pain Pract. 2015 Feb;15(2):98-106. doi: 10.1111/papr.12181. Epub 2014 Feb 17.	OBJECTIVE: Temporal summation (TS) of pain, conditioned pain modulation (CPM), and exercise-induced analgesia (EIA) are often investigated in chronic pain populations as an indicator for enhanced pain facilitation and impaired endogenous pain inhibition, respectively, but interactions are not yet clear both in healthy controls and in chronic pain patients. Therefore, the present double-blind randomized placebo-controlled study evaluates pains cores, TS, and CPM in response to exercise in healthy controls, patients with chronic fatigue syndrome and comorbid fibromyalgia (CFS/FM), and patients with rheumatoid arthritis (RA), both under placebo and paracetamol condition. METHODS: Fifty-three female volunteers - of which 19 patients with CFS/FM, 16 patients with RA, and 18 healthy controls - underwent a submaximal exercise test on a bicycle ergometer on 2 different occasions (paracetamol vs. placebo), with an interval of 7 days. Before and after exercise, participants rated pain intensity during TS and CPM. RESULTS: Patients with rheumatoid arthritis showed decreased TS after exercise, both after paracetamol and placebo ($P < 0.05$). In patients with CFS/FM, results were less univocal. A nonsignificant decrease in TS was only observed after taking paracetamol. CPM responses to exercise are inconclusive, but seem to worsen after exercise. No adverse effects were seen. CONCLUSION: This study evaluates pain scores, TS, and CPM in response to submaximal exercise in 2 different chronic pain populations and healthy controls. In patients with RA, exercise had positive effects on TS, suggesting normal EIA. In patients with CFS/FM, these positive effects were only observed after paracetamol and results were inconsistent.
Mensah F(1), Bansal A(2), Berkovitz S(3), Sharma A(1), Reddy V(1), Leandro MJ(1), Cambridge G(1).	(1)Department of Rheumatology Research, Division of Medicine, University College of London, London, United Kingdom.	Extended B-cell phenotype in patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A cross-sectional study.	Clin Exp Immunol. 2015 Dec 8. doi: 10.1111/cei.12749. [Epub ahead of print]	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a heterogeneous condition of unknown etiology characterized by multiple symptoms including fatigue, post-exertional malaise and cognitive impairment, lasting for at least 6 months. Recently, two clinical trials of B-cell depletion therapy with rituximab (anti-CD20) reported convincing improvement in symptoms. A possible but undefined role for B-cells has therefore been proposed. Studies of the relative percentages of B-cell subsets in patients with ME/CFS have not revealed any reproducible differences from healthy

	(2)Department of Immunology, Epsom and St Helier University Hospitals NHS Trust, London, United Kingdom. (3)Department of Neurology, Royal London Hospital Of Integrated Medicine, London, United Kingdom.			controls (HC). In order to explore whether more subtle alterations in B-cell subsets related to B-cell differentiation exist in ME/CFS patients we used flow cytometry to immunophenotype CD19(+) B-cells. The panel utilized IgD, CD27 and CD38 (classical B-cell subsets) together with additional markers. A total of 38 patients fulfilling Canadian, Centre for Disease Control, and Fukuda ME/CFS criteria and 32 age/sex-matched HC were included. We found no difference in percentages of classical subsets between ME/CFS patients and HC. However, we observed an increase in frequency ($p<0.01$) and expression (MFI; $p=0.03$) of CD24 on total B-cells, confined to IgD(+) subsets. Within memory subsets, a higher frequency of CD21(+) CD38(-) B-cells (>20%) was associated with the presence of ME/CFS (Odds ratio: 3.47 (1.15-10.46); $p=0.03$) compared with HC and there was a negative correlation with disease duration. In conclusion, we identified possible changes in B-cell phenotype in patients with ME/CFS. These may reflect altered B-cell function and if confirmed in other patient cohorts, could provide a platform for studies based on clinical course or responsiveness to rituximab-therapy.
Meyer B(1), Nguyen CB(1), Moen A(2), Fagermoen E(3), Sulheim D(4), Nilsen H(5), Wyller VB(6), Gjerstad J(2).	(1)Dept. of Paediatrics, Akershus University Hospital, Oslo, Norway.	Maintenance of Chronic Fatigue Syndrome (CFS) in Young CFS Patients Is Associated with the 5-HTTLPR and SNP rs25531 A > G Genotype.	PLoS One. 2015 Oct 16;10(10):e0140883. doi: 10.1371/journal.pone.0140883. eCollection 2015.	Earlier studies have shown that genetic variability in the SLC6A4 gene encoding the serotonin transporter (5-HTT) may be important for the re-uptake of serotonin (5-HT) in the central nervous system. In the present study we investigated how the 5-HTT genotype i.e. the short (S) versus long (L) 5-HTTLPR allele and the SNP rs25531 A > G affect the physical and psychosocial functioning in patients with chronic fatigue syndrome (CFS). All 120 patients were recruited from The Department of Paediatrics at Oslo University Hospital, Norway, a national referral center for young CFS patients (12-18 years). Main outcomes were number of steps per day obtained by an accelerometer and disability scored by the Functional Disability Inventory (FDI). Patients with the 5-HTT SS or SLG genotype had a significantly lower number of steps per day than patients with the 5-HTT LALG, SLA or LALA genotype. Patients with the 5-HTT SS or SLG genotype also had a significantly higher FDI score than patients with the 5-HTT LALG, SLA or LALA genotype. Thus, CFS patients with the 5-HTT SS or SLG genotype had worse 30 weeks outcome than CFS patients with the 5-HTT LALG, SLA or LALA genotype. The present study suggests that the 5-HTT genotype may be a factor that contributes to maintenance of CFS.
Miglis MG(1), Muppidi S(2), Feakins C(2), Fong L(2), Prieto T(2), Jaradeh S(2).	(1)Division of Autonomic Neurology, Stanford University Medical Center, 211 Quarry Rd, 2nd Fl, MC 5992, Stanford, CA, 94305, USA. mmiglis@stanford.edu. (2)Division of Autonomic Neurology,	Sleep disorders in patients with postural tachycardia syndrome.	Clin Auton Res. 2015 Dec 22. [Epub ahead of print]	OBJECTIVE: Patients with postural tachycardia syndrome (POTS) often describe symptoms of fatigue, sleepiness, and lack of refreshing sleep. We aimed to provide further objective measures of sleep in patients with POTS. METHODS: POTS patients ($n = 18$) were selected based on autonomic testing and evaluation at our center. Controls ($n = 16$) of similar age, gender, and BMI were selected from new patients referred to the Stanford Sleep Disorders Clinic for any sleep-related complaint. All patients underwent polysomnography and completed several sleep questionnaires and a 2-week sleep diary. RESULTS: POTS patients and control subjects were of similar age (27 ± 10.2 vs. 29 ± 5.4 years, $p = 0.92$) and Body Mass Index (21 ± 3.8 vs. 24 ± 4.1, $p = 0.14$). The majority of subjects in both groups were females (72 % POTS vs. 81 %

	Stanford University Medical Center, 211 Quarry Rd, 2nd Fl, MC 5992, Stanford, CA, 94305, USA.			controls). POTS patients scored higher on subjective fatigue scales but not sleepiness scales. POTS patients scored in the normal range on the BDI and the "evening" category on the MEQ. Their sleep diaries were not different from controls. With the exception of mild OSA, slightly reduced %REM and prolonged REM latency, their PSG data were normal and no different from controls. CONCLUSIONS: It is unlikely that the sleep-related complaints of POTS patients are the result of a primary sleep disorder unique to POTS. We propose that a combination of factors such as body fatigue, chronic pain, and other somatic symptoms common in POTS patients might be the underlying reason for sleep-related symptoms in POTS.
Mihelicova M(1), Siegel Z(2), Evans M(2), Brown A(2), Jason L(2).	(1)DePaul University, USA mmiheli1@depaul.edu. (2)DePaul University, USA.	Caring for people with severe myalgic encephalomyelitis: An interpretative phenomenological analysis of parents' experiences.	J Health Psychol. 2015 Jun 10. pii: 1359105315587137. [Epub ahead of print]	Experiences of parents who care for sons or daughters with severe myalgic encephalomyelitis are rarely discussed within the literature. Narratives of parent-carers in Lost Voices from a Hidden Illness were analyzed using interpretative phenomenological analysis. This study aimed to give voices to those who care for individuals with myalgic encephalomyelitis and are often stigmatized and inform future research supporting parent-carers. Results included themes of identity change, guilt, feeling like outsiders, uncertainty, changing perceptions of time, coping mechanisms, and improvement/symptom management. Findings could inform the development of carer-focused interventions and provide vital information to health professionals about parent-carers' lived experience.
Miller RR(1), Reid WD(2), Mattman A(3), Yamabayashi C(4), Steiner T(5), Parker S(6), Gardy J(7), Tang P(8), Patrick DM(9,)(10).	(1)School of Population and Public Health, British Columbia Centre for Disease Control, University of British Columbia, 655 West 12th Avenue, Vancouver, BC, V5Z 4R4, Canada. ruth.miller@bccdc.ca.	Submaximal exercise testing with near-infrared spectroscopy in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome patients compared to healthy controls: a case-control study.	J Transl Med. 2015 May 20;13:159. doi: 10.1186/s12967-015-0527-8.	BACKGROUND: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a debilitating illness. Symptoms include profound fatigue and distinctive post-exertional malaise (PEM). We asked whether a submaximal exercise test would prove useful for identifying different patterns of tissue oxygen utilization in individuals with ME/CFS versus healthy subjects. Such a test has potential to aid with ME/CFS diagnosis, or to characterize patients' illness. METHODS: A case-control study of 16 patients with ME/CFS compared to 16 healthy controls completing a 3-min handgrip protocol was performed. Response was measured using near-infrared spectroscopy, resulting in measurements of oxygenated (O2Hb) and deoxygenated hemoglobin (HHb) over wrist extensors and flexors. Changes in O2Hb (delta (d)O2Hb) and HHb (dHHb) absorbance between the first and last contraction were calculated, as were the force-time product of all contractions, measured as tension-time index (TTI), and ratings of perceived exertion (RPE). RESULTS: Individuals with ME/CFS demonstrated smaller dO2Hb and dHHb than controls. However, after adjusting for TTI and change in total hemoglobin (delta (d)tHb), differences in dO2Hb and dHHb were reduced, with large overlapping variances. RPE was significantly higher for cases than controls, particularly at rest. CONCLUSIONS: Relative to controls, participants with ME/CFS demonstrated higher RPE, lower TTI, and reduced dO2Hb and dHHb during repetitive handgrip exercise, although considerable variance was observed. With further study, submaximal exercise testing may prove useful for stratifying patients with a lower propensity for inducing PEM, and have the ability to establish baseline intensities for exercise prescription.

Miwa K(1).	(1)Department of Internal Medicine, Miwa Naika Clinic, 1-4-3 Shintomicho, Toyama, 930-0002, Japan. info@miwa-naika.com.	Variability of postural orthostatic tachycardia in patients with myalgic encephalomyelitis and orthostatic intolerance.	Heart Vessels. 2015 Sep 15. [Epub ahead of print]	Central nervous system dysfunction with myalgic encephalomyelitis (ME) has been suggested as the main cause of chronic fatigue syndrome. Fluctuation of the symptom severity and hierarchy is a characteristic feature in ME patients. The characteristics of the sympathetic activation may differ between the "good days" and "bad days" in them. Twenty-four ME patients with orthostatic intolerance underwent a conventional 10-min active standing test and echocardiography both on a "good day" and a "bad day", defined according to the severity of their symptoms. The mean heart rate at rest was significantly higher on the "bad days" than on the "good days". During the standing test on a "bad day", 5 patients (21 %) failed to maintain an upright posture for 10 min, whereas on a "good day" all the 24 patients maintained it. Postural orthostatic tachycardia (POT) (increase in heart rate ≥30 beats/min) or severe POT (heart rate ≥120 beats/min) was observed on the "bad days" in 10 patients (43 %) who did not suffer from the severe tachycardia on the "good days", suggesting the exaggerated sympathetic nervous activation. In contrast, POT did not occur or severe POT was attenuated on the "bad days" in 5 patients (21 %) who developed POT or severe POT on the "good days", suggesting the impaired sympathetic activation. Echocardiography revealed significantly lower mean values of both the left ventricular end-diastolic diameter and stroke volume index on the "bad days" compared with the "good days". In conclusion, in ME patients with orthostatic intolerance, the exaggerated activation of the sympathetic nervous system while standing appears to switch to the impaired sympathetic activation after the system is loaded with the additional accentuated stimuli associated with the preload reduction.
Miwa K(1).	(1)Department of Internal Medicine, Miwa Naika Clinic, 1-4-3 Shintomicho, Toyama, 930-0002, Japan, info@miwa-naika.com.	Cardiac dysfunction and orthostatic intolerance in patients with myalgic encephalomyelitis and a small left ventricle.	Heart Vessels. 2015 Jul;30(4):484-9. doi: 10.1007/s00380-014-0510-y. Epub 2014 Apr 16.	The etiology of chronic fatigue syndrome (CFS) is unknown. Myalgic encephalomyelitis (ME) has been recently postulated to be the cause of CFS. Orthostatic intolerance (OI) has been known as an important symptom in predicting quality of life in CFS patients. Cardiac function may be impaired in patients with ME. The presence or absence of OI was determined both symptomatically and by using a 10-min stand-up test in 40 ME patients. Left ventricular (LV) dimensions and function were determined echocardiographically in the ME patients compared to 40 control subjects. OI was noted in 35 (97%) of the 36 ME patients who could stand up quickly. The mean values for the cardiothoracic ratio, systemic systolic and diastolic pressures, LV end-diastolic diameter (EDD), LV end-systolic diameter, stroke volume index, cardiac index and LV mass index were all significantly smaller in the ME group than in the controls. Both a small LVEDD (<40 mm, 45 vs. 3%) and a low cardiac index (<2 l/ min/mm2, 53 vs. 8%) were significantly more common in the ME group than in the controls. Both heart rate and LV ejection fraction were similar between the groups. In conclusion, a small LV size with a low cardiac output was common in ME patients, in whom OI was extremely common. Cardiac dysfunction with a small heart appears to be related to the symptoms of ME.
Miyamoto ST(1),	(1)Escola Paulista de	Assessment of fatigue and	Rev Bras Reumatol. 2015	OBJECTIVE: To perform a cross-cultural adaptation and validation of the Profile of

Paganotti MA(2), Serrano ÉV(3), Giovelli RA(3), Valim V(4).	Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brasil; Universidade Federal do Espírito Santo, Vitória, ES, Brasil. (2)Universidade Vila Velha, Vila Velha, ES, Brasil. (3)Universidade Federal do Espírito Santo, Vitória, ES, Brasil; Escola Superior de Ciências, Santa Casa de Misericórdia de Vitória, Vitória, ES, Brasil. (4)Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, SP, Brasil; Universidade Federal do Espírito Santo, Vitória, ES, Brasil. Electronic address: val.valim@gmail.com.	dryness in primary Sjögren's syndrome: Brazilian version of "Profile of Fatigue and Discomfort - Sicca Symptoms Inventory (short form) (PROFAD-SSI-SF)".	Mar-Apr;55(2):113-22. doi: 10.1016/j.rbr.2014.10.002 . Epub 2014 Nov 7.	Fatigue and Discomfort - Sicca Symptoms Inventory (short form) (PROFAD-SSI-SF) questionnaire assessing the subjective aspects of the symptoms of primary Sjögren syndrome (pSS), for the Brazilian Portuguese language. METHOD: Conceptual, of the item, semantic and operational equivalences were evaluated. The Brazilian version of PROFAD-SSI-SF was administered to 62 women with pSS according to the European-American consensus 2002 to assess measurement equivalence. α-Cronbach was used for internal consistency; intraclass correlation coefficient (ICC) for intraobserver reproducibility; and Spearman correlation coefficient for validity by comparing with Patient Global Assessment (PaGA), EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI), Functional Assessment of Chronic Illness Therapy Fatigue Subscale (FACIT-F) and EuroQOL (EQ-5D). RESULTS: The internal consistency of PROFAD, SSI and total score was 0.80; 0.78; and 0.87, respectively. The intraobserver reproducibility of total PROFAD was 0.89; of total SSI of 0.86; and total score of 0.89. In terms of validity, PROFAD correlated significantly with PaGA (r = 0.50), FACIT-F (r = 0.59), ESSPRI (r = 0.58) and all domains of EQ-5D, with the exception of Mobility. On the other hand, SSI correlated significantly with PaGA (r = 0.43), FACIT-F (r = 0.57), ESSPRI (r = 0.55) and most areas of EQ-5D. The total score of PROFAD-SSI-SF had a non-statistically significant correlation only with Mobility domain and with 1-100 range of EQ-5D. CONCLUSION: The Portuguese version of PROFAD-SSI-SF proved to be an adaptable, reproducible and valid tool for the Brazilian Portuguese language.
Mizuno K(1), Tanaka M(2), Tanabe HC(3), Joudoi T(4), Kawatani J(4), Shigihara Y(2), Tomoda A(5), Miike T(6), Imai-Matsumura K(7), Sadato N(8), Watanabe Y(9).	(1)Pathophysiological and Health Science Team, RIKEN Center for Life Science Technologies, 6-7-3 Minatojima-minamimachi, Chuo-ku, Kobe, Hyogo 650-0047, Japan ; Department of Medical Science on Fatigue, Osaka City University Graduate School of Medicine, 1-	Less efficient and costly processes of frontal cortex in childhood chronic fatigue syndrome.	Neuroimage Clin. 2015 Sep 10;9:355-68. doi: 10.1016/j.nicl.2015.09.001. eCollection 2015.	The ability to divide one's attention deteriorates in patients with childhood chronic fatigue syndrome (CCFS). We conducted a study using a dual verbal task to assess allocation of attentional resources to two simultaneous activities (picking out vowels and reading for story comprehension) and functional magnetic resonance imaging. Patients exhibited a much larger area of activation, recruiting additional frontal areas. The right middle frontal gyrus (MFG), which is included in the dorsolateral prefrontal cortex, of CCFS patients was specifically activated in both the single and dual tasks; this activation level was positively correlated with motivation scores for the tasks and accuracy of story comprehension. In addition, in patients, the dorsal anterior cingulate gyrus (dACC) and left MFG were activated only in the dual task, and activation levels of the dACC and left MFG were positively associated with the motivation and fatigue scores, respectively. Patients with CCFS exhibited a wider area of activated frontal regions related to attentional resources in order to increase their poorer task performance with massive mental effort. This is likely to be less efficient and costly in

	4-3 Asahimachi, Abeno-ku, Osaka City, Osaka 545-8585, Japan.			terms of energy requirements. It seems to be related to the pathophysiology of patients with CCFS and to cause a vicious cycle of further increases in fatigue.
Mohanty AF(1), Muthukutty A, Carter ME, Palmer MN, Judd J, Helmer D, McAndrew LM, Garvin JH, Samore MH, Gundlapalli AV.	(1)*Informatics, Decision Enhancement, and Surveillance (IDEAS) Center, VA Salt Lake City Health Care System, Department of Internal Medicine, University of Utah School of Medicine †Department of Biomedical Informatics, University of Utah School of Medicine, Salt Lake City, UT ‡Department of Veteran Affairs, War Related Illness and Injury Study Center, New Jersey Health Care System, East Orange, NJ §Department of Education and Counseling Psychology, University of Albany, Albany, NY.	Chronic multisymptom illness among female Veterans deployed to Iraq and Afghanistan.	Med Care. 2015 Apr;53(4 Suppl 1):S143-8. doi: 10.1097/MLR.0000000000000314.	BACKGROUND: Chronic multisymptom illness (CMI) may be more prevalent among female Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) deployed Veterans due to deployment-related experiences. OBJECTIVES: To investigate CMI-related diagnoses among female OEF/OIF/OND Veterans. RESEARCH DESIGN: We estimated the prevalence of the International Classification of Disease-9th edition-Clinical Modification coded CMI-related diagnoses of chronic fatigue syndrome, fibromyalgia (FM), and irritable bowel syndrome (IBS) among female OEF/OIF/OND Veterans with Veterans Health Administration (VHA) visits, FY2002-2012 (n=78,435). We described the characteristics of female Veterans with and without CMI-related diagnoses and VHA settings of first CMI-related diagnoses. RESULTS: The prevalence of CMI-related diagnoses among female OEF/OIF/OND Veterans was 6397 (8.2%), over twice as high as the prevalence 95,424 (3.9%) among the totality of female Veterans currently accessing VHA (P<0.01). There were statistically significant differences in age, education, marital status, military component, service branch, and proportions of those with depression and/or post-traumatic stress disorder diagnoses across females with and without CMI-related diagnoses. Diagnoses were mainly from primary care, women's health, and physical medicine and rehabilitation clinics. CONCLUSIONS: CMI-related diagnoses were more prevalent among female OEF/OIF/OND Veterans compared with all female Veterans who currently access VHA. Future studies of the role of mental health diagnoses as confounders or mediators of the association of OEF/OIF/OND deployment and CMI are warranted. These and other factors associated with CMI may provide a basis for enhanced screening to facilitate recognition of these conditions. Further work should evaluate models of care and healthcare utilization related to CMI in female Veterans.
Monaco S(1), Mariotto S(1), Ferrari S(1), Calabrese M(1), Zanusso G(1), Gajofatto A(1), Sansonno D(1), Dammacco F(1).	(1)Salvatore Monaco, Sara Mariotto, Sergio Ferrari, Massimiliano Calabrese, Gianluigi Zanusso, Alberto Gaiofatto, Department of Neurological and Movement Sciences,	Hepatitis C virus-associated neurocognitive and neuropsychiatric disorders: Advances in 2015.	World J Gastroenterol. 2015 Nov 14;21(42):11974-83. doi: 10.3748/wjg.v21.i42.11974.	Since its identification in 1989, hepatitis C virus (HCV) has emerged as a worldwide health problem with roughly 185 million chronic infections, representing individuals at high risk of developing cirrhosis and liver cancer. In addition to being a frequent cause of morbidity and mortality due to liver disease, HCV has emerged as an important trigger of lymphoproliferative disorders, owing to its lymphotropism, and of a wide spectrum of extra-hepatic manifestations (HCV-EHMs) affecting different organ systems. The most frequently observed HCV-EHMs include mixed cryoglobulinemia and cryoglobulinemic vasculitis, B-cell non-Hodgkin's lymphoma, nephropathies, thyreopathies, type 2 diabetes mellitus, cardiovascular diseases, and several

	University of Verona, 37134 Verona, Italy.			neurological conditions. In addition, neuropsychiatric disorders and neurocognitive dysfunction are reported in nearly 50% of patients with chronic HCV infection, which are independent of the severity of liver disease or HCV replication rates. Fatigue, sleep disturbance, depression and reduced quality of life are commonly associated with neurocognitive alterations in patients with non-cirrhotic chronic HCV infection, regardless of the stage of liver fibrosis and the infecting genotype. These manifestations, which are the topic of this review, typically occur in the absence of structural brain damage or signal abnormalities on conventional brain magnetic resonance imaging (MRI), although metabolic and microstructural changes can be detected by in vivo proton magnetic resonance spectroscopy, perfusion-weighted and diffusion tensor MRI, and neurophysiological tests of cognitive processing. Several lines of evidence, including comparative and longitudinal neuropsychological assessments in patients achieving spontaneous or treatment-induced viral clearance, support a major pathogenic role for HCV in neuropsychiatric and neurocognitive disorders.
Moriya J(1), He Q(1), Uenishi H(1), Akazawa S(1), Yamakawa J(1), Kobayashi J(1), Ishigaki Y(2).	(1)Department of General Internal Medicine, Kanazawa Medical University, Ishikawa 920-0293, Japan. (2)Division of Molecular and Cell Biology, Kanazawa Medical University, Ishikawa 920-0293, Japan.	Induction Murine Models of Chronic Fatigue Syndrome by Brucella abortus Antigen Injections: Is Anemia Induced or Not?	Biomed Res Int. 2015;2015:191489. doi: 10.1155/2015/191489. Epub 2015 Jun 11.	To investigate whether Brucella abortus (BA) antigen injections lead to anemia, and to establish an appropriate Chronic Fatigue Syndrome (CFS) animal model by BA injections, 6 repeated injections of BA antigen were fulfilled every 2 weeks. At a high dose of 1∗10(10) particles/mouse, anemia was induced within 2 weeks and then recovered a lot at the end of the research, while at a moderate dose of 1∗10(8) (3 injections) shifting to 1∗10(9)/mouse (3 injections) anemia was absent. In both groups running wheel activity remained very low even 6 weeks after the last injection.
Morris G(1), Berk M(2,)(3), Walder K(4), Maes M(5,)(6).	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, SA15 2LW, Wales, UK. (2)IMPACT Strategic Research Centre, School of Medicine, Deakin University, Geelong, Australia. (3)Orygen, The National Centre of Excellence in Youth Mental Health, Department of Psychiatry and The Florey Institute of	The Putative Role of Viruses, Bacteria, and Chronic Fungal Biotoxin Exposure in the Genesis of Intractable Fatigue Accompanied by Cognitive and Physical Disability.	Mol Neurobiol. 2015 Jun 17. [Epub ahead of print]	Patients who present with severe intractable apparently idiopathic fatigue accompanied by profound physical and or cognitive disability present a significant therapeutic challenge. The effect of psychological counseling is limited, with significant but very slight improvements in psychometric measures of fatigue and disability but no improvement on scientific measures of physical impairment compared to controls. Similarly, exercise regimes either produce significant, but practically unimportant, benefit or provoke symptom exacerbation. Many such patients are afforded the exclusionary, non-specific diagnosis of chronic fatigue syndrome if rudimentary testing fails to discover the cause of their symptoms. More sophisticated investigations often reveal the presence of a range of pathogens capable of establishing life-long infections with sophisticated immune evasion strategies, including Parvoviruses, HHV6, variants of Epstein-Barr, Cytomegalovirus, Mycoplasma, and Borrelia burgdorferi. Other patients have a history of chronic fungal or other biotoxin exposure. Herein, we explain the epigenetic factors that may render such individuals susceptible to the chronic pathology induced by such agents, how such agents induce pathology, and, indeed,

	Neuroscience and Mental Health, The University of Melbourne, Parkville, Australia. (4)Centre for Molecular and Medical Research, School of Medicine, Deakin University, Geelong, Australia. (5)IMPACT Strategic Research Centre, School of Medicine, Deakin University, Geelong, Australia. dr.michaelmaes@hotmail.com. (6)Department of Psychiatry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. dr.michaelmaes@hotmail.com.			how such pathology can persist and even amplify even when infections have cleared or when biotoxin exposure has ceased. The presence of active, reactivated, or even latent Herpes virus could be a potential source of intractable fatigue accompanied by profound physical and or cognitive disability in some patients, and the same may be true of persistent Parvovirus B12 and mycoplasma infection. A history of chronic mold exposure is a feasible explanation for such symptoms, as is the presence of B. burgdorferi. The complex tropism, life cycles, genetic variability, and low titer of many of these pathogens makes their detection in blood a challenge. Examination of lymphoid tissue or CSF in such circumstances may be warranted.
Morris G(1), Berk M(2,)(3,)(4,)(5), Galecki P(6), Walder K(7), Maes M(8,)(9,)(10,)(11).	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, SA152LW, Wales, UK.	The Neuro-Immune Pathophysiology of Central and Peripheral Fatigue in Systemic Immune-Inflammatory and Neuro-Immune Diseases.	Mol Neurobiol. 2015 Jan 20. [Epub ahead of print]	Many patients with systemic immune-inflammatory and neuro-inflammatory disorders, including depression, rheumatoid arthritis, systemic lupus erythematosus, Sjögren's disease, cancer, cardiovascular disorder, Parkinson's disease, multiple sclerosis, stroke, and chronic fatigue syndrome/myalgic encephalomyelitis, endure pathological levels of fatigue. The aim of this narrative review is to delineate the wide array of pathways that may underpin the incapacitating fatigue occurring in systemic and neuro-inflammatory disorders. A wide array of immune, inflammatory, oxidative and nitrosative stress (O&NS), bioenergetic, and neurophysiological abnormalities are involved in the etiopathology of these disease states and may underpin the incapacitating fatigue that accompanies these disorders. This range of abnormalities comprises: increased levels of pro-inflammatory cytokines, e.g., interleukin-1 (IL-1), IL-6, tumor necrosis factor (TNF) α and interferon (IFN) α; O&NS-induced muscle fatigue; activation of the Toll-Like Receptor Cycle through pathogen-associated (PAMPs) and damage-associated (DAMPs) molecular patterns, including heat shock proteins; altered glutaminergic and dopaminergic neurotransmission; mitochondrial dysfunctions; and O&NS-induced

				defects in the sodium-potassium pump. Fatigue is also associated with altered activities in specific brain regions and muscle pathology, such as reductions in maximum voluntary muscle force, downregulation of the mitochondrial biogenesis master gene peroxisome proliferator-activated receptor gamma coactivator 1-alpha, a shift to glycolysis and buildup of toxic metabolites within myocytes. As such, both mental and physical fatigue, which frequently accompany immune-inflammatory and neuro-inflammatory disorders, are the consequence of interactions between multiple systemic and central pathways.
Morris G, Berk M, Walder K, Maes M.		Central pathways causing fatigue in neuro-inflammatory and autoimmune illnesses.	BMC Med. 2015 Feb 6;13:28. doi: 10.1186/s12916-014-0259-2.	BACKGROUND: The genesis of severe fatigue and disability in people following acute pathogen invasion involves the activation of Toll-like receptors followed by the upregulation of proinflammatory cytokines and the activation of microglia and astrocytes. Many patients suffering from neuroinflammatory and autoimmune diseases, such as multiple sclerosis, Parkinson's disease and systemic lupus erythematosus, also commonly suffer from severe disabling fatigue. Such patients also present with chronic peripheral immune activation and systemic inflammation in the guise of elevated proinflammtory cytokines, oxidative stress and activated Toll-like receptors. This is also true of many patients presenting with severe, apparently idiopathic, fatigue accompanied by profound levels of physical and cognitive disability often afforded the non-specific diagnosis of chronic fatigue syndrome. DISCUSSION: Multiple lines of evidence demonstrate a positive association between the degree of peripheral immune activation, inflammation and oxidative stress, gray matter atrophy, glucose hypometabolism and cerebral hypoperfusion in illness, such as multiple sclerosis, Parkinson's disease and chronic fatigue syndrome. Most, if not all, of these abnormalities can be explained by a reduction in the numbers and function of astrocytes secondary to peripheral immune activation and inflammation. This is also true of the widespread mitochondrial dysfunction seen in otherwise normal tissue in neuroinflammatory, neurodegenerative and autoimmune diseases and in many patients with disabling, apparently idiopathic, fatigue. Given the strong association between peripheral immune activation and neuroinflammation with the genesis of fatigue the latter group of patients should be examined using FLAIR magnetic resonance imaging (MRI) and tested for the presence of peripheral immune activation. SUMMARY: It is concluded that peripheral inflammation and immune activation, together with the subsequent activation of glial cells and mitochondrial damage, likely account for the severe levels of intractable fatigue and disability seen in many patients with neuroimmune and autoimmune diseases.This would also appear to be the case for many patients afforded a diagnosis of Chronic Fatigue Syndrome.
Morris G, Carvalho A, Anderson G, Galecki P, Maes	(1)IMPACT Strategic Research Center Barwon Health Deakin University Geelong,	The many neuroprogressive actions of tryptophan catabolites (TRYCATs) that may be	Curr Pharm Des. 2015 Dec 14. [Epub ahead of print]	Many if not all chronic medical, neurodegenerative and neuroprogressive illnesses are characterised by chronic immune activation, oxidative and nitrosative stress (O&NS) and systemic inflammation. These environmental factors notably elevated pro-inflammatory cytokines activate indoleamine 2,3-dioxygenase (IDO) leading to an

M(1).	Vic Australia. dr.michaelmaes@hotmail.com.	associated with the pathophysiology of neuro-immune disorders.		upregulated tryptophan catabolite (TRYCAT) pathway of tryptophan degradation in the periphery and in the brain. In such conditions the TRYCAT pathway becomes the predominant system for tryptophan degradation in all body compartments. In this paper we review the pathways whereby TRYCATs may play a role in neuro-inflammatory and neuroprogressive disease. Thus chronic activation of the TRYCAT pathway leads to the production of a range of neuroactive, neuroprotective and neurotoxic TRYCATs. Some TRYCATs such as quinolinic acid act as potent neurotoxins which inhibit ATP production by mitochondria, provoke increases in O&NS, disrupt neuron glial communication and blood brain barrier integrity, induce apoptosis of glial cells, directly damage neurons and function as a N-methyl D-aspartate (NMDA) receptor agonist. Other TRYCATs such as kynurenic acid function as antagonists of NMDA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid and kainate receptors and act to regulate levels of glutamate and dopamine. The neuroprotective functions of this TRYCAT are likely exercised via engagement with alpha7 nicotinic acetylcholine and aryl hydrocarbon receptors but the neuroprotective effects stemming from elevated kynurenic acid levels come at the price of severely compromised neurocognitive function and emotional processing. Other TRYCATS also possess neurotoxic or neuroprotective properties via pro-oxidant and antioxidant effects. Here we discuss the involvement of the abovementioned TRYCAT pathways in schizophrenia, Alzheimer's disease and chronic fatigue syndrome.
Morris G(1), Walder K, Puri BK, Berk M, Maes M.	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, SA152LW, Wales, UK.	The Deleterious Effects of Oxidative and Nitrosative Stress on Palmitoylation, Membrane Lipid Rafts and Lipid-Based Cellular Signalling: New Drug Targets in Neuroimmune Disorders.	Mol Neurobiol. 2015 Aug 27. [Epub ahead of print]	Oxidative and nitrosative stress (O&NS) is causatively implicated in the pathogenesis of Alzheimer's and Parkinson's disease, multiple sclerosis, chronic fatigue syndrome, schizophrenia and depression. Many of the consequences stemming from O&NS, including damage to proteins, lipids and DNA, are well known, whereas the effects of O&NS on lipoprotein-based cellular signalling involving palmitoylation and plasma membrane lipid rafts are less well documented. The aim of this narrative review is to discuss the mechanisms involved in lipid-based signalling, including palmitoylation, membrane/lipid raft (MLR) and n-3 polyunsaturated fatty acid (PUFA) functions, the effects of O&NS processes on these processes and their role in the abovementioned diseases. S-palmitoylation is a post-translational modification, which regulates protein trafficking and association with the plasma membrane, protein subcellular location and functions. Palmitoylation and MRLs play a key role in neuronal functions, including glutamatergic neurotransmission, and immune-inflammatory responses. Palmitoylation, MLRs and n-3 PUFAs are vulnerable to the corruptive effects of O&NS. Chronic O&NS inhibits palmitoylation and causes profound changes in lipid membrane composition, e.g. n-3 PUFA depletion, increased membrane permeability and reduced fluidity, which together lead to disorders in intracellular signal transduction, receptor dysfunction and increased neurotoxicity. Disruption of lipid-based signalling is a source of the neuroimmune disorders involved in the pathophysiology of the abovementioned diseases. n-3 PUFA supplementation is a rational therapeutic approach targeting

				disruptions in lipid-based signalling.
Morris G(1), Berk M(2,)(3,)(4,)(5).	(1)Tir Na Nog, Bryn Road seaside 87, Llanelli, Cardiff, Wales, SA152LW, UK. activatedmicroglia@gmail.com. (2)IMPACT Strategic Research Centre, School of Medicine, Deakin University, PO Box 291, Geelong, 3220, Australia. mikebe@barwonhealth.org.au. (3)Orygen Youth Health Research Centre and the Centre of Youth Mental Health, Poplar Road 35, Parkville, 3052, Australia. mikebe@barwonhealth.org.au. (4)The Florey Institute for Neuroscience and Mental Health, University of Melbourne, Kenneth Myer Building, Royal Parade 30, Parkville, 3052, Australia. mikebe@barwonhealth.org.au. (5)Department of Psychiatry, University of Melbourne, Level 1 North, Main Block, Royal Melbourne Hospital, Parkville, 3052, Australia.	The many roads to mitochondrial dysfunction in neuroimmune and neuropsychiatric disorders.	BMC Med. 2015 Apr 1;13:68. doi: 10.1186/s12916-015-0310-y.	BACKGROUND: Mitochondrial dysfunction and defects in oxidative metabolism are a characteristic feature of many chronic illnesses not currently classified as mitochondrial diseases. Examples of such illnesses include bipolar disorder, multiple sclerosis, Parkinson's disease, schizophrenia, depression, autism, and chronic fatigue syndrome. DISCUSSION: While the majority of patients with multiple sclerosis appear to have widespread mitochondrial dysfunction and impaired ATP production, the findings in patients diagnosed with Parkinson's disease, autism, depression, bipolar disorder schizophrenia and chronic fatigue syndrome are less consistent, likely reflecting the fact that these diagnoses do not represent a disease with a unitary pathogenesis and pathophysiology. However, investigations have revealed the presence of chronic oxidative stress to be an almost invariant finding in study cohorts of patients afforded each diagnosis. This state is characterized by elevated reactive oxygen and nitrogen species and/or reduced levels of glutathione, and goes hand in hand with chronic systemic inflammation with elevated levels of pro-inflammatory cytokines. SUMMARY: This paper details mechanisms by which elevated levels of reactive oxygen and nitrogen species together with elevated pro-inflammatory cytokines could conspire to pave a major road to the development of mitochondrial dysfunction and impaired oxidative metabolism seen in many patients diagnosed with these disorders.

	mikebe@barwonhealth.org.au.			
Moylan S(1), Eyre HA(2), Berk M(3).	(1)School of Medicine, Deakin University, Geelong, VIC, Australia; Barwon Health, Geelong, VIC 3220, Australia. Electronic address: steven.moylan@deakin.edu.au.	Chronic fatigue syndrome: what is it and how to treat?	Lancet Psychiatry. 2015 Dec;2(12):1044-5. doi: 10.1016/S2215-0366(15)00475-7. Epub 2015 Oct 28.	
Nam TS(1), Choi SY(2), Park DJ(3), Lee SS(3), Kim YO(4), Kim MK(5).	(1)Department of Neurology, Chonnam National University Medical School, Gwangju, Korea.; Department of Neurology, Chonnam National University Hwasun Hospital, Hwasun, Korea. (2)Department of Biomedical Sciences, Chonnam National University Medical School, Gwangju, Korea. (3)Department of Rheumatology, Chonnam National University Medical School, Gwangju, Korea. (4)Department of Pediatrics, Chonnam National University Medical School, Gwangju, Korea. (5)Department of Neurology, Chonnam National	The Overlap between Fibromyalgia Syndrome and Myotonia Congenita.	J Clin Neurol. 2015 Apr;11(2):188-91. doi: 10.3988/jcn.2015.11.2.188. Epub 2014 Nov 11.	BACKGROUND: Fibromyalgia syndrome (FMS) is a complex disorder characterized by chronic widespread pain (CWP), multiple areas of tenderness, sleep disturbance, fatigue, and mood or cognitive dysfunction. Myotonia congenita (MC) is an inherited myopathic disorder that is caused by mutations in the gene encoding the skeletal muscle chloride channel, which can infrequently manifest as generalized muscle cramps or myalgia. CASE REPORT: The first case was a 33-year-old woman who complained of CWP and chronic headache occurring during pregnancy, and the second case was a 37-year-old man with CWP and depression who suffered from cold-induced muscle cramps. These two patients were initially diagnosed with FMS by rheumatologists, based on CWP of longer than 3 months duration and mechanical tenderness in specific body regions. However, these two FMS patients were subsequently also diagnosed with MC. CONCLUSIONS: These two cases are the first report of an overlap of CWP between FMS and MC.

	University Medical School, Gwangju, Korea. mkkim@jnu.ac.kr.			
Natarajan R(1), Northrop NA(1), Yamamoto BK(1).	(1)a Department of Neurosciences , University of Toledo College of Medicine , Toledo , OH , USA.	Protracted effects of chronic stress on serotonin-dependent thermoregulation.	Stress. 2015 Nov;18(6):668-76. doi: 10.3109/10253890.2015.1087502. Epub 2015 Sep 28.	Chronic stress is known to affect serotonin (5HT) neurotransmission in the brain and to alter body temperature. The body temperature is controlled in part, by the medial preoptic area (mPOA) of the hypothalamus. To investigate the effect of chronic stress on 5HT and how it affects body temperature regulation, we examined whether exposure to a chronic unpredictable stress (CUS) paradigm produces long-term alterations in thermoregulatory function of the mPOA through decreased 5HT neurotransmission. Adult male Sprague-Dawley rats underwent 21 d of CUS. Four days after the last stress exposure, basal body temperature in the home cage and body temperature in a cold room maintained at 10 °C were recorded. The CUS rats had significantly higher subcutaneous basal body temperature at 13:00 h compared to unstressed (NoStress) rats. Whereas the NoStress rats were able to significantly elevate body temperature from basal levels at 30 and 60 min of exposure to the cold room, the CUS rats showed a hypothermic response to the cold. Treatment during CUS with metyrapone, a corticosterone synthesis inhibitor, blocked stress-induced decrease in body temperature in response to the cold challenge. CUS also decreased 5HT transporter protein immunoreactivity in the mPOA and 5HT2A/C agonist injection into the mPOA after CUS exposure caused stressed rats to exhibit a sensitized hyperthermic response to cold. These results indicate that the CUS induced changes to the 5HTergic system alter mPOA function in thermoregulation. These findings help us to explain the mechanisms underlying chronic stress-induced disorders such as chronic fatigue syndrome wherein long lasting thermoregulatory deficits are observed.
Natelson BH(1), Vu D(2), Mao X(3), Weiduschat N(3), Togo F(4), Lange G(2), Blate M(2), Kang G(3), Coplan JD(5), Shungu DC(3).	(1)Department of Neurology, Mount Sinai Beth Israel, New York, New York. Electronic address: bnatelson@bethisraelny.org. (2)Department of Neurology, Mount Sinai Beth Israel, New York, New York. (3)Department of Radiology, Weill Medical College of Cornell University, New York, New York.	Effect of Milnacipran Treatment on Ventricular Lactate in Fibromyalgia: A Randomized, Double-Blind, Placebo-Controlled Trial.	J Pain. 2015 Nov;16(11):1211-9. doi: 10.1016/j.jpain.2015.08.004. Epub 2015 Aug 31.	Milnacipran, a serotonin/norepinephrine reuptake inhibitor, has been approved by the US Food and Drug Administration for the treatment of fibromyalgia (FM). This report presents the results of a randomized, double-blind, placebo-controlled trial of milnacipran conducted to test the hypotheses that a) similar to patients with chronic fatigue syndrome, patients with FM have increased ventricular lactate levels at baseline; b) 8 weeks of treatment with milnacipran will lower ventricular lactate levels compared with baseline levels and with ventricular lactate levels after placebo; and c) treatment with milnacipran will improve attention and executive function in the Attention Network Test compared with placebo. In addition, we examined the results for potential associations between ventricular lactate and pain. Baseline ventricular lactate measured by proton magnetic resonance spectroscopic imaging was found to be higher in patients with FM than in healthy controls ($F1,37 = 22.11$, $P < .0001$, partial $\eta(2) = .37$). Milnacipran reduced pain in patients with FM relative to placebo but had no effect on cognitive processing. At the end of the study, ventricular lactate levels in the milnacipran-treated group had decreased significantly compared with baseline and

	(4)Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, Tokyo, Japan. (5)Department of Psychiatry & Behavioral Sciences, State University of New York Downstate Medical Center, Brooklyn, New York.			after placebo (F1,18 = 8.18, P = .01, partial η(2) = .31). A significantly larger proportion of patients treated with milnacipran showed decreases in both ventricular lactate and pain than those treated with placebo (P = .03). These results suggest that proton magnetic resonance spectroscopic imaging measurements of lactate may serve as a potential biomarker for a therapeutic response in FM and that milnacipran may act, at least in part, by targeting the brain response to glial activation and neuroinflammation.PERSPECTIVE: Patients treated with milnacipran showed decreases in both pain and ventricular lactate levels compared with those treated with placebo, but, even after treatment, levels of ventricular lactate remained higher than in controls. The hypothesized mechanism for these decreases is via drug-induced reductions of a central inflammatory state.
Neu D(1), Mairesse O(2), Verbanck P(3), Le Bon O(4).	(1)Brugmann University Hospital, Sleep Laboratory & Unit for Chronobiology U78, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium; UNI, ULB Neurosciences Institute, Faculty of Medicine, Laboratory for Medical Psychology ULB312, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium. Electronic address: daniel.neu@chu-brugmann.be.	Slow wave sleep in the chronically fatigued: Power spectra distribution patterns in chronic fatigue syndrome and primary insomnia.	Clin Neurophysiol. 2015 Oct;126(10):1926-33. doi: 10.1016/j.clinph.2014.12.016. Epub 2015 Jan 10.	OBJECTIVES: To investigate slow wave sleep (SWS) spectral power proportions in distinct clinical conditions sharing non-restorative sleep and fatigue complaints without excessive daytime sleepiness (EDS), namely the chronic fatigue syndrome (CFS) and primary insomnia (PI). Impaired sleep homeostasis has been suspected in both CFS and PI. METHODS: We compared perceived sleep quality, fatigue and sleepiness symptom-intensities, polysomnography (PSG) and SWS spectral power distributions of drug-free CFS and PI patients without comorbid sleep or mental disorders, with a good sleeper control group. RESULTS: Higher fatigue without EDS and impaired perceived sleep quality were confirmed in both patient groups. PSG mainly differed in sleep fragmentation and SWS durations. Spectral analysis revealed a similar decrease in central ultra slow power (0.3-0.79Hz) proportion during SWS for both CFS and PI and an increase in frontal power proportions of faster frequencies during SWS in PI only. The latter was correlated to affective symptoms whereas lower central ultra slow power proportions were related to fatigue severity and sleep quality impairment. CONCLUSIONS: In combination with normal (PI) or even increased SWS durations (CFS), we found consistent evidence for lower proportions of slow oscillations during SWS in PI and CFS. SIGNIFICANCE: Observing normal or increased SWS durations but lower proportions of ultra slow power, our findings suggest a possible quantitative compensation of altered homeostatic regulation.
Nickel JC(1), Tripp DA(2); International Interstitial Cystitis Study Group.	(1)Departments of Urology (JCN), Psychology and Anesthesiology, Queen's University, Kingston, Ontario,	Clinical and psychological parameters associated with pain pattern phenotypes in women with interstitial cystitis/bladder pain	J Urol. 2015 Jan;193(1):138-44. doi: 10.1016/j.juro.2014.07.108. Epub 2014 Aug 1.	PURPOSE: It was recently suggested that 2 distinct clinical phenotypes can be described in patients with urological chronic pelvic pain syndrome, including pelvic pain only and pelvic pain beyond. We examined data on patients with interstitial cystitis/bladder pain syndrome, including body pain location mapping, and associated medical and psychosocial phenotyping to validate these body pain maps in a cohort of female patients with interstitial cystitis/bladder pain syndrome undergoing tertiary care.

	Canada. Electronic address: jcn@queensu.ca. (2)Departments of Urology (JCN), Psychology and Anesthesiology, Queen's University, Kingston, Ontario, Canada.	syndrome.		MATERIALS AND METHODS: Validated questionnaires from 173 diagnosed outpatient female patients with interstitial cystitis/bladder pain syndrome included a body pain area diagram, demographics/history, pain assessment, interstitial cystitis/bladder pain syndrome symptoms, depression, anxiety, stress, fatigue, sexual functioning, catastrophizing, quality of life and data on other chronic pain conditions. Two pain phenotypes based on counts of body locations, pelvic pain only and pelvic pain beyond, were comprehensively examined. RESULTS: The 157 patients (81%) identified with pelvic pain beyond reported more sensory type pain, poorer physical quality of life, and greater somatic depression and sleep disturbance than the 36 (19%) categorized with pelvic pain only. The sexual pain score was higher in the pelvic pain only group. Furthermore, patients with the pelvic pain beyond phenotype reported a higher prevalence of irritable bowel syndrome and fibromyalgia as well as more general fatigue symptoms and psychiatric conditions. CONCLUSIONS: Two distinct pain location phenotypes, including pelvic pain only and pelvic pain beyond, were identified by our independent analysis of patients with interstitial cystitis/bladder pain syndrome. Assessing clinical phenotypes based on pain patterns has significant ramifications in our improved understanding of the etiology and treatment of female patients diagnosed with interstitial cystitis/bladder pain syndrome.
Nijhof LN(1), Nijhof SL, Bleijenberg G, Stellato RK, Kimpen JL, Pol HE, van de Putte EM.	(1)Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, HP KE.04.133.1, Post box 85090, 3508 AB, Utrecht, The Netherlands, L.N.Nijhof@umcutrecht.nl.	The impact of chronic fatigue syndrome on cognitive functioning in adolescents.	Eur J Pediatr. 2015 Sep 3. [Epub ahead of print]	Chronic fatigue syndrome (CFS) is characterized by persistent fatigue and severe disability. Most adolescent patients report attention and concentration problems, with subsequent poor performance at school. This study investigated the impact of CFS on intellectual capacity by (1) assessing discrepancies between current intelligence quotient (IQ) and school level and (2) exploring differences in current IQ and pre-CFS school performance, compared with healthy individuals. Current data was cross-sectionally gathered and compared with retrospective pre-CFS school performance data. Fifty-nine CFS adolescents and 40 controls were evaluated on performance on age-appropriate intelligence tests and school level. Current IQ scores of CFS adolescents were lower than expected on the basis of their school level. Furthermore, there was a difference in intelligence performance across time when current IQ scores were compared with pre-CFS cognitive achievement. Healthy controls did not show any discrepancies.CONCLUSION: According to their pre-CFS intelligence assessments, CFS patients started with appropriate secondary school levels at the age of 12. Our data suggest that CFS may be accompanied by a decline in general cognitive functioning. Given the critical age for intellectual development, we recommend a timely diagnosis followed by appropriate treatment of CFS in adolescents. What is Known: • Adolescent chronic fatigue syndrome (CFS) is a debilitating condition with major impact on social and intellectual development. • Most patients report concentration problems, with subsequent poor performance at school. Little is known about the influence of CFS on intellectual performances. What is New: • IQ scores of CFS adolescents are lower than the IQ scores of healthy peers with an equivalent school level. • There is a decrease in

				intelligence performance across time when current IQ scores are compared with pre-CFS cognitive achievement. Healthy controls do not show any discrepancies between their current IQ, school level and previous cognitive functioning. This suggest that adolescent CFS may be accompanied by a decline in general cognitive functioning.
Nijs J(1,)(2,)(3), Malfliet A(1,)(2).	(1)Pain in Motion International Research Group, Vrije Universiteit Brussel, Brussel, Belgium. (2)Department of Physiotherapy, Human Physiology and Anatomy, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium. (3)Department of Physical Medicine and Physiotherapy, University Hospital Brussels, Brussels, Belgium.	Rehabilitation for patients with myalgic encephalomyelitis/chronic fatigue syndrome: time to extent the boundaries of this field.	J Intern Med. 2015 Sep 16. doi: 10.1111/joim.12431. [Epub ahead of print]	
O'Halloran KD(1).	(1)Department of Physiology, School of Medicine, University College Cork, Cork, Ireland. Electronic address: k.ohalloran@ucc.ie.	Chronic intermittent hypoxia creates the perfect storm with calamitous consequences for respiratory control.	Respir Physiol Neurobiol. 2015 Oct 31. pii: S1569-9048(15)30067-7. doi: 10.1016/j.resp.2015.10.013. [Epub ahead of print]	Obstructive sleep apnoea syndrome (OSAS) is a common respiratory disorder with devastating consequences for integrative body systems. A picture is emerging to illustrate wide-ranging deleterious consequences of disordered breathing during sleep for major homeostatic control systems, with considerable interest in cardiorespiratory and autonomic morbidity underpinning the development of hypertension. The vista is bleak when one also considers the link between OSAS and a host of other maladies. Exposure to chronic intermittent hypoxia (CIH), resulting from repeated obstructions of the pharyngeal airway, is a hallmark feature of OSAS that appears, in animal models, to drive the development and maintenance of several key morbidities. A growing body of evidence now points to aberrant respiratory plasticity at multiple levels following exposure to CIH. Herein, we review the experimental data revealing that CIH causes: respiratory muscle weakness and fatigue; impaired motor control of the upper airway; and, discordant respiratory rhythm and pattern generation. This multifaceted conspiracy creates the perfect storm with the potential to exacerbate OSAS-serving to establish an inescapable cycle of respiratory morbidity. Several pharmacological interventions in animal models appear wholly effective in preventing the calamitous consequences of CIH and may have application as adjunctive therapies in the treatment

				of OSAS.
Okamoto LE(1), Raj SR(2), Gamboa A(1), Shibao CA(1), Arnold AC(1), Garland EM(1), Black BK(1), Farley G(1), Diedrich A(3), Biaggioni I(4).	(1)Vanderbilt Autonomic Dysfunction Center, Vanderbilt University School of Medicine, Nashville, Tennessee; Division of Clinical Pharmacology, Vanderbilt University School of Medicine, Nashville, Tennessee; Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee;	Sympathetic activation is associated with increased IL-6, but not CRP in the absence of obesity: lessons from postural tachycardia syndrome and obesity.	Am J Physiol Heart Circ Physiol. 2015 Dec 15;309(12):H2098-107. doi: 10.1152/ajpheart.00409.2015. Epub 2015 Oct 9.	Sympathetic activation is thought to contribute to the inflammatory process associated with obesity, which is characterized by elevated circulating C-reactive protein (hsCRP) and interleukin-6 (IL-6). To evaluate whether sympathetic activation is associated with inflammation in the absence of obesity, we studied patients with postural tachycardia syndrome (POTS), a condition characterized by increased sympathetic tone in otherwise healthy individuals. Compared with 23 lean controls, 43 lean female POTS had greater vascular sympathetic modulation (low-frequency blood pressure variability, LFSBP, 3.2 ± 0.4 vs. 5.5 ± 0.6 mmHg(2), respectively, P = 0.006), lower cardiac parasympathetic modulation (high-frequency heart rate variability, 1,414 ± 398 vs. 369 ± 66 ms(2), P = 0.001), and increased serum IL-6 (2.33 ± 0.49 vs. 4.15 ± 0.54 pg/ml, P = 0.011), but this was not associated with increases in hsCRP, which was low in both groups (0.69 ± 0.15 vs. 0.82 ± 0.16 mg/l, P = 0.736). To explore the contribution of adiposity to inflammation, we then compared 13 obese female POTS patients and 17 obese female controls to matched lean counterparts (13 POTS and 11 controls). Compared with lean controls, obese controls had increased LFSBP (3.3 ± 0.5 vs. 7.0 ± 1.1 mmHg(2); P = 0.016), IL-6 (2.15 ± 0.58 vs. 3.92 ± 0.43 pg/ml; P = 0.030) and hsCRP (0.69 ± 0.20 vs. 3.47 ± 0.72 mg/l; P = 0.001). Obese and lean POTS had similarly high IL-6 but only obese POTS had increased hsCRP (5.76 ± 1.99 mg/l vs. 0.65 ± 0.26; P < 0.001). In conclusion, sympathetic activation in POTS is associated with increased IL-6 even in the absence of obesity. The coupling between IL-6 and CRP, however, requires increased adiposity, likely through release of IL-6 by visceral fat.
Olson K(1), Zimka O(2), Stein E(3).	(1)University of Alberta, Edmonton, Alberta, Canada kolson@ualberta.ca. (2)University of Alberta, Edmonton, Alberta, Canada. (3)University of Calgary, Calgary, Alberta, Canada.	The Nature of Fatigue in Chronic Fatigue Syndrome.	Qual Health Res. 2015 Oct;25(10):1410-22. doi: 10.1177/1049732315573954. Epub 2015 Feb 26.	In this article, we report the findings of our study on the nature of fatigue in patients diagnosed with chronic fatigue syndrome. Using ethnoscience as a design, we conducted a series of unstructured interviews and card sorts to learn more about how people with chronic fatigue syndrome describe fatigue. Participants (N = 14) described three distinct domains: tiredness, fatigue, and exhaustion. Most participants experienced tiredness prior to diagnosis, fatigue during daily life, and exhaustion after overexertion. We also discuss participants' ability to adapt to a variety of stressors and prevent shifts to exhaustion, and relate our findings to stress theory and other current research. Primary strategies that promoted adaptation to stressors included pacing and extended rest periods. These findings can aid health care professionals in detecting impending shifts between tiredness, fatigue, and exhaustion and in improving adaptive strategies, thereby improving quality of life.
Overman CL(1), Kool MB, Da Silva JA, Geenen R.	(1)Department of Clinical and Health Psychology, Utrecht University, PO Box 80.140, 3508 TC, Utrecht, The	The prevalence of severe fatigue in rheumatic diseases: an international study.	Clin Rheumatol. 2015 Aug 15. [Epub ahead of print]	Fatigue is a common, disabling, and difficult-to-manage problem in rheumatic diseases. Prevalence estimates of fatigue within rheumatic diseases vary considerably. Data on the prevalence of severe fatigue across multiple rheumatic diseases using a similar instrument is missing. Our aim was to provide an overview of the prevalence of severe fatigue across a broad range of rheumatic diseases and to examine its association with clinical and demographic variables. Online questionnaires were filled out by an

	Netherlands, C.L.Overman@uu.nl.			international sample of 6120 patients (88 % female, mean age 47) encompassing 30 different rheumatic diseases. Fatigue was measured with the RAND(SF)-36 Vitality scale. A score of ≤35 was taken as representing severe fatigue (90 % sensitivity and 81 % specificity for chronic fatigue syndrome). Severe fatigue was present in 41 to 57 % of patients with a single inflammatory rheumatic disease such as rheumatoid arthritis, systemic lupus erythematosus, ankylosing spondylitis, Sjögren's syndrome, psoriatic arthritis, and scleroderma. Severe fatigue was least prevalent in patients with osteoarthritis (35 %) and most prevalent in patients with fibromyalgia (82 %). In logistic regression analysis, severe fatigue was associated with having fibromyalgia, having multiple rheumatic diseases without fibromyalgia, younger age, lower education, and language (French: highest prevalence; Dutch: lowest prevalence). In conclusion, one out of every two patients with a rheumatic disease is severely fatigued. As severe fatigue is detrimental to the patient, the near environment, and society at large, unraveling the underlying mechanisms of fatigue and developing optimal treatment should be top priorities in rheumatologic research and practice.
Pacey V(1,)(2,)(3,)(4), Tofts L(2,)(5), Adams RD(6), Munns CF(5,)(7), Nicholson LL(2,)(3).	(1)Physiotherapy Department, The Children's Hospital at Westmead, Sydney, New South Wales, Australia.	Quality of life prediction in children with joint hypermobility syndrome.	J Paediatr Child Health. 2015 Jul;51(7):689-95. doi: 10.1111/jpc.12826. Epub 2015 Jan 26.	AIMS: To assess the child- and parent-reported health-related quality of life (HRQOL) of children with joint hypermobility syndrome (JHS), to compare these with other chronic paediatric conditions and to determine whether symptoms experienced by children with JHS can predict their HRQOL. METHODS: Eighty-nine children with JHS and one of their parents completed the Pediatric Quality of Life Inventory 4.0 Generic Core Scale, the Multidimensional Fatigue Scale and the Pediatric Pain Questionnaire. Anthropometric measures and reported symptoms were recorded. Child-reported HRQOL scores were compared with parent report, and both child- and parent-reported HRQOL scores of children with JHS were compared with those of children with other chronic conditions. Stepwise multiple regression was undertaken to determine whether any combination of measures could predict HRQOL. RESULTS: Parent- and child-reported HRQOL scores were strongly correlated ($r = 0.6$-0.84, all $P < 0.001$); however, parents of children with JHS perceived lower overall HRQOL (mean difference = 4.44, $P = 0.001$), physical (mean difference = 7.11, $P < 0.0001$) and emotional functioning (mean difference = 5.24, $P = 0.011$) than their children. When considered together with previously reported HRQOL scores for children with other chronic conditions, parent and child scores were similarly strongly correlated ($r = 0.93$, $P = 0.001$). Multiple regression revealed that 75% of the variance in child-reported HRQOL scores was accounted for by a child's level of pain and fatigue, and presence of stress incontinence symptoms ($P < 0.0001$). CONCLUSION: Children with JHS experience poor HRQOL and disabling fatigue, with parent scores providing a good proxy. Pain, fatigue and the presence of stress incontinence symptoms have the greatest impact on their HRQOL.
Paganotti MA(1), Valim V(2), Serrano ÉV(3),	(1)Universidade de Vila Velha (UVV), Vila Velha, ES, Brasil. .	Validation and psychometric properties of the Eular Sjögren's	Rev Bras Reumatol. 2015 Sep-Oct;55(5):439-45. doi: 10.1016/j.rbr.2015.06.004	OBJECTIVE: To carry out the cross-cultural adaptation of Eular Sjögren's Syndrome Patient Reported Index (ESSPRI) for Portuguese language and evaluate its psychometric properties. METHOD: Cross-sectional study of patients with primary Sjögren's

Miyamoto ST(4), Giovelli RA(5), Santos MC(6).		Syndrome Patient Reported Index (ESSPRI) into Brazilian Portuguese.	. Epub 2015 Aug 6.	syndrome (SS). The psychometric properties (intraobserver reproducibility and construct validity) were studied. In construct validity, ESSPRI was compared with the Patient's Global Assessment (PGA), Profile of Fatigue and Discomfort (Profad), Sicca Symptoms Inventory (SSI) and Functional Assessment of Chronic Illness Therapy (Facit-F). Statistical tests used were:Cronbach's alpha, intraclass correlation coefficient (ICC), Bland-Altman method and Spearman coefficient. A value of $p \leq 0.05$ was considered significant. RESULTS: There was no difference between versions in both languages; thus, a Brazilian consensual version was obtained. All subjects were women aged 49.4 ± 11.6 years, with onset of symptoms of 7.2 ± 5.4 years, and time of diagnosis of 3.0 ± 3.3 years. The mean ESSPRI was 6.87 ± 1.97. The intraobserver reproducibility was high and significant (0.911) and, with Bland-Altman method, there was no systematic bias in the agreement of measures among evaluations. A moderate correlation of ESSPRI with all tested instruments was observed. CONCLUSION: The Brazilian Portuguese version of ESSPRI is a valid and reproducible version.
Parslow R(1), Patel A(2), Beasant L(1), Haywood K(3), Johnson D(1), Crawley E(1).	(1)Centre for Child and Adolescent Health, School of Social & Community Medicine, University of Bristol, Bristol, UK. (2)Psychology Department, University of Bath, Bath, UK. (3)Royal College of Nursing Research Institute, Warwick Medical School, University of Warwick, Coventry, UK.	What matters to children with CFS/ME? A conceptual model as the first stage in developing a PROM.	Arch Dis Child. 2015 Dec;100(12):1141-7. doi: 10.1136/archdischild-2015-308831. Epub 2015 Oct 9.	BACKGROUND: Paediatric chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) is relatively common and disabling. Research is hampered because current patient-reported outcome measures (PROMs) do not capture outcomes that are important to children with CFS/ME. AIM: The aim of this study was to explore the aspects of life and health outcomes that matter to children with CFS/ME. METHODS: Twenty-five children with CFS/ME were interviewed (11 males, 14 females; mean age 12.9 years (SD 2.2), range 8-17). Twelve were trial participants interviewed during the trial and 13 were recruited as part of a follow-up qualitative study. Parents were present in 19 interviews with their children. Three mothers participated in a focus group. All the interviews and the focus group were audio-recorded and transcribed. Data were analysed thematically using techniques of constant comparison. NVivo was used to structure and categorise data in a systematic way. RESULTS: Children identified four key themes (health outcome domains): 'symptoms' that fluctuated, which caused an unpredictable reduction in both 'physical activity' and 'social participation' all of which impacted on 'emotional well-being'. These domains were influenced by both 'management' and 'contextual factors', which could be positive and negative. The relationship between healthcare and school was considered pivotal. CONCLUSIONS: Children's descriptions helped to inform a conceptual model that is necessary to develop a new paediatric CFS/ME PROM. Doctors need to be aware of how children conceptualise CFS/ME; the relationship between healthcare and school is fundamental to ameliorate the impact of CFS/ME. TRIAL REGISTRATION NUMBER: ISRCTN81456207.
Pastuszak Ż(1), Tomczykiewicz K(1), Stępień A(1).	(1)Department of Neurology, Central Clinical Hospital of the Ministry of National Defense, Military	[Post-polio syndrome - a case report].[Article in Polish]	Pol Merkur Lekarski. 2015 Jul;39(229):37-9.	Post-polio syndrome occurs 30-40 years after polio virus infection. The main symptoms of PPS are slowly progressive muscle limbs paresis with muscle atrophy, joints pain, paresthesia. In 90% of patients the main symptom is fatigue that leads to physical and mental activity deterioration. The cause of disease remains unknown. Probably it is an effect of motoneurons damage during acute virus polio infection, their overloading and

	Institute of Medicine in Warsaw, Poland.			degeneration of remaining ones. In this study we described a case of man who developed PPS 36 years after Heine-Medin disease. The main symptom was intensification of right limb paresis and muscle atrophy. In electromyography there were damage features of muscle clinically affected and unaffected. Changes in lifestyle made possible to continue occupational activity.
Patrick DM(1), Miller RR(2), Gardy JL(1), Parker SM(3), Morshed MG(4), Steiner TS(5), Singer J(6), Shojania K(5), Tang P(4); Complex Chronic Disease Study Group.	(1)School of Population and Public Health, University of British Columbia British Columbia Centre for Disease Control. Vancouver, Canada. (6)School of Population and Public Health, University of British Columbia Centre for Health Evaluation and Outcome Sciences.	Lyme Disease Diagnosed by Alternative Methods: A Phenotype Similar to That of Chronic Fatigue Syndrome.	Clin Infect Dis. 2015 Oct 1;61(7):1084-91. doi: 10.1093/cid/civ470. Epub 2015 Jun 16.	BACKGROUND: A subset of patients reporting a diagnosis of Lyme disease can be described as having alternatively diagnosed chronic Lyme syndrome (ADCLS), in which diagnosis is based on laboratory results from a nonreference Lyme specialty laboratory using in-house criteria. Patients with ADCLS report symptoms similar to those reported by patients with chronic fatigue syndrome (CFS). METHODS: We performed a case-control study comparing patients with ADCLS and CFS to each other and to both healthy controls and controls with systemic lupus erythematosus (SLE). Subjects completed a history, physical exam, screening laboratory tests, 7 functional scales, reference serology for Lyme disease using Centers for Disease Control and Prevention criteria, reference serology for other tick-associated pathogens, and cytokine expression studies. RESULTS: The study enrolled 13 patients with ADCLS (12 of whom were diagnosed by 1 alternative US laboratory), 25 patients with CFS, 25 matched healthy controls, and 11 SLE controls. Baseline clinical data and functional scales indicate significant disability among ADCLS and CFS patients and many important differences between these groups and controls, but no significant differences between each other. No ADCLS patient was confirmed as having positive Lyme serology by reference laboratory testing, and there was no difference in distribution of positive serology for other tick-transmitted pathogens or cytokine expression across the groups. CONCLUSIONS: In British Columbia, a setting with low Lyme disease incidence, ADCLS patients have a similar phenotype to that of CFS patients. Disagreement between alternative and reference laboratory Lyme testing results in this setting is most likely explained by false-positive results from the alternative laboratory.
Pejovic S(1), Natelson BH(2), Basta M(3), Fernandez-Mendoza J(4), Mahr F(5), Vgontzas AN(6).	(1)Department of Psychiatry, Sleep Research and Treatment Center, Penn State College of Medicine, Hershey, PA, 17033, USA. bobapejovic@gmail.com.	Chronic fatigue syndrome and fibromyalgia in diagnosed sleep disorders: a further test of the 'unitary' hypothesis.	BMC Neurol. 2015 Apr 12;15:53. doi: 10.1186/s12883-015-0308-2.	BACKGROUND: Since chronic fatigue syndrome (CFS) and fibromyalgia (FM) often co-exist, some believe they reflect the same process, somatization. Against that hypothesis are data suggesting FM but not CFS was common in patients with sleep-disordered breathing (SDB). The presence of discrete case definitions for CFS and FM allowed us to explore rates of CFS alone, CFS with FM, and FM alone in SDB patients compared to those with sleep complaints that fulfilled criteria for insomnia. METHODS: Participants were 175 sequential patients with sleep-related symptoms (122 had SDB and 21 had insomnia) and 39 healthy controls. Diagnoses were made by questionnaires, tender point count, and rule out labs; sleepiness was assessed with Epworth Sleepiness Scale and mood with Beck Depression Inventory. RESULTS: Rates of CFS, FM or CFS + FM were high: 13% in SDB and 48% in insomnia. CFS occurred frequently in SDB and insomnia, but FM occurred frequently only in insomnia. SDB patients with CFS and/or FM had higher daytime sleepiness than those without these disorders. CONCLUSION:

				CFS patients should complete Epworth scales, and sleep evaluation should be considered for those with scores ≥ 16 before receiving the diagnosis of CFS; the coexistence of depressed mood in these patients suggests some may be helped by treatment of their depression. That FM was underrepresented in SDB suggests FM and CFS may have different underlying pathophysiological causes.
Penna F(1,)(2), Pin F(1,)(2), Ballarò R(1,)(2), Baccino FM(1), Costelli P(1,)(2).	(1)a Department of Clinical and Biological Sciences , University of Turin , Turin , Italy. (2)b Interuniversity Institute of Myology , Italy.	Novel investigational drugs mimicking exercise for the treatment of cachexia.	Expert Opin Investig Drugs. 2015 Nov 26:1-10. [Epub ahead of print]	INTRODUCTION: Cachexia is a syndrome characterized by body weight loss, muscle wasting and metabolic abnormalities, that frequently complicates the management of people affected by chronic diseases. No effective therapy is actually available, although several drugs are under clinical evaluation. Altered energy metabolism markedly contributes to the pathogenesis of cachexia; it can be improved by exercise, which is able to both induce anabolism and inhibit catabolism. Areas covered: This review focuses on exercise mimetics and their potential inclusion in combined protocols to treat cachexia. The authors pay with particular reference to the cancer-associated cachexia. Expert opinion: Even though exercise improves muscle phenotype, most patients retain sedentary habits which are quite difficult to disrupt. Moreover, they frequently present with chronic fatigue and comorbidities that reduce exercise tolerance. For these reasons, drugs mimicking exercise could be beneficial to those who are unable to comply with the practice of physical activity. Since some exercise mimetics may exert serious side effects, further investigations should focus on treatments which maintain their effectiveness on muscle phenotype while remaining tolerable at the same time.
Persson R(1), Wensaas KA(2), Hanevik K(3), Eide GE(4,)(5), Langeland N(6,)(7), Rortveit G(8,)(9).	(1)Research Unit for General Practice, Uni Research Health, Bergen, Norway. persson.robert@gmail.com.	The relationship between irritable bowel syndrome, functional dyspepsia, chronic fatigue and overactive bladder syndrome: a controlled study 6 years after acute gastrointestinal infection.	BMC Gastroenterol. 2015 Jun 10;15:66. doi: 10.1186/s12876-015-0296-0.	BACKGROUND: To investigate in a cohort with previous gastrointestinal infection and a control group the prevalence of overactive bladder syndrome (OAB), and how it was associated with three other functional disorders; irritable bowel syndrome (IBS), functional dyspepsia (FD) and chronic fatigue (CF). METHODS: Controlled historic cohort study including 724 individuals with laboratory confirmed giardiasis six years earlier, and 847 controls matched by gender and age. Prevalence and odds ratios (OR) with 95 % confidence intervals (CI) were calculated. RESULTS: The prevalence of OAB was 18.7 % (134/716) in the exposed group and 13.6 % (113/833) in the control group (p = 0.007). The association between OAB and IBS was strong in the control group (OR: 2.42; 95 % CI: 1.45 to 4.04), but insignificant in the Giardia exposed (OR: 1.29; 95 % CI: 0.88 to 1.88). The association between OAB and FD was weak in both groups. CF was strongly associated with OAB (OR: 2.73; 95 % CI: 1.85 to 4.02 in the exposed and OR: 2.79; 95 % CI: 1.69 to 4.62 in the controls), and this association remained when comorbid conditions were excluded. CONCLUSIONS: Sporadic IBS was associated with increased risk of OAB, whereas post-infectious IBS was not. An apparent association between OAB and previous Giardia infection can be ascribed to comorbid functional disorders.
Peterson D(1), Brenu EW(2),	(1)Simmaron Research, 948 Incline	Cytokines in the cerebrospinal fluids of	Mediators Inflamm. 2015;2015:929720. doi:	OBJECTIVES: Previous research has provided evidence for dysregulation in peripheral cytokines in patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis

Gottschalk G(1), Ramos S(2), Nguyen T(2), Staines D(2), Marshall-Gradisnik S(2).	Way, Incline Village, NV 89451, USA. (2)Griffith Health Institute, School of Medial Sciences, National Centre for Neuroimmunology and Emerging Diseases, Griffith University, Parklands, QLD 4222, Australia.	patients with chronic fatigue syndrome/myalgic encephalomyelitis.	10.1155/2015/929720. Epub 2015 Mar 5.	(CFS/ME). To date only one study has examined cytokines in cerebrospinal fluid (CSF) samples of CFS/ME patients. The purpose of this pilot study was to examine the role of cytokines in CSF of CFS/ME patients. METHODS: CSF was collected from 18 CFS/ME patients and 5 healthy controls. The CSF samples were examined for the expression of 27 cytokines (interleukin- (IL-) 1β, IL-1ra, IL-2, IL-4, IL-6, IL-7, IL-8, IL-9, IL-10, IL-12p70, IL-13, IL-15, IL-17, basic FGF, eotaxin, G-CSF, GM-CSF, IFN-γ, IP-10, MCP-1 (MCAF), MIP-1α, MIP-1β, PDGF-BB, RANTES, TNF-α, and VEGF) using the Bio-Plex Human Cytokine 27-plex Assay. RESULTS: Of the 27 cytokines examined, only IL-10 was significantly reduced in the CFS/ME patients in comparison to the controls. CONCLUSIONS: This preliminary investigation suggests that perturbations in inflammatory cytokines in the CSF of CFS/ME patients may contribute to the neurological discrepancies observed in CFS/ME.
Petrie M(1), Suneja M(2), Shields RK(3).	(1)Department of Physical Therapy and Rehabilitation Science, Carver College of Medicine, University of Iowa, Iowa City, Iowa; (2)Department of Internal Medicine, Carver College of Medicine, University of Iowa, Iowa City, Iowa; and. (3)Department of Physical Therapy and Rehabilitation Science, Carver College of Medicine, University of Iowa, Iowa City, Iowa; Department of Veterans Affairs, Veterans Affairs Medical Center, Iowa City, Iowa richard-shields@uiowa.edu.	Low-frequency stimulation regulates metabolic gene expression in paralyzed muscle.	J Appl Physiol (1985). 2015 Mar 15;118(6):723-31. doi: 10.1152/japplphysiol.00628.2014. Epub 2015 Jan 29.	The altered metabolic state after a spinal cord injury compromises systemic glucose regulation. Skeletal muscle atrophies and transforms into fast, glycolytic, and insulin-resistant tissue. Osteoporosis is common after spinal cord injury and limits the ability to exercise paralyzed muscle. We used a novel approach to study the acute effect of two frequencies of stimulation (20 and 5 Hz) on muscle fatigue and gene regulation in people with chronic paralysis. Twelve subjects with chronic (>1 yr) and motor complete spinal cord injury (ASIA A) participated in the study. We assessed the twitch force before and after a single session of electrical stimulation (5 or 20 Hz). We controlled the total number of pulses delivered for each protocol (10,000 pulses). Three hours after the completion of the electrical stimulation (5 or 20 Hz), we sampled the vastus lateralis muscle and examined genes involved with metabolic transcription, glycolysis, oxidative phosphorylation, and mitochondria remodeling. We discovered that the 5-Hz stimulation session induced a similar amount of fatigue and a five- to sixfold increase ($P < 0.05$) in key metabolic transcription factors, including PGC-1α, NR4A3, and ABRA as the 20-Hz session. Neither session showed a robust regulation of genes for glycolysis, oxidative phosphorylation, or mitochondria remodeling. We conclude that a low-force and low-frequency stimulation session is effective at inducing fatigue and regulating key metabolic transcription factors in human paralyzed muscle. This strategy may be an acceptable intervention to improve systemic metabolism in people with chronic paralysis.
Pham TV(1), Torres M(2).	(1)Department of Emergency Medicine, University of Maryland School of	Human Immunodeficiency Virus Infection-Related Heart Disease.	Emerg Med Clin North Am. 2015 Aug;33(3):613-22. doi: 10.1016/j.emc.2015.04.00	Human immunodeficiency virus (HIV) infection and antiretroviral medications are independent risk factors for cardiovascular disease. In the pre-antiretroviral therapy (ART) era, HIV-infected patients had increased morbidity and mortality from opportunistic infections; in the post-ART era, these patients are at increased risk of

	Medicine, 110 South Paca Street, Sixth Floor, Suite 200, Baltimore, MD 21201, USA. Electronic address: tpham@umem.org. (2)Department of Emergency Medicine, University of Maryland School of Medicine, 110 South Paca Street, Sixth Floor, Suite 200, Baltimore, MD 21201, USA.		9. Epub 2015 Jun 10.	chronic diseases such as acute coronary syndrome, coronary artery disease, cardiac arrhythmias, and cardiomyopathy. They may present with vague symptoms such as weakness, dyspnea, or fatigue as the initial presentation of their cardiovascular disease. An overview of the clinical presentation, workup, management, and treatment of different cardiovascular disease is provided in this article.
Picariello F(1), Ali S(2), Moss-Morris R(3), Chalder T(4).	(1)King's College London, United Kingdom; South London and Maudsley NHS Foundation Trust, United Kingdom. (2)South London and Maudsley NHS Foundation Trust, United Kingdom. (3)King's College London, United Kingdom. (4)King's College London, United Kingdom. Electronic address: Trudie.chalder@kcl.ac.uk.	The most popular terms for medically unexplained symptoms: the views of CFS patients.	J Psychosom Res. 2015 May;78(5):420-6. doi: 10.1016/j.jpsychores.2015.02.013. Epub 2015 Feb 27.	OBJECTIVE: Medically unexplained symptoms/syndromes are common, highly distressing and are often associated with profound disability. One of the controversies surrounding this area relates to which umbrella term should be used to group such symptoms. The purpose of this research was to establish the preferences of patients with chronic fatigue syndrome (CFS) for an umbrella term for medically unexplained symptoms. METHODS: A cross-sectional mixed methods survey design was used. Participants were asked to indicate their three most preferred terms out of a list of commonly used terms and to provide any extra comments. Frequency analysis was employed to look at the preferences of terms for each rank. Comments were analysed using principles of inductive thematic analysis. RESULTS: Eighty-seven patients with CFS completed a self-report survey. The term "Persistent Physical Symptoms" was the most popular first choice term chosen by 20.7% of patients. Terms containing the word "physical" were consistently more likely to be chosen. Three main themes emerged from the thematic analysis: 1) Physical nature of the illness, 2) Stigma, and 3) Evaluation of the terms, giving a more in-depth understanding of the findings. CONCLUSION: According to CFS patients, an umbrella term has to reflect the physical experience of MUS.
Pin F(1), Busquets S(2,)(3), Toledo M(2), Camperi A(1), Lopez-Soriano FJ(2,)(3), Costelli P(1),	(1)Department of Clinical and Biological Sciences, University of Torino, Torino, Italy. (2)Cancer Research Group, Departament	Combination of exercise training and erythropoietin prevents cancer-induced muscle alterations.	Oncotarget. 2015 Dec 22;6(41):43202-15. doi: 10.18632/oncotarget.6439.	Cancer cachexia is a syndrome characterized by loss of skeletal muscle mass, inflammation, anorexia and anemia, contributing to patient fatigue and reduced quality of life. In addition to nutritional approaches, exercise training (EX) has been proposed as a suitable tool to manage cachexia. In the present work the effect of mild exercise training, coupled to erythropoietin (EPO) administration to prevent anemia, has been tested in tumor-bearing mice. In the C26 hosts, acute exercise does not prevent and

Argilés JM(2,)(3), Penna F(1).	de Bioquímica i Biologia Molecular, Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain. (3)Institut de Biomedicina de la Universitat de Barcelona (IBUB), Barcelona, Spain.			even worsens muscle wasting. Such pattern is prevented by EPO co-administration or by the adoption of a chronic exercise protocol. EX and EPO co-treatment spares oxidative myofibers from atrophy and counteracts the oxidative to glycolytic shift, inducing PGC-1α. LLC hosts are responsive to exercise and their treatment with the EX-EPO combination prevents the loss of muscle strength and the onset of mitochondrial ultrastructural alterations, while increases muscle oxidative capacity and intracellular ATP content, likely depending on PGC-1α induction and mitophagy promotion. Consistently, muscle-specific PGC-1α overexpression prevents LLC-induced muscle atrophy and Atrogin-1 hyperexpression. Overall, the present data suggest that low intensisty exercise can be an effective tool to be included in combined therapeutic approaches against cancer cachexia, provided that anemia is coincidently treated in order to enhance the beneficial action of exercise.
Pinxsterhuis I(1), Hellum LL, Aannestad HH, Sveen U.	(1)Division of Medicine, Oslo University Hospital, and Faculty of Medicine, University of Oslo , Oslo , Norway.	Development of a group-based self-management programme for individuals with chronic fatigue syndrome: a pilot study.	Scand J Occup Ther. 2015 Mar;22(2):117-25. doi: 10.3109/11038128.2014.985608. Epub 2015 Jan 12.	OBJECTIVE: The aim of the study was to develop a group-based self-management programme for individuals with chronic fatigue syndrome (CFS) by using the participants' experiences with the initial version of the programme, which intends to promote coping with the illness in a primary healthcare setting. METHODS: An initial programme was developed, based on self-efficacy theory and the concepts of client-centred practice and empowerment. Subsequently, the programme was tested and further developed by drawing on the participants' experiences with the programme. Focus-group interviews were applied. The interviews were analysed using thematic analysis. RESULTS: The initial programme was found to be feasible, although several modifications regarding the content and practical organization of the programme were proposed. CONCLUSION: In line with the participants' experiences, the final self-management programme was developed, which includes short presentations of eight topics, exchange of experiences among participants, goal-setting, construction of action plans, and relaxation exercises, in addition to a meeting for relatives. The programme will be provided in eight biweekly sessions and be led by juxtaposed peer counsellors and occupational therapists. The effects of the final programme will be evaluated in a randomized controlled trial.
Pinxsterhuis I(1), Sandvik L(2), Strand EB(3), Bautz-Holter E(4), Sveen U(5).	(1)Division of Medicine, Oslo University Hospital, Oslo, Norway Department of Occupational Therapy, Prosthetics and Orthotics, Oslo, Norway Akershus University College of	Effectiveness of a group-based self-management program for people with chronic fatigue syndrome: A randomized controlled trial.	Clin Rehabil. 2015 Dec 16. pii: 0269215515621362. [Epub ahead of print]	OBJECTIVE: To evaluate the effectiveness of a group-based self-management program for people with chronic fatigue syndrome. DESIGN: A randomized controlled trial. SETTING: Four mid-sized towns in southern Norway and two suburbs of Oslo. SUBJECTS: A total of 137 adults with chronic fatigue syndrome. INTERVENTION: A self-management program including eight biweekly meetings of 2.5 hours duration. The control group received usual care. MAIN MEASURES: Primary outcome measure: Medical Outcomes Study-Short Form-36 physical functioning subscale. SECONDARY OUTCOME MEASURES: Fatigue severity scale, self-efficacy scale, physical and mental component summary of the Short Form-36, and the illness cognition questionnaire (acceptance subscale). Assessments were performed at baseline, and at six-month and

	Applied Sciences, Oslo, Norway irpi@uus.no. (2)Center for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway. (3)Division of Medicine, Oslo University Hospital, Oslo, Norway. (4)Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Oslo, Norway. (5)Department of Physical Medicine and Rehabilitation, Oslo University Hospital, Oslo, Norway Department of Occupational Therapy, Prosthetics and Orthotics, Oslo, Norway Akershus University College of Applied Sciences, Oslo, Norway.			one-year follow-ups. RESULTS: At the six-month follow-up, a significant difference between the two groups was found concerning fatigue severity (p = 0.039) in favor of the control group, and concerning self-efficacy in favor of the intervention group (p = 0.039). These significant differences were not sustained at the one-year follow-up. No significant differences were found between the groups concerning physical functioning, acceptance, and health status at any of the measure points. The drop-out rate was 13.9% and the median number of sessions attended was seven (out of eight). CONCLUSIONS: The evaluated self-management program did not have any sustained effect, as compared with receiving usual care.
Poteliakhoff A, Watts G.		Alex Poteliakhoff: campaigner for a less violent world.	Lancet. 2015 May 30;385(9983):2143. doi: 10.1016/S0140-6736(15)61012-1.	
Powell A(1), McNeil J(2).	(1)The Queen Elizabeth Hospital, Adelaide, SA, Australia. alice.c.powell@gmail.com. (2)University	Primary sclerosing cholangitis associated with CREST (calcinosis, Raynaud phenomenon, oesophageal dysmotility, sclerodactyly and	J Med Case Rep. 2015 Nov 25;9(1):272. doi: 10.1186/s13256-015-0747-9.	INTRODUCTION: CREST (calcinosis, Raynaud phenomenon, oesophageal dysmotility, sclerodactyly, and telangiectasia) syndrome comprising calcinosis cutis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia and primary sclerosing cholangitis are both chronic fibrotic diseases but the association between them is extremely rare. While primary sclerosing cholangitis has been associated with diffuse cutaneous scleroderma, the association with limited cutaneous scleroderma or

	Department of Medicine, Modbury Hospital, Adelaide, SA, Australia. julian.mcneil@adelaide.edu.au.	telangiectasia) in an elderly woman: a case report.		CREST has not been previously reported in the literature. This case report illustrates the association between CREST and primary sclerosing cholangitis. CASE PRESENTATION: We report the case of an 84-year-old Asian woman with a long history of CREST who was admitted with abdominal pain, fatigue and progressive derangement of her liver enzymes. This was initially thought to be secondary to her bosentan therapy for pulmonary hypertension but it persisted despite bosentan being ceased. Primary sclerosing cholangitis was subsequently diagnosed on magnetic resonance cholangiopancreatography and she was referred to a hepatologist for treatment. CONCLUSIONS: This case highlights the need to consider primary sclerosing cholangitis in patients with CREST who present with abdominal symptoms and deranged liver enzymes when other causes have been excluded. Relevant differential diagnoses for this presentation, which can be difficult to exclude, include immunoglobulin G4-associated cholangitis and antimitochondrial antibody negative primary biliary cirrhosis. It is of particular significance to rheumatologists and gastroenterologists but has broader relevance to all medical specialists involved in the care of patients with CREST.
Pratt SD(1), Jachna BR(2).	(1)Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA. Electronic address: spratt@bidmc.harvard.edu. (2)Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA.	Care of the clinician after an adverse event.	Int J Obstet Anesth. 2015 Feb;24(1):54-63. doi: 10.1016/j.ijoa.2014.10.001. Epub 2014 Oct 23.	The past two decades has seen a growing understanding that health care leads to harm in a large number of patients. With this insight has come an understanding that clinicians who care for patients who are harmed experience an understandable and predictable emotional response. After an adverse event, medical care givers may experience a wide range of symptoms including anger, guilt, shame, fear, loneliness, frustration and decreased job satisfaction. These may be accompanied by physical signs of fatigue, sleep disturbances, concentration difficulties, tachycardia and hypertension. These clinicians have been referred to as the "second victims." While many clinicians recover relatively quickly from an adverse event, for some this syndrome can last for weeks, months or indefinitely. Some have even contemplated or completed suicide. Being involved in an adverse event or error may also negatively impact the quality of care the clinician subsequently provides, either because of acute emotional distraction or chronic burnout. This can lead to additional errors and a vicious cycle of error, burnout and error. Health care systems have a moral responsibility to care for second victims. Care might be as simple as asking, "Are you OK?" and acknowledging the normal human emotional response to adverse events. Some centers have developed formal peer support programs in which clinicians are trained to act as peer supporter for emotional recovery after adverse events. Finally, more formal emotional support systems might be needed by some clinicians, including employee assistance programs, hospital clergy or psychological and psychiatric services.
Purohit T(1), Cappell MS(1).	(1)Treta Purohit, Mitchell S Cappell,	Primary biliary cirrhosis: Pathophysiology, clinical	World J Hepatol. 2015 May 8;7(7):926-41. doi:	Primary biliary cirrhosis (PBC) is an autoimmune, slowly progressive, cholestatic, liver disease characterized by a triad of chronic cholestasis, circulating anti-mitochondrial

	Division of Gastroenterology and Hepatology, William Beaumont Hospital, Royal Oak, MI 48073, United States.	presentation and therapy.	10.4254/wjh.v7.i7.926.	antibodies (AMA), and characteristic liver biopsy findings of nonsuppurative destructive cholangitis and interlobular bile duct destruction. About 10% of PBC patients, however, lack AMA. A variant, called PBC-autoimmune hepatitis (AIH) overlap, is characterized by the above findings of PBC together with findings of elevated serum alanine aminotransferase, elevated serum immunoglobulin G, and circulating anti-smooth muscle antibodies, with liver biopsy demonstrating periportal or periseptal, lymphocytic, piecemeal necrosis. PBC is hypothesized to be related to environmental exposure in genetically vulnerable individuals. It typically occurs in middle-aged females. Prominent clinical features include fatigue, pruritis, jaundice, xanthomas, osteoporosis, and dyslipidemia. The Mayo Risk score is the most widely used and best prognostic system. Ursodeoxycholic acid is the primary therapy. It works partly by reducing the concentration and injury from relatively toxic bile acids. PBC-AIH overlap syndrome is treated with ursodeoxycholic acid and corticosteroids, especially budesonide. Obeticholic acid and fibrate are promising new, but incompletely tested, therapies. Liver transplantation is the definitive therapy for advanced disease, with about 70% 10-year survival after transplantation. Management of pruritis includes local skin care, dermatologist referral, avoiding potential pruritogens, cholestyramine, and possibly opioid antagonists, sertraline, or rifaximin. Management of osteoporosis includes life-style modifications, administration of calcium and vitamin D, and alendronate. Statins are relatively safe to treat the osteopenia associated with PBC. Associated Sjogren's syndrome is treated by artificial tears, cyclosporine ophthalmic emulsion to stimulate tear production; and saliva substitutes, cholinergic agents, and scrupulous oral and dental care. Complications of cirrhosis from advanced PBC include esophageal varices, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, and hepatoma formation.
Qanneta R(1), Fontova R(2), Castel A(3).	(1)Unidad de Fibromialgia y Síndrome de Fatiga Crónica, Departamento de Reumatología, Hospital Universitari de Tarragona Joan XXIII, Tarragona, España. Electronic address: rami_kanita229@hotmail.com.	Response to: fibromyalgia and chronic fatigue syndrome caused by non-celiac gluten sensitivity.	Reumatol Clin. 2015 May-Jun;11(3):185. doi: 10.1016/j.reuma.2014.09.008. Epub 2014 Nov 7.	Comment on Reumatol Clin. 2015 Jan-Feb;11(1):56-7.
Rajeevan MS(1), Dimulescu I(2),	(1)Division of High-Consequence	Pathway-focused genetic evaluation of immune and	Hum Immunol. 2015 Aug;76(8):553-60. doi:	Recent evidence suggests immune and inflammatory alterations are important in chronic fatigue syndrome (CFS). This study was done to explore the association of

Murray J(2), Falkenberg VR(2), Unger ER(2).	Pathogens & Pathology, Centers for Disease Control and Prevention, Atlanta, GA, USA. Electronic address: mor4@cdc.gov. (2)Division of High-Consequence Pathogens & Pathology, Centers for Disease Control and Prevention, Atlanta, GA, USA.	inflammation related genes with chronic fatigue syndrome.	10.1016/j.humimm.2015.06.014. Epub 2015 Jun 24.	functionally important genetic variants in inflammation and immune pathways with CFS. Peripheral blood DNA was isolated from 50 CFS and 121 non-fatigued (NF) control participants in a population-based study. Genotyping was performed with the Affymetrix Immune and Inflammation Chip that covers 11K single nucleotide polymorphisms (SNPs) following the manufacturer's protocol. Genotyping accuracy for specific genes was validated by pyrosequencing. Golden Helix SVS software was used for genetic analysis. SNP functional annotation was done using SPOT and GenomePipe programs. CFS was associated with 32 functionally important SNPs: 11 missense variants, 4 synonymous variants, 11 untranslated regulatory region (UTR) variants and 6 intronic variants. Some of these SNPs were in genes within pathways related to complement cascade (SERPINA5, CFB, CFH, MASP1 and C6), chemokines (CXCL16, CCR4, CCL27), cytokine signaling (IL18, IL17B, IL2RB), and toll-like receptor signaling (TIRAP, IRAK4). Of particular interest is association of CFS with two missense variants in genes of complement activation, rs4151667 (L9H) in CFB and rs1061170 (Y402H) in CFH. A 5' UTR polymorphism (rs11214105) in IL18 also associated with physical fatigue, body pain and score for CFS case defining symptoms. This study identified new associations of CFS with genetic variants in pathways including complement activation providing additional support for altered innate immune response in CFS. Additional studies are needed to validate the findings of this exploratory study.
Regal Ramos RJ(1).	(1)Dirección Provincial del INSS de Madrid, Madrid, España. Electronic address: raul-jesus.regal@inss.seg-social.es.	[Can we rule out that fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity are psychosomatic diseases?[Article in Spanish].	Semergen. 2015 Oct;41(7):349-53. doi: 10.1016/j.semerg.2015.04.015. Epub 2015 Jul 26.	
Regland B(1), Forsmark S(1), Halaouate L(1), Matousek M(1), Peilot B(1), Zachrisson O(1), Gottfries CG(1).	(1)Gottfries Clinic, affiliated with Institute of Neuroscience and Physiology, Gothenburg University, Gothenburg, Sweden.	Response to vitamin B12 and folic acid in myalgic encephalomyelitis and fibromyalgia.	PLoS One. 2015 Apr 22;10(4):e0124648. doi: 10.1371/journal.pone.0124648. eCollection 2015.	BACKGROUND: Patients with myalgic encephalomyelitis (ME, also called chronic fatigue syndrome) may respond most favorably to frequent vitamin B12 injections, in vital combination with oral folic acid. However, there is no established algorithm for individualized optimal dosages, and rate of improvement may differ considerably between responders. OBJECTIVE: To evaluate clinical data from patients with ME, with or without fibromyalgia, who had been on B12 injections at least once a week for six months and up to several years. METHODS: 38 patients were included in a cross-sectional survey. Based on a validated observer's rating scale, they were divided into Good (n = 15) and Mild (n = 23) responders, and the two groups were compared from various clinical aspects. RESULTS: Good responders had used significantly more

				frequent injections (p<0.03) and higher doses of B12 (p<0.03) for a longer time (p<0.0005), higher daily amounts of oral folic acid (p<0.003) in good relation with the individual MTHFR genotype, more often thyroid hormones (p<0.02), and no strong analgesics at all, while 70% of Mild responders (p<0.0005) used analgesics such as opioids, duloxetine or pregabalin on a daily basis. In addition to ME, the higher number of patients with fibromyalgia among Mild responders was bordering on significance (p<0.09). Good responders rated themselves as "very much" or "much" improved, while Mild responders rated "much" or "minimally" improved. CONCLUSIONS: Dose-response relationship and long-lasting effects of B12/folic acid support a true positive response in the studied group of patients with ME/fibromyalgia. It's important to be alert on co-existing thyroid dysfunction, and we suspect a risk of counteracting interference between B12/folic acid and certain opioid analgesics and other drugs that have to be demethylated as part of their metabolism. These issues should be considered when controlled trials for ME and fibromyalgia are to be designed.
Riccio P(1), Rossano R(2).	(1)Department of Sciences, University of Basilicata, Potenza, Italy paoloxriccio@gmail.com. (2)Department of Sciences, University of Basilicata, Potenza, Italy.	Nutrition facts in multiple sclerosis.	ASN Neuro. 2015 Feb 18;7(1). pii: 1759091414568185. doi: 10.1177/1759091414568185. Print 2015 Jan-Feb.	The question whether dietary habits and lifestyle have influence on the course of multiple sclerosis (MS) is still a matter of debate, and at present, MS therapy is not associated with any information on diet and lifestyle. Here we show that dietary factors and lifestyle may exacerbate or ameliorate MS symptoms by modulating the inflammatory status of the disease both in relapsing-remitting MS and in primary-progressive MS. This is achieved by controlling both the metabolic and inflammatory pathways in the human cell and the composition of commensal gut microbiota. What increases inflammation are hypercaloric Western-style diets, characterized by high salt, animal fat, red meat, sugar-sweetened drinks, fried food, low fiber, and lack of physical exercise. The persistence of this type of diet upregulates the metabolism of human cells toward biosynthetic pathways including those of proinflammatory molecules and also leads to a dysbiotic gut microbiota, alteration of intestinal immunity, and low-grade systemic inflammation. Conversely, exercise and low-calorie diets based on the assumption of vegetables, fruit, legumes, fish, prebiotics, and probiotics act on nuclear receptors and enzymes that upregulate oxidative metabolism, downregulate the synthesis of proinflammatory molecules, and restore or maintain a healthy symbiotic gut microbiota. Now that we know the molecular mechanisms by which dietary factors and exercise affect the inflammatory status in MS, we can expect that a nutritional intervention with anti-inflammatory food and dietary supplements can alleviate possible side effects of immune-modulatory drugs and the symptoms of chronic fatigue syndrome and thus favor patient wellness.
Riegel B(1), Broicher W, Wegscheider K, Andresen V, Brähler E, Lohse	(1)Department of Psychosomatic Medicine and Psychotherapy, University Medical	Quality of life one year post-Shiga toxin-producing Escherichia coli O104 infection--a prospective cohort study.	Neurogastroenterol Motil. 2015 Mar;27(3):370-8. doi: 10.1111/nmo.12503. Epub 2015 Jan 11.	BACKGROUND: In 2011, a major outbreak of hemolytic-uremic syndrome (HUS) and bloody diarrhea related to infections from Shiga toxin-producing Escherichia coli O104 (STEC) occurred in Germany. While previous research has focused on the medical components of this disease, we aimed to investigate the course of health-related quality of life (HrQoL) over 12 months including somatic and psychosocial risk factors.

AW, Löwe B.	Centre Hamburg-Eppendorf, and Schön Klinik Hamburg Eilbek, Hamburg, Germany.			Furthermore, the influence of chronic fatigue (CF) on HrQoL was examined. METHODS: A prospective cohort study with n = 389 patients completing self-report scales at baseline, after 6 months (participation rate: 79%) and after 12 months (participation rate: 77%). The courses of physical and mental HrQoL over the 12 month period were calculated by employing general linear mixed models. KEY RESULTS: While the physical component score of HrQoL reached a score comparable to the general population, the mental component score remained below average 12 months after STEC infection. Female gender, prior psychiatric disorder, and prior traumatic events were risk factors for a worse HrQoL course after 12 months, while social support was identified to be protective. CF was associated with low HrQoL. In addition, the somatic symptom burden remained persistently high. CONCLUSIONS & INFERENCES: Our results show high somatic and psychosocial burden in patients 12 months after STEC infection. We recommend considering the risk factors and protective factors of poor HrQoL early in the treatment of STEC or similar diseases. Patients who are suffering from persisting somatic symptoms, CF, and impaired HrQoL may require specific aftercare.
Robinson LJ(1,)(2), Durham J(3), Newton JL(4,)(5).	(1)Academic Psychiatry, Newcastle University, Newcastle upon Tyne, UK. (2)Northumberland Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK. (3)Centre for Oral Health Research and Institute of Health & Society, Newcastle University, Newcastle upon Tyne, UK. (4)Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK. (5)Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.	A systematic review of the comorbidity between Temporomandibular Disorders and Chronic Fatigue Syndrome.	J Oral Rehabil. 2015 Nov 9. doi: 10.1111/joor.12367. [Epub ahead of print]	The most common cause of chronic oro-facial pain is a group of disorders collectively termed temporomandibular disorders (TMDs). Chronic painful TMD is thought to be a 'central sensitivity syndrome' related to hypersensitivity of the nervous system, but the cause is unknown. A similar understanding is proposed for other unexplained conditions, including chronic fatigue syndrome (CFS). Exploring the comorbidity of the two conditions is a valuable first step in identifying potential common aetiological mechanisms or treatment targets.METHOD: Systematic literature review. Studies were included if they recruited community or control samples and identified how many reported having both TMD and CFS, or if they recruited a sample of patients with either TMD or CFS and measured the presence of the other condition. RESULTS: Six papers met inclusion criteria. In studies of patients with CFS (n = 3), 21-32% reported having TMD. In a sample of people with CFS and fibromyalgia, 50% reported having TMD. Studies in people with TMD (n = 3) reported 0-43% having CFS. Studies in samples recruited from oro-facial pain clinics (n = 2) reported a lower comorbidity with CFS (0-10%) than a study that recruited individuals from a TMD self-help organisation (43%). CONCLUSION: The review highlights the limited standard of evidence addressing the comorbidity between oro-facial pain and CFS. There is a valuable signal that the potential overlap in these two conditions could be high; however, studies employing more rigorous methodology including standardised clinical assessments rather than self-report of prior diagnosis are needed.
Rodriguez-Rodriguez L(1),	(1)Rheumatology Department and	The rs3771863 single nucleotide polymorphism	Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl	OBJECTIVES: Fibromyalgia (FM) has been associated with affective spectrum disorders and other chronic pain disorders, which tend to co-occur in individuals and co-

Ramón Lamas J(1), Abásolo L(1), Baena S(1), Olano-Martin E(2), Collado A(3), Rivera J(4), Fernández-Gutiérrez B(1).	Health Research Institute (IdISsC), Hospital Clínico San Carlos, Madrid, Spain. (2)Progenika Biopharma SA, Derio, Spain. (3)Fibromyalgia Specialised Unit, Servicio de Reumatologia, ICEMEQ, Hospital Clínic de Barcelona, Barcelona, Spain. (4)Rheumatology Unit, Instituto Provincial de Rehabilitación, Hospital Universitario Gregorio Marañón, Madrid, Spain.	of the TACR1 gene is associated to a lower risk of sicca syndrome in fibromyalgia patients.	88):S33-40. Epub 2015 Mar 10.	aggregate among families. The objective of our study was to investigate the genetic risk factors associated with the presence of related symptoms and with disease severity in subjects affected with FM. METHODS: Two independent cohorts of subjects diagnosed with FM according to the 1990 ACR criteria were studied. A genetic array composed of 320 single nucleotide polymorphisms (SNPs) was analysed in a discovery cohort comprised by 564 patients, and the most suggestive variants were genotyped in a replication cohort, comprised by 397 subjects. The associated conditions and related symptoms analysed were: the presence of depression, sleep disorders, headache, myofascial syndrome, irritable bowel syndrome, chronic fatigue syndrome, vertiginous syndrome, chronic cystitis, and sicca syndrome. FM severity was assessed by the Fibromyalgia Impact Questionnaire and the Hospital Anxiety and Depression Scale. Analyses were adjusted by elapsed time from pain onset, and a meta-analysis was performed to pool the results. RESULTS: Minor allele of the rs3771863 SNP from the TACR1 gene showed a significant association with a lower risk of sicca syndrome (pooled and adjusted OR 0.56, [95%CI 0.42-0.76], p=0.00022). CONCLUSIONS: Our findings indicate a role of the TACR1 gene in the development of sicca syndrome in subjects affected with FM.
Roerink ME(1), Knoop H(2), Bredie SJ(3), Heijnen M(4), Joosten LA(5), Netea MG(6), Dinarello CA(7), van der Meer JW(8).	(1)Department of Internal Medicine, Radboud University Medical Center, Post Box 9101, 6500 HB, Nijmegen, The Netherlands. Megan.Roerink@radboudumc.nl.	Cytokine inhibition in chronic fatigue syndrome patients: study protocol for a randomized controlled trial.	Trials. 2015 Oct 5;16:439. doi: 10.1186/s13063-015-0971-z.	BACKGROUND: Chronic fatigue syndrome (CFS) is a medically unexplained syndrome for which no somatic or pharmacological treatment has been proven effective. Dysfunction of the cytokine network has been suspected to play a role in the pathophysiology of CFS. The disturbances of the cytokine network detected in CFS patients are highly variable, in part due to the lack of adequate controls in many studies. Furthermore, all studies have been performed on peripheral venous blood of patients. As cytokines mainly act in tissues, for example, the brain, the information that can be derived from peripheral blood cells is limited. The information regarding the possible role of cytokines in the pathophysiology could come from intervention studies in which the activities of relevant cytokines are reduced, for example, reducing interleukin-1, interleukin-6 or tumor necrosis factor. In this study, the clinical usefulness of anakinra, an IL-1 antagonist, will be assessed in patients with CFS. METHODS/DESIGN: A randomized placebo-controlled, double-blind trial will be conducted. Fifty adult female patients meeting the Centers for Disease Control (CDC) criteria for CFS and without psychiatric co-morbidity will be included. After inclusion, patients will be randomized between treatment with anakinra (recombinant human interleukin-1 receptor antagonist) or placebo. Each group will be treated for 4 weeks. Outcome measures will be assessed at baseline, after 4 weeks of intervention, and 6 months after baseline assessment. The primary outcome measure will be fatigue severity at 4 weeks, measured with the validated Checklist of Individual Strength (CIS). Secondary outcome measures are functional impairment, physical and social

				functioning, psychological distress, pain severity, presence of accompanying symptoms, and cytokine and cortisol concentrations. DISCUSSION: This is the first randomized placebo-controlled trial that will evaluate the effect of interference with IL-1 on the experience of fatigue in patients with CFS. The results of this study may expand treatment options for patients with CFS, for whom graded exercise therapy and cognitive behavioral therapy are the only evidence-based interventions that exist at this moment. TRIAL REGISTRATION: Clinicaltrials.gov: NCT02108210 . Clinicaltrials.gov registration date: 8 April 2014. EudraCT: 2013-005466-19.
Rogalska-Płońska M(1), Lapinski TW, Grzeszczuk A, Parfieniuk-Kowerda A, Flisiak R.	(1)Department of Infectious Diseases and Hepatology, Medical University of Białystok , Białystok, Poland .	Influence of HCV and HIV on development of cryoglobulinemia.	Viral Immunol. 2015 Apr;28(3):145-52. doi: 10.1089/vim.2014.0114. Epub 2015 Feb 27.	Cryoglobulinemic syndrome refers to a systemic inflammatory process that involves small and medium-sized vessels accompanied by multi-organ damage. The aim of the present study was to determine the incidence of cryoglobulinemia among patients infected with human immunodeficiency virus (HIV), hepatitis C virus (HCV) and HCV/HIV co-infection, as well as evaluation of cryoglobulinemia type. The association was evaluated between cryoglobulinemia and clinical symptoms, selected biochemical measures of liver and kidney function, virologic measures, as well as histopathological changes in the liver. One hundred and forty-one patients were enrolled (59 HCV mono-infected, 48 HIV mono-infected, and 34 HCV/HIV co-infected). Cryoglobulinemia was nearly five times less frequent among HIV mono-infected patients (10%) than HCV mono-infected (53%) and HCV/HIV co-infected patients (59%). Cryoglobulinemia was more frequent in patients infected with genotype 1 HCV than genotype 3 (63% vs. 46%, p=0.12). There was a lower incidence of cryoglobulinemia in HIV mono-infected patients treated with antiretroviral drugs (p=0.04). Cryoglobulinemia correlated with ALT activity (p=0.01) and HIV viral load (p<0.001). Symptoms were significantly more frequent among cryoglobulinemic patients than those without cryoglobulinemia (38% vs. 9%, p<0.001). The most common symptoms related to cryoglobulinemia, regardless of cryoglobulinemia type, were fatigue (38%), arthralgia (20%), polineuropathy (18%), and skin lesions (14%). In conclusion, HCV mono-infection and HCV/HIV co-infection, regardless of HCV genotype, are potent stimulators of cryoglobulinemia, with its symptomatic form occurring in about 40% of cases. Effective antiretroviral therapy seems to be protective against cryoglobulinemia development in HIV mono-infected patients.
Roizenblatt S(1), Souza AL(2), Palombini L(2), Godoy LM(2), Tufik S(2), Bittencourt LR(2).	(1)Department of Internal Medicine, UNIFESP, São Paulo, Brazil. (2)Department of Psychobiology, UNIFESP, São Paulo, Brazil.	Musculoskeletal Pain as a Marker of Health Quality. Findings from the Epidemiological Sleep Study among the Adult Population of São Paulo City.	PLoS One. 2015 Nov 24;10(11):e0142726. doi: 10.1371/journal.pone.0142726. eCollection 2015.	BACKGROUND: We are witnessing the growth of urban populations, particularly in the developing world. São Paulo, the largest city in South America, continues to grow, and this growth is dramatically effecting the environment and human health. The aim of this study was to estimate the point prevalence of chronic pain in São Paulo city dwellers and to explore the influence of aspects related to urbanicity. METHODS: A two-stage cluster randomized sample included 1100 individuals of the city of Sao Paulo, representing the population proportionally in terms of gender, age and social classes in 2007. For this observational cross-sectional study, the household sample was interviewed using validated questionnaires for sociodemographic aspects, the Beck

				inventories for anxiety and depression, the WHOQoL-REF for quality of life, the Chalder Fatigue Scale. Musculoskeletal pain was defined as diffuse pain or pain located in the back, joints or limbs. Data regarding sleep complaints and polysomnography were obtained from the Epidemiologic Sleep Study conducted in São Paulo city in 2007. RESULTS: The prevalence estimate of chronic musculoskeletal pain was approximately 27%, with a female/male ratio of approximately 2.6/1. The predictors were being in the age-range of 30-39 years, low socioeconomic and schooling levels, obesity, sedentarism, fatigue, non-restorative sleep, daytime sleepiness, poor sleep quality, poor life quality, anxiety and depression symptoms. Psychological wellbeing was the main discriminator between responders with chronic musculoskeletal pain and the controls, followed by depression for the participants with poor psychological wellbeing, and fatigue, for the remaining ones. Insomnia syndrome was the third-level discriminator for those with fatigue, whereas sleep quality for those without fatigue. CONCLUSIONS: Musculoskeletal pain was frequently reported by São Paulo city dwellers and its correlates with psychological and sleep aspects are suggestive of a response to urbanicity. TRIAL REGISTRATION: ClinicalTrials.gov NCT00596713.
Romano GF(1), Tomassi S, Russell A, Mondelli V, Pariante CM.	(1)Stress, Psychiatry and Immunology Laboratory, Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK.	Fibromyalgia and chronic fatigue: the underlying biology and related theoretical issues.	Adv Psychosom Med. 2015;34:61-77. doi: 10.1159/000369085. Epub 2015 Mar 30.	There is an increasing interest in understanding the biological mechanism underpinning fibromyalgia (FM) and chronic fatigue syndrome (CFS). Despite the presence of mixed findings in this area, a few biological systems have been consistently involved, and the increasing number of studies in the field is encouraging. This chapter will focus on inflammatory and oxidative stress pathways and on the neuroendocrine system, which have been more commonly examined. Chronic inflammation, together with raised levels of oxidative stress and mitochondrial dysfunction, has been increasingly associated with the manifestation of symptoms such as pain, fatigue, impaired memory, and depression, which largely characterise at least some patients suffering from CFS and FM. Furthermore, the presence of blunted hypothalamic-pituitary-adrenal axis activity, with reduced cortisol secretion both at baseline and in response to stimulation tests, suggests a role for the hypothalamic-pituitary-adrenal axis and cortisol in the pathogenesis of these syndromes. However, to what extent these systems' abnormalities could be considered as primary or secondary factors causing FM and CFS has yet to be clarified.
Rombaut L(1), Scheper M, De Wandele I, De Vries J, Meeus M, Malfait F, Engelbert R, Calders P.	(1)Department of Rehabilitation Sciences and Physiotherapy, Ghent University-Artevelde University College, De Pintelaan 185, 3B3, 9000, Ghent, Belgium, Lies.Rombaut@ugent.	Chronic pain in patients with the hypermobility type of Ehlers-Danlos syndrome: evidence for generalized hyperalgesia.	Clin Rheumatol. 2015 Jun;34(6):1121-9. doi: 10.1007/s10067-014-2499-0. Epub 2014 Feb 4.	Chronic widespread pain is highly present in patients with the Ehlers-Danlos syndrome hypermobility type (EDS-HT), but up to now, evidence for generalized hyperalgesia is lacking. The aim of this study is to investigate whether pressure pain thresholds (PPTs) at both symptomatic and asymptomatic body areas differ in EDS-HT patients compared to healthy subjects. Twenty-three women with EDS-HT and 23 gender- and age-matched healthy controls participated. All subjects marked on Margolis Pain Diagram where they felt pain lasting longer than 24 h in the past 4 weeks. Then, they completed several questionnaires assessing pain cognitions, fatigue, disability, and general health status, in order to take the possible influence of these factors on PPTs into account.

	be.			Patients also completed a form concerning the type of pain they experienced. Thereupon, a blinded researcher assessed PPTs at 14 body locations on the trunk and extremities. PPTs were compared for the two complete groups. In addition, PPTs of patients and controls who did not report pain in a respective zone were compared. PPTs of the patients were significantly lower compared to those of the control group, also when pain-free samples per zone were compared. The mean (SD) PPT was 2.9 (1.62) kg/cm(2) in the EDS-HT patients and 5.2 (1.88) kg/cm(2) in the controls ($P < 0.001$). No confounding factors responsible for the observed differences could be revealed. In half of the patient group, a predominantly neuropathic pain component was likely present. This study provides evidence for the existence of hyperalgesia even in asymptomatic areas (generalized secondary hyperalgesia). The generalized hyperalgesia may represent the involvement of a sensitized central nervous system, which inquires an adapted pain management for this patient group.
Roncati L(1), Gatti AM(2), Pusiol T(3), Barbolini G(1), Maiorana A(1).	(1)Department of Diagnostic and Clinical Medicine and of Public Health, University of Modena and Reggio Emilia, Modena (MO), Italy. (2)Institute of Science and Technology for Ceramics, National Research Council, Faenza (RA), Italy. (3)Provincial Health Care Services, Santa Maria del Carmine Hospital, Rovereto (TN), Italy.	Acquired immunodeficiency similar to Gulf War illness in a dead former serviceman.	J R Army Med Corps. 2015 Jun;161(2):153-5. doi: 10.1136/jramc-2014-000345. Epub 2014 Nov 26.	A 38-year-old non-commissioned officer was certified unfit for military duty several months before his death. The forensic autopsy revealed a severe bone marrow aplasia and a pulmonary angioinvasive aspergillosis. Moreover, the presence of inorganic foreign particles in the pulmonary macrophages and intestinal endothelia was observed. The microanalysis implemented on these last selected specimens revealed the presence of silica particles microimpregnated by lanthanides and steel. The patient's acquired immunodeficiency appears comparable with that of Iraqi civilians suffering from Gulf War illness. This is the first report in the literature of the presence of intestinal endothelia engulfed by foreign war particulates; the silica particles may have entered the intestinal endothelia via the blood stream or by ingestion of impregnated fruit and vegetable foodstuffs. This finding provides new perspectives in the assessment of war-associated diseases and includes electron probe microanalysis among the new techniques of military and forensic medicine.
Rosato L(1), Pacini F, Panier Suffat L, Mondini G, Ginardi A, Maggio M, Bosco MC, Della Pepa C.	(1)Department of Surgery - Endocrine Surgical Unit, Ivrea Hospital, School of Medicine, ASL TO4, University of Turin, Turin, Italy.	Post-thyroidectomy chronic asthenia: self-deception or disease?	Endocrine. 2015 Mar;48(2):615-20. doi: 10.1007/s12020-014-0353-4. Epub 2014 Jul 18.	There is clinical evidence that post-total thyroidectomy (TT) patients can present persistent asthenia. The aim of this study was to evaluate the prevalence of asthenia symptoms in such patients, assess whether a chronic asthenia syndrome could be caused by TT or become evident after it. An observational study was carried out comparing two groups of 100 patients each, all with homogeneous characteristics. Group A was treated with total lobectomy (TL), Group B with TT. All patients presented normal thyroid hormone levels. The patients were interviewed in order to identify the ones affected by post-operative asthenia persisting for at least six months, with reduced ability to perform physical and mental work, not showing improvement with rest. The severity of the symptoms has been measured by means of the brief fatigue

				inventory (BFI). Statistical analysis was performed to evaluate statistically significative differences between groups and prognostic factors in TT group. The incidence of post-operative asthenia was 0 % after TL and 25 % after TT, with the operation being the only significant variable. Asthenia is well known as symptom of post-thyroidectomy, but it has not been adequately investigated as consequence of surgery. We demonstrated that the complete removal of the thyroid gland could determine chronic post-thyroidectomy asthenia, although with intensity limited to low/moderate. Post-thyroidectomy asthenia is a relevant sequela interfering with quality of life of at least 25 % of patients operated, suggesting the need to identify its real causes and limit the indication to TT only when strictly required.
Ross LJ(1), Capra S(2), Baguley B(2), Sinclair K(3), Munro K(3), Lewindon P(2,)(3,)(4,)(5,)(6), Lavin M(7).	(1)Department of Nutrition and Dietetics, The Royal Brisbane & Women's Hospital, Brisbane, Queensland, Australia.	Nutritional status of patients with ataxia-telangiectasia: A case for early and ongoing nutrition support and intervention.	J Paediatr Child Health. 2015 Aug;51(8):802-7. doi: 10.1111/jpc.12828. Epub 2015 Feb 6.	AIM: Ataxia-telangiectasia (A-T) is a rare genomic syndrome resulting in severe disability. Chronic childhood disorders can profoundly influence growth and development. Nutrition-related issues in A-T are not well described, and there are no nutritional guidelines. This study investigated the nutrition-related characteristics and behaviours of Australian A-T patients attending a national clinic. METHODS: A cross-sectional analysis of 13 A-T patients (nine females; aged: 4-23 years): nutritional status was assessed by anthropometric and body cell mass (BCM) calculations. Parents reported their child's diet history and physical and behavioural factors that affect nutrition including fatigue and need for assistance. RESULTS: Ten (77%) had short stature (height for age z scores <-1), and seven (54%) were underweight for height (weight/height z scores <-1). Significant malnutrition (BCM z scores <-2) was detected in nine (69%) including the one adult who was severely malnourished. Malnutrition increased significantly with age (BCM for height z scores and age, $r = -0.937$, $P < 0.001$). Eight (62%) patients ate poorly compared with estimated energy requirement for weight. Poor diet quality was characterised by high fat and sugar choices. Parents reported significant nutritional barriers as chronic tiredness and the need for care giver assistance with meals. CONCLUSIONS: This study confirms profound malnutrition in Australian A-T patients. Poor intakes and diet quality suggest the need for early nutrition intervention. Ongoing support for families and early discussions on tube feeding are required to address changing needs in childhood and likely nutritional decline into adulthood. A prospective study is required to assess feasibility and effectiveness of nutrition interventions in young people with A-T.
Rossi A(1), Di Lollo AC(2), Guzzo MP(2), Giacomelli C(1), Atzeni F(3), Bazzichi L(1), Di Franco M(2).	(1)Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy. (2)Department of Internal Medicine and	Fibromyalgia and nutrition: what news?	Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl 88):S117-25. Epub 2015 Mar 18.	Fibromyalgia syndrome (FM) is a chronic, generalised pain condition usually accompanied by several associated symptoms, such as fatigue, sleep disturbance, headache, irritable bowel syndrome and mood disorders. Different medical treatments are used to treat fibromyalgia and the recent guidelines suggest that the optimal treatment consists in a multidisciplinary approach with a combination of pharmacological and non-pharmacological treatment modalities. Among non-pharmacological treatment, nutrition is a promising tool for FM patients. The aim of this review is to update the present knowledge about fibromyalgia and nutrition by

	Medical Specialties, Rheumatology Unit, La Sapienza University, Rome, Italy. (3)IRCCS Galeazzi Orthopaedic Institute, Milan, Italy.			means of a systematic search performed on Medline from January 2000 to December 2014. Nutritional deficiencies have been described in FM patients and the benefits of specific diet and nutritional supplementation are shown. Obesity and overweight, often present in FM patients, are related to the severity of FM worsening the quality of life in terms of higher pain, fatigue, worsened sleep quality and higher incidence of mood disorders. Weight control is thus an effective tool to improve the symptoms. Moreover, it seems reasonable to eliminate some foods from the diet of FM patients, for example excitotoxins. Non-coeliac gluten sensitivity is increasingly recognised as a frequent condition with similar manifestations which overlap with those of FM. The elimination of gluten from the diet of FM patients is recently becoming a potential dietary intervention for clinical improvement. In summary, this review reveals the potential benefit of specific dietary interventions as non-pharmacological tools as part of a multidisciplinary treatment for FM patients.
Russell C, Wearden AJ, Fairclough G, Emsley RA, Kyle SD.		Subjective But Not Actigraphy-Defined Sleep Predicts Next-Day Fatigue in Chronic Fatigue Syndrome: A Prospective Daily Diary Study.	Sleep. 2015 Dec 22. pii: sp-00453-15. [Epub ahead of print]	STUDY OBJECTIVES: This study aimed to (1) examine the relationship between subjective and actigraphy-defined sleep, and next-day fatigue in chronic fatigue syndrome (CFS); and (2) investigate the potential mediating role of negative mood on this relationship. We also sought to examine the effect of presleep arousal on perceptions of sleep. METHODS: Twenty-seven adults meeting the Oxford criteria for CFS and self-identifying as experiencing sleep difficulties were recruited to take part in a prospective daily diary study, enabling symptom capture in real time over a 6-day period. A paper diary was used to record nightly subjective sleep and presleep arousal. Mood and fatigue symptoms were rated four times each day. Actigraphy was employed to provide objective estimations of sleep duration and continuity. RESULTS: Multilevel modelling revealed that subjective sleep variables, namely sleep quality, efficiency, and perceiving sleep to be unrefreshing, predicted following-day fatigue levels, with poorer subjective sleep related to increased fatigue. Lower subjective sleep efficiency and perceiving sleep as unrefreshing predicted reduced variance in fatigue across the following day. Negative mood on waking partially mediated these relationships. Increased presleep cognitive and somatic arousal predicted self-reported poor sleep. Actigraphy-defined sleep, however, was not found to predict following-day fatigue. CONCLUSIONS: For the first time we show that nightly subjective sleep predicts next-day fatigue in CFS and identify important factors driving this relationship. Our data suggest that sleep specific interventions, targeting presleep arousal, perceptions of sleep and negative mood on waking, may improve fatigue in CFS.
Rusu C(1), Gee ME(1), Lagacé C(1), Parlor M(2).	(1)Centre for Chronic Disease Prevention, Public Health Agency of Canada, Ottawa, Ontario, Canada. (2)National ME/FM	Chronic fatigue syndrome and fibromyalgia in Canada: prevalence and associations with six health status indicators.	Health Promot Chronic Dis Prev Can. 2015 Mar;35(1):3-11.	INTRODUCTION: Few studies have considered the factors independently associated with chronic fatigue syndrome (CFS) and/or fibromyalgia (FM) or considered the impact of these conditions on health status using population-based data. METHODS: We used data from the nationally representative 2010 Canadian Community Health Survey (n = 59 101) to describe self-reported health professional-diagnosed CFS and/or FM, and their associations with 6 health status indicators. RESULTS: In 2010, diagnosed CFS and

	Action Network, Nepean, Ontario, Canada.			FM are reported by 1.4% (95% confidence interval [CI]: 1.3%-1.6%) and 1.5% (1.4%-1.7%), respectively, of the Canadian household population aged 12 years and over, with comorbid CFS and FM affecting 0.3% (0.3%-0.4%) of that population. Prevalent CFS and/or FM were more common among women, adults aged 40 years and over, those with lowest income, and those with certain risk factors for chronic disease (i.e. obesity, physical inactivity and smoking). After controlling for differences between the groups, people with CFS and/or FM reported poorer health status than those with neither condition on 5 indicators of health status, but not on the measure of fair/poor mental health. Having both CFS and FM and having multiple comorbid conditions was associated with poorer health status. CONCLUSION: Co-occurrence of CFS and FM and having other chronic conditions were strongly related to poorer health status and accounted for much of the differences in health status. Understanding factors contributing to improved quality of life in people with CFS and/or FM, particularly in those with both conditions and other comorbidities, may be an important area for future research.
Ryan JC(1,)(2), Wu Q(3), Shoemaker RC(4,)(5).	(1)ProteoGenomics, LLC, Vero Beach, FL, 32963, Florida. ryan.jimmy@progenome.com.	Transcriptomic signatures in whole blood of patients who acquire a chronic inflammatory response syndrome (CIRS) following an exposure to the marine toxin ciguatoxin.	BMC Med Genomics. 2015 Apr 2;8:15. doi: 10.1186/s12920-015-0089-x.	BACKGROUND: Ciguatoxins (CTXs) are polyether marine neurotoxins found in multiple reef-fish species and are potent activators of voltage-gated sodium channels. It is estimated that up to 500,000 people annually experience acute ciguatera poisoning from consuming toxic fish and a small percentage of these victims will develop a chronic, multisymptom, multisystem illness, which can last years, termed a Chronic Inflammatory Response Syndrome (CIRS). Symptoms of ciguatera CIRS include fatigue, cognitive deficits, neurologic deficits, pain and sensitivity to light. There are few treatment options for ciguatera CIRS since little is known about its pathophysiology. METHODS: This study characterizes the transcriptional profile in whole blood of 11 patients with ciguatera-induced CIRS and 11 normal controls run in duplicate using Agilent one color whole genome microarrays. Differential expression was determined by using a combination of moderated t-test p-value and fold change (FC). Significant genes were subjected to gene ontology, principal component analysis and SVM classification. Seven significant genes found by microarray were validated by PCR. RESULTS: Using a low stringency ($p < 0.05$ and $FC > 1.4$) and a high stringency ($p < 0.01$ and $FC > 1.5$) filter, the resulting gene sets of 185 and 55, respectively, showed clear separation of cases and controls by PCA as well as 100% classification accuracy by SVM, indicating that the gene profiles can separate patients from controls. PCR results of 7 genes showed a 95% correlation to microarray data. Several genes identified by microarray are important in wound healing (CD9, CD36, vWF and Factor XIII), adaptive immunity (HLA-DQB1, DQB2, IL18R1 and IL5RA) and innate immunity (GZMK, TOLLIP, SIGIRR and VIPR2), overlapping several areas shown to be disrupted in a mouse model of acute exposure to ciguatoxin. Another area of interest was differential expression of long, non-coding sequences, or lncRNA. CONCLUSIONS: Disruptions of innate and

				adaptive immune mechanisms were recorded at both the genomic and proteomic level. A disruption in the HLA-T cell receptor axis could indicate HLA haplotype sensitivity for this chronic syndrome, as noted in many autoimmune conditions. Taken together, these indicators of illness provide additional insights into pathophysiology and potential therapies.
Salsman JM(1), Beaumont JL, Wortman K, Yan Y, Friend J, Cella D.	(1)Department of Medical Social Sciences, Feinberg School of Medicine at Northwestern University, 633 North St. Clair, 19th Floor, Chicago, IL, 60611, USA, j-salsman@northwestern.edu.	Brief versions of the FACIT-fatigue and FAACT subscales for patients with non-small cell lung cancer cachexia.	Support Care Cancer. 2015 May;23(5):1355-64. doi: 10.1007/s00520-014-2484-9. Epub 2014 Oct 29.	PURPOSE: Cancer anorexia-cachexia syndrome (CACS) is common in advanced cancer patients and associated with weight loss, fatigue, impaired quality of life (QoL), and poor prognosis. The goal of this project was to identify the most responsive items from two QoL measures in the ROMANA 2 (NCT01387282) phase III global study evaluating anamorelin HCl in the treatment of non-small cell lung cancer (NSCLC) cachexia: the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and the Functional Assessment of Anorexia/Cachexia Therapy (FAACT). METHODS: In the ROMANA 2 trial, 477 patients with unresectable stage III or IV NSCLC and cachexia were to be enrolled and randomized (2:1) to receive anamorelin HCl or placebo once daily for 12 weeks. All 203 patients who reached the week 12 visit at the time of data analysis were included. Co-primary endpoints were change from baseline in lean body mass and handgrip strength. QoL was a secondary outcome with FACIT-F and FAACT questionnaires administered at baseline and at weeks 3, 6, 9, and 12. RESULTS: Two 4-item scales (fatigue/activity and appetite/eating) from the FACIT-F and FAACT questionnaires, respectively, demonstrated good internal consistency reliability, validity, and responsiveness (also referred to as the Simplified Evaluation of Fatigue (SEF) and Simplified Evaluation of Appetite (SEA), respectively). The estimated important difference for each scale was 1-2 points. CONCLUSIONS: These brief scales provide the psychometric properties necessary to promote future research in NSCLC patients with CACS. Additional work should examine the clinical utility of these scales and their impact on treatment decision-making.
Samsel A(1), Seneff S(2).	(1)Research Scientist and Consultant, Deerfield, NH 03037, USA. (2)Spoken Language Systems Group, Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge MA 02139, USA.	Glyphosate, pathways to modern diseases III: Manganese, neurological diseases, and associated pathologies.	Surg Neurol Int. 2015 Mar 24;6:45. doi: 10.4103/2152-7806.153876. eCollection 2015.	Manganese (Mn) is an often overlooked but important nutrient, required in small amounts for multiple essential functions in the body. A recent study on cows fed genetically modified Roundup(®)-Ready feed revealed a severe depletion of serum Mn. Glyphosate, the active ingredient in Roundup(®), has also been shown to severely deplete Mn levels in plants. Here, we investigate the impact of Mn on physiology, and its association with gut dysbiosis as well as neuropathologies such as autism, Alzheimer's disease (AD), depression, anxiety syndrome, Parkinson's disease (PD), and prion diseases. Glutamate overexpression in the brain in association with autism, AD, and other neurological diseases can be explained by Mn deficiency. Mn superoxide dismutase protects mitochondria from oxidative damage, and mitochondrial dysfunction is a key feature of autism and Alzheimer's. Chondroitin sulfate synthesis depends on Mn, and its deficiency leads to osteoporosis and osteomalacia. Lactobacillus, depleted in autism, depend critically on Mn for antioxidant protection. Lactobacillus probiotics can treat anxiety, which is a comorbidity of autism and chronic

				fatigue syndrome. Reduced gut Lactobacillus leads to overgrowth of the pathogen, Salmonella, which is resistant to glyphosate toxicity, and Mn plays a role here as well. Sperm motility depends on Mn, and this may partially explain increased rates of infertility and birth defects. We further reason that, under conditions of adequate Mn in the diet, glyphosate, through its disruption of bile acid homeostasis, ironically promotes toxic accumulation of Mn in the brainstem, leading to conditions such as PD and prion diseases.
Santiago T(1), Rebelo O, Negrão L, Matos A.	(1)Rheumatology Unit, Centro Hospitalar e Universitário de Coimbra, Praceta Prof. Mota Pinto, 3000-075, Coimbra, Portugal, tlousasantiago@hotmail.com.	Macrophagic myofasciitis and vaccination: consequence or coincidence?	Rheumatol Int. 2015 Jan;35(1):189-92. doi: 10.1007/s00296-014-3065-4. Epub 2014 Jun 13.	Macrophagic myofasciitis (MMF) characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization has been reported with increasing frequency in the past 10 years. We describe clinical and laboratory findings in patients with MMF. We did a retrospective analysis of 16 cases observed in our Neuropathology Laboratory, between January 2000 and July 2013. The mean age of the 16 patients was 48.8 ± 18.0 years; 80.0 % were female. Chronic fatigue syndrome was found in 8 of 16 patients. Half of the patients had elevated creatinine kinase levels, and 25.0 % had a myopathic electromyogram. Thirteen patients received intramuscular administration of aluminum-containing vaccine prior to the onset of symptoms. MMF may mirror a distinctive pattern of an inflammatory myopathy. The vaccines containing this adjuvant may trigger MMF in some patients.
Sarma P(1), Borah M(1), Das S(1).	(1)Department of Pharmacology, Assam Medical College, Dibrugarh, Assam, India.	Evaluation of the effect of ethanolic extract of fruit pulp of Cassia fistula Linn. on forced swimming induced chronic fatigue syndrome in mice.	Res Pharm Sci. 2015 May-Jun;10(3):206-13.	The fruit of Cassia fistula Linn. is a legume, has antioxidant and lots of other medicinal properties. As oxidants are involved in the pathogenesis of chronic fatigue syndrome, the present study was done to evaluate the effect of ethanolic extract of fruit pulp of C. fistula Linn. (EECF) on forced swimming induced chronic fatigue syndrome (CFS). Albino mice of 25-40 grams were grouped into five groups (n=5). Group A served as naive control and group B served as stress control. Group C received EECF 200 mg/kg and group D received EECF 400 mg/kg respectively. Group E received imipramine 20 mg/kg (standard). All animals were treated with their respective agent orally daily for 7 days. Except for group A, animals in other groups were subjected to force swimming 6 min daily for 7 days to induce a state of chronic fatigue. Duration of immobility was assessed on day 1(st), 3(rd), 5(th) and 7(th). Anxiety level (by elevated plus maze and mirrored chamber) and loco-motor activity (by open field test) were assessed 24 h after last force swimming followed by biochemical estimations of oxidative biomarkers in brain homogenate at the end of study. Treatment with EECF resulted in significant reduction in the duration of immobility, reduced anxiety and increased loco-motor activity. Malondialdehyde level was also reduced and catalase level was increased in the extract treated group and standard group compared to stress control group. The study indicates that EECF has protective effect against experimentally induced CFS.
Schafer C(1), Evans M, Jason LA, So S, Brown	(1)a Center for Community Research, DePaul University ,	Measuring substantial reductions in activity.	J Prev Interv Community. 2015;43(1):5-19. doi: 10.1080/10852352.2014.9	The case definitions for Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS), ME, and CFS each include a disability criterion requiring substantial reductions in activity in order to meet diagnostic criteria. Difficulties have been encountered in

A.	Chicago , Illinois , USA.		73242.	defining and operationalizing the substantial reduction disability criterion within these various illness definitions. The present study sought to relate measures of past and current activities in several domains including the SF-36, an objective measure of activity (e.g., actigraphy), a self-reported quality of life scale, and measures of symptom severity. Results of the study revealed that current work activities had the highest number of significant associations with domains such as the SF-36 subscales, actigraphy, and symptom scores. As an example, higher self-reported levels of current work activity were associated with better health. This suggests that current work related activities may provide a useful domain for helping operationalize the construct of substantial reductions in activity.
Scherber RM(1,)(2), Kosiorek HE(3), Senyak Z(4), Dueck AC(3), Clark MM(5), Boxer MA(6), Geyer HL(1), McCallister A(4), Cotter M(4), Van Husen B(7), Harrison CN(8,)(9), Mesa RA(1).	(1)Division of Hematology and Medical Oncology, Mayo Clinic, Scottsdale, Arizona. (2)Department of Hematology and Oncology, Oregon Health and Science University, Portland, Oregon. (3)Division of Biostatistics, Mayo Clinic, Scottsdale, Arizona. (4)MPN Forum, MPN Research Foundation, Chicago, Illinois. (5)Department of Psychiatry and Psychology, Mayo Clinic, Rochester, Minnesota. (6)Arizona Oncology, Tucson, Arizona. (7)MPN Research Foundation, Chicago, Illinois. (8)Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom. (9)MPN	Comprehensively understanding fatigue in patients with myeloproliferative neoplasms.	Cancer. 2015 Dec 15. doi: 10.1002/cncr.29753. [Epub ahead of print]	BACKGROUND: Patients with myeloproliferative neoplasms (MPNs) experience a high persistence, prevalence, and severity of fatigue. There is currently only limited information regarding factors that contribute to fatigue in patients with MPNs. METHODS: A 70-item, Internet-based survey regarding fatigue was developed by MPN investigators and patients/advocates and hosted by the Mayo Clinic Survey Research Center. RESULTS: Fatigue was found to be prevalent and severe among international survey respondents (1788 respondents). Higher body mass index (P<.001), current use of alcohol (P<.001), and current tobacco use (P = .0025) were found to be significantly associated with greater fatigue. Moderate/severe fatigue was present more frequently in those individuals who did not exercise compared with those who reported exercising at least once per week (P<.001). Medical comorbidities found to be significantly associated with greater fatigue included restless leg syndrome (P = .006), diabetes mellitus (P = .045), fibromyalgia (P < 0.001), chronic fatigue syndrome (P = .006), and chronic kidney disease (P = .02). Current use of antidepressants (P<.001), antihistamines (P = .0276), antianxiety medications (P = .0357), and prescription pain medications (P<.001) were found to be associated with worsened fatigue. Nearly 25% of respondents scored > 2 on the Patient Health Questionnaire, indicating a high probability of depression. Higher Brief Fatigue Inventory score, Myeloproliferative Neoplasm Total Symptom Score, and individual symptom items were all associated with a higher likelihood of depressive symptoms (P<.0001). CONCLUSIONS: The management of fatigue should be multifactorial, with a comprehensive assessment and treatment plan to address all modifiable fatigue etiologies. Patients with MPNs likely have a higher prevalence of mood disturbances compared with the general population, suggesting the need to assess and intervene in this domain. Cancer 2015. © 2015 American Cancer Society.

	Voice, London, United Kingdom.			
Schmaling KB(1), Betterton KL(2).	(1)Department of Psychology, Washington State University, 14204 NE Salmon Creek Avenue, Vancouver, WA, 98686, USA. karen.schmaling@wsu.edu. (2)Department of Psychology, Washington State University, 14204 NE Salmon Creek Avenue, Vancouver, WA, 98686, USA.	Neurocognitive complaints and functional status among patients with chronic fatigue syndrome and fibromyalgia.	Qual Life Res. 2015 Oct 15. [Epub ahead of print]	PURPOSE: The purpose of this study was to conduct a longitudinal examination of cognitive complaints and functional status in patients with chronic fatigue syndrome (CFS) alone and those who also had fibromyalgia (CFS/FM). METHODS: A total of 93 patients from a tertiary care fatigue clinic were evaluated on four occasions, each 6 months apart. Each evaluation included a tender point assessment, and self-reported functional status and cognitive complaints. RESULTS: Patients with CFS/FM reported significantly worse physical functioning, more bodily pain, and more cognitive difficulties (visuo-perceptual ability and verbal memory) than patients with CFS alone. Over time, bodily pain decreased only for participants with CFS alone. Verbal memory problems were associated with more bodily pain for both patient groups, whereas visuo-perceptual problems were associated with worse functional status for patients with CFS alone. CONCLUSIONS: This study adds to the literature on functional status, longitudinal course, and cognitive difficulties among patients with CFS and those with CFS and FM. The results suggest that patients with CFS/FM are more disabled, have more cognitive complaints, and improve more slowly over time than patients with CFS alone. Specific cognitive difficulties are related to worse functional status, which supports the addition of cognitive difficulties to the FM case criteria.
Schneck AS(1,)(2), Anty R(3,)(2), Tran A(3,)(2), Hastier A(3), Amor IB(1), Gugenheim J(1,)(2), Iannelli A(1,)(2), Piche T(4,)(5).	(1)Service de Chirurgie Digestive et Transplantation Hépatique, Hôpital Archet 2, Pôle Digestif, CHU Nice, Université de Nice Sophia-Antipolis, Nice, France. (2)INSERM, U1065, Team 8 "Hepatic complications in obesity", C3M, Nice, France. (3)Service d'Hépato-Gastroentérologie et de Cancérologie Digestive, Hôpital Archet 2, Pôle Digestif, CHU de Nice, Université de Nice	Increased Prevalence of Irritable Bowel Syndrome in a Cohort of French Morbidly Obese Patients Candidate for Bariatric Surgery.	Obes Surg. 2015 Sep 30. [Epub ahead of print]	BACKGROUND: Only a few recent reports have suggested a correlation between obesity and irritable bowel syndrome (IBS). We aimed to determine the prevalence and severity of IBS in a prospective cohort of obese patients undergoing bariatric surgery in Nice Hospital (France). METHODS: One hundred obese patients were included prospectively before bariatric surgery. A diagnosis of IBS and each subtype was performed according to Rome-III criteria using a Bristol scale for stool consistency. Patients provided information on IBS-related comorbidities, including chronic fatigue, migraine, lower back pain, gastroesophageal reflux disease (GERD), genitourinary problems, and dyspepsia. Patients completed questionnaires to assess the severity of IBS, GERD, psychological factors (anxiety, depression), fatigue, and quality of life. RESULTS: Thirty patients fulfilled the Rome-III criteria for IBS. There was no difference in age, gender, or BMI between obese patients with or without IBS. Obese patients with IBS reported a significantly higher prevalence of GERD, migraines, lower back pain, genitourinary problems, chronic fatigue, and dyspepsia. Obese patients with IBS had significant higher scores of fatigue, anxiety, depression, and poorer quality of life. Obese patients that had both IBS and GERD had significantly higher IBS severity scores than those without GERD. In a logistic regression model including BMI, anxiety, depression, gender, and GERD score, only anxiety was significantly and independently associated with IBS. CONCLUSIONS: Thirty percent of obese patients had IBS: its severity was not correlated with BMI. However, anxiety was independently associated with IBS, suggesting that psychological factors are key features of IBS, whatever the

	Sophia-Antipolis, Nice, France. (4)Service d'Hépato-Gastroentérologie et de Cancérologie Digestive, Hôpital Archet 2, Pôle Digestif, CHU de Nice, Université de Nice Sophia-Antipolis, Nice, France. piche.t@chu-nice.fr. (5)Service d'Immunologie, Pôle Biologie, EA 6302 Tolérance Immunitaire, Hôpital Archet 1 Université de Nice Sophia-Antipolis, Nice, France. piche.t@chu-nice.fr.			presence of obesity.
Sharpe M(1), Goldsmith KA(2), Johnson AL(3), Chalder T(4), Walker J(5), White PD(6).	(1)Psychological Medicine Research, University of Oxford Department of Psychiatry, Oxford, UK. Electronic address: michael.sharpe@psych.ox.ac.uk. (2)Department of Biostatistics, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. (3)Medical Research Council Clinical Trials Unit at UCL, London, UK. (4)Academic	Rehabilitative treatments for chronic fatigue syndrome: long-term follow-up from the PACE trial.	Lancet Psychiatry. 2015 Dec;2(12):1067-74. doi: 10.1016/S2215-0366(15)00317-X. Epub 2015 Oct 28.	BACKGROUND: The PACE trial found that, when added to specialist medical care (SMC), cognitive behavioural therapy (CBT), or graded exercise therapy (GET) were superior to adaptive pacing therapy (APT) or SMC alone in improving fatigue and physical functioning in people with chronic fatigue syndrome 1 year after randomisation. In this pre-specified follow-up study, we aimed to assess additional treatments received after the trial and investigate long-term outcomes (at least 2 years after randomisation) within and between original treatment groups in those originally included in the PACE trial. METHODS: The PACE trial was a parallel-group randomised controlled trial of patients meeting Oxford criteria for chronic fatigue syndrome who were recruited from six secondary care clinics in the UK between March 18, 2005, and Nov 28, 2008. Participants were randomly allocated to receive SMC alone or plus APT, CBT, or GET. Primary outcomes (were fatigue measured with Chalder fatigue questionnaire score and physical functioning with short form-36 subscale score, assessed 1 year after randomisation. In this long-term follow-up, we sent postal questionnaires to assess treatment received after the trial and outcomes a minimum of 2 years after randomisation. We assessed long-term differences in outcomes within and between originally randomised groups. The PACE trial is registered at http://isrctn.org, number ISRCTN54285094. FINDINGS: Between May 8, 2008, and April 26, 2011, 481 (75%) participants from the PACE trial returned questionnaires. Median time from randomisation to return of long-term follow-up assessment was 31 months (IQR 30-32;

	Department of Psychological Medicine, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK. (5)Psychological Medicine Research, University of Oxford Department of Psychiatry, Oxford, UK. (6)Centre for Psychiatry, Wolfson Institute of Preventive Medicine, Bart's and The London Medical School, Queen Mary University of London, London, UK.			range 24-53). 210 (44%) participants received additional treatment (mostly CBT or GET) after the trial; with participants originally assigned to SMC alone (73 [63%] of 115) or APT (60 [50%] of 119) more likely to seek treatment than those originally assigned to GET (41 [32%] of 127) or CBT (36 [31%] of 118; p<0·0001). Improvements in fatigue and physical functioning reported by participants originally assigned to CBT and GET were maintained (within-group comparison of fatigue and physical functioning, respectively, at long-term follow-up as compared with 1 year: CBT -2·2 [95% CI -3·7 to -0·6], 3·3 [0·02 to 6·7]; GET -1·3 [-2·7 to 0·1], 0·5 [-2·7 to 3·6]). Participants allocated to APT and to SMC alone in the trial improved over the follow-up period compared with 1 year (fatigue and physical functioning, respectively: APT -3·0 [-4·4 to -1·6], 8·5 [4·5 to 12·5]; SMC -3·9 [-5·3 to -2·6], 7·1 [4·0 to 10·3]). There was little evidence of differences in outcomes between the randomised treatment groups at long-term follow-up. INTERPRETATION: The beneficial effects of CBT and GET seen at 1 year were maintained at long-term follow-up a median of 2·5 years after randomisation. Outcomes with SMC alone or APT improved from the 1 year outcome and were similar to CBT and GET at long-term follow-up, but these data should be interpreted in the context of additional therapies having being given according to physician choice and patient preference after the 1 year trial final assessment. Future research should identify predictors of response to CBT and GET and also develop better treatments for those who respond to neither. FUNDING: UK Medical Research Council, Department of Health for England, Scottish Chief Scientist Office, Department for Work and Pensions, National Institute for Health Research (NIHR), NIHR Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust, King's College London.
Sheridan A(1).	(1)Glasgow , UK.	Response to Gladwell et al.: concerns about safety for GET.	Disabil Rehabil. 2015;37(5):464. doi: 10.3109/09638288.2014.952455. Epub 2014 Aug 21.	Comment on Disabil Rehabil. 2014;36(5):387-94
Shukla SK(1), Cook D(2,)(3), Meyer J(2), Vernon SD(4), Le T(1), Clevidence D(3), Robertson CE(5), Schrodi SJ(1), Yale S(6), Frank DN(5).	(1)Marshfield Clinic Research Foundation, Marshfield, WI, United States of America. (2)William S. Middleton Memorial Veterans Hospital, Madison, WI, United States of America. (3)University of Wisconsin, Madison, WI, United States of America. (4)Bateman	Changes in Gut and Plasma Microbiome following Exercise Challenge in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS).	PLoS One. 2015 Dec 18;10(12):e0145453. doi: 10.1371/journal.pone.0145453. eCollection 2015.	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a disease characterized by intense and debilitating fatigue not due to physical activity that has persisted for at least 6 months, post-exertional malaise, unrefreshing sleep, and accompanied by a number of secondary symptoms, including sore throat, memory and concentration impairment, headache, and muscle/joint pain. In patients with post-exertional malaise, significant worsening of symptoms occurs following physical exertion and exercise challenge serves as a useful method for identifying biomarkers for exertion intolerance. Evidence suggests that intestinal dysbiosis and systemic responses to gut microorganisms may play a role in the symptomology of ME/CFS. As such, we hypothesized that post-exertion worsening of ME/CFS symptoms could be due to increased bacterial translocation from the intestine into the systemic circulation. To test this hypothesis, we collected symptom reports and blood and stool samples from ten clinically characterized ME/CFS patients and ten matched healthy controls before

	Horne Center of Excellence, Salt Lake City, UT, United States of America. (5)University of Colorado Denver Anschutz Medical Campus, Aurora, CO, United States of America. (6)Marshfield Clinic, Marshfield, WI, United States of America.			and 15 minutes, 48 hours, and 72 hours after a maximal exercise challenge. Microbiomes of blood and stool samples were examined. Stool sample microbiomes differed between ME/CFS patients and healthy controls in the abundance of several major bacterial phyla. Following maximal exercise challenge, there was an increase in relative abundance of 6 of the 9 major bacterial phyla/genera in ME/CFS patients from baseline to 72 hours post-exercise compared to only 2 of the 9 phyla/genera in controls ($p = 0.005$). There was also a significant difference in clearance of specific bacterial phyla from blood following exercise with high levels of bacterial sequences maintained at 72 hours post-exercise in ME/CFS patients versus clearance in the controls. These results provide evidence for a systemic effect of an altered gut microbiome in ME/CFS patients compared to controls. Upon exercise challenge, there were significant changes in the abundance of major bacterial phyla in the gut in ME/CFS patients not observed in healthy controls. In addition, compared to controls clearance of bacteria from the blood was delayed in ME/CFS patients following exercise. These findings suggest a role for an altered gut microbiome and increased bacterial translocation following exercise in ME/CFS patients that may account for the profound post-exertional malaise experienced by ME/CFS patients.
Sieminski M(1), Losy J(2), Partinen M(3).	(1)Department of Adult Neurology, Medical University of Gdansk, Gdansk, Poland. Electronic address: msiem@wp.pl. (2)Department of Clinical Neuroimmunology, Chair of Neurology, Poznan University School of Medicine, Poznan, Poland; Neuroimmunlogical Unit, Mossakowski Medical Research Centre Polish Academy of Sciences, Poznan, Poland. (3)Helsinki Sleep Clinic, Vitalmed Research Centre,	Restless legs syndrome in multiple sclerosis.	Sleep Med Rev. 2015 Aug;22:15-22. doi: 10.1016/j.smrv.2014.10.002. Epub 2014 Oct 12.	Restless legs syndrome (RLS) is a sleep-related sensory-motor disorder characterized by an irresistible urge to move the legs accompanied by unpleasant sensations in the lower extremities. According to many recent studies patients with multiple sclerosis (MS) suffer frequently from symptoms of RLS. The prevalence of RLS in MS patients varies 13.3%-65.1%, which is higher than the prevalence of RLS in people of the same age in the general population. MS patients with RLS have higher scores in the Expanded Disability Status Scale compared to MS patients without RLS. Presence of RLS has a negative impact on sleep quality and fatigue of MS patients. Iron deficiency and chronic inflammation may be factors contributing to development of RLS in MS. The relationship between the course and treatment of MS and RLS requires further prospective studies.

	Helsinki, Finland; Department of Clinical Neurosciences, University of Helsinki, Helsinki, Finland.			
Singh K(1), Gupta R(2), Kamal H(2), Silvestri NJ(2), Wolfe GI(2).	(1)Department of Neurology, University at Buffalo School of Medicine and Biomedical Sciences, The State University of New York, 100 High Street, Building D, Buffalo, NY 14203-1126, USA. Electronic address: Karanbirsinghmd@gmail.com. (2)Department of Neurology, University at Buffalo School of Medicine and Biomedical Sciences, The State University of New York, 100 High Street, Building D, Buffalo, NY 14203-1126, USA.	Posterior reversible encephalopathy syndrome secondary to blood transfusion.	J Clin Neurosci. 2015 Mar;22(3):592-4. doi: 10.1016/j.jocn.2014.10.005. Epub 2014 Dec 23.	The appearance of posterior reversible encephalopathy syndrome (PRES) after blood transfusion is rare and has only been reported in three patients to our knowledge. We report a fourth patient with PRES secondary to blood transfusion. A 36-year-old woman with a history of menorrhagia presented to the emergency department with severe fatigue. She had a hemoglobin of 1.7 g/dl and received four units of red blood cells over 15 hours. On day 6 post-transfusion she returned with confusion, headache and a generalized tonic-clonic seizure. The MRI of her brain was consistent with PRES. The following day her confusion worsened, repeat MRI of the brain showed new T2-weighted lesions. Over next 10 days her mental status gradually improved close to her baseline. A repeat MRI of the brain showed resolution of the T2-weighted lesions. The clinical presentation, radiological findings and disease progression in our patient was consistent with PRES. Other than the blood transfusions, there were no apparent risk factors for PRES. The prior three patients with post-transfusion PRES have been reported in middle-aged women with uterine fibroids. It is suspected that these patients have a subacute to chronic anemic state due to ongoing menorrhagia. It is interesting to note that no cases of PRES post-transfusion have been reported in the setting of acute blood loss, such as from trauma. It is postulated that an abrupt increase in hemoglobin causes a rapid rise in blood viscosity and loss of hypoxic vasodilation. Subsequent endothelial damage and brain capillary leakage results in PRES. This constellation of changes may not occur after transfusion in patients with more acute blood loss.
Slim M(1), Calandre EP, Rico-Villademoros F.	(1)Instituto de Neurociencias "Federico Olóriz", Universidad de Granada, Avenida de Madrid, 11., 18012, Granada, Spain.	An insight into the gastrointestinal component of fibromyalgia: clinical manifestations and potential underlying mechanisms.	Rheumatol Int. 2015 Mar;35(3):433-44. doi: 10.1007/s00296-014-3109-9. Epub 2014 Aug 14.	Fibromyalgia syndrome is characterized by chronic generalized pain accompanied by a broad symptomatologic spectrum. Besides chronic fatigue, sleep disturbances, headaches and cognitive dysfunction that are extensively described in the literature, a considerable proportion of patients with fibromyalgia experience gastrointestinal symptoms that are commonly overlooked in the studies that are not specifically dedicated to evaluate these manifestations. Nevertheless, various attempts were undertaken to explore the gastrointestinal dimension of fibromyalgia. Several studies have demonstrated an elevated comorbidity of irritable bowel syndrome (IBS) among patients with fibromyalgia. Other studies have investigated the frequency of presentation of gastrointestinal symptoms in fibromyalgia in a nonspecific approach describing several gastrointestinal complaints frequently reported by these patients such as abdominal pain, dyspepsia and bowel changes, among others. Several

				underlying mechanisms that require further investigation could serve as potential explanatory hypotheses for the appearance of such manifestations. These include sensitivity to dietary constituents such as gluten, lactose or FODMAPs or alterations in the brain-gut axis as a result of small intestinal bacterial overgrowth or subclinical enteric infections such as giardiasis. The gastrointestinal component of fibromyalgia constitutes a relevant element of the multidisciplinary pathophysiologic mechanisms underlying fibromyalgia that need to be unveiled, as this would contribute to the adequate designation of relevant treatment alternatives corresponding to these manifestations.
Smith ME, Haney E, McDonagh M, Pappas M, Daeges M, Wasson N, Fu R, Nelson HD.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop.	Ann Intern Med. 2015 Jun 16;162(12):841-50. doi: 10.7326/M15-0114.	BACKGROUND: Myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) is a debilitating multisystem condition affecting more than 1 million adults in the United States. PURPOSE: To determine benefits and harms of treatments for adults with ME/CFS and identify future research needs. DATA SOURCES: MEDLINE, PsycINFO, and Cochrane databases (January 1988 to September 2014); clinical trial registries; reference lists; and manufacturer information. STUDY SELECTION: English-language randomized trials of the effectiveness and adverse effects of ME/CFS treatments. DATA EXTRACTION: Data on participants, study design, analysis, follow-up, and results were extracted and confirmed. Study quality was dual-rated by using prespecified criteria; discrepancies were resolved through consensus. DATA SYNTHESIS: Among 35 treatment trials enrolling participants primarily meeting the 1994 Centers for Disease Control and Prevention and Oxford case definitions of CFS, the immune modulator rintatolimod improved some measures of exercise performance compared with placebo in 2 trials (low strength of evidence). Trials of galantamine, hydrocortisone, IgG, valganciclovir, isoprinosine, fluoxetine, and various complementary medicines were inconclusive (insufficient evidence). Counseling therapies and graded exercise therapy compared with no treatment, relaxation, or support improved fatigue, function, global improvement, and work impairment in some trials; counseling therapies also improved quality of life (low to moderate strength of evidence). Harms were rarely reported across studies (insufficient evidence). LIMITATION: Trials were heterogeneous and were limited by size, number, duration, applicability, and methodological quality. CONCLUSION: Trials of rintatolimod, counseling therapies, and graded exercise therapy suggest benefit for some patients meeting case definitions for CFS, whereas evidence for other treatments and harms is insufficient. More definitive studies comparing participants meeting different case definitions, including ME, and providing subgroup analysis are needed to fill research gaps.
Smith ME, Haney E, Nelson HD.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):888. doi: 10.7326/L15-5176.	
Snodgrass K(1,)(2), Harvey	(1)Clinical Sciences, Murdoch Childrens	Sleep Disturbances in Pediatric Chronic Fatigue	J Clin Sleep Med. 2015 Jul 15;11(7):757-64. doi:	OBJECTIVE: Children and adolescents with chronic fatigue syndrome (CFS) frequently report sleep disturbances. However, little is known about the nature and severity of

A(1,)(2,)(3), Scheinberg A(1,)(3,)(4), Knight S(1,)(2,)(5).	Research Institute. (2)Department of Paediatrics, The University of Melbourne. (3)Victorian Paediatric Rehabilitation Service, The Royal Children's Hospital. (4)Faculty of Medicine, Monash University, Melbourne, Victoria, Australia. (5)Victorian Paediatric Rehabilitation Service, Monash Children's, Parkville, Victoria, Australia.	Syndrome: A Review of Current Research.	10.5664/jcsm.4854.	sleep disturbance and factors associated with sleep problems in pediatric CFS. The purpose of this review was to synthesize and critically appraise existing literature relating to sleep disturbances in pediatric CFS. METHODS: Embase, CINAHL, PsychINFO, PubMed. and Medline databases were searched to retrieve all studies that included an assessment of sleep in pediatric CFS. Two reviewers independently assessed eligibility, extracted data, and systematically assessed reporting quality. RESULTS: Six studies were included and these were mostly case-controlled designs. Findings varied across studies; however, most studies found that children and adolescents with CFS had significantly more sleep disturbances when compared to healthy controls. Significant methodological variations and limitations were apparent. CONCLUSIONS: This review suggests that children and adolescents with CFS experience sleep disturbances. However, results need to be interpreted cautiously given the limited evidence available and its overall low quality. More research is required to elucidate the nature and extent of sleep disturbance in pediatric CFS and should focus on (1) identifying the specific types, causes, and severity of sleep disturbances; (2) the specific consequences of sleep disturbances; and (3) the most effective interventions for sleep problems in this population.
So S(1), Evans M, Jason LA, Brown A.	(1)a Center for Community Research, DePaul University , Chicago , Illinois , USA.	Are stamina and fatigue polar opposites? A case study.	J Prev Interv Community. 2015;43(1):32-41. doi: 10.1080/10852352.2014.973235.	Most individuals with Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) (Carruthers et al., 2003), Myalgic Encephalomyelitis (ME) (Carruthers et al., 2011), and chronic fatigue syndrome (CFS) (Fukuda et al., 1994) indicate that they experience fatigue and sharp decreases in energy levels, which hinder the ability to engage in physical activities (Friedberg & Jason, 1998). However, there are some individuals who reduce activity engagement in order to avoid a worsening of symptoms; thus these individuals may endorse lower levels of fatigue. Accordingly, those with low levels of fatigue but low endurance/stamina might be inadvertently excluded from some criteria based on the fatigue requirement. The current study serves as an exploration of the relationship between fatigue and stamina and the effects of these constructs on illness symptomology and their implications for assessment and diagnosis.
Soejima Y(1), Munemoto T, Masuda A, Uwatoko Y, Miyata M, Tei C.	(1)Department of Cardiovascular, Respiratory and Metabolic Medicine, Graduate School of Medicine, Kagoshima University, Japan.	Effects of Waon therapy on chronic fatigue syndrome: a pilot study.	Intern Med. 2015;54(3):333-8. doi: 10.2169/internalmedicine.54.3042.	OBJECTIVE: Chronic fatigue syndrome (CFS) is a disabling condition of unknown etiology, and no definitive therapy has been identified to date. We developed Waon therapy, a form of thermal therapy using a far-infrared dry sauna, and in this study herein examined its feasibility and safety in patients with CFS. METHODS: Ten consecutive inpatients with CFS stayed in a 60°C sauna for 15 minutes and then rested on a bed under a blanket for an additional 30 minutes outside the sauna room. The treatments were performed once a day, five days a week for four weeks. Perceived fatigue, the primary outcome measure, was evaluated using a numerical rating scale before, during (two weeks after the commencement of therapy) and after therapy. The pain level, evaluated using a numerical rating scale, mood, assessed using the Profile of

				Mood States questionnaire, and performance status, assessed using a scale developed for CFS patients were also examined before and after therapy. RESULTS: Perceived fatigue significantly decreased after therapy, although no significant reductions were observed during therapy. In addition, a negative mood, including anxiety, depression and fatigue, and the performance status significantly improved after therapy. However, the levels of pain and vigor did not change significantly. No patients reported any adverse effects during the therapy. CONCLUSION: These findings suggest that Waon therapy may be a useful and safe treatment for CFS.
Speedy M.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):884-5. doi: 10.7326/L15-5170.	
Speer L(1), Mushkbar S.	(1)Department of Family Medicine, University of Toledo College of Medicine and Life Sciences, OH, USA. Email: linda.speer@utoledo.edu.	"Doctor, I'm so tired!" Refining your work-up for chronic fatigue.	J Fam Pract. 2015 Feb;64(2):84-91.	Recent advances in our understanding of the pathophysiology of chronic fatigue and related disorders can help guide your response to this common complaint.
Staud R(1), Mokthech M, Price DD, Robinson ME.	(1)Departments of aMedicine, bOral and Maxillofacial Surgery, and cClinical and Health Psychology, University of Florida, Gainesville, FL, USA.	Evidence for sensitized fatigue pathways in patients with chronic fatigue syndrome.	Pain. 2015 Apr;156(4):750-9. doi: 10.1097/j.pain.0000000000000110.	Patients with chronic fatigue syndrome (CFS) frequently demonstrate intolerance to physical exertion that is often reported as increased and long-lasting fatigue. Because no specific metabolic alterations have been identified in CFS patients, we hypothesized that sensitized fatigue pathways become activated during exercise corresponding with increased fatigue. After exhausting handgrip exercise, muscle metabolites were trapped in the forearm tissues of 39 CFS patients and 29 normal control (NC) by sudden occlusion for up to 5 minutes. A nonocclusive condition of similar duration was used as control. Repeated fatigue and pain ratings were obtained before and after exercise. Mechanical and heat hyperalgesia were assessed by quantitative sensory testing. All subjects fulfilled the 1994 Fukuda Criteria for CFS. Normal control and CFS subjects exercised for 6.6 (2.4) and 7.0 (2.7) minutes ($P > 0.05$). Forearm occlusion lasted for 4.7 (1.3) and 4.9 (1.8) minutes in NC and CFS subjects, respectively ($P > 0.05$). Although fatigue ratings of CFS subjects increased from 4.8 (2.0) to 5.6 (2.1) visual analogue scale (VAS) units during forearm occlusion, they decreased from 5.0 (1.8) to 4.8 (2.0) VAS units during the control condition without occlusion ($P = 0.04$). A similar time course of fatigue ratings was observed in NC ($P > 0.05$), although their ratings were significantly lower than those of CFS subjects ($P < 0.001$). Quantitative sensory testing demonstrated heat and mechanical hyperalgesia in CFS subjects. Our findings provide indirect evidence for significant contributions of peripheral tissues to the increased exercise-related fatigue in CFS patients consistent with sensitization of fatigue pathways. Future interventions that reduce sensitization of fatigue pathways in CFS

				patients may be of therapeutic benefit.
Stenhoff AL(1), Sadreddini S(2), Peters S(2), Wearden A(2).	(1)University of Manchester, UK stenhoff.alexandra@gmail.com. (2)University of Manchester, UK.	Understanding medical students' views of chronic fatigue syndrome: a qualitative study.	J Health Psychol. 2015 Feb;20(2):198-209. doi: 10.1177/1359105313501534. Epub 2013 Sep 20.	Chronic fatigue syndrome receives little attention in the medical curriculum. This study explores UK medical students' knowledge of and attitudes towards chronic fatigue syndrome. Semi-structured interviews (average length 22 minutes) were conducted with 21 participants (7 females and 14 males) in years 3 (n = 4), 4 (n = 11) and 5 (n = 6) of their studies. Inductive thematic analysis taking a realist perspective produced three themes: limited knowledge, influences on attitudes and training needs. Students acquired their knowledge and attitudes largely from informal sources and expressed difficulty understanding chronic fatigue syndrome within a traditional biomedical framework. Incorporating teaching about chronic fatigue syndrome into the medical curriculum within the context of a biopsychosocial understanding of illness could encourage more positive attitudes towards chronic fatigue syndrome.
Stormorken E(1), Jason LA(2), Kirkevold M(1).	(1)Department of Nursing Science, Institute of Health and Society, University of Oslo, P.O.B. 1130, Blindern, 0318 Oslo Norway. (2)Center for Community Research, DePaul University, 990 W. Fullerton Ave, Suite 3100, Chicago, Illinois 60614 USA.	Fatigue in adults with post-infectious fatigue syndrome: a qualitative content analysis.	BMC Nurs. 2015 Nov 28;14:64. doi: 10.1186/s12912-015-0115-5. eCollection 2015.	BACKGROUND: Fatigue is a major problem among individuals with post-infectious fatigue syndrome (PIFS), also known as chronic fatigue syndrome or myalgic encephalomyelitis. It is a complex phenomenon that varies across illnesses. From a nursing perspective, knowledge and understanding of fatigue in this illness is limited. Nurses lack confidence in caring for these patients and devalue their professional role. The aim of this study was to explore in-depth the experiences of fatigue among individuals with PIFS. A detailed description of the phenomenon of fatigue is presented. Increased knowledge would likely contribute to more confident nurses and improved nursing care. METHODS: A qualitative study with open interviews was employed. In-depth interviews with patients were fully transcribed and underwent a qualitative content analysis. A maximum variation sample of 26 affected adults between 26-59 years old was recruited from a population diagnosed at a fatigue outpatient clinic. RESULTS: The fatigue was a post-exertional, multidimensional, fluctuating phenomenon with varying degrees of severity and several distinct characteristics and was accompanied by concomitant symptoms. Fatigue was perceived to be an all-pervasive complex experience that substantially reduced the ability to function personally or professionally. A range of trigger mechanisms evoked or worsened the fatigue, but the affected were not always aware of what triggered it. There was an excessive increase in fatigue in response to even minor activities. An increase in fatigue resulted in the exacerbation of other concomitant symptoms. The term fatigue does not capture the participants' experiences, which are accompanied by a considerable symptom burden that contributes to the illness experience and the severe disability. CONCLUSIONS: Although some aspects of the fatigue experience have been reported previously, more were added in our study, such as the dimension of awakening fatigue and the characteristic beyond time, when time passes unnoticed. We also identified trigger mechanisms such as emotional, neurological, social, financial, and pressure on oneself or from others. This in-depth exploration of fatigue in PIFS provides an overview of the dimensions, characteristics, and trigger mechanisms of fatigue, thus making better

				clinical observations, early recognition, improved communication with patients and more appropriate nursing interventions possible.
Sulheim D(1), Fagermoen E(2), Sivertsen ØS(3), Winger A(4), Wyller VB(5), Øie MG(6).	(1)Department of Paediatrics, Oslo University Hospital, Oslo, Norway Department of Paediatrics, Innlandet Hospital Trust, Lillehammer, Norway.	Cognitive dysfunction in adolescents with chronic fatigue: a cross-sectional study.	Arch Dis Child. 2015 Sep;100(9):838-44. doi: 10.1136/archdischild-2014-306764. Epub 2015 Mar 19.	OBJECTIVE: To compare cognitive function in adolescents with chronic fatigue with cognitive function in healthy controls (HC). STUDY DESIGN: Cross-sectional study. SETTING: Paediatric department at Oslo University Hospital, Norway. PARTICIPANTS: 120 adolescents with chronic fatigue (average age 15.4 years; range 12-18) and 39 HC (average age 15.2 years; range 12-18). METHODS: The adolescents completed a neurocognitive test battery measuring processing speed, working memory, cognitive inhibition, cognitive flexibility, verbal learning and verbal memory, and questionnaires addressing demographic data, depression symptoms, anxiety traits, fatigue and sleep problems. Parents completed the Behaviour Rating Inventory of Executive Function (BRIEF), which measures the everyday executive functions of children. RESULTS: Adolescents with chronic fatigue had impaired cognitive function compared to HC regarding processing speed (mean difference 3.3, 95% CI 1.1 to 5.5, p=0.003), working memory (-2.4, -3.7 to -1.1, p<0.001), cognitive inhibition response time (6.2, 0.8 to 11.7, p=0.025) and verbal learning (-1.7, -3.2 to -0.3, p=0.022). The BRIEF results indicated that everyday executive functions were significantly worse in the chronic fatigue group compared to the HC (11.2, 8.2 to 14.3, p<0.001). Group differences remained largely unaffected when adjusted for symptoms of depression, anxiety traits and sleep problems. CONCLUSIONS: Adolescents with chronic fatigue had impaired cognitive function of clinical relevance, measured by objective cognitive tests, in comparison to HC. Working memory and processing speed may represent core difficulties.
Sunnquist M(1), Jason LA, Brown A, Evans M, Berman A.	(1)a Center for Community Research, DePaul University , Chicago , Illinois , USA.	Complications in operationalizing lifelong fatigue as an exclusionary criterion.	J Prev Interv Community. 2015;43(1):42-53. doi: 10.1080/10852352.2014.973238.	The case definitions for chronic fatigue syndrome (CFS) and chronic fatigue syndrome/Myalgic Encephalomyelitis (ME) stipulate that the experience of lifelong fatigue is an exclusionary criterion (Carruthers et al., 2003 ; Fukuda et al., 1994). This article examines the lifelong fatigue construct and identifies potential validity and reliability issues in using lifelong fatigue as an exclusionary condition. Participants in the current study completed the DePaul Symptom Questionnaire (Jason et al., 2010), and responses were examined to determine if they had experienced lifelong fatigue. This article discusses the extensive process that was needed to confidently discern which participants had or did not have lifelong fatigue. Using the most rigorous standards, few individuals were classified as having lifelong fatigue. In addition, those with and without lifelong fatigue had few significant differences in symptoms and functional areas. This article concludes with a recommendation that lifelong fatigue should no longer be used as an exclusionary criterion for CFS or ME/CFS.
Sáez-Francàs N(1), Calvo N(2), Alegre J(3), Castro-Marrero J(4), Ramírez	(1)Servei de Psiquiatria, Hospital Sant Rafael, FIDMAG, Hospital Universitari Vall d'Hebron,	Childhood trauma in Chronic Fatigue Syndrome: focus on personality disorders and psychopathology.	Compr Psychiatry. 2015 Oct;62:13-9. doi: 10.1016/j.comppsych.2015.06.010. Epub 2015 Jun 17.	INTRODUCTION: Personality Disorders (PDs) and childhood traumatic experiences have been considered risk factors for Chronic Fatigue Syndrome (CFS). However, the relationship between these factors and their associated psychopathological impact has not been explored in this population. This study was designed to evaluate the association between different childhood traumas and the presence and number of PDs

N(5), Hernández-Vara J(6), Casas M(7).	CIBERSAM, Department of Psychiatry, Universitat Autònoma de Barcelona, Passeig Vall d´Hebron 107-117, 08035, Barcelona, Spain. Electronic address: nasaez2@gmail.com.			and current psychopathology in a sample of CFS patients. MATERIAL AND METHODS: For this purpose, 166 CFS patients were evaluated with the Personality Diagnostic Questionnaire-4+ (PDQ-4+) and the Child Trauma Questionnaire. Other instruments were used to assess the associated psychopathology and the impact of fatigue. RESULTS: Of the total sample, 55 (33.1%) presented childhood trauma, the most frequent of which were emotional neglect (21.7%) and emotional abuse (18.1%). Considering PD presence, 79 (47.6%) patients presented some PD. There were no differences in frequency of physical childhood trauma in patients with and without PD. However, patients with PD had more frequently experienced emotional childhood trauma (OR=2.18, p=0.034). Severity of childhood trauma was related to a higher number of PDs, more severe depressive symptoms (p=0.025) and suicide risk (p=0.001). Patients with PD and any childhood trauma presented more severe depressive and irritable symptoms and a higher suicide risk than those without any PD and non-childhood traumatic event. These patients' psychopathological symptoms were similar to those of patients with childhood trauma and without PD. CONCLUSIONS: These results suggest that emotional childhood trauma but not physical childhood trauma is related to higher frequency of PD presence. More severe childhood emotional and physical traumas are related to a higher number of PDs and to more severe psychopathological symptoms.
Talotta R(1), Atzeni F(2), Bazzichi L(3), Giacomelli C(3), Di Franco M(4), Salaffi F(5), Sarzi-Puttini P(1).	(1)Rheumatology Unit, L. Sacco University Hospital, Milan, Italy. (2)IRCCS Galeazzi Orthopaedic Institute, Milan, Italy. (3)Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Italy. (4)Rheumatology Unit, Department of Internal Medicine and Medical Specialities, La Sapienza University of Rome, Italy. (5)Rheumatology Department, Polytechnic University of the Marche,	Algo-dysfunctional syndromes: a critical digest of the recent literature.	Clin Exp Rheumatol. 2015 Jan-Feb;33(1 Suppl 88):S102-8. Epub 2015 Mar 18.	The etiopathogenesis of the algo-dysfunctional syndromes, which include chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome, is still debated, but it is widely accepted that it is best described by a multifactorial model that include genes, environmental factors such as external infections, inflammation, dietary habits, impaired endogenous cortisol production, the aberrant activation of some areas of the central nervous system, and small peripheral nervous fibre damage. This complexity suggests that they should be managed by means of a multidisciplinary approach involving the use of both pharmacological and non-pharmacological treatments. The aim of this review is to discuss the most recent scientific acquisitions concerning these syndromes and their treatment.

	Ancona, Italy.			
Tandon P(1), Wong N(2), Zaltzman JS(3).	(1)Department of Medicine, Michigan State University College of Osteopathic Medicine, Lansing, Michigan, United States. (2)Department of Medicine, Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada. (3)Division of Nephrology, St. Michael's Hospital, Toronto, Ontario, Canada.	Lithium-Induced Minimal Change Disease and Acute Kidney Injury.	N Am J Med Sci. 2015 Jul;7(7):328-31. doi: 10.4103/1947-2714.161252.	CONTEXT: Lithium carbonate is a psychiatric medication commonly used in the treatment of bipolar disorder. It has been implicated in inducing nephrogenic diabetes inspidus, chronic tubulointerstitial nephropathy, and acute tubular necrosis. We describe a case of lithium-induced minimal change disease (MCD) and acute kidney injury (AKI). CASE REPORT: A 32-year-old female with a medical history of bipolar disorder treated with chronic lithium therapy presented with anasarca, fatigue, and tremors. Work-up revealed supra-therapeutic lithium levels, hypoalbuminemia, and significant proteinuria. The patient was treated conservatively with fluids and discontinuation of lithium therapy. Subsequently, she developed significant AKI and persistent proteinuria. She underwent a renal biopsy that demonstrated effacement of podocyte foot processes consistent with lithium-induced MCD. This was treated with corticosteroids, which decreased the proteinuria and resolved all the patient's symptoms. CONCLUSION: Lithium-induced MCD is a rare disease that affects patients of all ages. It is often associated with therapeutic lithium and is typically resolved with discontinuation of lithium. In some cases, concurrent AKI may result due to vascular obstruction from hyperalbuminuria and associated renal interstitial edema. Corticosteroids may be needed to reduce the proteinuria and prevent progression to chronic kidney disease. As such, patients on lithium therapy may benefit from monitoring of glomerular function via urinalysis to prevent the onset of nephrotic syndrome.
Tang LW(1), Zheng H(1), Chen L(1), Zhou SY(1), Huang WJ(2), Li Y(1), Wu X(1).	(1)Acupuncture and Tuina School, The 3rd Teaching Hospital, Chengdu University of Traditional Chinese Medicine, No. 37 Shi'er Qiao Road, Chengdu, Sichuan 610075, China. (2)Institute for Social Medicine, Epidemiology and Health Economics, Charité University Medical Center, 10117 Berlin, Germany.	Gray matter volumes in patients with chronic fatigue syndrome.	Evid Based Complement Alternat Med. 2015;2015:380615. doi: 10.1155/2015/380615. Epub 2015 Feb 22.	Chronic fatigue syndrome (CFS) is a debilitating and complex disorder characterized by profound fatigue with uncertain pathologic mechanism. Neuroimage may be an important key to unveil the central nervous system (CNS) mechanism in CFS. Although most of the studies found gray matter (GM) volumes reduced in some brain regions in CFS, there are many factors that could affect GM volumes in CFS, including chronic pain, stress, psychiatric disorder, physical activity, and insomnia, which may bias the results. In this paper, through reviewing recent literatures, we discussed these interferential factors, which overlap with the symptoms of CFS.
Tavel ME(1).	(1)Indiana University School of Medicine, St. Vincent Hospital,	Somatic symptom disorders without known physical causes: one	Am J Med. 2015 Oct;128(10):1054-8. doi: 10.1016/j.amjmed.2015.0	Patients complaining of pain or fatigue in the absence of known physical diseases constitute a high percentage of those seeking general medical care. Depending upon the type of physician/specialist consulted, those individuals may receive disease labels

	Indianapolis. Electronic address: tavelmorton@gmail.com.	disease with many names?	4.041. Epub 2015 May 30.	that range from an implied psychological origin such as somatoform or psychosomatic disease, or to a presumed physical disease such as fibromyalgia. Although all these conditions are regularly associated with fatigue, we have provided a new label suggesting another disease category, "systemic exertion intolerance disease," which replaces the previous "chronic fatigue syndrome." All these conditions have common, overlapping features that usually consist of both fatigue and pain, and, in the absence of definitive objective confirmation, might be best classified under one heading such as somatic symptom disorder. Management of these disorders is challenging, but suggestions for proper identification and treatment are presented.
Tekdöş Demircioğlu D(1), Kavadar G(2), Esen Öre Ö(3), Emre TY(3), Yaka U(3).	(1)Department of Physical Medicine and Rehabilitation, İstanbul Memorial Hizmet Hospital, İstanbul, Turkey. drtekdos@gmail.com. (2)Department of Physical Medicine and Rehabilitation, İstanbul Bağcılar Medicine Hospital, İstanbul, Turkey. (3)Department of Physical Medicine and Rehabilitation, İstanbul Memorial Hizmet Hospital, İstanbul, Turkey.	Relationship between restless leg syndrome and quality of life in uremic patients.	Agri. 2015;27(2):73-8. doi: 10.5505/agri.2015.19327.	OBJECTIVES: Patients with RLS suffer nonrestorative sleep, daytime sleepiness, fatigue, and concentration problems. In addition, dialysis itself effects the psychological and social life of the patient negatively. The aim of this study was to determine the prevalence of RLS in patients on regular hemodialysis, and its relationship with patients' quality of life, socio-demographic and laboratory data. METHODS: One hundred and eighteen stable chronic hemodialysis (HD) patients referring to the hemodialysis unit of Turkish Kidney Foundation and 49 patients that met IRLSSG diagnostic criteria were included into the study. IRLSSG Diagnostic Criteria and International Restless Leg Syndrome rating scale were used as a guideline to diagnose and evaluate the severity of RLS. Short form-36 health survey was used to evaluate the quality of life. For statistical analysis, the "SPSS for Windows" package program was used. RESULTS: A total of forty-nine patients, of whom 26 were female and 23 were male, that met IRLSSG diagnostic criteria were included into the study. Mean age of the patients was 61.35 ± 13.17 years. There was a negative correlation between the IRLSS score and SF36 Physical Score, Mental Score and Total Score, respectively (p=0.018 r=-0.351, p=0.01 r=-0.380, p=0.00 r=-0.499). There was no significant correlation between the IRLSS score and dialysis duration, blood ferritin and parathyroid hormone and other comorbid diseases. CONCLUSION: RLS is a common distressing problem in patients with ESRD, which negatively impacts functional health status. Clinicians should be aware of the symptoms of RLS to decrease morbidities related with quality of life.
Terzi R(1), Altın F(2).	(1)Department of Physical Medicine and Rehabilitation, Derince Training and Research Hospital, Kocaeli, Turkey. drrabia1@yahoo.com. (2)Department of Physical Medicine and Rehabilitation, Esenler	[The prevalence of low back pain in hospital staff and its relationship with chronic fatigue syndrome and occupational factors].[Article in Turkish]	Agri. 2015;27(3):149-54. doi: 10.5505/agri.2015.26121.	OBJECTIVES: This study aimed to investigate the occurrence of low back pain in hospital employees during the previous year and its correlation with demographic data, occupational factors and chronic fatigue syndrome. METHODS: All participants provided information on their socio-demographic background, occupational characteristics, their experience of low back pain during the previous year, and chronic fatigue syndrome. RESULTS: The study included 365 volunteers (221 male and 144 female). The mean age was 33.1 ± 7.2. Of the 365 participants, 218 (59.7%) had experienced low back pain in the last year. No statistically significant difference was detected in age, height, weight, level of education, smoking habits, occupation, professional working hours, shift work or levels of income between the groups with and without low back pain. Low back pain

	Medipol University and Reseach Hospital, Istanbul, Turkey.			was more frequent (p<0.05) in male workers. Chronic fatigue syndrome was statistically significant in the group suffering from low back pain (p<0.05), of whom 21.5% had chronic fatigue syndrome. We detected a statistically significant relationship (p<0.05) between chronic fatigue syndrome, occupational duration and shift work. CONCLUSION: To the best of our knowledge, this is the first to show the relationship between low back pain and chronic fatigue syndrome in hospital employees. Shift work and length of time in occupation are risk factors for chronic fatigue syndrome.
Theadom A(1), Cropley M(2), Kantermann T(3,)(4).	(1)National Institute for Stroke and Applied Neuroscience, Auckland University of Technology, 90 Akoranga Drive, Private Bag 92006, Auckland, New Zealand. alice.theadom@aut.ac.nz. (2)Department of Psychology, University of Surrey, Surrey, UK. MCropley@surrey.ac.uk. (3)Chronobiology Unit, Groningen institute for Evolutionary Life Sciences, University of Groningen, Groningen, The Netherlands. thomas@kantermann.de. (4)Institute for Occupational, Social and Environmental Medicine, Clinical Centre Ludwig-Maximilians University Munich, Ziemssenstrasse 1, 80336, Munich, Germany.	Daytime napping associated with increased symptom severity in fibromyalgia syndrome.	BMC Musculoskelet Disord. 2015 Feb 7;16:13. doi: 10.1186/s12891-015-0464-y.	BACKGROUND: Previous qualitative research has revealed that people with fibromyalgia use daytime napping as a coping strategy for managing symptoms against clinical advice. Yet there is no evidence to suggest whether daytime napping is beneficial or detrimental for people with fibromyalgia. The purpose of this study was to explore how people use daytime naps and to determine the links between daytime napping and symptom severity in fibromyalgia syndrome. METHODS: A community based sample of 1044 adults who had been diagnosed with fibromyalgia syndrome by a clinician completed an online questionnaire. Associations between napping behavior, sleep quality and fibromyalgia symptoms were explored using Spearman correlations, with possible predictors of napping behaviour entered into a logistic regression model. Differences between participants who napped on a daily basis and those who napped less regularly, as well as nap duration were explored. RESULTS: Daytime napping was significantly associated with increased pain, depression, anxiety, fatigue, memory difficulties and sleep problems. Sleep problems and fatigue explained the greatest amount of variance in napping behaviour, $p < 0.010$. Those who engaged in daytime naps for >30 minutes had higher memory difficulties ($t = -3.45$) and levels of depression ($t = -2.50$) than those who napped for shorter periods (<30 mins) ($p < 0.010$). CONCLUSIONS: Frequent use and longer duration of daytime napping was linked with greater symptom severity in people with fibromyalgia. Given the common use of daytime napping in people with fibromyalgia evidence based guidelines on the use of daytime napping in people with chronic pain are urgently needed.

	thomas@kantermann.de.			
Theoharides TC(1), Tsilioni I(2), Arbetman L(2), Panagiotidou S(2), Stewart JM(2), Gleason RM(2), Russell IJ(2).	(1)Department of Integrative Physiology and Pathobiology, Tufts University School of Medicine, Boston, Massachusetts	Fibromyalgia syndrome in need of effective treatments.	J Pharmacol Exp Ther. 2015 Nov;355(2):255-63. doi: 10.1124/jpet.115.227298. Epub 2015 Aug 25.	Fibromyalgia syndrome (FMS) is a chronic, idiopathic condition of widespread musculoskeletal pain, affecting primarily women. It is clinically characterized by chronic, nonarticular pain and a heightened response to pressure along with sleep disturbances, fatigue, bowel and bladder abnormalities, and cognitive dysfunction. The diagnostic criteria have changed repeatedly, and there is neither a definitive pathogenesis nor reliable diagnostic or prognostic biomarkers. Clinical and laboratory studies have provided evidence of altered central pain pathways. Recent evidence suggests the involvement of neuroinflammation with stress peptides triggering the release of neurosenzitizing mediators. The management of FMS requires a multidimensional approach including patient education, behavioral therapy, exercise, and pain management. Here we review recent data on the pathogenesis and propose new directions for research and treatment.
Theoharides TC(1), Stewart JM(2), Hatziagelaki E(3), Kolaitis G(4).	(1)Laboratory of Molecular Immunopharmacology and Drug Discovery, Department of Integrative Physiology and Pathobiology, Tufts University School of Medicine Boston, MA, USA ; Departments of Internal Medicine, Tufts University School of Medicine and Tufts Medical Center Boston, MA, USA ; Psychiatry, Tufts University School of Medicine and Tufts Medical Center Boston, MA, USA ; Sackler School of Graduate Biomedical Sciences, Tufts University School of Medicine Boston, MA,	Brain "fog," inflammation and obesity: key aspects of neuropsychiatric disorders improved by luteolin.	Front Neurosci. 2015 Jul 3;9:225. doi: 10.3389/fnins.2015.00225. eCollection 2015.	Brain "fog" is a constellation of symptoms that include reduced cognition, inability to concentrate and multitask, as well as loss of short and long term memory. Brain "fog" characterizes patients with autism spectrum disorders (ASDs), celiac disease, chronic fatigue syndrome, fibromyalgia, mastocytosis, and postural tachycardia syndrome (POTS), as well as "minimal cognitive impairment," an early clinical presentation of Alzheimer's disease (AD), and other neuropsychiatric disorders. Brain "fog" may be due to inflammatory molecules, including adipocytokines and histamine released from mast cells (MCs) further stimulating microglia activation, and causing focal brain inflammation. Recent reviews have described the potential use of natural flavonoids for the treatment of neuropsychiatric and neurodegenerative diseases. The flavone luteolin has numerous useful actions that include: anti-oxidant, anti-inflammatory, microglia inhibition, neuroprotection, and memory increase. A liposomal luteolin formulation in olive fruit extract improved attention in children with ASDs and brain "fog" in mastocytosis patients. Methylated luteolin analogs with increased activity and better bioavailability could be developed into effective treatments for neuropsychiatric disorders and brain "fog."

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Togo F(1), Lange G, Natelson BH, Quigley KS.	(1)Educational Physiology Laboratory, Graduate School of Education, University of Tokyo, Japan.	Attention network test: assessment of cognitive function in chronic fatigue syndrome.	J Neuropsychol. 2015 Mar;9(1):1-9. doi: 10.1111/jnp.12030. Epub 2013 Sep 24.	Information processing difficulties are common in patients with chronic fatigue syndrome (CFS). It has been shown that the time it takes to process a complex cognitive task, rather than error rate, may be the critical variable underlying CFS patients' cognitive complaints. The Attention Network Task (ANT) developed by Fan and colleagues may be of clinical utility to assess cognitive function in CFS, because it allows for simultaneous assessment of mental response speed, also called information processing speed, and error rate under three conditions challenging the attention system. Comparison of data from two groups of CFS patients (those with and without comorbid major depressive disorder; n = 19 and 22, respectively) to controls (n = 29) consistently showed that error rates did not differ among groups across conditions, but speed of information processing did. Processing time was prolonged in both CFS groups and most significantly affected in response to the most complex task conditions. For simpler tasks, processing time was only prolonged in CFS participants with depression. The data suggest that the ANT may be a task that could be used clinically to assess information processing deficits in individuals with CFS.
Torjesen I(1).	(1)London.	Tackling fear about exercise produces long term benefit in chronic fatigue syndrome.	BMJ. 2015 Oct 28;351:h5771. doi: 10.1136/bmj.h5771.	
Torjesen I(1).	(1)London.	Tackling fears about exercise is important for ME treatment, analysis indicates.	BMJ. 2015 Jan 14;350:h227. doi: 10.1136/bmj.h227.	
Twisk F(1).	(1)ME-de-patiënten Foundation, Zonnedauw, Limmen, 1906HB, Netherlands. Electronic address: frank.twisk@hetnet.nl.	Post-exertional malaise in chronic fatigue syndrome.	Lancet Psychiatry. 2015 Apr;2(4):e8-9. doi: 10.1016/S2215-0366(15)00044-9. Epub 2015 Mar 31.	Comment in Lancet Psychiatry. 2015 Apr;2(4):e10-1.
Twisk FN(1).	(1)Frank NM Twisk, ME-de-patiënten Foundation, 1906 HB Limmen, The Netherlands.	Accurate diagnosis of myalgic encephalomyelitis and chronic fatigue syndrome based upon objective test methods for characteristic symptoms.	World J Methodol. 2015 Jun 26;5(2):68-87. doi: 10.5662/wjm.v5.i2.68. eCollection 2015.	Although myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS) are considered to be synonymous, the definitional criteria for ME and CFS define two distinct, partially overlapping, clinical entities. ME, whether defined by the original criteria or by the recently proposed criteria, is not equivalent to CFS, let alone a severe variant of incapacitating chronic fatigue. Distinctive features of ME are: muscle weakness and easy muscle fatigability, cognitive impairment, circulatory deficits, a marked variability of the symptoms in presence and severity, but above all, post-exertional "malaise": a (delayed) prolonged aggravation of symptoms after a minor exertion. In contrast, CFS is primarily defined by (unexplained) chronic fatigue, which

				should be accompanied by four out of a list of 8 symptoms, e.g., headaches. Due to the subjective nature of several symptoms of ME and CFS, researchers and clinicians have questioned the physiological origin of these symptoms and qualified ME and CFS as functional somatic syndromes. However, various characteristic symptoms, e.g., post-exertional "malaise" and muscle weakness, can be assessed objectively using well-accepted methods, e.g., cardiopulmonary exercise tests and cognitive tests. The objective measures acquired by these methods should be used to accurately diagnose patients, to evaluate the severity and impact of the illness objectively and to assess the positive and negative effects of proposed therapies impartially.
Twisk FN(1).	(1)ME-de-patiënten Foundation , The Netherlands.	A critical analysis of the proposal of the Institute of Medicine to replace myalgic encephalomyelitis and chronic fatigue syndrome by a new diagnostic entity called systemic exertion intolerance disease.	Curr Med Res Opin. 2015;31(7):1333-47. doi: 10.1185/03007995.2015.1045472. Epub 2015 May 29.	The Institute of Medicine (IOM) recently published their report in response to an assignment "to define diagnostic criteria for Myalgic Encephalomyelitis (ME)/chronic fatigue syndrome (CFS), to propose a process for reevaluation of these criteria in the future, and to consider whether a new name for this disease is warranted". The basic pre-assumption of the IOM committee for the development of evidence-based diagnostic criteria for ME/CFS was that ME and CFS denote conditions with similar symptoms, hence ME/CFS. The IOM committee recommends: (1) that ME/CFS will be renamed 'systemic exertion intolerance disease' (SEID); and that a new code should be assigned to SEID in the International Classification of Diseases (ICD), replacing the existing codes for ME (a neurological disease: G93.3) and CFS ('signs, symptoms, and abnormal clinical and laboratory findings, not elsewhere classified': R53.82); (2) that a diagnosis of SEID should be made if the new diagnostic criteria are met; (3) that the Department of Health and Human Services develops a toolkit appropriate for screening and diagnosing patients; and (4) that a multidisciplinary group re-examines the new diagnostic criteria when necessary. This editorial reviews the working procedure of the IOM and two of the outcomes: the recommendation to introduce a new clinical entity (SEID) and new diagnostic criteria. Based upon the contents of the report, and the arguments of the IOM, a search of PubMed and the archive of the Journal of Chronic Fatigue Syndrome using the search terms ME (and old synonyms) and CFS, and a search of PubMed related to the five core symptoms of SEID was conducted. Reviewing the working method and the recommendations, it is concluded that the new diagnostic criteria for SEID are based upon important methodological shortcomings and that the introduction of SEID to replace both ME and CFS has several profound negative consequences outweighing the advantages.
Underhill RA.		Myalgic encephalomyelitis, chronic fatigue syndrome: An infectious disease.	Med Hypotheses. 2015 Oct 19. pii: S0306-9877(15)00382-5. doi: 10.1016/j.mehy.2015.10.011. [Epub ahead of print]	The etiology of myalgic encephalomyelitis also known as chronic fatigue syndrome or ME/CFS has not been established. Controversies exist over whether it is an organic disease or a psychological disorder and even the existence of ME/CFS as a disease entity is sometimes denied. Suggested causal hypotheses have included psychosomatic disorders, infectious agents, immune dysfunctions, autoimmunity, metabolic disturbances, toxins and inherited genetic factors. Clinical, immunological and epidemiological evidence supports the hypothesis that: ME/CFS is an infectious disease;

				the causal pathogen persists in patients; the pathogen can be transmitted by casual contact; host factors determine susceptibility to the illness; and there is a population of healthy carriers, who may be able to shed the pathogen. ME/CFS is endemic globally as sporadic cases and occasional cluster outbreaks (epidemics). Cluster outbreaks imply an infectious agent. An abrupt flu-like onset resembling an infectious illness occurs in outbreak patients and many sporadic patients. Immune responses in sporadic patients resemble immune responses in other infectious diseases. Contagion is shown by finding secondary cases in outbreaks, and suggested by a higher prevalence of ME/CFS in sporadic patients' genetically unrelated close contacts (spouses/partners) than the community. Abortive cases, sub-clinical cases, and carrier state individuals were found in outbreaks. The chronic phase of ME/CFS does not appear to be particularly infective. Some healthy patient-contacts show immune responses similar to patients' immune responses, suggesting exposure to the same antigen (a pathogen). The chronicity of symptoms and of immune system changes and the occurrence of secondary cases suggest persistence of a causal pathogen. Risk factors which predispose to developing ME/CFS are: a close family member with ME/CFS; inherited genetic factors; female gender; age; rest/activity; previous exposure to stress or toxins; various infectious diseases preceding the onset of ME/CFS; and occupational exposure of health care professionals. The hypothesis implies that ME/CFS patients should not donate blood or tissue and usual precautions should be taken when handling patients' blood and tissue. No known pathogen has been shown to cause ME/CFS. Confirmation of the hypothesis requires identification of a causal pathogen. Research should focus on a search for unknown and known pathogens. Finding a causal pathogen could assist with diagnosis; help find a biomarker; enable the development of anti-microbial treatments; suggest preventive measures; explain pathophysiological findings; and reassure patients about the validity of their symptoms.
Urban & Vogel.		[Tired, tired, constantly and always tired].[Article in German]	MMW Fortschr Med. 2015 Apr 16;157(7):30. doi: 10.1007/s15006-015-2962-0.	
van Der Schaaf ME(1,)(2,)(3), Schmits IC(4), Roerink M(5), Geurts DE(6), Toni I(7), Roelofs K(8), De Lange FP(9), Nater UM(10), van der Meer JW(11),	(1)Radboud University Medical Center, Expert Centre for Chronic Fatigue, Nijmegen, The Netherlands. marieke.vanderschaaf@donders.ru.nl.	Investigating neural mechanisms of change of cognitive behavioural therapy for chronic fatigue syndrome: a randomized controlled trial.	BMC Psychiatry. 2015 Jul 3;15:144. doi: 10.1186/s12888-015-0515-9.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by profound and disabling fatigue with no known somatic explanation. Cognitive behavioral therapy (CBT) has proven to be a successful intervention leading to a reduction in fatigue and disability. Based on previous neuroimaging findings, it has been suggested that central neural mechanisms may underlie CFS symptoms and play a role in the change brought on by CBT. In this randomized controlled trial we aim to further investigate the neural mechanisms that underlie fatigue in CFS and their change by CBT. METHODS/DESIGN: We will conduct a randomized controlled trial in which we collect anatomical and functional magnetic resonance imaging (MRI) measures from female CFS patients before and after CBT (N = 60) or waiting list (N = 30) and compare these with measures

Knoop H(12).				from age and education matched healthy controls (N = 30). By including a large treatment group we will also be able to compare patients that benefit from CBT with those that do not. In addition, to further investigate the role of endocrine and immune biomarkers in CFS, we will determine cortisol and cytokine concentrations in blood, hair and/or saliva. DISCUSSION: This project creates an unique opportunity to enhance our understanding of CFS symptoms and its change by CBT in terms of neuroanatomical, neurofunctional, endocrinological and immunological mechanisms and can help to further improve future treatments strategies. TRIAL REGISTRATION: Dutch Trial Register #15852. Registered 9 December 2013 (http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=4311).
van Geelen SM(1), Fuchs CE, van Geel R, Luyten P, van de Putte EM.	(1)Centre for Research on Child and Adolescent Mental Health, Karlstad University, Karlstad, Sweden.	The Self beyond Somatic Symptoms: A Narrative Approach to Self-Experience in Adolescent Chronic Fatigue Syndrome.	Psychopathology. 2015;48(5):278-86. doi: 10.1159/000431258. Epub 2015 Sep 12.	BACKGROUND: The self and self-experience are often assumed to play an important role in adolescent patients presenting with severe somatic symptoms and bodily distress. Nonetheless, most empirical work on this subject is confined to studies of personality and patients' experience of negative emotionality. This study aims to move beyond mere descriptions of symptoms, traits and distress, and consequently adopts a narrative approach to self-experience in adolescent chronic fatigue syndrome (CFS). SAMPLING AND METHODS: The self-confrontation method (SCM) is a well-validated instrument to systematically analyze narrative self-experience. The SCM was used to study 42 adolescents with CFS, compared to 36 adolescents with juvenile idiopathic arthritis (JIA) and 25 matched healthy controls. The Child Health Questionnaire (CHQ-CF87) was used to assess mental health, self-esteem, and physical and psychosocial functioning. RESULTS: Both patient groups reported significantly less positive self-experience of autonomy and success compared to healthy controls. Furthermore, patients with CFS described significantly more negative self-experience of powerlessness, isolation and unfulfilled longing. In the CHQ-CF87, both patient groups scored significantly lower on physical functioning than controls. Adolescents with CFS also scored significantly lower on mental health and self-esteem. CONCLUSIONS: Adolescent CFS entails a serious threat to the self, which might be inherent to the condition. Not only are patients more impaired in mental health, self-esteem, and physical and psychosocial functioning than patients with JIA, they also suffer from a distinct combination of high negative and low positive self-experience. These findings stress the need for strategies that empower patients towards a 'management of the self'.
van Leeuwen N(1), Bossema ER(2), Knoop H(2), Kruize AA(2), Bootsma	(1)Department of Clinical and Health Psychology, Utrecht University, Department of	Psychological profiles in patients with Sjögren's syndrome related to fatigue: a cluster analysis.	Rheumatology (Oxford). 2015 May;54(5):776-83. doi: 10.1093/rheumatology/keu387. Epub 2014 Oct 6.	OBJECTIVE: Fatigue is a highly prevalent and debilitating symptom in the autoimmune disease SS. Although the disease process plays a role in fatigue, psychological factors may influence fatigue and the ability to deal with its consequences. Profiles of co-occurring psychological factors may suggest potential targets for the treatment of fatigue. The aim of this study was to identify psychological profiles in patients with SS

H(2), Bijlsma JW(2), Geenen R(3).	Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen and Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, The Netherlands Department of Clinical and Health Psychology, Utrecht University, Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht, Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen and Department of Rheumatology and Clinical Immunology, University Medical Center Groningen, Groningen, The Netherlands N.vanLeeuwen@uu.nl.			and the accompanying levels of fatigue. METHODS: Three hundred patients with primary SS (mean age 57 years, 93% female) completed questionnaires on fatigue (multidimensional fatigue inventory), physical activity cognitions (TAMPA-SK), illness cognitions, cognitive regulation, emotion processing and regulation [Toronto Alexithymia Scale 20, Emotion Regulation Questionnaire (ERQ), Berkeley Expressivity Questionnaire], coping strategies (Brief COPE) and social support. RESULTS: Principal axis factor analysis (oblimin rotation) yielded six psychological factors: social support, negative thinking, positive thinking, emotional expressivity, avoidance and alexithymia (i.e. the inability to differentiate emotions). Using cluster analyses, these factors were grouped in four psychological profiles: functional (39%), alexithymic (27%), self-reliant (23%) and dysfunctional (11%). Irrespective of the psychological profile, the level of fatigue was substantially higher in patients than in the general population. Patients with a dysfunctional or an alexithymic profile reported more fatigue than those with a self-reliant profile. CONCLUSION: Our study in SS yielded four psychological profiles that were differentially associated with fatigue. These profiles can be used to examine determinants and prognosis of fatigue as well as the possibility of customizing cognitive behavioural interventions for chronic fatigue.
Vangeel E(1), Van Den Eede F,	(1)From the Genetic Research About Stress	Chronic Fatigue Syndrome and DNA	Psychosom Med. 2015 Oct;77(8):853-62. doi:	OBJECTIVES: Chronic fatigue syndrome (CFS) has been associated with hypothalamic-pituitary-adrenal axis hypofunction and enhanced glucocorticoid receptor (GR)

Hompes T, Izzi B, Del Favero J, Moorkens G, Lambrechts D, Freson K, Claes S.	and Psychiatry (GRASP) (Vangeel, Hompes, Claes), University Psychiatric Center (Hompes, Claes), Department of Cardiovascular Sciences, Center for Molecular and Vascular Biology (Izzi, Freson), and Laboratory of Translational Genetics, Department of Oncology (Lambrechts), University of Leuven, Leuven, Belgium	Hypomethylation of the Glucocorticoid Receptor Gene Promoter 1F Region: Associations With HPA Axis Hypofunction and Childhood Trauma.	10.1097/PSY.0000000000000224.	sensitivity. In addition, childhood trauma is considered a major risk factor for the syndrome. This study examines DNA methylation of the GR gene (NR3C1) in CFS and associations with childhood sexual and physical trauma. METHODS: Quantification of DNA methylation within the 1F promoter region of NR3C1 was performed in 76 female patients (46 with no/mild and 30 with moderate/severe childhood trauma) and 19 healthy controls by using Sequenom EpiTYPER. Further, we examined the association of NR3C1-1F promoter methylation with the outcomes of the low-dose (0.5 mg) dexamethasone/corticotropin-releasing factor test in a subset of the study population. Mann-Whitney U tests and Spearman correlations were used for statistical analyses. RESULTS: Overall NR3C1-1F DNA methylation was lower in patients with CFS than in controls. After cytosine guanine dinucleotide (CpG)-specific analysis, CpG_1.5 remained significant after Bonferroni correction (adjusted p = .0014). Within the CFS group, overall methylation (ρ = 0.477, p = .016) and selective CpG units (CpG_1.5: ρ = 0.538, p = .007; CpG_12.13: ρ = 0.448, p = .025) were positively correlated with salivary cortisol after dexamethasone administration. There was no significant difference in NR3C1-1F methylation between traumatized and nontraumatized patients. CONCLUSIONS: We found evidence of NR3C1 promoter hypomethylation in female patients with CFS and the functional relevance of these differences was consistent with the hypothalamic-pituitary-adrenalaxis hypofunction hypothesis (GR hypersuppression). However, we found no evidence of an additional effect of childhood trauma on CFS via alterations in NR3C1 methylation.
Velleman S(1), Collin SM(2), Beasant L(2), Crawley E(2).	(1)Paediatric CFS/ME Service, Royal National Hospital for Rheumatic Diseases NHS Foundation Trust, UK sophie.velleman@rnhrd.nhs.uk. (2)Centre for Child and Adolescent Health, University of Bristol, UK.	Psychological wellbeing and quality-of-life among siblings of paediatric CFS/ME patients: A mixed-methods study.	Clin Child Psychol Psychiatry. 2015 Sep 22. pii: 1359104515602373. [Epub ahead of print]	Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is a disabling condition known to have a negative impact on all aspects of a child's life. However, little is understood about the impact of CFS/ME on siblings. A total of 34 siblings completed questionnaires measuring depression (Hospital Anxiety and Depression Scale (HADS)), anxiety (HADS and Spence Children's Anxiety Scale (SCAS)) and European Quality-of-life-Youth (EQ-5D-Y). These scores were compared with scores from normative samples. Siblings had higher levels of anxiety on the SCAS than adolescents of the same age recruited from a normative sample; however, depression and quality-of-life were similar. Interviews were undertaken with nine siblings of children with CFS/ME who returned questionnaires. Interview data were analysed using a framework approach to thematic analysis. Siblings identified restrictions on family life, 'not knowing' and lack of communication as negative impacts on their family, and change of role/focus, emotional reactions and social stigma as negative impacts on themselves. They also described positive communication, social support and extra activities as protective factors. Paediatric services should be aware of the impact of CFS/ME on the siblings of children with CFS/ME, understand the importance of assessing paediatric

				CFS/ME patients within the context of their family and consider providing information for siblings about CFS/ME.
Velvin G(1,)(2), Bathen T(1), Rand-Hendriksen S(1,)(3), Østertun Geirdal A(2).	(1)Sunnaas Rehabilitation Hospital, TRS National Resource Centre for Rare Disorders, Norway. (2)Department of Social Work, Child Welfare and Social Policy, Faculty of Social Sciences, Oslo and Akershus University College of Applied Sciences, Norway. (3)Faculty of Medicine, Institute of Clinical Medicine, University of Oslo, Norway.	Work participation in adults with Marfan syndrome: Demographic characteristics, MFS related health symptoms, chronic pain, and fatigue.	Am J Med Genet A. 2015 Sep 30. doi: 10.1002/ajmg.a.37370. [Epub ahead of print]	Marfan syndrome (MFS) is a severe autosomal dominant connective tissue disorder that might influence peoples work ability. This cross sectional study aims to investigate work participation in adults with verified MFS diagnosis and to explore how the health related consequences of MFS and other factors might influence work participation. The prevalence of health problems in young adults compared to older adults with MFS was examined in association to work participation. A postal questionnaire including questions about work participation, demographic characteristics, MFS related health problems, chronic pain, and fatigue was sent to 117 adults with verified MFS (Ghent 1), and 62% answered. Fifty-nine percent were employed or students, significantly lower work participation than the General Norwegian Population (GNP), but higher than the Norwegian population of people with disability. Most young adults worked full-time despite extensive health problems, but the average age for leaving work was low. Few had received any work adaptations prior to retiring from work. In multiple logistic regression analysis, only age, lower educational level and severe fatigue were significantly associated with low work participation; not MFS related health problems or chronic pain. Fatigue appears to be the most challenging health problem to deal with in work, but the covariance is complex. Focus on vocational guidance early in life, more appropriate work adaptations, and psychosocial support might improve the possibility for sustaining in work for adults with MFS. More research about work challenges in adults with MFS is needed. © 2015 Wiley Periodicals, Inc.
Vergauwen K(1), Huijnen IP, Kos D, Van de Velde D, van Eupen I, Meeus M.	(1)Faculty of Medicine and Health Sciences, Department of Occupational Therapy, Ghent University , Ghent , Belgium .	Assessment of activity limitations and participation restrictions with persons with chronic fatigue syndrome: a systematic review.	Disabil Rehabil. 2015;37(19):1706-16. doi: 10.3109/09638288.2014.978507. Epub 2014 Nov 3.	PURPOSE: To summarize measurement instruments used to evaluate activity limitations and participation restrictions in patients with chronic fatigue syndrome (CFS) and review the psychometric properties of these instruments. METHOD: General information of all included measurement instruments was extracted. The methodological quality was evaluated using the COSMIN checklist. Results of the measurement properties were rated based on the quality criteria of Terwee et al. Finally, overall quality was defined per psychometric property and measurement instrument by use of the quality criteria by Schellingerhout et al. RESULTS: A total of 68 articles were identified of which eight evaluated the psychometric properties of a measurement instrument assessing activity limitations and participation restrictions. One disease-specific and 37 generic measurement instruments were found. Limited evidence was found for the psychometric properties and clinical usability of these instruments. However, the CFS-activities and participation questionnaire (APQ) is a disease-specific instrument with moderate content and construct validity. CONCLUSION: The psychometric properties of the reviewed measurement instruments to evaluate activity limitations and participation restrictions are not sufficiently evaluated. Future research is needed to evaluate the psychometric properties of the measurement instruments, including the other properties of the CFS-APQ. If it is

				necessary to use a measurement instrument, the CFS-APQ is recommended. IMPLICATIONS FOR REHABILITATION: Chronic fatigue syndrome (CFS). Chronic fatigue syndrome causes activity limitations and participation restrictions in one or more areas of life. Standardized, reliable and valid measurement instruments are necessary to identify these limitations and restrictions. Currently, no measurement instrument is sufficiently evaluated with persons with CFS. If a measurement instrument is needed to identify activity limitations and participation restrictions with persons with CFS, it is recommended to use the CFS-APQ in clinical practice and scientific research.
Verspaandonk J(1), Coenders M(2), Bleijenberg G(1), Lobbestael J(3), Knoop H(1).	(1)Expert Centre for Chronic Fatigue, Radboud University Medical Centre,Nijmegen,The Netherlands. (2)Faculty of Social and Behavioural Sciences,Utrecht University,The Netherlands. (3)Faculty of Clinical Psychological Science,Maastricht University,The Netherlands and RINO Zuid,Postdoctoral Education Institute,Eindhoven,The Netherlands.	The role of the partner and relationship satisfaction on treatment outcome in patients with chronic fatigue syndrome.	Psychol Med. 2015 Aug;45(11):2345-52. doi: 10.1017/S0033291715000288. Epub 2015 Mar 3.	BACKGROUND: Cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) leads to a significant decrease in CFS-related symptoms and disability. The primary objective of this study was to explore whether partners' solicitous responses and patients' and partners' perceived relationship satisfaction had an effect on treatment outcome. METHOD: The treatment outcome of a cohort of 204 consecutively referred patients treated with CBT was analysed. At baseline, CFS patients completed the Maudsley Marital Questionnaire. The Checklist Individual Strength subscale Fatigue and the Sickness Impact Profile total scores completed by CFS patients post-treatment were used as measures of clinically significant improvement. Partners completed the Family Response Questionnaire, the Maudsley Marital Questionnaire, the Brief Illness Perception Questionnaire, and the Causal Attribution List. Logistic regression analyses were performed with clinically significant improvement in fatigue and disability as dependent variables and scores on questionnaires at baseline as predictors. RESULTS: Solicitous responses of the partner were associated with less clinically significant improvement in fatigue and disability. Partners more often reported solicitous responses when they perceived CFS as a severe condition. Patients' relationship dissatisfaction was negatively associated with clinically significant improvement in fatigue. CONCLUSIONS: Partners' solicitous responses and illness perceptions at the start of the therapy can negatively affect the outcome of CBT for CFS. We emphasize the importance of addressing this in therapy.
Vij B(1), Whipple MO(2), Tepper SJ(1), Mohabbat AB(2), Stillman M(1), Vincent A(2).	(1)Headache Center, Neurology Institute, Cleveland Clinic, Cleveland, OH, USA. (2)Division of General Internal Medicine, Mayo Clinic, Rochester, MN, USA.	Frequency of Migraine Headaches in Patients With Fibromyalgia.	Headache. 2015 Jun;55(6):860-5. doi: 10.1111/head.12590. Epub 2015 May 21.	OBJECTIVE: The purpose of this study was to evaluate the frequency of migraine headache in a large cohort of patients with fibromyalgia using a brief migraine headache-screening tool. BACKGROUND: Several studies report a high prevalence of fibromyalgia among patients with migraine headaches, but there is a dearth of research evaluating the frequency of migraine headaches in patients with fibromyalgia, despite clinical observations suggesting that migraine headaches are common in patients with fibromyalgia. DESIGN AND METHODS: This was a cross-sectional survey study. Patients (N = 3717) with a previous diagnosis of fibromyalgia who were members of the Mayo Clinic Fibromyalgia Registry were contacted by electronic survey and asked to complete a brief demographic and medical history questionnaire and the validated ID-Migraine screener. RESULTS: A total of 1730 patients (46.5%) completed the electronic survey. The majority of participants were white (97.2%), female (92.5%), with a mean age of

				56.2 (±13.1) years. Of the respondents, 966 (55.8%) met criteria for migraine headaches. Hypertension (309 [32.3%] vs. 294 [40.1%], P = .004), asthma (312 [32.5%] vs. 189 [25.9%], P = .011), irritable bowel syndrome (520 [54.6%] vs. 348 [47.6], P = .017), chronic fatigue syndrome (486 [50.7%] vs. 271 [37.1], P < .0001), depression (634 [66.5%] vs. 413 [56.7%], P = .0002), anxiety (415 [43.5%] vs. 252 [34.7%], P = .0011), and post-traumatic stress disorder (172 [18.0%] vs. 96 [13.2%], P = .006) were all significantly more common in those who met criteria for migraine headaches than those who did not. CONCLUSION: The results of this study suggest that migraine headaches are common in patients with fibromyalgia. Clinicians who care for either population must be aware that these conditions commonly overlap and can significantly increase a patient's cumulative disease burden.
Vos-Vromans DC(1), Smeets RJ(2,)(3,)(4), Huijnen IP(2,)(3,)(4), Köke AJ(4), Hitters WM(5), Rijnders LJ(1), Pont M(6), Winkens B(7), Knottnerus JA(8).	(1)Revant Rehabilitation Centre Breda, Breda, The Netherlands.	Multidisciplinary rehabilitation treatment versus cognitive behavioural therapy for patients with chronic fatigue syndrome: a randomized controlled trial.	J Intern Med. 2015 Aug 26. doi: 10.1111/joim.12402. [Epub ahead of print]	OBJECTIVES: The aim of this trial was to evaluate the difference in treatment effect, at 26 and 52 weeks after the start of treatment, between cognitive behavioural therapy (CBT) and multidisciplinary rehabilitation treatment (MRT) for patients with chronic fatigue syndrome (CFS). DESIGN: Multicentre, randomized controlled trial of patients with CFS. Participants were randomly assigned to MRT or CBT. SETTING: Four rehabilitation centres in the Netherlands. SUBJECTS: A total of 122 patients participated in the trial. MAIN OUTCOME MEASURES: Primary outcomes were fatigue measured by the fatigue subscale of the Checklist Individual Strength and health-related quality of life measured by the Short-Form 36. Outcomes were assessed prior to treatment and at 26 and 52 weeks after treatment initiation. RESULTS: A total of 114 participants completed the assessment at 26 weeks, and 112 completed the assessment at 52 weeks. MRT was significantly more effective than CBT in reducing fatigue at 52 weeks. The estimated difference in fatigue between the two treatments was -3.02 [95% confidence interval (CI) -8.07 to 2.03; P = 0.24] at 26 weeks and -5.69 (95% CI -10.62 to -0.76; P = 0.02) at 52 weeks. Patients showed an improvement in quality of life over time, but between-group differences were not significant. CONCLUSION: This study provides evidence that MRT is more effective in reducing long-term fatigue severity than CBT in patients with CFS. Although implementation in comparable populations can be recommended based on clinical effectiveness, it is advisable to analyse the cost-effectiveness and replicate these findings in another multicentre trial.
Walitt B, Urrútia G, Nishishinya MB, Cantrell SE, Häuser W.		Selective serotonin reuptake inhibitors for fibromyalgia syndrome.	Sao Paulo Med J. 2015 Oct;133(5):454. doi: 10.1590/1516-3180.20151335T1.	BACKGROUND: Fibromyalgia is a clinically well-defined chronic condition with a biopsychosocial aetiology. Fibromyalgia is characterized by chronic widespread musculoskeletal pain, sleep problems, cognitive dysfunction, and fatigue. Patients often report high disability levels and poor quality of life. Since there is no specific treatment that alters the pathogenesis of fibromyalgia, drug therapy focuses on pain reduction and improvement of other aversive symptoms. OBJECTIVES: To assess the benefits and harms of selective serotonin reuptake inhibitors (SSRIs) in the treatment of fibromyalgia. METHODS: SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 5), MEDLINE (1966 to June 2014),

				EMBASE (1946 to June 2014), and the reference lists of reviewed articles. SELECTION CRITERIA: We selected all randomized, double-blind trials of SSRIs used for the treatment of fibromyalgia symptoms in adult participants. We considered the following SSRIs in this review: citalopram, fluoxetine, escitalopram, fluvoxamine, paroxetine, and sertraline. DATA COLLECTION AND ANALYSIS: Three authors extracted the data of all included studies and assessed the risks of bias of the studies. We resolved discrepancies by discussion. MAIN RESULTS: The quality of evidence was very low for each outcome. We downgraded the quality of evidence to very low due to concerns about risk of bias and studies with few participants. We included seven placebo-controlled studies, two with citalopram, three with fluoxetine and two with paroxetine, with a median study duration of eight weeks (4 to 16 weeks) and 383 participants, who were pooled together. All studies had one or more sources of potential major bias. There was a small (10%) difference in patients who reported a 30% pain reduction between SSRIs (56/172 (32.6%)) and placebo (39/171 (22.8%)) risk difference (RD) 0.10, 95% confidence interval (CI) 0.01 to 0.20; number needed to treat for an additional beneficial outcome (NNTB) 10, 95% CI 5 to 100; and in global improvement (proportion of patients who reported to be much or very much improved: 50/168 (29.8%) of patients with SSRIs and 26/162 (16.0%) of patients with placebo) RD 0.14, 95% CI 0.06 to 0.23; NNTB 7, 95% CI 4 to 17. SSRIs did not statistically, or clinically, significantly reduce fatigue: standard mean difference (SMD) -0.26, 95% CI -0.55 to 0.03; 7.0% absolute improvement on a 0 to 10 scale, 95% CI 14.6% relative improvement to 0.8% relative deterioration; nor sleep problems: SMD 0.03, 95 % CI -0.26 to 0.31; 0.8 % absolute deterioration on a 0 to 100 scale, 95% CI 8.3% relative deterioration to 6.9% relative improvement. SSRIs were superior to placebo in the reduction of depression: SMD -0.39, 95% CI -0.65 to -0.14; 7.6% absolute improvement on a 0 to 10 scale, 95% CI 2.7% to 13.8% relative improvement; NNTB 13, 95% CI 7 to 37. The dropout rate due to adverse events was not higher with SSRI use than with placebo use (23/146 (15.8%) of patients with SSRIs and 14/138 (10.1%) of patients with placebo) RD 0.04, 95% CI -0.06 to 0.14. There was no statistically or clinically significant difference in serious adverse events with SSRI use and placebo use (3/84 (3.6%) in patients with SSRIs and 4/84 (4.8%) and patients with placebo) RD -0.01, 95% CI -0.07 to 0.05. AUTHORS' CONCLUSIONS: There is no unbiased evidence that SSRIs are superior to placebo in treating the key symptoms of fibromyalgia, namely pain, fatigue and sleep problems. SSRIs might be considered for treating depression in people with fibromyalgia. The black box warning for increased suicidal tendency in young adults aged 18 to 24, with major depressive disorder, who have taken SSRIs, should be considered when appropriate.
Walitt B(1), Urrútia G,	(1)National Center for Complementary and	Selective serotonin reuptake inhibitors for	Cochrane Database Syst Rev. 2015 Jun	BACKGROUND: Fibromyalgia is a clinically well-defined chronic condition with a biopsychosocial aetiology. Fibromyalgia is characterized by chronic widespread

Nishishinya MB, Cantrell SE, Häuser W.	Integrative Health, National Institutes of Health, 10 Center Drive, Bethesda, MD, USA, 20892.	fibromyalgia syndrome.	5;6:CD011735. doi: 10.1002/14651858.CD011735.	musculoskeletal pain, sleep problems, cognitive dysfunction, and fatigue. Patients often report high disability levels and poor quality of life. Since there is no specific treatment that alters the pathogenesis of fibromyalgia, drug therapy focuses on pain reduction and improvement of other aversive symptoms. OBJECTIVES: The objective was to assess the benefits and harms of selective serotonin reuptake inhibitors (SSRIs) in the treatment of fibromyalgia. SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2014, Issue 5), MEDLINE (1966 to June 2014), EMBASE (1946 to June 2014), and the reference lists of reviewed articles. SELECTION CRITERIA: We selected all randomized, double-blind trials of SSRIs used for the treatment of fibromyalgia symptoms in adult participants. We considered the following SSRIs in this review: citalopram, fluoxetine, escitalopram, fluvoxamine, paroxetine, and sertraline. DATA COLLECTION AND ANALYSIS: Three authors extracted the data of all included studies and assessed the risks of bias of the studies. We resolved discrepancies by discussion. MAIN RESULTS: The quality of evidence was very low for each outcome. We downgraded the quality of evidence to very low due to concerns about risk of bias and studies with few participants. We included seven placebo-controlled studies, two with citalopram, three with fluoxetine and two with paroxetine, with a median study duration of eight weeks (4 to 16 weeks) and 383 participants, who were pooled together.All studies had one or more sources of potential major bias. There was a small (10%) difference in patients who reported a 30% pain reduction between SSRIs (56/172 (32.6%)) and placebo (39/171 (22.8%)) risk difference (RD) 0.10, 95% confidence interval (CI) 0.01 to 0.20; number needed to treat for an additional beneficial outcome (NNTB) 10, 95% CI 5 to 100; and in global improvement (proportion of patients who reported to be much or very much improved: 50/168 (29.8%) of patients with SSRIs and 26/162 (16.0%) of patients with placebo) RD 0.14, 95% CI 0.06 to 0.23; NNTB 7, 95% CI 4 to 17.SSRIs did not statistically, or clinically, significantly reduce fatigue: standard mean difference (SMD) -0.26, 95% CI -0.55 to 0.03; 7.0% absolute improvement on a 0 to 10 scale, 95% CI 14.6% relative improvement to 0.8% relative deterioration; nor sleep problems: SMD 0.03, 95 % CI -0.26 to 0.31; 0.8 % absolute deterioration on a 0 to 100 scale, 95% CI 8.3% relative deterioration to 6.9% relative improvement.SSRIs were superior to placebo in the reduction of depression: SMD -0.39, 95% CI -0.65 to -0.14; 7.6% absolute improvement on a 0 to 10 scale, 95% CI 2.7% to 13.8% relative improvement; NNTB 13, 95% CI 7 to 37. The dropout rate due to adverse events was not higher with SSRI use than with placebo use (23/146 (15.8%) of patients with SSRIs and 14/138 (10.1%) of patients with placebo) RD 0.04, 95% CI -0.06 to 0.14. There was no statistically or clinically significant difference in serious adverse events with SSRI use and placebo use (3/84 (3.6%) in patients with SSRIs and 4/84 (4.8%) and patients with placebo) RD -0.01, 95% CI -0.07 to 0.05. AUTHORS' CONCLUSIONS: There is no unbiased evidence that SSRIs are superior to placebo in treating the key symptoms of fibromyalgia, namely pain, fatigue and sleep problems. SSRIs might be considered for

				treating depression in people with fibromyalgia. The black box warning for increased suicidal tendency in young adults aged 18 to 24, with major depressive disorder, who have taken SSRIs, should be considered when appropriate.
Walitt B(1), Ceko M, Gracely J, Gracely RH.	(1)National Center for Complementary and Integrative Health, National Institutes of Health 10 Center Drive Bethesda, MD 20814. Brian.walitt@nih.gov.	Neuroimaging of Central Sensitivity Syndromes: Key Insights from the Scientific Literature.	Curr Rheumatol Rev. 2015 Dec 30. [Epub ahead of print]	Central sensitivity syndromes are characterized by distressing symptoms, such as pain and fatigue, in the absence of clinically obvious pathology. The scientific underpinnings of these disorders are not currently known. Modern neuroimaging techniques promise new insights into mechanisms mediating these postulated syndromes. We review the results of neuroimaging applied to five central sensitivity syndromes: fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, temporomandibular joint disorder, and vulvodynia syndrome. Neuroimaging studies of basal metabolism, anatomic constitution, molecular constituents, evoked neural activity, and treatment effect are compared across all of these syndromes. Evoked sensory paradigms reveal sensory augmentation to both painful and non-painful stimulation. This is a transformative observation for these syndromes, which were historically considered to be completely of hysterical or feigned in origin. However, whether sensory augmentation represents the cause of these syndromes, a predisposing factor, an endophenotype, or an epiphenomenon cannot be discerned from the current literature. Further, the result from cross-sectional neuroimaging studies of basal activity, anatomy, and molecular constituency are extremely heterogeneous within and between the syndromes. A defining neuroimaging "signature" cannot be discerned for any of the particular syndromes or for an over-arching central sensitization mechanism common to all of the syndromes. Several issues confound initial attempts to meaningfully measure treatment effects in these syndromes. At this time, the existence of "central sensitivity syndromes" is based more soundly on clinical and epidemiological evidence. A coherent picture of a "central sensitization" mechanism that bridges across all of these syndromes does not emerge from the existing scientific evidence.
Wasek M, Giebułtowicz J, Sochacka M, Zawada K, Modzelewska W, Krześniak LM, Wroczyński P.		THE MEASUREMENT OF ANTIOXIDANT CAPACITY AND POLYPHENOL CONTENT IN SELECTED FOOD SUPPLEMENTS.	Acta Pol Pharm. 2015 Sep-Oct;72(5):877-87.	Oxidative stress (OS), defined as a disturbance in the balance between the production of reactive oxygen species (ROS) and antioxidant defenses, can result in the development of many serious diseases like diabetes or cancer. Moreover, the role of oxidative stress in the acceleration of the aging process is also confirmed. ROS are constantly produced in the natural biochemical processes, mainly during cellular respiration. Their enhanced production may be the result of e.g., an inappropriate diet high in saturated fats, low in fiber, fruits and vegetables, insufficient physical activity or smoking. To prevent oxidative stress, besides changes in life style, the additional supplementation of antioxidants is proposed. On the Polish market, the number of food supplements with declared antioxidant activity is still increasing. However, their antioxidant properties are rarely confirmed experimentally. The aim of our study was to determine the antioxidant potential of selected dietary supplements available on the

				market and recommended in chronic fatigue syndrome. The antioxidant potential was measured using four methods: FRAP, ORAC, HORAC, EPR/DPPH. Moreover, the content of polyphenols in the dietary supplements was also determined.
Watanabe A(1), Satoh K(2), Maniwa T(2), Matsumoto KI(2).	(1)Division of Clinical Genetics, Nippon Medical School Hospital, Tokyo 113-8603, Japan. (2)Department of Biosignaling and Radioisotope Experiment, Interdisciplinary Center for Science Research, Organization for Research, Shimane University, Izumo, Shimane 693-8501, Japan.	Proteomic analysis for the identification of serum diagnostic markers for joint hypermobility syndrome.	Int J Mol Med. 2015 Dec 18. doi: 10.3892/ijmm.2015.2437. [Epub ahead of print]	Joint hypermobility syndrome (JHS) (also termed Ehlers-Danlos syndrome, hypermobility type) is a heritable connective tissue disorder which is characterized by generalized joint hypermobility, chronic pain, dizziness, fatigue, and minor skin changes. However, it has yet to be determined in patients with JHS whether specific genetic factors are involved in the risk of developing the disorder. Therefore, interventions have been limited to symptomatic treatments, and biomarkers for diagnosis and therapy have not yet been identified. In the present study, to identify potential serum biomarkers for JHS, we examined proteins with differential levels in sera from patients with JHS and in sera from control individuals using isobaric tags for relative and absolute quantitation (iTRAQ) labeling in combination with nano LC-MALDI-TOF/TOF-MS/MS followed by ProteinPilot analysis. In the sera of patients with JHS, a total of 106 proteins with differential levels were identified, and they were further narrowed down to 6 proteins ($p<0.05$, patient vs. control). Of the 6 proteins, proteins involved in the complement system including complement C1r subcomponent (C1R), vitronectin (VTN), complement component C9 (C9), and C4b-binding protein alpha chain (C4BPA) were identified as increased proteins in sera from patients with JHS compared with those in sera from controls. We confirmed increased levels of C1R and VTN in sera from patients with JHS by western blot analyses. The results indicate the possibility of a locally occurring inflammatory process in patients with JHS.
Weiler JJ(1).	(1)Disabled by ME/CFS and unable to work as a professional social worker since 1995, Ontario, Canada.	Living with ME/CFS. challenge for scientists?	Neuro Endocrinol Lett. 2015;36(1):96-9.	A Graded Exercise Therapy (GET) - Myalgic Encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS) Running Anomaly. Imagine you have been disabled with ME/CFS's cluster of symptoms for 19 years. Yet, this morning you just ran an easy 10K with no flare up of your exercise intolerance symptoms during the run or post-exertional malaise after the run. Then later in the day you go browsing for books and after 30 minutes or so your exercise intolerance and post-exertional malaise symptoms flare up. You experience a wave of exhaustion, achy muscles and additional cognitive fog, all of which carry into the next day. To me, this is a confusing anomaly that needs an explanation.
Wenz H(1), Wenz R(2), Groden C(3), Schmieder K(4), Fontana J(5).	(1)Department of Neuroradiology, University Medicine Mannheim, Medical Faculty Mannheim of the University of Heidelberg, Theodor-Kutzer-Ufer 1-3,	The pre-interventional psychiatric history - an underestimated confounder in benign intracranial lesions studies.	Clin Neurol Neurosurg. 2015 Oct;137:116-20. doi: 10.1016/j.clineuro.2015.06.022. Epub 2015 Jul 2.	OBJECTIVES: The current study was designed to analyze the influence of a positive pre-interventional psychiatric history on the quality of life (QOL) after successful treatment of benign intracranial extra-cerebral lesions. METHODS: Patients treated due to meningioma WHO I or unruptured intracranial aneurysms in two German neurosurgical centers between 2007 and 2013 were screened for exclusion criteria including malignant/chronic diseases, recurrence of the tumor/aneurysm and neurological deficits among others. 131 patients who met the criteria of an objectively unaffected health status were included. The pre-interventional psychiatric histories and the rates

	68161 Mannheim, Germany. Electronic address: holger.wenz@umm.de.			of post-interventional headaches, sleeping disorders, symptoms of chronic fatigue syndrome (CFS), post-traumatic stress disorder (PTSD) and QOL were determined by questionnaires which were mailed to the patients. RESULTS: 103 patients returned the questionnaires. Despite the objectively unaffected health status, the patients with a positive pre-interventional psychiatric history demonstrated a post-interventionally significantly lower QOL (p=0.002), a significantly higher Pittsburgh Sleep Quality Index sum score (p=0.009), as well as significantly higher rates of symptoms of a chronic fatigue syndrome (p=0.003) and PTSD (p=0.024), compared to the patient collective with a negative pre-interventional psychiatric status. CONCLUSION: The results of the current study demonstrate the importance of taking the pre-interventional psychiatric history as a significant and independent confounder into consideration when evaluating the outcome after treatment of benign intracranial extra-cerebral lesions. A pre-interventional psychiatric screening and an early psychological intervention might help to improve the overall outcome after successful treatment of such lesions.
White CM(1), Hadden RD(2), Robert-Lewis SF(3), McCrone PR(4), Petty JL(5).	(1)Division of Health and Social Care, King's College London, London, SE1 1UL, UK. claire.white@kcl.ac.uk. (2)Department of Neurology, King's College Hospital, London, UK. robert.hadden@nhs.net. (3)Division of Health and Social Care, King's College London, London, SE1 1UL, UK. sarah.roberts-lewis@kcl.ac.uk. (4)Centre for the Economics of Mental and Physical Health, Institute of Psychiatry, King's College London, London, UK. paul.mccrone@kcl.ac.uk. (5)Division of Health and Social	Observer blind randomised controlled trial of a tailored home exercise programme versus usual care in people with stable inflammatory immune mediated neuropathy.	BMC Neurol. 2015 Aug 21;15:147. doi: 10.1186/s12883-015-0398-x.	BACKGROUND: Inflammatory neuropathies such as Guillain-Barré syndrome, chronic inflammatory demyelinating polyradiculoneuropathy and paraproteinaemic demyelinating neuropathy are a heterogenous group of peripheral nerve disorders that affect around one to two people per 100,000. Whilst treatments such as intravenous immunoglobulin, plasma exchange and corticosteroids have generally positive results, long-term residual symptoms and associated activity limitations are common. There is currently no standardised care for patients with ongoing activity limitation and participation restriction as a result of inflammatory neuropathy IN but data from observational studies and a randomised controlled trial suggest that exercise either alone or as part of a multidisciplinary rehabilitation programme may be beneficial in improving activity limitation. Tailoring the intervention for participants following physiotherapy assessment and incorporating patient preference for type and location of exercise may be important. METHODS/DESIGN: The current study is a pragmatic, prospective, parallel observer-blind, randomised controlled trial to evaluate the efficacy and cost-effectiveness of a twelve week tailored home exercise programme versus advice and usual care. Seventy adults with stable immune mediated inflammatory neuropathy IN will be recruited to the study from two main sources: patients attending selected specialist peripheral nerve clinics in the South East and West Midlands of England and people with who access the GAIN charity website or newsletter. Participants will be randomised to receive either advice about exercise and usual care or a 12 week tailored home exercise programme. The primary outcome of activity limitation and secondary outcomes of fatigue, quality of life, self-efficacy, illness beliefs, mood and physical activity will be assessed via self-report questionnaire at baseline, 12 weeks and 12 months post intervention. Cost effectiveness and cost utility will be assessed via interview at baseline and 12 months post intervention. Intention to treat analysis will be our primary model for efficacy analysis. Semi-structured interviews will

	Care, King's College London, London, SE1 1UL, UK. jane.petty@kcl.ac.uk.			be conducted with a selected sample of participants in order to explore the acceptability of the intervention and factors affecting adherence to the exercise programme. DISCUSSION: This is the first randomised controlled trial to compare the efficacy and cost-effectiveness of tailored home exercise with advice about exercise and usual care for adults with inflammatory neuropathy. TRIAL REGISTRATION: Current Controlled Trials ISRCTN13311697.
White PD(1), Chalder T(2), Sharpe M(3).	(1)Queen Mary University of London. (2)King's College London. (3)University of Oxford.	The planning, implementation and publication of a complex intervention trial for chronic fatigue syndrome: the PACE trial.	BJPsych Bull. 2015 Feb;39(1):24-7. doi: 10.1192/pb.bp.113.045005.	The PACE trial was a four-arm trial of specialist medical care, compared with specialist medical care with a supplementary therapy: adaptive pacing therapy, cognitive-behavioural therapy or graded exercise therapy, for patients with chronic fatigue syndrome. The trial found that both cognitive-behavioural and graded exercise therapies were more effective than either of the other two treatments in reducing fatigue and improving physical disability. This paper describes the design, conduct and main results of the trial, along with a description of the challenges that had to be overcome in order to produce clear answers to the clinically important questions the trial posed.
White PD, Clauw DJ, van der Meer JW, Moss-Morris R, Taylor RR.		Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Ann Intern Med. 2015 Dec 1;163(11):885. doi: 10.7326/L15-5171.	
Whiting PF(1), Wolff RF(2), Deshpande S(2), Di Nisio M(3), Duffy S(2), Hernandez AV(4), Keurentjes JC(5), Lang S(2), Misso K(2), Ryder S(2), Schmidlkofer S(6), Westwood M(2), Kleijnen J(7).	(1)School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom	Cannabinoids for Medical Use: A Systematic Review and Meta-analysis.	JAMA. 2015 Jun 23-30;313(24):2456-73. doi: 10.1001/jama.2015.6358.	IMPORTANCE: Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear. OBJECTIVE: To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids. DATA SOURCES: Twenty-eight databases from inception to April 2015. STUDY SELECTION: Randomized clinical trials of cannabinoids for the following indications: nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome. DATA EXTRACTION AND SYNTHESIS: Study quality was assessed using the Cochrane risk of bias tool. All review stages were conducted independently by 2 reviewers. Where possible, data were pooled using random-effects meta-analysis. MAIN OUTCOMES AND MEASURES: Patient-relevant/disease-specific outcomes, activities of daily living, quality of life, global impression of change, and AEs. RESULTS: A total of 79 trials (6462 participants) were included; 4 were judged at low risk of bias. Most trials showed improvement in symptoms associated with cannabinoids but these associations did not reach statistical significance in all trials. Compared with placebo, cannabinoids were associated with a greater average number of patients showing a complete nausea and vomiting response (47% vs 20%; odds ratio [OR], 3.82 [95% CI, 1.55-9.42]; 3 trials), reduction in pain (37% vs 31%; OR, 1.41 [95% CI, 0.99-2.00]; 8 trials), a greater average reduction in numerical rating scale pain assessment (on a 0-10-point scale; weighted mean difference [WMD], -0.46 [95% CI, -0.80 to -0.11]; 6 trials), and average reduction in the Ashworth spasticity

				scale (WMD, -0.36 [95% CI, -0.69 to -0.05]; 7 trials). There was an increased risk of short-term AEs with cannabinoids, including serious AEs. Common AEs included dizziness, dry mouth, nausea, fatigue, somnolence, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination. CONCLUSIONS AND RELEVANCE: There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term AEs.
Wiborg JF(1), van Bussel J, van Dijk A, Bleijenberg G, Knoop H.	(1)Expert Centre for Chronic Fatigue, Radboud University Medical Center, Nijmegen, The Netherlands.	Randomised controlled trial of cognitive behaviour therapy delivered in groups of patients with chronic fatigue syndrome.	Psychother Psychosom. 2015;84(6):368-76. doi: 10.1159/000438867. Epub 2015 Sep 25.	BACKGROUND: Meta-analyses have been inconclusive about the efficacy of cognitive behaviour therapies (CBTs) delivered in groups of patients with chronic fatigue syndrome (CFS) due to a lack of adequate studies. METHODS: We conducted a pragmatic randomised controlled trial with 204 adult CFS patients from our routine clinical practice who were willing to receive group therapy. Patients were equally allocated to therapy groups of 8 patients and 2 therapists, 4 patients and 1 therapist or a waiting list control condition. Primary analysis was based on the intention-to-treat principle and compared the intervention group (n = 136) with the waiting list condition (n = 68). The study was open label. RESULTS: Thirty-four (17%) patients were lost to follow-up during the course of the trial. Missing data were imputed using mean proportions of improvement based on the outcome scores of similar patients with a second assessment. Large and significant improvement in favour of the intervention group was found on fatigue severity (effect size = 1.1) and overall impairment (effect size = 0.9) at the second assessment. Physical functioning and psychological distress improved moderately (effect size = 0.5). Treatment effects remained significant in sensitivity and per-protocol analyses. Subgroup analysis revealed that the effects of the intervention also remained significant when both group sizes (i.e. 4 and 8 patients) were compared separately with the waiting list condition. CONCLUSIONS: CBT can be effectively delivered in groups of CFS patients. Group size does not seem to affect the general efficacy of the intervention which is of importance for settings in which large treatment groups are not feasible due to limited referral.
Wilson RL(1), Paterson KB(1), Hutchinson CV(2).	(1)College of Medicine, Biological Sciences and Psychology, University of Leicester, UK. (2)College of Medicine, Biological Sciences and Psychology, University	Increased Vulnerability to Pattern-Related Visual Stress in Myalgic Encephalomyelitis.	Perception. 2015 Dec;44(12):1422-6. doi: 10.1177/0301006615614467. Epub 2015 Nov 3.	The objective of this study was to determine vulnerability to pattern-related visual stress in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). A total of 20 ME/CFS patients and 20 matched (age, gender) controls were recruited to the study. Pattern-related visual stress was determined using the Pattern Glare Test. Participants viewed three patterns, the spatial frequencies (SF) of which were 0.3 (low-SF), 2.3 (mid-SF), and 9.4 (high-SF) cycles per degree (c/deg). They reported the number of distortions they experienced when viewing each pattern. ME/CFS patients exhibited significantly higher pattern glare scores than controls for the mid-SF pattern. Mid-high SF differences were also significantly higher in patients than controls. These findings

	of Leicester, UK. ch190@le.ac.uk.			provide evidence of altered visual perception in ME/CFS. Pattern-related visual stress may represent an identifiable clinical feature of ME/CFS that will prove useful in its diagnosis. However, further research is required to establish if these symptoms reflect ME/CFS-related changes in the functioning of sensory neural pathways.
Winger A(1), Kvarstein G(2), Wyller VB(3,)(4,)(5), Ekstedt M(6,)(7), Sulheim D(8,)(9), Fagermoen E(10), Småstuen MC(11), Helseth S(12).	(1)Institute of Nursing, Faculty of Health Sciences, Oslo and Akershus University College of Applied Sciences, Postboks 4 St. Olavs plass, NO-0130, Oslo, Norway. anette.winger@hioa.no.	Health related quality of life in adolescents with chronic fatigue syndrome: a cross-sectional study.	Health Qual Life Outcomes. 2015 Jul 3;13:96. doi: 10.1186/s12955-015-0288-3.	AIM: To study health related quality of life (HRQOL) and depressive symptoms in adolescents with chronic fatigue syndrome (CFS) and to investigate in which domains their HRQOL and depressive symptoms differ from those of healthy adolescents. BACKGROUND AND OBJECTIVE: Several symptoms such as disabling fatigue, pain and depressive symptoms affect different life domains of adolescents with CFS. Compared to adolescents with other chronic diseases, young people with CFS are reported to be severely impaired, both physiologically and mentally. Despite this, few have investigated the HRQOL in this group. METHOD: This is a cross-sectional study on HRQOL including 120 adolescents with CFS and 39 healthy controls (HC), between 12 and 18 years. The Pediatric Quality of Life Inventory™, 4.0 (PedsQL) was used to assess HRQOL. The Mood and Feelings Questionnaire assessed depressive symptoms. Data were collected between March 2010 and October 2012 as part of the NorCAPITAL project (Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial). Linear and logistic regression models were used in analysis, and all tests were two-sided. RESULTS: Adolescents with CFS reported significantly lower overall HRQOL compared to HCs. When controlling for gender differences, CFS patients scored 44 points lower overall HRQOL on a scale from 0-100 compared to HCs. The domains with the largest differences were interference with physical health (B = -59, 95 % CI -54 to -65) and school functioning (B = -52, 95 % CI -45 to -58). Both depressive symptoms and being a patient were independently associated with lower levels of HRQOL CONCLUSION: The difference in HRQOL between CFS patients and healthy adolescents was even larger than we expected. The large sample of adolescents with CFS in our study confirms previous findings from smaller studies, and emphasizes that CFS is a seriously disabling condition that has a strong impact on their HRQOL. Even though depressive symptoms were found in the group of patients, they could not statistically explain the poor HRQOL.
Wise S(1), Ross A(2), Brown A(3), Evans M(3), Jason L(3).	(1)DePaul University, USA SWISE6@depaul.edu. (2)Johns Hopkins Medical College, USA. (3)DePaul University, USA.	An assessment of fatigue in patients with postural orthostatic tachycardia syndrome.	J Health Psychol. 2015 Nov 4. pii: 1359105315613624. [Epub ahead of print]	Individuals with postural orthostatic tachycardia syndrome share many symptoms with those who have chronic fatigue syndrome; one of which is severe fatigue. Previous literature found that those with chronic fatigue syndrome experience many forms of fatigue. The goal of this study was to investigate whether individuals with postural orthostatic tachycardia syndrome also experience multidimensional fatigue and whether these individuals can be clustered into subgroups based on the types of fatigue they endorse. A convenience sample of 138 participants (aged 14-29) with postural orthostatic tachycardia syndrome completed questionnaires that assessed fatigue, brain fog symptom severity, activities that improve brain fog, and brain fog-related disability. An exploratory factor analysis was conducted on the Fatigue Types

				Questionnaire, and a three-factor solution was produced. Factor scores were then used to cluster the patients into groups using a TwoStep cluster analysis. This resulted in two clusters, a high severity group and a low severity group. The clusters were then compared on a number of items related to symptom expression. Individuals within the more severe cluster had significantly more brain fog at the beginning and end of the survey when compared to cluster two. Those in the more severe cluster also described more activity impairment as well as more frequent, more severe, and more debilitation from postural orthostatic tachycardia syndrome and brain fog. The findings of the factor analysis suggest that patients with postural orthostatic tachycardia syndrome experience fatigue as a multidimensional construct and they also can be subgrouped based on symptom severity.
Witham MD(1), Adams F(2), McSwiggan S(2), Kennedy G(2), Kabir G(2), Belch JJ(2), Khan F(2).	(1)Medical Research Institute, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, Scotland, UK. Electronic address: m.witham@dundee.ac.uk. (2)Medical Research Institute, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, Scotland, UK.	Effect of intermittent vitamin D3 on vascular function and symptoms in chronic fatigue syndrome--a randomised controlled trial.	Nutr Metab Cardiovasc Dis. 2015 Mar;25(3):287-94. doi: 10.1016/j.numecd.2014.10.007. Epub 2014 Oct 22.	BACKGROUND AND AIMS: Low 25-hydroxyvitamin D levels are common in patients with chronic fatigue syndrome; such patients also manifest impaired vascular health. We tested whether high-dose intermittent oral vitamin D therapy improved markers of vascular health and fatigue in patients with chronic fatigue syndrome. METHODS AND RESULTS: Parallel-group, double-blind, randomised placebo-controlled trial. Patients with chronic fatigue syndrome according to the Fukuda (1994) and Canadian (2003) criteria were randomised to receive 100,000 units oral vitamin D3 or matching placebo every 2 months for 6 months. The primary outcome was arterial stiffness measured using carotid-femoral pulse wave velocity at 6 months. Secondary outcomes included flow-mediated dilatation of the brachial artery, blood pressure, cholesterol, insulin resistance, markers of inflammation and oxidative stress, and the Piper Fatigue scale. As many as 50 participants were randomised; mean age 49 (SD 13) years, mean baseline pulse wave velocity 7.8 m/s (SD 2.3), mean baseline office blood pressure 128/78 (18/12) mmHg and mean baseline 25-hydroxyvitamin D level 46 (18) nmol/L. 25-hydroxyvitamin D levels increased by 22 nmol/L at 6 months in the treatment group relative to placebo. There was no effect of treatment on pulse wave velocity at 6 months (adjusted treatment effect 0.0 m/s; 95% CI -0.6 to 0.6; p = 0.93). No improvement was seen in other vascular and metabolic outcomes, or in the Piper Fatigue scale at 6 months (adjusted treatment effect 0.2 points; 95% CI -0.8 to 1.2; p = 0.73). CONCLUSION: High-dose oral vitamin D3 did not improve markers of vascular health or fatigue in patients with chronic fatigue syndrome. TRIAL REGISTRATION: www.controlled-trials.com, ISRCTN59927814.
Wyller VB(1), Sørensen Ø(2), Sulheim D(3), Fagermoen E(4), Ueland T(5), Mollnes TE(6).	(1)Dept. of Paediatrics, Oslo University Hospital, Norway; Division of Medicine and Laboratory Sciences, Medical Faculty,	Plasma cytokine expression in adolescent chronic fatigue syndrome.	Brain Behav Immun. 2015 May;46:80-6. doi: 10.1016/j.bbi.2014.12.025. Epub 2014 Dec 31.	Chronic fatigue syndrome (CFS) is a prevalent and disabling condition among adolescents. The pathophysiology is poorly understood, but low-grade systemic inflammation has been suggested as an important component. This study compared circulating levels of individual cytokines and parameters of cytokine networks in a large set of adolescent CFS patients and healthy controls, and explored associations between cytokines and symptoms in the CFS group. CFS patients (12-18years old) were recruited nation-wide to a single referral center as part of the NorCAPITAL project (ClinicalTrials

	University of Oslo, Norway; Dept. of Paediatrics, Akershus University Hospital, Nordbyhagen, Norway.			ID: NCT01040429). A broad case definition of CFS was applied, requiring three months of unexplained, disabling chronic/relapsing fatigue of new onset, whereas no accompanying symptoms were necessary. Thus, the case definition was broader than the Fukuda-criteria of CFS. Healthy controls having comparable distribution of gender and age were recruited from local schools. Twenty-seven plasma cytokines, including interleukins, chemokines and growth factors were assayed using multiplex technology. The results were subjected to network analyses using the ARACNE algorithm. Symptoms were charted by a questionnaire, and patients were subgrouped according to the Fukuda-criteria. A total of 120 CFS patients and 68 healthy controls were included. CFS patients had higher scores for fatigue ($p<0.001$) and inflammatory symptoms ($p<0.001$) than healthy controls. All cytokine levels and cytokine network parameters were similar, and none of the differences were statistically different across the two groups, also when adjusting for adherence to the Fukuda criteria of CFS. Within the CFS group, there were no associations between aggregate cytokine network parameters and symptom scores. Adolescent CFS patients are burdened by symptoms that might suggest low-grade systemic inflammation, but plasma levels of individual cytokines as well as cytokine network measures were not different from healthy controls, and there were no associations between symptoms and cytokine expression in the CFS group. Low-grade systemic inflammation does not appear to be a central part of adolescent CFS pathophysiology.
Wyller VB, Reme SE, Mollnes TE.		Chronic fatigue syndrome/myalgic encephalo-myelitis - pathophysiology, diagnosis and treatment.	Tidsskr Nor Laegeforen. 2015 Dec 15;135(23-24):2172-2175. eCollection 2015.	
Xu MQ(1), Cao HL(1), Wang WQ(1), Wang S(1), Cao XC(1), Yan F(1), Wang BM(1).	(1)Meng-Que Xu, Hai-Long Cao, Wei-Qiang Wang, Shan Wang, Xiao-Cang Cao, Fang Yan, Bang-Mao Wang, Department of Gastroenterology and Hepatology, General Hospital, Tianjin Medical University, Tianjin 300052, China.	Fecal microbiota transplantation broadening its application beyond intestinal disorders.[Article in English, Norwegian]	World J Gastroenterol. 2015 Jan 7;21(1):102-11. doi: 10.3748/wjg.v21.i1.102.	Intestinal dysbiosis is now known to be a complication in a myriad of diseases. Fecal microbiota transplantation (FMT), as a microbiota-target therapy, is arguably very effective for curing Clostridium difficile infection and has good outcomes in other intestinal diseases. New insights have raised an interest in FMT for the management of extra-intestinal disorders associated with gut microbiota. This review shows that it is an exciting time in the burgeoning science of FMT application in previously unexpected areas, including metabolic diseases, neuropsychiatric disorders, autoimmune diseases, allergic disorders, and tumors. A randomized controlled trial was conducted on FMT in metabolic syndrome by infusing microbiota from lean donors or from self-collected feces, with the resultant findings showing that the lean donor feces group displayed increased insulin sensitivity, along with increased levels of butyrate-producing intestinal microbiota. Case reports of FMT have also shown favorable outcomes in Parkinson's disease, multiple sclerosis, myoclonus dystonia, chronic fatigue syndrome, and idiopathic thrombocytopenic purpura. FMT is a promising approach in the manipulation

				of the intestinal microbiota and has potential applications in a variety of extra-intestinal conditions associated with intestinal dysbiosis.
Yadav RK(1), Sarvottam K, Magan D, Yadav R.	(1)Integral Health Clinic, Department of Physiology, All India Institute of Medical Sciences , New Delhi, India .	A two-year follow-up case of chronic fatigue syndrome: substantial improvement in personality following a yoga-based lifestyle intervention.	J Altern Complement Med. 2015 Apr;21(4):246-9. doi: 10.1089/acm.2014.0055. Epub 2015 Mar 31.	BACKGROUND AND OBJECTIVE: Chronic Fatigue Syndrome (CFS) is characterized by excessive fatigue after minimal physical or mental exertion, muscle and joint pain, poor concentration, dizziness, and sleep disturbances. We report here the effect of a yoga-based lifestyle intervention in a 30-year old male patient with a documented diagnosis of CFS with compromised quality of life (QoL) and altered personality. METHODS: The patient initially attended a short-term yoga-based lifestyle intervention program that consisted of yoga-postures, breathing exercises (pranayama), meditation, group discussions, and individualized advice on stress management, diet and physical activity besides group support. Thereafter, patient attended 5 more such programs. RESULTS: There was a notable and consistent improvement in his clinical profile, positive aspects of personality and subjective well-being, and reduction in anxiety following this yoga-based lifestyle intervention. CONCLUSION: Overall, the results suggest that lifestyle intervention may improve clinical condition and personality in patients with CFS.
Yadlapati S(1), Efthimiou P(2).	(1)a Associate chief, Rheumatology Division, New York Methodist Hospital , Brooklyn , NY , USA. (2)b Rheumatology Division, New York Methodist Hospital, Associate Professor of Clinical Medicine and Rheumatology, Weill Cornell Medical College , New York , NY , USA.	Impact of IL-1 inhibition on fatigue associated with autoinflammatory syndromes.	Mod Rheumatol. 2016 Jan;26(1):3-8. doi: 10.3109/14397595.2015.1069459. Epub 2015 Aug 3.	Cryopyrin-associated periodic syndromes (CAPS) is a rare group of autoinflammatory disorders that includes familial cold autoinflammatory syndrome or FCAS, Muckle-wells syndrome or MWS, and neonatal-onset multisystem inflammatory disease or NOMID. CAPS is caused by a mutation in the NOD-like receptor family, pyrin domain containing 3 (NLRP3) gene. This ultimately leads to increased production of interleukin (IL)-1β. IL-1β is a biologically active member of the IL-1 family. It is not only a pro-inflammatory cytokine responsible for features such as fever, rash, and arthritis, but is also a major mediator in the central pathways of fatigue. Fatigue is a major component of CAPS and is associated with severely compromised quality of life. In clinical studies, fatigue was measured using functional assessment of chronic illness therapy-fatigue or FACIT-F and short form-36 or SF-36, physical component score instruments. These questionnaires can also be used to monitor improvement of fatigue following initiation of therapy. IL-1 inhibitors block the IL-1 signaling cascade, thereby preventing systemic inflammation in CAPS. The decrease in systemic inflammation is accompanied by improvement in fatigue.
Yang TY(1), Kuo HT, Chen HJ, Chen CS, Lin WM, Tsai SY, Kuo CN, Kao CH.	(1)From the Molecular and Genomic Epidemiology Center, China Medical University Hospital, China Medical University, Taichung	Increased Risk of Chronic Fatigue Syndrome Following Atopy: A Population-Based Study.	Medicine (Baltimore). 2015 Jul;94(29):e1211. doi: 10.1097/MD.0000000000001211.	Several hypotheses have been proposed to explain the etiopathogenesis of chronic fatigue syndrome (CFS), including immune dysregulation. However, few population-based prospective cohort studies have been conducted on CFS and atopy. We investigated the relationship between atopy and CFS by using a population-based cohort study. In this prospective, population-based cohort study of the National Health Insurance Research Database, we identified 42,558 patients with atopy and 170,232 patients without atopy from 2005 to 2007 with follow-up to 2011. The incidence rates and risks for CFS were estimated using Cox proportion hazards regression. The overall incidence rate of CFS was higher in the atopy cohort compared with the nonatopy cohort (1.37 versus 0.87 per 1000 person-year), with an adjusted hazard ratio of 1.48

				(95% confidence interval 1.30-1.69). The risk of CFS in the atopy cohort increased 1.47- to 1.50-fold for each nonexisting comorbidity. Patients with numerous atopic symptoms exhibited a biological gradient of increasing risk for CFS, and the risk changed significantly after adjustment for age, sex, and comorbidities, increasing from 1.46- to 2.59-fold. We revealed that atopy is associated with CFS, particularly in patients with numerous atopic syndromes. The actual mechanism for CFS development in patients with atopy remains unclear and requires further investigation. We recommend researching the subsequent fatigue symptom in patients with atopy, particularly those with multiple atopic syndromes.
Yao F, Zhao Y, Jiang S, Fang M.		[The theorotical basis for chronic fatigue syndrome from bladder meridian of foot-taiyang].[Article in Chinese]	Zhongguo Zhen Jiu. 2015 Mar;35(3):295-8.	The bladder meridian of foot-taiyang is considered as key of six meridians and the yang of the yang, which is the pivot of transportation for qi and blood in the meridians and zang-fu. The running route and treatment characteristic of bladder meridian is closely related with chronic fatigue syndrome (CFS). The bladder meridian belongs to brain and connects with governor vessel, which has a close relationship with zang-fu function, quality of sleep and fatigue. Besides, the running route of bladder meridian is highly consistent with the surface projections of important anatomical structures such as muscle, nerve and sympathetic trunk, etc. Therefore, regulating the meridian-qi of bladder meridian can harmonize five-zang and calm the mind, but also effectively relieve physical and mental fatigue in CFS.
Yazmalar L(1), Deveci Ö(2), Batmaz İ(1), İpek D(2), Çelepkolu T(3), Alpaycı M(4), Hattapoğlu E(1), Akdeniz D(1), Sarıyıldız MA(1).	(1)Departments of Physical Medicine and Rehabilitation, Dicle University, Diyarbakır, Turkey. (2)Departments of Infectious Disease and Clinical Microbiology, Dicle University, Diyarbakır, Turkey. (3)Departments of Family Physician, Faculty of Medicine, Dicle University, Diyarbakır, Turkey. (4)Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Yüzüncüyıl University, Van, Turkey.	Fibromyalgia incidence among patients with hepatitis B infection.	Int J Rheum Dis. 2015 Jul 1. doi: 10.1111/1756-185X.12593. [Epub ahead of print]	AIM: The purpose of our investigation was to evaluate the incidence of fibromyalgia syndrome (FMS) and identify FMS-related clinical symptoms in hepatitis B virus (HBV) patients. METHODS: One hundred and eighteen HBV surface antigen (HbsAg)-positive patients (40 with chronic active hepatitis B, 40 hepatitis B carriers and 38, all of whom had been antiretroviral-treated for at least 3 months) were included in this study. In addition, 60 age- and gender-matched HbsAg-negative healthy controls were included in the study. RESULTS: There was no significant difference in age, gender or body mass index (BMI) between the two groups ($P > 0.05$). Serum aspartate aminotransferase and alanine aminotransferase levels were significantly higher in HBV patients relative to the control group ($P < 0.05$). The incidence of FMS, widespread body pain, fatigue, sleep disturbance, anxiety, morning stiffness, arthralgia was significantly greater among HBV patients relative to the control group. Additionally, the mean tender point counts and the visual analog scale values were significantly higher among the HBV patients ($P < 0.05$). CONCLUSIONS: The results of the present study demonstrate that FMS incidence is greater among HBV patients relative to control subjects. However, there were no differences in FMS incidence among the subgroups of HBV diagnoses.

Ylikoski A(1), Martikainen K, Partinen M.	(1)Vitalmed Research Center, Helsinki Sleep Clinic, Helsinki, Finland.	Parkinson's disease and restless legs syndrome.	Eur Neurol. 2015;73(3-4):212-9. doi: 10.1159/000375493. Epub 2015 Mar 11.	AIMS: Various sleep-related complications are common in Parkinson's disease (PD). The prevalence of restless legs syndrome (RLS) and its association with other symptoms were studied. METHODS: Altogether, 1,447 Parkinson patients, aged 43-89, participated in a questionnaire study. RESULTS: The response rate was 59.0% and of these, 68% returned fully answered questionnaires (n = 577). RLS occurred in 20.3% of the PD subjects. In patients with RLS, the symptoms occurred in 81.9% at least once weekly. The degree of severity was moderate in 42.7%, severe in 23.9% and very severe in 15.4%. Daytime sleepiness, fatigue, chronic insomnia, sleep maintenance insomnia, intense dreaming, and low quality of life were more common in patients with RLS than in patients without RLS. The occurrence of early onset RLS (onset ≤ age of 45 years) was 4.2%. The occurrences of late onset (>45 years) drug naïve RLS and late onset RLS (with dopaminergic medication) were 5.4 and 10.4%, respectively. CONCLUSION: In patients with PD, the early onset of RLS resembles idiopathic RLS with typical gender distribution and familial trait. Late onset of RLS is more common than idiopathic RLS.
Yukumi S(1), Ichiki H(2), Funada J(3), Suzuki H(1), Morimoto M(1), Fujita T(3), Izumi N(3), Abe M(2).	(1)Department of Surgery, National Hospital Organization Ehime Medical Center, 366 Yokogawara, Toon, Ehime 791-0281, Japan. (2)Respiratory Medicine, National Hospital Organization Ehime Medical Center, 366 Yokogawara, Toon, Ehime 791-0281, Japan. (3)Cardiology, National Hospital Organization Ehime Medical Center, 366 Yokogawara, Toon, Ehime 791-0281, Japan.	Postcardiac injury syndrome following vascular interventional radiofrequency ablation for paroxysmal atrial fibrillation.	Respir Med Case Rep. 2015 Jun 4;15:89-91. doi: 10.1016/j.rmcr.2015.03.008. eCollection 2015.	Postcardiac injury syndrome (PCIS) occurs following a pericardial or myocardial injury. On the other hand, PCIS following cardiac catheter intervention is rare and can be difficult to diagnose because of its delayed onset. A 24-year-old man underwent radiofrequency ablation (RFA) for paroxysmal atrial fibrillation and suffered from general fatigue and left-sided pleural effusion three months after the procedure. His symptoms and effusion were effectively treated within a month by administrating nonsteroidal anti-inflammatory drugs. However, seven months later, he developed left-sided chest pain and low-grade fever. Computed tomography showed a thickening of the parietal pleura and reccurence of the pleural effusion. Pleural biopsy by video-assisted thoracoscopy demonstrated chronic pleuritis with a non-necrotizing granulomatous reaction. Given the previous RFA, and in the absence of infection or malignant disease, he was diagnosed with PCIS and treated with colchicine.
Zdunek M(1), Jason LA(1), Evans M(1), Jantke R(1), Newton JL(2).	(1)Center for Community Research, DePaul University, Chicago, USA. (2)Institute for Ageing	A Cross Cultural Comparison of Disability and Symptomatology Associated with CFS.	Int J Psychol Behav Sci. 2015;5(2):98-107.	Few studies have compared symptomatology and functional differences experienced by patients with chronic fatigue syndrome (CFS) across cultures. The current study compared patients with CFS from the United States (US) to those from the United Kingdom (UK) across areas of functioning, symptomatology, and illness onset characteristics. Individuals in each sample met criteria for CFS as defined by Fukuda et

	and Health, Newcastle University, Newcastle upon Tyne, UK.			al. (1994). These samples were compared on two measures of disability and impairment, the DePaul Symptom Questionnarie (DSQ) and the Medical outcomes study 36-item short-form health survey (SF-36). Results revealed that the UK sample was significantly more impaired in terms of mental health and role emotional functioning, as well as specific symptoms of pain, neurocognitive difficulties, and immune manifestations. In addition, the UK sample was more likely to be working rather than on disability. Individuals in the US sample reported more difficulties falling asleep, more frequently reported experiencing a sudden illness onset (within 24 hours), and more often reported that the cause of illness was primarily due to physical causes. These findings suggest that there may be important differences in illness characteristics across individuals with CFS in the US and the UK, and this has implications for the comparability of research findings across these two countries.
Zeineh MM(1), Kang J, Atlas SW, Raman MM, Reiss AL, Norris JL, Valencia I, Montoya JG.	(1)From the Department of Radiology, Lucas Center for Imaging, Stanford University School of Medicine, 1201 Welch Rd, Room P271, Stanford, CA 94305-5488.	Right arcuate fasciculus abnormality in chronic fatigue syndrome.	Radiology. 2015 Feb;274(2):517-26. doi: 10.1148/radiol.14141079. Epub 2014 Oct 29.	PURPOSE: To identify whether patients with chronic fatigue syndrome (CFS) have differences in gross brain structure, microscopic structure, or brain perfusion that may explain their symptoms. MATERIALS AND METHODS: Fifteen patients with CFS were identified by means of retrospective review with an institutional review board-approved waiver of consent and waiver of authorization. Fourteen age- and sex-matched control subjects provided informed consent in accordance with the institutional review board and HIPAA. All subjects underwent 3.0-T volumetric T1-weighted magnetic resonance (MR) imaging, with two diffusion-tensor imaging (DTI) acquisitions and arterial spin labeling (ASL). Open source software was used to segment supratentorial gray and white matter and cerebrospinal fluid to compare gray and white matter volumes and cortical thickness. DTI data were processed with automated fiber quantification, which was used to compare piecewise fractional anisotropy (FA) along 20 tracks. For the volumetric analysis, a regression was performed to account for differences in age, handedness, and total intracranial volume, and for the DTI, FA was compared piecewise along tracks by using an unpaired t test. The open source software segmentation was used to compare cerebral blood flow as measured with ASL. RESULTS: In the CFS population, FA was increased in the right arcuate fasciculus (P = .0015), and in right-handers, FA was also increased in the right inferior longitudinal fasciculus (ILF) (P = .0008). In patients with CFS, right anterior arcuate FA increased with disease severity (r = 0.649, P = .026). Bilateral white matter volumes were reduced in CFS (mean ± standard deviation, 467 581 mm(3) ± 47 610 for patients vs 504 864 mm(3) ± 68 126 for control subjects, P = .0026), and cortical thickness increased in both right arcuate end points, the middle temporal (T = 4.25) and precentral (T = 6.47) gyri, and one right ILF end point, the occipital lobe (T = 5.36). ASL showed no significant differences. CONCLUSION: Bilateral white matter atrophy is present in CFS. No differences in perfusion were noted. Right hemispheric increased FA may reflect degeneration of crossing fibers or strengthening of short-range fibers. Right anterior arcuate FA may serve as a biomarker for CFS.

Zhang Z, Cai Z, Yu Y, Wu L, Zhang Y.		Effect of Lixujieyu recipe in combination with Five Elements music therapy on chronic fatigue syndrome.	J Tradit Chin Med. 2015 Dec;35(6):637-41.	OBJECTIVE: To observe the clinical effects of the Lixujieyu recipe combined with Five Elements music therapy on chronic fatigue syndrome (CFS) identified as the symptom patterns of liver stagnation and spleen deficiency in terms of Traditional Chinese Medicine. METHODS: Patients with CFS were randomly divided into treatment group 1 (Lixujieyu recipe combined with Gong-Tune, n = 15); treatment group 2 (Lixujieyu recipe combined with Jiao-Tune, n = 15); treatment group 3 (Lixujieyu recipe combined with Yu-Tune, n = 15); treatment group 4 (Lixujieyu recipe combined with Shang-Tune, n = 15); treatment group 5 (Lixuiievu recipe combined with Zhi-Tune, n = 15); and the control group (Lixujieyu recipe alone, n = 15). Chinese medicine was given twice daily, and music was listened to for 45 minutes daily, 5 days a week. All patients were treated for 4 weeks. Patients were assessed via the Fatigue Scale, the Hamilton Depression Rating Scale, and the Hamilton Anxiety Rating Scale before and after treatment. RESULTS: Treatment groups 1 and 2 had better effects on relieving the symptoms of physical fatigue related to anxiety and depression than the control group ($P < 0.05$). CONCLUSION: Lixujieyu recipe combined with Gong-Tune or Jiao-Tune significantly relieved the symptoms of CFS.
Zhao RH, Liu JN, Li C, Zhang JS, Wang BZ, Yao YC, Xie M, Wang DH.		[Changes of HPAA in Different Rat Models of Gan Stagnation, Pi Deficiency, Gan Stagnation Pi Defi- ciency and Interventional Effect of Chaishu Sijun Decoction].[Article in Chinese]	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2015 Jul;35(7):834-8.	OBJECTIVE: To compare changes of hypothalamus-pituitary-adrenal axis (HPAA) in different rat models of Gan stagnation (GS), Pi deficiency (PD), Gan stagnation Pi deficiency (GSPD) syndromes, and to observe interventional effect of Chaishu Sijun Decoction (CSD, capable of soothing Gan-qi invigorating Pi) on them. METHODS: Seventy Wistar rats were divided into the normal control group (group 1), the GS group (group 2), the PD group (group 3), the GSPD group (group 4), the GS intervention group (group 5), the PD intervention group (group 6), and the GSPD intervention group (group 7) according to random digit table, 10 in each group. Rats in group 1 received no treatment. Rats in group 2 and 5 were modeled by chronic restraint method. Rats in group 3 and 6 were modeled by excess fatigue plus alimentary abstinence method. Rats in group 4 and 7 were modeled by chronic restraint, excess fatigue, and alimentary abstinence method. At the 2nd weekend of modeling, CSD at 2.86 g/kg was fed to rats in group 5, 6, and 7 by gastrogavage for 2 successive weeks. Equal volume of distilled water was given to rats in the rest 4 groups. On the 29th day, rats were killed, adrenal weight weighed, and adrenal index calculated. Levels of plasma and hypothalamus corticotropin-releasing hormone (CRH), plasma and pituitary adrenocorticotrophic hormone (ACTH), and plasma corticosterone (CORT) were determined using radioimmunity. RESULTS: Compared with group 1, adrenal index significantly decreased in group 2, 3, and 4 ($P < 0.05$). Of them, plasma and hypothalamus CRH, plasma CORT increased significantly in group 2 and 4 ($P < 0.05$). Besides, plasma and pituitary ACTH increased in group 4 ($P < 0.05$). Plasma and pituitary ACTH, as well as plasma CORT decreased significantly in group 3 ($P < 0.05$). Compared with group 2, 3, and 4, adrenal index increased significantly in group 5, 6, and 7 ($P < 0.05$). Compared with group 2, plasma CORT, hypothalamus CRH, and pituitary ACTH decreased significantly in group 5

				(P < 0.05). Compared with group 3, plasma ACTH and CORT increased significantly in group 6 (P < 0.05). Compared with group 4, plasma CRH, ACTH, CORT, hypothalamus CRH, and pituitary ACTH decreased in group 7 (P < 0.05). CONCLUSIONS: The function of HPA .axis was damaged to varying degrees in rats of the three models in this experiment. Hyperactivity of HPA axis existed in GS syndrome and GSPD syndrome. Impairment of feedback regulation in hypothalamus and pituitary was accompanied in GSPD syndrome. Hypofunction of HPA axis existed in PDS. CSD, capable of soothing Gan-qi invigorating'Pi, showed improvement on disarranged HPAA, but with optimal effect on GSPD syndrome. CSD had higher correlation with GSPD syndrome.
Zundel MT(1), Pattyn M(2), Chelimsky TC(3), Riess ML(4).	(1)Anesthesia Service, Clement J. Zablocki VA Medical Center, 5000 West National Avenue, Milwaukee, WI 53295, USA; Department of Anesthesiology, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226, USA.	Arterial flow waveforms, vascular tone, and chronic fatigue: a case report.	Auton Neurosci. 2015 Jul;190:58-60. doi: 10.1016/j.autneu.2015.03.003. Epub 2015 Mar 24.	We present the case of a patient with chronic fatigue secondary to Postural Orthostatic Tachycardia Syndrome (POTS) who had distinctive abnormalities in his arterial waveform morphology as assessed by pulse oximetry. Moreover, the patient's arterial waveform changed markedly from being supine to upright, suggesting that arterial flow patterns may be abnormal in our patient. Analysis of the waveform suggested a positional hypovolemia as the cause of his orthostatic intolerance. We review general aspects of arterial flow waveform analysis pertinent to health care providers and discuss the pathophysiology of POTS.
Üçeyler N(1), Sommer C.	(1)Neurologische Klinik, Universitätsklinikum Würzburg, Josef-Schneider-Str. 11, 97080, Würzburg, Deutschland, ueceyler_n@ukw.de.	[Fibromyalgia syndrome: A disease of the small nerve fibers?].[Article in German]	Z Rheumatol. 2015 Aug;74(6):490-2, 494-5. doi: 10.1007/s00393-014-1546-1.	Fibromyalgia syndrome (FMS) is characterized by chronic widespread pain and additional associated symptoms, such as fatigue, sleep disturbances and depressive moods. The pathophysiology of pain in FMS is unclear. In recent years, an involvement of the thinly myelinated A-delta and the unmyelinated C-nerve fibers has been reported in FMS patients. Independent research groups published consistent objective and multidimensional findings of damage to these small nerve fibers, such as disturbances of fiber function, electrical properties and morphological changes. All these alterations are not specific for FMS; however, they were described for the first time in subgroups of FMS patients. While the reasons for this small fiber pathology and its contribution to FMS pain are still unclear, a new research field has now been opened that will focus on uncovering the underlying pathophysiology. This review article summarizes these new findings and discusses the significance for the understanding of FMS.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**

No authors listed		Branch N 2 of the Vishnevskiy Central Military Clinical Hospital N 3 celebrates the 25th anniversary.	Voen Med Zh. 2014 Aug;335(8):76-81. Russian.	Article in Russian
Abed J, Judeh H, Abed E, Kim M, Arabelo H, Gurunathan R.	Department of Medicine, Icahn School of Medicine, Mount Sinai St, Luke's and Mount Sinai Roosevelt Hospitals, New York, NY, USA. hjudeh@chpnet.org.	Fixing a heart: the game of electrolytes in anorexia nervosa.	Nutr J. 2014 Sep 5;13:90. doi: 10.1186/1475-2891-13-90.	CASE: A 25-year-old woman with chronic anorexia nervosa and depression presented with sudden weakness and fatigue. Psychosocial history was notable for binge-starve cycles over the past year and a decline in overall well-being. Vitals on presentation were notable for hypothermia, hypotension, and bradycardia. Initial exam was significant for emaciation, lethargy, and lower extremity edema. Laboratory work-up revealed markedly elevated LFTs, hypoglycemia, thrombocytopenia and elevated INR and lipase. ECG showed sinus bradycardia with prolonged QTc. Ultrasound revealed normal liver and biliary tree. Serum acetaminophen, alcohol level, and urinary toxicology were unremarkable. Work up for infectious, autoimmune, and genetic causes of hepatitis was negative. Echocardiogram revealed left ventricular hypokinesis and EF 10-15%. Nutritional support was begun slowly, however electrolyte derangements began to manifest on hospital day 2, with hypophosphatemia, hypokalemia, hypocalcemia, and hypomagnesemia. Multiple medical and psychiatric disciplines were consulted, and aggressive electrolyte monitoring and repletion were done. The patient's overall clinical status improved slowly during her hospital course. Her liver enzymes trended down, and her QTc interval eventually returned toward the normal range. Repeat echocardiogram following treatment revealed improvement of her EF to 40%. DISCUSSION: Anorexia nervosa is an eating disorder characterized by extremely low body weight, fear of gaining weight or distorted perception of body image, and amenorrhea. Anorexia can lead to life threatening medical complications, and thus constitutes a major challenge to manage. Central to the pathogenesis of the refeeding syndrome is a weakened cardiopulmonary system, electrolytes abnormalities, hepatic dysfunction, liver hypoperfusion and failure. CONCLUSION: Given the clinical presentation, this patient likely presented on the brink of developing frank refeeding syndrome, with cardiac dysfunction and hypovolemia, leading to hepatic hypoperfusion and ischemic hepatitis. Subsequently, she developed electrolyte disturbances characteristic of refeeding syndrome, which were managed without major complication. Her hospital course is encouraging not only for her recovery, but for the collaboration of the different teams involved in her care, and it highlights the importance of a multidisciplinary approach to caring for patients with the potential dire complications of a complex psychiatric illness.

Ablin JN, Buskila D.	Institute of Rheumatology, Tel Aviv Sourasky Medical Center and Sackler School of Medicine, Tel Aviv University, Israel.	Predicting fibromyalgia, a narrative review: are we better than fools and children?	Eur J Pain. 2014 Sep;18(8):1060-6. doi: 10.1002/j.1532-2149.2014.00481.x. Epub 2014 Mar 11.	Fibromyalgia syndrome (FMS) is a common and intriguing condition, manifest by chronic pain and fatigue. Although the pathogenesis of FMS is not yet completely understood, predicting the future development of FMS and chronic pain is a major challenge with great potential advantages, both from an individual as well as an epidemiological standpoint. Current knowledge indicates a genetic underpinning for FMS, and as increasing data are accumulated regarding the genetics involved, the prospect of utilizing these data for prediction becomes ever more attractive. The co-existence of FMS with multiple other functional disorders indicates that the clinical identification of such symptom constellations in a patient can alert the physician to the future development of FMS. Hypermobility syndrome is another clinical (as well as genetic) phenotype that has emerged as a risk factor for the development of FMS. Stressful events, including early life trauma, are also harbingers of the future development of FMS. Functional neuroimaging may help to elucidate the neural processes involved in central sensitization, and may ultimately also evolve into markers of predictive value. Last but not least, obesity and disturbed sleep are clinical (inter-related) features relevant for this spectrum. Future efforts will aim at integrating genetic, clinical and physiological data in the prediction of FMS and chronic pain
Adamowicz JL, Caikauskaite I, Friedberg F.	(1)Department of Psychiatry and Behavioral Sciences, Stony Brook University, Putnam Hall/South Campus, Stony Brook, NY, 11794-8790, USA, Jenna.Adamowicz@stonybrook.edu	Defining recovery in chronic fatigue syndrome: a critical review.	Qual Life Res. 2014 Nov;23(9):2407-16. doi: 10.1007/s11136-014-0705-9. Epub 2014 May 3.	PURPOSE: In chronic fatigue syndrome (CFS), the lack of consensus on how recovery should be defined or interpreted has generated controversy and confusion. The purpose of this paper was to systematically review, compare, and evaluate the definitions of recovery reported in the CFS literature and to make recommendations about the scope of recovery assessments. METHODS: A search was done using the MEDLINE, PubMed, PsycINFO, CINAHL, and Cochrane databases for peer review papers that contained the search terms "chronic fatigue syndrome" and "recovery," "reversal," "remission," and/or "treatment response." RESULTS: From the 22 extracted studies, recovery was operationally defined by reference with one or more of these domains: (1) pre-morbid functioning; (2) both fatigue and function; (3) fatigue (or related symptoms) alone; (4) function alone; and/or (5) brief global assessment. Almost all of the studies measuring recovery in CFS did so differently. The brief global assessment was the most common outcome measure used to define recovery. Estimates of recovery ranged from 0 to 66 % in intervention studies and 2.6 to 62 % in naturalistic studies. CONCLUSIONS: Given that the term "recovery" was often based on limited assessments and less than full restoration of health, other more precise and accurate labels (e.g., clinically significant improvement) may be more appropriate and informative. In keeping with common understandings of the term recovery, we recommend a consistent definition that captures a broad-based return to health with assessments of both fatigue and function as well as the patient's perceptions of his/her recovery status.

Aerenhouts D, Ickmans K, Clarys P, Zinzen E, Meersdom G, Lambrecht L, Nijs J.	(1)Department of Human Biometry and Biomechanics	Sleep characteristics, exercise capacity and physical activity in patients with chronic fatigue syndrome.	Disabil Rehabil. 2014 Dec 16:1-7.	Abstract Purpose: Unrefreshing sleep and lowered physical activity are commonly observed in chronic fatigue syndrome (CFS) patients, but how they might influence each other remains unexplored. Therefore, this study simultaneously examined the exercise capacity, sleep characteristics and physical activity in CFS patients. Methods: Handgrip strength and cycle exercise capacity were assessed in 42 female CFS patients and 24 inactive control subjects. During four consecutive days and nights, energy expenditure, activity and sleep-wake pattern were objectively registered using a Sensewear Armband. Results: Exercise capacity was significantly lower in CFS patients. In both groups VO2peak correlated with the time subjects were physically active. In CFS patients only, VO2peak correlated negatively with sleeping during the day whilst physical activity level and energy expenditure correlated negatively with sleep latency and lying awake at night. Conclusions: In the present study, CFS patients with higher VO2peak tend to sleep less over day. Occupation in physical activities was negatively associated with sleep latency and lying awake at night. Increased physical activity potentially has beneficial effects on sleep quality in CFS. However, a close monitoring of the effects of increasing physical activity is essential to avoid negative effects on the health status of patients. Implications for Rehabilitation Female patients with chronic fatigue syndrome (CFS) have normal sleep latency and sleep efficiency, but sleep more and spent more time in bed as compared to healthy inactive women. Female CFS patients have lower exercise capacity, and a lower physical activity level as compared to healthy inactive women. CFS patients appear to be more sensitive for sleep quality (sleep latency and lying awake at night), which is associated with a low physical activity level
Afari N, Ahumada SM, Wright LJ, Mostoufi S, Golnari G, Reis V, Cuneo JG.	Department of Psychiatry, 9500 Gilman Dr, La Jolla, CA 92093-0737. nafari@ucsd.edu.	Psychological trauma and functional somatic syndromes: a systematic review and meta-analysis.	Psychosom Med. 2014 Jan;76(1):2-11. doi: 10.1097/PSY.0000000000000010. Epub 2013 Dec 12. Review.	OBJECTIVE: This meta-analysis systematically examined the association of reported psychological trauma and posttraumatic stress disorder (PTSD) with functional somatic syndromes including fibromyalgia, chronic widespread pain, chronic fatigue syndrome, temporomandibular disorder, and irritable bowel syndrome. Our goals were to determine the overall effect size of the association and to examine moderators of the relationship. METHODS: Literature searches identified 71 studies with a control or comparison group and examined the association of the syndromes with traumatic events including abuse of a psychological, emotional, sexual, or physical nature sustained during childhood or adulthood, combat exposure, or PTSD. A random-effects model was used to estimate the pooled odds ratio and 95% confidence interval. Planned subgroup analyses and meta-regression examined potential moderators. RESULTS: Individuals who reported exposure to trauma were 2.7 (95% confidence interval = 2.27-3.10) times more likely to have a functional somatic syndrome. This association was robust against both publication bias and the generally low quality of the literature. The magnitude of the association with PTSD was significantly larger than that with sexual or physical abuse. The association of

				reported trauma with chronic fatigue syndrome was larger than the association with either irritable bowel syndrome or fibromyalgia. Studies using non-validated questionnaires or self-report of trauma reported larger associations than did those using validated questionnaires. CONCLUSIONS: Findings are consistent with the hypothesis that traumatic events are associated with an increased prevalence of functional somatic syndromes. The analyses also highlight limitations of the existing literature and emphasize the importance of prospective studies, examining the potential similarities and differences of these conditions, and pursuing hypothesis-driven studies of the mechanisms underlying the link between trauma, PTSD, and functional somatic syndromes.
Agmon-Levin N, Zafrir Y, Kivity S, Balofsky A, Amital H, Shoenfeld Y.	The Zabludowicz Center for Autoimmune Diseases, Chaim Sheba Medical Center, 52621, Tel-Hashomer, Israel.	Chronic fatigue syndrome and fibromyalgia following immunization with the hepatitis B vaccine: another angle of the 'autoimmune (auto-inflammatory) syndrome induced by adjuvants' (ASIA).	Immunol Res. 2014 Dec;60(2-3):376-83. doi: 10.1007/s12026-014-8604-2.	The objectives of this study were to gather information regarding demographic and clinical characteristics of patients diagnosed with either fibromyalgia (FM) or chronic fatigue (CFS) following hepatitis B vaccination (HBVv) and furthermore to apply the recently suggested criteria of autoimmune (auto-inflammatory) syndromes induced by adjuvants (ASIA), in the aim of identifying common characteristics that may suggest an association between fibromyalgia, chronic fatigue and HBV vaccination. Medical records of 19 patients with CFS and/or fibromyalgia following HBVv immunization were analyzed. All of which were immunized during 1990-2008 in different centers in the USA. All medical records were evaluated for demographics, medical history, the number of vaccine doses, as well as immediate and long term post-immunization adverse events and clinical manifestations. In addition, available blood tests, imaging results, treatments and outcomes were analyzed. ASIA criteria were applied to all patients. The mean age of patients was 28.6 ± 11 years, of which 68.4 % were females. 21.05 % had either personal or familial background of autoimmune disease. The mean latency period from the last dose of HBVv to onset of symptoms was 38.6 ± 79.4 days, ranging from days to a year. Eight (42.1 %) patients continued with the immunization program despite experiencing adverse events. Manifestations that were commonly reported included neurological manifestations (84.2 %), musculoskeletal (78.9 %), psychiatric (63.1 %), fatigue (63.1 %), gastrointestinal complains (58 %) and mucocutaneous manifestations (36.8 %). Autoantibodies were detected in 71 % of patients tested. All patients fulfilled the ASIA criteria. This study suggests that in some cases CFS and FM can be temporally related to immunization, as part of ASIA syndrome. The appearance of adverse event during immunization, the presence of autoimmune susceptibility and higher titers of autoantibodies all can be suggested as risk factors. ASIA criteria were fulfilled in all patients eluding the plausible link between ASIA and CFS/FM.

Alevizos M, Karagkouni A, Panagiotidou S, Vasiadi M, Theoharides TC.	Molecular Immunopharmacology and Drug Discovery Laboratory, Department of Integrative Physiology and Pathobiology, Tufts University School of Medicine, Tufts Medical Center, Boston, Massachusetts; Present address: Department of Internal Medicine, Jacoby Medical Center, New York, New York.	Stress triggers coronary mast cells leading to cardiac events.	Ann Allergy Asthma Immunol. 2014 Apr;112(4):309-16. doi: 10.1016/j.anai.2013.09.017. Epub 2013 Oct 10. Review.	OBJECTIVE: Stress precipitates and worsens not only asthma and atopic dermatitis but also acute coronary syndromes (ACSs), which are associated with coronary inflammation. Evidence linking stress to ACS was reviewed and indicated that activation of coronary mast cells (MCs) by stress, through corticotropin-releasing hormone (CRH) and other neuropeptides, contributes to coronary inflammation and coronary artery disease. DATA SOURCES: PubMed was searched (2005-2013) for articles using the following keywords: allergies, anaphylaxis, anxiety, coronary arteries, coronary artery disease, C-reactive protein, cytokines, chymase, histamine, hypersensitivity, interleukin-6 (IL-6), inflammation, mast cells, myocardial ischemia, niacin, platelet-activating factor, rupture, spasm, statins, stress, treatment, tryptase, and uroctortin. STUDY SELECTIONS: Articles were selected based on their relevance to how stress affects ACS and how it activates coronary MCs, leading to coronary hypersensitivity, inflammation, and coronary artery disease. RESULTS: Stress can precipitate allergies and ACS. Stress stimulates MCs through the activation of high-affinity surface receptors for CRH, leading to a CRH-dependent increase in serum IL-6. Moreover, neurotensin secreted with CRH from peripheral nerves augments the effect of CRH and stimulates cardiac MCs to release IL-6, which is elevated in ACS and is an independent risk factor for myocardial ischemia. MCs also secrete CRH and uroctortin, which induces IL-6 release from cardiomyocytes. The presence of atherosclerosis increases the risk of cardiac MC activation owing to the stimulatory effect of lipoproteins and adipocytokines. Conditions such as Kounis syndrome, mastocytosis, and myalgic encephalopathy/chronic fatigue syndrome are particularly prone to coronary hypersensitivity reactions. CONCLUSION: Inhibition of cardiac MCs may be a novel treatment approach.
Ali S, Chalder T, Madan I.	(1)South London and Maudsley NHS Foundation Trust, London, UK. (2)Department of Psychological Medicine, King's College London, London, UK. (3)Guys and St Thomas' NHS Foundation Trust and Division of Health and Social Care, King's College London, London, UK.	Evaluating Interactive Fatigue Management Workshops for Occupational Health Professionals in the United Kingdom.	Saf Health Work. 2014 Dec;5(4):191-7. doi: 10.1016/j.shaw.2014.07.002. Epub 2014 Jul 27.	BACKGROUND: Disabling fatigue is common in the working age population. It is essential that occupational health (OH) professionals are up-to-date with the management of fatigue in order to reduce the impact of fatigue on workplace productivity. Our aim was to evaluate the impact of one-day workshops on OH professionals' knowledge of fatigue and chronic fatigue syndrome (CFS), and their confidence in diagnosing and managing these in a working population. METHODS: Five interactive problem-based workshops were held in the United Kingdom. These workshops were developed and delivered by experts in the field. Questionnaires were self-administered immediately prior to, immediately after, and 4 months following each workshop. Questionnaires included measures of satisfaction, knowledge of fatigue and CFS, and confidence in diagnosing and managing fatigue. Open-ended questions were used to elicit feedback about the workshops. RESULTS: General knowledge of fatigue increased significantly after training (with a 25% increase in the median score). Participants showed significantly higher levels of confidence in diagnosing and managing CFS (with a 62.5% increase in the median score), and high scores were maintained 4 months after the workshops. OH

				physicians scored higher on knowledge and confidence than nurses. Similarly, thematic analysis revealed that participants had increased knowledge and confidence after attending the workshops. CONCLUSION: Fatigue can lead to severe functional impairment with adverse workplace outcomes. One-day workshops can be effective in training OH professionals in how to diagnose and manage fatigue and CFS. Training may increase general knowledge of fatigue and confidence in fatigue management in an OH setting.
Amihăesei IC, Cojocaru E.	No address given	Main neuroendocrine features, diagnosis and therapeutic possibilities in the chronic fatigue syndrome, an underdiagnosed entity.	Rev Med Chir Soc Med Nat Iasi. 2014 Jul-Sep;118(3):688-91.	Chronic fatigue syndrome is characterized by severe, persistent fatigue which is not relieved by rest and is not associated to other medical conditions. Other common symptoms are including concentration and memory impairment, muscle and multiple joints pain, extreme exhaustion after physical or mental exertions, irritable bowel syndrome-like symptoms and depression, anxiety, mood swings and panic attacks. Etiology of the syndrome is not yet clear, post-viral and stress hypotheses were not verified. Diagnosis is confirmed in case of new onset of severe fatigue, for six consecutive months or more; fatigue is leading to significant reduction of the activity levels and is accompanied by other four or more of the specific associated symptoms, which are also lasting for six months or longer. The management of the disease is based on cognitive behavioral therapy, graded exercise therapy and pacing; medication plays a minor role in therapy. The occupational status is severely affected, more than half of the cases being unable to work. Full recovery rate is in average of about 5%.
Anderson G, Berk M, Maes M.	CRC, Glasgow, UK.	Biological phenotypes underpin the physio-somatic symptoms of somatization, depression, and chronic fatigue syndrome.	Acta Psychiatr Scand. 2014 Feb;129 (2):83-97. doi: 10.1111/acps.12182. Epub 2013 Aug 17. Review.	OBJECTIVE: Somatization is a symptom cluster characterized by 'psychosomatic' symptoms, that is, medically unexplained symptoms, and is a common component of other conditions, including depression and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). This article reviews the data regarding the pathophysiological foundations of 'psychosomatic' symptoms and the implications that this has for conceptualization of what may more appropriately be termed physio-somatic symptoms. METHOD: This narrative review used papers published in PubMed, Scopus, and Google Scholar electronic databases using the keywords: depression and chronic fatigue, depression and somatization, somatization and chronic fatigue syndrome, each combined with inflammation, inflammatory, tryptophan, and cell-mediated immune (CMI). RESULTS: The physio-somatic symptoms of depression, ME/CFS, and somatization are associated with specific biomarkers of inflammation and CMI activation, which are correlated with, and causally linked to, changes in the tryptophan catabolite (TRYCAT) pathway. Oxidative and nitrosative stress induces damage that increases neoepitopes and autoimmunity that contribute to the immuno-inflammatory processes. These pathways are all known to cause physio-somatic symptoms, including fatigue, malaise, autonomic symptoms, hyperalgesia, intestinal hypermotility, peripheral neuropathy, etc. CONCLUSION: Biological underpinnings, such as immune-

				inflammatory pathways, may explain, at least in part, the occurrence of physio-somatic symptoms in depression, somatization, or myalgic encephalomyelitis/chronic fatigue syndrome and thus the clinical overlap among these disorders.
Anderson VR, Jason LA, Hlavaty LE.	Department of Psychology Michigan State University , East Lansing , Michigan , USA.	A qualitative natural history study of ME/CFS in the community.	Health Care Women Int. 2014 Jan;35(1):3-26. doi: 10.1080/07399332.2012.684816. Epub 2013 Feb 27.	In previous qualitative research on Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS), researchers have focused on the experiences of patients with ME/CFS in tertiary care samples. This qualitative study examined the natural history of people with ME/CFS (n = 19) from a community-based sample. Findings highlighted multilayered themes involving the illness experience and the physical construction of ME/CFS. In addition, this study further illuminated unique subthemes regarding community response and treatment, which have implications for understanding the progression of ME/CFS as well as experiences of those within patient networks. There is a need for more longitudinal qualitative research on epidemiological samples of patients with ME/CFS.
Argento AC, Wolfe CR, Wahidi MM, Shofer SL, Mahmood K.	Emory, Interventional Pulmonology, Division of Pulmonary, Allergy and Critical Care Medicine, Atlanta, Georgia, United States ; christine.argento@emory.edu.	Broncho-Mediastinal Fistula Caused by Endobronchial Aspergilloma.	Ann Am Thorac Soc. 2014 Dec 16.	INTRODUCTION: Endobronchial aspergilloma is a rare condition affecting immunocompromised patients. We present 3 cases resulting in airway sinus tractsfistulae . CASE PRESENTATIONS: 68 year old male with orthotopic heart transplantation presented with fatigue, cough and dyspnea. Computerized tomography (CT) scan of the chest and bronchoscopy revealed an endobronchial right mainstem mass and airway fistulasinus to the mediastinum. The mass was debrided and biopsy showed Aspergillus fumigatus. He was treated with antifungals and recovered. 52 year old male with acquired immunodeficiency syndrome presented with cough, dyspnea and hypoxemia. Chest CT showed a bronchus intermedius mass and fistulasinus to the mediastinum. Bronchoscopy revealed a necrotic endobronchial mass and pseudomembranes and confirmed the presence of with a fistulasinus opening. The mass was resected bronchoscopically and Aspergillus fumigatus was isolated. He was treated with anti-fungals and . Tthe fistulasinus healed; however, he developed stenosis of the bronchus intermedius which required multiple dilations and stent placement... 63 year old male with chronic lymphoid leukemia was admitted for dyspnea, cough, weakness and dysphagia. Chest CT and bronchoscopy showed a mass causing obstruction of the subglottic trachea and a fistulasinus to the mediastinum. Biopsy showed Aspergillus fumigatus and he was treated with anti-fungals. The sinus healed but the patient died of leukemia. DISCUSSION: Risk factors for airway aspergilloma include immune-deficiency, mucosal damage and ischemia. We report airway fistulasinus formation as a complication of this infection which has not been previously emphasized. CONCLUSIONS: Endobronchial aspergillomas may form fistulaesinus tracts to the mediastinum. Aggressive treatment with anti-fungals and bronchoscopic

				interventions are required.
Armstrong CW, McGregor NR, Butt HL, Gooley PR.	No address given.	Metabolism in chronic fatigue syndrome.	Adv Clin Chem. 2014;66:121-72. Review.	Chronic fatigue syndrome (CFS) is a poorly understood condition that presents as long-term physical and mental fatigue with associated symptoms of pain and sensitivity across a broad range of systems in the body. The poor understanding of the disorder comes from the varying clinical diagnostic definitions as well as the broad array of body systems from which its symptoms present. Studies on metabolism and CFS suggest irregularities in energy metabolism, amino acid metabolism, nucleotide metabolism, nitrogen metabolism, hormone metabolism, and oxidative stress metabolism. The overwhelming body of evidence suggests an oxidative environment with the minimal utilization of mitochondria for efficient energy production. This is coupled with a reduced excretion of amino acids and nitrogen in general. Metabolomics is a developing field that studies metabolism within a living system under varying conditions of stimuli. Through its development, there has been the optimisation of techniques to do large-scale hypothesis-generating untargeted studies as well as hypothesis-testing targeted studies. These techniques are introduced and show an important future direction for research into complex illnesses such as CFS.
Arroll MA, Attree EA, Marshall CL, Dancey CP.	Chronic Illness Research Team, School of Psychology, University of East London, London, UK.	Pilot study investigating the utility of a specialized online symptom management program for individuals with myalgic encephalomyelitis/chronic fatigue syndrome as compared to an online meditation program.	Psychol Res Behav Manag. 2014;7:213-21. doi: 10.2147/PRBM.S63193.	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a long-term, debilitating condition that impacts numerous areas of individuals' lives. The two predominant treatment options for ME/CFS are cognitive behavioral therapy and graded exercise therapy; however, many people have found these techniques unacceptable or even damaging. This pilot study aimed to evaluate the utility of a specialized online symptom management program for ME/CFS in comparison to an online meditation program in an effort to ascertain whether this tool could be a further option for those with ME/CFS. METHODS: THIS EXPERIMENTAL DESIGN CONSISTED OF TWO INTERVENTIONS: a specialized online symptoms management program (N=19) and a control intervention based on an online meditation website (N=9). A battery of questionnaires, including measures of multidimensional fatigue, illness specific symptoms, perceived control, and mindful awareness, were completed before the participants commenced use of the programs and following 8 weeks' use. RESULTS: Significant differences were found in the areas of chance and powerful others' locus of control, and sleeping difficulties, but not in ME/CFS symptomatology overall. CONCLUSION: The specialized online program described in this study warrants further investigation, as it appears to influence perceived control and key ME/CFS symptoms over time.

Attard L, Bonvicini F, Gelsomino F, Manfredi R, Cascavilla A, Viale P, Varani S, Gallinella G.	University of Bologna, Department of Medicine and Surgery, Division of Infectious Diseases, S.Orsola-Malpighi Hospital, Bologna, Italy. Electronic address: giorgio.gallinella@unibo.it.	Paradoxical response to intravenous immunoglobulin in a case of Parvovirus B19-associated chronic fatigue syndrome.	J Clin Virol. 2015 Jan;62:54-7. doi: 10.1016/j.jcv.2014.11.021. Epub 2014 Nov 22.	We describe a case of chronic fatigue syndrome (CFS) associated to Parvovirus B19 infection where administration of intravenous immunoglobulins (IVIG), previously reported as effective, induced a paradoxical clinical response and increased viral replication. The indication of IVIG administration in the treatment of Parvovirus B19-associated CFS should be carefully reconsidered.
Attree EA, Arroll MA, Dancey CP, Griffith C, Bansal AS.	(1)Chronic Illness Research Team, School of Psychology, University of East London, London, UK. (2)Chronic Illness Research Team, School of Psychology, University of East London, London, UK ; Department of Immunology and the Sutton CFS Service, St Helier Hospital, Carshalton, UK.	Psychosocial factors involved in memory and cognitive failures in people with myalgic encephalomyelitis/chronic fatigue syndrome.	Psychol Res Behav Manag. 2014;7:67-76. doi: 10.2147/PRBM.S50645.	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is characterized by persistent emotional, mental, and physical fatigue accompanied by a range of neurological, autonomic, neuroendocrine, immune, and sleep problems. Research has shown that psychosocial factors such as anxiety and depression as well as the symptoms of the illness, have a significant impact on the quality of life of people with ME/CFS. In addition, individuals may suffer from deficits in memory and concentration. This study set out to explore the relationships between variables which have been found to contribute to cognitive performance, as measured by prospective and retrospective memory, and cognitive failures. METHODS: Eighty-seven people with ME/CFS answered questionnaires measuring fatigue, depression, anxiety, social support, and general self-efficacy. These were used in a correlational design (multiple regression) to predict cognitive function (self-ratings on prospective and retrospective memory), and cognitive failures. RESULTS: Our study found that fatigue, depression, and general self-efficacy were directly associated with cognitive failures and retrospective (but not prospective) memory. CONCLUSION: Although it was not possible in this study to determine the cause of the deficits, the literature in this area leads us to suggest that although the pathophysiological mechanisms of ME/CFS are unclear, abnormalities in the immune system, including proinflammatory cytokines, can lead to significant impairments in cognition. We suggest that fatigue and depression may be a result of the neurobiological effects of ME/CFS and in addition, that the neurobiological effects of the illness may give rise to both fatigue and cognitive deficits independently.
Bakken I, Tveito K, Gunnes N, Ghaderi S, Stoltenberg C, Trogstad L, HÃ¥berg S, Magnus P.	No address given	Two age peaks in the incidence of chronic fatigue syndrome/myalgic encephalomyelitis: a population-based registry study from	BMC Med. 2014 Oct 1;12(1):167	Background - The aim of the current study was to estimate sex- and age-specific incidence rates of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) using population-based registry data. CFS/ME is a debilitating condition with large impact on patients and their families. The etiology is unknown, and the distribution of the disease in the general population has not been well described. MethodsCases of CFS/ME were identified in the Norwegian Patient Register (NPR) for the years 2008 to 2012. The NPR is nationwide and contains diagnoses assigned by specialist

		Norway 2008Â¿2012.		health care services (hospitals and outpatient clinics). We estimated sex- and age-specific incidence rates by dividing the number of new cases of CFS/ME in each category by the number of person years at risk. Incidence rate ratios were estimated by Poisson regression with sex, age categories, and year of diagnosis as covariates. total of 5,809 patients were registered with CFS/ME during 2008 to 2012. The overall incidence rate was 25.8 per 100,000 person years (95% confidence interval (CI): 25.2 to 26.5). The female to male incidence rate ratio of CFS/ME was 3.2 (95% CI: 3.0 to 3.4). The incidence rate varied strongly with age for both sexes, with a first peak in the age group 10 to 19 years and a second peak in the age group 30 to 39 years. Conclusions - Early etiological clues can sometimes be gained from examination of disease patterns. The strong female preponderance and the two age peaks suggest that sex- and age-specific factors may modulate the risk of CFS/ME.
Band R, Barrowclough C, Wearden A.	School of Psychological Sciences, University of Manchester	The impact of significant other expressed emotion on patient outcomes in chronic fatigue syndrome.	Health Psychol. 2014 Sep;33(9):1092-101. doi: 10.1037/hea0000086.	OBJECTIVE: Previous literature has identified the importance of interpersonal processes for patient outcomes in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), particularly in the context of significant other relationships. The current study investigated expressed emotion (EE), examining the independent effects of critical comments and emotional overinvolvement (EOI) in association with patient outcomes. METHOD: Fifty-five patients with CFS/ME and their significant others were recruited from specialist CFS/ME services. Significant other EE status was coded from a modified Camberwell Family Interview. Patient outcomes (fatigue severity, disability, and depression) were derived from questionnaire measures. Forty-four patients (80%) completed follow-up questionnaires 6-months after recruitment. RESULTS: Significant other high-EE categorized by both high levels of critical comments and high EOI was predictive of worse fatigue severity at follow-up. High-critical EE was associated with higher levels of patient depressive symptoms longitudinally; depressive symptoms were observed to mediate the relationship between high critical comments and fatigue severity reported at follow-up. There were higher rates of high-EE in parents than in partners, and this was because of higher rates of EOI in parents. CONCLUSIONS: Patients with high-EE significant others demonstrated poorer outcomes at follow-up compared with patients in low-EE dyads. One mechanism for this appears to be as a result of increased patient depression. Future research should seek to further clarify whether the role of interpersonal processes in CFS/ME differs across different patient-significant other relationships. The development of significant other-focused treatment interventions may be particularly beneficial for both patients and significant others.

Barah F, Whiteside S, Batista S, Morris J.	Center for Neuroscience and Cell Biology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal.	Neurological aspects of human parvovirus B19 infection: a systematic review.	Rev Med Virol. 2014 May;24(3):154-68. doi: 10.1002/rmv.1782. Epub 2014 Jan 24. Review.	Parvovirus B19 has been linked with various clinical syndromes including neurological manifestations. However, its role in the latter remains not completely understood. Although the last 10 years witnessed a surge of case reports on B19-associated neurological aspects, the literature data remains scattered and heterogeneous, and epidemiological information on the incidence of B19-associated neurological aspects cannot be accurately extrapolated. The aim of this review is to identify the characteristics of cases of B19-associated neurological manifestations. A computerized systematic review of existing literature concerning cases of B19-related neurological aspects revealed 89 articles describing 129 patients; 79 (61.2%) were associated with CNS manifestations, 41 (31.8%) were associated with peripheral nervous system manifestations, and 9 (7.0%) were linked with myalgic encephalomyelitis. The majority of the cases (50/129) had encephalitis. Clinical characteristic features of these cases were analyzed, and possible pathological mechanisms were also described. In conclusion, B19 should be included in differential diagnosis of encephalitic syndromes of unknown etiology in all age groups. Diagnosis should rely on investigation of anti-B19 IgM antibodies and detection of B19 DNA in serum or CSF. Treatment of severe cases might benefit from a combined regime of intravenous immunoglobulins and steroids. To confirm these outcomes, goal-targeted studies are recommended to exactly identify epidemiological scenarios and explore potential pathogenic mechanisms of these complications. Performing retrospective and prospective and multicenter studies concerning B19 and neurological aspects in general, and B19 and encephalitic syndromes in particular, are required.
Bathen T, Velvin G, Rand-Hendriksen S, Robinson HS.	TRS National Resource Centre for Rare Disorders, Sunnaas Rehabilitation Hospital, Nesoddtangen, Norway.	Fatigue in adults with Marfan syndrome, occurrence and associations to pain and other factors.	Am J Med Genet A. 2014 Aug;164A(8):1931-9. doi: 10.1002/ajmg.a.36574. Epub 2014 Apr 9.	This study aims to investigate how fatigue affects adults with verified Marfan syndrome (MFS) in their daily lives, by examining fatigue levels and prevalence of severe fatigue compared to the general Norwegian population and individuals with other comparable chronic conditions. We investigated associations between socio-demographic characteristics, Marfan-related health problems, pain and fatigue. A cross-sectional study was conducted, using a postal questionnaire including the Fatigue Severity Scale (FSS) and questions on socio-demographic characteristics, Marfan-related health problems and pain. One hundred seventeen persons with MFS were invited to participate, 73 answered (62%). Participants reported significantly higher FSS scores and prevalence of severe fatigue compared to the general Norwegian population and patients with rheumatoid arthritis (RA), but lower than for other chronic conditions. Participants with chronic pain reported higher fatigue scores than those without chronic pain. Participants on disability benefits reported higher fatigue scores than participants who were working or enrolled in higher education. Marfan-related health problems like aortic dissection and use of blood pressure medication were not significantly associated with fatigue. In multivariable regression analyses chronic pain and employment status were

				significantly associated with fatigue. The final multivariable model explained 24% of the variance in fatigue scores. Our results show that fatigue is common in MFS patients and that it interferes with their daily lives. Chronic pain and employment status show significant associations to fatigue. This implies that fatigue is important to address when meeting MFS patients in clinical practice. There is need for more research on fatigue in Marfan syndrome.
Bayliss K, Goodall M, Chisholm A, Fordham B, Chew-Graham C, Riste L, Fisher L, Lovell K, Peters S, Wearden A.	Institute of Population Health, University of Manchester, Manchester, UK. kerin.bayliss@manchester.ac.uk.	Overcoming the barriers to the diagnosis and management of chronic fatigue syndrome/ME in primary care: a meta synthesis of qualitative studies.	BMC Fam Pract. 2014 Mar 7;15:44. doi: 10.1186/1471-2296-15-44.	BACKGROUND: The NICE guideline for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) emphasises the need for an early diagnosis in primary care with management tailored to patient needs. However, GPs can be reluctant to m ake a diagnosis and are unsure how to manage people with the condition. METHODS: A meta synthesis of published qualitative studies was conducted, producing a multi-perspective description of barriers to the diagnosis and management of CFS/ME, and the ways that some health professionals have been able to overcome them. Analysis provided second-order interpretation of the original findings and developed third-order constructs to provide recommendations for the medical curriculum. RESULTS: Twenty one qualitative studies were identified. The literature shows that for over 20 years health professionals have reported a limited understanding of CFS/ME. Working within the framework of the biomedical model has also led some GPs to be sceptical about the existence of the condition. GPs who provide a diagnosis tend to have a broader, multifactorial, model of the condition and more positive attitudes towards CFS/ME. These GPs collaborate with patients to reach agreement on symptom management, and use their therapeutic skills to promote self care. CONCLUSIONS: In order to address barriers to the diagnosis and management of CFS/ME in primary care, the limitations of the biomedical model needs to be recognised. A more flexible bio-psychosocial approach is recommended where medical school training aims to equip practitioners with the skills needed to understand, support and manage patients and provide a pathway to refer for specialist input
Bayliss K, Riste L, Fisher L, Wearden A, Peters S, Lovell K, Chew-Graham C.	Research Associate, Institute of Population Health, University of Manchester, Manchester, UK..	Diagnosis and management of chronic fatigue syndrome/myalgic encephalitis in black and minority ethnic people: a qualitative study.	Prim Health Care Res Dev. 2014 Apr;15(2):143-55. doi: 10.1017/S1463423613000145. Epub 2013 May 23.	AIM: This study aims to explore the possible reasons for the lower levels of diagnosis of chronic fatigue syndrome/myalgic encephalitis (CFS/ME) in the black and minority ethnic (BME) population, and the implications for management. BACKGROUND: Population studies suggest CFS/ME is more common in people from BME communities compared with the White British population. However, the diagnosis is made less frequently in BME groups. METHODS: Semi-structured qualitative interviews were conducted with 35 key stakeholders in NW England. Interviews were analysed using open explorative thematic coding. FINDINGS: There are barriers at every stage to the diagnosis and management of CFS/ME in people from BME groups. This begins with a lack of awareness of CFS/ME among BME respondents. Religious beliefs and the expectation of roles in the family and community mean that some people in BME groups may choose to manage their

				symptoms outside primary care using alternative therapies, prayer or spiritual healing. When accessing primary care, all participants recognised the possible influence of language barriers in reducing the likelihood of a diagnosis of CFS/ME. Stereotypical beliefs, including labels such as 'lazy' or 'work shy' were also believed to act as a barrier to diagnosis. Patients highlighted the importance of an on-going relationship with the general practitioner (GP), but perceived a high turnover of GPs in inner city practices, which undermined the holistic approach necessary to achieve a diagnosis. CONCLUSION: Training is required for health professionals to challenge inaccurate assumptions about CFS/ME in BME groups. The focus on the individual in UK primary care may not be appropriate for this group due to the role played by the family and community in how symptoms can be presented and managed. Culturally sensitive, educational resources for patients are also needed to explain symptoms and legitimise consultation
BaÄdina TV, Akintseva IV, Trushnikova TN.	No address given	A chronic fatigue syndrome and blood platelet serotonin levels in patients with multiple sclerosis.]	Zh Nevrol Psikhiatr Im S S Korsakova. 2014;114(2 Vypusk 2 Rasseiannyi skleroz):25-28. Russian.	Article in Russian Sixty patients with multiple sclerosis and 12 healthy controls were examined. The fatigue was measured by the Fatigue Severity Scale (FSS). Concentration of platelet serotonin was analyzed with immunoassay techniques («Serotonin ELISA"). The results of the study have shown the primary role of fatigue in multiple sclerosis, with the prevalence of this syndrome reached 57.6%. The patients with multiple sclerosis had low concentration of platelet serotonin that was correlated with clinical features of the disease.
Beasant L, Mills N, Crawley E.	(1) School of Social & Community Medicine, Centre for Child & Adolescent Health, University of Bristol, Oakfield Grove, UK. (2) School of Social and Community Medicine, University of Bristol, Canynge Hall, 39 Whatley Road, UK.	Adolescents and mothers value referral to a specialist service for chronic fatigue syndrome or myalgic encephalopathy (CFS/ME).	Prim Health Care Res Dev. 2014 Apr;15(2):134-42. doi: 10.1017/S1463423613000121. Epub 2013 Apr 25.	BACKGROUND: Paediatric chronic fatigue syndrome or myalgic encephalopathy (CFS/ME) is relatively common and disabling. Current guidance recommends referral to specialist services, although some general practitioners believe the label of CFS/ME is harmful and many are not confident about diagnosing CFS/ME. Aim Explore whether or not adolescents and their mothers value referral to a specialist service for young people with CFS/ME. METHODS: A qualitative study nested within a feasibility study of interventions for CFS/ME [Specialist Medical Intervention and Lightning Evaluation (SMILE)]. In-depth interviews were undertaken with 13 mothers and 12 adolescents participating in the SMILE study. Transcripts were systematically assigned codes using the qualitative data organisation package NVivo and analysed thematically using techniques of constant comparison. RESULTS: Gaining access to the specialist service was difficult and took a long time. Mothers felt that they needed to be proactive and persistent, partly because of a lack of knowledge in primary and secondary care. Having gained access, mothers felt the CFS/ME service was useful because it recognised and acknowledged their child's condition and opened channels of dialogue between health-care professionals and education providers. Adolescents reported that specialist medical care resulted in better symptom management, although some adolescents did not like the fact that

				the treatment approach limited activity. CONCLUSIONS: Adolescents and their mothers value receiving a diagnosis from a specialist service and making progress in managing CFS/ME. General practitioners should support adolescents with CFS/ME in accessing CFS/ME specialist services, consistent with current guidance.
Belcaro G, Cornelli U, Luzzi R, Ledda A, Cacchio M, Saggino A, Cesarone MR, Dugall M, Feragalli B, Hu S, Pellegrini L, Ippolito E.	Circulation/Vascular Labs, University Chieti-Pescara, Chieti, Italy - cardres@abol.it.	QR (Quercus Robur Extract, Robuvit) supplementation in subjects with chronic fatigue syndrome (CFS) and increased oxidative stress. A pilot registry.	J Neurosurg Sci. 2014 Nov 14.	The aim of this registry was to evaluate the effects of supplementation with Robuvit (French Quercus robur extract) capsules in subjects with Chronic Fatigue Syndrome (CFS) associated with an increased oxidative stress. Robuvit is a wood extract from Quercus robur (Horphag Research Ltd) used to improve liver dysfunction and chronic fatigue. After excluding any disease, subjects observed a defined management plan to improve CFS. Signs/symptoms had been present for more than 6 months in association with an increase in oxidative stress (measured as plasma free radicals). Blood tests were within normal values.METHODS: The registry included 38 CFS subjects and 42 comparable controls. There were no dropouts in the 4 weeks of follow up; the subjects were evaluated for a further period of 6 months. The management plan included: improved/increased sleep; reduction/abolition in smoking and alcohol or any other agent that may have affected them; control of diet, increase in dietary proteins; good hydration; rest (1/2-1 hr/day) and exercise (at least 30 min/day); planned relaxation time; increased time in open spaces. In the Robuvit supplementation group - 300 mg/day of Robuvit was used. RESULTS: symptoms improved in both groups with a significantly more important improvement in the supplement group ($p<0.05$). The single items in the MAF questionnaire were statistically better improved ($p<0.05$) in the supplement group. A parallel improvement in oxidative stress was observed in the supplemented subjects. In the post-registry follow up, at 6 months no organic disease was discovered or disease markers found. CONCLUSIONS: this preliminary registry indicates that supplementation with Robuvit improves CFS in otherwise healthy subjects with no presence of clinical disease or risk conditions. The effects of Robuvit in CFS may be partially mediated by an important action on plasma free radicals and oxidative stress.
Belcaro G, Cornelli U, Luzzi R, Cesarone MR, Dugall M, Feragalli B, Hu S, Pellegrini L, Ippolito E.	Circulation/Vascular Labs, University Chieti-Pescara, Chieti, Italy - cardres@abol.it.	Improved management of primary chronic fatigue syndrome with the supplement French oak wood extract (RobuvitÂ®): a pilot, registry	Panminerva Med. 2014 Mar;56(1):63-72. Epub 2013 Nov 14.	AIM: The aim of this supplement study was to evaluate French oak wood extract (Robuvit®, Horphag Research Ltd) used as a supplement in association with a defined management plan for chronic fatigue syndrome (CFS) in healthy subjects with CFS, a condition that has, so far, no specific treatment or management standards. METHODS: Robuvit® is a new proprietary and exclusive extract of oak wood with important antoxidant actions. The dosage of the supplementation was 200 mg/day for at least 6 months. The CFS questionnaire and the Brief Mood Introspection Scale (BMIS) questionnaire were used to evaluate mood variations

		evaluation.		associated with CFS patients. The CFS form includes an analogue scale to record the variations of single symptoms with a score range of 0-10. At inclusion into the registry study, at least 5 symptoms were present. All subjects (age range 35-44; BMI range 24-26) with CFS were tested for oxidative stress: 61 out of 91 subjects had an increased value of oxidative stress. The BMIS scale evaluating mood changes in time was also used. The evaluation was repeated at 3 and 6 months. RESULTS: Out of 91 eligible subjects with CFS, 48 subjects (31 with increased oxidative stress) were accepted as part of the supplement registry study using Robuvit; 43 (30 with increased oxidative stress) were accepted as controls using only the management plan. In the Robuvit® group there were 3 drop outs; also 3 controls were lost. Oxidative stress was increased in 64.58% of subjects that used Robuvit and in 69.7% of controls. The average values of oxidative stress were expressed for the whole group. The average follow up was 199.3;9.2 days in the Robuvit group and 202.2;5.5 in the control group with a minimum of 6 months. Considering variations in oxidative stress, there was no significant average change in controls, but a significant decrease from the initial values was observed in Robuvit subjects after 3 and 6 months. The CFS questionnaire variations in score indicated that there was a significant improvement for most symptoms after 3 and 6 months in the Robuvit group. Positive variations were also present in controls, indicating the positive effect of an increased attention to CFS. The improvement in signs/symptoms was significantly more valuable in subjects using the oak wood extract considering the main 8 symptoms and the accessory symptoms. Considering the BMIS variations, the totals for positive and negative items were significantly more favourable for Robuvit subjects. Overall mood evaluation in the oak wood extract group improved from an inclusion average of -6.93;2.1 to +4.32;2.6 at 6 months; in contrast it changed from -6.5;2.5 to -3.4;1.5 in controls. No side effects were observed during the supplementation with Robuvit. The compliance was optimal with 93% of the capsules correctly used. CONCLUSION: This promising pilot supplement registry study indicates a new opportunity of management for these difficult and often neglected patients. Correlation between oxidative stress and CFS has to be better explored.
Bennett BK, Goldstein D, Chen M, Davenport TA, Vollmer-Conna U, Scott EM, Hickie IB, Lloyd AR.	No address given	Characterization of fatigue states in medicine and psychiatry by structured interview.	Psychosom Med. 2014 Jun;76(5):379-88.	CONTEXT: Unexplained fatigue states are prevalent, with uncertain diagnostic boundaries. OBJECTIVE: Patients with fatigue-related illnesses were investigated by questionnaire and a novel semistructured interview to identify discriminatory features. METHODS: Cross-sectional samples of women from specialist practices with chronic fatigue syndrome (n = 20), postcancer fatigue (PCF; n = 20), or major depression (n = 16) were recruited. Additionally, two longitudinal samples were studied: women with fatigue associated with acute infection who subsequently developed postinfective fatigue syndrome (n = 20) or recovered uneventfully (n = 21), and women undergoing adjuvant therapy for breast cancer experiencing

				treatment-related fatigue who subsequently developed PCF (n = 16) or recovered uneventfully (n = 16). Patients completed self-report questionnaires, and trained interviewers applied the Semi-structured Clinical Interview for Neurasthenia. The receiver operating characteristics curves of the interview were measured against clinician-designated diagnoses. Cluster analyses were performed to empirically partition participants by symptom characteristics. RESULTS: The interview had good internal consistency (Cronbach alpha "fatigue" = .83), and diagnostic sensitivity and specificity for chronic fatigue syndrome (100% and 83%) and major depression (100% and 72%), with reasonable parameters for PCF (72% and 58%). Empirical clustering by "fatigue" or "neurocognitive difficulties" items allocated most patients to one group, whereas "mood disturbance" items correctly classified patients with depression only. CONCLUSIONS: The Semi-structured Clinical Interview for Neurasthenia offers reliable diagnostic use in assessing fatigue-related conditions. The symptom domains of fatigue and neurocognitive difficulties are shared across medical and psychiatric boundaries, whereas symptoms of depression such as anhedonia are distinguishing.
Bertagna X, Pivonello R, Fleseriu M, Zhang Y, Robinson P, Taylor A, Watson CE, Maldonado M, Hamrahian AH, Boscaro M, Biller BM.	Department of Endocrinology (X.B.), Centre de Référence des Maladies Rares de la Surrénale, Hôpital Cochin, Faculté de Médecine Paris Descartes, Université Paris 5, Paris 75014, France;	LCI699, a potent 11Î²-hydroxylase inhibitor, normalizes urinary cortisol in patients with Cushing's disease: results from a multicenter, proof-of-concept study.	J Clin Endocrinol Metab. 2014 Apr;99(4):1375-83. doi: 10.1210/jc.2013-2117. Epub 2013 Dec 11.	INTRODUCTION: The clinical features and increased mortality associated with Cushing's syndrome result from a chronic excess of circulating cortisol. As LCI699 potently inhibits 11β-hydroxylase, which catalyzes the final step of cortisol synthesis, it is a potential new treatment for Cushing's disease, the most common cause of endogenous Cushing's syndrome. METHODS: Adult patients with moderate-to-severe Cushing's disease (urinary free cortisol [UFC] levels >1.5 × ULN [upper limit of normal]) received oral LCI699 for 10 weeks in this proof-of-concept study. LCI699 was initiated at 4 mg/d in two equal doses; the dose was escalated every 14 days to 10, 20, 40, and 100 mg/d until UFC normalized, whereupon the dose was maintained until treatment ended (day 70). The primary endpoint was UFC ≤ ULN or a ≥50% decrease from baseline at day 70. RESULTS: Twelve patients were enrolled and completed the study. Baseline UFC ranged over 1.6-17.0 × ULN. All 12 patients achieved UFC ≤ULN or a ≥50% decrease from baseline at day 70; 11 (92%) had normal UFC levels at that time. After treatment discontinuation (day 84), UFC was >ULN in 10 patients with available measurements. Mean 11-deoxycortisol, 11-deoxycorticosterone, and adrenocorticotropic hormone levels increased during treatment and declined after discontinuation. Mean systolic and diastolic blood pressure decreased from baseline by 10.0 and 6.0 mmHg, respectively. LCI699 was generally well tolerated; most adverse events (AEs) were mild or moderate. The most common AEs included fatigue (7/12), nausea (5/12), and headache (3/12). No serious drug-related AEs were reported. CONCLUSIONS: LCI699 was efficacious and well tolerated in patients with Cushing's disease enrolled in this proof-of-concept study.

Bhardwaj N, Coffin JM.	Department of Molecular Biology and Microbiology, Graduate Program in Molecular Microbiology, Sackler School of Graduate Biomedical Sciences, Tufts University, 136 Harrison Avenue, Boston, MA 02111, USA. Electronic address: john.coffin@tufts.edu.	Endogenous retroviruses and human cancer: is there anything to the rumors?	Cell Host Microbe. 2014 Mar 12;15(3):255-9. doi: 10.1016/j.chom.2014.02.013.	Xenotropic murine leukemia virus-related virus (XMRV) infection was incorrectly associated with prostate cancer and chronic fatigue syndrome (CFS) in recent years. In this forum, we discuss the story of XMRV and how we can apply lessons learned here to inform the debate surrounding cancers associated with human endogenous retroviruses (HERVs).
Bhargava S, Tyagi SC.	Department of Biochemistry, Sir Ganga Ram Hospital, New Delhi, India, bhargavaseema6@gmail.com.	Nutriepigenetic regulation by folate-homocysteine-methionine axis: a review.	Mol Cell Biochem. 2014 Feb;387(1-2):55-61. doi: 10.1007/s11010-013-1869-2. Epub 2013 Nov 10. Review.	Although normally folic acid is given during pregnancy, presumably to prevent neural tube defects, the mechanisms of this protection are unknown. More importantly it is unclear whether folic acid has other function during development. It is known that folic acid re-methylates homocysteine (Hcy) to methionine by methylene tetrahydrofolate reductase-dependent pathways. Folic acid also generates high-energy phosphates, behaves as an antioxidant and improves nitric oxide (NO) production by endothelial NO synthase. Interestingly, during epigenetic modification, methylation of DNA/RNA generate homocysteine unequivocally. The enhanced overexpression of methyl transferase lead to increased yield of Hcy. The accumulation of Hcy causes vascular dysfunction, reduces perfusion in the muscles thereby causing musculopathy. Another interesting fact is that children with severe hyperhomocysteinaemia (HHcy) have skeletal deformities, and do not live past teenage. HHcy is also associated with the progeria syndrome. Epilepsy is primarily caused by inhibition of gamma-amino-butyric-acid (GABA) receptor, an inhibitory neurotransmitter in the neuronal synapse. Folate deficiency leads to HHcy which then competes with GABA for binding on the GABA receptors. With so many genetic and clinical manifestations associated with folate deficiency, we propose that folate deficiency induces epigenetic alterations in the genes and thereby results in disease.
Bjartveit K, Helskog EH, Kryvi PD, Brauer H.	No address given	Woman in her 30s with chronic fatigue	Tidsskr Nor Laegeforen. 2014 Feb 25;134(4):423-5. doi: 10.4045/tidsskr.13.0142. Norwegian. No abstract available.	Article in Norwegian Comment in Tidsskr Nor Laegeforen. 2014 Apr 8;134(7):691. Tidsskr Nor Laegeforen. 2014 Apr 8;134(7):690-1. Tidsskr Nor Laegeforen. 2014 Apr 29;134(8):811-2.

Blazquez A, Ruiz E, Aliste L, GarcÃa-Quintana A, Alegre J.	Unit of CFS and Fibromyalgia, Vall Hebron Hospital, Internal Medicine , Barcelona , Spain.	The effect of fatigue and fibromyalgia on sexual dysfunction in women with chronic fatigue syndrome.	J Sex Marital Ther. 2015;41(1):1-10. doi: 10.1080/0092623X.2013.864370. Epub 2014 Mar 11.	Sexual dysfunction in patients with chronic fatigue syndrome is attracting growing interest but, to date, few studies have analyzed it. For this reason, the authors evaluated sexual dysfunction in women with chronic fatigue syndrome (using the Golombok Rust Inventory of Sexual Satisfaction) and explore correlations with fatigue and other symptoms. Sexual dysfunction was greater in patients with chronic fatigue syndrome (n = 615) with a higher number of cognitive, neurological, and neurovegetative symptoms, concomitant fibromyalgia, Sjögren's syndrome, or myofascial pain syndrome, and more intense fatigue (p <.05).
Bloot L, Heins MJ, Donders R, Bleijenberg G, Knoop H.	Expert Centre for Chronic Fatigue, Radboud University Medical Center, The Netherlands †Department for Health Evidence, Radboud University Medical Center, The Netherlands.	The Process of Change in Pain During Cognitive Behavior Therapy for Chronic Fatigue Syndrome.	Clin J Pain. 2014 Dec 11.	BACKGROUND:: Cognitive behavior therapy (CBT) leads to a reduction of fatigue and pain in chronic fatigue syndrome (CFS). The processes underlying the reduction in pain have not been investigated. Recently, it was shown that increased self-efficacy, decreased focusing on symptoms, increased physical functioning and a change in beliefs about activity contribute to the decrease in fatigue. OBJECTIVES:: The present study has two objectives: (1) to determine the relationship between the reduction of fatigue and pain during CBT; (2) test to what extent the model for change in fatigue is applicable to the reduction in pain. METHODS:: 142 patients meeting US center for disease criteria for CFS, currently reporting pain, and starting CBT were included. A cross-lagged analysis was performed to study the causal direction of change between pain and fatigue. Pain and process variables were assessed before therapy, three times during CBT and after therapy. Actual physical activity was also assessed. The model was tested with multiple regression analyses. RESULTS:: The direction of change between pain and fatigue could not be determined. An increase in physical functioning and decrease in focusing on symptoms explained 4 to 14% of the change in pain. CONCLUSIONS:Pain and fatigue most probably decrease simultaneously during CBT. Pain reduction can partly be explained by a reduction of symptom focusing and increased physical functioning. Additional, yet unknown cognitive-behavioral factors also play a role in the reduction of pain.
Borah M, Sarma P, Das S.	Department of Pharmacology, Assam Medical College, Dibrugarh, Assam, India	A Study of the Protective Effect of Triticum aestivum L. in an Experimental Animal Model of Chronic Fatigue Syndrome.	Pharmacognosy Res. 2014 Oct;6(4):285-91. doi: 10.4103/0974-8490.138251.	BACKGROUND: Oxidative stress plays a major role in the pathogenesis of chronic fatigue syndrome (CFS). Keeping in view the proven antioxidant activity of Triticum aestivum L., this study has been undertaken to explore the potential therapeutic benefit of this plant in the treatment of CFS. OBJECTIVE: To study the protective effect of the ethanolic extract of the leaves of Triticum aestivum (EETA) in an experimental mice model of CFS. MATERIALS AND METHODS: Five groups of albino mice (20-25 g) were selected for the study, with five animals in each group. Group A served as the naïve control and Group B served as the stressed control. Groups C and D received EETA (100 mg/kg and 200 mg/kg b.w.). Group E received imipramine (20 mg/kg b.w.). Except for Group A, mice in each group were forced to swim 6 min each for 7 days to induce a state of chronic fatigue. Duration of immobility was measured on every alternate day. After 7 days, various behavioral tests (mirror

				chamber and elevated plus maize test for anxiety, open field test for locomotor activity) and biochemical estimations (malondialdehyde [MDA] and catalase activity) in mice brain were performed. RESULTS: Forced swimming in the stressed group resulted in a significant increase in immobility period, decrease in locomotor activity and elevated anxiety level. The brain homogenate showed significantly increased MDA and decreased catalase levels. The extract-treated groups showed significantly ($P < 0.05$) improved locomotor activity, decreased anxiety level, elevated catalase levels and reduction of MDA. CONCLUSION: The study confirms the protective effects of EETA in CFS.
Borsini A, Hepgul N, Mondelli V, Chalder T, Pariante CM.	(1)Section of Stress, Psychiatry and Immunology and Perinatal Psychiatry, Department of Psychological Medicine, Institute of Psychiatry,King's College London,UK. (2)Department of Psychological Medicine, Institute of Psychiatry,King's College London,UK.	Childhood stressors in the development of fatigue syndromes: a review of the past 20 years of research.	Psychol Med. 2014 Jul;44(9):1809-23. doi: 10.1017/S0033291713002468. Epub 2013 Oct 7.	BACKGROUND: Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are both highly prevalent conditions associated with extreme disability and with the development of co-morbid psychiatric disorders, such as depression and anxiety. Childhood stressors have been shown to induce persistent changes in the function of biological systems potentially relevant to the pathogenesis of both CFS and FM, such as the inflammatory system and the hypothalamic-pituitary-adrenal (HPA) axis. In this review, we examined whether multiple forms of childhood stressors are contributing factors to the development of these disorders, and of the associated psychiatric symptoms. METHOD: Using PubMed, we identified 31 papers relevant to this narrative review. We included cohort studies and case-control studies, without any exclusion in terms of age and gender. No study characteristics or publication date restrictions were imposed. RESULTS: Most studies across the literature consistently show that there is a strong association between experiences of childhood stressors and the presence of CFS and FM, with rates of CFS/FM being two- to three-fold higher in exposed than in unexposed subjects. We also found evidence for an increased risk for the development of additional symptoms, such as depression, anxiety and pain, in individuals with CFS and FM with a previous history of childhood stressors, compared with individuals with CFS/FM and no such history. CONCLUSIONS: Our review confirms that exposure to childhood stressors is associated with the subsequent development of fatigue syndromes such as CFS and FM, and related symptoms. Further studies are needed to identify the mechanisms underlying these associations.
Bourke JH, Johnson AL, Sharpe M, Chalder T, White PD.	(1)Centre for Psychiatry, Wolfson Institute for Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, UK. (2)MRC	Pain in chronic fatigue syndrome: response to rehabilitative treatments in the PACE trial.	Psychol Med. 2014 May;44(7):1545-52. doi: 10.1017/S0033291713002201. Epub 2013 Aug 23.	BACKGROUND: Pain is a common symptom of chronic fatigue syndrome (CFS). We investigated the effects of the treatments used in the PACE trial [cognitive behavioural therapy (CBT), graded exercise therapy (GET), adaptive pacing therapy (APT) and specialist medical care (SMC)] on pain in CFS. METHOD: We compared pain outcomes including individual painful symptoms, taken from the CDC criteria for CFS and co-morbid fibromyalgia. We modelled outcomes adjusting for baseline variables with multiple linear regression. RESULTS: Significantly less frequent muscle pain was reported by patients following treatment with CBT compared to SMC (mean difference = 0.38 unit change in frequency, p = 0.02), GET versus SMC (0.42, p

	Biostatistics Unit, University of Cambridge Institute of Public Health. (3)Department of Psychiatry, University of Oxford, Oxford, UK. (4)Academic Department of Psychological Medicine, King's College London, UK.			= 0.01) and GET versus APT (0.37, p = 0.01). Significantly less joint pain was reported following CBT versus APT (0.35, p = 0.02) and GET versus APT (0.36, p = 0.02). Co-morbid fibromyalgia was less frequent following GET versus SMC (0.03, p = 0.03). The effect sizes of these differences varied between 0.25 and 0.31 for muscle pain and 0.24 and 0.26 for joint pain. Treatment effects on pain were independent of 'change in fatigue'. CONCLUSIONS: CBT and GET were more effective in reducing the frequency of both muscle and joint pain than APT and SMC. When compared to SMC, GET also reduced the frequency of co-morbid fibromyalgia; the size of this effect on pain was small.
Bratis D, Tselebis A, Zafeiropoulos G, Tsaraklis A, Dumitru S, Moussas G, Kosmas E, Koutsilieris M.	(1)Psychiatric Department, "Sotiria" General Hospital of Chest Diseases, Athens. (2)Sleep Laboratory of 3rd Pulmonary Department, "Sotiria" General Hospital of Chest Diseases, Athens. (3)Pulmonary Department, "Metropolitan" Hospital, Athens. (4)Department of Experimental Physiology, University of Athens Medical School, Athens, Greece.	Psychological burden of patients diagnosed with obstructive sleep apnea.	Psychiatriki. 2014 Apr-Jun;25(2):95-103.	[Article in Greek] Obstructive sleep apnea syndrome (OSAS) is characterized by repeated episodes of upper airway obstruction during sleep, which leads to the presence of excessive daytime drowsiness. Regarding the psychological comorbidity in patients diagnosed with OSAS, previous studies focused mainly on depressive and secondarily on anxiety symptoms. Due to the lack of research data regarding the prevalence of anxiety and depressive symptoms as well as of alexithymic characteristics in patients with OSAS in Greece, the aim of the study was to record the above symptomatology in a sample of Greek OSAS patients and to investigate its relation to the respiratory parameter (Apnea-Hypopnea Index, AHI) of polysomnography. The study was conducted in a certified sleep laboratory. Thirty five randomly selected patients who attended the laboratory with symptoms of daytime drowsiness, fatigue, disrupted sleep and snoring, were examined for anxiety, depression and alexithymia using the Spielberger Trait Anxiety Inventory (STAI), the Beck Depression Inventory (BDI) and the Toronto Alexithymia Scale (TAS-20), respectively, 24 hours prior to being submitted to polysomnography. All 35 patients met the inclusion criteria of the study (age≤75 years, no other chronic diseases and no history of major psychiatric disorders). Six patients did not meet the diagnostic criteria for OSAS and were thus used as the control group of the study. A high prevalence of anxiety (41.4%) and depressive (55.2%) symptoms and of alexithymic characteristics (41.4%) was observed in OSAS patients. Although the control group showed a higher prevalence of anxiety (66.7%) and depressive (83.3%) symptoms, there were no differences between the two groups (STAI: t=-0.927, p=0.360, BDI: t=-1.537, p=0.134, TAS-20: t=0.196, p=0.846). With regard to severity, no differences were observed between control, mild, moderate and severe OSAS subgroups (STAI: F=0.583, p=0.660, BDI: F=0.829, p=0.488, TAS-20: F=0.987, p=0.412). Females scored higher on the BDI and on the STAI compared to males (STAI: t=-2.38, p=0.039, BDI: t=-3.59, p=0.01).

				Finally, no correlation was observed between psychometric scores and AHI (Pearson correlation p>0.05). The study confirms the high prevalence of anxiety and depressive symptoms which has been found in previous studies. Furthermore, we found a high prevalence of alexithymic characteristics, a factor that has not been investigated previously and which is positively correlated with anxiety symptoms. The coexistence of alexithymic characteristics may further complicate the clinical manifestations of OSAS due to the fact that patients with alexithymia typically have difficulty in indentifying and describing their underlying psychological symptomatology and, moreover, tend to exhibit more, and often atypical, physical symptoms. In conclusion, the study supports the presence of a high degree of psychological burden in patients diagnosed with OSAS, regardless of the severity of their symptoms, as determined by the AHI. This comorbidity should be taken into consideration during the clinical assessment of OSAS and for the treatment planning.
Brenu EW, Huth TK, Hardcastle SL, Fuller K, Kaur M, Johnston S, Ramos SB, Staines DR, Marshall-Gradisnik SM.	School of Medical Science, Griffith University, Gold Coast, QLD 4215, Australia.	Role of adaptive and innate immune cells in chronic fatigue syndrome/myalgic encephalomyelitis.	Int Immunol. 2014 Apr;26(4):233-42. doi: 10.1093/intimm/dxt068. Epub 2013 Dec 16.	Perturbations in immune processes are a hallmark of a number of autoimmune and inflammatory disorders. Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is an inflammatory disorder with possible autoimmune correlates, characterized by reduced NK cell activity, elevations in regulatory T cells (Tregs) and dysregulation in cytokine levels. The purpose of this article is to examine innate and adaptive immune cell phenotypes and functional characteristics that have not been previously examined in CFS/ME patients. Thirty patients with CFS/ME and 25 non-fatigued controls were recruited for this study. Whole blood samples were collected from all participants for the assessment of cell phenotypes, functional properties, receptors, adhesion molecules, antigens and intracellular proteins using flow cytometric protocols. The cells investigated included NK cells, dendritic cells, neutrophils, B cells, T cells, γδT cells and Tregs. Significant changes were observed in B-cell subsets, Tregs, CD4(+)CD73(+)CD39(+) T cells, cytotoxic activity, granzyme B, neutrophil antigens, TNF-α and IFN-γ in the CFS/ME patients in comparison with the non-fatigued controls. Alterations in B cells, Tregs, NK cells and neutrophils suggest significant impairments in immune regulation in CFS/ME and these may have similarities to a number of autoimmune disorders.
Brenu EW, Ashton KJ, Batovska J, Staines DR, Marshall-Gradisnik SM.	School of Medical Science, Griffith Health Centre, Griffith University, Gold Coast, Queensland, Australia; The National Centre for Neuroimmunology and Emerging Diseases, Griffith University,	High-throughput sequencing of plasma microRNA in chronic fatigue syndrome/myalgic encephalomyelitis.	PLoS One. 2014;9(9):e102783. doi: 10.1371/journal.pone.0102783.	BACKGROUND: MicroRNAs (miRNAs) are known to regulate many biological processes and their dysregulation has been associated with a variety of diseases including Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). The recent discovery of stable and reproducible miRNA in plasma has raised the possibility that circulating miRNAs may serve as novel diagnostic markers. The objective of this study was to determine the role of plasma miRNA in CFS/ME. RESULTS: Using Illumina high-throughput sequencing we identified 19 miRNAs that were differentially expressed in the plasma of CFS/ME patients in comparison to non-fatigued controls. Following RT-qPCR analysis, we were able to confirm the

	Gold Coast, Queensland, Australia.			significant up-regulation of three miRNAs (hsa-miR-127-3p, hsa-miR-142-5p and hsa-miR-143-3p) in the CFS/ME patients. CONCLUSION: Our study is the first to identify circulating miRNAs from CFS/ME patients and also to confirm three differentially expressed circulating miRNAs in CFS/ME patients, providing a basis for further study to find useful CFS/ME biomarkers.
Broderick JE, Gold MS, Amin MM, Gold AR.	Department of Psychiatry and Behavioral Sciences, Stony Brook University School of Medicine, Stony Brook, NY 11794, USA. (Electronic address: avram.gold@va.gov	The association of somatic arousal with the symptoms of upper airway resistance syndrome.	Sleep Med. 2014 Apr;15(4):436-43. doi: 10.1016/j.sleep.2014.01.014. Epub 2014 Feb 15.	OBJECTIVES: We tested the hypothesis that the symptoms of upper airway resistance syndrome (UARS) are manifestations of chronic stress. To accomplish this, we utilized the score on a self-report questionnaire for somatic arousal (a component of stress) to compare somatic arousal between UARS patients and healthy controls and, among all participants, to correlate the level of somatic arousal with the severity of UARS symptoms. METHODS: We administered the Mood and Anxiety Symptom Questionnaire anxious arousal subscale (MASQaas; a 17-item questionnaire with increasing levels of arousal scored 17-85) to 12 UARS patients and 12 healthy controls and compared scores between groups. For all participants, we correlated the MASQaas scores with scores for the Epworth Sleepiness Scale (ESS), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale, Pittsburgh Sleep Quality Index (PSQI), SF-36 Health Survey, and Perceived Deficits Questionnaire (PDQ; assessing cognitive function). RESULTS: Compared to healthy controls, UARS patients demonstrated increased somatic arousal (MASQaas scores of 18±2 and 28±7, respectively; $p<0.0001$). For all participants, the MASQaas scores correlated significantly with scores of the ESS ($r=0.64$; $p=0.0008$), the FACIT-Fatigue scale ($r=-0.89$; $p<0.0001$), the PSQI ($r=0.70$; $p=0.0002$), SF-36 Physical component ($r=-0.78$; $p<0.0001$), SF-36 Mental component ($r=-0.74$; $p<0.0001$), and the PDQ ($r=0.89$; $p<0.0001$). CONCLUSIONS: Our findings suggest that UARS patients have increased levels of the stress component, somatic arousal, proportionate to the severity of their symptoms.
Brooks J, King N, Wearden A.	Centre for Applied Psychological Research, University of Huddersfield, UK.	Couples' experiences of interacting with outside others in chronic fatigue syndrome: a qualitative study.	Chronic Illn. 2014 Mar;10(1):5-17. doi: 10.1177/1742395312474478. Epub 2013 Apr 12.	OBJECTIVES: Social isolation and stigma are frequently reported by patients with chronic fatigue syndrome/myalgic encephalomyelitis and relationships in the home environment with those close to the patients (their 'significant others') may thus be particularly important. Rather little attention has yet been paid to the beliefs and experiences of 'significant others' themselves in this context. This study sought to explore in-depth the beliefs and experiences of both patients and 'significant others' in relation to chronic fatigue syndrome/myalgic encephalomyelitis. METHODS: In-depth interviews using a semi-structured interview schedule designed around the core constructs of the Common-Sense Model of self-regulation were conducted with two patients with chronic fatigue syndrome/myalgic encephalomyelitis and their spouses. Interpretative Phenomenological Analysis was used to analyse interview data. RESULTS: Experiences of social interactions in relation to chronic fatigue syndrome/myalgic encephalomyelitis with others outside of the relationship dyad emerged as a key issue for all participants when reflecting on their experiences

				of living with the condition. These concerns are presented under two themes: interactions with healthcare professionals and interactions with the social world. CONCLUSIONS: It is evident that significant others play an important role in the lived experience of chronic fatigue syndrome/myalgic encephalomyelitis. For both patients and significant others, the wider social world and interactions with outside others may be important influences on dyadic coping in chronic fatigue syndrome/myalgic encephalomyelitis. Both future research and treatment interventions could usefully include a 'significant other' perspective.
Brown BI.	No address given	Chronic fatigue syndrome: a personalized integrative medicine approach.	Altern Ther Health Med. 2014 Jan-Feb;20(1):29-40. Review.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a relatively common illness, yet despite considerable investigation, current treatments have modest benefits, and the prognosis remains poor. Because CFS/ME is a heterogeneous disorder with diverse etiological factors and pathological features, a patient-centered integrative framework based on modifiable physiological and environmental factors may offer hope for more effective management and better clinical outcomes. An individualized approach may also help target interventions for subgroups most likely to respond to specific treatments. This review summarizes a number of avenues for integrative management, including dietary modification, functional nutritional deficiencies, physical fitness, psychological and physical stress, environmental toxicity, gastrointestinal disturbances, immunological aberrations, inflammation, oxidative stress, and mitochondrial dysfunction. A personalized, integrative approach to CFS/ME deserves further consideration as a template for patient management and future research.
Brurberg KG, FÃ¸nhus MS, Larun L, Flottorp S, Malterud K.	Norwegian Knowledge Centre for the Health Services, Oslo, Norway.	Case definitions for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review.	BMJ Open. 2014 Feb 7;4(2):e003973. doi: 10.1136/bmjopen-2013-003973.	OBJECTIVE: To identify case definitions for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), and explore how the validity of case definitions can be evaluated in the absence of a reference standard. DESIGN: Systematic review. SETTING: International. PARTICIPANTS: A literature search, updated as of November 2013, led to the identification of 20 case definitions and inclusion of 38 validation studies. PRIMARY AND SECONDARY OUTCOME MEASURE: Validation studies were assessed for risk of bias and categorised according to three validation models: (1) independent application of several case definitions on the same population, (2) sequential application of different case definitions on patients diagnosed with CFS/ME with one set of diagnostic criteria or (3) comparison of prevalence estimates from different case definitions applied on different populations. RESULTS: A total of 38 studies contributed data of sufficient quality and consistency for evaluation of validity, with CDC-1994/Fukuda as the most frequently applied case definition. No study rigorously assessed the reproducibility or feasibility of case definitions. Validation studies were small with methodological weaknesses and inconsistent results. No empirical data indicated that any case definition specifically identified patients with a neuroimmunological condition. CONCLUSIONS: Classification of patients according to severity and symptom patterns, aiming to predict prognosis or

				effectiveness of therapy, seems useful. Development of further case definitions of CFS/ME should be given a low priority. Consistency in research can be achieved by applying diagnostic criteria that have been subjected to systematic evaluation.
Castro-Marrero J, Cordero MD, Segundo MJ, SÃ¡ez-FrancÃ s N, Calvo N, RomÃ¡n-Malo L, Aliste L, FernÃ¡ndez de Sevilla T, Alegre J.	CFS Clinical Unit, Vall d'Hebron Research Institute, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona , Barcelona, Spain .	Does Oral Coenzyme Q(10) Plus NADH Supplementation Improve Fatigue and Biochemical Parameters in Chronic Fatigue Syndrome?	Antioxid Redox Signal. 2014 Nov 11.	Abstract Chronic fatigue syndrome (CFS) is a chronic and extremely debilitating illness characterized by prolonged fatigue and multiple symptoms with unknown cause, diagnostic test, or universally effective treatment. Inflammation, oxidative stress, mitochondrial dysfunction, and CoQ10 deficiency have been well documented in CFS. We conducted an 8-week, randomized, double-blind placebo-controlled trial to evaluate the benefits of oral CoQ10 (200 mg/day) plus NADH (20 mg/day) supplementation on fatigue and biochemical parameters in 73 Spanish CFS patients. This study was registered in ClinicalTrials.gov (NCT02063126). A significant improvement of fatigue showing a reduction in fatigue impact scale total score ($p<0.05$) was reported in treated group versus placebo. In addition, a recovery of the biochemical parameters was also reported. NAD+/NADH ($p<0.001$), CoQ10 ($p<0.05$), ATP ($p<0.05$), and citrate synthase ($p<0.05$) were significantly higher, and lipoperoxides ($p<0.05$) were significantly lower in blood mononuclear cells of the treated group. These observations lead to the hypothesis that the oral CoQ10 plus NADH supplementation could confer potential therapeutic benefits on fatigue and biochemical parameters in CFS. Larger sample trials are warranted to confirm these findings. Antioxid. Redox Signal. 00, 000-000.
Cervigni M, Natale F.	Obstetrics and Gynecology Department, Catholic University, Rome, Italy; Urogynecologic Department, S.Carlo-IDI, Rome, Italy.	Gynecological disorders in bladder pain syndrome/interstitial cystitis patients.	Int J Urol. 2014 Apr;21 Suppl 1:85-8. doi: 10.1111/iju.12379.	OBJECTIVES: Bladder pain syndrome/interstitial cystitis, a chronic inflammatory condition of the bladder, is the source of pain in over 30% of female patients with chronic pelvic pain. The aim of the present study was to evaluate the most frequent associations between bladder pain syndrome/interstitial cystitis and gynecological disorders. METHODS: A literature review of the previous 10 years was carried out to evaluate the incidence of gynecological diseases in patients with bladder pain syndrome/interstitial cystitis. RESULTS: Hypertonic pelvic floor dysfunction with associated voiding dysfunction can be present in bladder pain syndrome/interstitial cystitis patients. It has been estimated that the prevalence ranges from 50% to 87%. Endometriosis affects 1-7% of the general population and up to 70% of women with endometriosis have some type of pain symptoms, a recent systematic review estimated the prevalence of bladder pain syndrome to be 61%, of endometriosis to be 70%, and coexisting bladder pain syndrome and endometriosis to be 48%. Vulvodynia is represented by pain, or an unpleasant altered sensation, in the vulva. Women with vestibulodynia are likely to have other additional pain conditions, such as fibromyalgia, irritable bowel syndrome or chronic fatigue syndrome. Recent data reported that vestibulodynia affects 25% of women with bladder pain

				syndrome/interstitial cystitis. CONCLUSIONS: Bladder pain syndrome/interstitial cystitis is a complex pathology often associated with vulvodynia, endometriosis and pelvic floor dysfunctions. Therefore, it is of utmost importance to obtain an accurate evaluation ruling out confusable disease, such as pudendal neuropathy. The optimal approach is a combined treatment oriented not only to treat the bladder, but also the other components responsible for the pain disorder.
Chassagne P, Bahri O, Roca F.	Service de médecine interne gériatrique, CHU de Rouen, France	Iron deficiency in elderly people: clinical presentation and management.	Geriatr Psychol Neuropsychiatr Vieil. 2014 Jun;12 Suppl 2:11-5. doi: 10.1684/pnv.2014.0479.	[Article in French] Iron deficiency (absolute or functional) is commonly observed (frequently without associated anemia) in up to one third of old people. Iron deficiency is the most cause of anemia in adults. Many non hematological consequences of iron deficiency are described like: cardiac failure, mood or cognitive disorders, chronic fatigue or restless leg syndrome. Iron deficiency can be orally or with intravenous iron replacement treates if necessary. Long term compliance of patients orally treated for iron deficiency is poor mainly because of fair tolerability of drugs. New regimenof intravenous iron replacement are now available when orally iron administration cannot be achieved. In functional iron deficiency iron intravenous replacement seems especially relevant. However further controlled studies are necessary to assess their clinical benefits.
Check JH, Cohen R.	No address given	Severe headaches from intracranial hypertension (pseudotumor cerebri) abrogated by treatment with dextroamphetamine sulfate.	Clin Exp Obstet Gynecol. 2014;41(2):211-3.	PURPOSE: To determine if sympathomimetic amines may relieve migraine headache pain from pseudotumor cerebri (PTC) similar to its effect on helping other types of migraine headaches that were recalcitrant to other therapies. MATERIALS AND METHODS: A woman with severe migraine headaches which did not respond to treatment with acetazolamide was treated with dextroamphetamine sulfate sustained release capsules 25 mg daily. RESULTS: The patient demonstrated marked improvement within a month. The marked decrease in headache pain has persisted over a year. Her papilledema also completely disappeared. CONCLUSIONS: The sympathetic neural hyperalgesia edema syndrome can manifest as PTC. Besides headaches, other symptoms that the patient manifested were part of this syndrome including chronic fatigue, inability to lose weight despite dieting, and backache. All of these additional symptoms also improved with sympathomimetic amine therapy.
Check JH, Chan S.	No address given	Complete eradication of chronic long standing eczema and keratosis pilaris following treatment with dextroamphetamine sulfate.	Clin Exp Obstet Gynecol. 2014;41(2):202-4.	PURPOSE: To present two other dermatologic conditions related to a disorder of sympathetic nervous system hypofunction common in women that respond to treatment with dextroamphetamine sulfate--chronic eczema and keratosis pilaris. MATERIALS AND METHODS: Case 1 was a patient with chronic eczema of 30 years duration was started on treatment for other conditions related to the sympathetic neural hyperalgesia edema syndrome, i.e., migraine headaches and chronic fatigue syndrome. Case 2 who also had chronic eczema also had a skin condition frequently associated with eczema--keratosis pilaris and he was started on dextroamphetamine sulfate for chronic fatigue syndrome. RESULTS: Not only did

				the headaches and chronic fatigue syndrome in both patients markedly improve following sympathomimetic amine therapy but so did the eczema and keratosis pilaris. CONCLUSIONS: Eczema and keratosis pilaris are two more chronic dermatologic conditions besides chronic urticaria and prurigo nodularis that respond extremely well to treatment with dextroamphetamine sulfate. Case 2 shows this condition is not restricted to females.
Check JH, Cohen R.	No address given	Marked improvement of pain from long-term fibromyalgia with dextroamphetamine sulfate in a woman who failed to improve with conventional pharmacologic treatment.	Clin Exp Obstet Gynecol. 2014;41(1):90-2.	PURPOSE: To determine if treatment with the sympathomimetic amine dextroamphetamine sulfate, which has been so effective in treating a variety of pain syndromes, including severe pelvic pain and interstitial cystitis in women with the sympathetic neural hyperalgesia edema syndrome would also mitigate pain from fibromyalgia which was resistant to multiple therapies. MATERIALS AND METHODS: Dextroamphetamine sulfate extended release capsules once daily was gradually increased to 25 mg per day in a woman with treatment resistant fibromyalgia of 20 years duration. RESULTS: Within a short time, the woman experienced dramatic relief of pain. Furthermore, her edema improved resulting in a 27 pound weight loss and her chronic fatigue improved. CONCLUSIONS: Fibromyalgia can be effectively treated with an innocuous dose of dextroamphetamine sulfate.
Chen CS, Lin WM, Yang TY, Chen HJ, Kuo CN, Kao CH.	China Medical University Hospital, China Medical University,	Chronic fatigue syndrome is associated with the risk of fracture: a nationwide cohort study.	QJM. 2014 Aug;107(8):635-41. doi: 10.1093/qjmed/hcu037. Epub 2014 Mar 11.	PURPOSE: Chronic fatigue syndrome (CFS) is a complex disorder that is associated with unreasonable persistent fatigue. CFS has also been reported to be a possible risk factor for osteopathy. We propose that CFS might be associated with an increased risk of fracture. METHODS: We used the National Health Insurance Research Database to conduct a prospective cohort study, identifying 3744 patients with a CFS diagnosis (International Classification of Diseases, Ninth Revision, Clinical Modification code 780.71) and 14 976 patients without CFS until 2006, with follow-up observed until the end of 2010. RESULTS: The incidence rate of fracture was higher in the CFS cohort than in the non-CFS cohort (17.44 vs. 14.53 per 1000 person-year, respectively), with an adjusted hazard ratio of 1.14 (95% confidence interval = 1.00-1.30). The risks of fracture between CFS and non-CFS were shown without comorbidity for each would be elevated than with other comorbidities, particularly in osteoporosis. The patients without osteoporosis in the CFS cohort exhibited a 1.16-fold higher risk of fracture than did those in the non-CFS cohort. CONCLUSIONS: We propose that CFS-related fracture might not be associated with osteoporosis. The mechanism for developing CFS-related fracture remains unclear; however, we recommend noticing the prevention of fracture for CFS patients before clarifying the aetiology of CFS-related fracture.
Chen PY, Lai SC, Yang CC, Lee MJ, Chiu YH, Yan SH, Lu CS, Yeh TH.	Department of Neurology, Taipei City Hospital, Renai branch, Taipei, Taiwan.	A novel XK gene mutation in a Taiwanese family with McLeod	J Neurol Sci. 2014 May 15;340(1-2):221-4. doi: 10.1016/j.jns.2014.02.027. Epub 2014 Feb 27.	McLeod syndrome is one subtype of rare neuroacanthocytosis syndromes characterized by misshapen red blood cells and progressive degeneration of the basal ganglia. It is an X-linked recessive disorder with mutation in the XK gene of the Kell blood group system with multisystem involvements. Concerning the movement

	do2739@adm.cgmh.org.tw	syndrome.		disorders, its dyskinesias are various and difficult to differentiate from those in Huntington's disease or other hyperkinetic movement disorders. In this report, we described a 62-year-old male patient presenting with insidious myalgia and muscle fatigue. Progressive motor restlessness and toes choreoathetosis were noted. Previously, he had chronic psychotic disorder with irregular treatment for 14 years. The laboratory tests revealed elevated creatine phosphokinase and acanthocytes (36.3%). The electrophysiological test demonstrated an axonal type polyneuropathy. The neuroimaging of brain showed striatal degeneration. Genetic analysis revealed a nonsense hemizygous mutation c.154C>T (p.Gln52X) at exon 1 of XK gene. The genetic counseling of his family revealed one elder brother carrying the same mutation and showing a similar but very mild syndrome. Several offspring were the asymptomatic carriers. We suggest that for a patient with multiple system disorders including dyskinetic movement disorders, psychiatric symptoms, polyneuropathy, and elevated CPK, a genetic test for XK gene mutation is highly indicated to confirm the McLeod syndrome and to guide the possible therapy.
Chen Z, Lin SY, Zhou YH, Wu LQ, Zhang Y, Shen YP, Zheng ZY, Chen JF, Shen YY, Chen YY.	Department of Hematology, First Affiliated Hospital, Zhejiang Chinese Medical University, Hangzhou 310006, China. (2)Center for Clinical Assessment and Analysis, First Clinical College of Zhejiang Chinese Medical University, Hangzhou 310006, China.	Analysis of clinical features of traditional Chinese medicine symptoms and syndromes of 220 patients with chronic aplastic anemia.	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2014 Jan;34(1):43-5.	[Article in Chinese] OBJECTIVE: To study Chinese medicine (CM) syndrome types of chronic aplastic anemia (CAA) patients and the distribution laws of typical CM symptoms in different genders. METHODS: From June 2002 to June 2012, 220 CAA outpatients/inpatients at Department of Hematology, Zhejiang Chinese Medical Hospital were recruited. Patients' symptoms and signs, as well as four diagnostic information at the first onset were collected. CM syndrome differentiation was performed. The syndrome types and typical symptoms were analyzed. RESULTS: (1) In the 220 CAA patients, there were 121 cases of Shen yang deficiency syndrome (55.0%), 18 of Shen yin deficiency syndrome type (8.18%), 81 cases of Shen yin-yang deficiency syndrome (36.82%). (2) The distribution of typical symptoms: fatigue and shortness of breath (77.12% males and 73.53% females), pale complexion (64.41% males and 57.84% females), low temperature of four limbs (12.71% males and 26.47% females), spontaneous perspiration and night sweating (32.20% males and 26.47% females), dry mouth and throat (6.78% males and 6.86% females), feverish feelings in palms and soles (14.41% males and 20.59% females), loose stool (6.78% males and 2.94% females), petechiae and ecchymosis (42.37% males and 43.14% females). CONCLUSIONS: Shen yang deficiency syndrome was most often seen in CAA patients at the initial diagnosis, followed by Shen yin-yang deficiency syndrome. Shen yin deficiency syndrome was the least seen. In CM symptoms, fatigue and shortness of breath were most common seen, followed by pale complexion, skin petechia and ecchymosis

Cheng Z, Zhou B, Shi X, Zhang Y, Zhang L, Chen L, Liu X.	Department of Infectious Diseases, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100730, China.	Extrahepatic manifestations of chronic hepatitis C virus infection: 297 cases from a tertiary medical center in Beijing, China.	Chin Med J (Engl). 2014;127(7):1206-10.	BACKGROUND: Chronic hepatitis C virus (HCV) infection can affect multiple organ systems and cause a variety of extrahepatic manifestations (EMs). We sought to assess the constituent ratio of EMs in Chinese patients with chronic HCV infection and identify the clinical and biological factors associated with EM. METHODS: The medical records of 297 patients with chronic HCV infection were analyzed and demographic and epidemiological information was collected. The diagnosis of chronic HCV infection was based on positive anti-HCV combined with a positive HCV-RNA or at least two times of elevated aminotransferases attributable to HCV infection. Patients with HBV and/or HIV coinfection, autoimmune hepatitis, and history of alcohol abuse were excluded. RESULTS: Sixty-two percent (184/297) of the patients had at least one EM, including fatigue (29.4%), type 2 diabetes mellitus (28.2%), renal involvement (12.5%), lymphadenopathy (9.6%), fever (9.4%), thyroid dysfunction (8.1%), and arthralgia (7.4%). Neuropathy, sicca syndrome, B-cell lymphoma, Raynaud's phenomenon, and lichen planus were rare. The mean age of patients with EM was older compared with those without EM. CONCLUSIONS: EMs were common in Chinese patients with chronic HCV infection, particularly fatigue, type 2 diabetes, renal impairment, lymphadenophy, fever, and thyroid dysfunction. Older age was associated with EMs.
Chhabra P, Law AD, Sharma U, Suri V, Sachdeva MS, Kumari S, Varma S, Malhotra P.	Department of Internal Medicine, PGIMER, Chandigarh, 160012 India. (	Epstein-barr virus infection masquerading as acute leukemia: a report of two cases and review of literature.	Indian J Hematol Blood Transfus. 2014 Mar;30(1):26-8. doi: 10.1007/s12288-012-0207-2. Epub 2012 Oct 25.	Epstein-Barr virus (EBV) is the first herpes virus to be completely sequenced. It is implicated in diseases from the benign infectious mononucleosis to malignant nasopharyngeal carcinoma, Burkitt's lymphoma and primary CNS lymphoma in AIDS patients. It has also been found to be associated with some miscellaneous diseases like chronic fatigue syndrome, multiple sclerosis etc. however causality still remains an issue of debate. As the virus mainly targets the lymphomonuclear cells and the reticuloendothelial system of the body, it's various manifestations are often mistaken as leukemic malignancies. We report two such cases of young adults who had been diagnosed as having acute leukemia on the basis of atypical cells in the peripheral blood. One patient later turned out to be a classical infectious mononucleosis and second patient had EBV associated hemophagocytic lymphohistiocytosis syndrome.
Christensen SS, Frostholm L, Ã˜rnbÃ¸l E, SchrÃ¶der A.	(1)The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 44, Aarhus C, Denmark. (2)The Research Clinic for Functional	Changes in illness perceptions mediated the effect of cognitive behavioural therapy in severe functional somatic syndromes.	J Psychosom Res. 2014 Dec 13. doi:pii: S0022-3999(14)00441-3. 10.1016/j.jpsychores.2014.12.005.	OBJECTIVE: Although there is substantial evidence that cognitive behavioural therapy alleviates symptoms in functional somatic syndromes, the mechanisms of change are less investigated. This study examined whether changes in illness perceptions mediated the effect of cognitive behavioural therapy. METHODS: We analysed additional data from a randomised controlled trial comparing completers of cognitive behavioural group therapy (46 patients) to an enhanced usual care group (66 patients). Proposed mediators (illness perceptions) and primary (physical health) and secondary (somatic symptoms and illness worry) outcomes were assessed by means of questionnaires at referral, baseline, end of treatment, and 10 and 16months after randomisation. Multiple mediation analysis determined

	Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 44, Aarhus C, Denmark. Electronic address: andreas.schroeder@aarhus.rm.dk.			whether (1) changes in specific illness perceptions during treatment mediated the effect of cognitive behavioural therapy (primary analysis), and (2) whether changes in illness perceptions during the whole trial period were associated with improved outcome (secondary analysis). RESULTS: Improvements in illness perceptions during treatment partially mediated the effect of cognitive behavioural therapy on physical health one year after treatment (sum of indirect effects 1.556, BCa 95% CI (0.006; 3.620)). Improving perceived control was particularly important. Changes in illness perceptions from baseline to 16months after randomisation were associated with clinically meaningful improvements in physical health, somatic symptoms and illness worry during the same period. CONCLUSION: Our results suggest that changing patients' illness perceptions is an important process in cognitive behavioural therapy for functional somatic syndromes. Challenging patients' own understanding of their illness may hence be a key element of successful treatment.
Chung KF, Yu BY, Yung KP, Yeung WF, Ng TH, Ho FY.	Department of Psychiatry, The University of Hong Kong, Hong Kong SAR, China. Electronic address: kfchung@hkucc.hku.hk.	Assessment of fatigue using the Multidimensional Fatigue Inventory in patients with major depressive disorder.	Compr Psychiatry. 2014 Oct;55(7):1671-8. doi: 10.1016/j.comppsych.2014.06.006. Epub 2014 Jun 13.	OBJECTIVES: There are problems with the fatigue measures currently used in depressed patients. The Multidimensional Fatigue Inventory (MFI-20) covering general fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation has been widely used in patients with cancer and chronic fatigue syndrome. To address the multidimensional nature of fatigue, we examined the validity and reliability of a Chinese version of the MFI-20 in major depressive disorder (MDD). METHODS: Data were derived from a randomized controlled trial of acupuncture in 137 patients with partially remitted MDD. The test-retest reliability, internal consistency, construct and concurrent validity and sensitivity to change of the MFI-20 were analyzed. RESULTS: The MFI-20 was found to have good internal consistency (Cronbach's alpha=0.89) and 1-week test-retest reliability (Pearson correlation of the total score=0.73). Factor analysis showed 5 factors, but the factor structure was different from that in medical conditions. The 2 most prominent factors, explaining 46% of the total variance, were both associated with physical and mental energy but different in directions. There were adequate concurrent validity and sensitivity to change as evidenced by the significant correlations between the MFI-20 scores and depressive and anxiety symptoms, general health and quality of life. CONCLUSION: The Chinese MFI-20 is a valid and reliable instrument for the assessment of fatigue in MDD patients with residual symptoms. The construct of fatigue in MDD seems to be different from that in medical conditions. Further studies are needed to examine the MFI-20 in MDD patients from other cultures.
Chung SD, Lin CC, Liu SP, Lin HC.	(1)Division of Urology, Department of Surgery, Far Eastern Memorial Hospital, Ban Ciao, Taipei, Taiwan; School of	Obstructive sleep apnea increases the risk of bladder pain syndrome/interstitial cystitis: a population-based matched-	Neurourol Urodyn. 2014 Mar;33(3):278-82. doi: 10.1002/nau.22401. Epub 2013 Mar 28.	AIMS: Previous studies indicated a possible association between bladder pain syndrome/interstitial cystitis (BPS/IC) and sleep disorders including sleep abnormalities with delayed onset of sleep, waking up before needed, and snoring. Nevertheless, no previous study has reported the association between obstructive sleep apnea (OSA) and BPS/IC. In this retrospective cohort study, we examined the risk of BPS/IC among subjects with OSA during a 3-year follow-up in Taiwan using a

	Health Care Administration, Taipei Medical University, Taipei, Taiwan; Sleep Research Center, Taipei Medical University Hospital, Taipei, Taiwan.	cohort study.		population-based dataset. METHODS: This study comprised 2,940 study subjects with OSA, and 29,400 randomly selected comparison subjects. We individually followed-up each sampled subject (n = 32,340) for a 3-year period to identify those subjects who subsequently received a diagnosis of BPS/IC. A Cox proportional hazards regression model was constructed to estimate the risk of subsequent BPS/IC following a diagnosis of OSA. RESULTS: Incidences of BPS/IC during the 3-year follow-up period were 13.61 (95% confidence interval [CI] = 7.37-23.13) and 3.60 (95% CI = 2.06-4.39) for subjects with and those without OSA, respectively. After adjusting for diabetes, hypertension, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraines, sicca syndrome, allergies, endometriosis, asthma, tobacco use disorder, and alcohol abuse, the stratified Cox proportional hazards regressions revealed that the hazard ratio for BPS/IC among subjects with OSA was 3.71 (95% CI = 1.81-7.62, P < 0.001) that of comparison subjects. CONCLUSIONS: This study provides epidemiological evidence of a link between OSA and a subsequent BPS/IC diagnosis. We suggest that clinical practitioners treating subjects with OSA be alert to urinary complaints in this population.
Cockshell SJ, Mathias JL.	School of Psychology, The University of Adelaide.	Cognitive functioning in people with chronic fatigue syndrome: a comparison between subjective and objective measures.	Neuropsychology. 2014 May;28(3):394-405. doi: 10.1037/neu0000025. Epub 2013 Dec 23.	OBJECTIVE: The purpose of this study was to examine the relationship between subjective and objective assessments of memory and attention in people with chronic fatigue syndrome (CFS), using tests that have previously detected deficits in CFS samples and measures of potential confounds. METHOD: Fifty people with CFS and 50 healthy controls were compared on subjective (memory and attention symptom severity, Cognitive Failures Questionnaire, Everyday Attention Questionnaires) and objective (California Verbal Learning Test, Rey-Osterreith Complex Figure Test, Paced Auditory Serial Addition Test, Stroop task) measures of memory and attention. Fatigue, sleep, depression, and anxiety were also assessed. RESULTS: The CFS group reported experiencing more cognitive problems than the controls, but the two groups did not differ on the cognitive tests. Scores on the subjective and objective measures were not correlated in either group. Depression was positively correlated with increased severity of cognitive problems in both the CFS and control groups. CONCLUSIONS: There is little evidence for a relationship between subjective and objective measures of cognitive functioning for both people with CFS and healthy controls, which suggests that they may be capturing different constructs. Problems with memory and attention in everyday life are a significant part of CFS. Depression appears to be related to subjective problems but does not fully explain them.

Collin SM, Tilling K, Joinson C, Rimes KA, Pearson RM, Hughes RA, Sterne JA, Crawley E.	School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom; Centre for Child and Adolescent Health, University of Bristol, Bristol, United Kingdom. Electronic address: simon.collin@bristol.ac.uk.	Maternal and Childhood Psychological Factors Predict Chronic Disabling Fatigue at Age 13 Years.	J Adolesc Health. 2014 Nov 18. doi:pii: S1054-139X(14)00382-6. 10.1016/j.jadohealth.2014.09.002.	PURPOSE: To investigate whether premorbid maternal and childhood psychological problems are risk factors for chronic disabling fatigue at age 13 years among children in the Avon Longitudinal Study of Parents and Children birth cohort. METHODS: Chronic disabling fatigue was defined as fatigue of at least 3-month, and up to 5-year, duration that prevented school attendance or hobbies/sport/leisure activities, and for which other causes were not identified. Maternal psychological factors were symptoms of anxiety and depression assessed up to eight times between pregnancy and age 6 years. We investigated critical periods for maternal effects and effects of paternal depression at three time points. Child psychological factors included internalizing and externalizing problems and upsetting life events occurring at age 7-8 years. RESULTS: Of 5,657 children, 110 (1.9%) had chronic disabling fatigue at age 13 years. Maternal anxiety (adjusted odds ratio [AOR], 1.19; 95% confidence interval [CI], 1.09-1.31 per episode), maternal depression (AOR, 1.24; CI, 1.11-1.39 per episode), child psychological problems (AOR, 1.19; CI, 1.00-1.41 per problem), and upsetting events (AOR, 1.22; CI, .99-1.58 per event) were associated with chronic disabling fatigue. Associations of child psychological problems and upsetting events were attenuated (AOR, 1.12; CI, .93-1.33 per problem; AOR, 1.19; CI, .94-1.52 per event) after further adjusting for maternal anxiety and depression. CONCLUSIONS: Pediatricians need to be aware that children whose mothers experience anxiety and/or depression between pregnancy and child's age 6 years have an increased risk of developing chronic disabling fatigue in early adolescence. Conversely, clinicians need to be alert to fatigue in children whose mothers have longstanding anxiety and depression. These findings suggest the importance of family-based approaches to treatment.
Cordero MD, Alcocer-GÃ³mez E, Culic O, CarriÃ³n AM, de Miguel M, DÃaz-Parrado E, PÃ©rez-Villegas EM, BullÃ³n P, Battino M, SÃ¡nchez-Alcazar JA.	Dpto. Citología e Histología Normal y Patológica, Facultad de Medicina, Universidad de Sevilla , Sevilla, Spain .	NLRP3 inflammasome is activated in fibromyalgia: the effect of coenzyme Q10.	Antioxid Redox Signal. 2014 Mar 10;20(8):1169-80. doi: 10.1089/ars.2013.5198. Epub 2013 Sep 19.	AIMS: Fibromyalgia (FM) is a prevalent chronic pain syndrome characterized by generalized hyperalgesia associated with a wide spectrum of symptoms such as fatigue and joint stiffness. Diagnosis of FM is difficult due to the lack of reliable diagnostic biomarkers, while treatment is largely inadequate. We have investigated the role of coenzyme Q10 (CoQ10) deficiency and mitochondrial dysfunction in inflammasome activation in blood cells from FM patients, and in vitro and in vivo CoQ10 deficiency models. RESULTS: Mitochondrial dysfunction was accompanied by increased protein expression of interleukin (IL)-1β, NLRP3 (NOD-like receptor family, pyrin domain containing 3) and caspase-1 activation, and an increase of serum levels of proinflammatory cytokines (IL-1β and IL-18). CoQ10 deficiency induced by p-aminobenzoate treatment in blood mononuclear cells and mice showed NLRP3 inflammasome activation with marked algesia. A placebo-controlled trial of CoQ10 in FM patients has shown a reduced NLRP3 inflammasome activation and IL-1β and IL-18 serum levels. INNOVATION: These results show an important role for the NLRP3 inflammasome in the pathogenesis of FM, and the capacity of CoQ10 in the control of inflammasome. CONCLUSION: These findings provide new insights into

				the pathogenesis of FM and suggest that NLRP3 inflammasome inhibition represents a new therapeutic intervention for the disease.
Courtney R.	London, United Kingdom, information785@gmail.com.	Improvement rates in adolescent patients with chronic fatigue syndrome after receiving cognitive behavioural therapy.	Eur J Pediatr. 2014 May;173(5):691. doi: 10.1007/s00431-013-2234-x. Epub 2013 Dec 10. No abstract available.	Comment in Eur J Pediatr. 2014 May;173(5):693-4. Comment on Eur J Pediatr. 2013 Oct;172(10):1293-8.
Cozon GJ.	Pavillon F, hôpital E.-Herriot, place d'Arsonval, 69437 Lyon cedex 03, France; UFR Lyon-Est UCBL, domaine Rockefeller, 8, avenue Rockefeller, 69373 Lyon cedex 08, France. Electronic address: gregoire.cozon@chu-lyon.fr.	Iron deficiency and digestive disorders.	Transfus Clin Biol. 2014 Nov;21(4-5):189-92. doi: 10.1016/j.tracli.2014.08.135. Epub 2014 Oct 2. French.	[Article in French] Iron deficiency anemia still remains problematic worldwide. Iron deficiency without anemia is often undiagnosed. We reviewed, in this study, symptoms and syndromes associated with iron deficiency with or without anemia: fatigue, cognitive functions, restless legs syndrome, hair loss, and chronic heart failure. Iron is absorbed through the digestive tract. Hepcidin and ferroportin are the main proteins of iron regulation. Pathogenic micro-organisms or intestinal dysbiosis are suspected to influence iron absorption.
Craddock TJ, Fritsch P, Rice MA Jr, del Rosario RM, Miller DB, Fletcher MA, Klimas NG, Broderick G.	Nova Southeastern University, Fort Lauderdale, Florida, United States of America ;	A role for homeostatic drive in the perpetuation of complex chronic illness: Gulf War Illness and chronic fatigue syndrome.	PLoS One. 2014;9(1):e84839. doi: 10.1371/journal.pone.0084839. Erratum in: PLoS One. 2014;9(4):e94161.	A key component in the body's stress response, the hypothalamic-pituitary-adrenal (HPA) axis orchestrates changes across a broad range of major biological systems. Its dysfunction has been associated with numerous chronic diseases including Gulf War Illness (GWI) and chronic fatigue syndrome (CFS). Though tightly coupled with other components of endocrine and immune function, few models of HPA function account for these interactions. Here we extend conventional models of HPA function by including feed-forward and feedback interaction with sex hormone regulation and immune response. We use this multi-axis model to explore the role of homeostatic regulation in perpetuating chronic conditions, specifically GWI and CFS. An important obstacle in building these models across regulatory systems remains the scarcity of detailed human in vivo kinetic data as its collection can present significant health risks to subjects. We circumvented this using a discrete logic representation based solely on literature of physiological and biochemical connectivity to provide a qualitative description of system behavior. This connectivity model linked molecular variables across the HPA axis, hypothalamic-pituitary-gonadal (HPG) axis in men and women, as well as a simple immune

				network. Inclusion of these interactions produced multiple alternate homeostatic states and sexually dimorphic responses. Experimental data for endocrine-immune markers measured in male GWI subjects showed the greatest alignment with predictions of a naturally occurring alternate steady state presenting with hypercortisolism, low testosterone and a shift towards a Th1 immune response. In female CFS subjects, expression of these markers aligned with an alternate homeostatic state displaying hypocortisolism, high estradiol, and a shift towards an anti-inflammatory Th2 activation. These results support a role for homeostatic drive in perpetuating dysfunctional cortisol levels through persistent interaction with the immune system and HPG axis. Though coarse, these models may nonetheless support the design of robust treatments that might exploit these regulatory regimes.
Crawley E.	No address given	Response to Derek Enlander.	QJM. 2014 Mar;107(3):247. doi: 10.1093/qjmed/hct171. Epub 2013 Aug 22. No abstract available.	Comment on QJM. 2014 Jan;107(1):87.
Crawley E.	No address given	The epidemiology of chronic fatigue syndrome/myalgic encephalitis in children.	Arch Dis Child. 2014 Feb;99(2):171-4. doi: 10.1136/archdischild-2012-302156. Epub 2013 Oct 21. Review.	Most paediatricians regularly see children with chronic fatigue syndrome or myalgic encephalitis (CFS/ME) in their clinics and yet we know little about how common it is, who is affected, whether there are risk factors and how likely a child is to recover (or what might predict recovery). Recent research suggests that this illness is more complicated than previously thought and that rather than being an illness found in middle class families, it is more common in those who are socially deprived. This article reviews what is currently known about this important but little understood condition.
Crinion SJ, McNicholas WT.	Department of Respiratory and Sleep Medicine, Pulmonary and Sleep Disorders Unit, St. Vincent's University Hospital, Elm Park, Dublin, Ireland.	Sleep-related disorders in chronic obstructive pulmonary disease.	Expert Rev Respir Med. 2014 Feb;8(1):79-88. doi: 10.1586/17476348.2014.860357. Epub 2013 Dec 30. Review.	Sleep may have several negative consequences in patients with chronic obstructive pulmonary disease (COPD). Sleep is typically fragmented with diminished slow wave and rapid-eye-movement sleep, which likely represents an important contributing factor to daytime symptoms such as fatigue and lethargy. Furthermore, normal physiological adaptations during sleep, which result in mild hypoventilation in normal subjects, are more pronounced in COPD, which can result in clinically important nocturnal oxygen desaturation. The co-existence of obstructive sleep apnea and COPD is also common, principally because of the high prevalence of each disorder, and there is little convincing evidence that one disorder predisposes to the other. Nonetheless, this co-existence, termed the overlap syndrome, typically results in more pronounced nocturnal oxygen desaturation and there is a high prevalence of pulmonary hypertension in such patients. Management of sleep disorders in patients with COPD should address both sleep quality and disordered gas exchange. Non-invasive pressure support is beneficial in selected cases,

				particularly during acute exacerbations associated with respiratory failure, and is particularly helpful in patients with the overlap syndrome. There is limited evidence of benefit from pressure support in the chronic setting in COPD patients without obstructive sleep apnea.
Cullen T, Thomas AW, Webb R, Hughes MG.	(1)Cardiff School of Sport, Cardiff Metropolitan University, Cardiff CF23 6XD, UK. Electronic address: tcullen@cardiffmet.ac.uk. (2)Cardiff School of Health Sciences, Cardiff Metropolitan University, Cardiff CF5 2YB, UK. (3)Cardiff School of Sport, Cardiff Metropolitan University, Cardiff CF23 6XD, UK.	The relationship between interleukin-6 in saliva, venous and capillary plasma, at rest and in response to exercise.	Cytokine. 2014 Nov 15. doi:pii: S1043-4666(14)00555-9. 10.1016/j.cyto.2014.10.011.	IL-6 plays a mechanistic role in conditions such as metabolic syndrome, chronic fatigue syndrome and clinical depression and also plays a major role in inflammatory and immune responses to exercise. The purpose of this study was to investigate the levels of resting and post exercise IL-6 when measured in venous plasma, saliva and capillary plasma. Five male and five females completed 2 separate exercise trials, both of which involved standardized exercise sessions on a cycle ergometer. Venous blood and saliva samples were taken immediately before and after Trial A, venous and capillary blood samples were taken immediately before and after Trial B. IL-6 values were obtained using a high-sensitivity enzyme-linked immunosorbent assay (ELISA). In Trial A venous plasma IL-6 increased significantly from 0.4±0.14pg/ml to 0.99±0.29pg/ml ($P<0.01$) while there was no increase in salivary IL-6. Venous plasma and salivary IL-6 responses were not correlated at rest, post exercise or when expressed as an exercise induced change. In Trial B venous and capillary plasma IL-6 increased significantly (venous: 0.22±0.18 to 0.74±0.28pg/ml ($P\leqslant0.01$); capillary: 0.37±0.22 to 1.08±0.30pg/ml ($P<0.01$). Venous and capillary plasma responses did not correlate at rest ($r=0.59$, $P=0.07$) but did correlate post exercise ($r=0.79$, $P\geqslant0.001$) and when expressed as an exercise induced change ($r=0.71$, $P=0.02$). Saliva does not appear to reflect systemic IL-6 responses, either at rest or in response to exercise. Conversely, capillary plasma responses are reflective of systemic IL-6 responses to exercise.
Davis AS, Viera AJ, Mead MD.	(1) AnMed Health Family Medicine Residency Program, Anderson, SC, USA. (2)University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, USA. (3)University of California-Los Angeles, Los Angeles, CA, USA.	Leukemia: an overview for primary care.	Am Fam Physician. 2014 May 1;89(9):731-8. Review.	Leukemia is a clonal proliferation of hematopoietic stem cells in the bone marrow. The four broad subtypes most likely to be encountered by primary care physicians are acute lymphoblastic, acute myelogenous, chronic lymphocytic, and chronic myelogenous. Acute lymphoblastic leukemia occurs more often in children, whereas the other subtypes are more common in adults. Risk factors include a genetic predisposition as well as environmental factors, such as exposure to ionizing radiation. Symptoms are nonspecific and include fever, fatigue, weight loss, bone pain, bruising, or bleeding. A complete blood count usually reveals leukocytosis and other abnormally elevated or depressed cell lines. Patients with suspected leukemia should be referred promptly to a hematologist-oncologist. The diagnosis is confirmed by further examination of the bone marrow or peripheral blood. Treatment may include chemotherapy, radiation, monoclonal antibodies, or hematopoietic stem cell transplantation. Complications of treatment include tumor lysis syndrome and serious infections from immunosuppression. Leukemia survivors

				should be monitored closely for secondary malignancies, cardiac complications, and endocrine disturbances such as metabolic syndrome, hypothyroidism, and hypogonadism. Five-year survival rates are highest in younger patients and in patients with chronic myelogenous leukemia or chronic lymphocytic leukemia.
de Vega WC, Vernon SD, McGowan PO.	(1)Centre for Environmental Epigenetics and Development, University of Toronto, Scarborough, ON, Canada; Department of Biological Sciences, University of Toronto, Scarborough, ON, Canada; Department of Cell and Systems Biology, University of Toronto, Toronto, ON, Canada.	DNA methylation modifications associated with chronic fatigue syndrome.	PLoS One. 2014;9(8):e104757. doi: 10.1371/journal.pone.0104757.	Chronic Fatigue Syndrome (CFS), also known as myalgic encephalomyelitis, is a complex multifactorial disease that is characterized by the persistent presence of fatigue and other particular symptoms for a minimum of 6 months. Symptoms fail to dissipate after sufficient rest and have major effects on the daily functioning of CFS sufferers. CFS is a multi-system disease with a heterogeneous patient population showing a wide variety of functional disabilities and its biological basis remains poorly understood. Stable alterations in gene function in the immune system have been reported in several studies of CFS. Epigenetic modifications have been implicated in long-term effects on gene function, however, to our knowledge, genome-wide epigenetic modifications associated with CFS have not been explored. We examined the DNA methylome in peripheral blood mononuclear cells isolated from CFS patients and healthy controls using the Illumina HumanMethylation450 BeadChip array, controlling for invariant probes and probes overlapping polymorphic sequences. Gene ontology (GO) and network analysis of differentially methylated genes was performed to determine potential biological pathways showing changes in DNA methylation in CFS. We found an increased abundance of differentially methylated genes related to the immune response, cellular metabolism, and kinase activity. Genes associated with immune cell regulation, the largest coordinated enrichment of differentially methylated pathways, showed hypomethylation within promoters and other gene regulatory elements in CFS. These data are consistent with evidence of multisystem dysregulation in CFS and implicate the involvement of DNA modifications in CFS pathology.
Desai CS, Martin SS, Blumenthal RS.	(1)Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Baltimore, MD 21287, USA cdesai6@jhmi.edu. (2)Johns Hopkins Ciccarone Center for the Prevention of Heart Disease, Baltimore, MD 21287, USA.	Non-cardiovascular effects associated with statins.	BMJ. 2014 Jul 17;349:g3743. doi: 10.1136/bmj.g3743. Review.	Statins form the pharmacologic cornerstone of the primary and secondary prevention of atherosclerotic cardiovascular disease. In addition to beneficial cardiovascular effects, statins seem to have multiple non-cardiovascular effects. Although early concerns about statin induced hepatotoxicity and cancer have subsided owing to reassuring evidence, two of the most common concerns that clinicians have are myopathy and diabetes. Randomized controlled trials suggest that statins are associated with a modest increase in the risk of myositis but not the risk of myalgia. Severe myopathy (rhabdomyolysis) is rare and often linked to a statin regimen that is no longer recommended (simvastatin 80 mg). Randomized controlled trials and meta-analyses suggest an increase in the risk of diabetes with statins, particularly with higher intensity regimens in people with two or more components of the metabolic syndrome. Other non-cardiovascular effects covered in this review are contrast induced nephropathy, cognition, cataracts, erectile

				dysfunction, and venous thromboembolism. Currently, systematic reviews and clinical practice guidelines indicate that the cardiovascular benefits of statins generally outweigh non-cardiovascular harms in patients above a certain threshold of cardiovascular risk. Literature is also accumulating on the potential non-cardiovascular benefits of statins, which could lead to novel applications of this class of drug in the future.
Dhingra MS, Dhingra S, Kumria R, Chadha R, Singh T, Kumar A, Karan M.	(1)University Institute of Pharmaceutical Sciences, UGC Center of Advanced Study (UGC-CAS) in Pharmaceutical Sciences, Panjab University, Chandigarh, India.	Effect of trimethylgallic acid esters against chronic stress-induced anxiety-like behavior and oxidative stress in mice.	Pharmacol Rep. 2014 Aug;66(4):606-12. doi: 10.1016/j.pharep.2014.01.004. Epub 2014 Apr 25.	BACKGROUND: Many studies have shown that the levels of oxidative stress (increased lipid peroxidation, decreased glutathione levels and endogenous antioxidant enzyme activities) and proinflammatory cytokines (e.g., TNF-α) are increased in patients with chronic fatigue syndrome. Gallic acid and other phenolic compounds are potent antioxidants and inhibitor of cytokine production. The present study was designed to investigate the effect of newly synthesized conjugated esters of trimethylgallic acid in an experimental model of chronic stress. METHODS: The animals were forced to swim individually for a period of 6min every day for 15 days to induce chronic stress. The locomotor activity, anxiety-like behavior, and memory retention were evaluated in chronically stressed animals, followed by biochemical estimations and neuroinflammatory surge in the brain. RESULTS: Chronic treatment with trimethylgallic acid esters for 15 days significantly reversed the chronic stress-induced behavioral (impaired locomotor activity, anxiety-like behavior, and decreased percentage of memory retention), biochemical (increased lipid peroxidation and nitrite levels; decreased glutathione levels, superoxide dismutase and catalase activities), and inflammation surge (serum TNF-α) in stressed mice. CONCLUSIONS: The study revealed that trimethylgallic acid esters could ameliorate chronic stress-induced various behavioral and biochemical alterations in mice, showing protective effects against chronic stress.
Djamshidian A, Lees AJ.	The National Hospital for Neurology and Neurosurgery, Queen Square and the Reta Lila Weston Institute of Neurological Studies, UCL, London, UK.	Can stress trigger Parkinson's disease?	J Neurol Neurosurg Psychiatry. 2014 Aug;85(8):878-81. doi: 10.1136/jnnp-2013-305911. Epub 2013 Nov 20. Review.	In this manuscript we summarize the role of chronic stress as a potential trigger factor for Parkinson's disease. Underlying mechanisms and stress-induced changes to the neuronal networks have been highlighted. Examples of stress induced reversible symptoms that resemble parkinsonism in humans and in animal models raise the question whether emotional stress can cause striatal degeneration in susceptible patients. A Pubmed literature review searching for the terms 'Stress', 'Distress and Parkinson's disease', 'Emotional Distress and Parkinson's disease', 'Stress and Parkinson's disease', 'Prodromal Parkinson's disease', 'Non motor symptoms and Parkinson's disease', 'Paradoxical kinesia', 'Psychogenic parkinsonism', 'Functional somatic syndromes', 'Chronic fatigue syndrome', 'Irritable bowel syndrome', 'Fibromyalgia', 'Dopamine and fibromyalgia', 'Dopamine and chronic fatigue syndrome' and 'Dopamine and irritable bowel syndrome' was carried out until April 2013. Articles were also identified through searches of the authors' own files. Only papers published in English were reviewed. The final reference list was generated on the basis of originality and relevance to the broad scope of this

				viewpoint.
Docampo E, EscaramÃs G, GratacÃ²s M, Villatoro S, Puig A, Kogevinas M, Collado A, Carbonell J, Rivera J, Vidal J, Alegre J, Estivill X, Rabionet R.	Genomics and Disease Group, Centre for Genomic Regulation (CRG), Dr. Aiguader 88, 08003 Barcelona, Catalonia, Spain;	Genome-wide analysis of single nucleotide polymorphisms and copy number variants in fibromyalgia suggest a role for the central nervous system.	Pain. 2014 Jun;155(6):1102-9. doi: 10.1016/j.pain.2014.02.016. Epub 2014 Feb 26.	Fibromyalgia (FM) is a highly disabling syndrome defined by a low pain threshold and a permanent state of pain. The mechanisms explaining this complex disorder remain unclear, and its genetic factors have not yet been identified. With the aim of elucidating FM genetic susceptibility factors, we selected 313 FM cases having low comorbidities, and we genotyped them on the Illumina 1 million duo array. Genotypic data from 220 control women (Illumina 610k array) was obtained for genome-wide association scan (GWAS) analysis. Copy number variants in FM susceptibility were analyzed by array comparative genomic hybridization (aCGH) experiments on pooled samples using the Agilent 2×400K platform. No single nucleotide polymorphism (SNP) reached GWAS association threshold, but 21 of the most associated SNPs were chosen for replication in 952 cases and 644 controls. Four of the SNPs selected for replication showed a nominal association in the joint analysis, and rs11127292 (MYT1L) was found to be associated to FM with low comorbidities (P=4.28×10(-5), odds ratio [95% confidence interval]=0.58 [0.44-0.75]). aCGH detected 5 differentially hybridized regions. They were followed up, and an intronic deletion in NRXN3 was demonstrated to be associated to female cases of FM with low levels of comorbidities (P=.021, odds ratio [95% confidence interval]=1.46 [1.05-2.04]). Both GWAS and aCGH results point to a role for the central nervous system in FM genetic susceptibility. If the proposed FM candidate genes were further validated in replication studies, this would highlight a neurocognitive involvement in agreement with latest reports.
dos Santos MR, Moro CM, Vosgerau DS.	No address given	Protocol for physical assessment in patients with fibromyalgia syndrome.	Rev Bras Reumatol. 2014 Mar-Apr;54(2):117-23. English, Portuguese.	[Article in English, Portuguese] INTRODUCTION: Fibromyalgia syndrome (FMS) is a chronic disease that causes pain and fatigue, presenting a negative impact on quality of life. Exercise helps maintaining physical fitness and influences directly on the improvement of quality of life. OBJECTIVE: Develop a protocol for health-related physical fitness assessment of patients with FMS with tests that are feasible and appropriate for this population. METHOD: An exploratory and analytical literature review was performed, seeking to determine the tests used by the scientific community. With this in mind, we performed a literature revision through the use of virtual libraries databases: PubMed, Bireme, Banco de Teses e Dissertações da Capes and Biblioteca Digital Brasileira de Teses e Dissertações, published in between 1992-2012. RESULTS: A variety of tests was found; the following, by number of citations, stood out: Body Mass Index (BMI) and bioimpedance; 6-minute walk; handgrip strength

				(dynamometer, 1RM [Repetition Maximum]); Sit and reach and Shoulder flexibility; Foot Up and Go, and Flamingo balance. CONCLUSION: These are the tests that should make up the protocol for the physical evaluation of FMS patients, emphasizing their ease of use.
Dougall D, Johnson A, Goldsmith K, Sharpe M, Angus B, Chalder T, White P.	East London Foundation NHS Trust, London, UK.	Adverse events and deterioration reported by participants in the PACE trial of therapies for chronic fatigue syndrome.	J Psychosom Res. 2014 Jul;77(1):20-6. doi: 10.1016/j.jpsychores.2014.04.002. Epub 2014 Apr 22.	OBJECTIVE: Adverse events (AEs) are health related events, reported by participants in clinical trials. We describe AEs in the PACE trial of treatments for chronic fatigue syndrome (CFS) and baseline characteristics associated with them. METHODS: AEs were recorded on three occasions over one year in 641 participants. We compared the numbers and nature of AEs between treatment arms of specialist medical care (SMC) alone, or SMC supplemented by adaptive pacing therapy (APT), cognitive behaviour therapy (CBT) or graded exercise therapy (GET). We examined associations with baseline measures by binary logistic regression analyses, and compared the proportions of participants who deteriorated by clinically important amounts. RESULTS: Serious adverse events and reactions were infrequent. Non-serious adverse events were common; the median (quartiles) number was 4 (2, 8) per participant, with no significant differences between treatments (P=.47). A greater number of NSAEs were associated with recruitment centre, and baseline physical symptom count, body mass index, and depressive disorder. Physical function deteriorated in 39 (25%) participants after APT, 15 (9%) after CBT, 18 (11%) after GET, and 28 (18%) after SMC (P<.001), with no significant differences in worsening fatigue. CONCLUSIONS: The numbers of adverse events did not differ significantly between trial treatments, but physical deterioration occurred most often after APT. The reporting of non-serious adverse events may reflect the nature of the illness rather than the effect of treatments. Differences between centres suggest that both standardisation of ascertainment methods and training are important when collecting adverse event data.
Dryden MS, Saeed K, Ogborn S, Swales P.	(1)Department of Microbiology, Royal Hampshire County Hospital, Winchester, UK. (2)Department of Medicine, Royal Hampshire County Hospital, Winchester, UK.	Lyme borreliosis in southern United Kingdom and a case for a new syndrome, chronic arthropod-borne neuropathy.	Epidemiol Infect. 2014 May 9:1-12.	SUMMARY This series of serologically confirmed Lyme disease is the largest reported in the UK and represents 508 patients who presented to one hospital in the South of England between 1992 and 2012. The mean rate of borreliosis throughout this period was 9·8/100 000 population, much higher than the reported national rate of 1·7/100 000. The actual rate increased each year until 2009 when it levelled off. Patients clinically presented with rash (71%), neurological symptoms (16%, of whom half had VII cranial nerve palsies), arthropathy (8%), pyrexia (5%), cardiac abnormalities (1%) or other manifestations (<1%). Twenty percent of patients had additional non-specific symptoms of fatigue, myalgia, and cognitive changes. Serological diagnosis was with a two-tiered system of ELISA and

				immunoblot. There was a marked seasonal presentation in the summer months and in the first and sixth decades of life. A third of patients gave a clear history of a tick bite. The median interval between tick bite and clinical symptoms was 15 days [interquartile range (IQR) 9-28 days], with a further interval of 14 days to clinical diagnosis/treatment (IQR 2-31 days). Most cases were acquired locally and only 5% abroad. Patients responded to standard antibiotic therapy and recurrence or persistence was extremely rare. A second group of patients, not included in the clinical case series, were those who believed they had Lyme disease based on a probable tick bite but were seronegative by currently available validated tests and presented with subjective symptoms. This condition is often labelled chronic Lyme disease. These patients have a different disease from Lyme disease and therefore an alternative name, chronic arthropod-borne neuropathy (CAN), and case definition for this condition is proposed. We suggest that this chronic condition needs to be distinguished from Lyme disease, as calling the chronic illness 'Lyme disease' causes confusion to patients and physicians. We recommend research initiatives to investigate the aetiology, diagnosis and therapy of CAN.
Enlander D.	No address given	RE: 'Treatment outcome in adults with chronic fatigue syndrome: a prospective study.	QJM. 2014 Jan;107(1):87. doi: 10.1093/qjmed/hct169. Epub 2013 Aug 22. No abstract available.	Comment in QJM. 2014 Mar;107(3):247. Comment on QJM. 2013 Jun;106(6):555-65.
Eriksen TE, RisÃ¸r MB.	(1) Department of Occupational and Environmental Medicine, University Hospital of North Norway, Box 6060, 9038, Tromsø, Norway, thor.eirik.eriksen@unn.no.	What is called symptom?	Med Health Care Philos. 2014 Feb;17(1):89-102. doi: 10.1007/s11019-013-9501-5.	There is one concept in medicine which is prominent, the symptom. The omnipresence of the symptom seems, however, not to be reflected by an equally prominent curiosity aimed at investigating this concept as a phenomenon. In classic, traditional or conventional medical diagnostics and treatment, the lack of distinction with respect to the symptom represents a minor problem. Faced with enigmatic conditions and their accompanying labels such as chronic fatigue syndrome, fibromyalgia, medically unexplained symptoms, and functional somatic syndromes, the contestation of the symptom and its origin is immediate and obvious and calls for further exploration. Based on a description of the diagnostic framework encompassing medically unexplained conditions and a brief introduction to how such symptoms are managed both within and outside of the medical clinic, we argue on one hand how unexplained conditions invite us to reconsider and re-think the concept we call a "symptom" and on the other hand how the concept "symptom" is no longer an adequate and necessary fulcrum and must be enriched by socio-cultural, phenomenological and existential dimensions. Consequently, our main aim is to expand both our interpretative horizon and the linguistic repertoire in the face of those appearances we label medically unexplained symptoms.

Esquinas AM, Ucar ZZ, Kirakli C.	(1)Intensive Care Unit, Hospital Morales Meseguer, Avenida Marques de los Velez s/n, Murcia, 30008, Spain, antmesquinas@gmail.com.	Deventilation syndrome in severe COPD patients during long-term noninvasive mechanical ventilation: poor sleep pattern, hyperinflation, or silent chronic muscular fatigue?	Sleep Breath. 2014 May;18(2):225-6. doi: 10.1007/s11325-013-0931-3. Epub 2014 Jan 23. No abstract available.	Comment on Sleep Breath. 2012 Dec;16(4):1081-90.
Evans S, Lung KC, Seidman LC, Sternlieb B, Zeltzer LK, Tsao JC.	Pediatric Pain Program, University of California, Los Angeles	Iyengar yoga for adolescents and young adults with irritable bowel syndrome.	J Pediatr Gastroenterol Nutr. 2014 Aug;59(2):244-53. doi: 10.1097/MPG.0000000000000366.	OBJECTIVES: Irritable bowel syndrome (IBS) is a chronic, disabling condition that greatly compromises patient functioning. The aim of this study was to assess the impact of a 6-week twice per week Iyengar yoga (IY) program on IBS symptoms in adolescents and young adults (YA) with IBS compared with a usual-care waitlist control group. METHODS: Assessments of symptoms, global improvement, pain, health-related quality of life, psychological distress, functional disability, fatigue, and sleep were collected pre- and post-treatment. Weekly ratings of pain, IBS symptoms, and global improvement were also recorded until 2-month follow-up. A total of 51 participants completed the intervention (yoga = 29; usual-care waitlist = 22). RESULTS: Baseline attrition was 24%. On average, the yoga group attended 75% of classes. Analyses were divided by age group. Relative to controls, adolescents (14-17 years) assigned to yoga reported significantly improved physical functioning, whereas YA (18-26 years) assigned to yoga reported significantly improved IBS symptoms, global improvement, disability, psychological distress, sleep quality, and fatigue. Although abdominal pain intensity was statistically unchanged, 44% of adolescents and 46% of YA reported a minimally clinically significant reduction in pain following yoga, and one-third of YA reported clinically significant levels of global symptom improvement. Analysis of the uncontrolled effects and maintenance of treatment effects for adolescents revealed global improvement immediately post-yoga that was not maintained at follow-up. For YA, global improvement, worst pain, constipation, and nausea were significantly improved postyoga, but only global improvement, worst pain, and nausea maintained at the 2-month follow-up. CONCLUSIONS: The findings suggest that a brief IY intervention is a feasible and safe adjunctive treatment for young people with IBS, leading to benefits in a number of IBS-specific and general functioning domains for YA. The age-specific results suggest that yoga interventions may be most fruitful when developmentally tailored.

Faro M, SÃ¡ez-FrancÃ s N, Castro-Marrero J, Aliste L, Collado A, Alegre J.	(1)EAP CAP Terrassa Nord, Consorci Sanitari de Terrassa, Terrassa, Barcelona, España. Electronic address: 34174mfc@comb.cat. (2)Unidad de Fatiga Crónica, Institut de Recerca Vall d'Hebron, Hospital Universitario Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, España. (3)Unidad de Fibromialgia, Hospital Clínic de Barcelona, Barcelona, España.	Impact of the fibromyalgia in the chronic fatigue syndrome.	Med Clin (Barc). 2014 Jun 16;142(12):519-25. doi: 10.1016/j.medcli.2013.06.030. Epub 2014 Jan 2. Spanish.	[Article in Spanish] BACKGROUND AND OBJECTIVE: Different studies have showed association of the chronic fatigue syndrome (CFS) with other pathologies, including fibromyalgia (FM). The objective of this study is to analyze whether there are differences in the clinic and in the assessment of fatigue in CFS patients associated or not with FM. PATIENTS AND METHODS: A cross-sectional, single-site observational study was undertaken on a consecutive cases of a register of CFS patients at CFS Unit in Vall d'Hebron Hospital, Barcelona, from January 2008 until March 2011. The variables analyzed were FM comorbidity, sleep and fatigue characteristics and cognitive, neurological and autonomic symptoms. Questionnaires of fatigue impact scale, fatigue strength and impact on quality of life SF-36 were evaluated. RESULTS: We included 980 CFS patients (mean age: 48±9 years; 91% women). Fibromyalgia was present in 528 patients (54%). The level of fatigue (P=.001) and pain (P<.001) was higher in FM patients. Patients with CFS and FM had more prevalence of sleep-related phenomena. The percentage of patients and the degree of severity of cognitive symptoms, neurological and autonomic dysfunction was higher in FM patients (P<.001). FM patients scored higher on the fatigue impact scale (P<.001) and showed worse results in the quality of life questionnaire (P<.001). CONCLUSIONS: FM co-morbidity worse clinical parameters, fatigue and the perception of quality of life in CFS patients.
Fernie BA, Maher-Edwards L, Murphy G, NikÄ□eviÄ‡ AV, Spada MM.	Department of Psychology, King's College London, London, UK; CASCAID, South London & Maudsley NHS Foundation Trust, London, UK.	The Metacognitions about Symptoms Control Scale: Development and Concurrent Validity.	Clin Psychol Psychother. 2014 Jun 4. doi: 10.1002/cpp.1906.	Objective This paper presents the development and preliminary validation of a self-report instrument designed to measure metacognitions pertaining to symptoms control in the form of the following: (1) symptoms focusing and (2) symptoms conceptual thinking. Methods A total of 124 patients (95 female and 29 male) presenting with chronic fatigue syndrome (CFS) contributed data to the study to test the structure and psychometric properties of the Metacognitions about Symptoms Control Scale (MaSCS). Results A principal components factor analysis indicated that a two-factor solution best fitted the data. The factors were labelled positive and negative metacognitions about symptoms control. Further analyses revealed that both factors had good internal consistency. Correlation analyses established preliminary concurrent validity, indicating that both positive and negative metacognitions about symptoms control were significantly associated with levels of fatigue in CFS. Regression analysis revealed that positive and negative metacognitions about symptoms control significantly predicted fatigue severity when controlling for anxiety and depression. Conclusions The newly developed instrument may help future research that examines the role of metacognitions in CFS, as well as aiding clinical assessment and case formulation. Copyright © 2014 John Wiley & Sons, Ltd.KEY PRACTITIONER MESSAGE: The MaSCS is a useful first instrument to assess metacognitions in CFS. The MaSCS may help to deepen our

				understanding of symptoms control (symptoms focusing and conceptual thinking about symptoms) in the experience of CFS symptoms. Assessing and conceptualizing symptoms control through the MaSCS may aid treatment of CFS.
Fischer DB, William AH, Strauss AC, Unger ER, Jason L, Marshall GD Jr, Dimitrakoff JD.	(1)Harvard Medical School, 25 Shattuck Street, Boston, MA, USA 02115. (2)Harvard Medical School, 25 Shattuck Street, Boston, MA, USA 02115 ;	Chronic Fatigue Syndrome: The Current Status and Future Potentials of Emerging Biomarkers.	Fatigue. 2014 Jun 1;2(2):93-109.	Chronic fatigue syndrome (CFS) remains an incompletely characterized illness, in part due to controversy regarding its definition, biological basis and diagnosis. Biomarkers are objective measures that may lead to improvements in our understanding of CFS by providing a more coherent and consistent approach to study, diagnosis and treatment of the illness. Such metrics may allow us to distinguish between CFS subtypes - each defined by characteristic biomarkers - currently conflated under the single, heterogeneous condition of CFS. These delineations, in turn, may guide more granular, focused, and targeted treatment strategies based on more precise characterizations of the illness. Here, we review potential CFS biomarkers related to neurological and immunological components of the illness, and discuss how these biomarkers may be used to move the field of CFS forward, emphasizing clinical utility and potential routes of future research.
Flo E, Chalder T.	(1)Norwegian Competence Center for Sleep Disorders, Haukeland University Hospital, Bergen, Norway; Centre for Elderly and Nursing Home Medicine, Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway. Electronic address: elisabeth.flo@psykp.uib.no. (2)Institute of Psychiatry, King's College London, London, United Kingdom.	Prevalence and predictors of recovery from chronic fatigue syndrome in a routine clinical practice.	Behav Res Ther. 2014 Dec;63:1-8. doi: 10.1016/j.brat.2014.08.013. Epub 2014 Aug 26.	Cognitive behavioural therapy (CBT) is one of the treatments of choice for patients with chronic fatigue syndrome (CFS). However, the factors that predict recovery are unknown. The objective of this study was to ascertain the recovery rate among CFS patients receiving CBT in routine practice and to explore possible predictors of recovery. Recovery was defined as no longer meeting Oxford or CDC criteria for CFS measured at 6 months follow-up. A composite score representing full recovery additionally included the perception of improvement, and normal population levels of fatigue and of physical functioning. Logistic regression was used to examine predictors of recovery. Predictors included age, gender, cognitive and behavioural responses to symptoms, work and social adjustment, beliefs about emotions, perfectionism, anxiety and depression at baseline. At 6 months follow-up 37.5% of the patients no longer met either the Oxford or the CDC criteria for CFS while 18.3% were fully recovered. Multivariate analyses showed that worse scores on the work and social adjustment scale, unhelpful beliefs about emotions, high levels of depression and older age were associated with reduced odds for recovery. Recovery rates in this routine practice were comparable to previous RCTs. There was a wide spectrum of significant predictors for recovery.

Floege J.	Division of Nephrology and Clinical Immunology, RWTH University of Aachen, Pauwelsstr. 30, 52057, Aachen, Germany, juergen.floege@rwth-aachen.de.	Magnesium in CKD: more than a calcification inhibitor?	J Nephrol. 2014 Sep 17.	Magnesium fulfils important roles in multiple physiological processes. Accordingly, a tight regulation of magnesium homeostasis is essential. Dysregulated magnesium serum levels, in particular hypomagnesaemia, are common in patients with chronic kidney disease (CKD) and have been associated with poor clinical outcomes. In cell culture studies as well as in clinical situations magnesium levels were associated with vascular calcification, cardiovascular disease and altered bone-mineral metabolism. Magnesium has also been linked to diseases such as metabolic syndrome, diabetes, hypertension, fatigue and depression, all of which are common in CKD. The present review summarizes and discusses the latest clinical data on the impact of magnesium and possible effects of higher levels on the health status of patients with CKD, including an outlook on the use of magnesium-based phosphate-binding agents in this context
Friedberg F, Coronel J, Seva V, Adamowicz JL, Napoli A.	Stony Brook University, USA fred.friedberg@stonybrookmedicine.edu. (2)Stony Brook University, USA.	Participant attributions for global change ratings in unexplained chronic fatigue and chronic fatigue syndrome.	J Health Psychol. 2014 Jun 8. doi:pii: 1359105314535458.	The purpose of this mixed methods study was to identify participants' attributions for their global impression of change ratings in a behavioral intervention for unexplained chronic fatigue and chronic fatigue syndrome. At 3-month follow-up, participants (N = 67) were asked "Why do you think you are (improved, unchanged, worse)?" Improved patients pointed to specific behavioral changes, unchanged patients referred to a lack of change in lifestyle, and worsened patients invoked stress and/or specific life events. Identifying patient perceptions of behaviors associated with patient global impression of change-rated improvement and non-improvement may assist in developing more effective management strategies in clinical care.
Friedberg F, Adamowicz J.	Department of Psychiatry, Stony Brook University, Stony Brook, New York, USA.	Reports of recovery in chronic fatigue syndrome may present less than meets the eye.	Evid Based Ment Health. 2014 Aug;17(3):95. doi: 10.1136/eb-2013-101652. Epub 2014 May 21.	Comment on Psychol Med. 2013 Oct;43(10):2227-35.
Gaber TA, Oo WW, Ringrose H.	(1)Neurological Rehabilitation, Wrightington Wigan and Leigh NHS Trust, Wigan, UK. (2)Neurological Rehabilitation, Royal Wolverhampton Hospitals NHS Trust, UK. (3)Rehabilitation Medicine, Wrightington Wigan and Leigh NHS Trust,	Multiple Sclerosis/Chronic Fatigue Syndrome overlap: When two common disorders collide.	NeuroRehabilitation. 2014;35(3):529-34. doi: 10.3233/NRE-141146.	INTRODUCTION: Fatigue is a major cause of disability and handicap in Multiple Sclerosis (MS) patients. The management of this common problem is often difficult. Chronic Fatigue Syndrome (CFS/ME) is another common cause of fatigue which is prevalent in the same population of middle aged females commonly affected by MS. AIM: This report aims at examining the potential coexistence of MS and CFS/ME in the same patients. METHOD: This is a retrospective study examining a cohort of MS patients referred for rehabilitation. The subjects were screened for CFS/ME symptoms. RESULTS: Sixty-four MS patients (43 females) were screened for CFS/ME. Nine patients (14%) with a mean age 52 (SD 9.7) who were all females fulfilled the Fukuda criteria for diagnosis of CFS/ME. Their symptoms, including muscular and joint pain, malaise and recurrent headaches, were not explained by the pattern of their MS. DISCUSSION: MS and CFS/ME are two common conditions with increased prevalence in middle aged females. As the diagnosis of CFS/ME is clinical with no

	Wigan, UK.			positive clinical signs or investigations; it can be made with difficulty in the presence of another clear explanation for the disabling fatigue. Our results suggest that the two conditions may co-exist. Considering CFS/ME as a potential co-morbidity may lead to more focused and appropriate management.
Galland L.	Foundation for Integrated Medicine , New York, New York, USA .	The gut microbiome and the brain.	J Med Food. 2014 Dec;17(12):1261-72. doi: 10.1089/jmf.2014.7000.	Abstract The human gut microbiome impacts human brain health in numerous ways: (1) Structural bacterial components such as lipopolysaccharides provide low-grade tonic stimulation of the innate immune system. Excessive stimulation due to bacterial dysbiosis, small intestinal bacterial overgrowth, or increased intestinal permeability may produce systemic and/or central nervous system inflammation. (2) Bacterial proteins may cross-react with human antigens to stimulate dysfunctional responses of the adaptive immune system. (3) Bacterial enzymes may produce neurotoxic metabolites such as D-lactic acid and ammonia. Even beneficial metabolites such as short-chain fatty acids may exert neurotoxicity. (4) Gut microbes can produce hormones and neurotransmitters that are identical to those produced by humans. Bacterial receptors for these hormones influence microbial growth and virulence. (5) Gut bacteria directly stimulate afferent neurons of the enteric nervous system to send signals to the brain via the vagus nerve. Through these varied mechanisms, gut microbes shape the architecture of sleep and stress reactivity of the hypothalamic-pituitary-adrenal axis. They influence memory, mood, and cognition and are clinically and therapeutically relevant to a range of disorders, including alcoholism, chronic fatigue syndrome, fibromyalgia, and restless legs syndrome. Their role in multiple sclerosis and the neurologic manifestations of celiac disease is being studied. Nutritional tools for altering the gut microbiome therapeutically include changes in diet, probiotics, and prebiotics
GarcÃa-Leiva JM, Carrasco JL, Slim M, Calandre EP.	Instituto de Neurociencias "Federico Olóriz", Universidad de Granada, Avenida de Madrid, 11, 18012, Granada, Spain.	Celiac symptoms in patients with fibromyalgia: a cross-sectional study.	Rheumatol Int. 2014 Aug 15.	Fibromyalgia is a chronic pain syndrome associated with numerous somatic symptoms including gastrointestinal manifestations of nonspecific nature. Celiac disease and nongluten sensitivity frequently evolve in adults with gastrointestinal and extraintestinal symptoms similar to those found among patients with fibromyalgia. The objective of the present study was to evaluate the presence of celiac-type symptoms among patients with fibromyalgia in comparison with healthy subjects and with those experienced by adult celiac patients and subjects with gluten sensitivity. A list of typical celiac-type symptoms was developed, comparing the frequency of presentation of these symptoms between patients with fibromyalgia (N = 178) and healthy subjects (N = 131), in addition to those of celiac patients and gluten-sensitive patients reported in the literature. The frequency of presentation of every celiac-type symptom, excepting anemia, was significantly higher among patients with fibromyalgia compared to controls ($p < 0.0001$). Regarding the existing data in the literature, the prevalence of fatigue, depression, cognitive symptoms and cutaneous lesions predominated among patients with fibromyalgia, whereas the prevalence of gastrointestinal symptoms was higher

				among patients with fibromyalgia compared to gluten-sensitive patients and was similar among patients with fibromyalgia and celiac disease patient. The symptomatological similarity of both pathologies, especially gastrointestinal symptoms, suggests that at least a subgroup of patients with fibromyalgia could experience subclinical celiac disease or nonceliac gluten intolerance.
Giannotti E, Koutsikos K, Pigatto M, Rampudda ME, Doria A, Masiero S.	Rehabilitation Unit, Department of Neurosciences, University of Padua, Via Giustiniani 3, 35128 Padua, Italy.	Medium-/long-term effects of a specific exercise protocol combined with patient education on spine mobility, chronic fatigue, pain, aerobic fitness and level of disability in fibromyalgia.	Biomed Res Int. 2014;2014:474029. doi: 10.1155/2014/474029. Epub 2014 Jan 29.	OBJECTIVE: To propose a rehabilitation protocol able to produce immediate and long-term beneficial effects on level of disability and overall performance in ADLs. MATERIALS AND METHODS: Forty-one FM patients were randomized to an exercise and educational-behavioral programme group (experimental group, EG = 21) or to a control group (CG = 20). Each subject was evaluated before, at the end (T1), and after 6 months (T6) from the conclusion of the rehabilitation treatment using the Fibromyalgia Impact Questionnaire (FIQ), the visual analogue scale (VAS), the Health Assessment Questionnaire (HAQ), the fatigue severity scale (FSS), the 6-minute walking test (6MWT), tender points count (TPC), and spinal active range of motion. The exercise protocol included 20 sessions consisting in self-awareness, stretching, strengthening, spine flexibility, and aerobic exercises, which patients were subsequently educated to perform at home. RESULTS: The two groups were comparable at baseline. At T1, the EG showed a positive trend in FIQ, VAS, HAQ, and FSS scales and significant improvement in 6MWT and in most spinal active range of motion measurements (P between 0.001 and 0.04). The positive results were maintained at the follow-up. CONCLUSION: The proposed programme was well tolerated and produced immediate and medium-term beneficial effects improving function and strain endurance. This trial is registered with DRKS00005071 on DRKS.
Giebels V, Repping-Wuts H, Bleijenberg G, Kroese JM, Stikkelbroeck N, Hermus A.	Nijmegen Expert Centre of Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.	Severe fatigue in patients with adrenal insufficiency: physical, psychosocial and endocrine determinants.	J Endocrinol Invest. 2014 Mar;37(3):293-301. doi: 10.1007/s40618-013-0042-9. Epub 2014 Jan 9.	BACKGROUND: Fatigue is a frequently experienced complaint in patients with adrenal insufficiency (AI) and may be influenced by cortisol levels. AIM: The objective of this study was to determine the prevalence of severe fatigue in adrenal insufficiency (AI) patients, to assess which dimensions contribute to fatigue severity and to determine the association between salivary cortisol levels and momentary fatigue. SUBJECTS AND METHODS: We performed a cross-sectional study in the outpatient department of a university hospital. Included were 27 patients with congenital adrenal hyperplasia (CAH), 26 patients with primary AI (PAI), 24 patients with secondary AI (SAI) and 31 patients with adrenal insufficiency after treatment for Cushing's syndrome (Cush-AI). Measurements included computerised questionnaires to determine fatigue severity and physical and psychosocial contributors. Patients took four saliva samples at home, in which cortisol levels were measured. RESULTS: Severe fatigue was experienced by 41 % of the CAH patients, 42 % of the PAI patients, 50 % of the SAI patients and 42 % of the Cush-AI patients. Psychological distress, functional impairment, sleep disturbance, physical activity, concentration problems and social functioning contributed to the subjective experience of fatigue. Salivary cortisol levels were not correlated with momentary

				fatigue. CONCLUSIONS: A considerable proportion of AI patients experience severe fatigue. Salivary cortisol level is not a significant predictor for momentary fatigue in AI patients.
Gladwell PW, Pheby D, Rodriguez T, Poland F.	North Bristol NHS Trust , Bristol , UK .	Use of an online survey to explore positive and negative outcomes of rehabilitation for people with CFS/ME.	Disabil Rehabil. 2014;36(5):387-94. doi: 10.3109/09638288.2013.797508. Epub 2013 Jun 4.	PURPOSE: First, to explore the experiences of people with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) of rehabilitation therapies so as to build an understanding of reasons for the discrepancy between the notably mixed experiences regarding effectiveness reported in patient surveys and the RCT evidence about the efficacy of Graded Exercise Therapy (GET). GET is a form of structured and supervised activity management that aims for gradual but progressive increases in physical activity. Second, to review patient experiences of two related rehabilitation approaches, Exercise on Prescription (EoP) and Graded Activity Therapy (GAT). METHOD: An online survey conducted by the charity Action for ME generated qualitative data about 76 patient experiences of rehabilitation undertaken during or after 2008, examined using thematic analysis. RESULTS: Both positive and negative experiences of rehabilitation were reported. Positive themes included supportive communication, the benefits of a routine linked with baseline setting and pacing, the value of goal setting, and increasing confidence associated with exercise. Negative themes included poor communication, feeling pushed to exercise beyond a sustainable level, having no setback plan, and patients feeling blamed for rehabilitation not working. CONCLUSIONS: The negative themes may help explain the negative outcomes from rehabilitation reported by previous patient surveys. The negative themes indicate rehabilitation processes which contradict the NICE (National Institute for Health and Clinical Excellence) Guideline advice regarding GET, indicating that some clinical encounters were not implementing these. These findings suggest areas for improving therapist training, and for developing quality criteria for rehabilitation in CFS/ME. Implications for Rehabilitation The insensitive delivery of rehabilitation support for people with CFS/ME can explain negative outcomes reported in patient surveys. Therapist-patient collaboration, establishing a sustainable baseline and agreeing a setback plan are all examples of higher quality rehabilitation indicated by this research. Greater awareness of the positive and negative experiences of rehabilitation therapies should enable avoidance of the potential pitfalls identified in this research. Positive experiences of rehabilitation therapies include supportive communication with a therapist, treatment which included routines and goals, and value attached to baselines and controlled pacing. By contrast, factors leading to negative experiences include poor communication and support, conflict in beliefs about CFS/ME and rehabilitation, pressure to comply with treatment, worsening of symptoms, baselines experienced as unsustainable, and feeling blamed for

				rehabilitation not working.
GodÃ¡s Sieso T, NoguÃ© Xarau S, Salamero BarÃ³ M, Fernandez SolÃ¡ J.	Unidad de Fatiga Crónica, Servicio de Psicología, Hospital Clínic, Instituto de Neurociencias, Universitat de Barcelona, Barcelona, España. Electronic address: tgodas@clinic.ub.es	Psychopathologic status in patients with chronic fatigue syndrome, associated or not with multiple chemical sensitivity.	Med Clin (Barc). 2014 Nov 18;143(10):467-8. doi: 10.1016/j.medcli.2013.11.012. Epub 2014 Jan 22. Spanish. No abstract available.	[Article in Spanish]
Goedendorp MM, Bleijenberg G, Knoop H.	Department of Health Sciences, University Medical Center Groningen, University of Groningen; Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre	Response to 'Underperformance of myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) patients at neurocognitive tests should be assessed objectively'.	J Psychosom Res. 2014 Apr;76(4):340. doi: 10.1016/j.jpsychores.2013.12.006. Epub 2013 Dec 21. No abstract available.	Comment on J Psychosom Res. 2013 Sep;75(3):242-8 , J Psychosom Res. 2014 Apr;76(4):339.
Goswami K, Saddichha S, Chaturvedi SK.	Department of Psychiatry, National Institute of Mental Health and Neurosciences, Bangalore, Karnataka, India.	Amisulpride treatment of somatoform disorders: not just chronic fatigue.	Am J Ther. 2014 Mar-Apr;21(2):e48-9. doi: 10.1097/MJT.0b013e3182383c78.	Amisulpride has been used to treat psychotic disorders and more recently even chronic fatigue. We describe 2 cases with somatoform disorders and who responded to low-dose amisulpride.
Grellety T, BrugÃ¨res-Chakiba C, Chaminade A, Roubaud G, Ravaud A, Gross-Goupil M.	(1)CHU de Bordeaux, Hôpital Saint-André, 1 rue Jean-Burguet, 33075 Bordeaux cedex, France. (2)Institut Bergonié, Centre de lutte contre le cancer	Revision of therapeutic index for targeted treatment in kidney cancer: What if toxicity could predict efficacy?.	Bull Cancer. 2014 Jun;101(6):608-18. doi: 10.1684/bdc.2014.1935. Review. French.	Since 2006, new treatments as targeted therapies (anti angiogenic and mTOR inhibitors) are prescribed in renal cell cancer. Toxicity of these treatments is ell known by clinicians. Occurrence of these side effects has been associated with anti tumoral efficacy. High blood pressure, hypothyroïdie and hand foot syndrome were reported to be predictive of anti tumoral response. Fatigue and hyponatremia are still largely discussed. Moreover, non infectious pneumonia, which frequently occurs with mTOR inhibitors, is associated with clinical benefit. The main objective

	de Bordeaux, 229 cours de l'Argonne, 33076 Bordeaux cedex, France. (3)CHU de Bordeaux, Hôpital Saint-André, 1 rue Jean-Burguet, 33075 Bordeaux cedex, France, Université Bordeaux 2, 146, rue Léo-Saignat, 33076 Bordeaux cedex, France.			of treatment of advanced kidney cancer, specially renal cell cancer, is obtaining clinical benefit (stabilization and response) with a chronic evolution of the disease. This prolong exposure to drugs, according to their toxicity profile, often contributes to dose reduction, moreover interruption of treatment, potentially associated with a loss of control of disease. Thus, the adverse effects, described hereby, may be considered as « positive events », predicting efficacy, and thus looked for… Moreover, the sequential approach, with new drugs, emphasizes the need of defining the optimal sequence. Thus, because of the lack of molecular biomarkers to date, this predictives secondary effects may help for selecting the therapeutic strategy.
Gremion G, Kuntzer T.	No address given	[Fatigue and reduction in motor performance in sportspeople or overtraining syndrome].	Rev Med Suisse. 2014 Apr 30;10(428):962, 964-5. French.	[Article in French] The main goal of training activities is to improve motor performance. After strenuous workouts, it is physiological to experience fatigue, which relieves within two weeks, and then induce an improvement in motor capacities. An overtraining syndrome is diagnosed when fatigue is postponed beyond two weeks, and affects mainly endurance athletes. It is a condition of chronic fatigue, underperformance and an increased vulnerability to infection leading to recurrent infections. The whole observed spectrum of symptoms is physiological, psychological, endocrinogical and immunological. All play a role in the failure to recover. Monitoring of athletes activities helps to prevent the syndrome with days with no sports. Rest, patience and empathy are the only ways of treatment options.
Haliloglu S, Carlioglu A, Akdeniz D, Karaaslan Y, Kosar A.	Department of Physical Medicine and Rehabilitation, Erzurum Regional Research and Training Hospital, 25240, Erzurum, Turkey, sema@haliloglu.org.	Fibromyalgia in patients with other rheumatic diseases: prevalence and relationship with disease activity.	Rheumatol Int. 2014 Sep;34(9):1275-80. doi: 10.1007/s00296-014-2972-8. Epub 2014 Mar 4.	Fibromyalgia (FM) is a syndrome characterized by chronic widespread pain and the presence of specific tender points. The prevalence of FM has been estimated at 2-7 % of the general global population. The presence of FM in several rheumatic diseases with a structural pathology has been reported as 11-30 %. The objectives of this study were to determine the prevalence of FM and to evaluate the possible relationship between FM existence and disease activity among rheumatic diseases. The study group included 835 patients--197 rheumatoid arthritis (RA), 67 systemic lupus erythematosus (SLE), 119 ankylosing spondylitis (AS), 238 osteoarthritis (OA), 14 familial Mediterranean fever (FMF), 53 Behçet's disease (BD), 71 gout, 25 Sjögren's syndrome (SS), 20 vasculitis, 29 polymyalgia rheumatica (PMR), and two polymyositis (PM)--with or without FM. Recorded information included age, gender, laboratory parameters, presence of fatigue, and disease activity indexes. The prevalence of FM in patients with rheumatologic diseases was found to be 6.6 % for RA, 13.4 % for SLE, 12.6 % for AS, 10.1 % for OA, 5.7 % for BD, 7.1 % for FMF, 12 %

				for SS, 25 % for vasculitis, 1.4 % for gout, and 6.9 % for PMR. One out of two patients with PM was diagnosed with FM. Some rheumatologic cases (AS, OA) with FM were observed mostly in female patients (p = 0.000). Also, there were significant correlations between disease activity indexes and Fibromyalgia Impact Questionnaire scores for most rheumatologic patients (RA, AS, OA, and BD) (p < 0.05; respectively, r = 0.6, 0.95, 0.887, and 1). Concomitant FM is a common clinical problem in rheumatologic diseases, and its recognition is important for the optimal management of these diseases. Increased pain, physical limitations, and fatigue may be interpreted as increased activity of these diseases, and a common treatment option is the prescription of higher doses of biologic agents or corticosteroids. Considerations of the FM component in the management of rheumatologic diseases increase the likelihood of the success of the treatment.
Hall DL, Lattie EG, Antoni MH, Fletcher MA, Czaja S, Perdomo D, Klimas NG.	(1)Department of Psychology, University of Miami, Coral Gables, FL, USA. Electronic address: dhall@psy.miami.edu. (2)Department of Psychology, University of Miami, Coral Gables, FL, USA. (3)Institute for Neuro Immune Medicine, Nova Southeastern University, Davie, FL, USA. (4)Department of Psychiatry and Behavioral Sciences, University of Miami, Miami, FL, USA.	Stress management skills, cortisol awakening response, and post-exertional malaise in Chronic Fatigue Syndrome.	Psychoneuroendocrinology. 2014 Nov;49:26-31. doi: 10.1016/j.psyneuen.2014.06.021. Epub 2014 Jul 6.	Chronic Fatigue Syndrome (CFS) is characterized in part by debilitating fatigue typically exacerbated by cognitive and/or physical exertion, referred to as post-exertional malaise (PEM). In a variety of populations, the cortisol awakening response (CAR) has stood out as a marker of endocrine dysregulation relevant to the experience of fatigue, and may therefore be particularly relevant in CFS. This is the first study to examine PEM and the CAR in a sample of individuals with CFS. The CAR has also been established as a stress-sensitive measure of HPA axis functioning. It follows that better management of stress could modulate the CAR, and in turn PEM. In this cross-sectional study, we hypothesized that greater Perceived Stress Management Skills (PSMS) would relate to lower reports of PEM, via the impact of PSMS on the CAR. A total of 117 adults (72% female) with a CFS diagnosis completed self-report measures of PSMS and PEM symptomatology and a two-day protocol of saliva collection. Cortisol values from awakening and 30 min post-awakening were used to compute the CAR. Regression analyses revealed that greater PSMS related to greater CAR and greater CAR related to less PEM severity. Bootstrapped analyses revealed an indirect effect of PSMS on PEM via the CAR, such that greater PSMS related to less PEM, via a greater CAR. Future research should examine these trends longitudinally and whether interventions directed at improving stress management skills are accompanied by improved cortisol regulation and less PEM in individuals with CFS.
Hanevik K, Wensaas KA, Rortveit G, Eide GE, MÃ¸rch K, Langeland N.	Department of Clinical Science, University of Bergen.	Irritable bowel syndrome and chronic fatigue 6 years after giardia infection: a controlled prospective cohort	Clin Infect Dis. 2014 Nov 15;59(10):1394-400. doi: 10.1093/cid/ciu629. Epub 2014 Aug 12.	BACKGROUND: Functional gastrointestinal disorders and fatigue may follow acute infections. This study aimed to estimate the persistence, prevalence, and risk of irritable bowel syndrome and chronic fatigue 6 years after Giardia infection. METHODS: We performed a controlled prospective study of a cohort of 1252 individuals who had laboratory-confirmed Giardia infection during a waterborne outbreak in 2004. In total, 748 cohort cases (exposed) and 878 matched controls responded to a postal questionnaire 6 years later (in 2010). Responses were

		study.		compared to data from the same cohort 3 years before (in 2007). RESULTS: The prevalences of irritable bowel syndrome (39.4%) by Rome III criteria and chronic fatigue (30.8%) in the exposed group 6 years after giardiasis were significantly elevated compared with controls, with adjusted relative risks (RRs) of 3.4 (95% confidence interval [CI], 2.9-3.9) and 2.9 (95% CI, 2.3-3.4), respectively. In the exposed group, the prevalence of irritable bowel syndrome decreased by 6.7% (RR, 0.85 [95% CI, .77-.93]), whereas the prevalence of chronic fatigue decreased by 15.3% from 3 to 6 years after Giardia infection (RR, 0.69 [95% CI, .62-.77]). Giardia exposure was a significant risk factor for persistence of both conditions, and increasing age was a risk factor for persisting chronic fatigue. CONCLUSIONS: Giardia infection in a nonendemic setting is associated with an increased risk for irritable bowel syndrome and chronic fatigue 6 years later. The prevalences of both conditions decrease over time, indicating that this intestinal protozoan parasite may elicit very long-term, but slowly self-limiting, complications.
Hannan LM, Dominelli GS, Chen YW, Darlene Reid W, Road J.	Institute for Breathing and Sleep, Austin Hospital, Heidelberg, Victoria, Australia; University of Melbourne, Medicine, Dentistry and Health Sciences, Melbourne, Victoria, Australia; University of British Columbia, Respiratory Division and Department of Medicine, Vancouver, British Columbia, Canada. Electronic address: liamhannan1@yahoo.com.au.	Systematic review of non-invasive positive pressure ventilation for chronic respiratory failure.	Respir Med. 2014 Feb;108(2):229-43. doi: 10.1016/j.rmed.2013.11.010. Epub 2013 Nov 20. Review.	BACKGROUND: This systematic review examined the effect of non-invasive positive pressure ventilation (NIPPV) on patient reported outcomes (PROs) and survival for individuals with or at risk of chronic respiratory failure (CRF). METHODS: Randomised controlled trials (RCTs) and prospective non-randomised studies in those treated with NIPPV for CRF were identified from electronic databases, reference lists and grey literature. Diagnostic groups included in the review were amyotrophic lateral sclerosis/motor neuron disease (ALS/MND), Duchenne muscular dystrophy (DMD), restrictive thoracic disease (RTD) and obesity hypoventilation syndrome (OHS). RESULTS: Eighteen studies were included and overall study quality was weak. Those with ALS/MND had improved somnolence and fatigue as well as prolonged survival with NIPPV. For OHS, improvements in somnolence and fatigue, dyspnoea and sleep quality were demonstrated, while for RTD, measures of dyspnoea, sleep quality, physical function and health, mental and emotional health and social function improved. There was insufficient evidence to form conclusions regarding the effect of NIPPV for those with DMD. CONCLUSIONS: This review has demonstrated that NIPPV influences PROs differently depending on the underlying cause of CRF. These findings may provide assistance to patients and clinicians to determine the relative costs and benefits of NIPPV therapy and also highlight areas in need of further research.
Hardcastle SL, Brenu EW, Johnston S, Staines D, Marshall-Gradisnik S.	National Centre for Neuroimmunology and Emerging Diseases, Griffith Health Centre, School of Medical Science , Griffith	Severity Scales for Use in Primary Health Care to Assess Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.	Health Care Women Int. 2014 Oct 14:1-16.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a physical and cognitive disabling illness, characterized by severe fatigue and a range of physiological symptoms, that primarily affects women. The immense variation in clinical presentation suggests differences in severity based on symptomology and physical and cognitive functional capacities. In this article, we examine a number of severity scales used in assessing severity of patients with CFS/ME and the clinical

	University , Gold Coast , Queensland , Australia.			aspects of CFS/ME severity subgroups. The use of severity scales may be important in CFS/ME because it permits the establishment of subgroups that may improve accuracy in both clinical and research settings.
Hausteiner-Wiehle C, Henningsen P.	Constanze Hausteiner-Wiehle, Psychosomatic Consultation Service, Murnau Trauma Center, 82418 Murnau, Germany.	Irritable bowel syndrome: relations with functional, mental, and somatoform disorders.	World J Gastroenterol. 2014 May 28;20(20):6024-30. doi: 10.3748/wjg.v20.i20.6024.	This review describes the conceptual and clinical relations between irritable bowel syndrome (IBS), other functional, somatoform, and mental disorders, and points to appropriate future conceptualizations. IBS is considered to be a functional somatic syndrome (FSS) with a considerable symptom overlap with other FSSs like chronic fatigue syndrome or fibromyalgia syndrome. IBS patients show an increased prevalence of psychiatric symptoms and disorders, especially depression and anxiety. IBS is largely congruent with the concepts of somatoform and somatic symptom disorders. Roughly 50% of IBS patients complain of gastrointestinal symptoms only and have no psychiatric comorbidity. IBS concepts, treatment approaches, as well as health care structures should acknowledge its variability and multidimensionality by: (1) awareness of additional extraintestinal and psychobehavioral symptoms in patients with IBS; (2) general and collaborative care rather than specialist and separated care; and (3) implementation of "interface disorders" to abandon the dualistic classification of purely organic or purely mental disorders.
Hawkrigg S, Payne DN.	Adolescent Medicine Department, Princess Margaret Hospital, Perth, Western Australia, Australia	Prolonged school non-attendance in adolescence: a practical approach.	Arch Dis Child. 2014 Oct;99(10):954-7. doi: 10.1136/archdischild-2013-304595. Epub 2014 Jun 9. Review.	Prolonged school non-attendance in adolescence poses a significant public health concern. Adverse outcomes for adolescents who have missed out on the social and academic benefits of high school include mental health disorders and economic, social and relationship difficulties that may persist into adulthood. Healthcare professionals are often consulted in cases of prolonged school non-attendance. Diagnosis and management of specific physical and mental health problems must be the health professional's initial priority, with the subsequent development of a management plan to assist with school reintegration. Using a specific framework, an understanding of the factors contributing to a young person's school non-attendance can be developed. Intervention leading to a successful return to school has the potential to lower the risk of associated long-term adverse health outcomes.
Haywood KL, Collin SM, Crawley E.	Royal College of Nursing Research Institute, Warwick Medical School, University of Warwick, Coventry, UK.	Assessing severity of illness and outcomes of treatment in children with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis	Child Care Health Dev. 2014 Nov;40(6):806-24. doi: 10.1111/cch.12135. Epub 2014 Mar 24.	Chronic Fatigue Syndrome or Myalgic Encephalomyelitis (CFS/ME) in children is characterized by persistent or recurrent debilitating fatigue which results in a substantial reduction in activity. There is a growing interest in the use of questionnaires, or patient-reported outcome measures (PROMs), to assess how patients function and feel in relation to their health and associated healthcare. However, guidance for PROM selection for children with CFS/ME does not exist. We reviewed the quality and acceptability of PROMs used with children with CFS/ME to

		(CFS/ME): a systematic review of patient-reported outcome measures (PROMs).		inform recommendations for practice. We conducted a systematic review of PROMs completed by children with CFS/ME. The quality of the evaluative studies and the reviewed measures were assessed against recommended criteria using an appraisal framework and the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) checklist. We sought evidence of measurement (reliability, validity, responsiveness, interpretability, data quality) and practical properties (acceptability, relevance, feasibility). Sixteen articles were included in the review, providing evidence of reliability and/or validity for 13 PROMs. Of these, five were child-specific (one health-related quality-of-life; four emotional well-being) and eight were not (four emotional well-being, three fatigue-specific; and one generic). All measures had limited evidence of measurement properties and no evidence of practical properties. Recommendations for patient-reported assessment are difficult to make because of limited evidence of the quality and acceptability of PROMs for children with CFS/ME. The appraisal method highlighted significant methodological and quality issues which must be addressed in future research. There is a lack of qualitative evidence describing the outcomes of healthcare that are important to children with CFS/ME, and the relevance or appropriateness of available measures. Future PROM development and evaluation in this group must seek to involve children collaboratively to ensure that the outcomes that children care about are assessed in an acceptable way.
Helskog E, Bjartveit K.	No address given	E. Helskog and colleagues reply.	Tidsskr Nor Laegeforen. 2014 May 27;134(10):1023. doi: 10.4045/tidsskr.14.0609. Norwegian. No abstract available.	[Article in Norwegian] Comment on Tidsskr Nor Laegeforen. 2014 Apr 29;134(8):811-2.
Helskog EH, Bjartveit K.	No address given	[E.H. Helskog and colleagues reply].	Tidsskr Nor Laegeforen. 2014 Apr 8;134(7):691. doi: 10.4045/tidsskr.14.0368. Norwegian. No abstract available.	[Article in Norwegian] Comment on Tidsskr Nor Laegeforen. 2014 Feb 25;134(4):423-5. Tidsskr Nor Laegeforen. 2014 Apr 8;134(7):690-1.

Henderson TA.	No address given	Valacyclovir treatment of chronic fatigue in adolescents.	Adv Mind Body Med. 2014 Winter;28(1):4-14.	Chronic fatigue syndrome (CFS) presents with fatigue, low motivation, diminished mood, and reduced activity, all symptoms having extensive diagnostic overlaps with depression. Studies have linked chronic viral infections with CFS, and antiviral therapy has effectively treated CFS in adult patients. In a retrospective case series, 15 adolescents and preteens referred to the author for treatment-resistant depression or mood disorder were evaluated and found to have met the Fukuda diagnostic criteria for CFS. While a subset (4/15) had been diagnosed in the past with CFS, the majority had a current diagnosis of depression or a mood disorder. The Diagnostic and Statistical Manual-IV Text Revision (DSM-IV TR) criteria for depression were not met in all patients, although 3 cases of mood disorder not otherwise specified (MD-NOS) and 1 case of Tourette syndrome (TS) plus MD-NOS were diagnosed. Baseline scores on the Children's Depression Inventory (CDI) were below the cutoff for depression in all but 1 patient. Baseline self-assessment scales for CFS or fatigue were obtained and sleep was evaluated with sleep logs. All patients were treated subsequently with valacyclovir, with 93% having a positive response. At the end of treatment, scores on fatigue self-assessment scales improved significantly ($P < .001$). Vigor subscale scores also improved significantly ($P < .001$). Some patients experienced complete resolution of symptoms. Although not every patient was tested, available laboratory testing revealed increased counts of natural killer (NK) cells and decreased human herpesvirus 6 (HHV-6) antibody titers in all patients who responded to valacyclovir. This article discusses the significance of infectious agents in the pathogenesis of psychiatric symptoms. The study's data support an intriguing hypothesis that a portion of treatment-resistant depression in fact may be undiagnosed CFS or other chronic viral infection.
Hommel B, Charuel JL, Jaureguiberry S, Arnaud L, Courtin R, Kassab P, Prendki V, Paris L, Ghillani-Dalbin P, Thellier M, Caumes E, Amoura Z, Mazier D, Musset L, Buffet P, Miyara M.	Immunology Department - Immune Chemistry and Autoimmunity Laboratory, Groupe Hospitalier Pitié-Salpêtrière, AP-HP, Paris, France ; Parasitology-Mycology Laboratory, Assistance Publique Hôpitaux de Paris, Groupe Hospitalier Pitié-Salpêtrière, Paris, France	Chronic malaria revealed by a new fluorescence pattern on the antinuclear autoantibodies test.	PLoS One. 2014;9(2):e88548. doi: 10.1371/journal.pone.0088548. Erratum in: PLoS One. 2014;9(3):e92361.	BACKGROUND: Several clinical forms of malaria such as chronic carriage, gestational malaria or hyper-reactive malarial splenomegaly may follow a cryptic evolution with afebrile chronic fatigue sometimes accompanied by anemia and/or splenomegaly. Conventional parasitological tests are often negative or not performed, and severe complications may occur. Extensive explorations of these conditions often include the search for antinuclear autoantibodies (ANA). METHODS: We analysed fluorescence patterns in the ANA test in patients with either chronic cryptic or acute symptomatic malaria, then conducted a one-year prospective study at a single hospital on all available sera drawn for ANA detections. We then identified autoantibodies differentially expressed in malaria patients and in controls using human protein microarray. RESULTS: We uncovered and defined a new, malaria-related, nucleo-cytoplasmic ANA pattern displaying the specific association of a nuclear speckled pattern with diffuse cytoplasmic perinuclearly-enhanced fluorescence. In the one-year prospective analysis, 79% of sera displaying this new nucleo-cytoplasmic fluorescence were from patients with malaria. This specific pattern, not seen in other parasitic diseases, allowed a timely reorientation of the

				diagnosis toward malaria. To assess if the autoantibody immune response was due to autoreactivity or molecular mimicry we isolated 42 autoantigens, targets of malarial autoantibodies. BLAST analysis indicated that 23 of recognized autoantigens were homologous to plasmodial proteins suggesting autoimmune responses directly driven by the plasmodial infection. CONCLUSION: In patients with malaria in whom parasitological tests have not been performed recognition of this new, malaria-related fluorescence pattern on the ANA test is highly suggestive of the diagnosis and triggers immediate, easy confirmation and adapted therapy.
Hou R, Moss-Morris R, Risdale A, Lynch J, Jeevaratnam P, Bradley BP, Mogg K.	Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, United Kingdom.	Attention processes in chronic fatigue syndrome: attentional bias for health-related threat and the role of attentional control.	Behav Res Ther. 2014 Jan;52:9-16. doi: 10.1016/j.brat.2013.10.005. Epub 2013 Oct 24.	Cognitive behavioural models of chronic fatigue syndrome (CFS) propose that attention processes, specifically, enhanced selective attention to health-threat related cues, may play an important role in symptom maintenance. The current study investigated attentional bias towards health-threat stimuli in CFS. It also examined whether individuals with CFS have impaired executive attention, and whether this was related to attentional bias. 27 participants with CFS and 35 healthy controls completed a Visual Probe Task measuring attentional bias, and an Attention Network Test measuring executive attention, alerting and orienting. Participants also completed self-report measures of CFS and mood symptoms. Compared to the control group, the CFS group showed greater attentional bias for health-threat words than pictures; and the CFS group was significantly impaired in executive attention. Furthermore, CFS individuals with poor executive attention showed greater attentional bias to health-threat related words, compared not only to controls but also to CFS individuals with good executive attention. Thus, this study revealed a significant relationship between attentional bias and executive attention in CFS: attentional bias to threat was primarily evident in those with impaired executive attention control. Taking account of individual differences in executive attention control in current intervention models may be beneficial for CFS.
Hu C, Lv L, Liu D, Huo J.	Department of Gastroenterology, Second Xiang Ya Hospital, Central South University, 139 Mid RenMin Road, Changsha, 410011 Hunan People's Republic of China.	Treatment of Crohn's disease complicated with myelodysplastic syndrome via allogeneic hematopoietic stem cell transplantation: case report and literature review.	Clin J Gastroenterol. 2014;7:299-304. Epub 2014 May 22.	Crohn's disease (CD) is a chronic inflammatory disease of the gastrointestinal tract arising in individuals with genetic predisposing factors and abnormalities of the immune system. Myelodysplastic syndrome (MDS), an acquired clonal hematologic disorder, is characterized by peripheral blood cytopenia, dysplastic changes in several types of hematopoietic cells of the bone marrow and peripheral blood, and a high risk of transformation to acute leukemia. CD rarely occurs in combination with MDS, and MDS treatment with hematopoietic stem cell transplantation (HSCT) has not been frequently reported. We report the case of a 50-year-old Chinese male who presented with abdominal pain, diarrhea, and fatigue. CD was diagnosed by colonoscopy, imaging studies, and pathological examination. He was initially treated with mesalazine and prednisone and thereafter he presented with pancytopenia. MDS (RAEB-I) was diagnosed by bone marrow examination, and karyotyping revealed 47, XY, +8. The patient was treated with thalidomide, andriol, and decitabine. Allogeneic HSCT was performed with a human leukocyte antigen-

				matched sibling as the donor. The patient is currently well at 14 months after HSCT, without abdominal pain, diarrhea, or fatigue. HSCT may be a promising treatment option for patients with combined CD and MDS.
Huibregtse KE, Wolfgram P, Winer KK, Connor EL.	No address given	Polyglandular autoimmune syndrome type I - a novel AIRE mutation in a North American patient.	J Pediatr Endocrinol Metab. 2014 Nov;27(11-12):1257-60. doi: 10.1515/jpem-2013-0328.	Autoimmune polyglandular syndrome type 1 (APS-1), also referred to as autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED), is a rare autoimmune disease that results from autosomal recessive mutations of the human autoimmune regulatory (AIRE) gene. We present the case of a 17-year-old North American girl of primarily Norwegian descent with a novel AIRE gene mutation causing APS-1. In addition to the classic triad of chronic candidiasis, hypoparathyoidism and autoimmune adrenocortical insufficiency, she also has vitiligo, intestinal malabsorption, autoimmune hepatitis, autoimmune hypothyroidism, myositis, myalgias, chronic fatigue, and failure to thrive. Genetic testing revealed heterozygosity for c.20_115de196 and c.967_979del13 mutations in the AIRE gene. The AIRE gene c.20_115de196 mutation has not been previously reported.
Hull A, Reinhard M, McCarron K, Allen N, Jecmen MC, Akhter J, Duncan A, Soltes K.	War Related Illness and Injury Study Center, Veteran Affairs Medical Center, Washington, DC, United States	Acupuncture and meditation for military veterans: first steps of quality management and future program development.	Glob Adv Health Med. 2014 Jul;3(4):27-31. doi: 10.7453/gahmj.2013.050.	Veterans of all war eras have a high rate of chronic disease, mental health disorders, and chronic multi-symptom illnesses (CMI).(1-3) Many veterans report symptoms that affect multiple biological systems as opposed to isolated disease states. Standard medical treatments often target isolated disease states such as headaches, insomnia, or back pain and at times may miss the more complex, multisystem dysfunction that has been documented in the veteran population. Research has shown that veterans have complex symptomatology involving physical, cognitive, psychological, and behavioral disturbances, such as difficult to diagnose pain patterns, irritable bowel syndrome, chronic fatigue, anxiety, depression, sleep disturbance, or neurocognitive dysfunction.(2-4) Meditation and acupuncture are each broad-spectrum treatments designed to target multiple biological systems simultaneously, and thus, may be well suited for these complex chronic illnesses. The emerging literature indicates that complementary and integrative medicine (CIM) approaches augment standard medical treatments to enhance positive outcomes for those with chronic disease, mental health disorders, and CMI.(5-12.)

Hutchinson CV, Maltby J, Badham SP, Jason LA.	College of Medicine, Biological Sciences and Psychology, School of Psychology, University of Leicester, , Leicester, UK	Vision-related symptoms as a clinical feature of chronic fatigue syndrome/myalgic encephalomyelitis? Evidence from the DePaul Symptom Questionnaire.	Br J Ophthalmol. 2014 Jan;98(1):144-5. doi: 10.1136/bjophthalmol-2013-304439. Epub 2013 Nov 1. No abstract available.	No abstract available
Hock AD.	Mariawaldstraße 7, 50935 Cologne, Germany. ad.hoeck@t-online.de.	Review: Vitamin D3 deficiency results in dysfunctions of immunity with severe fatigue and depression in a variety of diseases.	In Vivo. 2014 Jan-Feb;28(1):133-45. Review.	Recent immune data on vitamin D3 deficiency help to more clearly understand chronic fatiguing illnesses, such as autoimmune disorders, cancer and chronic fatigue syndrome (CFS). The vitamin D3 pathway is activated by stress and requires sufficient stores of precursor 25-hydroxyvitamin D3 for proper cell and immune functions. In vitamin D3 deficiency, secretion of the antimicrobial peptide cathelicidin is reduced, leading to impaired auto/xenophagy. As a result, phagocytosis, cytotoxicity, antigen processing and antigen presentation become dysregulated. In addition, vitamin D3 deficiency affects T- and B-lymphocyte activation, as well as quantity, maturation and function of regulatory natural killer T-cells and their counterparts in the gut, i.e. T-cell receptor-αβ, cluster of differentiation-8αα-positive intraepithelial lymphocytes. Consequently, innate and adaptive immunity become de-regulated, with microbial effects contributing further to this. Persistent infections, chronic inflammation and fatigue follow. Vitamin D3 substitution in such conditions may help to prevent or to ameliorate such chronic conditions, even in patients with cancer
Ickmans K, Meeus M, De Kooning M, Lambrecht L, Nijs J.	Pain in Motion Research Group, Department of Human Physiology and Physiotherapy, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium;	Recovery of upper limb muscle function in chronic fatigue syndrome with and without fibromyalgia.	Eur J Clin Invest. 2014 Feb;44(2):153-9. doi: 10.1111/eci.12201. Epub 2013 Dec 9.	BACKGROUND: Chronic fatigue syndrome (CFS) patients frequently complain of muscle fatigue and abnormally slow recovery, especially of the upper limb muscles during and after activities of daily living. Furthermore, disease heterogeneity has not yet been studied in relation to recovery of muscle function in CFS. Here, we examine recovery of upper limb muscle function from a fatiguing exercise in CFS patients with (CFS+FM) and without (CFS-only) comorbid fibromyalgia and compare their results with a matched inactive control group. DESIGN: In this case-control study, 18 CFS-only patients, 30 CFS+FM patients and 30 healthy inactive controls performed a fatiguing upper limb exercise test with subsequent recovery measures. RESULTS: There was no significant difference among the three groups for maximal handgrip strength of the non-dominant hand. A significant worse recovery of upper limb muscle function was found in the CFS+FM, but not in de CFS-only group compared with the controls ($P < 0{\cdot}05$). CONCLUSIONS: This study reveals, for the first time, delayed recovery of upper limb muscle function in CFS+FM, but not in CFS-only patients. The results underline that CFS is a heterogeneous disorder suggesting that reducing the heterogeneity of the disorder in future research is important to make

				progress towards a better understanding and uncovering of mechanisms regarding the nature of divers impairments in these patients.
Ickmans K, Meeus M, De Kooning M, Lambrecht L, Pattyn N, Nijs J.	K. Ickmans, PT, MSc, Pain in Motion Research Group, Department of Human Physiology and Physiotherapy, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium;	Can recovery of peripheral muscle function predict cognitive task performance in chronic fatigue syndrome with and without fibromyalgia?	Phys Ther. 2014 Apr;94(4):511-22. doi: 10.2522/ptj.20130367. Epub 2013 Dec 20.	BACKGROUND: Both good physical and cognitive functioning have a positive influence on the execution of activities of daily living. Patients with chronic fatigue syndrome (CFS) as well as patients with fibromyalgia have marked cognitive deficits. Furthermore, a good physical and functional health status may have a positive impact on a variety of cognitive skills-a link that has been observed in young and old individuals who are healthy, although evidence is limited in patients with CFS. OBJECTIVE: The purpose of this study was to examine whether recovery of upper limb muscle function could be a significant predictor of cognitive performance in patients with CFS and in patients with CFS and comorbid fibromyalgia. Furthermore, this study determined whether cognitive performance is different between these patient groups. DESIGN: A case-control design was used. METHODS: Seventy-eight participants were included in the study: 18 patients with CFS only (CFS group), 30 patients with CFS and comorbid fibromyalgia (CFS+FM group), and 30 individuals who were healthy and inactive (control group) were studied. Participants first completed 3 performance-based cognitive tests designed to assess selective and sustained attention, cognitive inhibition, and working memory capacity. Seven days later, they performed a fatiguing upper limb exercise test, with subsequent recovery measures. RESULTS: Recovery of upper limb muscle function was found to be a significant predictor of cognitive performance in patients with CFS. Participants in the CFS+FM group but not those in the CFS group showed significantly decreased cognitive performance compared with the control group. LIMITATIONS: The cross-sectional nature of this study does not allow for inferences of causation. CONCLUSIONS: The results suggest that better physical health status could predict better mental health in patients with CFS. Furthermore, they underline disease heterogeneity, suggesting that reducing this factor in future research is important to better understand and uncover mechanisms regarding the nature of diverse impairments in these patients.
Ifuku M, Hossain SM, Noda M, Katafuchi T.	Department of Integrative Physiology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan	Induction of interleukin-1Î² by activated microglia is a prerequisite for immunologically induced fatigue.	Eur J Neurosci. 2014 Oct;40(8):3253-63. doi: 10.1111/ejn.12668. Epub 2014 Jul 5.	We previously reported that an intraperitoneal (i.p.) injection of synthetic double-stranded RNA, polyriboinosinic:polyribocytidylic acid (poly-I:C), produced prolonged fatigue in rats, which might serve as a model for chronic fatigue syndrome. The poly-I:C-induced fatigue was associated with serotonin transporter (5-HTT) overexpression in the prefrontal cortex (PFC), a brain region that has been suggested to be critical for fatigue sensation. In the present study, we demonstrated that microglial activation in the PFC was important for poly-I:C-induced fatigue in rats, as pretreatment with minocycline, an inhibitor of microglial activation, prevented the decrease in running wheel activity. Poly-I:C injection increased the microglial interleukin (IL)-1β expression in the PFC. An intracerebroventricular (i.c.v.)

				injection of IL-1β neutralising antibody limited the poly-I:C-induced decrease in activity, whereas IL-1β (i.c.v.) reduced the activity in a dose-dependent manner. 5-HTT expression was enhanced by IL-1β in primary cultured astrocytes but not in microglia. Poly-I:C injection (i.p.) caused an increase in 5-HTT expression in astrocytes in the PFC of the rat, which was inhibited by pretreatment with minocycline (i.p.) and rat recombinant IL-1 receptor antagonist (i.c.v.). Poly-I:C injection (i.p.) led to a breakdown of the blood-brain barrier and enhanced Toll-like receptor 3 signaling in the brain. Furthermore, direct application of poly-I:C enhanced IL-1β expression in primary microglia. We therefore propose that poly-I:C-induced microglial activation, which may be at least partly caused by a direct action of poly-I:C, enhances IL-1β expression. Then, IL-1β induces 5-HTT expression in astrocytes, resulting in the immunologically induced fatigue.
Ijaz M, Tariq H, Niazi M, Lvovsky D.	Division of Pulmonary and Critical Care Medicine, Department of Medicine, Bronx Lebanon Hospital Center, 1650 Selwyn Avenue, Suit No. 12 F, Bronx, NY 10457, USA.	Complete heart block and persistent lactic acidosis as an initial presentation of non-hodgkin lymphoma in a critically ill newly diagnosed AIDS patient.	Case Rep Crit Care. 2014;2014:214970. doi: 10.1155/2014/214970. Epub 2014 Nov 6.	A 66-year-old male with newly diagnosed untreated acquired immunodeficiency syndrome (AIDS) presented with chronic nonspecific complaints of weakness, fatigue, myalgia, and weight loss. His initial EKG showed complete heart block necessitating temporary pacemaker placement. He had no previous history of cardiac disease. He was also found to have a persistent lactic acidosis and imaging studies showed abdominal lymphadenopathy. The patient underwent biopsy of these lymph nodes and was found to have diffuse large B-cell lymphoma. The hospital course was complicated by respiratory failure requiring mechanical ventilator support and cardiac arrest. Patient remained critically ill; he was not a candidate for chemotherapy and, after a month of hospitalization, he died. Lactic acidosis and heart block as an initial presentation of non-Hodgkin lymphoma in an AIDS patient are an unusual and unique presentation.
Irlbeck DM, Vernon SD, McCleary KK, Bateman L, Klimas NG, Lapp CW, Peterson DL, Brown JR, Remlinger KS, Wilfret DA, Gerondelis P.	Division of Infectious Diseases, GlaxoSmithKline, Research Triangle Park, NC, USA. peter.z.gerondelis@gsk.com	No association found between the detection of either xenotropic murine leukemia virus-related virus or polytropic murine leukemia virus and chronic fatigue syndrome in a blinded, multi-site, prospective study by the establishment and use of the SolveCFS BioBank.	BMC Res Notes. 2014 Aug 4;7:461. doi: 10.1186/1756-0500-7-461.	BACKGROUND: In 2009, a retrospective study reported the detection of xenotropic murine leukemia virus-related virus (XMRV) in clinical isolates derived from individuals with chronic fatigue syndrome or myalgic encephalomyelitis (CFS). While many efforts to confirm this observation failed, one report detected polytropic murine leukemia virus (pMLV), instead of XMRV. In both studies, Polymerase Chain Reaction (PCR)-based methods were employed which could provide the basis for the development of a practical diagnostic tool. To confirm these studies, we hypothesized that the ability to detect these viruses will not only depend upon the technical details of the methods employed but also on the criteria used to diagnose CFS and the availability of well characterized clinical isolates. METHODS: A repository of clinical isolates from geographically distinct sites was generated by the collection of fresh blood samples from well characterized CFS and healthy subjects. Molecular techniques were used to generate assay positive controls and to determine the lower limit of detection (LLOD) for murine retroviral and Intracisternal A particle (Cell 12(4):963-72, 1977) detection methods. RESULTS: We report the establishment of a repository of well-defined, clinical isolates from five,

				geographically distinct regions of the US, the comparative determination of the LLODs and validation efforts for the previously reported detection methods and the results of an effort to confirm the association of these retroviral signatures in isolates from individuals with CFS in a blinded, multi-site, prospective study. We detected various, murine retroviral DNA signatures but were unable to resolve a difference in the incidence of their detection between isolates from CFS (5/72; 6.7%) and healthy (2/37; 5.4%) subjects (Fisher's Exact Test, p-value = 1). The observed sequences appeared to reflect the detection of endogenous murine retroviral DNA, which was not identical to either XMRV or pMLV. CONCLUSIONS: We were unable to confirm a previously reported association between the detection of XMRV or pMLV sequences and CFS in a prospective, multi-site study. Murine retroviral sequences were detected at a low frequency that did not differ between CFS and control subjects. The nature of these sequences appeared to reflect the detection of pre-existing, endogenous, murine retroviral DNA in the PCR reagents employed.
Isasi C, Tejerina E, Fernandez-Puga N, Serrano-Vela JI.	Servicio de Reumatología, Hospital Puerta de Hierro, Majadahonda, Madrid, España. Electronic address: carlosmaria.isasi@salud.madrid.org.	Fibromyalgia and chronic fatigue syndrome caused by non-celiac gluten sensitivity.	Reumatol Clin. 2014 Jul 18. doi:pii: S1699-258X(14)00132-6. 10.1016/j.reuma.2014.06.005. English, Spanish. No abstract available.	[Article in English, Spanish] No abstract available
Isasi ZaragozÃ¡ C.	(Servicio de Reumatología, Hospital Puerta de Hierro, Majadahonda, España. Electronic address: cisasi.hpth@salud.madrid.org.	Chronic fatigue syndrome and non-celiac gluten sensitivity. Association or cause?	Reumatol Clin. 2014 Dec 9. doi:pii: S1699-258X(14)00221-6. 10.1016/j.reuma.2014.10.010. English, Spanish. No abstract available.	Article in English, Spanish] No abstract available
Jason LA, Katz BZ, Shiraishi Y, Mears CJ, Im Y, Taylor R.	DePaul University; Center for Community Research, 990 W. Fullerton Ave, Chicago, Il. 60614, (773-325-	Predictors of Post-Infectious Chronic Fatigue Syndrome in Adolescents.	Health Psychol Behav Med. 2014 Jan 1;2(1):41-51.	This study focused on identifying risk factors for adolescent post-infectious chronic fatigue syndrome (CFS), utilizing a prospective, nested case-control longitudinal design in which over 300 teenagers with Infectious Mononucleosis (IM) were identified through primary care sites and followed. Baseline variables that were gathered several months following IM, included autonomic symptoms, days in bed

	2018)(ljason@depaul.edu).			since IM, perceived stress, stressful life events, family stress, difficulty functioning and attending school, family stress and psychiatric disorders. A number of variables were predictors of post-infectious CFS at 6 months; however, when autonomic symptoms were used as a control variable, only days spent in bed since mono was a significant predictor. Step-wise logistic regression findings indicated that baseline autonomic symptoms as well as days spent in bed since mono, which reflect the severity of illness, were the only significant predictors of those who met CFS criteria at 6 months.
Jason LA, Sunnquist M, Brown A, Evans M, Vernon SD, Furst J, Simonis V.	(1)Center for Community Research, DePaul University, Chicago, IL USA. (2)The CFIDS Association of America. (3)College of Computing and Digital Media, DePaul University, Chicago, USA.	Examining case definition criteria for chronic fatigue syndrome and myalgic encephalomyelitis.	Fatigue. 2014 Jan 1;2(1):40-56.	BACKGROUND: Considerable controversy has transpired regarding the core features of myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS). Current case definitions differ in the number and types of symptoms required. This ambiguity impedes the search for biological markers and effective treatments. PURPOSE: This study sought to empirically operationalize symptom criteria and identify which symptoms best characterize the illness. METHODS: Patients (n=236) and controls (n=86) completed the DePaul Symptom Questionnaire, rating the frequency and severity of 54 symptoms. Responses were compared to determine the threshold of frequency/severity ratings that best distinguished patients from controls. A Classification and Regression Tree (CART) algorithm was used to identify the combination of symptoms that most accurately classified patients and controls. RESULTS: A third of controls met the symptom criteria of a common CFS case definition when just symptom presence was required; however, when frequency/severity requirements were raised, only 5% met criteria. Employing these higher frequency/severity requirements, the CART algorithm identified three symptoms that accurately classified 95.4% of participants as patient or control: fatigue/extreme tiredness, inability to focus on multiple things simultaneously, and experiencing a dead/heavy feeling after starting to exercise. CONCLUSIONS: Minimum frequency/severity thresholds should be specified in symptom criteria to reduce the likelihood of misclassification. Future research should continue to seek empirical support of the core symptoms of ME and CFS to further progress the search for biological markers and treatments
Jason LA, Sunnquist M, Brown A, Evans M, Newton JL.	Center for Community Research, DePaul University, USA	Are Myalgic Encephalomyelitis and chronic fatigue syndrome different illnesses? A preliminary analysis.	J Health Psychol. 2014 Feb 7.	Considerable discussion has transpired regarding whether chronic fatigue syndrome is a distinct illness from Myalgic Encephalomyelitis. A prior study contrasted the Myalgic Encephalomyelitis International Consensus Criteria with the Fukuda and colleagues' chronic fatigue syndrome criteria and found that the Myalgic Encephalomyelitis International Consensus Criteria identified a subset of patients with greater functional impairment and physical, mental, and cognitive problems than the larger group who met Fukuda and colleagues' criteria. The current study analyzed two discrete data sets and found that the Myalgic Encephalomyelitis International Consensus Criteria identified more impaired individuals with more

				severe symptomatology
Jeffery DD, Bulathsinhala L, Kroc M, Dorris J.	(1)Department of Defense, Defense Health Agency, 7700 Arlington Boulevard, Suite 5101, Falls Church, VA 22042-5101. (2)U.S. Army Research Institute of Environmental Medicine, Kansas Street, Natick, MA 01760-5007. (3)Altarum Institute, 4401 Ford Avenue #800, Alexandria, VA 22302. (4)Altarum Institute, 3520 Green Court #300, Ann Arbor, MI 48105	Prevalence, health care utilization, and costs of fibromyalgia, irritable bowel, and chronic fatigue syndromes in the military health system, 2006-2010.	Mil Med. 2014 Sep;179(9):1021-9. doi: 10.7205/MILMED-D-13-00419.	OBJECTIVE: We compared prevalence, health care utilization, and costs over time for nonelderly adults diagnosed with fibromyalgia syndrome (FMS), irritable bowel syndrome (IBS), and chronic fatigue syndrome (CFS) in relation to timing of federal approvals for FMS drugs. DATA SOURCE: We used military health care claims from October 2006 to September 2010. STUDY DESIGN/ANALYSIS: Retrospective, multiple-year comparisons were conducted using trend analyses, and time series regression-based generalized linear models. RESULTS: Over 5 years, FMS prevalence rates increased from 0.307% to 0.522%, whereas IBS and CFS prevalence rates remained stable. The largest increase in FMS prevalence occurred between 2007 and 2008. Health care utilization was higher for FMS cases compared to IBS and CFS cases. Over 5 years, the total cost for FMS-related care increased $163.2 million, whereas IBS costs increased $14.9 million and CFS cost increased $3.7 million. Between 2006 and 2010, total pharmacy cost for FMS cases increased from $55 million ($3,641/person) to $96.3 million ($3,557/person). CONCLUSION: Although cause and effect cannot be established, the advent of federally approved drugs for FMS in concert with pharmaceutical industry marketing of these drugs coincide with the observed changes in prevalence, health care utilization, and costs of FMS relative to IBS and CFS.
Jensen NE.	No address given	Re: Woman in her 30s with chronic fatigue.	Tidsskr Nor Laegeforen. 2014 Apr 29;134(8):811-2. doi: 10.4045/tidsskr.14.0461. Norwegian. No abstract available.	[Article in Norwegian] Comment in Tidsskr Nor Laegeforen. 2014 May 27;134(10):1023. Comment on Tidsskr Nor Laegeforen. 2014 Feb 25;134(4):423-5.
Jin H, Patil PM, Sharma A.	No address given	Topical review: the enigma of fibromyalgia.	J Oral Facial Pain Headache. 2014 Spring;28(2):107-18. doi: 10.11607/ofph.1220. Review. Retraction in: J Oral Facial Pain Headache. 2014 Fall;28(4):preceding 297.	Fibromyalgia is a syndrome characterized by chronic widespread pain, stiffness, nonrestorative sleep, fatigue, and comorbid conditions. Recognition of the condition and its associated medications and challenges, along with knowledge of treatment modifications and precautions in drug prescription, can ensure safe and effective delivery of oral health care in fibromyalgia patients. The ever-evolving research into the condition makes it necessary for the oral health re provider to be informed about the current state of the literature and treatment standards regarding the management of fibromyalgia patients. This article reviews the epidemiology, etiology, pathophysiology, and clinical presentation of fibromyalgia, as well as therapeutic advances. Also highlighted are issues that are important to the oral health care provider, including orofacial manifestations and oral health care

				considerations for patients with fibromyalgia.
Johnston SC, Brenu EW, Hardcastle SL, Huth TK, Staines DR, Marshall-Gradisnik SM.	(1)Griffith Health Institute, School of Medical Sciences, National Centre for Neuroimmunology and Emerging Diseases, Griffith University, Parklands, QLD 4222, Australia. samantha.johnston3@griffithuni.edu.au	A comparison of health status in patients meeting alternative definitions for chronic fatigue syndrome/myalgic encephalomyelitis.	Health Qual Life Outcomes. 2014 Apr 30;12:64. doi: 10.1186/1477-7525-12-64.	BACKGROUND: Several diagnostic definitions are available for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) that varies significantly in their symptom criteria. This pilot study was conducted to determine whether simple biological and clinical measures differed between CFS/ME patients meeting the 1994 Centres for Disease Control and Prevention (CDC) criteria, the International Consensus Criteria (ICC), as well as healthy controls. METHODS: A total of 45 CFS/ME patients and 30 healthy controls from the South East Queensland region of Australia provided a blood sample, reported on their current symptoms, as well as aspects of their physical and social health using the Short-Form Health Survey (SF-36), and the World Health Organisation Disability Adjustment Schedule 2.0 (WHO DAS 2.0). Differences were examined using independent sample t-testing. RESULTS: Patients fulfilling the ICC definition reported significantly lower scores ($p < 0.05$) for physical functioning, physical role, bodily pain, and social functioning than those that only fulfilled the 1994 CDC definition. ICC patients reported significantly greater ($p < 0.05$) disability across all domains of the WHO DAS 2.0. CONCLUSIONS: These preliminary findings suggest that the ICC identifies a distinct subgroup found within patients complying with the 1994 CDC definition, with more severe impairment to their physical and social functioning.
Kairys AE, Schmidt-Wilcke T, Puiu T, Ichesco E, Labus JS, Martucci K, Farmer MA, Ness TJ, Deutsch G, Mayer EA, Mackey S, Apkarian AV, Maravilla K, Clauw DJ, Harris RE.	Department of Anesthesiology, and the Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, Michigan.	Increased Brain Gray Matter in the Primary Somatosensory Cortex is Associated with Increased Pain and Mood Disturbance in Patients with Interstitial Cystitis/Painful Bladder Syndrome.	J Urol. 2015 Jan;193(1):131-7. doi: 10.1016/j.juro.2014.08.042. Epub 2014 Aug 14.	PURPOSE: Interstitial cystitis is a highly prevalent pain condition estimated to affect 3% to 6% of women in the United States. Emerging data suggest there are central neurobiological components to the etiology of this disease. We report the first brain structural imaging findings from the MAPP network with data on more than 300 participants. MATERIALS AND METHODS: We used voxel based morphometry to determine whether human patients with chronic interstitial cystitis display changes in brain morphology compared to healthy controls. A total of 33 female patients with interstitial cystitis without comorbidities and 33 age and gender matched controls taken from the larger sample underwent structural magnetic resonance imaging at 5 MAPP sites across the United States. RESULTS: Compared to controls, females with interstitial cystitis displayed significant increased gray matter volume in several regions of the brain including the right primary somatosensory cortex, the superior parietal lobule bilaterally and the right supplementary motor area. Gray matter volume in the right primary somatosensory cortex was associated with greater pain, mood (anxiety) and urological symptoms. We explored these

				correlations in a linear regression model, and found independent effects of these 3 measures on primary somatosensory cortex gray matter volume, namely clinical pain (McGill pain sensory total), a measure of urgency and anxiety (HADS). CONCLUSIONS: These data support the notion that changes in somatosensory gray matter may have an important role in pain sensitivity as well as affective and sensory aspects of interstitial cystitis. Further studies are needed to confirm the generalizability of these findings to other pain conditions.
Kallestad H, Jacobsen HB, LandrÃ¸ NI, Borchgrevink PC, Stiles TC.	Norwegian University of Science and Technology, Department of Neuroscience, Trondheim, Norway; St. Olav's University Hospital, Department of Østmarka, Trondheim, Norway. Electronic address: havard.kallestad@ntnu.no.	The role of insomnia in the treatment of chronic fatigue.	J Psychosom Res. 2014 Dec 5. doi:pii: S0022-3999(14)00422-X. 10.1016/j.jpsychores.2014.11.022.	BACKGROUND: The definition of Chronic Fatigue Syndrome (CFS) overlaps with definitions of insomnia, but there is limited knowledge about the role of insomnia in the treatment of chronic fatigue. AIMS: To test if improvement of insomnia during treatment of chronic fatigue was associated with improved outcomes on 1) fatigue and 2) cortisol recovery span during a standardized stress exposure. METHODS: Patients (n=122) with chronic fatigue received a 3.5-week inpatient return-to-work rehabilitation program based on Acceptance and Commitment Therapy, and had been on paid sick leave>8weeks due their condition. A physician and a psychologist examined the patients, assessed medication use, and SCID-I diagnoses. Patients completed self-report questionnaires measuring fatigue, pain, depression, anxiety, and insomnia before and after treatment. A subgroup (n=25) also completed the Trier Social Stress Test for Groups (TSST-G) before and after treatment. Seven cortisol samples were collected during each test and cortisol spans for the TSST-G were calculated. RESULTS: A hierarchical regression analysis in nine steps showed that insomnia improvement predicted improvement in fatigue, independently of age, gender, improvement in pain intensity, depression and anxiety. A second hierarchical regression analysis showed that improvement in insomnia significantly predicted the cortisol recovery span after the TSST-G independently of improvement in fatigue. CONCLUSION: Improvement in insomnia severity had a significant impact on both improvement in fatigue and the ability to recover from a stressful situation. Insomnia severity may be a maintaining factor in chronic fatigue and specifically targeting this in treatment could increase treatment response.
Kang S, Lee KP, Park SJ, Noh DY, Kim JM, Moon HR, Lee YG, Choi YW, Im DS.	Molecular Inflammation Research Center for Aging Intervention (MRCA) and College of Pharmacy, Pusan National University, 63 Beon-gil 2, Busandaehag-ro, Geumjeong-gu, Busan 609-735, Republic of	Identification of a novel anti-inflammatory compound, Î±-cubebenoate from Schisandra chinensis.	J Ethnopharmacol. 2014 Apr 11;153(1):242-9. doi: 10.1016/j.jep.2014.02.027. Epub 2014 Feb 21.	AIMS OF THE STUDY: Extracts of Schisandra chinensis have been used as an anti-fatigue and tonic agent. Because chronic fatigue syndrome is related to inflammatory and oxidative stress, we assessed whether Schisandra chinensis has anti-inflammatory constituents and studied the effect of a novel α-cubebenoate isolated from Schisandra chinensis. MATERIALS AND METHODS: α-Cubebenoate was isolated from an extract of Schisandra chinensis fruits. The inductions of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) by lipopolysaccharide (LPS) were quantified by RT-PCR and Western blotting in mouse peritoneal macrophages. Nitric oxide (NO) and prostaglandin E2 (PGE2) were also measured in the media by Griess reagent and EIA method. A mouse model of LPS-induced peritonitis was used to test the in vivo efficacy of α-cubebenoate. RESULTS: α-

	Korea.			Cubebenoate (5-10μg/ml) inhibited the inductions of iNOS and COX-2 in mouse peritoneal macrophages at the mRNA and protein levels. LPS-induced productions of NO and PGE2 were inhibited by α-cubebenoate (5-10μg/ml). In addition, α-cubebenoate inhibited the LPS-induced activation of JNK, but not those of ERK and p38 MAPK in mouse peritoneal macrophages. Furthermore, in the LPS-induced in vivo peritonitis model, α-cubebenoate (1mg/kg) strongly inhibited the accumulation of polymorph nuclear lymphocytes in the peritoneal cavity. CONCLUSION: α-Cubebenoate inhibited LPS-induced expression of iNOS and COX-2 in a concentration-dependent manner, thereby suppressing productions of NO and PGE2 in vitro in peritoneal macrophages. α-Cubebenoate also inhibited LPS-induced accumulation of polymorph nuclear lymphocytes in LPS-induced peritonitis model in vivo. α-Cubebenoate may act as an anti-fatigue constituent of Schisandra chinensis through anti-inflammation and could be of therapeutic use as a treatment for inflammatory diseases.
Kawada T.	Department of Hygiene and Public Health, Nippon Medical School, Tokyo, Japan	Chronic fatigue syndrome in adolescents: definition and epidemiological characteristics.	J Paediatr Child Health. 2014 Oct;50(10):840. doi: 10.1111/jpc.12721. No abstract available.	Comment on J Paediatr Child Health. 2014 Oct;50(10):775-81
Keller BA, Pryor JL, Giloteaux L.	Department of Exercise & Sport Sciences, Ithaca College, School of Health Sciences & Human Performance, 318 Center for Health Sciences, Ithaca, NY 14850, USA. keller@ithaca.edu.	Inability of myalgic encephalomyelitis/chronic fatigue syndrome patients to reproduce VOâ,,peak indicates functional impairment.	J Transl Med. 2014 Apr 23;12:104. doi: 10.1186/1479-5876-12-104.	BACKGROUND: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a multi-system illness characterized, in part, by increased fatigue following minimal exertion, cognitive impairment, poor recovery to physical and other stressors, in addition to other symptoms. Unlike healthy subjects and other diseased populations who reproduce objective physiological measures during repeat cardiopulmonary exercise tests (CPETs), ME/CFS patients have been reported to fail to reproduce results in a second CPET performed one day after an initial CPET. If confirmed, a disparity between a first and second CPET could serve to identify individuals with ME/CFS, would be able to document their extent of disability, and could also provide a physiological basis for prescribing physical activity as well as a metric of functional impairment. METHODS: 22 subjects diagnosed with ME/CFS completed two repeat CPETs separated by 24 h. Measures of oxygen consumption (VO_2), heart rate (HR), minute ventilation (Ve), workload (Work), and respiratory exchange ratio (RER) were made at maximal (peak) and ventilatory threshold (VT) intensities. Data were analyzed using ANOVA and Wilcoxon's Signed-Rank Test (for RER). RESULTS: ME/CFS patients showed significant decreases from CPET1 to CPET2 in VO_2peak (13.8%), HRpeak (9 bpm), Ve peak (14.7%), and Work@peak (12.5%). Decreases in VT measures included VO_2@VT (15.8%), Ve@VT (7.4%), and Work@VT (21.3%). Peak RER was high (≥1.1) and did not differ between tests, indicating maximum effort by participants during both CPETs. If data from only a single CPET test is used,

				a standard classification of functional impairment based on VO_2peak or VO_2@VT results in over-estimation of functional ability for 50% of ME/CFS participants in this study. CONCLUSION: ME/CFS participants were unable to reproduce most physiological measures at both maximal and ventilatory threshold intensities during a CPET performed 24 hours after a prior maximal exercise test. Our work confirms that repeated CPETs warrant consideration as a clinical indicator for diagnosing ME/CFS. Furthermore, if based on only one CPET, functional impairment classification will be mis-identified in many ME/CFS participants
Kempke S, Luyten P, De Coninck S, Van Houdenhove B, Mayes LC, Claes S.	Faculty of Psychology and Educational Sciences, University of Leuven, Leuven, Belgium. Electronic address: stefan.kempke@ppw.kuleuven.be	Effects of early childhood trauma on hypothalamic-pituitary-adrenal (HPA) axis function in patients with Chronic Fatigue Syndrome.	Psychoneuroendocrinology. 2014 Nov 8;52C:14-21. doi: 10.1016/j.psyneuen.2014.10.027.	BACKGROUND: There is a paucity of studies that have investigated the assumption that early childhood trauma is associated with hypothalamic-pituitary-adrenal (HPA) axis dysfunction in Chronic Fatigue Syndrome (CFS). The current study is the first to simultaneously investigate relationships among early childhood trauma, cortisol activity, and cortisol stress reactivity to psychosocial stress in a sample of well-screened CFS patients. We also examined whether self-critical perfectionism (SCP) plays a mediating role in the potential relationship between early trauma and neurobiological stress responses. METHODS: A total of 40 female patients diagnosed with CFS were asked to provide morning saliva cortisol samples (after awakening, 30min later, and 1h later) for seven consecutive days as a measure of cortisol activity. In addition, patients were exposed to the Trier Social Stress Test, a well-validated stress test, to investigate the relationship between early childhood trauma and cortisol stress reactivity. Before the start of the study, patients completed the Childhood Trauma Questionnaire-Short form (CTQ-SF) as a measure of early childhood trauma (i.e. sexual, physical and emotional traumatic experiences). SCP was measured with the Depressive Experiences Questionnaire (DEQ). Data were analyzed by calculating several indices of cortisol secretion (i.e. Cortisol Awakening Response and Area Under the Curve). RESULTS: There was no association between early childhood trauma and cortisol as measured over the 7-day period. However, emotional neglect was significantly negatively related to cortisol reactivity in the TSST. SCP did not significantly mediate this association. CONCLUSION: Findings of this study suggest that emotional neglect is associated with blunted HPA axis reactivity, congruent with the assumption that CFS may reflect loss of adaptability of the neuroendocrine stress response system in at least a subgroup of patients.
Khaiboullina SF, DeMeirleir KL, Rawat S, Berk GS, Gaynor-Berk RS, Mijatovic T, Blatt N, Rizvanov AA, Young SG, Lombardi VC.	Gail and Gerald Oppenheimer Family Center for Neurobiology of Stress, David Geffen School of Medicine, University of California-Los Angeles	Cytokine expression provides clues to the pathophysiology of Gulf War illness and myalgic encephalomyelitis.	Cytokine. 2014 Dec 13;72(1):1-8. doi: 10.1016/j.cyto.2014.11.019.	Gulf War illness (GWI) is a chronic disease of unknown etiology characterized by persistent symptoms such as cognitive impairment, unexplained fatigue, pervasive pain, headaches, and gastrointestinal abnormalities. Current reports suggest that as many as 200,000 veterans who served in the 1990-1991 Persian Gulf War were afflicted. Several potential triggers of GWI have been proposed including chemical exposure, toxins, vaccines, and unknown infectious agents. However, a definitive cause of GWI has not been identified and a specific biological marker that can consistently delineate the disease has not been defined. Myalgic encephalomyelitis

				(ME) is a disease with similar and overlapping symptomology, and subjects diagnosed with GWI typically fit the diagnostic criteria for ME. For these reasons, GWI is often considered a subgroup of ME. To explore this possibility and identify immune parameters that may help to understand GWI pathophysiology, we measured 77 serum cytokines in subjects with GWI and compared these data to that of subjects with ME as well as healthy controls. Our analysis identified a group of cytokines that identified ME and GWI cases with sensitivities of 92.5% and 64.9%, respectively. The five most significant cytokines in decreasing order of importance were IL-7, IL-4, TNF-α, IL-13, and IL-17F. When delineating GWI and ME cases from healthy controls, the observed specificity was only 33.3%, suggesting that with respect to cytokine expression, GWI cases resemble control subjects to a greater extent than ME cases across a number of parameters. These results imply that serum cytokines are representative of ME pathology to a greater extent than GWI and further suggest that the two diseases have distinct immune profiles despite their overlapping symptomology
Kilpatrick LA, Kutch JJ, Tillisch K, Naliboff BD, Labus JS, Jiang Z, Farmer MA, Apkarian AV, Mackey S, Martucci KT, Clauw DJ, Harris RE, Deutsch G, Ness TJ, Yang CC, Maravilla K, Mullins C, Mayer EA.		Alterations in resting state oscillations and connectivity in sensory and motor networks in women with interstitial cystitis/painful bladder syndrome.	J Urol. 2014 Sep;192(3):947-55. doi: 10.1016/j.juro.2014.03.093. Epub 2014 Mar 26.	PURPOSE: The pathophysiology of interstitial cystitis/painful bladder syndrome remains incompletely understood but is thought to involve central disturbance in the processing of pain and viscerosensory signals. We identified differences in brain activity and connectivity between female patients with interstitial cystitis/painful bladder syndrome and healthy controls to advance clinical phenotyping and treatment efforts for interstitial cystitis/painful bladder syndrome. MATERIALS AND METHODS: We examined oscillation dynamics of intrinsic brain activity in a large sample of well phenotyped female patients with interstitial cystitis/painful bladder syndrome and female healthy controls. Data were collected during 10-minute resting functional magnetic resonance imaging as part of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain Research Network project. The blood oxygen level dependent signal was transformed to the frequency domain. Relative power was calculated for multiple frequency bands. RESULTS: Results demonstrated altered frequency distributions in viscerosensory (post insula), somatosensory (postcentral gyrus) and motor regions (anterior paracentral lobule, and medial and ventral supplementary motor areas) in patients with interstitial cystitis/painful bladder syndrome. Also, the anterior paracentral lobule, and medial and ventral supplementary motor areas showed increased functional connectivity to the midbrain (red nucleus) and cerebellum. This increased functional connectivity was greatest in patients who reported pain during bladder filling. CONCLUSIONS: Findings suggest that women with interstitial cystitis/painful bladder syndrome have a sensorimotor component to the pathological condition involving an alteration in intrinsic oscillations and connectivity in a cortico-cerebellar network previously associated with bladder function.

Kindlon T, Baldwin A.	(1)Irish ME/CFS Association, Dublin, Ireland. (2)Bristol, UK	Response to: reports of recovery in chronic fatigue syndrome may present less than meets the eye.	Evid Based Ment Health. 2014 Sep 19. doi:pii: ebmental-2014-101961. 10.1136/eb-2014-101961. No abstract available.	No abstract available
Kizilbash SJ, Ahrens SP, Bruce BK, Chelimsky G, Driscoll SW, Harbeck-Weber C, Lloyd RM, Mack KJ, Nelson DE, Ninis N, Pianosi PT, Stewart JM, Weiss KE, Fischer PR.	Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN	Adolescent fatigue, POTS, and recovery: a guide for clinicians.	Curr Probl Pediatr Adolesc Health Care. 2014 May-Jun;44(5):108-33. doi: 10.1016/j.cppeds.2013.12.014. Review.	Many teenagers who struggle with chronic fatigue have symptoms suggestive of autonomic dysfunction that may include lightheadedness, headaches, palpitations, nausea, and abdominal pain. Inadequate sleep habits and psychological conditions can contribute to fatigue, as can concurrent medical conditions. One type of autonomic dysfunction, postural orthostatic tachycardia syndrome, is increasingly being identified in adolescents with its constellation of fatigue, orthostatic intolerance, and excessive postural tachycardia (more than 40 beats/min). A family-based approach to care with support from a multidisciplinary team can diagnose, treat, educate, and encourage patients. Full recovery is possible with multi-faceted treatment. The daily treatment plan should consist of increased fluid and salt intake, aerobic exercise, and regular sleep and meal schedules; some medications can be helpful. Psychological support is critical and often includes biobehavioral strategies and cognitive-behavioral therapy to help with symptom management. More intensive recovery plans can be implemented when necessary
Klasnja A, Grujic N, Popadic Gacesa J, Barak O, Tomic S, Brkic S.	Department of Physiology, Medical faculty University of Novi Sad, Novi Sad, Serbia - aklasnja@gmail.com	Influence of graded exercise therapy on anxiety levels and health-related quality of life in chronic fatigue syndrome.	J Sports Med Phys Fitness. 2014 Apr;54(2):210-5.	AIM: The purpose of the present study was twofold: 1) to determine to what extent graded exercise therapy (GET) improves health-related quality of life (HRQOL) and anxiety levels in patients with chronic fatigue syndrome (CFS); and 2) to correlate scores of HRQOL and anxiety levels in CFS patients. METHODS: Anxiety and HRQOL were assessed in 26 CFS patients before and after 12 weeks of GET. Anxiety was measured using the State-Trait Anxiety Inventory questionnaire (STAI) and HRQOL using the Medical Outcomes Study Short-Form questionnaire (SF-36). RESULTS: GET significantly decreased trait anxiety (STAI-T) levels in patients with CFS. Patients' scores on SF-36 following GET showed higher levels of functioning, but only the "vitality" subscale scores showed a statistically significant difference. A negative correlation was present between all eight subscales of SF-36 and anxiety levels. The strongest negative correlation for both state and trait anxiety scores (STAI-S and STAI-T) was found with the scores on the "Limitations due to emotional problems" subscale of SF-36 (r=-0.69 and r=-0.55, respectively), while the weakest negative correlation was with the "Physical functioning" subscale scores (r=-0.30 and r=-0.31, respectively). CONCLUSION: Graded exercise therapy has a positive effect on both physical and psychological state of CFS patients. GET can decrease anxiety and improve quality of life of CFS patients. CFS patients with higher state and trait anxiety levels have lower quality of life, and vice versa.

Klineberg E, Rushworth A, Bibby H, Bennett D, Steinbeck K, Towns S.	(1)Academic Department of Adolescent Medicine, The Children's Hospital at Westmead, Sydney, New South Wales, Australia; Sydney Medical School, The University of Sydney, Sydney, New South Wales, Australia.	Adolescent chronic fatigue syndrome and somatoform disorders: a prospective clinical study.	J Paediatr Child Health. 2014 Oct;50(10):775-81. doi: 10.1111/jpc.12653. Epub 2014 Jun 18.	Comment in J Paediatr Child Health. 2014 Oct;50(10):840. AIM: To examine and compare the presenting characteristics and the change in the physical and psychosocial functioning of adolescents with chronic fatigue syndrome (CFS) or somatoform disorders who have received an adaptable multidisciplinary intervention over a 12-month period. METHODS: Fifty adolescents presenting to the Complex Adolescent Clinic at The Children's Hospital at Westmead, Sydney, Australia were assessed. Their physical and psychosocial functioning was rated by the adolescents and their parents using the Child Health Questionnaire. Participants were assessed at baseline, 4 months and 12 months after initiating treatment. Analyses examined whether diagnosis and/or illness precipitants were related to treatment outcome. RESULTS: Adolescents with both CFS and somatoform disorders demonstrated improvement in physical and psychosocial functioning over the first 4 months of treatment, sustained at 12-month follow-up. A diagnosis of CFS was associated with poorer physical functioning over time and a trend towards a longer illness time course compared with somatoform disorder. Adjustment for a physical precipitant reduced the association between diagnosis and physical functioning. Those who had a physical precipitant to their illness had significantly poorer physical functioning over time than those who did not, regardless of diagnostic category. Diagnosis and physical precipitant were not associated with psychosocial functioning. CONCLUSIONS: Improvement in adolescent physical and psychosocial functioning over time suggests that a multidisciplinary treatment model may be effective for varied complex medico-psychosocial presentations, irrespective of diagnosis and illness precipitant. Illness precipitant may have a greater influence on treatment outcome than diagnostic category
Knight S, Harvey A, Towns S, Payne D, Lubitz L, Rowe K, Reveley C, Hennel S, Hiscock H, Scheinberg A.	(1)Clinical Sciences, Murdoch Childrens Research Institute, Perth, Western Australia, Australia; Victorian Paediatric Rehabilitation Service, The University of Melbourne, Perth, Western Australia, Australia; Department of Paediatrics, The University of Melbourne, Perth, Western Australia,	How is paediatric chronic fatigue syndrome/myalgic encephalomyelitis diagnosed and managed by paediatricians? An Australian Paediatric Research Network Study.	J Paediatr Child Health. 2014 Dec;50(12):1000-7. doi: 10.1111/jpc.12677. Epub 2014 Jul 10.	AIM: The diagnosis and management of paediatric chronic fatigue syndrome/myalgic encepnalomyelitis (CFS/ME) represent ongoing challenges for paediatricians. A better understanding of current approaches at a national level is important in informing where research and education could improve treatment outcomes. We aimed to examine current diagnosis and management practices for CFS/ME by Australian paediatricians. METHOD: An online survey was sent to members of the Australian Paediatric Research Network. The primary outcomes of interest included diagnostic criteria used, medical investigations and management practices in paediatric CFS/ME. RESULTS: One hundred seventy-eight (41%) of 430 eligible paediatricians responded, with 70 of the 178 (39%) reporting that they diagnose and manage CFS/ME as part of their practice. Medical investigations used for diagnosis were variable. Conditions that more than half of the paediatricians reported as commonly co-occurring (i.e. present in >50% of cases) included somatisation disorders, anxiety, depression and fibromyalgia. There was wide variation in behavioural and pharmacological management strategies but most

	Australia; The Melbourne School of Psychological Sciences, The University of Melbourne, Perth, Western Australia, Australia.			paediatricians commonly engaged a school teacher, physiotherapist and/or psychologist as part of their management. CONCLUSION: The diagnostic and management practices of paediatricians for CFS/ME within Australia vary widely. This likely reflects a paucity of paediatric-specific guidelines, together with limited evidence to guide best practice and limited training in this area. There is a need for guidance and education for the diagnosis and management of paediatric CFS/ME in Australia.
Kovacic K, Chelimsky TC, Sood MR, Simpson P, Nugent M, Chelimsky G.	Division of Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Center for Pediatric Neurogastroenterology , Motility, and Autonomic Disorders, Medical College of Wisconsin, Milwaukee, WI	Joint hypermobility: a common association with complex functional gastrointestinal disorders.	J Pediatr. 2014 Nov;165(5):973-8. doi: 10.1016/j.jpeds.2014.07.021. Epub 2014 Aug 20.	OBJECTIVE: To evaluate the prevalence of joint hypermobility (JH) and comorbid conditions in children and young adults referred to a tertiary care neurogastroenterology and autonomic disorders clinic for functional gastrointestinal complaints. STUDY DESIGN: This was a retrospective chart review of 66 new patients aged 5-24 years who fulfilled at least 1 pediatric Rome III criteria for a functional gastrointestinal disorder (FGID) and had a recorded Beighton score (n = 45) or fibromyalgia tender point score (n = 45) based on physician examination. Comorbid symptoms were collected and autonomic testing was performed for evaluation of postural tachycardia syndrome (POTS). RESULTS: The median patient age was 15 years (range, 5-24 years), 48 (73%) were females, and 56% had JH, a significantly higher rate compared with population studies of healthy adolescents (P < .001; OR, 10.03; 95% CI, 5.26-19.13). POTS was diagnosed in 34% of patients and did not correlate significantly with hypermobility. Comorbid conditions were common, including sleep disturbances (77%), chronic fatigue (93%), dizziness (94%), migraines (94%), chronic nausea (93%), and fibromyalgia (24%). CONCLUSION: JH and other comorbid symptoms, including fibromyalgia, occur commonly in children and young adults with complex FGIDs. POTS is prevalent in FGIDs but is not associated with hypermobility. We recommend screening patients with complex FGIDs for JH, fibromyalgia, and comorbid symptoms such as sleep disturbances, migraines, and autonomic dysfunction
Kovacic K, Miranda A, Chelimsky G, Williams S, Simpson P, Li BU.	Center for Pediatric Neurogastroenterology , Division of Gastroenterology, Hepatology, and Nutrition, Medical College of Wisconsin, Milwaukee, WI. Electronic address: kkovacic@mcw.edus.	Chronic idiopathic nausea of childhood.	J Pediatr. 2014 May;164(5):1104-9. doi: 10.1016/j.jpeds.2014.01.046. Epub 2014 Mar 5.	OBJECTIVES: To compare children with primary, chronic idiopathic nausea to those with secondary nausea associated with functional abdominal pain. STUDY DESIGN: Retrospective chart review of 45 children with a primary complaint of chronic nausea several times per week. Comparisons were made to prospectively collected data on 49 children with functional abdominal pain and comorbid nausea. RESULTS: The majority of those affected were adolescent Caucasian females. Subjects with chronic nausea had a more severe presentation with daily 88% (vs 26%) and constant 60% (vs 10%) nausea (P < .001), one-half with peak morning intensity. In the chronic nausea group, 62% had migraines, and 71% (vs 22%) had familial migraines (P < .001), 36% had postural tachycardia syndrome and 27% cyclic vomiting syndrome. Both groups suffered comorbid symptoms (anxiety, dizziness, fatigue, and sleep problems). The chronic nausea cohort underwent extensive, negative medical evaluations. CONCLUSIONS: Chronic idiopathic nausea of

				childhood is a poorly described symptom. Patients with primary (vs secondary) chronic nausea were more likely Caucasian, older adolescent females with severe, daily nausea and comorbid conditions such as anxiety, dizziness, and fatigue as well as significantly more migraine features. Chronic nausea is a major, disabling symptom that requires increased recognition as a separate functional entity. Future studies may need to focus on comorbid conditions including migraine and dysautonomia.
Krieger JN, Stephens AJ, Landis JR, Clemens JQ, Kreder K, Lai HH, Afari N, Rodriguez L, Schaeffer A, Mackey S, Andriole GL, Williams DA; MAPP Research Network.	Department of Urology, University of Washington, Seattle, WA. Electronic address: jkrieger@uw.edu	Relationship between Chronic Non-Urological Associated Somatic Syndromes (NUAS) and Symptom Severity in Urological Chronic Pelvic Pain Syndromes: Baseline Evaluation of the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) Study.	J Urol. 2014 Oct 22. doi:pii: S0022-5347(14)04767-3. 10.1016/j.juro.2014.10.086.	PURPOSE: We report data from the Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) network to: (1) identify participants having either (a) urologic chronic pelvic pain syndromes (UCPPS) only or (b) chronic functional non-urological associated somatic syndromes (NUAS) in addition to UCPPS, (2) characterize these two subgroups, and (3) explore these two subgroups using three criteria: (a) the MAPP eligibility criteria, (b) self-reported medical history, or (c) RAND interstitial cystitis epidemiologic (RICE) criteria. MATERIALS AND METHODS: Self-reported cross-sectional data were collected from men and women with UCPPS including: predominant symptoms, symptom duration and severity, NUAS symptoms, and psychosocial factors. RESULTS: Of 424 UCPPS participants, 162 (38%) had NUAS: 93 (22%) irritable bowel syndrome, 15 (4%) fibromyalgia, 13 (3%) chronic fatigue syndrome, and 41 (10%) with multiple syndromes. Among 233 females, 103 (44%) had NUAS compared to 59 (31%) of 191 males ($p = 0.006$). Participants with NUAS had more severe urological symptoms, and more frequent depression and anxiety. Of 424 participants, 228 (54%) met RICE criteria. Among 228 RICE-positive participants, 108 (47%) had NUAS compared to 54 (28%) of 203 RICE-negative patients with NUAS ($p < 0.001$). CONCLUSIONS: NUAS represent important clinical characteristics of UCPPS. Participants with NUAS have more severe symptoms, longer duration and higher rates of depression and anxiety. RICE-positive patients are more likely to have NUAS and more severe symptoms. Because NUAS are more common in women, future studies need to account for this potential confounding factor in UCPPS.
Krzeczkowska A, Karatzias T, Dickson A.	School of Life, Sport and Social Sciences, Edinburgh Napier University , Edinburgh , UK.	Pain in people with chronic fatigue syndrome/myalgic encephalomyelitis: The role of traumatic stress and coping strategies.	Psychol Health Med. 2015 Mar;20(2):210-6. doi: 10.1080/13548506.2014.951370. Epub 2014 Sep 2.	Pain is a significant problem for many people with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME). This exploratory study investigated the extent to which severity of pain was related to coping strategies and post-traumatic symptomatology in people with CFS/ME. Participants comprised 27 individuals with CFS/ME and 27 healthy controls. All participants completed the CFS/ME Symptom Questionnaire, the brief pain inventory, the impact of event scale-revised and the brief-COPE. It was found that CFS/ME participants present with significantly more post-traumatic stress symptoms and report significantly less emotion focused strategies and problem focused coping strategies compared with healthy controls. Severity of pain in the CFS/ME subgroup was not associated with traumatic symptomatology, although those with severe pain reported less use of self-

				distraction, positive re-framing and acceptance than those with mild pain. Our results suggest that the enhancement of certain coping strategies (facilitated by psychological interventions such as acceptance and commitment therapy) may be beneficial in alleviating pain in people with CFS/ME.
Landis JR, Williams DA, Lucia MS, Clauw DJ, Naliboff BD, Robinson NA, van Bokhoven A, Sutcliffe S, Schaeffer AJ, Rodriguez LV, Mayer EA, Lai HH, Krieger JN, Kreder KJ, Afari N, Andriole GL, Bradley CS, Griffith JW, Klumpp DJ, Hong BA, Lutgendorf SK, Buchwald D, et al.	Department of Urology, Division of Neurourology and Pelvic Reconstructive Surgery, University of Michigan, Ann Arbor, MI, USA. qclemens@med.umich.edu	The MAPP research network: design, patient characterization and operations.	BMC Urol. 2014 Aug 1;14:58. doi: 10.1186/1471-2490-14-58.	BACKGROUND: The "Multidisciplinary Approach to the Study of Chronic Pelvic Pain" (MAPP) Research Network was established by the NIDDK to better understand the pathophysiology of urologic chronic pelvic pain syndromes (UCPPS), to inform future clinical trials and improve clinical care. The evolution, organization, and scientific scope of the MAPP Research Network,and the unique approach of the network's central study and common data elements are described. METHODS: The primary scientific protocol for the Trans-MAPP Epidemiology/Phenotyping (EP) Study comprises a multi-site, longitudinal observational study, including bi-weekly internet-based symptom assessments, following a comprehensive in-clinic deep-phenotyping array of urological symptoms, non-urological symptoms and psychosocial factors to evaluate men and women with UCPPS. Healthy controls, matched on sex and age, as well as "positive" controls meeting the non-urologic associated syndromes (NUAS) criteria for one or more of the target conditions of Fibromyalgia (FM), Chronic Fatigue Syndrome (CFS) or Irritable Bowel Syndrome (IBS), were also evaluated. Additional, complementary studies addressing diverse hypotheses are integrated into the Trans-MAPP EP Study to provide a systemic characterization of study participants, including biomarker discovery studies of infectious agents, quantitative sensory testing, and structural and resting state neuroimaging and functional neurobiology studies. A highly novel effort to develop and assess clinically relevant animal models of UCPPS was also undertaken to allow improved translation between clinical and mechanistic studies. Recruitment into the central study occurred at six Discovery Sites in the United States, resulting in a total of 1,039 enrolled participants, exceeding the original targets. The biospecimen collection rate at baseline visits reached nearly 100%, and 279 participants underwent common neuroimaging through a standardized protocol. An extended follow-up study for 161 of the UCPPS participants is ongoing. DISCUSSION: The MAPP Research Network represents a novel, comprehensive approach to the study of UCPPS, as well as other concomitant NUAS. Findings are expected to provide significant advances in understanding UCPPS pathophysiology that will ultimately inform future clinical trials and lead to improvements in patient care. Furthermore, the structure and methodologies developed by the MAPP Network provide the foundation upon which future studies of other urologic or non-urologic disorders can be based. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT01098279 "Chronic Pelvic Pain Study of Individuals with Diagnoses or Symptoms of Interstitial Cystitis and/or Chronic Prostatitis (MAPP-EP)". http://clinicaltrials.gov/show/NCT01098279.

Lasselin J, Capuron L.	Nutrition and Integrative Neurobiology (NutriNeuro), UMR 1286, National Institute of Agricultural Research (INRA) and Bordeaux University, Bordeaux, France	Chronic low-grade inflammation in metabolic disorders: relevance for behavioral symptoms.	Neuroimmunomodulation. 2014;21(2-3):95-101. doi: 10.1159/000356535. Epub 2014 Feb 14. Review.	The ability of cytokines to influence cerebral functions and to induce the development of behavioral alterations is well established in conditions of acute or chronic high-grade activation of the innate immune system. Recent evidence suggests that the release of these immune mediators during chronic low-grade endogenous inflammatory processes may also contribute to the development of behavioral alterations. Metabolic disorders, including obesity, type 2 diabetes and the metabolic syndrome, represent examples of those conditions which are both characterized by a chronic low-grade inflammatory state and an increased prevalence of behavioral disorders. In metabolic disorders, the increased production of acute-phase proteins and cytokines (e.g. C-reactive protein, interleukin-6 and tumor necrosis factor-α), but at relatively low levels, may promote and contribute to the development of behavioral symptoms, including depressive symptoms, cognitive impairment, fatigue, sleep problems and pain. This hypothesis is supported by a growing literature referring both to experimental and clinical findings that will be reviewed here
Lau M, Lebert B, Jung M.	No address given	Assessment of cancer-induced fatigue by nurses and patients in pediatric oncology.	Kinderkrankenschwester. 2014 Mar;33(3):103-8. German. No abstract available.	[Article in German] No abstract available
Learmonth YC, Paul L, McFadyen AK, Marshall-McKenna R, Mattison P, Miller L, McFarlane NG.	College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, Scotland, UK	Short-term effect of aerobic exercise on symptoms in multiple sclerosis and chronic fatigue syndrome: a pilot study.	Int J MS Care. 2014 Summer;16(2):76-82. doi: 10.7224/1537-2073.2013-005.	BACKGROUND: This pilot study was conducted to determine whether a 15-minute bout of moderate-intensity aerobic cycling exercise would affect symptoms (pain and fatigue) and function (Timed 25-Foot Walk test [T25FW] and Timed Up and Go test [TUG]) in people with multiple sclerosis (MS) or chronic fatigue syndrome (CFS), and to compare these results with those of a healthy control group. METHODS: Eight people with MS (Expanded Disability Status Scale score 5-6; Karnofsky score 50-80), eight people with CFS (Karnofsky score 50-80), and eight healthy volunteers participated in the study. Pain and fatigue levels and results of the T25FW and TUG were established at baseline as well as at 30 minutes, 2 hours, and 24 hours following a 15-minute stationary cycling aerobic exercise test. Repeated-measures

				analysis of variance (ANOVA) and covariance (ANCOVA) were used to analyze the findings over time. RESULTS: At baseline there were statistically significant differences between groups in fatigue (P = .039), T25FW (P = .034), and TUG (P = .010). A significant group/time interaction emerged for fatigue levels (P= .005). We found no significant group/time interaction for pain levels or function. CONCLUSIONS: Undertaking 15 minutes of moderate-intensity aerobic cycling exercise had no significant adverse effects on pain or function in people with MS and CFS (with a Karnofsky score of 50-80) within a 24-hour time period. These initial results suggest that people with MS or CFS may undertake 15 minutes of cycling as moderate aerobic exercise with no expected negative impact on pain or function
LeBlanc TW, Nipp RD, Rushing CN, Samsa GP, Locke SC, Kamal AH, Cella D, Abernethy AP.	Duke Cancer Institute, Duke University School of Medicine; Center for Learning Health Care, Duke Clinical Research Institute; Divisions of Hematologic Malignancies and Cellular Therapy	Correlation Between the International Consensus Definition of the Cancer Anorexia Cachexia Syndrome (CACS) and Patient-Centered Outcomes in Advanced Non-Small Cell Lung Cancer.	J Pain Symptom Manage. 2014 Nov 4. doi:pii: S0885-3924(14)00545-4. 10.1016/j.jpainsymman.2014.09.008.	CONTEXT: The cancer anorexia-cachexia syndrome (CACS) is common in patients with advanced solid tumors and is associated with adverse outcomes including poor quality of life (QOL), impaired functioning, and shortened survival. OBJECTIVES: To apply the recently posed weight-based international consensus CACS definition to a population of patients with advanced non-small cell lung cancer (NSCLC) and explore its impact on patient-reported outcomes. METHODS: Ninety-nine patients participated in up to four study visits over a six-month period. Longitudinal assessments included measures of physical function, QOL, and other clinical variables like weight and survival. RESULTS: Patients meeting the consensus CACS criteria at visit 1 had a significantly shorter median survival (239.5 vs. 446 days, HR 2.06, P<0.05). Physical function was worse in the CACS group (mean Karnofsky Performance Status score 68 vs. 77, Eastern Cooperative Oncology Group Performance Status score 1.8 s. 1.3, P<0.05 for both), as was QOL (Functional Assessment of Cancer Therapy-General (FACT-G) Lung Cancer Subscale of 17.2 vs. 19.9, Anorexia/Cachexia Subscale of 31.4 vs. 37.9, P<0.05 for both). Differences in the FACT-G and the Functional Assessment of Chronic Illness Therapy Fatigue Subscale approached but did not reach statistical significance. Longitudinally, all measures of physical function and QOL worsened regardless of CACS status, but the rate of decline was more rapid in the CACS group. CONCLUSION: The weight-based component of the recently-proposed international consensus CACS definition is useful in identifying patients with advanced NSCLC who are likely to have significantly inferior survival and who will develop more precipitous declines in physical function and QOL. This definition may be useful for clinical screening purposes and identify patients with high palliative care needs
Lee YC, Frits ML, Iannaccone CK, Weinblatt ME, Shadick NA, Williams DA, Cui J.	Harvard Medical School and Brigham and Women's Hospital, Boston, Massachusetts	Subgrouping of patients with rheumatoid arthritis based on pain, fatigue, inflammation, and	Arthritis Rheumatol. 2014 Aug;66(8):2006-14. doi: 10.1002/art.38682.	OBJECTIVE: Among patients with rheumatoid arthritis (RA), pain may be attributed to peripheral inflammation or other causes, such as central pain mechanisms. The aim of this study was to use self-report measures and physical examination findings to identify clusters of RA patients who may have different causes of pain as well as different prognoses and treatment options. METHODS: Data from 169 RA patients with pain scores of >0 (on a 10-point numeric rating scale) in the Brigham and

		psychosocial factors.		Women's Hospital Rheumatoid Arthritis Sequential Study were analyzed. The patients completed questionnaires on pain, fatigue, and psychosocial factors. A hierarchical agglomerative clustering procedure with Ward's method was used to obtain subgroups. Multivariate analysis of variance was used to determine the contribution of each variable in a cluster. General linear regression models were used to examine differences in clinical characteristics across subgroups. Discriminant analyses were performed to determine coefficients for linear combinations of variables that assigned cluster membership to individual cases. RESULTS: Three clusters best fit these data. Cluster 1 consisted of 89 individuals with low levels of inflammation, pain, fatigue, and psychosocial distress. Cluster 2 consisted of 57 individuals with minimal inflammation but high levels of pain, fatigue, and psychosocial distress. Cluster 3 consisted of 23 individuals with active inflammatory disease, manifested by high swollen joint counts, high C-reactive protein levels, and high levels of pain and fatigue. CONCLUSION: Although most patients had low levels of inflammation, pain, and fatigue, 47.3% continued to report having moderate to high levels of pain and fatigue. Most of these patients had minimal signs of inflammation but high levels of fatigue, pain catastrophizing, and sleep disturbance, indicative of a chronic widespread pain syndrome
Lendrem D, Mitchell S, McMeekin P, Bowman S, Price E, Pease CT, Emery P, Andrews J, Lanyon P, Hunter J, Gupta M, Bombardieri M, Sutcliffe N, Pitzalis C, McLaren J, Cooper A, Regan M, Giles I, Isenberg D, Vadivelu S, Coady D, Dasgupta B, et al.	Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK	Health-related utility values of patients with primary SjÃ¶gren's syndrome and its predictors.	Ann Rheum Dis. 2014 Jul;73(7):1362-8. doi: 10.1136/annrheumdis-2012-202863. Epub 2013 Jun 12.	OBJECTIVES: EuroQoL-5 dimension (EQ-5D) is a standardised preference-based tool for measurement of health-related quality of life and EQ-5D utility values can be converted to quality-adjusted life years (QALYs) to aid cost-utility analysis. This study aimed to evaluate the EQ-5D utility values of 639 patients with primary Sjögren's syndrome (PSS) in the UK. METHODS: Prospective data collected using a standardised pro forma were compared with UK normative data. Relationships between utility values and the clinical and laboratory features of PSS were explored. RESULTS: The proportion of patients with PSS reporting any problem in mobility, self-care, usual activities, pain/discomfort and anxiety/depression were 42.2%, 16.7%, 56.6%, 80.6% and 49.4%, respectively, compared with 5.4%, 1.6%, 7.9%, 30.2% and 15.7% for the UK general population. The median EQ-5D utility value was 0.691 (IQR 0.587-0.796, range -0.239 to 1.000) with a bimodal distribution. Bivariate correlation analysis revealed significant correlations between EQ-5D utility values and many clinical features of PSS, but most strongly with pain, depression and fatigue (R values>0.5). After adjusting for age and sex differences, multiple regression analysis identified pain and depression as the two most important predictors of EQ-5D utility values, accounting for 48% of the variability. Anxiety, fatigue and body mass index were other statistically significant predictors, but they accounted for <5% in variability. CONCLUSIONS: This is the first report on the EQ-5D utility values of patients with PSS. These patients have significantly impaired utility values compared with the UK general population. EQ-5D utility values are significantly related to pain and depression scores in PSS.

Levy J, Bernstein L, Silber N.	Department of Pediatrics, New York University School of Medicine, New York, NY	Celiac disease: an immune dysregulation syndrome.	Curr Probl Pediatr Adolesc Health Care. 2014 Dec;44(11):324-7. doi: 10.1016/j.cppeds.2014.10.002.	Celiac disease is a chronic immune-mediated condition that develops in genetically predisposed individuals. It is characterized by the presence of circulating auto-antibodies in addition to an enteropathy and at times, other extra-intestinal manifestations triggered by exposure to the gliadin fraction of gluten, a family of proteins found in wheat, barley, and rye. There seems to be a rise in reported adverse reactions to gluten, an entity currently termed non-celiac gluten (or perhaps more accurately, wheat) sensitivity, where neither the enteropathy nor the auto-antibodies are present. Celiac disease has protean extra-intestinal manifestations, and an accurate diagnosis should be sought in people suffering from seemingly unrelated complaints, such as fatigue, anorexia, delayed puberty, short stature, decreased bone density, unusual skin rashes, unexplained iron deficiency, and infertility. The presence of an enteropathy, in conjunction with the positive serology, is considered the diagnostic gold standard for making the diagnosis of celiac disease. It is important to stress that the elimination of gluten, even in asymptomatic patients, brings about health benefits, particularly in relation to bone health, as well as a decrease in the incidence of small bowel malignancy, especially lymphoma. Better understanding of the pathophysiology of celiac disease and the molecular mechanisms involved in antigen recognition and processing has provided the impetus for the development of pharmacologic agents that might block the recognition of gluten and its conversion to a toxic antigenic target. Inhibition of tight junction dysregulation could also prevent or minimize the damage triggered by gluten. Work on genetically modified wheat cultivars has progressed, and the possibility of a vaccine to block the immune mediated trigger is being actively investigated. Education and guidance by a knowledgeable nutritionist or registered dietitian can go a long way in minimizing the stress and facilitating the acceptance of the diet and the life-style changes that it represents
LeÅ›niak K, Kade G, Niemczyk S.	No address given	[Acute renal failure in the course of renal-ocular syndrome].	Pol Merkur Lekarski. 2014 Jan;36(211):34-8. Review. Polish.	[Article in Polish] Acute tubulointerstitial nephritis with uveitis is described as TINU syndrome. This syndrome, known as a renal-ocular disease, is a rare problem. Until now there have been described 200 cases of TINU all over the world. The most frequent morbidity concerns girls and young women although it may occur at any age. Etiology of this syndrom is unknown. Diagnosis is often difficult as in approximately 65% of cases, ocular symptoms occur later than tubulointerstitial nephritis. General symptoms (fever, weight loss, weakening, fatigue) are frequently nonspecific. There are no randomized studies dealing with treatment of TINU syndrome. Glucocoticosteroids and immunosuppressive drugs are mainly administered. The prospects are generally good, particularly among young children. However, in some patients chronic renal failure develops. Uveitis is treated locally with steroids. The prospects are good as well but inflammation process returns. A study of TINU syndrome has a general

				purpose of reminding of this disease which is often forgotten by doctors and the problems connected with diagnostics and treatment.
Li C, Xie M, Zhao RH, Wang BZ, Yao YC.	No address given	[Effect of chaishu sijun decoction on the gonad axis of gan-qi stagnation, Pi deficiency, and gan-qi stagnation pi deficiency model rats].	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2014 Jun;34(6):694-7. Chinese.	[Article in Chinese] OBJECTIVE: To observe changes of gonad functions of Gan-qi stagnation (GS), Pi deficiency (PD), Gan-qi stagnation Pi deficiency (GSPD) model rats, and the effect of Chaishu Sijun Decoction (CSD) on them. METHODS: Rats were randomly divided into 7 groups according to romdom digit table, i.e., the normal control group, the GS model group, the GS medication group, the PD model group, the PD medication group, the GSPD model group,and the GSPD medication group, 10 in each group. Rats in the GS model group, the PD model group, and the GSPD model group were treated with chronic restraint, improper diet +excessive fatigue, chronic restraint +improper diet +excessive fatigue. The model was established for 4 successive weeks. Starting from the 15th day of modeling, CSD at the daily dose of 3.57 g/kg was given by gastrogavage to them for 14 successive days. Equal volume of distilled water was given by gastrogavage to rats in each model group and the normal control group for 14 successive days. The blood contents of gonadotrophin releasing hormone (GnRH), follicular stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), and testosterone (T) were detected in rats of each group. RESULTS: Compared with the normal control group, there was statistical difference in GnRH, T, E, and FSH in the GS, PD, and GSPD model groups ($P < 0.05$, $P < 0.01$). The content of LH was elevated in the GS model group ($P < 0.05$) and declined in the GSPD model group ($P < 0.01$). Compared with the GS model group, the contents of FSH, LH, and T decreased and E2 increased in the PD model group (all $P < 0.05$); the contents of FSH and LH also declined in the GSPD model group ($P < 0.05$). Compared with the PD model group, the T content increased and FSH decreased in the GSPD model group (all $P < 0.05$). Compared with each corresponding model group, the FSH content decreased ($P < 0.01$) and LH increased in the GS medication group; the T content increased, E2 and LH decreased ($P < 0.05$, $P < 0.01$) in the PD medication group; the T content decreased ($P < 0.01$), GnRH, E2, FSH, and LH increased ($P < 0. 05$, $P < 0.01$) in the GSPD medication group. CONCLUSIONS: There exist different degrees of abnormal function of the gonad axis in the GS, PD, and GSPD models. CSD had certain regulatory effect on the 3 syndromes. Of them, it showed a more comprehensive role in improving the gonad function axis. Results of this experiment had provided the experimental evidence for higher correlation between CSD and GSPD syndrome.

Li M, Xu C, Yao W, Mahan CM, Kang HK, Sandbrink F, Zhai P, Karasik PA.	Department of Veterans Affairs Medical Center, War-Related Illness and Injury Study Center Washington, DC, USA ; Neurology Service, Department of Veterans Affairs Medical Center Washington, DC, USA ; Research Service, Department of Veterans Affairs Medical Center Washington, DC, USA.	Self-reported post-exertional fatigue in Gulf War veterans: roles of autonomic testing.	Front Neurosci. 2014 Jan 7;7:269. doi: 10.3389/fnins.2013.00269.	To determine if objective evidence of autonomic dysfunction exists from a group of Gulf War veterans with self-reported post-exertional fatigue, we evaluated 16 Gulf War ill veterans and 12 Gulf War controls. Participants of the ill group had self-reported, unexplained chronic post-exertional fatigue and the illness symptoms had persisted for years until the current clinical study. The controls had no self-reported post-exertional fatigue either at the time of initial survey nor at the time of the current study. We intended to identify clinical autonomic disorders using autonomic and neurophysiologic testing in the clinical context. We compared the autonomic measures between the 2 groups on cardiovascular function at both baseline and head-up tilt, and sudomotor function. We identified 1 participant with orthostatic hypotension, 1 posture orthostatic tachycardia syndrome, 2 distal small fiber neuropathy, and 1 length dependent distal neuropathy affecting both large and small fiber in the ill group; whereas none of above definable diagnoses was noted in the controls. The ill group had a significantly higher baseline heart rate compared to controls. Compound autonomic scoring scale showed a significant higher score (95% CI of mean: 1.72-2.67) among ill group compared to controls (0.58-1.59). We conclude that objective autonomic testing is necessary for the evaluation of self-reported, unexplained post-exertional fatigue among some Gulf War veterans with multi-symptom illnesses. Our observation that ill veterans with self-reported post-exertional fatigue had objective autonomic measures that were worse than controls warrants validation in a larger clinical series.
Lian OS, Nettleton S.	(1)University of Tromsø-The Arctic University of Norway, Tromsø, Norway olaug.lian@uit.no. (2)University of Tromsø-The Arctic University of Norway, Tromsø, Norway University of York, York, United Kingdom.	United We Stand": Framing Myalgic Encephalomyelitis in a Virtual Symbolic Community."	Qual Health Res. 2014 Dec 8. doi:pii: 1049732314562893.	In this article, we report on a study that seeks to explore how the contested chronic condition myalgic encephalomyelitis (ME), one of the current medical diagnoses for medically unexplained long-term exhaustion, is negotiated within the context of Norwegian internet sites. From an analysis of discussions on 14 internet forums sustained by and for people living with ME, we seek to understand how their online activity sustains a virtual symbolic community (VSC). After exploring the content on these sites, we identified four discursive domains, or fields of conversation, that are demarcated by a discursive frame, or norms, values, and goals that define and reinforce the boundaries of the community. Interpreting discursive domains and their discursive frame provides insight not only to the culture of the ME VSC but also to its role in an international social health movement, including its potential for becoming politically influential.
Lievesley K, Rimes KA, Chalder T.	Chronic Fatigue Research and Treatment Unit, South London and Maudsley NHS Trust, 1st Floor, Mapother House, De Crespigny Park,	A review of the predisposing, precipitating and perpetuating factors in Chronic Fatigue Syndrome in children and adolescents.	Clin Psychol Rev. 2014 Apr;34(3):233-48. doi: 10.1016/j.cpr.2014.02.002. Epub 2014 Mar 1. Review.	Chronic Fatigue Syndrome (CFS) is a condition characterised by severe mental and physical fatigue coupled with profound disability. The purpose of this review was to investigate psychological, social and physiological factors associated with fatigue and disability in CFS in children and adolescents. The review aimed to gain an overview of the strength of evidence for the relationship between these different factors and CFS in young people. Seventy-nine studies met the inclusion criteria and were included in the review. A narrative synthesis of these studies was conducted.

	Denmark Hill, London SE5 8AZ, UK			The strongest and most consistent finding was that rates of psychiatric co-morbidity, predominantly anxiety and depressive disorders, were higher in young people with CFS compared to healthy controls or illness control groups. Studies suggested that many children and adolescents with CFS reported that their illness began with an infection and there was some objective and prospective evidence to support this. Preliminary evidence suggested a link between CFS and a family history of CFS, high expectations from both the parent and child, personality traits such as conscientiousness and physical illness attributions. The evidence was limited by methodological problems. Few studies were prospective in nature and future research should address this. Clinical implications of the findings are discussed and a hypothesised model of the factors associated with CFS in children and adolescents is presented.
Lin Y, Liu HL, Fang J, Yu CH, Xiong YK, Yuan K.	The Nurturing Station for the State Key Laboratory of Subtropical Silviculture, Zhejiang Agriculture and Forestry University, Lin'an 311300, China; School of Pharmacy, East China University of Science and Technology, Shanghai 200237, China	Anti-fatigue and vasoprotective effects of quercetin-3-O-gentiobiose on oxidative stress and vascular endothelial dysfunction induced by endurance swimming in rats.	Food Chem Toxicol. 2014 Jun;68:290-6. doi: 10.1016/j.fct.2014.03.026. Epub 2014 Mar 29.	Chronic fatigue accumulation increases the incidence of cardiovascular disease while the treatment of antioxidants could prevent this development. We have previously shown that quercetin-3-O-gentiobiose (QG), a flavonoid isolated from tonic herb Okra, possesses anti-oxidative properties. In the present study, the protective effects of QG were evaluated in a rat model of load-induced endurance swimming. Oral administration of QG at the doses of 25-75mg/kg could significantly improve the endurance capability of rats to fatigue along with decrease serum lactic acid and blood urea nitrogen levels were decreased. Moreover, QG could alleviate vascular impairments, enhance the activities of antioxidant enzymes and attenuate the levels of inflammatory cytokines (MCP-1, IL-6 and TNF-α). The results indicated that QG had anti-fatigue and vasoprotective effects and represented a potential agent for the treatment of aortic pathology involved with fatigue- and related syndrome.
Littlejohns P.	No address given	Who values evidence?	J Neurol Neurosurg Psychiatry. 2014 Feb;85(2):123-4. doi: 10.1136/jnnp-2012-304208. Epub 2012 Dec 1. No abstract available.	Comment on J Neurol Neurosurg Psychiatry. 2014 Feb;85(2):214-9
Liu Z, Cappola AR, Crofford LJ, Guo W.	Department of Biostatistics, Richard M. Fairbanks School of Public Health and School of Medicine, Indiana University, Indianapolis, IN 46202 (ziliu@iupui.edu).	Modeling Bivariate Longitudinal Hormone Profiles by Hierarchical State Space Models.	J Am Stat Assoc. 2014 Jan 1;109(505):108-118.	The hypothalamic-pituitary-adrenal (HPA) axis is crucial in coping with stress and maintaining homeostasis. Hormones produced by the HPA axis exhibit both complex univariate longitudinal profiles and complex relationships among different hormones. Consequently, modeling these multivariate longitudinal hormone profiles is a challenging task. In this paper, we propose a bivariate hierarchical state space model, in which each hormone profile is modeled by a hierarchical state space model, with both population-average and subject-specific components. The bivariate model is constructed by concatenating the univariate models based on the hypothesized relationship. Because of the flexible framework of state space form,

				the resultant models not only can handle complex individual profiles, but also can incorporate complex relationships between two hormones, including both concurrent and feedback relationship. Estimation and inference are based on marginal likelihood and posterior means and variances. Computationally efficient Kalman filtering and smoothing algorithms are used for implementation. Application of the proposed method to a study of chronic fatigue syndrome and fibromyalgia reveals that the relationships between adrenocorticotropic hormone and cortisol in the patient group are weaker than in healthy controls
Loebel M, Strohschein K, Giannini C, Koelsch U, Bauer S, Doebis C, Thomas S, Unterwalder N, von Baehr V, Reinke P, Knops M, Hanitsch LG, Meisel C, Volk HD, Scheibenbogen C.	Institute for Medical Immunology, Charité University Medicine Berlin, Campus Virchow, Berlin, Germany	Deficient EBV-specific B- and T-cell response in patients with chronic fatigue syndrome.	PLoS One. 2014;9(1):e85387. doi: 10.1371/journal.pone.0085387.	Epstein-Barr virus (EBV) has long been discussed as a possible cause or trigger of Chronic Fatigue Syndrome (CFS). In a subset of patients the disease starts with infectious mononucleosis and both enhanced and diminished EBV-specific antibody titers have been reported. In this study, we comprehensively analyzed the EBV-specific memory B- and T-cell response in patients with CFS. While we observed no difference in viral capsid antigen (VCA)-IgG antibodies, EBV nuclear antigen (EBNA)-IgG titers were low or absent in 10% of CFS patients. Remarkably, when analyzing the EBV-specific memory B-cell reservoir in vitro a diminished or absent number of EBNA-1- and VCA-antibody secreting cells was found in up to 76% of patients. Moreover, the ex vivo EBV-induced secretion of TNF-α and IFN-γ was significantly lower in patients. Multicolor flow cytometry revealed that the frequencies of EBNA-1-specific triple TNF-α/IFN-γ/IL-2 producing CD4(+) and CD8(+) T-cell subsets were significantly diminished whereas no difference could be detected for HCMV-specific T-cell responses. When comparing EBV load in blood immune cells, we found more frequently EBER-DNA but not BZLF-1 RNA in CFS patients compared to healthy controls suggesting more frequent latent replication. Taken together, our findings give evidence for a deficient EBV-specific B- and T-cell memory response in CFS patients and suggest an impaired ability to control early steps of EBV reactivation. In addition the diminished EBV response might be suitable to develop diagnostic marker in CFS.
Lu C, Yang XJ, Hu J.	No address given	[Randomized controlled clinical trials of acupuncture and moxibustion treatment of chronic fatigue syndrome patients].	Zhen Ci Yan Jiu. 2014 Aug;39(4):313-7.	[Article in Chinese] OBJECTIVE: To observe the therapeutic effect of acupuncture and moxibustion interventions in the treatment of chronic fatigue syndrome (CFS). METHODS: A total of 133 CFS patients were randomized into acupuncture group (47 cases), warm-needling group (44 cases) and non-acupoint group (42 cases). Manual acupuncture (MA) stimulation was applied to Baihui (GV 20), Danzhong (CV 17), Qihai (CV 6), Guanyuan (CV 4), bilateral Zusanli (ST 36), Hegu (LI 4), Taichong (LR 3) and Sanyinjiao (SP 6) for patients in the acupuncture group. For patients n the warm-needling group, moxa-heated needle was applied to Baihui (GV 20), Qihai (CV 6), Guanyuan (CV 4) and bilateral Zusanli (ST 36). Non-acupoints were located about 1-2 cm beside the Baihui (GV 20), Danzhong (CV 17), Qihai (CV 6), Guanyuan (CV 4),

				Zusanli (ST 36), Taichong (LR 3), Sanyinjiao (SP 6) and Hegu (LI 4). The treatment was given once daily for 20 days. The Chalder Fatigue Scale (14-item fatigue scale) was adopted to evaluate the changes of CFS before and after the treatment. RESULTS: In comparison with pre-treatment, the scores of Chalder Fatigue Scale including physical and mental fatigue and total score were significantly decreased in both acupuncture and warm-needling groups ($P < 0.05$, $P < 0.01$), but not in the non-acupoint group ($P > 0.05$) except physical score ($P < 0.05$). The physical, mental and total scores of the acupuncture and warm-needling groups were significantly lower than those of the non-acupoint group ($P < 0.05$, $P < 0.01$), while the physical and total scores of the warm-needling group were markedly lower than those of the acupuncture group ($P < 0.05$). After the treatment, the CFS patients' satisfactory rates of the acupuncture, warm-needling and non-acupoint groups were 36.2% (17/47), 72.7% (32/44) and 35.7% (15/42), respectively. CONCLUSION: Both MA and warm-needling interventions have a good therapeutic effect in the treatment of CFS patients, while the latter is obviously better.
Lu Y, Liu Y, Li Y.	(1)Laboratory of Oral Biomedical Science and Translational Medicine, Department of Orthodontics, School of Stomatology, Tongji University, Shanghai, China. (2)Laboratory of Oral Biomedical Science and Translational Medicine, Department of Orthodontics, School of Stomatology, Tongji University, Shanghai, China. Electronic address: liuyuehua@tongji.edu.cn	Comparison of natural estrogens and synthetic derivative on genioglossus function and estrogen receptors expression in rats with chronic intermittent hypoxia.	J Steroid Biochem Mol Biol. 2014 Mar;140:71-9. doi: 10.1016/j.jsbmb.2013.12.006. Epub 2013 Dec 12.	The pathogenesis of obstructive sleep apnea--hypopnea syndrome (OSAHS) is summarized as the narrow anatomic structure of upper airway (UA) and the defective function of UA dilator muscles. Up to now, there have been no specific reatments for the UA dilator muscle deficiency. We previously found that some estrogen-like compounds exert protective effects on genioglossus, but this protection tends to be less satisfactory. A novel phytoestrogen derivative was synthesized in recent years and was verified to have some cytoprotective activity. This study was designed to compare the effects of natural estrogens and the synthetic resveratrol dimer on genioglossus contraction and expression of estrogen receptors (ERs) under chronic intermittent hypoxia (CIH) condition. Genioglossus myoblasts of rat were isolated and cultured in a culture medium with different agents (estradiol, genistein, resveratrol, and resveratrol dimer, respectively) under hypoxia condition, and ERs expressions were detected. In vivo study, 48 ovariectomized female rats were randomized into six groups. After CIH exposure and agents injection, rats were tested for genioglossus contractile properties and further analysis of ERs expression. Estradiol up-regulated ERα level and exerted the best protective effect of fatigue resistance. Genistein, resveratrol and resveratrol dimer primarily up-regulated the expression of ERβ. Resveratrol dimer exhibited better protection of fatigue resistance than genistein and resveratrol, and expressed higher binding affinity for ERβ than for ERα. Besides estrogenic effects, there may be some other mechanisms for the fatigue resistance improvement contributed by phytoestrogens and their derivatives.

Lum E, Medveczky MM, Medveczky PG.	The HHV-6 Foundation, Santa Barbara, CA 93101, USA	Is inherited human herpesvirus 6 the perpetrator behind some cases of chronic fatigue syndrome?	Future Microbiol. 2014;9(4):433-6. doi: 10.2217/fmb.14.11.	No abstract available
LÃ¶we B, Andresen V, Fraedrich K, Gappmayer K, Wegscheider K, Treszl A, Riegel B, Rose M, Lohse AW, Broicher W.	Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Hamburg-Eppendorf and Schön Klinik Hamburg-Eilbek, Hamburg, Germany. Electronic address: b.loewe@uke.uni-hamburg.de.	Psychological Outcome, Fatigue, and Quality of Life After Infection With Shiga Toxin-Producing Escherichia coli O104.	Clin Gastroenterol Hepatol. 2014 Nov;12(11):1848-55. doi: 10.1016/j.cgh.2014.02.035. Epub 2014 Mar 13.	BACKGROUND & AIMS: From May through July 2011 in northern Germany, there was a large outbreak of hemolytic uremic syndrome and bloody diarrhea, which was related to infections from Shiga toxin-producing Escherichia coli O104 (STEC). We investigated the depression, posttraumatic symptoms, fatigue, and health-related quality of life among patients within the first 6 months after STEC infection and aimed to identify factors associated with poor outcome. METHODS: In a cohort study, we performed baseline assessments of 389 patients (69% female) 3 months after STEC infection (82 ± 36 days) and follow-up assessments of 308 of the patients 6 months afterward (199 ± 17 days). Data were collected at 13 hospitals in northern Germany. Patients completed validated self-report scales and a diagnostic interview. RESULTS: At baseline, hemolytic uremic syndrome was diagnosed in 31% of the patients. Six months after the infection, mean self-reported severity of depression and posttraumatic symptoms and fatigue were significantly greater than in the general population, and the mean score from the mental component of health-related quality of life survey was significantly lower than average. Posttraumatic stress disorder had recently developed in 3% of patients (95% confidence interval, 1%-5%), and 43% of patients had clinically relevant fatigue (95% confidence interval, 41%-45%). The most important baseline factors associated with poor psychological health 6 months after STEC infection were previous traumatic events, neuroticism, and low social support (all P < .05). CONCLUSIONS: Six months after the major outbreak of STEC infection in northern Germany, a substantial number of patients had poor psychological health, persistent fatigue, and impaired quality of life. For future outbreaks, patients' premorbid risk factors should be considered, which might minimize the long-term effects of infections on mental health.
Maes M, Leunis JC, Geffard M, Berk M.	(1)Maes Clinics @ TRIA, Bangkok, Thailand, Thailand. (2)Laboratory Ategis, Wavre, Belgium. (3)Association Institute	Evidence for the existence of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) with and without	Neuro Endocrinol Lett. 2014 Nov 2;35(6):445-453.	BACKGROUND: There is evidence that Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is accompanied by gastro-intestinal symptoms; and IgA and IgM responses directed against lipopolysaccharides (LPS) of commensal bacteria, indicating bacterial translocation. METHODS: This study was carried out to examine gastro-intestinal symptoms in subjects with ME/CFS versus those with chronic fatigue (CF). The two groups were issected by dichotomizing those fulfilling and not

	for Research and Development in Human Pathology and Therapy, Talence, France. (4)Department of Psychiatry, Deakin University, Geelong, Australia.	abdominal discomfort (irritable bowel) syndrome.		fulfilling Fukuda's critera. In these groups, we examined the association between gastro-intestinal symptoms and the IgA and IgM responses directed against commensal bacteria. RESULTS: Using cluster analysis performed on gastro-intestinal symptoms we delineated that the cluster analysis-generated diagnosis of abdominal discomfort syndrome (ADS) was significantly higher in subjects with ME/CFS (59.6%) than in those with CF (17.7%). The diagnosis of ADS was strongly associated with the diagnosis of irritable bowel syndrome (IBS). There is evidence that ME/CFS consists of two subgroups, i.e. ME/CFS with and without ADS. Factor analysis showed four factors, i.e. 1) inflammation-hyperalgesia; 2) fatigue-malaise; 3) gastro-intestinal symptoms/ADS; and 4) neurocognitive symptoms. The IgA and IgM responses to LPS of commensal bacteria were significantly higher in ME/CFS patients with ADS than in those without ADS. CONCLUSIONS: The findings show that ADS is a characteristic of a subset of patients with ME/CFS and that increased bacterial translocation (leaky gut) is associated with ADS symptoms. This study has defined a pathway phenotype, i.e bacterial translocation, that is related to ME/CFS and ADS/IBS and that may drive systemic inflammatory processes.
Maric D, Brkic S, Tomic S, Novakov Mikic A, Cebovic T, Turkulov V.	(1)Clinic for Infectious Diseases, Clinical Center Vojvodina, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia. (2)Faculty of Medicine, University of Novi Sad, Serbia. (3)Biochemistry Department, Clinical Center Vojvodina, Faculty of Medicine, University of Novi Sad, Serbia.	Multivitamin mineral supplementation in patients with chronic fatigue syndrome.	Med Sci Monit. 2014 Jan 14;20:47-53. doi: 10.12659/MSM.889333.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by medically unexplained persistent or reoccurring fatigue lasting at least 6 months. CFS has a multifactorial pathogenesis in which oxidative stress (OS) plays a prominent role. Treatment is with a vitamin and mineral supplement, but this therapeutic option so far has not been properly researched. MATERIAL AND METHODS: This prospective study included 38 women of reproductive age consecutively diagnosed by CDC definition of CFS and treated with a multivitamin mineral supplement. Before and after the 2-month supplementation, SOD activity was determined and patients self-assessed their improvement in 2 questionnaires: the Fibro Fatigue Scale (FFS) and the Quality of Life Scale (SF36). Results There was a significant improvement in SOD activity levels; and significant decreases in fatigue (p=0.0009), sleep disorders (p=0.008), autonomic nervous system symptoms (p=0.018), frequency and intensity of headaches (p=0.0001), and subjective feeling of infection (p=0.0002). No positive effect on quality of life was found. CONCLUSIONS: Treatment with a vitamin and mineral supplement could be a safe and easy way to improve symptoms and quality of life in patients with CFS.
MartÃ-Carvajal AJ, Anand V, Cardona AF, SolÃ I.	Iberoamerican Cochrane Network, Valencia, Venezuela	Eculizumab for treating patients with paroxysmal nocturnal hemoglobinuria.	Cochrane Database Syst Rev. 2014 Oct 30;10:CD010340. doi: 10.1002/14651858.CD010340.pub2. Review.	BACKGROUND: Paroxysmal nocturnal hemoglobinuria (PNH) is a chronic, not malignant, disease of the hematopoietic stem cells, associated with significant morbidity and mortality. It is a rare disease with an estimated incidence of 1.3 new cases per one million individuals per year. The treatment of PNH has been largely empirical and symptomatic, with blood transfusions, anticoagulation, and supplementation with folic acid or iron. Eculizumab, a biological agent that inhibits complement cascade, was developed for preventing hemolytic anemia and severe thrombotic episodes. OBJECTIVES: To assess the clinical benefits and harms of

				eculizumab for treating patients with paroxysmal nocturnal hemoglobinuria (PNH). SEARCH METHODS: We conducted a comprehensive search strategy. We searched the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library 2014, Issue 5), Ovid MEDLINE (from 1946 to 15 May 2014), EMBASE (from 1980 to 25 June 2014), and LILACS (from 1982 to 25 June 2014). We did not apply any language restrictions. SELECTION CRITERIA: We included randomized controlled trials (RCTs) irrespective of their publication status or language. No limits were applied with respect to period of follow-up. We excluded quasi-RCTs. We included trials comparing eculizumab with placebo or best available therapy. We included any patient with a confirmed diagnosis of PNH. Primary outcome was overall survival. DATA COLLECTION AND ANALYSIS: We independently performed a duplicate selection of eligible trials, risk of bias assessment, and data extraction. We estimated risk ratios (RRs) and 95% confidence interval (CIs) for dichotomous outcomes, and mean differences (MDs) and 95% CIs for continuous outcomes. We used a random-effects model for analysis. MAIN RESULTS: We identified one multicenter (34 sites) phase III RCT involving 87 participants. The trial compared eculizumab versus placebo, and was conducted in the US, Canada, Europe, and Australia with 26 weeks of follow-up. This small trial had high risk of bias in many domains (attrition and selective reporting). It was sponsored by a pharmaceutical company. No patients died during the study. By using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (scores can range from 0 to 100, with higher scores on the global health status and functioning scales indicating improvement), the trial showed improvement in health-related quality of life in patients treated with eculizumab (mean difference (MD) 19.4, 95% CI 8.25 to 30.55; P = 0.0007; low quality of evidence). By using the Functional Assessment of Chronic Illness Therapy Fatigue instrument (scores can range from 0 to 52, with higher scores indicating improvement in fatigue), the trial showed a reduction in fatigue (MD 10.4, 95% CI 9.97 to 10.83; P = 0.00001; moderate quality of evidence) in the eculizumab group compared with placebo. Eculizumab compared with placebo showed a greater proportion of patients with transfusion independence: 51% (22/43) versus 0% (0/44); risk ratio (RR) 46.02, 95% CI 2.88 to 735.53; P = 0.007; moderate quality of evidence; and withdrawal for any reason: 4.7% (2/43) versus 22.72% (10/44); RR 0.20, 95% CI 0.05 to 0.88; P = 0.03; moderate quality of evidence. Due to the low rate of events observed, the included trial did not show any difference between eculizumab and placebo in terms of serious adverse events: 9.3% (4/43) versus 20.4% (9/44); RR 0.15, 95% CI 0.15 to 1.37; P = 0.16; low quality of evidence. We did not observe any difference between intervention and placebo for the most frequent adverse events. One participant receiving placebo showed an episode of thrombosis. The trial did not assess overall survival, transformation to myelodysplastic syndrome and acute myelogenous

				leukemia, or development or recurrence of aplastic anemia on treatment. AUTHORS' CONCLUSIONS: This review has detected an absence of evidence for eculizumab compared with placebo for treating paroxysmal nocturnal hemoglobinuria (PNH), in terms of overall survival, nonfatal thrombotic events, transformation to myelodysplastic syndrome and acute myelogenous leukemia, and development and recurrence of aplastic anemia on treatment. Current evidence indicates that compared with placebo, eculizumab increases health-related quality of life and increases transfusion independence. During the execution of the included trial, no patients died. Furthermore, the intervention seems to reduce fatigue and withdrawals for any reason. The safety profile of eculizumab is unclear. These conclusions are based on one small trial with risk of attrition and selective reporting bias.Therefore, prescription of eculizumab for treating patients with PNH can neither be supported nor rejected, unless new evidence from a large high quality trial alters this conclusion. Therefore, we urge the reader to interpret the trial results with much caution. Future trials on this issue should be conducted according to the SPIRIT statement and reported according to the CONSORT statement by independent investigators, and using the Foundation of Patient-Centered Outcomes Research recommendations.
MartÃnez-MartÃ-nez LA, Mora T, Vargas A, Fuentes-Iniestra M, MartÃ-nez-LavÃn M.	Instituto Nacional de Cardiología Ignacio Chávez, Mexico City, Mexico	Sympathetic nervous system dysfunction in fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, and interstitial cystitis: a review of case-control studies.	J Clin Rheumatol. 2014 Apr;20(3):146-50. doi: 10.1097/RHU.0000000000000089. Review.	BACKGROUND: Fibromyalgia often coexists and overlaps with other syndromes such as chronic fatigue, irritable bowel syndrome, and interstitial cystitis. Chronic stress has been implicated in the pathogenesis of these illnesses. The sympathetic nervous system is a key element of the stress response system. Sympathetic dysfunction has been reported in these syndromes, raising the possibility that such dysautonomia could be their common clustering underlying pathogenesis. OBJECTIVE: The objective of this study was to carry out a review of all published comparative case-control studies investigating sympathetic nervous system performance in fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, and interstitial cystitis. METHODS: Online databases PubMed and EMBASE were accessed using the following key words: autonomic (OR) sympathetic (AND) fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, and interstitial cystitis. All entries up to December 10th 2012 were reviewed by 2 independent investigators searching for case-control studies in humans. The Method for Evaluating Research and Guidelines Evidence adapted to the Scottish Intercollegiate Guidelines Network was used to rank the level of evidence contained in the selected articles. RESULTS: A total of 196 articles are included in this review. The most often used methods to assess sympathetic functionality were heart rate variability analysis, sympathetic skin response, tilt table testing, and genetic studies. The majority of studies (65%) described sympathetic nervous system predominance in these overlapping syndromes. In contrast, 7% of the studies found parasympathetic predominance. CONCLUSIONS: This review demonstrates that sympathetic nervous system

				predominance is common in fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, and interstitial cystitis. This concordance raises the possibility that sympathetic dysfunction could be their common underlying pathogenesis that brings on overlapping clinical features. The recognition of sympathetic predominance in these 4 syndromes may have potential clinical implications. It may be worth exploring the use of nonpharmacological measures as well as drug therapies aimed to regain autonomic balance.
Matthees A.	P.O. Box 6483, East Perth, WA, 6892, Australia, alem.matthees@gmail.com	Assessment of recovery status in chronic fatigue syndrome using normative data.	Qual Life Res. 2014 Oct 11.	INTRODUCTION: Adamowicz et al. have reviewed criteria previously employed to define recovery in chronic fatigue syndrome (CFS). They suggested such criteria have generally lacked stringency and consistency between studies and recommended future research should require "normalization of symptoms and functioning". METHODS: Options regarding how "normalization of symptoms and functioning" might be operationalized for CFS cohorts are explored. RESULTS: A diagnosis of CFS excludes many chronic disabling illnesses present in the general population, and CFS cohorts can almost exclusively consist of people of working age; therefore, it is suggested that thresholds for recovery should not be based on population samples which include a significant proportion of sick, disabled or elderly individuals. It is highlighted how a widely used measure in CFS research, the SF-36 physical function subscale, is not normally distributed. This is discussed in relation to how recovery was defined for a large intervention trial, the PACE trial, using a method that assumes a normal distribution. Summary data on population samples are also given, and alternative methods to assess recovery are proposed. CONCLUSIONS: The "normalization of symptoms and function" holds promise as a means of defining recovery from CFS at the current time. However, care is required regarding how such requirements are operationalized, otherwise recovery rates may be overstated, and perpetuate the confusion and controversy noted by Adamowicz et al
Maughan D, Toth M.	(1)Department of Molecular Physiology & Biophysics, University of Vermont, Burlington, VT 05405, USA. dmaughan@uvm.edu. (2) Department of Molecular Physiology & Biophysics, University of Vermont, Burlington, VT 05405,	Discerning primary and secondary factors responsible for clinical fatigue in multisystem diseases.	Biology (Basel). 2014 Sep 22;3(3):606-22. doi: 10.3390/biology3030606. Review.	Fatigue is a common symptom of numerous acute and chronic diseases, including myalgic encephalomyelitis/chronic fatigue syndrome, multiple sclerosis, heart failure, cancer, and many others. In these multi-system diseases the physiological determinants of enhanced fatigue encompass a combination of metabolic, neurological, and myofibrillar adaptations. Previous research studies have focused on adaptations specific to skeletal muscle and their role in fatigue. However, most have neglected the contribution of physical inactivity in assessing disease syndromes, which, through deconditioning, likely contributes to symptomatic fatigue. In this commentary, we briefly review disease-related muscle phenotypes in the context of whether they relate to the primary disease or whether they develop secondary to reduced physical activity. Knowledge of the etiology of the skeletal muscle adaptations in these conditions and their contribution to fatigue symptoms

	USA. mtoth@uvm.edu.			is important for understanding the utility of exercise rehabilitation as an intervention to alleviate the physiological precipitants of fatigue
McDermott C, Al Haddabi A, Akagi H, Selby M, Cox D, Lewith G.	Department of Primary Care and Population Science, University of Southampton, Southampton, Hampshire, UK	What is the current NHS service provision for patients severely affected by chronic fatigue syndrome/myalgic encephalomyelitis? A national scoping exercise.	BMJ Open. 2014 Jul 1;4(6):e005083. doi: 10.1136/bmjopen-2014-005083.	BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), in its most severe clinical presentation, can result in patients becoming housebound and bedbound so unable to access most available specialist services. This presents particular clinical risks and treatment needs for which the National Institute for Health and Care Excellence (NICE) advises specialist medical care and monitoring. The extent of National Health Service (NHS) specialist provision in England for severe CFS/ME is currently unknown. OBJECTIVES: To establish the current NHS provision for patients with severe CFS/ME in England. SETTING AND PARTICIPANTS: All 49 English NHS specialist CFS/ME adult services in England, in 2013. METHOD: Cross-sectional survey by email questionnaire. PRIMARY OUTCOME MEASURES: Adherence to NICE guidelines for severe CFS/ME. RESULTS: All 49 services replied (100%). 33% (16/49) of specialist CFS/ME services provided no service for housebound patients. 55% (27/49) services did treat patients with severe CFS/ME and their interventions followed the NICE guidelines. The remaining services (12%, 6/49) offered occasional or minimal support where funding allowed. There was one NHS unit providing specialist inpatient CFS/ME provision in England. CONCLUSIONS: Study findings highlight substantial variation in access to specialist care for patients with severe presentation of CFS/ME. Where treatment was provided, this appeared to comply with NICE recommendations for this patient group
McDonald C, Koshi S, Busner L, Kavi L, Newton JL.	(1)Institute for Ageing & Health, Campus for Ageing & Vitality, Medical School, Newcastle University, Newcastle Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. (2)PoTs UK, www.potsuk.org.	Postural tachycardia syndrome is associated with significant symptoms and functional impairment predominantly affecting young women: a UK perspective.	BMJ Open. 2014 Jun 16;4(6):e004127. doi: 10.1136/bmjopen-2013-004127.	OBJECTIVE: To examine a large UK cohort of patients with postural tachycardia syndrome (PoTS), to compare demographic characteristics, symptoms and treatment of PoTS at one centre compared to the largest patient group PoTS UK and to verify if their functional limitation is similar to patients with chronic fatigue syndrome (CFS). DESIGN: A cross-sectional study assessed the frequency of symptoms and their associated variables. PATIENTS AND SETTING: Two PoTS cohorts were: (1) recruited via PoTS UK, (2) diagnosed at Newcastle Hospitals National Health Service (NHS) Foundation Trust 2009-2012. Patients with PoTS were then compared to a matched cohort with CFS. MAIN OUTCOME MEASURES: Patients' detailed demographics, time to diagnosis, education, disability, medications, comorbidity and precipitants. Symptom assessment tools captured, Fatigue Impact Scale, Epworth Sleepiness Scale, Orthostatic Grading Scale (OGS), Hospital Anxiety and Depression Scale, Health Assessment Questionnaire, Cognitive Failures Questionnaire. RESULTS: 136 patients with PoTS participated (84 members of PoTS UK (170 cohort; 50% return) and 52 (87 cohort; 60%) from Newcastle Clinics). The PoTS UK population was significantly younger than the clinic patients, with significantly fewer men (p=0.005). Over 60% had a university or postgraduate

				degree. Significantly more of the PoTS UK cohort were working, with hours worked being significantly higher (p=0.001). Time to diagnosis was significantly longer in the PoTS UK cohort (p=0.04). Symptom severity was comparable between cohorts. The PoTS total group was compared with a matched CFS cohort; despite comparable levels of fatigue and sleepiness, autonomic symptom burden (OGS) was statistically significantly higher. The most common treatment regime included β-blockers. Overall, 21 treatment combinations were described. Up to 1/3 were taking no treatment. CONCLUSIONS: Patients with PoTS are predominantly women, young, well educated and have significant and debilitating symptoms that impact significantly on quality of life. Despite this, there is no consistent treatment.
McInnis OA, McQuaid RJ, Bombay A, Matheson K, Anisman H.	Department of Neuroscience, Carleton University, Ottawa, ON, Canada	Finding benefit in stressful uncertain circumstances: relations to social support and stigma among women with unexplained illnesses.	Stress. 2014 Dec 29:1-32.	Abstract Living with a chronic illness can be challenging, but the ability to derive benefits and grow from this experience may enhance well-being. However, the possibility of obtaining such benefits may be dependent on the levels of stigmatization and lack of social support experienced by an individual as a result of the illness. Chronic fatigue syndrome (CFS) and fibromyalgia are chronic conditions that remain largely unexplained and those with these conditions must often contend with stigma and skepticism from others. Individuals with CFS/fibromyalgia often display stress-related biological alterations and the experience of stressful life events have been associated with illness development. The present study demonstrated that women with CFS/fibromyalgia (n=40) as well as community participants who were depressed/anxious (n=37), reported higher stigma levels than healthy women (n=33). Moreover, women with CFS/fibromyalgia and those with depression/anxiety also reported greater levels of stigma than women with a chronic yet more widely accepted condition (n=35; rheumatoid arthritis, osteoarthritis, and multiple sclerosis). Secrecy related to stigma among those with CFS/fibromyalgia declined with increased social support, but this was not apparent among those with other chronic conditions. In addition, posttraumatic growth was lower among women with CFS/fibromyalgia compared to those with other chronic conditions. Qualitative analysis examining both negative impacts and positive changes stemming from illness experience revealed many similarities between women with CFS/fibromyalgia and those with other chronic conditions, including elevated appreciation for life, personal growth, and compassion for others. However, women with CFS/fibromyalgia tended to report less positive change regarding interpersonal relationships compared to women with other chronic conditions. In general, unexplained illnesses were also accompanied by stigmatization which might ultimately contribute to women's lower ability to derive positive growth from their illness experience

McInnis OA, Matheson K, Anisman H.	Department of Neuroscience Carleton University Ottawa , ON Canada	Living with the unexplained: coping, distress, and depression among women with chronic fatigue syndrome and/or fibromyalgia compared to an autoimmune disorder.	Anxiety Stress Coping. 2014;27(6):601-18. doi: 10.1080/10615806.2014.888060. Epub 2014 Mar 3.	Chronic fatigue syndrome (CFS) and fibromyalgia are disabling conditions without objective diagnostic tests, clear-cut treatments, or established etiologies. Those with the disorders are viewed suspiciously, and claims of malingering are common, thus promoting further distress. It was hypothesized in the current study that levels of unsupportive social interactions and the coping styles used among those with CFS/fibromyalgia would be associated with perceived distress and depressive symptoms. Women with CFS/fibromyalgia (n=39), in fact, reported higher depression scores, greater perceived distress and more frequent unsupportive relationships than healthy women (n=55), whereas those with a chronic, but medically accepted illness comprising an autoimmune disorder (lupus erythematosus, multiple sclerosis, rheumatoid arthritis; n=28), displayed intermediate scores. High problem-focused coping was associated with low levels of depression and perceived distress in those with an autoimmune condition. In contrast, although CFS/fibromyalgia was also accompanied by higher depression scores and higher perceived distress, this occurred irrespective of problem-focused coping. It is suggested that because the veracity of ambiguous illnesses is often questioned, this might represent a potent stressor in women with such illnesses, and even coping methods typically thought to be useful in other conditions, are not associated with diminished distress among those with CFS/fibromyalgia
McLennan MT.	Obstetrics Gynecology and Women's Health, Saint Louis University School of Medicine, 6420 Clayton Road, St Louis, MO 63117, USA. Electronic address: mclennan@slu.edu	Interstitial cystitis: epidemiology, pathophysiology, and clinical presentation.	Obstet Gynecol Clin North Am. 2014 Sep;41(3):385-95. doi: 10.1016/j.ogc.2014.05.004. Epub 2014 Jul 9.	Interstitial cystitis, or painful bladder syndrome, can present with lower abdominal pain/discomfort and dyspareunia, and pain in any distribution of lower spinal nerves. Patients with this condition experience some additional symptoms referable to the bladder, such as frequency, urgency, or nocturia. It can occur across all age groups, although the specific additional symptoms can vary in prevalence depending on patient age. It should be considered in patients who have other chronic pain conditions such as fibromyalgia, chronic fatigue, irritable bowel, and vulvodynia. The cause is still largely not understood, although there are several postulated mechanisms
Medow MS, Sood S, Messer Z, Dzogbeta S, Terilli C, Stewart JM.	(1)Department of Pediatrics, New York Medical College, Valhalla, New York; and Department of Physiology, New York Medical College, Valhalla, New York marvin_medow@nymc.edu. (2)Department of Pediatrics, New York Medical College,	Phenylephrine alteration of cerebral blood flow during orthostasis: effect on n-back performance in chronic fatigue syndrome.	J Appl Physiol (1985). 2014 Nov 15;117(10):1157-64. doi: 10.1152/japplphysiol.00527.2014. Epub 2014 Oct 2.	Chronic fatigue syndrome (CFS) with orthostatic intolerance is characterized by neurocognitive deficits and impaired working memory, concentration, and information processing. In CFS, upright tilting [head-up tilt (HUT)] caused decreased cerebral blood flow velocity (CBFv) related to hyperventilation/hypocapnia and impaired cerebral autoregulation; increasing orthostatic stress resulted in decreased neurocognition. We loaded the baroreflex with phenylephrine to prevent hyperventilation and performed n-back neurocognition testing in 11 control subjects and 15 CFS patients. HUT caused a significant increase in heart rate (109.4 ± 3.9 vs. 77.2 ± 1.6 beats/min, $P < 0.05$) and respiratory rate (20.9 ± 1.7 vs. 14.2 ± 1.2 breaths/min, $P < 0.05$) and decrease in end-tidal CO_2 ($ETCO_2$; 42.8 ± 1.2 vs. 33.9 ± 1.1 Torr, $P < 0.05$) in CFS vs. control. HUT caused CBFv to decrease 8.7% in control subjects but fell 22.5% in CFS. In CFS, phenylephrine prevented the HUT-induced

	Valhalla, New York; and. (3)Department of Pediatrics, New York Medical College, Valhalla, New York; and Department of Physiology, New York Medical College, Valhalla, New York.			hyperventilation/hypocapnia and the significant drop in CBFv with HUT (-8.1% vs. -22.5% untreated). There was no difference in control subject n-back normalized response time (nRT) comparing supine to HUT (106.1 ± 6.9 vs. 97.6 ± 7.1 ms at n = 4), and no difference comparing control to CFS while supine (97.1 ± 7.1 vs 96.5 ± 3.9 ms at n = 4). However, HUT of CFS subjects caused a significant increase in nRT (148.0 ± 9.3 vs. 96.4 ± 6.0 ms at n = 4) compared with supine. Phenylephrine significantly reduced the HUT-induced increase in nRT in CFS to levels similar to supine (114.6 ± 7.1 vs. 114.6 ± 9.3 ms at n = 4). Compared with control subjects, CFS subjects are more sensitive both to orthostatic challenge and to baroreflex/chemoreflex-mediated interventions. Increasing blood pressure with phenylephrine can alter CBFv. In CFS subjects, mitigation of the HUT-induced CBFv decrease with phenylephrine has a beneficial effect on n-back outcome.
Meeus M, Nijs J, Vanderheiden T, Baert I, Descheemaeker F, Struyf F.	Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium Pain in Motion Research Group, Belgium mira.meeus@ugent.be	The effect of relaxation therapy on autonomic functioning, symptoms and daily functioning, in patients with chronic fatigue syndrome or fibromyalgia: a systematic review.	Clin Rehabil. 2014 Sep 8. doi:pii: 0269215514542635.	OBJECTIVE: To establish the effects of relaxation therapy on autonomic function, pain, fatigue and daily functioning in patients with chronic fatigue syndrome or fibromyalgia. METHOD: A systematic literature study was performed. Using specific keywords related to fibromyalgia or chronic fatigue syndrome and relaxation therapy, the electronic databases PubMed and Web of Science were searched. Included articles were assessed for their risk of bias and relevant information regarding relaxation was extracted. The review was conducted and reported according to the PRISMA-statement. RESULTS: Thirteen randomized clinical trials of sufficient quality were included, resulting in a total of 650 fibromyalgia patients (11 studies) and 88 chronic fatigue syndrome patients (3 studies). None of the studies reported effects on autonomic function. Six studies reported the effect of guided imagery on pain and daily functioning in fibromyalgia. The acute effect of a single session of guided imagery was studied in two studies and seems beneficial for pain relief. For other relaxation techniques (eg. muscle relaxation, autogenic training) no conclusive evidence was found for the effect on pain and functioning in fibromyalgia patients comparison to multimodal treatment programs. For fatigue a multimodal approach seemed better than relaxation, as shown in the sole three studies on chronic fatigue syndrome patients. CONCLUSION: There is moderate evidence for the acute effect of guided imagery on pain, although the content of the visualization is a matter of debate. Other relaxation formats and the effects on functionality and autonomic function require further study
Meeus M, Ickmans K, Struyf F, Kos D, Lambrecht L, Willekens B, Cras P, Nijs J.	Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium,	What is in a name? Comparing diagnostic criteria for chronic fatigue syndrome with or without fibromyalgia.	Clin Rheumatol. 2014 Oct 14.	The current study had two objectives. (1) to compare objective and self-report measures in patients with chronic fatigue syndrome (CFS) according to the 1994 Center for Disease Control (CDC) criteria, patients with multiple sclerosis (MS), and healthy controls, and (2) to contrast CFS patients who only fulfill CDC criteria to those who also fulfill the criteria for myalgic encephalomyelitis (ME), the 2003 Canadian criteria for ME/CFS, or the comorbid diagnosis of fibromyalgia (FM). One hundred six participants (48 CFS patients diagnosed following the 1994 CDC criteria,

	mira.meeus@ugent.be			19 MS patients, and 39 healthy controls) completed questionnaires assessing symptom severity, quality of life, daily functioning, and psychological factors. Objective measures consisted of activity monitoring, evaluation of maximal voluntary contraction and muscle recovery, and cognitive performance. CFS patients were screened whether they also fulfilled ME criteria, the Canadian criteria, and the diagnosis of FM. CFS patients scored higher on symptom severity, lower on quality of life, and higher on depression and kinesiophobia and worse on MVC, muscle recovery, and cognitive performance compared to the MS patients and the healthy subjects. Daily activity levels were also lower compared to healthy subjects. Only one difference was found between those fulfilling the ME criteria and those who did not regarding the degree of kinesiophobia (lower in ME), while comorbidity for FM significantly increased the symptom burden. CFS patients report more severe symptoms and are more disabled compared to MS patients and healthy controls. Based on the present study, fulfillment of the ME or Canadian criteria did not seem to give a clinically different picture, whereas a diagnosis of comorbid FM selected symptomatically worse and more disabled patients.
Meeus M, Hermans L, Ickmans K, Struyf F, Van Cauwenbergh D, Bronckaerts L, De Clerck LS, Moorken G, Hans G, Grosemans S, Nijs J.	Departments of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium;	Endogenous Pain Modulation in Response to Exercise in Patients with Rheumatoid Arthritis, Patients with Chronic Fatigue Syndrome and Comorbid Fibromyalgia, and Healthy Controls: A Double-Blind Randomized Controlled Trial.	Pain Pract. 2014 Feb 17. doi: 10.1111/papr.12181.	OBJECTIVE: Temporal summation (TS) of pain, conditioned pain modulation (CPM), and exercise-induced analgesia (EIA) are often investigated in chronic pain populations as an indicator for enhanced pain facilitation and impaired endogenous pain inhibition, respectively, but interactions are not yet clear both in healthy controls and in chronic pain patients. Therefore, the present double-blind randomized placebo-controlled study evaluates pains cores, TS, and CPM in response to exercise in healthy controls, patients with chronic fatigue syndrome and comorbid fibromyalgia (CFS/FM), and patients with rheumatoid arthritis (RA), both under placebo and paracetamol condition. METHODS: Fifty-three female volunteers - of which 19 patients with CFS/FM, 16 patients with RA, and 18 healthy controls - underwent a submaximal exercise test on a bicycle ergometer on 2 different occasions (paracetamol vs. placebo), with an interval of 7 days. Before and after exercise, participants rated pain intensity during TS and CPM. RESULTS: Patients with rheumatoid arthritis showed decreased TS after exercise, both after paracetamol and placebo ($P < 0.05$). In patients with CFS/FM, results were less univocal. A nonsignificant decrease in TS was only observed after taking paracetamol. CPM responses to exercise are inconclusive, but seem to worsen after exercise. No adverse effects were seen. CONCLUSION: This study evaluates pain scores, TS, and CPM in response to submaximal exercise in 2 different chronic pain populations and healthy controls. In patients with RA, exercise had positive effects on TS, suggesting normal EIA. In patients with CFS/FM, these positive effects were only observed after paracetamol and results were inconsistent

Mikirova N, Hunninghake R.	Bio-Communication Research Institute, Riordan Clinic, Wichita, USA	Effect of high dose vitamin C on Epstein-Barr viral infection.	Med Sci Monit. 2014 May 3;20:725-32. doi: 10.12659/MSM.890423.	Background Many natural compounds were tested for the ability to suppress viral replication. The present manuscript details an analysis of high dose vitamin C therapy on patients with EBV infection. Material and Methods The data were obtained from the patient history database at the Riordan Clinic. Among people in our database who were treated with intravenous vitamin C (7.5 g to 50 g infusions) between 1997 and 2006, 178 patients showed elevated levels of EBV EA IgG (range 25 to 211 AU) and 40 showed elevated levels of EBV VCA IgM (range 25 to 140 AU). Most of these patients had a diagnosis of chronic fatigue syndrome, with the rest being diagnosed as having mononucleosis, fatigue, or EBV infection. Results Our data provide evidence that high dose intravenous vitamin C therapy has a positive effect on disease duration and reduction of viral antibody levels. Plasma levels of ascorbic acid and vitamin D were correlated with levels of antibodies to EBV. We found an inverse correlation between EBV VCA IgM and vitamin C in plasma in patients with mononucleosis and CFS meaning that patients with high levels of vitamin C tended to have lower levels of antigens in the acute state of disease. In addition, a relation was found between vitamin D levels and EBV EA IgG with lower levels of EBV early antigen IgG for higher levels of vitamin D. Conclusions The clinical study of ascorbic acid and EBV infection showed the reduction in EBV EA IgG and EBV VCA IgM antibody levels over time during IVC therapy that is consistent with observations from the literature that millimolar levels of ascorbate hinder viral infection and replication in vitro
Milic S, Lulic D, Stimac D.	Sandra Milić, Davorka Lulić, Davor Štimac, Division of Gastroenterology, Department of Internal Medicine, University Hospital Rijeka, Rijeka 51000, Croatia	Non-alcoholic fatty liver disease and obesity: biochemical, metabolic and clinical presentations.	World J Gastroenterol. 2014 Jul 28;20(28):9330-7. doi: 10.3748/wjg.v20.i28.9330.	Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in the world. Presentation of the disease ranges from simple steatosis to non-alcoholic steatohepatitis (NASH). NAFLD is a hepatic manifestation of metabolic syndrome that includes central abdominal obesity along with other components. Up to 80% of patients with NAFLD are obese, defined as a body mass index (BMI) > 30 kg/m(2). However, the distribution of fat tissue plays a greater role in insulin resistance than the BMI. The large amount of visceral adipose tissue (VAT) in morbidly obese (BMI > 40 kg/m(2)) individuals contributes to a high prevalence of NAFLD. Free fatty acids derived from VAT tissue, as well as from dietary sources and de novo lipogenesis, are released to the portal venous system. Excess free fatty acids and chronic low-grade inflammation from VAT are considered to be two of the most important factors contributing to liver injury progression in NAFLD. In addition, secretion of adipokines from VAT as well as lipid accumulation in the liver further promotes inflammation through nuclear factor kappa B signaling pathways, which are also activated by free fatty acids, and contribute to insulin resistance. Most NAFLD patients are asymptomatic on clinical presentation, even though some may present with fatigue, dyspepsia, dull pain in the liver and hepatosplenomegaly. Treatment for NAFLD and NASH involves weight reduction through lifestyle modifications, anti-obesity medication and bariatric surgery. This article reviews the available

				information on the biochemical and metabolic phenotypes associated with obesity and fatty liver disease. The relative contribution of visceral and liver fat to insulin resistance is discussed, and recommendations for clinical evaluation of affected individuals is provided.
Miller AH, Jones JF, Drake DF, Tian H, Unger ER, Pagnoni G.	(1)Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia, United States of America. (2)Chronic Viral Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America. (3)Department of Neuroscience, Biomedical, Metabolic Sciences, Università Degli Studi Di Modena E Reggio Emilia, Modena, Italy.	Decreased basal ganglia activation in subjects with chronic fatigue syndrome: association with symptoms of fatigue.	PLoS One. 2014;9(5):e98156. doi: 10.1371/journal.pone.0098156.	Reduced basal ganglia function has been associated with fatigue in neurologic disorders, as well as in patients exposed to chronic immune stimulation. Patients with chronic fatigue syndrome (CFS) have been shown to exhibit symptoms suggestive of decreased basal ganglia function including psychomotor slowing, which in turn was correlated with fatigue. In addition, CFS patients have been found to exhibit increased markers of immune activation. In order to directly test the hypothesis of decreased basal ganglia function in CFS, we used functional magnetic resonance imaging to examine neural activation in the basal ganglia to a reward-processing (monetary gambling) task in a community sample of 59 male and female subjects, including 18 patients diagnosed with CFS according to 1994 CDC criteria and 41 non-fatigued healthy controls. For each subject, the average effect of winning vs. losing during the gambling task in regions of interest (ROI) corresponding to the caudate nucleus, putamen, and globus pallidus was extracted for group comparisons and correlational analyses. Compared to non-fatigued controls, patients with CFS exhibited significantly decreased activation in the right caudate ($p = 0.01$) and right globus pallidus ($p = 0.02$). Decreased activation in the right globus pallidus was significantly correlated with increased mental fatigue ($r2 = 0.49$, $p = 0.001$), general fatigue ($r2 = 0.34$, $p = 0.01$) and reduced activity ($r2 = 0.29$, $p = 0.02$) as measured by the Multidimensional Fatigue Inventory. No such relationships were found in control subjects. These data suggest that symptoms of fatigue in CFS subjects were associated with reduced responsivity of the basal ganglia, possibly involving the disruption of projections from the globus pallidus to thalamic and cortical networks
Mitchell WM, Nicodemus CF, Carter WA, Horvath JC, Strayer DR.	(1)Department of Pathology, Microbiology, and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee. Electronic address: bill.mitchell@vanderbilt.edu. (2)AIT Strategies, Franconia, New Hampshire.	Discordant biological and toxicological species responses to TLR3 activation.	Am J Pathol. 2014 Apr;184(4):1062-72. doi: 10.1016/j.ajpath.2013.12.006. Epub 2014 Jan 30.	Toll-like receptors (TLRs) are highly conserved type 1 membrane proteins that initiate a multiplicity of transient gene transcriptions, resulting in innate and adaptive immune responses. These essential immune responses are triggered by common TLR pattern recognition receptors of microbial products expressed through the cytoplasmic carboxy-terminal Toll/IL-1 domain. Toll/IL-1 adapter protein cascades are induced by an activated Toll/IL-1 to induce transient transcription responses. All TLRs, with the exception of TLR3, use an MyD88 adapter to Toll/IL-1 to initiate a proinflammatory cascade. TLR3 uses the toll receptor 3/4 induction factor adapter to initiate a different cytosolic adapter cascade with double-stranded RNA agonists. This non-MyD88 pathway induces both NF-κB and type 1 interferon responses. By using a TLR3-restricted double-stranded RNA agonist, rintatolimod, we demonstrate significant unexpected differences in toxic responses between rats

	(3)Hemispherx BioPharma, Inc., Philadelphia, Pennsylvania			and primates. The mechanism of this differential response is consistent with a relative down-regulation of the NF-κB inflammatory cytokine induction pathway in the cynomolgus monkey and humans, but not observed systemically in rat. Our findings suggest evaluation of TLR3 agonists in drug therapy.
Miwa K, Fujita M.	(1)Department of Internal Medicine, Miwa Naika Clinic, Toyama, Japan. Electronic address: info@miwa-naika.com. (2)Department of Cardiology, Uji Hospital, Kyoto, Japan.	Renin-aldosterone paradox in patients with myalgic encephalomyelitis and orthostatic intolerance.	Int J Cardiol. 2014 Mar 15;172(2):514-5. doi: 10.1016/j.ijcard.2014.01.043. Epub 2014 Jan 23. No abstract available.	No abstract available
Miwa K.	Department of Internal Medicine, Miwa Naika Clinic, 1-4-3 Shintomicho, Toyama, 930-0002, Japan, info@miwa-naika.com.	Cardiac dysfunction and orthostatic intolerance in patients with myalgic encephalomyelitis and a small left ventricle.	Heart Vessels. 2014 Apr 16.	The etiology of chronic fatigue syndrome (CFS) is unknown. Myalgic encephalomyelitis (ME) has been recently postulated to be the cause of CFS. Orthostatic intolerance (OI) has been known as an important symptom in predicting quality of life in CFS patients. Cardiac function may be impaired in patients with ME. The presence or absence of OI was determined both symptomatically and by using a 10-min stand-up test in 40 ME patients. Left ventricular (LV) dimensions and function were determined echocardiographically in the ME patients compared to 40 control subjects. OI was noted in 35 (97 %) of the 36 ME patients who could stand up quickly. The mean values for the cardiothoracic ratio, systemic systolic and diastolic pressures, LV end-diastolic diameter (EDD), LV end-systolic diameter, stroke volume index, cardiac index and LV mass index were all significantly smaller in the ME group than in the controls. Both a small LVEDD (<40 mm, 45 vs. 3 %) and a low cardiac index (<2 l/min/mm(2), 53 vs. 8 %) were significantly more common in the ME group than in the controls. Both heart rate and LV ejection fraction were similar between the groups. In conclusion, a small LV size with a low cardiac output was common in ME patients, in whom OI was extremely common. Cardiac dysfunction with a small heart appears to be related to the symptoms of ME.
Moens K, Higginson IJ, Harding R; EURO IMPACT.	(1)Department of Palliative Care, Policy & Rehabilitation, Cicely Saunders Institute, King's College London, London, United Kingdom. Electronic address: Katrien.Moens@kcl.ac.uk. (2)Department of	Are there differences in the prevalence of palliative care-related problems in people living with advanced cancer and eight non-cancer conditions? A systematic review.	J Pain Symptom Manage. 2014 Oct;48(4):660-77. doi: 10.1016/j.jpainsymman.2013.11.009. Epub 2014 May 5.	CONTEXT: If access to effective palliative care is to extend beyond cancer patients, an understanding of the comparative prevalence of palliative care problems among cancer and non-cancer patients is necessary. OBJECTIVES: This systematic review aimed to describe and compare the prevalence of seventeen palliative care-related problems across the four palliative care domains among adults with advanced cancer, acquired immune deficiency syndrome, chronic heart failure, end-stage renal disease (ESRD), chronic obstructive pulmonary disease, multiple sclerosis, motor neuron disease, Parkinson's disease, and dementia. METHODS: Three databases were searched using three groups of keywords. The results of the extraction of the prevalence figures were summarized. RESULTS: The electronic

	Palliative Care, Policy & Rehabilitation, Cicely Saunders Institute, King's College London, London, United Kingdom.			searches yielded 4697 hits after the removal of 1784 duplicates. Of these hits, 143 met the review criteria. The greatest number of studies were found for advanced cancer (n=57) and ESRD patients (n=47), and 75 of the 143 studies used validated scales. Few data were available for people living with multiple sclerosis (n=2) and motor neuron disease (n=3). The problems with a prevalence of 50% or more found across most of the nine studied diagnostic groups were: pain, fatigue, anorexia, dyspnea, and worry. CONCLUSION: There are commonalities in the prevalence of problems across cancer and non-cancer patients, highlighting the need for palliative care to be provided irrespective of diagnosis. The methodological heterogeneity across the studies and the lack of non-cancer studies need to be addressed in future research.
Moreno M.	No address given	JAMA Pediatrics patient page. Chronic fatigue syndrome among adolescents.	JAMA Pediatr. 2014 Apr;168(4):396. doi: 10.1001/jamapediatrics.2013.3337. No abstract available.	No abstract available
Morris G, Maes M.	(1) Tir Na Nog, Pembrey, Llanelli, UK. (2)Department of Psychiatry, Chulalongkorn University, Bangkok, Thailand ; Department of Psychiatry, Deakin University, Geelong, Australia	Oxidative and Nitrosative Stress and Immune-Inflammatory Pathways in Patients with Myalgic Encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS).	Curr Neuropharmacol. 2014 Mar;12(2):168-85. doi: 10.2174/1570159X11666131120224653.	Myalgic Encephalomyelitis (ME) / Chronic Fatigue Syndrome (CFS) has been classified as a disease of the central nervous system by the WHO since 1969. Many patients carrying this diagnosis do demonstrate an almost bewildering array of biological abnormalities particularly the presence of oxidative and nitrosative stress (O&NS) and a chronically activated innate immune system. The proposal made herein is that once generated chronically activated O&NS and immune-inflammatory pathways conspire to generate a multitude of self-sustaining and self-amplifying pathological processes which are associated with the onset of ME/CFS. Sources of continuous activation of O&NS and immune-inflammatory pathways in ME/CFS are chronic, intermittent and opportunistic infections, bacterial translocation, autoimmune responses, mitochondrial dysfunctions, activation of the Toll-Like Receptor Radical Cycle, and decreased antioxidant levels. Consequences of chronically activated O&NS and immune-inflammatory pathways in ME/CFS are brain disorders, including neuroinflammation and brain hypometabolism / hypoperfusion, toxic effects of nitric oxide and peroxynitrite, lipid peroxidation and oxidative damage to DNA, secondary autoimmune responses directed against disrupted lipid membrane components and proteins, mitochondrial dysfunctions with a disruption of energy metabolism (e.g. compromised ATP production) and dysfunctional intracellular signaling pathways. The interplay between all of these factors leads to self-amplifying feed forward loops causing a chronic state of activated O&NS, immune-inflammatory and autoimmune pathways which may sustain the disease

Morris G, Maes M.	Tir Na Nog, Pembrey, Llanelli, UK	Mitochondrial dysfunctions in myalgic encephalomyelitis/chronic fatigue syndrome explained by activated immuno-inflammatory, oxidative and nitrosative stress pathways.	Metab Brain Dis. 2014 Mar;29(1):19-36. doi: 10.1007/s11011-013-9435-x. Epub 2013 Sep 10.	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/cfs) is classified by the World Health Organization as a disorder of the central nervous system. ME/cfs is an neuro-immune disorder accompanied by chronic low-grade inflammation, increased levels of oxidative and nitrosative stress (O&NS), O&NS-mediated damage to fatty acids, DNA and proteins, autoimmune reactions directed against neoantigens and brain disorders. Mitochondrial dysfunctions have been found in ME/cfs, e.g. lowered ATP production, impaired oxidative phosphorylation and mitochondrial damage. This paper reviews the pathways that may explain mitochondrial dysfunctions in ME/cfs. Increased levels of pro-inflammatory cytokines, such as interleukin-1 and tumor necrosis factor-α, and elastase, and increased O&NS may inhibit mitochondrial respiration, decrease the activities of the electron transport chain and mitochondrial membrane potential, increase mitochondrial membrane permeability, interfere with ATP production and cause mitochondrial shutdown. The activated O&NS pathways may additionally lead to damage of mitochondrial DNA and membranes thus decreasing membrane fluidity. Lowered levels of antioxidants, zinc and coenzyme Q10, and ω3 polyunsaturated fatty acids in ME/cfs may further aggravate the activated immuno-inflammatory and O&NS pathways. Therefore, it may be concluded that immuno-inflammatory and O&NS pathways may play a role in the mitochondrial dysfunctions and consequently the bioenergetic abnormalities seen in patients with ME/cfs. Defects in ATP production and the electron transport complex, in turn, are associated with an elevated production of superoxide and hydrogen peroxide in mitochondria creating adaptive and synergistic damage. It is argued that mitochondrial dysfunctions, e.g. lowered ATP production, may play a role in the onset of ME/cfs symptoms, e.g. fatigue and post exertional malaise, and may explain in part the central metabolic abnormalities observed in ME/cfs, e.g. glucose hypometabolism and cerebral hypoperfusion.
Morris G, Anderson G, Dean O, Berk M, Galecki P, Martin-Subero M, Maes M.	Tir Na Nog, Bryn Road Seaside 87, Llanelli, SA152LW, Wales, UK	The glutathione system: a new drug target in neuroimmune disorders.	Mol Neurobiol. 2014 Dec;50(3):1059-84. doi: 10.1007/s12035-014-8705-x. Epub 2014 Apr 22.	Glutathione (GSH) has a crucial role in cellular signaling and antioxidant defenses either by reacting directly with reactive oxygen or nitrogen species or by acting as an essential cofactor for GSH S-transferases and glutathione peroxidases. GSH acting in concert with its dependent enzymes, known as the glutathione system, is responsible for the detoxification of reactive oxygen and nitrogen species (ROS/RNS) and electrophiles produced by xenobiotics. Adequate levels of GSH are essential for the optimal functioning of the immune system in general and T cell activation and differentiation in particular. GSH is a ubiquitous regulator of the cell cycle per se. GSH also has crucial functions in the brain as an antioxidant, neuromodulator, neurotransmitter, and enabler of neuron survival. Depletion of GSH leads to exacerbation of damage by oxidative and nitrosative stress; hypernitrosylation; increased levels of proinflammatory mediators and inflammatory potential; dysfunctions of intracellular signaling networks, e.g., p53, nuclear factor-κB, and Janus kinases; decreased cell proliferation and DNA synthesis; inactivation of

				complex I of the electron transport chain; activation of cytochrome c and the apoptotic machinery; blockade of the methionine cycle; and compromised epigenetic regulation of gene expression. As such, GSH depletion has marked consequences for the homeostatic control of the immune system, oxidative and nitrosative stress (O&NS) pathways, regulation of energy production, and mitochondrial survival as well. GSH depletion and concomitant increase in O&NS and mitochondrial dysfunctions play a role in the pathophysiology of diverse neuroimmune disorders, including depression, myalgic encephalomyelitis/chronic fatigue syndrome and Parkinson's disease, suggesting that depleted GSH is an integral part of these diseases. Therapeutical interventions that aim to increase GSH concentrations in vivo include N-acetyl cysteine; Nrf-2 activation via hyperbaric oxygen therapy; dimethyl fumarate; phytochemicals, including curcumin, resveratrol, and cinnamon; and folate supplementation
Morris G, Berk M, Galecki P, Maes M.	Mumbles Head, Pembrey, Llanelli, UK	The emerging role of autoimmunity in myalgic encephalomyelitis/chronic fatigue syndrome (ME/cfs).	Mol Neurobiol. 2014 Apr;49(2):741-56. doi: 10.1007/s12035-013-8553-0. Epub 2013 Sep 26. Review.	The World Health Organization classifies myalgic encephalomyelitis/chronic fatigue syndrome (ME/cfs) as a nervous system disease. Together with other diseases under the G93 heading, ME/cfs shares a triad of abnormalities involving elevated oxidative and nitrosative stress (O&NS), activation of immuno-inflammatory pathways, and mitochondrial dysfunctions with depleted levels of adenosine triphosphate (ATP) synthesis. There is also abundant evidence that many patients with ME/cfs (up to around 60 %) may suffer from autoimmune responses. A wide range of reported abnormalities in ME/cfs are highly pertinent to the generation of autoimmunity. Here we review the potential sources of autoimmunity which are observed in people with ME/cfs. The increased levels of pro-inflammatory cytokines, e.g., interleukin-1 and tumor necrosis factor-α, and increased levels of nuclear factor-κB predispose to an autoimmune environment. Many cytokine abnormalities conspire to produce a predominance of effector B cells and autoreactive T cells. The common observation of reduced natural killer cell function in ME/cfs is a source of disrupted homeostasis and prolonged effector T cell survival. B cells may be pathogenic by playing a role in autoimmunity independent of their ability to produce antibodies. The chronic or recurrent viral infections seen in many patients with ME/cfs can induce autoimmunity by mechanisms involving molecular mimicry and bystander activation. Increased bacterial translocation, as observed in ME/cfs, is known to induce chronic inflammation and autoimmunity. Low ATP production and mitochondrial dysfunction is a source of autoimmunity by inhibiting apoptosis and stimulating necrotic cell death. Self-epitopes may be damaged by exposure to prolonged O&NS, altering their immunogenic profile and become a target for the host's immune system. Nitric oxide may induce many faces of autoimmunity stemming from elevated mitochondrial membrane hyperpolarization and blockade of the methionine cycle with subsequent hypomethylation of DNA. Here we also outline options for treatment involving rituximab and endotherapia

Morriss R.	No address given	Chronic fatigue syndrome/myalgic encephalomyelitis: more heat, some light--directions for research and clinical practice.	J Neurol Neurosurg Psychiatry. 2014 Feb;85(2):127-8. doi: 10.1136/jnnp-2012-304824. Epub 2013 Feb 13. No abstract available.	Comment on J Neurol Neurosurg Psychiatry. 2014 Feb;85(2):214-9
Nacul L, O'Donovan DG, Lacerda EM, Gveric D, Goldring K, Hall A, Bowman E, Pheby D.	(1) London School of Hygiene & Tropical Medicine, ITD/CRD/International Centre for Evidence in Disability, K/490, Keppel Street, WC1E 7HT London, UK. Luis.Nacul@lshtm.ac.uk	Considerations in establishing a post-mortem brain and tissue bank for the study of myalgic encephalomyelitis/chronic fatigue syndrome: a proposed protocol.	BMC Res Notes. 2014 Jun 18;7:370. doi: 10.1186/1756-0500-7-370.	BACKGROUND: Our aim, having previously investigated through a qualitative study involving extensive discussions with experts and patients the issues involved in establishing and maintaining a disease specific brain and tissue bank for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), was to develop a protocol for a UK ME/CFS repository of high quality human tissue from well characterised subjects with ME/CFS and controls suitable for a broad range of research applications. This would involve a specific donor program coupled with rapid tissue collection and processing, supplemented by comprehensive prospectively collected clinical, laboratory and self-assessment data from cases and controls. FINDINGS: We reviewed the operations of existing tissue banks from published literature and from their internal protocols and standard operating procedures (SOPs). On this basis, we developed the protocol presented here, which was designed to meet high technical and ethical standards and legal requirements and was based on recommendations of the MRC UK Brain Banks Network. The facility would be most efficient and cost-effective if incorporated into an existing tissue bank. Tissue collection would be rapid and follow robust protocols to ensure preservation sufficient for a wide range of research uses. A central tissue bank would have resources both for wide-scale donor recruitment and rapid response to donor death for prompt harvesting and processing of tissue. CONCLUSION: An ME/CFS brain and tissue bank could be established using this protocol. Success would depend on careful consideration of logistic, technical, legal and ethical issues, continuous consultation with patients and the donor population, and a sustainable model of funding ideally involving research councils, health services, and patient charities. This initiative could revolutionise the understanding of this still poorly-understood disease and enhance development of diagnostic biomarkers and treatments.
Nakatomi Y, Mizuno K, Ishii A, Wada Y, Tanaka M, Tazawa S, Onoe K, Fukuda S, Kawabe J, Takahashi K, Kataoka Y, Shiomi	Department of Metabolism, Endocrinology and Molecular Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan	Neuroinflammation in Patients with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis: An 11C-(R)-PK11195 PET Study.	J Nucl Med. 2014 Mar 24;55(6):945-950.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a disease characterized by chronic, profound, disabling, and unexplained fatigue. Although it is hypothesized that brain inflammation is involved in the pathophysiology of CFS/ME, there is no direct evidence of neuroinflammation in patients with CFS/ME. Activation of microglia or astrocytes is related to neuroinflammation. (11)C-(R)-(2-chlorophenyl)-N-methyl-N-(1-methylpropyl)-3-isoquinoline-carboxamide ((11)C-(R)-PK11195) is a ligand of PET for a translocator protein that is expressed by activated

S, Yamaguti K, Inaba M, Kuratsune H, Watanabe Y.	RIKEN Center for Life Science Technologies, Hyogo, Japan.			microglia or astrocytes. We used (11)C-(R)-PK11195 and PET to investigate the existence of neuroinflammation in CFS/ME patients.METHODS: Nine CFS/ME patients and 10 healthy controls underwent (11)C-(R)-PK11195 PET and completed questionnaires about fatigue, fatigue sensation, cognitive impairments, pain, and depression. To measure the density of translocator protein, nondisplaceable binding potential (BPND) values were determined using linear graphical analysis with the cerebellum as a reference region. RESULTS: The BPND values of (11)C-(R)-PK11195 in the cingulate cortex, hippocampus, amygdala, thalamus, midbrain, and pons were 45%-199% higher in CFS/ME patients than in healthy controls. In CFS/ME patients, the BPND values of (11)C-(R)-PK11195 in the amygdala, thalamus, and midbrain positively correlated with cognitive impairment score, the BPND values in the cingulate cortex and thalamus positively correlated with pain score, and the BPND value in the hippocampus positively correlated with depression score. CONCLUSION: Neuroinflammation is present in widespread brain areas in CFS/ME patients and was associated with the severity of neuropsychologic symptoms. Evaluation of neuroinflammation in CFS/ME patients may be essential for understanding the core pathophysiology and for developing objective diagnostic criteria and effective medical treatments
Neu D, Mairesse O, Montana X, Gilson M, Corazza F, Lefevre N, Linkowski P, Le Bon O, Verbanck P.	(1)Sleep Laboratory and Unit for Chronobiology U78, Department of Psychiatry, Brugmann University Hospital, Université Libre de Bruxelles (U.L.B), Arthur Van Gehuchten Square, 1020, Brussels, Belgium, daniel.neu@chu-brugmann.be	Dimensions of pure chronic fatigue: psychophysical, cognitive and biological correlates in the chronic fatigue syndrome.	Eur J Appl Physiol. 2014 Sep;114(9):1841-51. doi: 10.1007/s00421-014-2910-1. Epub 2014 May 31.	OBJECTIVES: To investigate associated dimensions of fatigue regarding cognitive impairment, psychomotor performances, muscular effort power and circulating cytokine levels and their relations to symptom intensity in a sample of pure chronic fatigue syndrome (CFS) patients without overlapping objective sleepiness or sleep disorders. METHODS: 16 CFS patients were compared to 14 matched controls. We assessed structured symptom-scales, polysomnography, multiple sleep latency tests, attention (Zazzo-Cancellation ZCT, digit-symbol-substitution DSST), psychomotor vigilance and speed (PVT, finger tapping test, FTT), dynamometer handgrip force (tonic and phasic trials) and circulating cytokines (IFN-γ, IL-1b, IL-6, IL-8, IL-10, TNF-α). RESULTS: In addition to fatigue, CFS patients presented with higher affective symptom intensity and worse perceived sleep quality. Polysomnography showed more slow-wave sleep and microarousals in CFS but similar sleep time, efficiency and light-sleep durations than controls. Patients presented with impaired attention (DSST, ZCT), slower reaction times (PVT) but not with lower hit rates (FTT). Notwithstanding lower grip strength during tonic and phasic trials, CFS also presented with higher fatigability during phasic trials. Cytokine levels were increased for IL-1b, IL-8, IL-10 and TNF-α and fatigue intensity was correlated to grip strength and IL-8. CONCLUSIONS: In contrast to sleepiness, chronic fatigue is a more complex phenomenon that cannot be reduced to one single measured dimension (i.e., sleep propensity). Showing its relations to different measurements, our study reflects this multidimensionality, in a psychosomatic disorder such as CFS. To obtain objective information, routine assessments of

				fatigue should rule out sleepiness, combine aspects of mental and physical fatigue and focus on fatigability.
Neu D, Mairesse O, Verbanck P, Linkowski P, Le Bon O.	Brugmann University Hospital, Sleep Laboratory & Unit for Chronobiology U78, Free University of Brussels (U.L.B/V.U.B.), Brussels, Belgium; UNI, ULB Neurosciences Institute, Faculty of Medicine, Laboratory for Medical Psychology ULB312, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium. Electronic address: daniel.neu@chu-brugmann.be.	Non-REM sleep EEG power distribution in fatigue and sleepiness.	J Psychosom Res. 2014 Apr;76(4):286-91. doi: 10.1016/j.jpsychores.2014.02.002. Epub 2014 Feb 17.	OBJECTIVES: The aim of this study is to contribute to the sleep-related differentiation between daytime fatigue and sleepiness. METHODS: 135 subjects presenting with sleep apnea-hypopnea syndrome (SAHS, n=58) or chronic fatigue syndrome (CFS, n=52) with respective sleepiness or fatigue complaints and a control group (n=25) underwent polysomnography and psychometric assessments for fatigue, sleepiness, affective symptoms and perceived sleep quality. Sleep EEG spectral analysis for ultra slow, delta, theta, alpha, sigma and beta power bands was performed on frontal, central and occipital derivations. RESULTS: Patient groups presented with impaired subjective sleep quality and higher affective symptom intensity. CFS patients presented with highest fatigue and SAHS patients with highest sleepiness levels. All groups showed similar total sleep time. Subject groups mainly differed in sleep efficiency, wake after sleep onset, duration of light sleep (N1, N2) and slow wave sleep, as well as in sleep fragmentation and respiratory disturbance. Relative non-REM sleep power spectra distributions suggest a pattern of power exchange in higher frequency bands at the expense of central ultra slow power in CFS patients during all non-REM stages. In SAHS patients, however, we found an opposite pattern at occipital sites during N1 and N2. CONCLUSIONS: Slow wave activity presents as a crossroad of fatigue and sleepiness with, however, different spectral power band distributions during non-REM sleep. The homeostatic function of sleep might be compromised in CFS patients and could explain why, in contrast to sleepiness, fatigue does not resolve with sleep in these patients. The present findings thus contribute to the differentiation of both phenomena
Nichols TW Jr, Gaiteri C.	(1) CNDD, 721 Ash Dr., Hanover, PA 17331-1545, United States. (2)Sage Bionetworks, Seattle, 1100 Fairview Avenue North, WA 98109, United States. Electronic address: twnicholpa@comcast.net.	Morton's foot and pyridoxal 5'-phosphate deficiency: Genetically linked traits.	Med Hypotheses. 2014 Sep 16;83(6):644-648. doi: 10.1016/j.mehy.2014.09.003.	Vitamin B6 is an essential vitamin needed for many chemical reactions in the human body. It exists as several vitamins forms but pyridoxal 5'-phosphate (PLP) is the phosphorylated form needed for transamination, deamination, and decarboxylation. PLP is important in the production of neurotransmitters, acts as a Schiff base and is essential in the metabolism of homocysteine, a toxic amino acid involved in cardiovascular disease, stroke, thrombotic and Alzheimer's disease. This report announces the connection between a deficit of PLP with a genetically linked physical foot form known as the Morton's foot. Morton's foot has been associated with fibromyalgia/myofascial pain syndrome. Another gene mutation methylenetetrahydrofolate reductase (MTHFr) is now being recognized much commonly than previous with chronic fatigue, chronic Lyme diseases and as "the missing link" in other chronic diseases. PLP deficiency also plays a role in impaired

				glucose tolerance and may play a much bigger role in the obesity, diabetes, fatty liver and metabolic syndrome. Without the Schiff-base of PLP acting as an electron sink, storing electrons and dispensing them in the mitochondria, free radical damage occurs! The recognition that a phenotypical expression (Morton's foot) of a gene resulting in deficiency of an important cofactor enzyme pyridoxal 5'-phosphate will hopefully alert physicians and nutritionist to these phenomena. Supplementation with PLP, L5-MTHF, B12 and trimethylglycine should be used in those patients with hyperhomocysteinemia and/or MTHFR gene mutation
Nickel JC, Tripp DA; International Interstitial Cystitis Study Group.	(1)Departments of Urology (JCN), Psychology and Anesthesiology, Queen's University, Kingston, Ontario, Canada. Electronic address: jcn@queensu.ca. (2) Departments of Urology (JCN), Psychology and Anesthesiology, Queen's University, Kingston, Ontario, Canada.	Clinical and psychological parameters associated with pain pattern phenotypes in women with interstitial cystitis/bladder pain syndrome.	J Urol. 2015 Jan;193(1):138-44. doi: 10.1016/j.juro.2014.07.108. Epub 2014 Aug 1.	PURPOSE: It was recently suggested that 2 distinct clinical phenotypes can be described in patients with urological chronic pelvic pain syndrome, including pelvic pain only and pelvic pain beyond. We examined data on patients with interstitial cystitis/bladder pain syndrome, including body pain location mapping, and associated medical and psychosocial phenotyping to validate these body pain maps in a cohort of female patients with interstitial cystitis/bladder pain syndrome undergoing tertiary care. MATERIALS AND METHODS: Validated questionnaires from 173 diagnosed outpatient female patients with interstitial cystitis/bladder pain syndrome included a body pain area diagram, demographics/history, pain assessment, interstitial cystitis/bladder pain syndrome symptoms, depression, anxiety, stress, fatigue, sexual functioning, catastrophizing, quality of life and data on other chronic pain conditions. Two pain phenotypes based on counts of body locations, pelvic pain only and pelvic pain beyond, were comprehensively examined. RESULTS: The 157 patients (81%) identified with pelvic pain beyond reported more sensory type pain, poorer physical quality of life, and greater somatic depression and sleep disturbance than the 36 (19%) categorized with pelvic pain only. The sexual pain score was higher in the pelvic pain only group. Furthermore, patients with the pelvic pain beyond phenotype reported a higher prevalence of irritable bowel syndrome and fibromyalgia as well as more general fatigue symptoms and psychiatric conditions. CONCLUSIONS: Two distinct pain location phenotypes, including pelvic pain only and pelvic pain beyond,were identified by our independent analysis of patients with interstitial cystitis/bladder pain syndrome. Assessing clinical phenotypes based on pain patterns has significant ramifications in our improved understanding of the etiology and treatment of female patients diagnosed with interstitial cystitis/bladder pain syndrome.
Nicolson GL.	No address given	Mitochondrial dysfunction and chronic disease: treatment with natural supplements.	Altern Ther Health Med. 2014 Winter;20 Suppl 1:18-25.	Loss of function in mitochondria, the key organelle responsible for cellular energy production, can result in the excess fatigue and other symptoms that are common complaints in almost every chronic disease. At the molecular level, a reduction in mitochondrial function occurs as a result of the following changes: (1) a loss of maintenance of the electrical and chemical transmembrane potential of the inner mitochondrial membrane, (2) alterations in the function of the electron transport

				chain, or (3) a reduction in the transport of critical metabolites into mitochondria. In turn, these changes result in a reduced efficiency of oxidative phosphorylation and a reduction in production of adenosine-5'-triphosphate (ATP). Several components of this system require routine replacement, and this need can be facilitated with natural supplements. Clinical trials have shown the utility of using oral replacement supplements, such as L-carnitine, alpha-lipoic acid (α-lipoic acid [1,2-dithiolane-3-pentanoic acid]), coenzyme Q10 (CoQ10 [ubiquinone]), reduced nicotinamide adenine dinucleotide (NADH), membrane phospholipids, and other supplements. Combinations of these supplements can reduce significantly the fatigue and other symptoms associated with chronic disease and can naturally restore mitochondrial function, even in long-term patients with intractable fatigue
Nie LJ, Cai WJ, Zhang XM, Shen ZY.	No address given	[Effect of compound bushen recipe on chronic fatigue syndrome in C. elegans: an experimental study].	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2014 Jun;34(6):728-32.	[Article in Chinese] OBJECTIVE: To evaluate the effect of compound bushen recipe (CBR) in improving the survival state of stress and the overall life span in C. elegans by simulating chronic fatigue syndrome (CFS) under various stress states. METHODS: The tolerance and the average survival time of adult larvae against heat stress (35 degrees C), oxidative stress (250 microg/mL juglone), and in vivo Abeta protein toxicity (Abeta(1-42) transgenic mutant CL4176) under the intervention of the high (500 mg/L), middle (250 mg/L), and low (100 mg/L) dose CBR were observed. The effect of CBR on the average live time (at 25 degrees C), movement distance in 20 seconds, the frequency of pharyngeal pump in 30 seconds, and the reproductive capability were assessed. RESULTS: Compared with the control group, the survival time of heat stressed C. elegans could be significantly increased in each CBR group ($P < 0.01$). The survival time of heat stressed C. elegans could be elongated, the protein toxicity be attenuated, and the live time prolonged in the high and middle dose CBR groups ($P < 0.01$, $P < 0.05$).The movement distance and the frequency of pharyngeal pump could also be increased in the high dose CBR group ($P < 0.01$). There was no statistical difference in the reproductive capability among all groups ($P > 0.05$). CONCLUSIONS: CBR could significantly enhance the stress capacity of C. elegans against internal and external environment, and prolong their lifespan. It did not interfere their normal production, and also could improve the quality of life, thus laying a foundation for further mechanism studies and pharmacological researches on CBR in preventing and treating CFS.
Nijhof SL, Werker CL, van de Putte EM.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Office KE 04.133.1, Postbox	Improvement rates in adolescent patients with chronic fatigue syndrome after receiving cognitive behavioural therapy.	Eur J Pediatr. 2014 May;173(5):693-4. doi: 10.1007/s00431-013-2235-9. Epub 2013 Dec 10.	Comment on Eur J Pediatr. 2013 Oct;172(10):1293-8. Eur J Pediatr. 2014 May;173(5):691

	85090, 3508 AB, Utrecht, The Netherlands, s.l.nijhof@umcutrecht.nl.	Correspondence in response to: Clinical Practice: chronic fatigue syndrome-author's reply.		
Nijhof SL, Rutten JM, Uiterwaal CS, Bleijenberg G, Kimpen JL, Putte EM.	Department of Paediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht, The Netherlands. Electronic address: s.l.nijhof@umcutrecht.nl.	The role of hypocortisolism in chronic fatigue syndrome.	Psychoneuroendocrinology. 2014 Apr;42:199-206. doi: 10.1016/j.psyneuen.2014.01.017. Epub 2014 Jan 30.	BACKGROUND: There is accumulating evidence of hypothalamic-pituitary-adrenal (HPA) axis hypofunction in chronic fatigue syndrome (CFS). However, knowledge of this hypofunction has so far come exclusively from research in adulthood, and its clinical significance remains unclear. The objective of the current study was to assess the role of the HPA-axis in adolescent CFS and recovery from adolescent CFS. METHOD: Before treatment, we compared the salivary cortisol awakening response of 108 diagnosed adolescent CFS patients with that of a reference group of 38 healthy peers. Salivary cortisol awakening response was measured again after 6 months of treatment in CFS patients. RESULTS: Pre-treatment salivary cortisol levels were significantly lower in CFS-patients than in healthy controls. After treatment recovered patients had a significant rise in salivary cortisol output attaining normalization, whereas non-recovered patients improved slightly, but not significantly. The hypocortisolism found in CFS-patients was significantly correlated to the amount of sleep. Logistic regression analysis showed that an increase of one standard deviation in the difference between pre- and post-treatment salivary cortisol awakening response was associated with a 93% higher odds of recovery (adjusted OR 1.93 (1.18 to 3.17), p=0.009). Pre-treatment salivary cortisol did not predict recovery. CONCLUSIONS: Hypocortisolism is associated with adolescent CFS. It is not pre-treatment cortisol but its change to normalization that is associated with treatment success. We suggest that this finding may have clinical implications regarding the adaptation of future treatment strategies.
Nijs J, Lundberg M.	Pain in Motion Research Group, Departments of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium, Jo.Nijs@vub.ac.be.	Avoidance behavior towards physical activity in chronic fatigue syndrome and fibromyalgia: the fear for post-exertional malaise.	Clin Rheumatol. 2014 Jan;33(1):151-2. doi: 10.1007/s10067-013-2421-1. Epub 2013 Nov 7.	No abstract available

Nijs J, Nees A, Paul L, De Kooning M, Ickmans K, Meeus M, Van Oosterwijck J.	No address given	Altered immune response to exercise in patients with chronic fatigue syndrome/myalgic encephalomyelitis: a systematic literature review.	Exerc Immunol Rev. 2014;20:94-116. Review.	An increasing number of studies have examined how the immune system of patients with Chronic Fatigue Syndrome (CFS), or myalgic encephalomyelitis, responds to exercise. The objective of the present study was to systematically review the scientific literature addressing exercise-induced immunological changes in CFS patients compared to healthy control subjects. A systematic literature search was conducted in the PubMed and Web of science databases using different keyword combinations. We included 23 case control studies that examined whether CFS patients, compared to healthy sedentary controls, have a different immune response to exercise. The included articles were evaluated on their methodological quality. Compared to the normal response of the immune system to exercise as seen in healthy subjects, patients with CFS have a more pronounced response in the complement system (i.e. C4a split product levels), oxidative stress system (i.e. enhanced oxidative stress combined with a delayed and reduced anti-oxidant response), and an alteration in the immune cells' gene expression profile (increases in post-exercise interleukin-10 and toll-like receptor 4 gene expression), but not in circulating pro- or anti-inflammatory cytokines. Many of these immune changes relate to post-exertional malaise in CFS, a major characteristic of the illness. The literature review provides level B evidence for an altered immune response to exercise in patients with CFS.
Norheim KB, Le Hellard S, Nordmark G, Harboe E, GÃ¸ransson L, Brun JG, Wahren-Herlenius M, Jonsson R, Omdal R.	Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Pb. 8100 Forus, 4068, Stavanger, Norway, katnorheim@gmail.com.	A possible genetic association with chronic fatigue in primary SjÃ¶gren's syndrome: a candidate gene study.	Rheumatol Int. 2014 Feb;34(2):191-7. doi: 10.1007/s00296-013-2850-9. Epub 2013 Sep 3.	Fatigue is prevalent and disabling in primary Sjögren's syndrome (pSS). Results from studies in chronic fatigue syndrome (CFS) indicate that genetic variation may influence fatigue. The aim of this study was to investigate single nucleotide polymorphism (SNP) variations in pSS patients with high and low fatigue. A panel of 85 SNPs in 12 genes was selected based on previous studies in CFS. A total of 207 pSS patients and 376 healthy controls were genotyped. One-hundred and ninety-three patients and 70 SNPs in 11 genes were available for analysis after quality control. Patients were dichotomized based on fatigue visual analogue scale (VAS) scores, with VAS <50 denominated "low fatigue" (n = 53) and VAS ≥50 denominated "high fatigue" (n = 140). We detected signals of association with pSS for one SNP in SLC25A40 (unadjusted p = 0.007) and two SNPs in PKN1 (both p = 0.03) in our pSS case versus control analysis. The association with SLC25A40 was stronger when only pSS high fatigue patients were analysed versus controls (p = 0.002). One SNP in PKN1 displayed an association in the case-only analysis of pSS high fatigue versus pSS low fatigue (p = 0.005). This candidate gene study in pSS did reveal a trend for associations between genetic variation in candidate genes and fatigue. The results will need to be replicated. More research on genetic associations with fatigue is warranted, and future trials should include larger cohorts and multicentre collaborations with sharing of genetic material to increase the statistical power

Nyland M, Naess H, Birkeland JS, Nyland H.	(1) Institute of Clinical Medicine, University of Bergen, Bergen, Norway. (2)Institute of Clinical Medicine, University of Bergen, Bergen, Norway Department of Neurology, Haukeland University Hospital, Bergen, Norway. (3)Department of Neurology, Haukeland University Hospital, Bergen, Norway.	Longitudinal follow-up of employment status in patients with chronic fatigue syndrome after mononucleosis.	BMJ Open. 2014 Nov 26;4(11):e005798. doi: 10.1136/bmjopen-2014-005798.	OBJECTIVE: To examine the effect of early clinical and demographic factors on occupational outcome, return to work or awarded permanent disability pension in young patients with chronic fatigue syndrome (CFS). DESIGN: Longitudinal cohort study. INTERVENTION: A written self-management programme including a description of active coping strategies for daily life was provided. SETTING, PARTICIPANTS: Patients with CFS after mononucleosis were evaluated at Department of Neurology, Haukeland University Hospital during 1996-2006 (contact 1). In 2009 self-report questionnaires were sent to all patients (contact 2). PRIMARY AND SECONDARY OUTCOME MEASURES: Primary measure was employment status at contact 2. Secondary measures included clinical symptoms, and Fatigue Severity Scale (FSS) scores on both contacts, and Work and Social Adjustment Scale (WSAS) at contact 2. RESULTS: Of 111 patients at contact 1, 92 (83%) patients returned the questionnaire at contact 2. Mean disease duration at contact 1 was 4.7 years and at contact 2 11.4 years. At contact 1, 9 (10%) were part-time or full-time employed. At contact 2, 49 (55%) were part-time or full-time employed. Logical regression analysis showed that FSS≥5 at contact 2 was associated with depression, arthralgia and long disease duration (all at contact 1). CONCLUSIONS: About half of younger patients with CFS with long-term incapacity for work experienced marked improvement including full-time or part-time employment showing better outcomes than expected. Risk factors for transition to permanent disability were depression, arthralgia and disease duration.
NystrÃ¸m J.	No address given	[Re: Woman in her 30s with chronic fatigue].	Tidsskr Nor Laegeforen. 2014 Apr 8;134(7):690-1. doi: 10.4045/tidsskr.14.0367.	[Article in Norwegian] Comment in Tidsskr Nor Laegeforen. 2014 Apr 8;134(7):691. Comment on Tidsskr Nor Laegeforen. 2014 Feb 25;134(4):423-5.
Oka T, Tanahashi T, Chijiwa T, Lkhagvasuren B, Sudo N, Oka K.	(1) Department of Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, 812-8582 Japan. (2)Department of Pediatrics and Child Health, School of Medicine, Kurume University, Asahi-machi 67, Kurume, 830-0011	Isometric yoga improves the fatigue and pain of patients with chronic fatigue syndrome who are resistant to conventional therapy: a randomized, controlled trial.	Biopsychosoc Med. 2014;8(1):27. doi: 10.1186/s13030-014-0027-8.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) often complain of persistent fatigue even after conventional therapies such as pharmacotherapy, cognitive behavioral therapy, or graded exercise therapy. The aim of this study was to investigate in a randomized, controlled trial the feasibility and efficacy of isometric yoga in patients with CFS who are resistant to conventional treatments. METHODS: This trial enrolled 30 patients with CFS who did not have satisfactory improvement after receiving conventional therapy for at least six months. They were randomly divided into two groups and were treated with either conventional pharmacotherapy (control group, n = 15) or conventional therapy together with isometric yoga practice that consisted of biweekly, 20-minute sessions with a yoga instructor and daily in-home sessions (yoga group, n = 15) for approximately two months. The short-term effect of isometric yoga on fatigue was assessed by administration of the Profile of Mood Status (POMS) questionnaire immediately

	Japan			before and after the final 20-minute session with the instructor. The long-term effect of isometric yoga on fatigue was assessed by administration of the Chalder's Fatigue Scale (FS) questionnaire to both groups before and after the intervention. Adverse events and changes in subjective symptoms were recorded for subjects in the yoga group. RESULTS: All subjects completed the intervention. The mean POMS fatigue score decreased significantly (from 21.9 ± 7.7 to 13.8 ± 6.7, P < 0.001) after a yoga session. The Chalder's FS score decreased significantly (from 25.9 ± 6.1 to 19.2 ± 7.5, P = 0.002) in the yoga group, but not in the control group. In addition to the improvement of fatigue, two patients with CFS and fibromyalgia syndrome in the yoga group also reported pain relief. Furthermore, many subjects reported that their bodies became warmer and lighter after practicing isometric yoga. Although there were no serious adverse events in the yoga group, two patients complained of tiredness and one of dizziness after the first yoga session with the instructor. CONCLUSIONS: Isometric yoga as an add-on therapy is both feasible and successful at relieving the fatigue and pain of a subset of therapy-resistant patients with CFS. TRIAL REGISTRATION: University Hospital Medical Information Network (UMIN CTR) UMIN000009646.
Orlin MN, Cicirello NA, O'Donnell AE, Doty AK.	M.N. Orlin, PT, PhD, Department of Physical Therapy & Rehabilitation Sciences, Drexel University, 7th Floor, Room 729, 1601 Cherry St, MS 7502, Philadelphia, PA 19102 (USA). margo.n.orlin@drexel.edu.	The continuum of care for individuals with lifelong disabilities: role of the physical therapist.	Phys Ther. 2014 Jul;94(7):1043-53. doi: 10.2522/ptj.20130168. Epub 2014 Feb 20.	Many individuals with lifelong disabilities (LLDs) of childhood onset are living longer, participating in adult roles, and seeking comprehensive health care services, including physical therapy, with greater frequency than in the past. Individuals with LLDs have the same goals of health and wellness as those without disabilities. Aging with a chronic LLD is not yet well understood; however, impairments such as pain, fatigue, and osteoporosis often present earlier than in adults who are aging typically. People with LLDs, especially those living with developmental disabilities such as cerebral palsy, myelomeningocele, Down syndrome, and intellectual disabilities, frequently have complex and multiple body system impairments and functional limitations that can: (1) be the cause of numerous and varied secondary conditions, (2) limit overall earning power, (3) diminish insurance coverage, and (4) create unique challenges for accessing health care. Collaboration between adult and pediatric practitioners is encouraged to facilitate smooth transitions to health practitioners, including physical therapists. A collaborative client-centered emphasis to support the transition to adult-oriented facilities and promote strategies to increase accessibility should become standard parts of examination, goal setting, and intervention. This perspective article identifies barriers individuals with selected LLDs experience in accessing health care, including physical therapy. Strategies are suggested, including establishment of niche practices, physical accessibility improvement, and inclusion of more specific curriculum content in professional (entry-level) doctorate physical therapy schools.

Paquette AG, Marsit CJ.	Department of Pharmacology and Toxicology, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire.	The developmental basis of epigenetic regulation of HTR2A and psychiatric outcomes.	J Cell Biochem. 2014 Dec;115(12):2065-72. doi: 10.1002/jcb.24883.	The serotonin receptor 5-HT2A (encoded by HTR2A) is an important regulator of fetal brain development and adult cognitive function. Environmental signals that induce epigenetic changes of serotonin response genes, including HTR2A, have been implicated in adverse mental health outcomes. The objective of this perspective article is to address the medical implications of HTR2A epigenetic regulation, which has been associated with both infant neurobehavioral outcomes and adult mental health. Ongoing research has identified a region of the HTR2A promoter that has been associated with a number of medical outcomes in adults and infants, including bipolar disorder, schizophrenia, chronic fatigue syndrome, borderline personality disorder, suicidality, and neurobehavioral outcomes. Epigenetic regulation of HTR2A has been studied in several different types of tissues, including the placenta. The placenta is an important source of serotonin during fetal neurodevelopment, and placental epigenetic variation of HTR2A has been associated with infant neurobehavioral outcomes, which may represent the basis of adult mental health disorders. Further analysis is needed to identify intrinsic and extrinsic factors that modulate HTR2A methylation, and the mechanism by which this epigenetic variation influences fetal growth and leads to altered brain development, manifesting in psychiatric disorders
Pardini M, Cordano C, Benassi F, Mattei C, Sassos D, Guida S, Serrati C, Primavera A, Amore M, Cocito L, Emberti Gialloreti L.	(1)Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics and Maternal and Child Health, University of Genoa, Genoa, Italy; Center for Communication and Neurorehabilitation Research-CNAPP, Rome, Italy. Electronic address: matteo.pardini@gmail.com.	Agomelatine but not melatonin improves fatigue perception: a longitudinal proof-of-concept study.	Eur Neuropsychopharmacol. 2014 Jun;24(6):939-44. doi: 10.1016/j.euroneuro.2014.02.010. Epub 2014 Feb 25.	Chronic Fatigue Syndrome (CFS) represents a disabling condition characterized by persistent mental and physical fatigue, bodily discomfort and cognitive difficulties. To date the neural bases of CFS are poorly understood; however, mono-aminergic abnormalities, sleep-wake cycle changes and prefrontal dysfunctions are all thought to play a role in the development and maintenance of this condition. Here we explored in a group of 62 CFS subjects the impact on fatigue levels of agomelatine, an antidepressant with agonist activity at melatonin receptors (MT1 and MT2) and antagonist activity at serotoninergic 2C receptors (5HT2C). To tease out the relative effects of MT-agonism and 5HT2C antagonism on fatigue, we compared agomelatine 50mg u.i.d. with sustained release melatonin 10mg u.i.d. in the first 12-week-long phase of the study, and then switched all melatonin-treated subjects to agomelatine in the second 12-week-long phase of the study. Agomelatine treatment, but not melatonin, was associated with a significant reduction of perceived fatigue and an increase in perceived quality of life. Moreover the switch from melatonin to agomelatine was associated with a reduction of fatigue levels. Agomelatine was well tolerated by all enrolled subjects. Our data, albeit preliminary, suggest that agomelatine treatment could represent a novel useful approach to the clinical care of subjects with CFS.

Pemberton S, Cox DL.	Yorkshire Fatigue Clinic, Forsyth Business Centre , York, North Yorkshire ,	Experiences of daily activity in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and their implications for rehabilitation programmes.	Disabil Rehabil. 2014;36(21):1790-7. doi: 10.3109/09638288.2013.874503. Epub 2013 Dec 27.	PURPOSE: Chronic Fatigue Syndrome, also known as Myalgic Encephalomyelitis (CFS/ME), has a significant impact upon daily functioning. Most recommended treatments aim to alter activity patterns based upon assumptions of activity avoidance. However, as there is limited research on the experience of activity and occupational beliefs in people with CFS/ME, this study took a qualitative approach to understand the meaning of activity in people with this disabling condition. METHOD: This study applied a social constructivist grounded theory methodology. Semi-structured interviews took place with 14 participants attending a Specialist CFS/ME Service in England. FINDINGS: The emergent themes described a premorbid state of constant action with difficulty stopping an activity once it had commenced. When this pattern was interrupted by illness, participants attempted to maintain their previous level of occupational engagement. Negative associations and emotions were described in response to the concept of doing nothing or limited activity. A recurring cycle was reported of increasing activity levels when symptoms improved, followed by post exertional symptoms. CONCLUSIONS: Consequently, participants' beliefs about concepts of both activity and inactivity need to be considered within the application of rehabilitation programmes for CFS/ME that aim to modify activity related behaviours. IMPLICATIONS FOR REHABILITATION: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is commonly treated in the UK using activity modification. In this small qualitative study, patients expressed negative feelings and beliefs towards the concept of doing nothing and therefore sought to push their activity levels when this was available, leading to recurring cycles of symptoms and activity. Rehabilitation programmes need to consider how people with CFS/ME engaged with activity and inactivity before the condition and how this may impact upon engagement with activity-based rehabilitation programmes
Peng M, Ma HB, Si GM.	No address given	A literature review on Chinese medicine syndrome and syndrome elements of chronic fatigue syndrome.	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2014 Jun;34(6):691-3. Chinese.	[Article in Chinese] OBJECTIVE: To research the distribution characteristics of Chinese medicine (CM) syndrome and syndrome elements of chronic fatigue syndrome (CFS) by analyzing literature in recent 20 years. METHODS: Relevant literature on treating CFS by syndrome differentiation of CM at home were retrieved by computer and manual ways. Database wasestablished by using EpiData 3.1 to conduct frequency analysis of syndrome and syndrome elements. RESULTS: The most common clinical syndromes were Xin-Pi deficiency syndrome, Gan stagnation Pi deficiency syndrome, Gan-Shen yin deficiency syndrome, Gan qi stagnation syndrome, and Pi-Wei qi deficiency syndrome. Disease locations were sequenced as Pi, Gan, Shen, and Xin. The clinical pathogenesis of CFS was characterized by deficiency of vital energy, complicated with intermingled excess and deficiency. Asthenia of healthy energy was mainly manifested as qi deficiency, blood deficiency, and yin deficiency, while

				excess of sthenia was mainly manifested as qi stagnation, phlegm dampness, and static blood. CONCLUSIONS: Research of CM syndrome starting from syndrome elements can better unify and standardize clinical syndrome differentiation. Results of literature analysis can provide reference for further studies.
Petra AI, Panagiotidou S, Stewart JM, Conti P, Theoharides TC.	(1)Department of Molecular Physiology and Pharmacology, Molecular Immunopharmacology and Drug Discovery Laboratory, Tufts University School of Medicine and Tufts Medical Center, 136 Harrison Avenue, Boston, MA, USA	Spectrum of mast cell activation disorders.	Expert Rev Clin Immunol. 2014 Jun;10(6):729-39. doi: 10.1586/1744666X.2014.906302. Epub 2014 May 1.	Mast cell (MC) activation disorders present with multiple symptoms including flushing, pruritus, hypotension, gastrointestinal complaints, irritability, headaches, concentration/memory loss and neuropsychiatric issues. These disorders are classified as: cutaneous and systemic mastocytosis with a c-kit mutation and clonal MC activation disorder, allergies, urticarias and inflammatory disorders and mast cell activation syndrome (MCAS), idiopathic urticaria and angioedema. MCs are activated by IgE, but also by cytokines, environmental, food, infectious, drug and stress triggers, leading to secretion of multiple mediators. The symptom profile and comorbidities associated with these disorders, such as chronic fatigue syndrome and fibromyalgia, are confusing. We propose the use of the term 'spectrum' and highlight the main symptoms, useful diagnostic tests and treatment approaches.
Pianosi PT, Goodloe AH, Soma D, Parker KO, Brands CK, Fischer PR.	Department of Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, Minnesota	High flow variant postural orthostatic tachycardia syndrome amplifies the cardiac output response to exercise in adolescents.	Physiol Rep. 2014 Aug 28;2(8). doi:pii: e12122. 10.14814/phy2.12122. Print 2014 Aug 1.	Postural orthostatic tachycardia syndrome (POTS) is characterized by chronic fatigue and dizziness and affected individuals by definition have orthostatic intolerance and tachycardia. There is considerable overlap of symptoms in patients with POTS and chronic fatigue syndrome (CFS), prompting speculation that POTS is akin to a deconditioned state. We previously showed that adolescents with postural orthostatic tachycardia syndrome (POTS) have excessive heart rate (HR) during, and slower HR recovery after, exercise - hallmarks of deconditioning. We also noted exaggerated cardiac output during exercise which led us to hypothesize that tachycardia could be a manifestation of a high output state rather than a consequence of deconditioning. We audited records of adolescents presenting with long-standing history of any mix of fatigue, dizziness, nausea, who underwent both head-up tilt table test and maximal exercise testing with measurement of cardiac output at rest plus 2-3 levels of exercise, and determined the cardiac output () versus oxygen uptake () relationship. Subjects with chronic fatigue were diagnosed with POTS if their HR rose ≥40 beat·min(-1) with head-up tilt. Among 107 POTS patients the distribution of slopes for the , relationship was skewed toward higher slopes but showed two peaks with a split at ~7.0 L·min(-1) per L·min(-1), designated as normal (5.08 ± 1.17, N = 66) and hyperkinetic (8.99 ± 1.31, N = 41) subgroups. In contrast, cardiac output rose appropriately with in 141 patients with chronic fatigue but without POTS, exhibiting a normal distribution and an average slope of 6.10 ± 2.09 L·min(-1) per L·min(-1). Mean arterial blood pressure and pulse pressure from rest to exercise rose similarly in both groups. We conclude that 40% of POTS adolescents demonstrate a hyperkinetic circulation during exercise. We attribute this to failure of normal regional vasoconstriction during exercise, such that

				patients must increase flow through an inappropriately vasodilated systemic circulation to maintain perfusion pressure
Piven' BN.	No address given	A new essence or just new names?.	Zh Nevrol Psikhiatr Im S S Korsakova. 2014;114(5):104-7..	[Article in Russian] Some new terms and meanings in modern psychiatry ("emotional burnout syndrome", "chronic fatigue syndrome", "panic attacks", etc.) were analyzed, due to save clinic psychiatry traditions and succession of different generations of psychiatrists. Comparison of their content and well-known science concepts proves absence of any unknown phenomenon. These terms do not introduce some new items of classic determination of psychopathology catastasis, they just rename it. The reasons of this tendency were investigated.
Porter J, Al-Jarrah Q, Richardson S.	Department of Vascular Surgery, University Hospital of South, Manchester, Southmoor Road, Manchester M23 9LT, UK	A case of femoral arteriovenous fistula causing high-output cardiac failure, originally misdiagnosed as chronic fatigue syndrome.	Case Rep Vasc Med. 2014;2014:510429. doi: 10.1155/2014/510429. Epub 2014 May 20.	Percutaneous arterial catheterisation is commonly undertaken for a range of diagnostic and interventional procedures. Iatrogenic femoral arteriovenous fistulas are an uncommon complication of these procedures. Most are asymptomatic and close spontaneously, but can rarely increase in size leading to the development of symptoms. We report a case of an iatrogenic femoral arteriovenous fistula, causing worsening congestive cardiac failure, in a 34-year-old marathon runner. This was originally diagnosed as chronic fatigue syndrome. Following clinical examination, duplex ultrasound, and CT angiography a significant arteriovenous fistula was confirmed. Elective open surgery was performed, leading to a dramatic and rapid improvement in symptoms. Femoral arteriovenous fistulas have the potential to cause significant haemodynamic effects and can present many years after the initial procedure. Conservative, endovascular, and open surgical management strategies are available.
Potestio CP, Check JH, Mitchell-Williams J.	No address given	Improvement in symptoms of the syndrome of mitochondrial encephalopathy, lactic acidosis, and stroke-like symptoms (MELAS) following treatment with sympathomimetic amines--possible implications for	Clin Exp Obstet Gynecol. 2014;41(3):343-5.	PURPOSE: To evaluate the efficacy of sympathomimetic amine therapy on a mitochondrial abnormality known as the mitochondrial encephalopathy lactic acidosis and stroke-like symptoms syndrome (MELAS syndrome). MATERIALS AND METHODS: Dextroamphetamine sulfate 15 mg extended release capsule was prescribed to a woman with a 25 year history of MELAS syndrome refractory to most other therapies. RESULTS: Within one month of therapy the woman noticed considerable improvement in her chronic fatigue, pain, and edema. CONCLUSIONS: The MELAS syndrome is thus another condition to add to the list of various chronic refractory disorders that improve considerably after dextroamphetamine therapy. This is the first mitochondrial disorder shown to improve with sympathomimetic amines which could suggest that dextroamphetamine could prove useful in decreasing the risk of aneuploidy in women of advanced reproductive age.

		improving fecundity in women of advanced reproductive age.		
Pratt SD, Jachna BR.	(1)Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA. Electronic address: spratt@bidmc.harvard.edu. (2)Department of Anesthesia, Critical Care and Pain Medicine, Beth Israel Deaconess Medical Center, Boston, MA, USA	Care of the clinician after an adverse event.	Int J Obstet Anesth. 2014 Oct 23. doi:pii: S0959-289X(14)00140-X. 10.1016/j.ijoa.2014.10.001. Review.	The past two decades has seen a growing understanding that health care leads to harm in a large number of patients. With this insight has come an understanding that clinicians who care for patients who are harmed experience an understandable and predictable emotional response. After an adverse event, medical care givers may experience a wide range of symptoms including anger, guilt, shame, fear, loneliness, frustration and decreased job satisfaction. These may be accompanied by physical signs of fatigue, sleep disturbances, concentration difficulties, tachycardia and hypertension. These clinicians have been referred to as the "second victims." While many clinicians recover relatively quickly from an adverse event, for some this syndrome can last for weeks, months or indefinitely. Some have even contemplated or completed suicide. Being involved in an adverse event or error may also negatively impact the quality of care the clinician subsequently provides, either because of acute emotional distraction or chronic burnout. This can lead to additional errors and a vicious cycle of error, burnout and error. Health care systems have a moral responsibility to care for second victims. Care might be as simple as asking, "Are you OK?" and acknowledging the normal human emotional response to adverse events. Some centers have developed formal peer support programs in which clinicians are trained to act as peer supporter for emotional recovery after adverse events. Finally, more formal emotional support systems might be needed by some clinicians, including employee assistance programs, hospital clergy or psychological and psychiatric services.
Prior KN, Bond MJ.	General Practice, School of Medicine , Flinders University , Adelaide , Australia	Construct validity and temporal stability of the abridged 31-item Illness Behaviour Questionnaire.	Psychol Health. 2014;29(5):517-35. doi: 10.1080/08870446.2013.863885. Epub 2013 Dec 16.	OBJECTIVE: Key psychometric information was sought for three newly derived dimensions from an abridged Illness Behaviour Questionnaire (IBQ-31): Affirmation of Illness (AI), Concern for Health (CH) and General Affective State (GAS). The construct validity of these scales was examined along with their test-retest reliability and long-term stability. DESIGN: A longitudinal, observational study was conducted with 675 participants (general community members and those with either asthma, diabetes and chronic pain or chronic fatigue syndrome) providing self-report questionnaire data at baseline, with additional information sought at three (n = 483; 71.6%) and 12 months (n = 517, 76.6%). MAIN OUTCOME MEASURES: Construct validity of the IBQ-31 was explored using well-validated psychological measures of Symptom Attributions and Symptom Experience, Cognitive Distortion of Somatic Information and Illness Likelihood. RESULTS: In general, AI, CH and GAS shared predictable empirical overlap with related psychological indices across the five samples. Adequate three-month test-retest reliability was evident, with greater score variability over 12 months. CONCLUSION: The IBQ-31 comprises three

				theoretically relevant dimensions which demonstrate relative short- and long-term stability for individuals with diverse illness experiences. Future investigations should explore the predictive validity of AI, CH and GAS, along with the potential value of 'cut-off' scores for clinical use.
Qanneta R, Fontova R, Castel A.	No address given	Response to: Fibromyalgia and chronic fatigue syndrome caused by non-celiac gluten sensitivity.	Reumatol Clin. 2014 Nov 7. doi:pii: S1699-258X(14)00211-3. 10.1016/j.reuma.2014.09.008. [Epub ahead of print	[English, Spanish] No abstract available.
Qanneta R, Fontova R, Poveda MJ, Castro S.	Unidad de Fatiga Crónica, Departamento de Reumatología, Hospital Universitari Joan XXIII, Tarragona, España. Electronic address: rami_kanita229@hotmail.com.	Clinical typology of chronic fatigue syndrome: classificatory hypothesis.	Reumatol Clin. 2014 Mar-Apr;10(2):132-3. doi: 10.1016/j.reuma.2013.04.004. Epub 2013 Jul 9	[English, Spanish] No abstract available.
Qanneta R.	Chronic Fatigue Unit, Department of Rheumatology, Hospital Universitari Joan XXIII, Tarragona, Spain, rami_kanita229@hotmail.com.	Obstructive sleep apnea syndrome manifested as a subset of chronic fatigue syndrome: a comorbidity or an exclusion criterion?	Rheumatol Int. 2014 Mar;34(3):441-2. doi: 10.1007/s00296-013-2746-8. Epub 2013 Apr 18.	[English, Spanish] No abstract available.
Qanneta R, Fontova R, PÃ mies A.	Chronic Fatigue Unit, Department of Rheumatology, Hospital Universitari Joan XXIII, Tarragona, Spain, rami_kanita229@hotm	Etiology of sicca syndrome in a consecutive series of 199 patients with chronic fatigue syndrome.	Reumatol Clin. 2014 Jul-Aug;10(4):269-70. doi: 10.1016/j.reuma.2013.11.002. Epub 2013 Dec 17.	[English, Spanish] No abstract available.

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Rasa S, Nora-Krukle Z, Chapenko S, Krumina A, Roga S, Murovska M.	August Kirchenstein Institute of Microbiology and Virology, Riga Stradins University, Latvia	No evidence of XMRV provirus sequences in patients with myalgic encephalomyelitis/chronic fatigue syndrome and individuals with unspecified encephalopathy.	New Microbiol. 2014 Jan;37(1):17-24. Epub 2014 Jan 15.	Xenotropic murine leukemia virus-related virus (XMRV) has been considered a possible trigger of myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) and could also be linked with unspecified encephalopathy. The aim of this study was to analyse the frequency of XMRV proviral sequences in peripheral blood leukocyte (PBL) DNA from 150 patients with ME/CFS and 30 apparently healthy individuals, as well as in PBL and brain tissue DNA from 61 individuals with/without unspecified encephalopathy. Targeting the XMRV proviral gag gene sequence by nested polymerase chain reaction (nPCR) with previously reported primer sets, provirus was not detected either in DNA from patients with ME/CFS and individuals with unspecified encephalopathy, or in apparently healthy individuals. Only the positive control gave the amplimer of 410 base pairs (bp) after the second round that corresponds to the expected XMRV gag gene fragment. In addition, DNA was found to be negative in nPCR assays, targeting XMRV specific env gene sequence, using previously described primer sets. Also only positive control gave the amplimer of 218 bp after the second round, corresponding to the expected XMRV env gene fragment. Using nPCR we found no evidence of XMRV infection either in apparently healthy individuals or in patients with ME/CFS and individuals with unspecified encephalopathy.
Ratter J, Radlinger L, Lucas C.	(1)Hospital Rivierenland Tiel, The Netherlands. (2)Applied Research and Development Physiotherapy, Health Division, Bern University of Applied Sciences, Switzerland. (3)Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Medical Faculty, University of Amsterdam, Academic Medical Centre, Amsterdam, The	Several submaximal exercise tests are reliable, valid and acceptable in people with chronic pain, fibromyalgia or chronic fatigue: a systematic review.	J Physiother. 2014 Sep;60(3):144-50. doi: 10.1016/j.jphys.2014.06.011. Epub 2014 Jul 30.	QUESTION: Are submaximal and maximal exercise tests reliable, valid and acceptable in people with chronic pain, fibromyalgia and fatigue disorders? DESIGN: Systematic review of studies of the psychometric properties of exercise tests. PARTICIPANTS: People older than 18 years with chronic pain, fibromyalgia and chronic fatigue disorders. INTERVENTION: Studies of the measurement properties of tests of physical capacity in people with chronic pain, fibromyalgia or chronic fatigue disorders were included. OUTCOME MEASURES: Studies were required to report: reliability coefficients (intraclass correlation coefficient, alpha reliability coefficient, limits of agreements and Bland-Altman plots); validity coefficients (intraclass correlation coefficient, Spearman's correlation, Kendal T coefficient, Pearson's correlation); or dropout rates. RESULTS: Fourteen studies were eligible: none had low risk of bias, 10 had unclear risk of bias and four had high risk of bias. The included studies evaluated: Åstrand test; modified Åstrand test; Lean body mass-based Åstrand test; submaximal bicycle ergometer test following another protocol other than Åstrand test; 2-km walk test; 5-minute, 6-minute and 10-minute walk tests; shuttle walk test; and modified symptom-limited Bruce treadmill test. None of the studies assessed maximal exercise tests. Where they had been tested, reliability and validity were generally high. Dropout rates were generally acceptable. The 2-km

	Netherlands			walk test was not recommended in fibromyalgia. CONCLUSION: Moderate evidence was found for reliability, validity and acceptability of submaximal exercise tests in patients with chronic pain, fibromyalgia or chronic fatigue. There is no evidence about maximal exercise tests in patients with chronic pain, fibromyalgia and chronic fatigue. [Ratter J, Radlinger L, Lucas C (2014) Several submaximal exercise tests are reliable, valid and acceptable in people with chronic pain, fibromyalgia or chronic fatigue: a systematic review.Journal of Physiotherapy60: 144-150].
Rees CA.	School of Social and Community Medicine, University of Bristol, Bristol, UK	Lost among the trees? The autonomic nervous system and paediatrics.	Arch Dis Child. 2014 Jun;99(6):552-62. doi: 10.1136/archdischild-2012-301863. Epub 2014 Feb 26. Review.	The autonomic nervous system (ANS) has been strikingly neglected in Western medicine. Despite its profound importance for regulation, adjustment and coordination of body systems, it lacks priority in training and practice and receives scant attention in numerous major textbooks. The ANS is integral to manifestations of illness, underlying familiar physical and psychological symptoms. When ANS activity is itself dysfunctional, usual indicators of acute illness may prove deceptive. Recognising the relevance of the ANS can involve seeing the familiar through fresh eyes, challenging assumptions in clinical assessment and in approaches to practice. Its importance extends from physical and psychological well-being to parenting and safeguarding, public services and the functioning of society. Exploration of its role in conditions ranging from neurological, gastrointestinal and connective tissue disorders, diabetes and chronic fatigue syndrome, to autism, behavioural and mental health difficulties may open therapeutic avenues. The ANS offers a mechanism for so-called functional illnesses and illustrates the importance of recognising that 'stress' takes many forms, physical, psychological and environmental, desirable and otherwise. Evidence of intrauterine and post-natal programming of ANS reactivity suggests that neonatal care and safeguarding practice may offer preventive opportunity, as may greater understanding of epigenetic change of ANS activity through, for example, accidental or psychological trauma or infection. The aim of this article is to accelerate recognition of the importance of the ANS throughout paediatrics, and of the potential physical and psychological cost of neglecting it.
Reynolds GK, Lewis DP, Richardson AM, Lidbury BA.	Department of Genome Biology, The John Curtin School of Medical Research, The Australian National University, Canberra, Australian Capital Territory, Australia	Comorbidity of postural orthostatic tachycardia syndrome and chronic fatigue syndrome in an Australian cohort.	J Intern Med. 2014 Apr;275(4):409-17. doi: 10.1111/joim.12161. Epub 2013 Nov 29.	OBJECTIVE: Patients with chronic fatigue syndrome (CFS) are frequently diagnosed with comorbid postural orthostatic tachycardia syndrome (POTS), suggesting a shared pathogenesis. The aim of this study was to examine the relationship between demographic characteristics, autonomic functioning and fatigue levels amongst CFS patients with and without comorbid POTS. DESIGN AND SETTING: All patients presenting to the CFS Discovery Clinic between 2009 and 2012 completed a 20-min standing task as part of their initial assessment. Heart rate and pulse pressure were recorded at baseline, at 2-min intervals poststanding, at the end of the task and following a recovery period. Average heart rate and pulse pressure variability were calculated from this data. Age, gender, length of illness and self-reported fatigue scores were also recorded. POTS patients were diagnosed by an

				orthostatic increase in heart rate >30 beats per min, concomitant symptoms of orthostatic intolerance and no orthostatic hypotension. Differences in autonomic functioning between POTS and CFS patients were compared using independent samples t-tests, whilst logistic and linear regressions were performed to examine the contribution of autonomic functioning to task completion and perceived fatigue, respectively. RESULTS: Comorbidity of CFS and POTS (CFS-POTS) was observed in 11% (33/306) of patients. CFS-POTS patients were significantly younger (P < 0.001), had a shorter length of illness (P = 0.034), experienced greater task difficulty (P = 0.002) and were able to stand for significantly shorter periods compared to the CFS-only patients (P < 0.001). CFS-POTS patients experienced significantly lower baseline diastolic blood pressure (P = 0.002), significantly higher heart rate and lower pulse pressures at each standing measurement. Early heart rate changes (P = 0.002) and overall heart rate change (P < 0.001) were significant predictors of completion status, whereas heart rate variability (P < 0.001) and female gender (P < 0.001) were significant predictors of increased perceived task difficulty. CONCLUSIONS: Haemodynamic and demographic differences between CFS-POTS and CFS-only patients suggest that the former group reflects a distinct subgroup of the CFS population. The findings highlight the utility of screening younger patients with fatigue for POTS, and identified heart rate variability as an important marker of fatigue for CFS patients in general.
Rico-Villademoros F, Calandre EP.	Instituto de Neurociencias, Universidad de Granada, Granada, España. Electronic address: fernando.ricovillademoros@gmail.com. (2)Instituto de Neurociencias, Universidad de Granada, Granada, España.	Fibromyalgia: comorbidity indicative of vulnerability?.	Med Clin (Barc). 2014 Jun 16;142(12):538-9. doi: 10.1016/j.medcli.2013.09.030. Epub 2013 Dec 5.	[Spanish] Comment on Med Clin (Barc). 2014 Jun 16;142(12):519-25.
Rigolet M, Aouizerate J, Couette M, Ragunathan-Thangarajah N, Aoun-Sebaiti M, Gherardi RK,	Faculty of Medicine, INSERM U955-Team 10 , Créteil , France	Clinical features in patients with long-lasting macrophagic myofasciitis.	Front Neurol. 2014;5:230. doi: 10.3389/fneur.2014.00230. Review.	Macrophagic myofasciitis (MMF) is an emerging condition characterized by specific muscle lesions assessing abnormal long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients usually are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and marked cognitive deficits, not related to pain, fatigue, or depression. Clinical features usually correspond to that observed in chronic fatigue syndrome/myalgic encephalomyelitis. Representative features of MMF-associated

Cadusseau J, Authier FJ.				cognitive dysfunction include dysexecutive syndrome, visual memory impairment, and left ear extinction at dichotic listening test. Most patients fulfill criteria for non-amnestic/dysexecutive mild cognitive impairment, even if some cognitive deficits appear unusually severe. Cognitive dysfunction seems stable over time despite marked fluctuations. Evoked potentials may show abnormalities in keeping with central nervous system involvement, with a neurophysiological pattern suggestive of demyelination. Brain perfusion SPECT shows a pattern of diffuse cortical and subcortical abnormalities, with hypoperfusions correlating with cognitive deficiencies. The combination of musculoskeletal pain, chronic fatigue, and cognitive disturbance generates chronic disability with possible social exclusion. Classical therapeutic approaches are usually unsatisfactory making patient care difficult.
Rimes KA, Papadopoulos AS, Cleare AJ, Chalder T.	King's College London, Institute of Psychiatry, London, UK. Electronic address: Katharine.Rimes@kcl.ac.uk	Cortisol output in adolescents with chronic fatigue syndrome: Pilot study on the comparison with healthy adolescents and change after cognitive behavioural guided self-help treatment.	J Psychosom Res. 2014 Nov;77(5):409-14. doi: 10.1016/j.jpsychores.2014.08.018. Epub 2014 Sep 8.	OBJECTIVE: This study examined cortisol in adolescents with chronic fatigue syndrome (CFS) compared to healthy adolescents and changes in cortisol after cognitive behavioural guided self-help treatment. Exploratory analyses investigated the association between cortisol output and psychological variables. METHODS: Salivary cortisol was measured upon awakening, at 15, 30, 45 and 60min afterwards and at 12 noon, 4:00 p.m. and 8:00 p.m., in adolescents with CFS and healthy controls (HC). Groups were matched for age, gender, menarche status, menstrual cycle and awakening time. Twenty-four adolescents with CFS provided saliva samples six months after treatment. The main outcome measure was total salivary output over the day, calculated by area under the curve (AUC). The salivary awakening response was also assessed. RESULTS: Cortisol output over the day was significantly lower in the CFS group (n=46) than in healthy controls (n=33). Within the CFS group, lower daily cortisol output was associated with higher self-reported perfectionist striving and prosocial behaviour. There were no significant group differences in the awakening response (n=47 CFS versus n=34 HC). After treatment, adolescents with CFS (n=21) showed a significant increase in daily cortisol output, up to normal levels. CONCLUSION: The reduced daily cortisol output in adolescents with CFS is in line with adult findings. Associations between reduced cortisol output and two psychological variables-perfectionism and prosocial behaviour-are consistent with cognitive behavioural models of chronic fatigue syndrome. The mild hypocortisolism is reversible; cortisol output had returned to healthy adolescent levels by six months after cognitive behavioural guided self-help treatment
Rimes KA, Wingrove J, Moss-Morris R, Chalder T.	(1) King's College London Institute of Psychiatry,UK. (2)South London and Maudsley NHS Foundation Hospital	Competences required for the delivery of high and low-intensity cognitive behavioural interventions for	Behav Cogn Psychother. 2014 Nov;42(6):760-4. doi: 10.1017/S1352465814000290. Epub 2014 May 15.	BACKGROUND: Cognitive behavioural interventions are effective in the treatment of chronic fatigue, chronic fatigue syndrome (sometimes known as ME or CFS/ME) and irritable bowel syndrome (IBS). Such interventions are increasingly being provided not only in specialist settings but in primary care settings such as Improving Access to Psychological Therapies (IAPT) services. There are no existing competences for the delivery of "low-intensity" or "high-intensity" cognitive behavioural

	Trust,London,UK	chronic fatigue, chronic fatigue syndrome/ME and irritable bowel syndrome.		interventions for these conditions. AIMS: To develop "high-intensity" and "low-intensity" competences for cognitive behavioural interventions for chronic fatigue, CFS/ME and IBS. METHOD: The initial draft drew on a variety of sources including treatment manuals and other information from randomized controlled trials. Therapists with experience in providing cognitive behavioural interventions for CF, CFS/ME and IBS in research and clinical settings were consulted on the initial draft competences and their suggestions for minor amendments were incorporated into the final versions. RESULTS: Feedback from experienced therapists was positive. Therapists providing low intensity interventions reported that the competences were also helpful in highlighting training needs. CONCLUSIONS: These sets of competences should facilitate the training and supervision of therapists providing cognitive behavioural interventions for chronic fatigue, CFS/ME and IBS. The competences are available online (see table of contents for this issue: http://journals.cambridge.org/jid_BCP) or on request from the first author
Rombaut L, Scheper M, De Wandele I, De Vries J, Meeus M, Malfait F, Engelbert R, Calders P.	(1)Department of Rehabilitation Sciences and Physiotherapy, Ghent University-Artevelde University College, De Pintelaan 185, 3B3, 9000, Ghent, Belgium, Lies.Rombaut@ugent.be	Chronic pain in patients with the hypermobility type of Ehlers-Danlos syndrome: evidence for generalized hyperalgesia.	Clin Rheumatol. 2014 Feb 4.	Chronic widespread pain is highly present in patients with the Ehlers-Danlos syndrome hypermobility type (EDS-HT), but up to now, evidence for generalized hyperalgesia is lacking. The aim of this study is to investigate whether pressure pain thresholds (PPTs) at both symptomatic and asymptomatic body areas differ in EDS-HT patients compared to healthy subjects. Twenty-three women with EDS-HT and 23 gender- and age-matched healthy controls participated. All subjects marked on Margolis Pain Diagram where they felt pain lasting longer than 24 h in the past 4 weeks. Then, they completed several questionnaires assessing pain cognitions, fatigue, disability, and general health status, in order to take the possible influence of these factors on PPTs into account. Patients also completed a form concerning the type of pain they experienced. Thereupon, a blinded researcher assessed PPTs at 14 body locations on the trunk and extremities. PPTs were compared for the two complete groups. In addition, PPTs of patients and controls who did not report pain in a respective zone were compared. PPTs of the patients were significantly lower compared to those of the control group, also when pain-free samples per zone were compared. The mean (SD) PPT was 2.9 (1.62) kg/cm(2) in the EDS-HT patients and 5.2 (1.88) kg/cm(2) in the controls ($P < 0.001$). No confounding factors responsible for the observed differences could be revealed. In half of the patient group, a predominantly neuropathic pain component was likely present. This study provides evidence for the existence of hyperalgesia even in asymptomatic areas (generalized secondary hyperalgesia). The generalized hyperalgesia may represent the involvement of a sensitized central nervous system, which inquires an adapted pain management for this patient group

Rosato L, Pacini F, Panier Suffat L, Mondini G, Ginardi A, Maggio M, Bosco MC, Della Pepa C.	Department of Surgery - Endocrine Surgical Unit, Ivrea Hospital, School of Medicine, ASL TO4, University of Turin, Turin, Italy	Post-thyroidectomy chronic asthenia: self-deception or disease?	Endocrine. 2014 Jul 18.	There is clinical evidence that post-total thyroidectomy (TT) patients can present persistent asthenia. The aim of this study was to evaluate the prevalence of asthenia symptoms in such patients, assess whether a chronic asthenia syndrome could be caused by TT or become evident after it. An observational study was carried out comparing two groups of 100 patients each, all with homogeneous characteristics. Group A was treated with total lobectomy (TL), Group B with TT. All patients presented normal thyroid hormone levels. The patients were interviewed in order to identify the ones affected by post-operative asthenia persisting for at least six months, with reduced ability to perform physical and mental work, not showing improvement with rest. The severity of the symptoms has been measured by means of the brief fatigue inventory (BFI). Statistical analysis was performed to evaluate statistically significative differences between groups and prognostic factors in TT group. The incidence of post-operative asthenia was 0 % after TL and 25 % after TT, with the operation being the only significant variable. Asthenia is well known as symptom of post-thyroidectomy, but it has not been adequately investigated as consequence of surgery. We demonstrated that the complete removal of the thyroid gland could determine chronic post-thyroidectomy asthenia, although with intensity limited to low/moderate. Post-thyroidectomy asthenia is a relevant sequela interfering with quality of life of at least 25 % of patients operated, suggesting the need to identify its real causes and limit the indication to TT only when strictly required
Rowe PC, Marden CL, Flaherty MA, Jasion SE, Cranston EM, Johns AS, Fan J, Fontaine KR, Violand RL.	Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD. Electronic address: prowe@jhmi.edu	Impaired range of motion of limbs and spine in chronic fatigue syndrome.	J Pediatr. 2014 Aug;165(2):360-6. doi: 10.1016/j.jpeds.2014.04.051. Epub 2014 Jun 11.	OBJECTIVE: To determine whether adolescents and young adults with chronic fatigue syndrome (CFS) have a greater prevalence of impaired range of motion (ROM) of the limbs and spine than healthy control patients. STUDY DESIGN: Case-control study comparing rates of abnormal ROM in 48 consecutive adolescents and young adults with CFS and 48 healthy control patients matched by sex and joint hypermobility. We examined range of ankle dorsiflexion, passive straight-leg raise, seated slump, upper-limb neurodynamic test, prone knee bend, and prone press-up. Abnormal ROM was defined before the study began. The number of abnormal responses ranged from 0 (normal ROM throughout) to 11 (impaired ROM in all areas tested). RESULTS: The median number of areas with impaired ROM was greater in patients with CFS at the onset of stretch in the involved limb (5 vs 2, P<.001) and at end-range (2 vs 0, P<.001). Patients with CFS were more likely to have greater than 3 areas of impaired ROM (OR 6.0, 95% CI 2.1-17.3; P<.001) and were more likely to develop abnormal symptomatic responses to the individual tests and to the overall assessment (40% vs 4%; P<.001). CONCLUSIONS: Impaired ROM is more common in subjects with CFS than in healthy adolescents and young adults matched by sex and joint hypermobility. Adding a longitudinal strain to the nerves and soft tissues provoked symptoms in some subjects with CFS. The causes, functional impact, and optimal treatment of these abnormalities warrant further study.

Russek LN, LaShomb EA, Ware AM, Wesner SM, Westcott V.	Clarkson University, Potsdam, NY, USA; Canton-Potsdam Hospital, Potsdam, NY, USA	United States Physical Therapists' Knowledge About Joint Hypermobility Syndrome Compared with Fibromyalgia and Rheumatoid Arthritis.	Physiother Res Int. 2014 Dec 12. doi: 10.1002/pri.1613.	BACKGROUND: Joint hypermobility syndrome (JHS) is one of the most common inherited connective tissue disorders. It causes significant pain and disability for all age groups, ranging from developmental delay among children to widespread chronic pain in adults. Experts in JHS assert that the condition is under-recognized and poorly managed. PURPOSE: The aim of this study was to assess US physical therapists' knowledge about JHS compared with other causes of widespread pain and activity limitations: fibromyalgia, juvenile rheumatoid arthritis and adult rheumatoid arthritis. METHODS: Cross-sectional, Internet-based survey of randomly selected members of the American Physical Therapy Association and descriptive statistics were used to explore physical therapists' knowledge about JHS, fibromyalgia, juvenile rheumatoid arthritis and adult rheumatoid arthritis, and chi square was used to compare knowledge about the different conditions. RESULTS: The response rate was 15.5% (496). Although 36% recognized the Beighton Scale for assessing joint hypermobility, only 26.8% of respondents were familiar with the Brighton Criteria for diagnosing JHS. Few respondents (11-19%) realized that JHS has extra-articular features such as anxiety disorder, fatigue, headache, delayed motor development, easy bruising and sleep disturbance. Physical therapists working in environments most likely to see patients with JHS underestimated the likely prevalence in their patient population. CONCLUSIONS: The results suggest that many physical therapists in the United States are not familiar with the diagnostic criteria, prevalence or common clinical presentation of JHS
Saeed ID, Kheroo KN, Abdullah TJ, Salih KA.	(1)Department of Medicine, Mosul College of Medicine, Mosul, Iraq. (2)Endoscopy Unit, Ibn Sena Teaching Hospital, Mosul, Iraq. (3)Department of Medicine, Ibn Sena Teaching Hospital, Mosul, Iraq.	Blue rubber bleb naevus syndrome: a rare cause of iron deficiency anaemia.	BMJ Case Rep. 2014 Nov 11;2014. doi:pii: bcr2014205144. 10.1136/bcr-2014-205144.	We report a case in an adolescent male patient with a history of chronic fatigue, headache and unexplained iron deficiency anaemia since 2007. Numerous bluish-black lesions were found over his body surface. A surgical scar from a previous lumpectomy with a small lump were noted at the left submandibular region and another smaller lesion on the left lobe of the thyroid was also palpated. His most recent blood indices displayed the presence of moderately severe iron deficiency anaemia. Endoscopic evaluation exhibited multiple vascular lesions throughout the gastrointestinal tract. MRI of the brain revealed an irregular intracranial vascular lesion at the cerebellopontine angle. Further work-up with abdominal CT demonstrated the absence of similar lesions in the extraintestinal abdominal organs. Putting these together with histological findings, the diagnosis of blue rubber bleb naevus syndrome was confirmed. The patient was treated conservatively at this point and future management planning was discussed with him
Salsman JM, Beaumont JL, Wortman K, Yan Y, Friend J, Cella D.	Department of Medical Social Sciences, Feinberg School of Medicine at Northwestern	Brief versions of the FACIT-fatigue and FAACT subscales for patients with non-small cell lung cancer	Support Care Cancer. 2014 Oct 29.	PURPOSE: Cancer anorexia-cachexia syndrome (CACS) is common in advanced cancer patients and associated with weight loss, fatigue, impaired quality of life (QoL), and poor prognosis. The goal of this project was to identify the most responsive items from two QoL measures in the ROMANA 2 (NCT01387282) phase III global study evaluating anamorelin HCl in the treatment of non-small cell lung

	University, 633 North St. Clair, 19th Floor, Chicago, IL, 60611, USA, j-salsman@northwestern.edu	cachexia.		cancer (NSCLC) cachexia: the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and the Functional Assessment of Anorexia/Cachexia Therapy (FAACT). METHODS: In the ROMANA 2 trial, 477 patients with unresectable stage III or IV NSCLC and cachexia were to be enrolled and randomized (2:1) to receive anamorelin HCl or placebo once daily for 12 weeks. All 203 patients who reached the week 12 visit at the time of data analysis were included. Co-primary endpoints were change from baseline in lean body mass and handgrip strength. QoL was a secondary outcome with FACIT-F and FAACT questionnaires administered at baseline and at weeks 3, 6, 9, and 12. RESULTS: Two 4-item scales (fatigue/activity and appetite/eating) from the FACIT-F and FAACT questionnaires, respectively, demonstrated good internal consistency reliability, validity, and responsiveness (also referred to as the Simplified Evaluation of Fatigue (SEF) and Simplified Evaluation of Appetite (SEA), respectively). The estimated important difference for each scale was 1-2 points. CONCLUSIONS: These brief scales provide the psychometric properties necessary to promote future research in NSCLC patients with CACS. Additional work should examine the clinical utility of these scales and their impact on treatment decision-making
Santamarina-Perez P, Eiroa-Orosa FJ, Rodriguez-Urrutia A, Qureshi A, Alegre J.	Department of Child and Adolescent Psychiatry and Psychology , Institut Clínic de Neurociències, Hospital Clínic Universitari , Barcelona , Spain	Neuropsychological impairment in female patients with chronic fatigue syndrome: a preliminary study.	Appl Neuropsychol Adult. 2014;21(2):120-7. doi: 10.1080/09084282.2013.771264. Epub 2013 Aug 13.	This study examines neuropsychological impairments associated with chronic fatigue syndrome (CFS) and explores their association with related clinical factors. Sixty-eight women with CFS were assessed with a neuropsychological battery. Raw scores were adjusted for age and gender and were converted to T scores according to normative data extracted from a local sample of 250 healthy subjects. Neuropsychological dysfunction was calculated using summary impairment indexes (proportion of test scores outside normal limits-T score <40-for each cognitive domain). Finally, a linear regression was calculated to identify predictors of cognitive deficit, including intrinsic factors of the disease (level of fatigue and length of illness) and extrinsic factors (emotional factors, age, and education). Approximately 50% of scores showed impairment in attention and motor functioning, and nearly 40% showed impairment in speed information processing and executive functioning. Fatigue predicted attention and executive functioning impairment, and emotional factors predicted verbal memory dysfunction. According to our findings, cognitive dysfunction in CFS could be explained by pathophysiological processes of the disease. One implication of this would be the need to identify homogeneous subgroups of patients with CFS by taking into account common factors, which, in turn, would help to identify more specific cognitive profiles, which could then serve to implement appropriate therapeutic measures accordingly.

Santiago T, Rebelo O, NegrÃ£o L, Matos A.	Rheumatology Unit, Centro Hospitalar e Universitário de Coimbra, Praceta Prof. Mota Pinto, 3000-075, Coimbra, Portugal, tlousasantiago@hotmail.com	Macrophagic myofasciitis and vaccination: Consequence or coincidence?	Rheumatol Int. 2015 Jan;35(1):189-92. doi: 10.1007/s00296-014-3065-4. Epub 2014 Jun 13.	Macrophagic myofasciitis (MMF) characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization has been reported with increasing frequency in the past 10 years. We describe clinical and laboratory findings in patients with MMF. We did a retrospective analysis of 16 cases observed in our Neuropathology Laboratory, between January 2000 and July 2013. The mean age of the 16 patients was 48.8 ± 18.0 years; 80.0 % were female. Chronic fatigue syndrome was found in 8 of 16 patients. Half of the patients had elevated creatinine kinase levels, and 25.0 % had a myopathic electromyogram. Thirteen patients received intramuscular administration of aluminum-containing vaccine prior to the onset of symptoms. MMF may mirror a distinctive pattern of an inflammatory myopathy. The vaccines containing this adjuvant may trigger MMF in some patients.
Schmidt-Wilcke T, Ichesco E, Hampson JP, Kairys A, Peltier S, Harte S, Clauw DJ, Harris RE.	(1)Department of Anesthesiology, Chronic Pain and Fatigue Research Center, University of Michigan, Ann Arbor, USA. (2)Department of Biomedical Engineering and Functional MRI Laboratory, University of Michigan, Ann Arbor, USA.	Resting state connectivity correlates with drug and placebo response in fibromyalgia patients.	Neuroimage Clin. 2014;6:252-61. doi: 10.1016/j.nicl.2014.09.007.	Fibromyalgia is a chronic pain syndrome characterized by widespread pain, fatigue, and memory and mood disturbances. Despite advances in our understanding of the underlying pathophysiology, treatment is often challenging. New research indicates that changes in functional connectivity between brain regions, as can be measured by magnetic resonance imaging (fcMRI) of the resting state, may underlie the pathogenesis of this and other chronic pain states. As such, this parameter may be able to be used to monitor changes in brain function associated with pharmacological treatment, and might also be able to predict treatment response. We performed a resting state fcMRI trial using a randomized, placebo-controlled, cross-over design to investigate mechanisms of action of milnacipran (MLN), a selective serotonin and norepinephrine reuptake inhibitor (SNRI), in fibromyalgia patients. Our aim was to identify functional connectivity patterns at baseline that would differentially predict treatment response to MLN as compared to placebo. Since preclinical studies of MLN suggest that this medication works by augmenting antinociceptive processes, we specifically investigated brain regions known to be involved in pain inhibition. 15 fibromyalgia patients completed the study, consisting of 6 weeks of drug and placebo intake (order counterbalanced) with an interspersed 2 week wash out period. As a main finding we report that reductions in clinical pain scores during MLN were associated with decreased functional connectivity between pro-nociceptive regions and antinociceptive pain regions at baseline, specifically between the rostral part of the anterior cingulate cortex (ACC) and the insular cortex (IC), as well as between the periaqueductal gray (PAG) and the IC: patients with lower preexisting functional connectivity had the greatest reduction in clinical pain. This pattern was not observed for the placebo period. However a more robust placebo response was associated with lower baseline functional connectivity between the ACC and the dorsolateral prefrontal cortex. This study indicates that ACC-IC connectivity might play a role in the mechanism of action of MLN, and perhaps more importantly fcMRI might be a useful tool to predict pharmacological

				treatment response.
Schouwers S, Bonnet M, Verschueren P, Westhovens R, Blockmans D, MariÃ«n G, Bossuyt X.	No address given	Value-added reporting of antinuclear antibody testing by automated indirect immunofluorescence analysis.	Clin Chem Lab Med. 2014 Apr;52(4):547-51. doi: 10.1515/cclm-2013-0610.	BACKGROUND: Automated systems for antinuclear antibody analysis are being introduced. The aim was to evaluate whether automated quantitative reading of fluorescence intensity is clinically relevant and allows for value-added reporting of test results. METHODS: Consecutive samples (n=260) were used to correlate fluorescence intensity with end-point titer. Moreover, 434 samples from controls (150 healthy blood donors, 150 chronic fatigue syndrome, and 134 diseased controls) and 252 samples (obtained at diagnosis) from patients with systemic rheumatic diseases were screened for antinuclear antibodies (1:80) on HEp-2 cells using NOVA View, and likelihood ratios were calculated for fluorescence intensity result intervals. RESULTS: There was a significant correlation between end-point titer and fluorescence intensity. Likelihood ratios for a systemic rheumatic disease increased with increasing fluorescence intensity. The likelihood ratio for a systemic rheumatic disease was 0.06, 0.18, 0.51, 5.3, and 37.5 for a fluorescence intensity of ≤66, 67-150, 151-300, 301-1000, >1000, respectively. A range of 31%-37% of the patients with Sjögren's syndrome, systemic sclerosis or systemic lupus erythematosus had fluorescence intensities >1000. CONCLUSIONS: Estimation of fluorescence intensity by automated antinuclear antibody analysis offers clinically useful information. Likelihood ratios based on fluorescence intensity test result intervals aid with the interpretation of automated antinuclear antibody analysis and allow value-added reporting.
Schulte-Markwort M.	Klinik Kinder- und Jugendpsychiatrie, -psychotherapie und -psychosomatik, Universitätsklinikum Hamburg-Eppendorf.	[Does burnout exist among children and adolescents? a plea for studying an unclear mental state].	Z Kinder Jugendpsychiatr Psychother. 2014 Jul;42(4):209-10. doi: 10.1024/1422-4917/a000292.	[German] No abstract available.
Schulte-van Maaren YW, Giltay EJ, van Hemert AM, Zitman FG, de Waal MW, Van Rood YR, Carlier IV.	(1)Department of Psychiatry, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, The Netherlands. Electronic address: Y.W.M.Schulte-van_Maaren@lumc.nl. (2)Department of Psychiatry, Leiden	Reference values for the Body Image Concern Inventory (BICI), the Whitely Index (WI), and the Checklist Individual Strength (CIS-20R): The Leiden Routine Outcome Monitoring Study.	J Affect Disord. 2014 Aug;164:82-9. doi: 10.1016/j.jad.2014.03.013. Epub 2014 Mar 24.	BACKGROUND: The Body Image Concern Inventory (BICI), the Whitely Index (WI), and the Checklist Individual Strength (CIS-20R) are three questionnaires often incorporated in routine outcome monitoring (ROM). Respectively, they assess symptom severity in patients with body dysmorphic disorder, hypochondriasis, and chronic fatigue syndrome. We aimed to generate reference values for a healthy population and for a population of patients fulfilling diagnostic criteria for at least one of BDD, hypochondriasis, and CFS, treated in specialized mental health care. METHODS: The healthy ROM reference-group (n=648) was recruited through general practitioners. These subjects were matched for age and sex with the ROM patient-group (n=823). To define limits (i.e., cut-off-values) for one-sided reference intervals (5th percentile [P5] for ROM patient-group and 95th percentile [P95] for

	University Medical Center, P.O. Box 9600, 2300 RC Leiden, The Netherlands. (3)Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, The Netherlands.			ROM reference-group) the outermost 5% of observations were used. Discriminative powers were evaluated by receiver operating characteristics (ROC) analyses RESULTS: Cut-off-values (P95 ROM reference-group) were 55 for the BICI, 6 for the WI, and 92 for the CIS-20R. These values differed for men and women, being mostly higher for women. The discriminative power of all three somatoform questionnaires was very high. LIMITATIONS: Substantial non-response and limited generalizability. CONCLUSIONS: For the BICI, WI, and CIS-20R a comprehensive set of reference values was obtained. The reference values may support clinical decisions regarding adjusting or terminating therapy, and possible referral.
Sha S, Liang J, Chen M, Xu B, Liang C, Wei N, Wu K.	State Key Laboratory of Cancer Biology & Xijing Hospital of Digestive Diseases, Fourth Military Medical University, Xi'an, Shaanxi Province, China.	Systematic review: faecal microbiota transplantation therapy for digestive and nondigestive disorders in adults and children.	Aliment Pharmacol Ther. 2014 May;39(10):1003-32. doi: 10.1111/apt.12699. Epub 2014 Mar 18. Review. Comment in Aliment Pharmacol Ther. 2014 Jul;40(1):119. Aliment Pharmacol Ther. 2014 Jul;40(1):119-20.	BACKGROUND: There has been growing interest in the use of faecal microbiota transplantation (FMT) for the treatment of gastrointestinal and nongastrointestinal diseases. AIM: To review systematically the reported efficacy and safety of FMT in the management of gastrointestinal and nongastrointestinal disorders in adults and children. METHODS: The systematic review followed Cochrane and PRISMA recommendations. Available articles were identified using three electronic databases in addition to hand searching and contacting experts. Inclusion criteria were any reports of FMT therapy written in English. RESULTS: A total of 844 patients who had undergone FMT were identified from 67 published studies. The most common indications were refractory/relapsing Clostridium difficile infection (CDI) (76.3%) and inflammatory bowel disease (IBD) (13.2%). There has been only one placebo-controlled trial, a successful trial in 43 patients with recurrent CDI. Seven publications report FMT in paediatric patients with a total of 11 treated, 3 with chronic constipation and the remainder with recurrent CDI or ulcerative colitis (UC). 90.7% of patients with refractory/relapsing CDI were cured and 78.4% of patients with IBD were in remission after FMT. FMT therapy could also be effective in treatment of some nongastrointestinal disorders such as chronic fatigue syndrome. The only reported serious adverse event attributed to the therapy was a case of suspected peritonitis. CONCLUSIONS: Although more controlled trials are needed, faecal microbiota transplantation therapy shows promise in both adults and children with gastrointestinal diseases such as CDI and IBD.

Shimosako N, Kerr JR.	(1) CFS Group, Department of Cellular & Molecular Medicine, St George's University of London, London, UK. (2)CFS Group, Department of Cellular & Molecular Medicine, St George's University of London, London, UK Escuela de Medicina y Ciencias de Salud, Universidad del Rosario, Bogota, Colombia.	Use of single-nucleotide polymorphisms (SNPs) to distinguish gene expression subtypes of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).	J Clin Pathol. 2014 Dec;67(12):1078-83. doi: 10.1136/jclinpath-2014-202597. Epub 2014 Sep 19.	AIMS: We have reported gene expression changes in patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and the fact that such gene expression data can be used to identify subtypes of CFS/ME with distinct clinical phenotypes. Due to the difficulties in using a comparative gene expression method as an aid to CFS/ME disease and subtype-specific diagnosis, we have attempted to develop such a method based on single-nucleotide polymorphism (SNP) analysis. METHODS: To identify SNP allele associations with CFS/ME and CFS/ME subtypes, we tested genomic DNA of patients with CFS/ME (n=108), patients with endogenous depression (n=17) and normal blood donors (n=68) for 504 human SNP alleles located within 88 CFS-associated human genes using the SNP Genotyping GoldenGate Assay (Illumina, San Diego, California, USA). 360 ancestry informative markers (AIM) were also examined. RESULTS: 21 SNPs were significantly associated with CFS/ME compared with depression and normal groups. 148 SNP alleles had a significant association with one or more CFS/ME subtypes. For each subtype, associated SNPs tended to be grouped together within particular genes. AIM SNPs indicated that 4 subjects were of Asian origin while the remainder were Caucasian. Hierarchical clustering of AIM data revealed the relatedness between 2 couples of patients with CFS only and confirmed the overall heterogeneity of all subjects. CONCLUSIONS: This study provides evidence that human SNPs located within CFS/ME associated genes are associated with particular genomic subtypes of CFS/ME. Further work is required to develop this into a clinically useful subtype-specific diagnostic test.
Shiraishi W, Une H, Iwanaga Y, Yamamoto A.	Department of Neurology, Kyushu Kosei Nenkin Hospital.	A case of post-transfusion posterior reversible encephalopathy syndrome with cerebral hemorrhage that may be associated with fat-soluble vitamin deficiency	Rinsho Shinkeigaku. 2014;54(6):518-21.	[Article in Japanese] A 36-year-old woman with a 4 year history of lower legs edema, hypermenorrhea and melena without medical treatment was admitted to our hospital. At 18 days before admission, anasarca and general fatigue appeared and she was admitted to another hospital. Her hemoglobin concentration was 1.4 g/dl and chest X-ray showed cardiomegaly. Heart failure with severe chronic anemia was diagnosed, and blood transfusion was performed. Her hemoglobin concentration increased to 10 g/dl and the anasarca disappeared. The day after discharge, she was referred to our hospital with generalized convulsion. We diagnosed posterior reversible encephalopathy syndrome (PRES) from the typical MRI imaging. We started treatment and her consciousness recovered steadily. At a week after admission, left hemiparesis appeared. Her brain imaging revealed multiple intracranial hemorrhages. In addition, her visual disturbance revealed vitamin A and vitamin K deficiency. PRES sometimes occur secondary to blood transfusion, but secondary brain hemorrhage is rare. Her fat-soluble vitamin deficiency, which resulted from a peculiar eating habit, may have contributed to the brain hemorrhage.

Shmygalev S, Dagtekin O, Gerbershagen HJ, Marcus H, JÃ¼bner M, Sabatowski R, Petzke F.	Department of Anaesthesiology and Intensive Care Medicine, University Hospital Dresden, Technische Universität Dresden, Dresden, Germany, sergey.shmygalev@uniklinikum-dresden.de.	Assessing Cognitive and Psychomotor Performance in Patients with Fibromyalgia Syndrome.	Pain Ther. 2014 Oct 25.	INTRODUCTION: Patients with fibromyalgia syndrome (FMS) generally present with chronic widespread pain, accompanied by a range of additional and non-specific symptoms, such as fatigue, disturbed sleep, and cognitive dysfunction, which tend to increase with overall severity. Previous studies have shown moderate cognitive impairment in patients with FMS, but there are few valid data explicitly assessing the relevance of these findings to everyday functions, such as driving ability. Therefore, we studied patients with FMS to assess the impact of FMS on tests that predict driving ability. METHODS: Female patients with FMS were prospectively compared to a historical control group of healthy volunteers. The test battery comprised assessments of visual orientation, concentration, attention, vigilance, motor coordination, performance under stress, and reaction time. RESULTS: A total of 43 patients were matched to 129 controls. The results indicated that the patients' psychomotor and cognitive performances were significantly non-inferior when compared to healthy controls (with 0.05% alcohol), with the exception of motor coordination. Patients and healthy controls showed an age-related decline in test performance. Correlations were smaller in patients and reversed for vigilance which was linked to a greater FMS symptom load in younger patients. CONCLUSION: The results of the present study demonstrate that, in general, the driving ability of patients with FMS was not inferior to that of healthy volunteers based on a standardized computer-based test battery. However, variables, such as younger age, depression, anxiety, fatigue, pain, and poor motor coordination, likely contribute to the subjective perception of cognitive dysfunction in FMS.
Sieminski M, Losy J, Partinen M.	Department of Adult Neurology, Medical University of Gdansk, Gdansk, Poland. Electronic address: msiem@wp.pl.	Restless legs syndrome in multiple sclerosis.	Sleep Med Rev. 2014 Oct 12. doi:pii: S1087-0792(14)00101-4. 10.1016/j.smrv.2014.10.002. Review.	Restless legs syndrome (RLS) is a sleep-related sensory-motor disorder characterized by an irresistible urge to move the legs accompanied by unpleasant sensations in the lower extremities. According to many recent studies patients with multiple sclerosis (MS) suffer frequently from symptoms of RLS. The prevalence of RLS in MS patients varies 13.3%-65.1%, which is higher than the prevalence of RLS in people of the same age in the general population. MS patients with RLS have higher scores in the Expanded Disability Status Scale compared to MS patients without RLS. Presence of RLS has a negative impact on sleep quality and fatigue of MS patients. Iron deficiency and chronic inflammation may be factors contributing to development of RLS in MS. The relationship between the course and treatment of MS and RLS requires further prospective studies.
Singh K, Gupta R, Kamal H, Silvestri NJ, Wolfe GI.	Department of Neurology, University at Buffalo School of Medicine and Biomedical Sciences, The State University of New York, 100 High	Posterior reversible encephalopathy syndrome secondary to blood transfusion.	J Clin Neurosci. 2014 Dec 23. doi:pii: S0967-5868(14)00627-4. 10.1016/j.jocn.2014.10.005.	The appearance of posterior reversible encephalopathy syndrome (PRES) after blood transfusion is rare and has only been reported in three patients to our knowledge. We report a fourth patient with PRES secondary to blood transfusion. A 36-year-old woman with a history of menorrhagia presented to the emergency department with severe fatigue. She had a hemoglobin of 1.7g/dl and received four units of red blood cells over 15hours. On day 6 post-transfusion she returned with confusion, headache and a generalized tonic-clonic seizure. The MRI of her brain

	Street, Building D, Buffalo, NY 14203-1126, USA. Electronic address: Karanbirsinghmd@gmail.com.			was consistent with PRES. The following day her confusion worsened, repeat MRI of the brain showed new T2-weighted lesions. Over next 10days her mental status gradually improved close to her baseline. A repeat MRI of the brain showed resolution of the T2-weighted lesions. The clinical presentation, radiological findings and disease progression in our patient was consistent with PRES. Other than the blood transfusions, there were no apparent risk factors for PRES. The prior three patients with post-transfusion PRES have been reported in middle-aged women with uterine fibroids. It is suspected that these patients have a subacute to chronic anemic state due to ongoing menorrhagia. It is interesting to note that no cases of PRES post-transfusion have been reported in the setting of acute blood loss, such as from trauma. It is postulated that an abrupt increase in hemoglobin causes a rapid rise in blood viscosity and loss of hypoxic vasodilation. Subsequent endothelial damage and brain capillary leakage results in PRES. This constellation of changes may not occur after transfusion in patients with more acute blood loss.
Sirois FM, Molnar DS.		Perfectionism and maladaptive coping styles in patients with chronic fatigue syndrome, irritable bowel syndrome and fibromyalgia/arthritis and in healthy controls.	Psychother Psychosom. 2014;83(6):384-5. doi: 10.1159/000365174. Epub 2014 Oct 16. No abstract available.	Health and Well-Being Laboratory, Department of Psychology, Bishop's University, Sherbrooke, Que., Canada.
Slavich GM, Irwin MR.		From stress to inflammation and major depressive disorder: a social signal transduction theory of depression.	Psychol Bull. 2014 May;140(3):774-815. doi: 10.1037/a0035302. Epub 2014 Jan 13.	No abstract available
Slim M, Calandre EP, Rico-Villademoros F.	Cousins Center for Psychoneuroimmunology, University of California, Los Angeles.	An insight into the gastrointestinal component of fibromyalgia: clinical manifestations and potential underlying mechanisms.	Rheumatol Int. 2014 Aug 14.	Major life stressors, especially those involving interpersonal stress and social rejection, are among the strongest proximal risk factors for depression. In this review, we propose a biologically plausible, multilevel theory that describes neural, physiologic, molecular, and genomic mechanisms that link experiences of social-environmental stress with internal biological processes that drive depression pathogenesis. Central to this social signal transduction theory of depression is the hypothesis that experiences of social threat and adversity up-regulate components of the immune system involved in inflammation. The key mediators of this response, called proinflammatory cytokines, can in turn elicit profound changes in

				behavior, which include the initiation of depressive symptoms such as sad mood, anhedonia, fatigue, psychomotor retardation, and social-behavioral withdrawal. This highly conserved biological response to adversity is critical for survival during times of actual physical threat or injury. However, this response can also be activated by modern-day social, symbolic, or imagined threats, leading to an increasingly proinflammatory phenotype that may be a key phenomenon driving depression pathogenesis and recurrence, as well as the overlap of depression with several somatic conditions including asthma, rheumatoid arthritis, chronic pain, metabolic syndrome, cardiovascular disease, obesity, and neurodegeneration. Insights from this theory may thus shed light on several important questions including how depression develops, why it frequently recurs, why it is strongly predicted by early life stress, and why it often co-occurs with symptoms of anxiety and with certain physical disease conditions. This work may also suggest new opportunities for preventing and treating depression by targeting inflammation.
Smith C, Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, Weston Education Centre, London, UK.	Unity of opposites? Chronic fatigue syndrome and the challenge of divergent perspectives in guideline development.	J Neurol Neurosurg Psychiatry. 2014 Feb;85(2):214-9. doi: 10.1136/jnnp-2012-303208. Epub 2012 Nov 17.	Guideline development by its nature is a process and method of integration and synthesis of information, be it originating from research, evidence-based medicine, clinical findings, patient experience and/or individual narratives of an illness or disease. In the majority of cases, it can be assumed that this information and these ideas are travelling in the same direction; however, it is possible that the objective and subjective cannot be synthesised, and appear mutually contradictory. In this commentary, an example of where this might be the case has been analysed: a report published by the Scottish Public Health Network, a Health Care Needs Assessment of Services for people living with myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS). It appears from reflection and analysis of this document that this process may indeed have gone awry. We propose that, if followed, this document would lead to the adoption of dangerous diagnostic criteria for ME/CFS, as well as preventing patients from making informed decisions about treatment options, and discouraging clinicians from following evidence-based medicine and recommending proven treatments for ME/CFS, because of potential implications for future commissioning. This commentary seeks to highlight some of the problems, contradictions and unintended consequences of a divergence between patient perspectives and evidence-based medicine despite probably sharing the same aim, that of improving patient care and striving for better understanding and better treatments for disease.
Smith SC, Wagner MS.	No address given	Clinical endocannabinoid deficiency (CECD) revisited: can this concept explain the therapeutic benefits	Neuro Endocrinol Lett. 2014;35(3):198-201. Review.	OBJECTIVES: Ethan B. Russo's paper of December 1, 2003 explored the concept of a clinical endocannabinoid deficiency (CECD) underlying the pathophysiology of migraine, fibromyalgia, irritable bowel syndrome and other functional conditions alleviated by clinical cannabis. METHODS: Available literature was reviewed, including searches via the National Library of medicine database and other sources. RESULTS: A review of the literature indicates that significant progress has been

		of cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatment-resistant conditions?		made since Dr. Ethan B. Russo's landmark paper, just ten years ago (February 2, 2004). Investigation at that time suggested that cannabinoids can block spinal, peripheral and gastrointestional mechanisms that promote pain in headache, fibromyalgia, irritable bowel syndrome and muscle spasm. CONCLUSION: Subsequent research has confirmed that underlying endocannabinoid deficiencies indeed play a role in migraine, fibromyalgia, irritable bowel syndrome and a growing list of other medical conditions. Clinical experience is bearing this out. Further research and especially, clinical trials will further demonstrate the usefulness of medical cannabis. As legal barriers fall and scientific bias fades this will become more apparent.
Snekkevik H, Eriksen HR, Tangen T, Chalder T, Reme SE.	Friskvernklinikken, Asker, Norway	Fatigue and depression in sick-listed chronic low back pain patients.	Pain Med. 2014 Jul;15(7):1163-70. doi: 10.1111/pme.12435. Epub 2014 Apr 9.	OBJECTIVE: The relationship between fatigue and pain has been investigated previously, but little is known about the prevalence of substantial fatigue in patients sick-listed for chronic low back pain (CLBP) and about how fatigue is associated with depression, pain, and long-term disability. The aims of the study were to examine the prevalence of substantial fatigue; associations between fatigue, depression, and pain; and whether fatigue predicted long-term disability. METHODS: Five hundred sixty-nine patients participating in a randomized controlled trial and sick-listed 2-10 months for LBP were included in the study. Cross-sectional analyses were conducted to investigate the prevalence and independent associations between fatigue, depression, pain, and disability, while longitudinal analyses were done to investigate the association between fatigue and long-term disability. RESULTS: The prevalence of substantial fatigue was 69.7%. Women reported significantly more fatigue than men ($t = -3.6$, $df = 551$; $P < .001$). Those with substantial fatigue had higher pain intensity ($t = -3.3$, $df = 534$; $P = 0.01$), more depressive symptoms ($t = -10.9$, $df = 454$; $P < 0.001$), and more disability ($t = -7.6$, $df = 539$; $P < 0.001$) than those without substantial fatigue. Musculoskeletal pain and depression were independently associated with substantial fatigue. In the longitudinal analyses, fatigue predicted long-term disability at 3, 6, and 12 months' follow-up. After pain and depression were controlled for, fatigue remained a significant predictor of disability at 6 months' follow-up. CONCLUSIONS: The vast majority of the sick-listed CLBP patients reported substantial fatigue. Those with substantial fatigue had more pain and depressive symptoms and a significant risk of reporting more disability at 3, 6, and 12 months. Substantial fatigue is disabling in itself but also involves a risk of developing chronic fatigue syndrome and long-term disability.
Stahl D, Rimes KA, Chalder T.	(1)Department of Biostatistics, Institute of Psychiatry, King's College London, UK. (2)Department of	Mechanisms of change underlying the efficacy of cognitive behaviour therapy for chronic	Psychol Med. 2014 Apr;44(6):1331-44. doi: 10.1017/S0033291713002006. Epub 2013 Aug 12.	BACKGROUND: Several randomized controlled trials (RCTs) have shown that cognitive behavioural psychotherapy (CBT) is an efficacious treatment for chronic fatigue syndrome (CFS). However, little is known about the mechanisms by which the treatment has its effect. The aim of this study was to investigate potential mechanisms of change underlying the efficacy of CBT for CFS. We applied path

	Psychology, University of Bath, UK. (3)Department of Psychological Medicine, Institute of Psychiatry, King's College London, UK.	fatigue syndrome in a specialist clinic: a mediation analysis.		analysis and introduce novel model comparison approaches to assess a theoretical CBT model that suggests that fearful cognitions will mediate the relationship between avoidance behaviour and illness outcomes (fatigue and social adjustment). METHOD: Data from 389 patients with CFS who received CBT in a specialist service in the UK were collected at baseline, at discharge from treatment, and at 3-, 6- and 12-month follow-ups. Path analyses were used to assess possible mediating effects. Model selection using information criteria was used to compare support for competing mediational models. RESULTS: Path analyses were consistent with the hypothesized model in which fear avoidance beliefs at the 3-month follow-up partially mediate the relationship between avoidance behaviour at discharge and fatigue and social adjustment respectively at 6 months. CONCLUSIONS: The results strengthen the validity of a theoretical model of CBT by confirming the role of cognitive and behavioural factors in CFS.
Struyf F, Meeus M, Fransen E, Roussel N, Jansen N, Truijen S, Nijs J.	Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium; Chronic Pain and Chronic Fatigue Research Group (Pain in Motion). Electronic address: Filip.struyf@uantwerpen.be.	Interrater and intrarater reliability of the pectoralis minor muscle length measurement in subjects with and without shoulder impingement symptoms.	Man Ther. 2014 Aug;19(4):294-8. doi: 10.1016/j.math.2014.04.005. Epub 2014 Apr 21.	Measuring the pectoralis minor muscle length (PML) is of clinical interest, as a short PML has been associated with a decrease of scapular posterior tilting and shoulder pain. However, as no reliability data are available at present, the objective of this study was to examine the inter- and intrarater reliability of the PML measurement in both subjects with and without shoulder impingement symptoms (SIS). Therefore, two assessors performed the PML measurement (3 times/shoulder) in 25 patients with SIS and 25 pain-free controls. Both assessors were blinded for each other's findings. For reliability testing, intra-class coefficients (ICCs; model 2,1) and standard errors of measurements were calculated. Intrarater reliability analysis resulted with ICCs ranging from 0.87 (Standard error of measurement (SEM) 0.21-0.27%) (symptomatic) to 0.93 (SEM 0.19-0.30%) (asymptomatic) in patients with SIS, representing excellent test-retest agreement. Healthy subjects presented with ICCs ranging from 0.76 (SEM 0.29-0.32%) (dominant side) to 0.87 (SEM 0.21-0.32%) (non-dominant side), representing good test-retest agreement. ICCs and SEMs on the symptomatic and asymptomatic side (0.48 and 0.46%; 0.56 and 0.61%) in SIS patients, and on the two sides (non-dominant; 0.47 and 0.45%, dominant; 0.53 and 0.38% respectively) in healthy subjects showed moderate interrater reliability and low dispersion of the measurement errors. We concluded that the PML measurement has good to excellent intrarater reliability and poor to moderate interrater reliability.
Sulheim D, Fagermoen E, Winger A, Andersen AM, Godang K, MÃ¼ller F, Rowe PC, Saul	Department of Paediatrics, Oslo University Hospital, Oslo, Norway, Department of Paediatrics,	Disease mechanisms and clonidine treatment in adolescent chronic fatigue syndrome: a combined cross-	JAMA Pediatr. 2014 Apr;168(4):351-60. doi: 10.1001/jamapediatrics.2013.4647.	IMPORTANCE: Chronic fatigue syndrome (CFS) is a disabling condition with unknown disease mechanisms and few treatment options. OBJECTIVE: To explore the pathophysiology of CFS and assess clonidine hydrochloride pharmacotherapy in adolescents with CFS by using a hypothesis that patients with CFS have enhanced sympathetic activity and that sympatho-inhibition by clonidine would improve symptoms and function. DESIGN, SETTING, AND PARTICIPANTS: Participants were

JP, Skovlund E, Ã˜ie MG, Wyller VB.	Lillehammer County Hospital, Lillehammer, Norway.	sectional and randomized clinical trial.		enrolled from a single referral center recruiting nationwide in Norway. A referred sample of 176 adolescents with CFS was assessed for eligibility; 120 were included (34 males and 86 females; mean age, 15.4 years). A volunteer sample of 68 healthy adolescents serving as controls was included (22 males and 46 females; mean age, 15.1 years). The CSF patients and healthy controls were assessed cross-sectionally at baseline. Thereafter, patients with CFS were randomized 1:1 to treatment with low-dose clonidine or placebo for 9 weeks and monitored for 30 weeks; double-blinding was provided. Data were collected from March 2010 until October 2012 as part of the Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial. INTERVENTIONS: Clonidine hydrochloride capsules (25 µg or 50 µg twice daily for body weight <35 kg or >35 kg, respectively) vs placebo capsules for 9 weeks. MAIN OUTCOMES AND MEASURES: Number of steps per day. RESULTS: At baseline, patients with CFS had a lower number of steps per day (P < .001), digit span backward score (P = .002), and urinary cortisol to creatinine ratio (P = .001), and a higher fatigue score (P < .001), heart rate responsiveness (P = .02), plasma norepinephrine level (P < .001), and serum C-reactive protein concentration (P = .04) compared with healthy controls. There were no significant differences regarding blood microbiology evaluation. During intervention, the clonidine group had a lower number of steps per day (mean difference, -637 steps; P = .07), lower plasma norepinephrine level (mean difference, -42 pg/mL; P = .01), and lower serum C-reactive protein concentration (mean ratio, 0.69; P = .02) compared with the CFS placebo group. CONCLUSIONS AND RELEVANCE: Adolescent CFS is associated with enhanced sympathetic nervous activity, low-grade systemic inflammation, attenuated hypothalamus-pituitary-adrenal axis function, cognitive impairment, and large activity reduction, but not with common microorganisms. Low-dose clonidine attenuates sympathetic outflow and systemic inflammation in CFS but has a concomitant negative effect on physical activity; thus, sympathetic and inflammatory enhancement may be compensatory mechanisms. Low-dose clonidine is not clinically useful in CFS. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT01040429.
Swenson ER.	VA Puget Sound Health Care System and Department of Medicine, University of Washington, Seattle, WA, USA, eswenson@u.washington.edu.	Carbonic anhydrase inhibitors and high altitude illnesses.	Subcell Biochem. 2014;75:361-86. doi: 10.1007/978-94-007-7359-2_18. Review.	Carbonic anhydrase (CA) inhibitors, particularly acetazolamide, have been used at high altitude for decades to prevent or reduce acute mountain sickness (AMS), a syndrome of symptomatic intolerance to altitude characterized by headache, nausea, fatigue, anorexia and poor sleep. Principally CA inhibitors act to further augment ventilation over and above that stimulated by the hypoxia of high altitude by virtue of renal and endothelial cell CA inhibition which oppose the hypocapnic alkalosis resulting from the hypoxic ventilatory response (HVR), which acts to limit the full expression of the HVR. The result is even greater arterial oxygenation than that driven by hypoxia alone and greater altitude tolerance. The severity of several additional diseases of high attitude may also be reduced by acetazolamide, including

				high altitude cerebral edema (HACE), high altitude pulmonary edema (HAPE) and chronic mountain sickness (CMS), both by its CA-inhibiting action as described above, but also by more recently discovered non-CA inhibiting actions, that seem almost unique to this prototypical CA inhibitor and are of most relevance to HAPE. This chapter will relate the history of CA inhibitor use at high altitude, discuss what tissues and organs containing carbonic anhydrase play a role in adaptation and maladaptation to high altitude, explore the role of the enzyme and its inhibition at those sites for the prevention and/or treatment of the four major forms of illness at high altitude.
SÃ¡ez-FrancÃ s N, Valero S, Calvo N, GomÃ -I-Freixanet M, Alegre J, de Sevilla TF, Casas M.	Dept of Psychiatry, Hospital Universitari Vall d'Hebron, Passeig de la Vall d'Hebron 119-129, 08035 Barcelona, Dept of Psychiatry and Legal Medicine, Universitat Autònoma de Barcelona, Catalonia, Spain. E- address: nasaez@vhebron.net.	Chronic fatigue syndrome and personality: a case-control study using the Alternative Five Factor Model.	Psychiatry Res. 2014 May 30;216(3):373-8. doi: 10.1016/j.psychres.2014.02.031 . Epub 2014 Mar 3.	Neuroticism is the personality dimension most frequently associated with chronic fatigue syndrome (CFS). Most studies have also shown that CFS patients are less extraverted than non-CFS patients, but results have been inconsistent, possibly because the facets of the extraversion dimension have not been separately analyzed. This study has the following aims: to assess the personality profile of adults with CFS using the Alternative Five-Factor Model (AFFM), which considers Activity and Sociability as two separate factors of Extraversion, and to test the discriminant validity of a measure of the AFFM, the Zuckerman-Kuhlman Personality Questionnaire, in differentiating CFS subjects from normal-range matched controls. The CFS sample consisted of 132 consecutive patients referred for persistent fatigue or pain to the Department of Medicine of a university hospital. These were compared with 132 matched normal population controls. Significantly lower levels of Activity and significantly higher levels of Neuroticism-Anxiety best discriminated CFS patients from controls. The results are consistent with existing data on the relationship between Neuroticism and CFS, and clarify the relationship between Extraversion and CFS by providing new data on the relationship of Activity to CFS.
Tak LM, Rosmalen JG.	Dimence Institute of Mental Health, Nico Bolkesteinlaan 1, 7416 SB Deventer, the Netherlands. Electronic address: L.Tak@dimence.nl.	Potential bias in research of heart rate variability in fibromyalgia and chronic fatigue syndrome.	Semin Arthritis Rheum. 2014 Apr;43(5):e1. doi: 10.1016/j.semarthrit.2013.09.002. Epub 2013 Oct 11. No abstract available.	Comment on Semin Arthritis Rheum. 2013 Oct;43(2):279-87.
Tarakji B, Ashok N, Alakeel R, Azzeghaibi S, Umair A, Darwish S, Mahmoud R, Elkhatat E.	(1) Department of Oral Maxillofacial Sciences, Alfarabi College of Dentistry and Nursing, Riyadh, Saudi Arabia. (2)Department of Clinical Laboratory	Hepatitis B vaccination and associated oral manifestations: a non-systematic review of literature and case reports.	Ann Med Health Sci Res. 2014 Nov;4(6):829-36. doi: 10.4103/2141-9248.144870. Review.	Hepatitis B vaccine has been administered in children and adults routinely to reduce the incidence of the disease. Even though, hepatitis B vaccine is considered as highly safe, some adverse reactions have been reported. A literature search was carried out in PubMed, accessed via the National Library of Medicine PubMed interface, searching used the following keywords: Hepatitis B vaccine and complications from 1980 to 2014. A total of 1147 articles were obtained out of which articles, which discuss the complications occurring orally or occurring elsewhere in the body, which

	Sciences, King Saud University, Alfarabi College of Medicine, Riyadh, Saudi Arabia. (3)Department of Restorative Dentistry Sciences, Alfarabi College of Dentistry and Nursing, Saudi Arabia.			have the potential to manifest orally after hepatitis B vaccination were selected. A total of 82 articles were identified which included 58 case series or case reports, 15 review articles, 4 cross sectional studies, 3 prospective cohort studies, one retrospective cohort study and a case control study. After reviewing the literature, we observed that complications seen after Hepatitis B vaccination are sudden infant death syndrome, multiple sclerosis, chronic fatigue syndrome, idiopathic thrombocytopenic purpura, vasculititis optic neuritis, anaphylaxis, systemic lupus erytymatosus, lichen planus and neuro-muscular disorder. Of these complications, some are manifested orally or have the potential to manifest orally. Although, most of the complications are self-limiting, some are very serious conditions, which require hospitalization with immediate medical attention.
Teitelbaum J.	No address given	Chronic fatigue syndrome, fibromyalgia, and myalgic encephalomyelitis: a clinical perspective.	Altern Ther Health Med. 2014 Jan-Feb;20(1):45-6..	No abstract available
The GK, Verkes RJ, Fekkes D, Bleijenberg G, van der Meer JW, Buitelaar JK.	Department of General Internal Medicine, Nijmegen Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Reinier Postlaan 4, 6525 GC Nijmegen, The Netherlands. g.the@adrz.nl.	Tryptophan depletion in chronic fatigue syndrome, a pilot cross-over study.	BMC Res Notes. 2014 Sep 16;7:650. doi: 10.1186/1756-0500-7-650.	BACKGROUND: Chronic fatigue syndrome (CFS) is still an enigmatic disorder. CFS can be regarded as a complex disorder with tremendous impact on lives of CFS-patients. Full recovery without treatment is rare. A somatic explanation for the fatigue is lacking. There is clinical and experimental evidence implicating enhanced serotonergic neurotransmission in CFS. Genetic studies and imaging studies support the hypothesis of upregulated serotonin system in CFS. In line with the hypothesis of an increased serotonergic state in CFS, we performed a randomised clinical trial investigated the effect of 5-HT3 receptor antagonism in CFS. No benefit was found of the 5-HT3 receptor antagonist ondansetron compared to placebo.To further investigate the involvement of serotonin in CFS we performed a placebo controlled cross over pilot study investigating the effect of Acute Tryptophan Depletion. FINDINGS: Five female CFS-patients who met the US Center for Disease Control and Prevention criteria for CFS were recruited. There were two test days, one week apart. Each participant received placebo and ATD. To evaluate the efficacy of the ATD procedure tryptophan and the large neutral amino acids were measured. The outcome measures were fatigue severity, concentration and mood states. ATD resulted in a significant plasma tryptophan to large neutral amino acid ratio reduction of 96%. There were no significant differences in fatigue-, depression and concentration between the placebo- and ATD condition. CONCLUSIONS: These first five CFS-patients did not respond to the ATD procedure. However, a much larger sample size is needed to draw final conclusions on the hypothesis of an increased serotonergic state in the pathophysiology of CFS. TRIAL REGISTRATION:

				ISRCTN07518149.
Tiemensma J, Andela CD, Kaptein AA, Romijn JA, van der Mast RC, Biermasz NR, Pereira AM.	Department of Endocrinology and MetabolismC7-Q, Center for Endocrine Tumors Leiden (CETL), Leiden University Medical Center, PO Box 9600, 2300 RC Leiden, The NetherlandsPsychological	Psychological morbidity and impaired quality of life in patients with stable treatment for primary adrenal insufficiency: cross-sectional study and review of the literature.	Eur J Endocrinol. 2014 Aug;171(2):171-82. doi: 10.1530/EJE-14-0023. Epub 2014 May 6. Review.	CONTEXT: A high prevalence of psychological morbidity and maladaptive personality as well as impaired quality of life (QoL) is observed in patients with and without hydrocortisone dependency following (cured) Cushing's syndrome. However, it is currently unclear whether a similar pattern is present in patients with chronic glucocorticoid replacement for primary adrenal insufficiency (PAI). OBJECTIVE: To evaluate psychological functioning, personality traits, and QoL in patients with PAI. DESIGN AND SUBJECTS: A cross-sectional study including 54 patients with stable treatment for PAI and 54 healthy matched controls. Both patients and controls completed questionnaires on psychological functioning (Apathy Scale, Irritability Scale, Mood and Anxiety Symptoms Questionnaire short form, and Hospital Anxiety and Depression Scale), personality traits (Dimensional Assessment of Personality Pathology short form), and QoL (Multidimensional Fatigue Inventory, Short Form 36, EuroQoL-5D, Nottingham Health Profile, and Physical Symptom Checklist). RESULTS: Patients with PAI suffered from more psychological morbidity (i.e. irritability and somatic arousal) and QoL impairments compared with controls (all $P<0.01$). There were no differences regarding maladaptive personality traits between patients and controls. However, there was a strong and consistent positive association between the daily hydrocortisone dose and prevalence of maladaptive personality traits (i.e. identity problems, cognitive distortion, compulsivity, restricted expression, callousness, oppositionality, rejection, conduct problems, social avoidance, narcissism, and insecure attachment, all $P<0.05$). There was also a strong relation between the mean daily hydrocortisone dose and both psychological morbidity (i.e. depression, $P<0.05$) and QoL impairments (i.e. general health perception, several measures of physical functioning, and vitality, all $P<0.05$). CONCLUSION: Patients on stable glucocorticoid replacement therapy for PAI report psychological morbidity and impaired QoL. Psychological morbidity, impaired QoL, and maladaptive personality traits were all associated with higher dosages of hydrocortisone.
Tobback E, Mariman A, Heytens S, Declercq T, Bouwen A, Spooren D, Snoeck P, Van Dessel K, D'Hooghe S, Rimbaut S, Vogelaers D.	No address given	A multidisciplinary network for the care of abnormal fatigue and chronic fatigue syndrome in the provinces of East and West Flanders in Belgium.	Acta Clin Belg. 2014 Oct;69(5):327-34. doi: 10.1179/2295333714Y.0000000056. Epub 2014 Jul 24.	The organization of care for patients with the chronic fatigue syndrome (CFS) in tertiary care referral centres from 2002 onwards, was negatively evaluated by the Belgian Health Care Knowledge Centre on the endpoint of socio-professional reintegration. Subsequently, the federal health authorities asked for the elaboration of a new and innovative model of stepped care, aiming at improved integration of diagnosis and treatment into primary care and between levels of health care for patients with CFS. The reference centre of the University Hospital Ghent took the initiative of recruiting partners in the Belgian provinces of East and West Flanders to guarantee the care for patients with medically unexplained symptoms, in particular abnormal fatigue and CFS. A new and innovative care model, in which general

				practitioners play a central role, emphasizes the importance of early recognition of the patient 'at risk', correct diagnosis and timely referral. Early detection and intervention is essential in order to avoid or minimize illness progression towards chronicity, to safeguard opportunities for significant health improvement as well as to enhance successful socio-professional reintegration. This approach covers both the large sample of patients developing somatic complaints without obvious disease in an early phase as well as the more limited group of patients with chronic illness, including CFS. Cognitive behavioural therapy and graded exposure/exercise therapy are the evidence based main components of therapy in the latter. A biopsychosocial model underlies the proposed path of care.
Tobback E, Mariman A, Vogelaers D.	No address given	Care for chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) patients in Belgium: time for a paradigm shift - Reply to letter to the editor.	Acta Clin Belg. 2014 Dec;69(6):468. doi: 10.1179/2295333714Y.0000000075. Epub 2014 Sep 18..	No abstract available
Tripp DA, Nickel JC, Katz L, Krsmanovic A, Ware MA, Santor D.	(1)Departments of Psychology, Anesthesiology and Urology, Queen's University, Kingston, ON; (2)Department of Urology, Queen's University, Kingston, ON; (3)Psychology, Queen's University, Kingston, ON; (4)Alan Edwards Pain Management Unit, McGill University Health Centre, Montreal, QC; (5)School of Psychology, University of Ottawa, Ottawa, ON	A survey of cannabis (marijuana) use and self-reported benefit in men with chronic prostatitis/chronic pelvic pain syndrome.	Can Urol Assoc J. 2014 Nov;8(11-12):E901-5. doi: 10.5489/cuaj.2268.	INTRODUCTION: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a chronic pelvic pain condition largely refractory to treatment. Cannabis (marijuana) use has been reported for a wide variety of chronic pain conditions, but no study has examined prevalence of cannabis use, symptom benefit or side effects, or frequency in CP/CPPS. METHODS: Participants were recruited from an outpatient CP/CPPS urology clinic (n = 98) and online through the Prostatitis Foundation website (n = 244). Participants completed questionnaires (demographics, CP/CPPS, depression, cannabis). RESULTS: The clinic sample included Canadian patients and the online sample included primarily American patients. Due to differences, groups were examined separately. Almost 50% of respondents reported using cannabis (clinic n = 49; online n = 89). Of the cannabis users, 36.8% of clinic and 75% of online respondents reported that it improved their symptoms. Most of the respondents (from the clinic and online groups) reported that cannabis improved their mood, pain, muscle spasms, and sleep. However, they did not note any improvements for weakness, fatigue, numbness, ambulation, and urination. Overall, the effectiveness of cannabis for CP/CPPS was "somewhat/very effective" (57% clinic; 63% online). There were no differences between side effects or choice of consumption and most reported using cannabis rarely. CONCLUSIONS: These are the first estimates in men suffering from CP/CPPS and suggest that while cannabis use is prevalent, its medical use and benefit are unknown. This is an understudied area and the benefit or hazard for cannabis use awaits further study.

Tsai SY, Yang TY, Chen HJ, Chen CS, Lin WM, Shen WC, Kuo CN, Kao CH.	Department of Laboratory Medicine, Mackay Memorial Hospital, Taipei, Taiwan	Increased risk of chronic fatigue syndrome following herpes zoster: a population-based study.	Eur J Clin Microbiol Infect Dis. 2014 Sep;33(9):1653-9. doi: 10.1007/s10096-014-2095-x. Epub 2014 Apr 9. Erratum in: Eur J Clin Microbiol Infect Dis. 2014 Sep;33(9):1661.	Chronic fatigue syndrome (CFS) is a complex disorder accompanied by unexplainable persistent fatigue, in which several etiological factors exist, such as viral infections. Using the National Health Insurance Research Database (NHIRD) of Taiwan, this study evaluated the association between herpes zoster (HZ) infection and the risk of CFS, and examined the possibility of patients developing postviral fatigue effects, including the possibility of developing other unexplainable chronic fatigue conditions. In this prospective cohort study using the NHIRD, we identified 9,205 patients with HZ infection [ICD-9 (International Classification of Disease, Ninth Revision), code 053] and 36,820 patients without HZ infection (non-HZ) from 2005 to 2007, and followed up to the end of 2010. The incidence rate of CFS was higher in the HZ cohort than in the non-HZ cohort (4.56 vs. 3.44 per 1,000 person-years), with an adjusted hazard ratio of 1.29 [95 % confidence interval (CI) = 1.09-1.53]. It was shown that the risk of CFS without comorbidity for each patient increased from 1.25- to 1.36-fold between the CFS and non-CFS cohorts; with long-term follow-up, the HZ cohort showed a significantly higher cumulative incidence rate of developing CFS than the non-HZ patients. We propose that patients with chronic fatigue might exist in a subset of patients that would be associated with HZ infection. The actual mechanism of development of CFS that is attributed to HZ infection remains unclear. The findings of this population cohort study provide pivotal evidence of postviral fatigue among patients with HZ infection.
Tschudi-Madsen H, Kjeldsberg M, Natvig B, Ihlebaek C, Straand J, Bruusgaard D.	Department of General Practice, Institute of Health and Society, Faculty of Medicine, University of Oslo, PO Box 1130, Blindern, N-0318 Oslo	Medically unexplained conditions considered by patients in general practice.	Fam Pract. 2014 Apr;31(2):156-63. doi: 10.1093/fampra/cmt081. Epub 2013 Dec 24.	BACKGROUND: Patients frequently present with multiple and 'unexplained' symptoms, often resulting in complex consultations. To better understand these patients is a challenge to health care professionals, in general, and GPs, in particular. OBJECTIVES: In our research on symptom reporting, we wanted to explore whether patients consider that they may suffer from conditions commonly regarded as unexplained, and we explored associations between these concerns and symptom load, life stressors and socio-demographic factors. METHODS: Consecutive, unselected patients in general practice completed questionnaires addressing eight conditions commonly regarded as unexplained (amalgam poisoning, Candida syndrome, fibromyalgia, food intolerance, electromagnetic hypersensitivity, burnout syndrome, chronic fatigue syndrome and irritable bowel syndrome). With logistic regression, we analysed associations with symptom load, burden of life stressors with negative impact on present health and socio-demographic variables. RESULTS: Out of the 909 respondents (response rate = 88.8%), 863 had complete data. In total, 39.6% of patients had considered that they may suffer from one or more unexplained conditions (UCs). These concerns were strongly and positively associated with recent symptom load and number of life stressors. If we excluded burnout and food intolerance, corresponding associations were found. CONCLUSION: Patients frequently considered that they may suffer from UCs. The likelihood of such concerns strongly increased with an increasing symptom load and

				with the number of life stressors with negative impact on present health. Hence, the number of symptoms may be a strong indicator of whether patients consider their symptoms part of such often controversial multisymptom conditions.
Tveito K.	No address given	So many things we do not know.	Tidsskr Nor Laegeforen. 2014 Jun 17;134(11):1117-8. doi: 10.4045/tidsskr.14.0726..	[Article in English, Norwegian] Comment in Tidsskr Nor Laegeforen. 2014 Sep 2;134(16):1543 Tidsskr Nor Laegeforen. 2014 Sep 2;134(16):1543.
Twisk F.	No address given	Care for chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) patients in Belgium: time for a paradigm shift.	Acta Clin Belg. 2014 Dec;69(6):467. doi: 10.1179/2295333714Y.0000000076. Epub 2014 Sep 16.	No abstract available
Twisk FN.	ME-de-patiënten Foundation, Zonnedauw 15, 1906 HB, Limmen, The Netherlands, frank.twisk@hetnet.nl.	A definition of recovery in myalgic encephalomyelitis and chronic fatigue syndrome should be based upon objective measures.	Qual Life Res. 2014 Nov;23(9):2417-8. doi: 10.1007/s11136-014-0737-1. Epub 2014 Jun 17.	Comment in Qual Life Res. 2014 Nov;23(9):2419. Comment on Qual Life Res. 2014 Nov;23(9):2407-16. INTRODUCTION: Adamowicz and colleagues recently proposed to use "a consistent definition of recovery that captures a broad-based return to health with assessments of both fatigue and function as well as the patients' perceptions of his/her recovery status" for patients with chronic fatigue syndrome (CFS). METHODS: A qualitative analysis of case definitions for Myalgic encephalomyelitis (ME) and CFS and methods to assess the symptoms and clinical status of ME and CFS patients objectively. RESULTS: The criteria of CFS define a heterogeneous disorder. ME, often used interchangeably with CFS, is principally defined by muscle weakness, cognitive impairment etc., but above all post-exertional "malaise": a long-lasting increase in symptoms, e.g. muscle pain and cognitive deficits, after a minor exertion. The principle symptom of CFS however is "chronic fatigue". Since post-exertional "malaise" is not obligatory for CFS, only part of the CFS patients meet the diagnostic criteria for ME, while not all ME patients qualify as CFS patients. There are several accepted methods to assess characteristic symptoms and the clinical status of ME and CFS patients using objective measures, e.g. (repeated) cardiopulmonary exercise tests. CONCLUSION: To resolve the debate about the clinical status,

				proposed effectiveness of therapies and recovery in ME and CFS, it is crucial to accurately diagnose patients using well-defined criteria for ME and CFS and an objective assessment of various typical symptoms, since subjective measures such as "fatigue" will perpetuate the debate.
Twisk FN.	ME-de-patiënten Foundation, The Netherlands. Electronic address: frank.twisk@hetnet.	Underperformance of myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) patients at neurocognitive tests should be assessed objectively without an a priori judgment about the etiology.	J Psychosom Res. 2014 Apr;76(4):339. doi: 10.1016/j.jpsychores.2013.10.016. Epub 2013 Nov 5	Comment in J Psychosom Res. 2014 Apr;76(4):340. Comment on J Psychosom Res. 2013 Sep;75(3):242-8.
Twisk FN.	ME-de-Patiënten Foundation Limmen, Netherlands.	The status of and future research into Myalgic Encephalomyelitis and Chronic Fatigue Syndrome: the need of accurate diagnosis, objective assessment, and acknowledging biological and clinical subgroups.	Front Physiol. 2014;5:109. doi: 10.3389/fphys.2014.00109.	Although Myalgic Encephalomyelitis (ME) and Chronic Fatigue Syndrome (CFS) are used interchangeably, the diagnostic criteria define two distinct clinical entities. Cognitive impairment, (muscle) weakness, circulatory disturbances, marked variability of symptoms, and, above all, post-exertional malaise: a long-lasting increase of symptoms after a minor exertion, are distinctive symptoms of ME. This latter phenomenon separates ME, a neuro-immune illness, from chronic fatigue (syndrome), other disorders and deconditioning. The introduction of the label, but more importantly the diagnostic criteria for CFS has generated much confusion, mostly because chronic fatigue is a subjective and ambiguous notion. CFS was redefined in 1994 into unexplained (persistent or relapsing) chronic fatigue, accompanied by at least four out of eight symptoms, e.g., headaches and unrefreshing sleep. Most of the research into ME and/or CFS in the last decades was based upon the multivalent CFS criteria, which define a heterogeneous patient group. Due to the fact that fatigue and other symptoms are non-discriminative, subjective experiences, research has been hampered. Various authors have questioned the physiological nature of the symptoms and qualified ME/CFS as somatization. However, various typical symptoms can be assessed objectively using standardized methods. Despite subjective and unclear criteria and measures, research has observed specific abnormalities in ME/CFS repetitively, e.g., immunological abnormalities, oxidative and nitrosative stress, neurological anomalies, circulatory deficits and mitochondrial dysfunction. However, to improve future research standards and patient care, it is crucial that patients with post-exertional malaise (ME) and patients without this odd phenomenon are

				acknowledged as separate clinical entities that the diagnosis of ME and CFS in research and clinical practice is based upon accurate criteria and an objective assessment of characteristic symptoms, as much as possible that well-defined clinical and biological subgroups of ME and CFS patients are investigated in more detail, and that patients are monitored before, during and after interventions with objective measures and biomarkers.
Tzanis G, Dimopoulos S, Agapitou V, Nanas S.	(1) 1st Critical Care Medicine Department, Cardiopulmonary Exercise Testing and Rehabilitation Laboratory, "Evgenidio Hospital", National & Kapodestrian University of Athens, Papadiamantopoulou str., 20, Athens, 11528, Greece.	Exercise intolerance in chronic heart failure: the role of cortisol and the catabolic state.	Curr Heart Fail Rep. 2014 Mar;11(1):70-9. doi: 10.1007/s11897-013-0177-1. Review.	Chronic heart failure (CHF) is a complex clinical syndrome leading to exercise intolerance due to muscular fatigue and dyspnea. Hemodynamics fail to explain the reduced exercise capacity, while a significant skeletal muscular pathology seems to constitute the main underlying mechanism for exercise intolerance in CHF patients. There have been proposed several metabolic, neurohormonal and immune system abnormalities leading to an anabolic/catabolic imbalance that plays a central role in the pathogenesis of the wasting process of skeletal muscle myopathy. The impairment of the anabolic axes is associated with the severity of symptoms and the poor outcome in CHF, whereas increased cortisol levels are predictive of exercise intolerance, ventilatory inefficiency and chronotropic incompetence, suggesting a significant contributing mechanism to the limited functional status. Exercise training and device therapy could have beneficial effects in preventing and treating muscle wasting in CHF. However, specific anabolic treatment needs more investigation to prove possible beneficial effects.
Udovika NO, Romanenko Ilu, Lieonov OO.	No address given	Effectiveness of medical rehabilitation of women of reproductive age with fatigue syndrome.	Lik Sprava. 2014 Mar-Apr;(3-4):78-82.	[Article in Ukrainian] Efficacy Erbisol in combination with Lymphomyosot and Echinacea compositum C in medical rehabilitation of women of reproductive age with fatigue syndrome and chronic gynecological pathology was studied. It was found that this complex of medications promotes faster and more effective reduction of the level of circulating immune complexes in the serum, achievement of persistent clinical remission of disease and liquidation of fatigue syndrome manifestations, what improves the quality of life of patients.
Van Cauwenbergh D, Nijs J, Kos D, Van Weijnen L, Struyf F, Meeus M.	(1)Pain in Motion Research Group, Departments of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium; Pain in Motion Research	Malfunctioning of the autonomic nervous system in patients with chronic fatigue syndrome: a systematic literature review.	Eur J Clin Invest. 2014 May;44(5):516-26. doi: 10.1111/eci.12256. Review.	INTRODUCTION: It is hypothesised that the autonomic nervous system responds differently to various stressors in patients with chronic fatigue syndrome (CFS) compared with healthy controls. The goal is to systematically review the scientific literature addressing the functioning of the autonomic nervous system in patients with CFS. MATERIALS AND METHODS: All studies that were identified through electronic databases (PubMed and Web of Science) were screened for eligibility based on the selection criteria and assessed (two independent raters) for methodological quality using a methodological checklist for case-control studies. RESULTS: Twenty-seven case-control studies were included. The methodological quality varied between 50% and 71·4%. Some studies showed different responses to head-up tilt and other autonomous testing. CONCLUSION: Although comparison

	Group, Faculty of Medicine and Health Sciences, University of Antwerp, Antwerp, Belgium.			between the included case-control studies was difficult, we can conclude that there are differences in autonomous response between patients with CFS and healthy controls. The heart rate dynamic response during the head-up tilt test differs between patients with CFS and healthy controls, supporting the increased prevalence of postural orthostatic tachycardia syndrome. The autonomic response can be useful for the diagnosis of CFS.
Van den Bergh M, Bauer FA, Posteraro AF, Thumma S, Dasanu CA.	No address given	An unusual presentation of Kikuchi-Fujimoto disease.	Conn Med. 2014 Apr;78(4):225-8.	Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare, self-limited disease of unknown etiology. This condition is most commonly encountered in Asian and Caucasian females of childbearing age who usually present with cervical lymphadenopathy and fever. Though rarely, KFD has been described in younger African-American females as well. It often mimics more serious conditions such as lymphoma, metastatic solid malignancy, HIV infection, tuberculosis, sarcoidosis, or systemic lupus erythematosus. Although its etiopathogenesis has not been fully elucidated, literature suggests viral or possibly autoimmune components to play a role. We describe a 34-year-old African-American female who presented with constitutional symptoms and polyadenopathy on clinical examination and imaging, of which the portacaval and portahepatis lymph nodes were most prominent. An extensive workup was otherwise unremarkable, and biopsy showed histiocytic necrotizing lymphadenitis. Initially, her clinical condition improved spontaneously, and she required only a short course of oral steroids. Three months later, she relapsed with bilateral cervical adenopathy and constitutional symptoms and was successfully managed again with steroids. Our case is unique with respect to (a) portahepatis and portacaval node enlargement as the dominant adenopathy and (b) her underlying conditions of fibromyalgia and chronic fatigue syndrome.
van Leeuwen N, Bossema ER, Knoop H, Kruize AA, Bootsma H, Bijlsma JW, Geenen R.	Department of Clinical and Health Psychology, Utrecht University, Department of Rheumatology and Clinical Immunology, University Medical Center Utrecht, Utrecht,	Psychological profiles in patients with SjÃ¶gren's syndrome related to fatigue: a cluster analysis.	Rheumatology (Oxford). 2014 Oct 6. doi:pii: keu387.	OBJECTIVE: Fatigue is a highly prevalent and debilitating symptom in the autoimmune disease SS. Although the disease process plays a role in fatigue, psychological factors may influence fatigue and the ability to deal with its consequences. Profiles of co-occurring psychological factors may suggest potential targets for the treatment of fatigue. The aim of this study was to identify psychological profiles in patients with SS and the accompanying levels of fatigue. METHODS: Three hundred patients with primary SS (mean age 57 years, 93% female) completed questionnaires on fatigue (multidimensional fatigue inventory), physical activity cognitions (TAMPA-SK), illness cognitions, cognitive regulation, emotion processing and regulation [Toronto Alexithymia Scale 20, Emotion Regulation Questionnaire (ERQ), Berkeley Expressivity Questionnaire], coping strategies (Brief COPE) and social support. RESULTS: Principal axis factor analysis (oblimin rotation) yielded six psychological factors: social support, negative thinking, positive thinking, emotional expressivity, avoidance and alexithymia (i.e. the inability to differentiate emotions). Using cluster analyses, these factors were

				grouped in four psychological profiles: functional (39%), alexithymic (27%), self-reliant (23%) and dysfunctional (11%). Irrespective of the psychological profile, the level of fatigue was substantially higher in patients than in the general population. Patients with a dysfunctional or an alexithymic profile reported more fatigue than those with a self-reliant profile. CONCLUSION: Our study in SS yielded four psychological profiles that were differentially associated with fatigue. These profiles can be used to examine determinants and prognosis of fatigue as well as the possibility of customizing cognitive behavioural interventions for chronic fatigue.
van Tilburg MA, Zaki EA, Venkatesan T, Boles RG.	Center for Functional GI and Motility Disorders, University of North Carolina, 130 Mason Farm Rd #4106, Chapel Hill, NC, 27599-7080, USA, tilburg@med.unc.edu.	Irritable bowel syndrome may be associated with maternal inheritance and mitochondrial DNA control region sequence variants.	Dig Dis Sci. 2014 Jul;59(7):1392-7. doi: 10.1007/s10620-014-3045-2. Epub 2014 Feb 6.	BACKGROUND AND AIM: Mitochondrial dysfunction has been implicated in various functional disorders that are co-morbid to irritable bowel syndrome (IBS) such as migraine, depression and chronic fatigue syndrome. The aim of the current case-control pilot study was to determine if functional symptoms in IBS show a maternal inheritance bias, and if the degree of this maternal inheritance is related to mitochondrial DNA (mtDNA) polymorphisms. METHODS: Pedigrees were obtained from 308 adult IBS patients, 102 healthy controls, and 36 controls with inflammatory bowel disease (IBD), all from Caucasian heritage, to determine probable maternal inheritance. Two mtDNA polymorphisms (16519T and 3010A), which have previously been implicated in other functional disorders, were assayed in mtDNA haplogroup H IBS subjects and compared to genetic data from 344 published haplogroup H controls. RESULTS: Probable maternal inheritance was found in 17.5 % IBS, 2 % healthy controls and 0 % IBD controls ($p < .0001$). No difference was found between IBS and control for 3010A, and a trend was found for 16519T ($p = 0.05$). IBS with maternal inheritance were significantly more likely to have the 16519T than controls (OR 5.8; 95 % CI 1.5-23.1) or IBS without maternal inheritance (OR 5.2; 95 % CI 1.2-22.6). CONCLUSIONS: This small pilot study shows that a significant minority (1/6) of IBS patients have pedigrees suggestive of maternal inheritance. The mtDNA polymorphism 16519T, which has been previously implicated in other functional disorders, is also associated with IBS patients who display maternal inheritance. These findings suggest that mtDNA-related mitochondrial dysfunction may constitute a sub-group within IBS. Future replication studies in larger samples are needed.
Vasiadi M, Newman J, Theoharides TC.	No address given	Isoflavones inhibit poly(I:C)-induced serum, brain, and skin inflammatory mediators - relevance to chronic fatigue syndrome.	J Neuroinflammation. 2014 Oct 31;11(1):168.	BackgroundChronic Fatigue Syndrome (CFS) is a neuroimmunoendocrine disease affecting about 1% of the US population, mostly women. It is characterized by debilitating fatigue for six or more months in the absence of cancer or other systemic diseases. Many CFS patients also have fibromyalgia and skin hypersensitivity that worsen with stress. Corticotropin-releasing hormone (CRH) and neurotensin (NT), secreted under stress, activate mast cells (MC) necessary for allergic reactions to release inflammatory mediators that could contribute to CFS

				symptoms.ObjectiveTo investigate the effect of isoflavones on the action of polyinosinic:polycytidylic acid (poly(I:C)), with or without swim stress, on mouse locomotor activity and inflammatory mediator expression, as well as on human MC activation.MethodsFemale C57BL/6 mice were randomly divided into four groups: (a) control/no-swim, (b) control/swim, (c) poly(I:C)/no swim, and (d) poly(I:C)/swim. Mice were provided with chow low or high in isoflavones for 2 weeks prior to ip injection with 20 mg/kg poly(I:C) followed or not by swim stress for 15 minutes. Locomotor activity was monitored overnight and animals were sacrificed the following day. Brain and skin gene expression, as well as serum levels, of inflammatory mediators were measured. Data were analyzed using the non-parametric Mann-Whitney U-test.ResultsPoly(I:C)-treated mice had decreased locomotor activity over 24 hours, and increased serum levels of TNF-¿, IL-6, KC (IL-8/CXCL8 murine homolog), CCL2,3,4,5, CXCL10, as well as brain and skin gene expression of TNF, IL-6, KC (Cxcl1, IL8 murine homolog), CCL2, CCL4, CCL5 and CXCL10. Histidine decarboxylase (HDC) and NT expression were also increased, but only in the skin, over the same period. High isoflavone diet reversed these effects.Conclusion -Poly(I:C) treatment decreased mouse locomotor activity and increased serum levels and brain and skin gene expression of inflammatory mediators. These effects were inhibited by isoflavones that may prove useful in CFS.
Vergauwen K, Huijnen IP, Kos D, Van de Velde D, van Eupen I, Meeus M.	Faculty of Medicine and Health Sciences, Department of Occupational Therapy, Ghent University , Ghent , Belgium .	Assessment of activity limitations and participation restrictions with persons with chronic fatigue syndrome: a systematic review.	Disabil Rehabil. 2014 Nov 3:1-11.	Abstract Purpose: To summarize measurement instruments used to evaluate activity limitations and participation restrictions in patients with chronic fatigue syndrome (CFS) and review the psychometric properties of these instruments. Method: General information of all included measurement instruments was extracted. The methodological quality was evaluated using the COSMIN checklist. Results of the measurement properties were rated based on the quality criteria of Terwee et al. Finally, overall quality was defined per psychometric property and measurement instrument by use of the quality criteria by Schellingerhout et al. Results: A total of 68 articles were identified of which eight evaluated the psychometric properties of a measurement instrument assessing activity limitations and participation restrictions. One disease-specific and 37 generic measurement instruments were found. Limited evidence was found for the psychometric properties and clinical usability of these instruments. However, the CFS-activities and participation questionnaire (APQ) is a disease-specific instrument with moderate content and construct validity. Conclusion: The psychometric properties of the reviewed measurement instruments to evaluate activity limitations and participation restrictions are not sufficiently evaluated. Future research is needed to evaluate the psychometric properties of the measurement instruments, including the other properties of the CFS-APQ. If it is necessary to use a measurement instrument, the CFS-APQ is recommended. Implications for Rehabilitation Chronic fatigue syndrome (CFS). Chronic fatigue syndrome causes activity limitations and participation restrictions in one or more

				areas of life. Standardized, reliable and valid measurement instruments are necessary to identify these limitations and restrictions. Currently, no measurement instrument is sufficiently evaluated with persons with CFS. If a measurement instrument is needed to identify activity limitations and participation restrictions with persons with CFS, it is recommended to use the CFS-APQ in clinical practice and scientific research.
Vermeulen RC, Vermeulen van Eck IW.	CFS/ME Medical Centre Amsterdam, Waalstraat 25-31, Amsterdam 1078BR, Netherlands. rv@cvscentrum.nl.	Decreased oxygen extraction during cardiopulmonary exercise test in patients with chronic fatigue syndrome.	J Transl Med. 2014 Jan 23;12:20. doi: 10.1186/1479-5876-12-20.	BACKGROUND: The insufficient metabolic adaptation to exercise in Chronic Fatigue Syndrome (CFS) is still being debated and poorly understood. METHODS: We analysed the cardiopulmonary exercise tests of CFS patients, idiopathic chronic fatigue (CFI) patients and healthy visitors. Continuous non-invasive measurement of the cardiac output by Nexfin (BMEYE B.V. Amsterdam, the Netherlands) was added to the cardiopulmonary exercise tests. The peak oxygen extraction by muscle cells and the increase of cardiac output relative to the increase of oxygen uptake ($\Delta Q'/\Delta V'O_2$) were measured, calculated from the cardiac output and the oxygen uptake during incremental exercise. RESULTS: The peak oxygen extraction by muscle cells was 10.83 ± 2.80 ml/100ml in 178 CFS women, 11.62 ± 2.90 ml/100 ml in 172 CFI, and 13.45 ± 2.72 ml/100 ml in 11 healthy women (ANOVA: P=0.001), 13.66 ± 3.31 ml/100 ml in 25 CFS men, 14.63 ± 4.38 ml/100 ml in 51 CFI, and 19.52 ± 6.53 ml/100 ml in 7 healthy men (ANOVA: P=0.008).The $\Delta Q'/\Delta V'O_2$ was > 6 L/L (normal $\Delta Q'/\Delta V'O_2 \approx 5$ L/L) in 70% of the patients and in 22% of the healthy group. CONCLUSION: Low oxygen uptake by muscle cells causes exercise intolerance in a majority of CFS patients, indicating insufficient metabolic adaptation to incremental exercise. The high increase of the cardiac output relative to the increase of oxygen uptake argues against deconditioning as a cause for physical impairment in these patients.
Vishnu VY, Modi M, Prabhakar S, Bhansali A, Goyal MK.	Department of Neurology, Post Graduate Institute of Medical Education and Research, Chandigarh 160012, India. Electronic address: vishnuvy16@yahoo.com.	A" motor neuron disease."	J Neurol Sci. 2014 Jan 15;336(1-2):251-3. doi: 10.1016/j.jns.2013.10.003. Epub 2013 Oct 8.	IMPORTANCE: Allgrove syndrome is a rare autosomal recessive disorder characterised by achalasia, alacrima, adrenal insufficiency, autonomic dysfunction and amyotrophy. The syndrome has been described in childhood and adult presentation, as in our case, is very rare. There is a considerable delay in diagnosis due to lack of awareness about the syndrome. OBSERVATIONS: We report a single case of a 36 year old man who was initially diagnosed and treated for achalasia cardia in our institute 14 years before. After 8 years he presented again with weakness and wasting predominantly distally. He had tongue fasciculations, brisk reflexes and extensor plantar. After supportive electrophysiological studies he was diagnosed as Amyotrophic lateral sclerosis. After 5 years he presented with generalised fatigue without any significant worsening of his neurological status. On reevaluation he had alacrimia, autonomic dysfunction and mild ACTH resistance. CONCLUSIONS AND RELEVANCE: Allgrove syndrome may be an underdiagnosed cause of multisystem neurological disease due to the heterogeneous clinical presentation as well as for ignorance of clinician about the syndrome. Based on our

				case, we also believe that there does exist a subgroup of patients who follow a less severe and chronic course. Recognition of syndrome allows for treatment of autonomic dysfunction, adrenal insufficiency and dysphagia.
von Polier GG, Zepf FD.	Clinic for Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, RWTH Aachen University, Aachen, Germany.	Physiosomatic complaints, immune-inflammatory pathways, and serotonin-related mood symptoms: relevance for tryptophan-related challenge procedures and clinical considerations with respect to the DSM-V.	Acta Psychiatr Scand. 2014 Feb;129(2):98-9. doi: 10.1111/acps.12197. Epub 2013 Sep 30..	Comment on Acta Psychiatr Scand. 2014 Feb;129(2):83-97.
Walter SM.	West Virginia University School of Nursing, PO Box 9640, 6400 Health Sciences South, Morgantown, WV 26506-9640, USA.	Case Report: Ehlers-Danlos Syndrome in an adolescent presenting with Chronic Daily Headache.	Surg Neurol Int. 2014;5(Suppl 13):S475-8. doi: 10.4103/2152-7806.144629.	BACKGROUND: Classic Ehlers-Danlos syndrome (EDS) is a connective tissue disorder characterized by skin hyperextensibility, skin fragility as well as joint hypermobility. EDS has been associated with psychiatric disorders, fatigue, dizziness, musculoskeletal pain, and stomach pain that are common complaints associated with adolescent chronic daily headache (CDH). This case report discusses an adolescent who presents with CDH and is subsequently diagnosed with EDS based upon the presenting symptoms for headache including syncope and chronic musculoskeletal pain as well as a history of hypermobility. CASE DESCRIPTION: A 15-year-old female presented to an outpatient headache clinic with a 10-year history of headache, which had become daily over the past 3 months and awakened her in the middle of the night. Past history also revealed chronic musculoskeletal pain, syncope, fatigue, and hypermobility of joints. Subsequent referral to a geneticist confirmed mild classic EDS. CONCLUSION: Along with the major manifestation of EDS, other signs and symptoms that characterize this disorder include musculoskeletal pain, fatigue, dizziness/vertigo, depression, and anxiety, which are often associated with CDH in adolescents. Clinicians treating CDH need to be aware of the major clinical manifestations of EDS as well as the other signs and symptoms that characterize both of these chronic pain disorders. An understanding of this syndrome will lead not only to a diagnosis of EDS but also initiation of a treatment plan specific for an adolescent with CDH and EDS.

Wang C, Xie WJ, Liu M, Yan J, Zhang JL, Liu Z, Guo LN.	No address given	Effect of manual acupuncture stimulation of Baihui" (GV 20)	Zhen Ci Yan Jiu. 2014 Oct;39(5):387-9.	[Article in Chinese] OBJECTIVE: To observe the effect of manual acupuncture stimulation of "Baihui" (GV 20), etc. on serum IFN- gamma and IL-4 contents in rats with chronic fatigue syndrome (CFS). METHODS: A total of 24 male SD rats were equally randomized into control group, model group and acupuncture group. CFS model was established by bounding and forced swimming in cold water once daily for 14 days. Rats in the acupuncture group were treated by manual acupuncture stimulation of bilateral "Zusanli" (ST 36), "Baihui" (GV 20), and "Guanyuan" (CV 4), once daily for 14 days. Serum IFN-gamma and IL-4 contents were detected by ELISA. RESULTS: Compared with the control group, the contention of serum IFN-gamma and ratio of IFN-gamma/IL-4 were significant decreased in the model group (P<0.01). While in comparison with the model group, the contention of IFN-gamma and ratio of IFN-gamma/IL-4 were obviously increased in the acupuncture group (P<0.05). No significant differences were found among the three groups in serum IL-4 levels (P>0.05). CONCLUSION: Manual acupuncture can inhibit CFS induced reduction of serum IFN-gamma level and the ratio of IFN-gamma/IL-4 in CFS rats, suggesting a favorable adjustment of acupuncture intervention for CFS by balancing the ratio of IFN-gamma/IL-4.
Wang H, Liu X, Lv B, Yang F, Hong Y.	(1)College of Computer Science and Technology, Huaqiao University, Xiamen, China. (2)School of Information Science and Engineering, Xiamen University, Xiamen, China. (3)Department of traditional Chinese medicine, Xiamen University, Xiamen, China.	Reliable multi-label learning via conformal predictor and random forest for syndrome differentiation of chronic fatigue in traditional Chinese medicine.	PLoS One. 2014;9(6):e99565. doi: 10.1371/journal.pone.0099565.	OBJECTIVE: Chronic Fatigue (CF) still remains unclear about its etiology, pathophysiology, nomenclature and diagnostic criteria in the medical community. Traditional Chinese medicine (TCM) adopts a unique diagnostic method, namely 'bian zheng lun zhi' or syndrome differentiation, to diagnose the CF with a set of syndrome factors, which can be regarded as the Multi-Label Learning (MLL) problem in the machine learning literature. To obtain an effective and reliable diagnostic tool, we use Conformal Predictor (CP), Random Forest (RF) and Problem Transformation method (PT) for the syndrome differentiation of CF. METHODS AND MATERIALS: In this work, using PT method, CP-RF is extended to handle MLL problem. CP-RF applies RF to measure the confidence level (p-value) of each label being the true label, and then selects multiple labels whose p-values are larger than the pre-defined significance level as the region prediction. In this paper, we compare the proposed CP-RF with typical CP-NBC(Naïve Bayes Classifier), CP-KNN(K-Nearest Neighbors) and ML-KNN on CF dataset, which consists of 736 cases. Specifically, 95 symptoms are used to identify CF, and four syndrome factors are employed in the syndrome differentiation, including 'spleen deficiency', 'heart deficiency', 'liver stagnation' and 'qi deficiency'. THE RESULTS: CP-RF demonstrates an outstanding performance beyond CP-NBC, CP-KNN and ML-KNN under the general metrics of subset accuracy, hamming loss, one-error, coverage, ranking loss and average precision. Furthermore, the performance of CP-RF remains steady at the large scale of confidence levels from 80% to 100%, which indicates its

				robustness to the threshold determination. In addition, the confidence evaluation provided by CP is valid and well-calibrated. CONCLUSION: CP-RF not only offers outstanding performance but also provides valid confidence evaluation for the CF syndrome differentiation. It would be well applicable to TCM practitioners and facilitate the utilities of objective, effective and reliable computer-based diagnosis tool.
Wang J, Sun C, Zheng Y, Pan H, Zhou Y, Fan Y.	Jilin Province Key Laboratory on Chemistry and Biology of Changbai Mountain Natural Drugs School of Life Sciences, Northeast Normal University, Changchun, 130024, People's Republic of China.	The effective mechanism of the polysaccharides from Panax ginseng on chronic fatigue syndrome.	Arch Pharm Res. 2014 Apr;37(4):530-8. doi: 10.1007/s12272-013-0235-y. Epub 2013 Aug 21.	Ginseng acidic polysaccharide WGPA isolated from the root of Panax ginseng C. A. Meyer was fractionated into WGPA-A and WGPA-N by anion-exchange chromatography. The antifatigue activity of ginseng acidic polysaccharide WGPA has been reported in our previous research. This present study was designed to identify its active component and elucidate the mechanism for preventing chronic fatigue syndrome (CFS). WGPA, WGPA-A and WGPA-N were orally administered to mice once daily for 15 days. The effects of these compounds on physiological biomarkers of oxidative stress and on the morphology of the mitochondria in striated skeletal muscle were assessed. The results of forced swimming test-induced indicated that WGPA and WGPA-A could lengthen the swimming time, while WGPA-N could not. In addition, malondialdehyde and lactate dehydrogenase levels in serum were enhanced; while those of superoxide dismutase and glutathione peroxidase were lowered. Interestingly, the structural degeneration of mitochondria were all ameliorated. These findings suggested that WGPA-A is the active component of WGPA, it might have potential therapeutic effects for CFS and the oxidative stress might be involved in the pathogenesis. Our results also provided essential data for a better understanding of the antifatigue effects of P. ginseng extracts.
Wang W, Russell A, Yan Y; Global Health Epidemiology Reference Group (GHERG).	School of Medical Sciences, Edith Cowan University, Perth, Western Australia WA6027, Australia. wei.wang@ecu.edu.au.	Traditional Chinese medicine and new concepts of predictive, preventive and personalized medicine in diagnosis and treatment of suboptimal health.	EPMA J. 2014 Feb 13;5(1):4. doi: 10.1186/1878-5085-5-4. Erratum in: EPMA J. 2014;5(1):12.	BACKGROUND: The premise of disease-related phenotypes is the definition of the counterpart normality in medical sciences. Contrary to clinical practices that can be carefully planned according to clinical needs, heterogeneity and uncontrollability is the essence of humans in carrying out health studies. Full characterization of consistent phenotypes that define the general population is the basis to individual difference normalization in personalized medicine. Self-claimed normal status may not represent health because asymptomatic subjects may carry chronic diseases at their early stage, such as cancer, diabetes mellitus and atherosclerosis. Currently, treatments for non-communicable chronic diseases (NCD) are implemented after disease onset, which is a very much delayed approach from the perspective of predictive, preventive and personalized medicine (PPPM). A NCD pandemic will develop and be accompanied by increased global economic burden for healthcare systems throughout both developed and developing countries. This paper examples the characterization of the suboptimal health status (SHS) which represents a new PPPM challenge in a population with ambiguous health complaints such as general weakness, unexplained medical syndrome (UMS), chronic fatigue syndrome (CFS), myalgic encephalomyelitis (ME), post-viral fatigue syndrome (PVFS) and chronic

				fatigue immune dysfunction syndrome (CFIDS). METHODS: We applied clinical informatic approaches and developed a questionnaire-suboptimal health status questionnaire-25 (SHSQ-25) for measuring SHS. The validity and reliability of this approach were evaluated in a small pilot study and then in a cross-sectional study of 3,405 participants in China. RESULTS: We found a correlation between SHS and systolic blood pressure, diastolic blood pressure, plasma glucose, total cholesterol and high-density lipoprotein (HDL) cholesterol among men, and a correlation between SHS and systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides and HDL cholesterol among women. CONCLUSIONS: The SHSQ-25 is a self-rated questionnaire of perceived health complaints, which can be used as a new instrument for PPPM. An ongoing longitudinal SHS cohort survey (China Sub-optimal Health Cohort Study, COACS) consisting of 50,000 participants will provide a powerful health trial to use SHSQ-25 for its application to PPPM through patient stratification and therapy monitoring using innovative technologies of predictive diagnostics and prognosis: an effort of paradigm shift from reactive to predictive medicine.
Wang YY, Li XX, Liu JP, Luo H, Ma LX, Alraek T.	Center for Evidence-Based Medicine, Beijing University of Chinese Medicine, Beijing, China	Traditional Chinese medicine for chronic fatigue syndrome: a systematic review of randomized clinical trials.	Complement Ther Med. 2014 Aug;22(4):826-33. doi: 10.1016/j.ctim.2014.06.004. Epub 2014 Jun 30.	BACKGROUND: There is no curative treatment for chronic fatigue syndrome (CFS). Traditional Chinese medicine (TCM) is widely used in the treatment of CFS in China. OBJECTIVE: To evaluate the effectiveness and safety of TCM for CFS. METHODS: The protocol of this review is registered at PROSPERO. We searched six main databases for randomized clinical trials (RCTs) on TCM for CFS from their inception to September 2013. The Cochrane risk of bias tool was used to assess the methodological quality. We used RevMan 5.1 to synthesize the results. RESULTS: 23 RCTs involving 1776 participants were identified. The risk of bias of the included studies was high. The types of TCM interventions varied, including Chinese herbal medicine, acupuncture, qigong, moxibustion, and acupoint application. The results of meta-analyses and several individual studies showed that TCM alone or in combination with other interventions significantly alleviated fatigue symptoms as measured by Chalder's fatigue scale, fatigue severity scale, fatigue assessment instrument by Joseph E. Schwartz, Bell's fatigue scale, and guiding principle of clinical research on new drugs of TCM for fatigue symptom. There was no enough evidence that TCM could improve the quality of life for CFS patients. The included studies did not report serious adverse events. CONCLUSIONS: TCM appears to be effective to alleviate the fatigue symptom for people with CFS. However, due to the high risk of bias of the included studies, larger, well-designed studies are needed to confirm the potential benefit in the future.
Warren JW, Clauw DJ, Wesselmann U, Howard FM, Gallicchio L,	Department of Medicine, University of Maryland School of Medicine, United	Functional somatic syndromes as risk factors for hysterectomy in early	J Psychosom Res. 2014 Nov;77(5):363-7. doi: 10.1016/j.jpsychores.2014.09.004. Epub 2014 Sep 16.	OBJECTIVE: We tested the hypothesis that functional somatic syndromes (FSSs) are risk factors for hysterectomy in early bladder pain syndrome/interstitial cystitis (BPS/IC). METHODS: In 312 women with incident BPS/IC, we diagnosed seven pre-BPS/IC syndromes: chronic pelvic pain (CPP), fibromyalgia, chronic fatigue

Morozov V.	States; Department of Epidemiology and Public Health, University of Maryland School of Medicine, United States. Electronic address: jwarren@medicine.umaryland.edu.	bladder pain syndrome/interstitial cystitis.		syndrome, irritable bowel syndrome (IBS), sicca syndrome, migraine, and panic disorder. Each was defined as present before 12months (existing syndrome) or onset within 12months (new syndrome) prior to BPS/IC onset. Retrospectively, we sought associations between prior hysterectomy and existing FSSs. Prospectively we studied associations of existing and new syndromes with subsequent hysterectomy. Logistic regression analyses adjusted for age, race, menopause and education. RESULTS: The retrospective study showed prior hysterectomy (N=63) to be associated with existing CPP and the presence of multiple existing FSSs. The prospective study revealed that 30/249 women with a uterus at baseline (12%) underwent hysterectomy in early BPS/IC. This procedure was associated with new CPP (OR 6.0; CI 2.0, 18.2), new IBS (OR 5.4; CI 1.3, 22.3), and ≥3 existing FSSs (OR 3.9; CI 1.1, 13.9). CONCLUSION: Accounting for CPP and IBS, the presence of multiple FSSs (most without pelvic pain) was a separate, independent risk factor for hysterectomy in early BPS/IC. This suggests that patient features in addition to abdominopelvic abnormalities led to this procedure. Until other populations are assessed, a prudent approach to patients who are contemplating hysterectomy (and possibly other surgeries) for pain and who have IBS or numerous FSSs is first to try alternative therapies including treatment of the FSSs.
Warren JW.	Department of Medicine, University of Maryland School of Medicine, 10 South Pine Street, #900, Baltimore, MD 21201, United States; Department of Epidemiology and Public Health, University of Maryland School of Medicine, United States. Electronic address: jwarren@medicine.umaryland.edu.	Bladder pain syndrome/interstitial cystitis as a functional somatic syndrome.	J Psychosom Res. 2014 Dec;77(6):510-5. doi: 10.1016/j.jpsychores.2014.10.003. Epub 2014 Oct 14.	PURPOSE: To determine whether bladder pain syndrome/interstitial cystitis (BPS/IC) has the characteristics of a functional somatic syndrome (FSS). MATERIALS AND METHODS: There is no accepted definition of an FSS. Consequently, this paper reviewed the literature for common FSS characteristics and for reports that BPS/IC has these characteristics. RESULTS: Eleven articles met inclusion and exclusion criteria and yielded 18 FSS characteristics. BPS/IC patients manifest all but two: the exceptions were normal light microscopic anatomy (after hydrodistention under anesthesia, some BPS/IC bladders have Hunner's lesions and most have petechial hemorrhages) and normal laboratory tests (many BPS/IC patients have hematuria). Petechial hemorrhages and hematuria are probably related and may appear during naturally-occurring bladder distention. Without such distention, then, the 90% of BPS/IC patients without a Hunner's lesion have all the characteristics of an FSS. Comparisons in the opposite direction were consistent: several additional features of BPS/IC were found in FSSs. CONCLUSIONS: This systematic but untested method is consistent with but does not test the hypothesis that BPS/IC in some patients might best be understood as an FSS. Like most conditions, BPS/IC is probably heterogeneous; hence only a proportion of BPS/IC cases are likely to be manifestations of an FSS. This hypothesis has several implications. Explorations of processes that connect the FSSs might contribute to understanding the pathogenesis of BPS/IC. Patients with FSSs are at risk for BPS/IC and may benefit from future preventive strategies. Therapies that are useful in FSSs also may be useful in some cases of BPS/IC.

Weidner J, Check JH.	No address given	Marked improvement of the autoimmune syndrome associated with autoimmune hepatitis by treatment with sympathomimetic amines.	Clin Exp Obstet Gynecol. 2014;41(4):460-1.	PURPOSE: To evaluate the effect of sympathomimetic amine therapy for a life threatening autoimmune disorder. MATERIALS AND METHODS: Dextroamphetamine sulfate was used to treat edema, myalgia, and chronic fatigue associated with autoimmune hepatitis (AIH). RESULTS: Sympathomimetic amine therapy completely abrogated the symptoms associated with AIH. CONCLUSIONS: AIH should be added to the long list of chronic treatment-refractory conditions that respond quickly and effectively to treatment with sympathomimetic amines.
Werner R, Meindl-Fridez C, Zimmerli L.	No address given	Chronic fatigue.	Praxis (Bern 1994). 2014 Mar 12;103(6):305-11; quiz 312-3. doi: 10.1024/1661-8157/a001611. Review	[Article in German] No abstract available
Wiborg JF, Wensing M, Tummers M, Knoop H, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands; Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Hamburg-Eppendorf & Schön Klinik Hamburg-Eilbek, Hamburg, Germany.	Implementing evidence-based practice for patients with chronic fatigue syndrome.	Clin Psychol Psychother. 2014 Mar-Apr;21(2):108-14. doi: 10.1002/cpp.1827. Epub 2012 Dec 11.	The aim of our study was to explore whether community-based mental health care centres (MHCs) are able to implement and sustain cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) with the help of an implementation manual. We monitored the implementation process and treatment outcome data of three Dutch MHCs that implemented or sustained CBT for CFS, one in the context of a stepped care programme. We compared these data with findings of other treatment studies conducted in the context of CBT for CFS. All three MHCs included at least 40 patients with dropout rates between 15% and 35% from intention-to-treat to second assessment. Effect sizes ranged between 0.88 and 1.76 for changes in fatigue severity and 0.43 and 1.23 for changes in physical functioning. With one exception, these outcomes were within the range of our benchmark. Contrary to original expectations, we provided additional implementation support to the two MHCs new with CBT for CFS. We concluded that our implementation manual does not seem to substitute external support for team leaders and associated professions during initial implementation of CBT for CFS but may have the potential to make this assistance more efficient. Particular attention should be paid to challenges of implementing stepped care for CFS.KEY PRACTITIONERS MESSAGE: Implementation of CBT for CFS in community-based MHCs was monitored. External support was provided in addition to an implementation manual during initial implementation of CBT for CFS. Participating MHCs were generally capable of successfully implementing and delivering CBT for CFS. Implementation of low-intensity interventions for CFS might better be postponed until therapists have sufficient experience with conventional CBT for CFS.

Winger A, Ekstedt M, Wyller VB, Helseth S.	Faculty of Nursing, Oslo and Akershus University College of Applied Sciences, Oslo, Norway; Medical Faculty, Institute of Clinical Medicine, University of Oslo, Oslo, Norway.	'Sometimes it feels as if the world goes on without me': adolescents' experiences of living with chronic fatigue syndrome.	J Clin Nurs. 2014 Sep;23(17-18):2649-57. doi: 10.1111/jocn.12522. Epub 2013 Dec 20.	AIMS AND OBJECTIVES: To explore the experience of being an adolescent with chronic fatigue syndrome. BACKGROUND: Despite ample research, chronic fatigue syndrome is still poorly understood, and there are still controversies related to the illness. Adolescents with chronic fatigue syndrome are often unable to attend school and lose social relations with friends. The challenges they face will affect their quality of life. DESIGN: A qualitative, phenomenological hermeneutical design. METHOD: Six boys and twelve girls, aged 12-18, were interviewed, emphasising their own experiences living with chronic fatigue syndrome. Analyses were performed using a phenomenological hermeneutical method. RESULTS: The core theme, 'Sometimes it feels as if the world goes on without me', encompasses the feelings an adolescent living with chronic fatigue syndrome might have about life. The core theme was supported by four subthemes: 'On the side of life--locked in and shut out'; 'the body, the illness and me'; 'if the illness is not visible to others, does it exist?'; and 'handling life while hoping for a better future'. The subthemes reflect the experience of social isolation, their own and others' understanding of the illness and hope for the future. CONCLUSIONS: Not being able to be with friends, or attend school, made the adolescents feel different and forgotten. They felt alienated in their own bodies and were struggling to be visible to themselves and to their surroundings. Spending less time with friends and more time with their parents constituted a threat to independence and development. Yet they managed to envision a better future despite all the difficulties. RELEVANCE FOR CLINICAL PRACTICE: To provide effective support and constructive relations to adolescents with chronic fatigue syndrome, all health professions involved need insight from the persons who are themselves ill. Health centres could function as resource centres for patients and healthcare professionals.
Winger A, Kvarstein G, Wyller VB, Sulheim D, Fagermoen E, SmÃ¥stuen MC, Helseth S.	Faculty of Health Sciences, Institute of Nursing, Oslo and Akershus University College of Applied Sciences, Oslo, Norway.	Pain and pressure pain thresholds in adolescents with chronic fatigue syndrome and healthy controls: a cross-sectional study.	BMJ Open. 2014 Oct 6;4(9):e005920. doi: 10.1136/bmjopen-2014-005920.	OBJECTIVES: Although pain is a significant symptom in chronic fatigue syndrome (CFS), pain is poorly understood in adolescents with CFS. The aim of this study was to explore pain distribution and prevalence, pain intensity and its functional interference in everyday life, as well as pressure pain thresholds (PPT) in adolescents with CFS and compare this with a control group of healthy adolescents (HC). METHODS: This is a case-control, cross-sectional study on pain including 120 adolescents with CFS and 39 HCs, aged 12-18 years. We measured pain frequency, pain severity and pain interference using self-reporting questionnaires. PPT was measured using pressure algometry. Data were collected from March 2010 until October 2012 as part of the Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial. RESULTS: Adolescents with CFS had significantly lower PPTs compared with HCs ($p<0.001$). The Pain Severity Score and the Pain Interference Score were significantly higher in adolescents with CFS compared with HCs ($p<0.001$). Almost all adolescents with CFS experienced headache, abdominal pain and/or pain in muscles and joints. Moreover, in all sites,

				the pain intensity levels were significantly higher than in HCs (p<0.001). CONCLUSIONS: We found a higher prevalence of severe pain among adolescents with CFS and lowered pain thresholds compared with HCs. The mechanisms, however, are still obscure. Large longitudinal population surveys are warranted measuring pain thresholds prior to the onset of CFS. TRIAL REGISTRATION NUMBER: Clinical Trials, NCT01040429; The Norwegian Study of Chronic Fatigue Syndrome in Adolescents: Pathophysiology and Intervention Trial (NorCAPITAL) http://www.clinicaltrials.gov.
Witham M, Kennedy G, Belch J, Hill A, Khan F.	Ageing and Health, Division of Cardiovascular & Diabetes Medicine, Ninewells Hospital & Medical School, University of Dundee, Dundee DD1 9SY, UK.	Association between vitamin D status and markers of vascular health in patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).	Int J Cardiol. 2014 Jun 1;174(1):139-40. doi: 10.1016/j.ijcard.2014.03.145. Epub 2014 Apr 2..	No abstract available
Witham MD, Adams F, McSwiggan S, Kennedy G, Kabir G, Belch JJ, Khan F.	(1) Medical Research Institute, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, Scotland, UK. Electronic address: m.witham@dundee.ac.uk. (2)Medical Research Institute, University of Dundee, Ninewells Hospital, Dundee DD1 9SY, Scotland, UK.	Effect of intermittent vitamin D3 on vascular function and symptoms in chronic fatigue syndrome - A randomised controlled trial.	Nutr Metab Cardiovasc Dis. 2014 Oct 22. doi:pii: S0939-4753(14)00315-9. 10.1016/j.numecd.2014.10.007.	BACKGROUND AND AIMS: Low 25-hydroxyvitamin D levels are common in patients with chronic fatigue syndrome; such patients also manifest impaired vascular health. We tested whether high-dose intermittent oral vitamin D therapy improved markers of vascular health and fatigue in patients with chronic fatigue syndrome. METHODS AND RESULTS: Parallel-group, double-blind, randomised placebo-controlled trial. Patients with chronic fatigue syndrome according to the Fukuda (1994) and Canadian (2003) criteria were randomised to receive 100,000 units oral vitamin D3 or matching placebo every 2 months for 6 months. The primary outcome was arterial stiffness measured using carotid-femoral pulse wave velocity at 6 months. Secondary outcomes included flow-mediated dilatation of the brachial artery, blood pressure, cholesterol, insulin resistance, markers of inflammation and oxidative stress, and the Piper Fatigue scale. As many as 50 participants were randomised; mean age 49 (SD 13) years, mean baseline pulse wave velocity 7.8 m/s (SD 2.3), mean baseline office blood pressure 128/78 (18/12) mmHg and mean baseline 25-hydroxyvitamin D level 46 (18) nmol/L. 25-hydroxyvitamin D levels increased by 22 nmol/L at 6 months in the treatment group relative to placebo. There was no effect of treatment on pulse wave velocity at 6 months (adjusted treatment effect 0.0 m/s; 95% CI -0.6 to 0.6; p = 0.93). No improvement was seen in other vascular and metabolic outcomes, or in the Piper Fatigue scale at 6 months (adjusted treatment effect 0.2 points; 95% CI -0.8 to 1.2; p = 0.73). CONCLUSION: High-dose oral vitamin D3 did not improve markers of vascular health or fatigue in patients with chronic fatigue syndrome. Trial registration: www.controlled-trials.com, ISRCTN59927814.

Won CH, Kryger M.	Section of Pulmonary, Critical Care and Sleep Medicine, Yale University School of Medicine, PO BOX 208057, 333 Cedar Street, New Haven, CT 06520-8057, USA. Electronic address: christine.won@yale.edu.	Sleep in patients with restrictive lung disease.	Clin Chest Med. 2014 Sep;35(3):505-12. doi: 10.1016/j.ccm.2014.06.006. Epub 2014 Jul 24. Review.	Restrictive lung disease leads to ventilatory defects and diffusion impairments. These changes may contribute to abnormal nocturnal pathophysiology, including sleep architecture disruption and impaired ventilation and oxygenation. Patients with restrictive lung disease may suffer significant daytime fatigue and dysfunction. Hypercarbia and hypoxemia during sleep may impact progression of lung disease and related symptoms. Little is known about the impact of treatment of sleep disruption on sleep quality and overall prognosis in restrictive lung disease. This review discusses the pathophysiology of sleep and comorbid sleep disorders in restrictive lung diseases including interstitial lung disease, neuromuscular disease, and obesity hypoventilation syndrome.
Wyller VB, SÃ¸rensen Ã˜, Sulheim D, Fagermoen E, Ueland T, Mollnes TE.	Dept. of Paediatrics, Oslo University Hospital, Norway; Division of Medicine and Laboratory Sciences, Medical Faculty, University of Oslo, Norway; Dept. of Paediatrics, Akershus University Hospital, Nordbyhagen, Norway. Electronic address: brwylle@online.no	Plasma cytokine expression in adolescent chronic fatigue syndrome.	Brain Behav Immun. 2014 Dec 31. doi:pii: S0889-1591(14)00614-X. 10.1016/j.bbi.2014.12.025.	Chronic fatigue syndrome (CFS) is a prevalent and disabling condition among adolescents. The pathophysiology is poorly understood, but low-grade systemic inflammation has been suggested as an important component. This study compared circulating levels of individual cytokines and parameters of cytokine networks in a large set of adolescent CFS patients and healthy controls, and explored associations between cytokines and symptoms in the CFS group. CFS patients (12-18years old) were recruited nation-wide to a single referral center as part of the NorCAPITAL project (ClinicalTrials ID: NCT01040429). A broad case definition of CFS was applied, requiring three months of unexplained, disabling chronic/relapsing fatigue of new onset, whereas no accompanying symptoms were necessary. Thus, the case definition was broader than the Fukuda-criteria of CFS. Healthy controls having comparable distribution of gender and age were recruited from local schools. Twenty-seven plasma cytokines, including interleukins, chemokines and growth factors were assayed using multiplex technology. The results were subjected to network analyses using the ARACNE algorithm. Symptoms were charted by a questionnaire, and patients were subgrouped according to the Fukuda-criteria. A total of 120 CFS patients and 68 healthy controls were included. CFS patients had higher scores for fatigue ($p<0.001$) and inflammatory symptoms ($p<0.001$) than healthy controls. All cytokine levels and cytokine network parameters were similar, and none of the differences were statistically different across the two groups, also when adjusting for adherence to the Fukuda criteria of CFS. Within the CFS group, there were no associations between aggregate cytokine network parameters and symptom scores. Adolescent CFS patients are burdened by symptoms that might suggest low-grade systemic inflammation, but plasma levels of individual cytokines as well as cytokine network measures were not different from healthy controls, and there were no associations between symptoms and cytokine expression in the CFS group. Low-grade systemic inflammation does not appear to be a central part of adolescent CFS pathophysiology.

Wyller VB, Fagermoen E, Sulheim D, Winger A, Skovlund E, Saul JP.	Department of Pediatrics, Oslo University Hospital, N-1478 Oslo, Norway ; Division of Medicine and Laboratory Sciences, Medical Faculty, University of Oslo, Oslo, Norway ; Department of Pediatrics, Akershus University Hospital, Nordbyhagen, Norway.	Orthostatic responses in adolescent chronic fatigue syndrome: contributions from expectancies as well as gravity.	Biopsychosoc Med. 2014;8:22. doi: 10.1186/1751-0759-8-22.	BACKGROUND: Orthostatic intolerance is common in chronic fatigue syndrome (CFS), and several studies have documented an abnormal sympathetic predominance in the autonomic cardiovascular response to gravitational stimuli. The aim of this study was to explore whether the expectancies towards standing are contributors to autonomic responses in addition to the gravitational stimulus itself. METHODS: A total of 30 CFS patients (12-18 years of age) and 39 healthy controls underwent 20° head-up tilt test and a motor imagery protocol of standing upright. Beat-to-beat cardiovascular variables were recorded. RESULTS: At supine rest, CFS patients had significantly higher heart rate, diastolic blood pressure, and mean arterial blood pressure, and lower stroke index and heart rate variability (HRV) indices. The response to 20° head-up tilt was identical in the two groups. The response to imaginary upright position was characterized by a stronger increase of HRV indices of sympathetic predominance (power in the low-frequency range as well as the ratio low-frequency: high-frequency power) among CFS patients. CONCLUSIONS: These results suggest that in CFS patients expectancies towards orthostatic challenge might be additional determinants of autonomic cardiovascular modulation along with the gravitational stimulus per se.
Yasui M, Yoshimura T, Takeuchi S, Tokizane K, Tsuda M, Inoue K, Kiyama H.	Department of Functional Anatomy and Neuroscience, Graduate School of Medicine, Nagoya University, Nagoya, Aichi, Japan; Core Research for Evolutional Science and Technology (CREST) of the Japan Science and Technology Agency, Saitama, Japan.	A chronic fatigue syndrome model demonstrates mechanical allodynia and muscular hyperalgesia via spinal microglial activation.	Glia. 2014 Sep;62(9):1407-17. doi: 10.1002/glia.22687. Epub 2014 May 23.	Patients with chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) display multiple symptoms, such as chronic widespread pain, fatigue, sleep disturbance, and cognitive dysfunction. Abnormal pain sensation may be the most serious of these symptoms; however, its pathophysiology remains unknown. To provide insights into the molecular basis underlying abnormal pain in CFS and FMS, we used a multiple continuous stress (CS) model in rats, which were housed in a cage with a low level of water (1.5 cm in depth). The von Frey and Randall-Seritto tests were used to evaluate pain levels. Results showed that mechanical allodynia at plantar skin and mechanical hyperalgesia at the anterior tibialis (i.e., muscle pain) were induced by CS loading. Moreover, no signs of inflammation and injury incidents were observed in both the plantar skin and leg muscles. However, microglial accumulation and activation were observed in L4-L6 dorsal horn of CS rats. Quantification analysis revealed a higher accumulation of microglia in the medial part of Layers I-IV of the dorsal horn. To evaluate an implication of microglia in pain, minocycline was intrathecally administrated (via an osmotic pump). Minocycline significantly attenuated CS-induced mechanical hyperalgesia and allodynia. These results indicated that activated microglia were involved in the development of abnormal pain in CS animals, suggesting that the pain observed in CFS and FMS patients may be partly caused by a mechanism in which microglial activation is involved.

Zeineh MM, Kang J, Atlas SW, Raman MM, Reiss AL, Norris JL, Valencia I, Montoya JG.	From the Department of Radiology, Lucas Center for Imaging, Stanford University School of Medicine, 1201 Welch Rd, Room P271, Stanford, CA 94305-5488.	Right Arcuate Fasciculus Abnormality in Chronic Fatigue Syndrome.	Radiology. 2014 Oct 29:141079.	Purpose To identify whether patients with chronic fatigue syndrome (CFS chronic fatigue syndrome) have differences in gross brain structure, microscopic structure, or brain perfusion that may explain their symptoms. Materials and Methods Fifteen patients with CFS chronic fatigue syndrome were identified by means of retrospective review with an institutional review board-approved waiver of consent and waiver of authorization. Fourteen age- and sex-matched control subjects provided informed consent in accordance with the institutional review board and HIPAA. All subjects underwent 3.0-T volumetric T1-weighted magnetic resonance (MR) imaging, with two diffusion-tensor imaging (DTI diffusion-tensor imaging) acquisitions and arterial spin labeling (ASL arterial spin labeling). Open source software was used to segment supratentorial gray and white matter and cerebrospinal fluid to compare gray and white matter volumes and cortical thickness. DTI diffusion-tensor imaging data were processed with automated fiber quantification, which was used to compare piecewise fractional anisotropy (FA fractional anisotropy) along 20 tracks. For the volumetric analysis, a regression was performed to account for differences in age, handedness, and total intracranial volume, and for the DTI diffusion-tensor imaging FA fractional anisotropy was compared piecewise along tracks by using an unpaired t test. The open source software segmentation was used to compare cerebral blood flow as measured with ASL arterial spin labeling. Results In the CFS chronic fatigue syndrome population, FA fractional anisotropy was increased in the right arcuate fasciculus (P = .0015), and in right-handers, FA fractional anisotropy was also increased in the right inferior longitudinal fasciculus (ILF inferior longitudinal fasciculus) (P = .0008). In patients with CFS chronic fatigue syndrome, right anterior arcuate FA fractional anisotropy increased with disease severity (r = 0.649, P = .026). Bilateral white matter volumes were reduced in CFS chronic fatigue syndrome (mean ± standard deviation, 467 581 mm(3) ± 47 610 for patients vs 504 864 mm(3) ± 68 126 for control subjects, P = .0026), and cortical thickness increased in both right arcuate end points, the middle temporal (T = 4.25) and precentral (T = 6.47) gyri, and one right ILF inferior longitudinal fasciculus end point, the occipital lobe (T = 5.36). ASL arterial spin labeling showed no significant differences. Conclusion Bilateral white matter atrophy is present in CFS chronic fatigue syndrome . No differences in perfusion were noted. Right hemispheric increased FA fractional anisotropy may reflect degeneration of crossing fibers or strengthening of short-range fibers. Right anterior arcuate FA fractional anisotropy may serve as a biomarker for CFS chronic fatigue syndrome .

Zeller B, Ruud E, Havard Loge J, Kanellopoulos A, Hamre H, Godang K, Bruun Wyller V.	Department of Pediatric Medicine, Oslo University Hospital, Oslo, Norway. Electronic address: bzeller@ous-hf.no	Chronic fatigue in adult survivors of childhood cancer: associated symptoms, neuroendocrine markers, and autonomic cardiovascular responses.	Psychosomatics. 2014 Nov-Dec;55(6):621-9. doi: 10.1016/j.psym.2013.12.005. Epub 2013 Dec 8.	BACKGROUND: Chronic fatigue (CF) is a common late effect after childhood cancer. OBJECTIVE: Based on findings among patients with the chronic fatigue syndrome (CFS), this study explored symptoms, neuroendocrine markers, and autonomic cardiovascular responses associated with CFS in childhood cancer survivors. METHODS: Long-term survivors of childhood lymphoma and acute lymphoblastic leukemia reporting CF were compared with survivors without CF. Data included patient-reported outcomes, clinical examination, head-up tilt test, and neuroendocrine markers in the blood and the urine. RESULTS: Of 102 included survivors, 15 were excluded from comparative analyses because of significant co-morbidity or pregnancy. Of the remaining 87 participants (median age 33.0 years, follow-up time 25.2 years), 35 had CF and 52 did not have CF. Compared with non-CF controls, CF cases reported a significantly ($P < 0.01$) higher frequency of symptoms typical of the CFS (muscle or joint pain or both and feeling confused/disoriented) and symptoms of autonomic dysfunction (palpitations, feeling intermittently heat and cold, and watery diarrhea). CF cases and controls did not differ regarding autonomic cardiovascular responses to orthostatic stress, but the CF group had lower levels of plasma adrenocorticotrophic hormone ($P = 0.002$) and higher levels of urine norepinephrine ($P = 0.017$). CONCLUSIONS: Survivors with CF reported a high symptom-burden compared with controls. There were few differences between both the groups regarding biomarkers, but slight alterations of the hypothalamus-pituitary-adrenal axis and sympathetic nervous activity were detected. CF in cancer survivors has features in common with the CFS, but further efforts are required to clarify the pathophysiology.
Zeller B, Loge JH, Kanellopoulos A, Hamre H, Wyller VB, Ruud E.	Departments of Pediatric Medicine Oncology, National Resource Center for Late Effects after Cancer Treatment Department of Behavioural Sciences in Medicine, University of Oslo, Oslo, Norway.	Chronic fatigue in long-term survivors of childhood lymphomas and leukemia: persistence and associated clinical factors.	J Pediatr Hematol Oncol. 2014 Aug;36(6):438-44. doi: 10.1097/MPH.0000000000000051.	BACKGROUND: Chronic fatigue (CF) is an important late effect after childhood malignancies. Our aim was to assess CF persistence over time, concurrent comorbidities, and associations with clinical symptoms. PROCEDURE: A total of 102 long-term survivors of childhood lymphomas and acute lymphoblastic leukemia, 53 and 49 reporting CF and no CF, respectively, at time point (TP)1, were evaluated for CF at a second TP after a median interval of 2.7 years. At TP2 a survey, including self-reported and objectively measured variables, assessed depressive symptoms, pain, and physical activity. RESULTS: A total of 32 of the 53 reported CF cases at both TPs and 40/49 survivors had no CF at both TPs, whereas 30 had changed their fatigue status between first and second assessment (converters). Major somatic comorbidities were equally distributed among the groups. After exclusion of converters and survivors with major comorbidity/pregnancy, 27 persistent CF (PCF) cases and 35 controls were compared. PCF cases reported significantly more depression, sleeping problems, anxiety, pain, and reduced physical function. Further, they were less physically active than controls (steps/d; $P=0.009$). In a multiple regression analysis, depressive symptoms remained the only significant predictor of PCF. CONCLUSIONS: Long-term survivors of childhood cancer with PCF

				are characterized by more depressive symptoms, anxiety, pain, insomnia, and less physical activity.
Zhang L, Xu MM, Zeng L, Liu S, Liu X, Wang X, Li D, Huang RZ, Zhao LB, Zhan QL, Zhu D, Zhang YY, Xu P, Xie P.	Department of Neurology, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuzhong District, 400016, Chongqing, People's Republic of China.	Evidence for Borna disease virus infection in neuropsychiatric patients in three western China provinces.	Eur J Clin Microbiol Infect Dis. 2014 Apr;33(4):621-7. doi: 10.1007/s10096-013-1996-4. Epub 2013 Oct 30.	Borna disease virus (BDV) is a non-cytolytic, neurotropic RNA virus that can infect a wide variety of vertebrate species from birds and primates to humans. Several studies have been carried out to investigate whether BDV is associated with neuropsychiatric diseases. However, this association is still inconclusive. Two panels of subjects consisting of 1,679 various neuropsychiatric patients and healthy people from three western China provinces were enrolled in this study. BDV p24 or p40 RNA in peripheral blood mononuclear cells (PBMCs) were detected in the first panel of 1,481 subjects using reverse transcription quantitative polymerase chain reaction (RT-qPCR) and cerebrospinal fluid (CSF) samples from the BDV RNA-positive individuals were subjected to BDV p24 antibodies testing by enzyme-linked immunosorbent assay (ELISA). BDV p24 or p40 RNA in PBMCs and p24 antibodies in plasma were detected in the second panel of 198 subjects by RT-qPCR and Western blot. A higher prevalence for BDV RNA was demonstrated in patients with viral encephalitis (6.70%), Guillain-Barré syndrome (6.70%), schizophrenia (9.90%) and chronic fatigue syndrome (CFS) (12.70%) compared to healthy controls in the first panel. CSF p24 antibodies were demonstrated in three viral encephalitis patients, two schizophrenia patients and two major depressive disorder (MDD) patients. The prevalences of p24 antibodies in plasma from patients with viral encephalitis (13.24%), multiple sclerosis (25.00%) and Parkinson's disease (22.73%) were significantly higher than healthy controls. This study demonstrates that BDV infection also exists in humans from three western China provinces, and suggests the involvement of the contribution of BDV in the aetiology of Chinese patients with some neuropsychiatric disorders, including viral encephalitis, schizophrenia, CFS, multiple sclerosis and Parkinson's disease.
L, Liao XJ, Yang GG, M Q, Wu WJ.	No address given	Distribution characteristics of basic syndromes of chronic functional constipation and its related factors analysis	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2014 Oct;34(10):1173-7.	[Article in Chinese] ıts with chronic functional constipation (CFC). METHODS: The complete data of 538 yping was performed. The distribution characteristics of basic syndromes were rformed with SPSS 17. 0 Software to determine basic syndrome related factors such gue, stimulating beverage, exercise conditions, Western medicine type of h to low as qi deficiency syndrome (380 cases, 70.6%), qi stagnation syndrome (337 , yang deficiency syndrome (197 cases, 36.6%), and others (58 cases, 10. 8%) . Most deficiency complicated qi stagnation syndrome (275 cases, 51.1%) and qi deficiency were main related factors for qi deficiency syndrome (P <0. 01, P <0. 05). Poor s constipation were main related factors for qi stagnation syndrome (P <0.01). Sleep ciency syndrome (P <0. 01, P < 0.05). Stimulating beverages were main related factor

				elated factors for yang deficiency syndrome (P < 0. 01, P <0. 05). CONCLUSIONS: CFC d qi stagnation syndrome and qi deficiency complicated blood deficiency syndrome. sion and anxiety tendencies), mental stress, interpersonal relations, work fatigue, he distribution of CFC syndromes.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No abstract given]	Department of Molecular Pathology, The Institute for Molecular Medicine, Huntington Beach, CA 92649, USA. Electronic address: gnicolson@immed.org.	Lipid Replacement Therapy: A natural medicine approach to replacing damaged lipids in cellular membranes and organelles and restoring function.	Biochim Biophys Acta. 2013 Nov 21. pii: S0005-2736(13)00407-0. doi: 10.1016/j.bbamem.2013.11.010. [Epub ahead of print]	Lipid Replacement Therapy, the use of functional oral supplements containing cell membrane phospholipids and antioxidants, has been used to replace damaged, usually oxidized, membrane glycerophospholipids that accumulate during aging and in various clinical conditions in order to restore cellular function. This approach differs from other dietary and intravenous phospholipid interventions in the composition of phospholipids and their defense against oxidation during storage, ingestion, digestion and uptake as well as the use of protective molecules that noncovalently complex with phospholipid micelles and prevent their enzymatic and bile disruption. Once the phospholipids have been taken in by transport processes, they are protected by several natural mechanisms involving lipid receptors, transport and carrier molecules and circulating cells and lipoproteins until their delivery to tissues and cells where they can again be transferred to intracellular membranes by specific and nonspecific transport systems. Once delivered to membrane sites, they naturally replace and stimulate removal of damaged membrane lipids. Various chronic clinical conditions are characterized by membrane damage, mainly oxidative but also enzymatic, resulting in loss of cellular function. This is readily apparent in mitochondrial inner membranes where oxidative damage to phospholipids like cardiolipin and other molecules results in loss of trans-membrane potential, electron transport function and generation of high-energy molecules. Recent clinical trials have shown the benefits of Lipid Replacement Therapy in restoring mitochondrial function and reducing fatigue in aged subjects and patients with a variety of clinical diagnoses that are characterized by loss of mitochondrial function and include fatigue as a major symptom. This article is part of a Special Issue entitled: Membrane structure and function: Relevance in the cell's physiology, pathology and therapy.
[No authors listed]	[No address quoted]	Information from your family doctor. Chronic fatigue syndrome.	Am Fam Physician. 2012 Oct 15; 86(8):1-1.	[No abstract given]
Abbi B, Natelson BH.	War Related Illness and Injury Study Center, DVA Medical Center, East Orange, NJ, USA.	Is chronic fatigue syndrome the same illness as fibromyalgia: evaluating the 'single syndrome' hypothesis.	QJM. 2013 Jan; 106(1):3-9. doi: 10.1093/qjmed/hcs156. Epub 2012 Aug 26.	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained syndromes that can and often do co-occur. For this reason, some have posited that the two are part of the same somatic syndrome--examples of symptom amplification. This hypothesis would suggest that few differences exist between the two syndromes. To evaluate this interpretation, we have searched the literature for articles comparing CFS to FM, reviewing only those articles which report differences between the two. This review presents data showing differences across a number of parameters--implying that the underlying pathophysiology in CFS may differ from that of FM. We hope that our review encourages other groups to look for additional differences between CFS and FM. By continuing to preserve the unique illness definitions of the

				two syndromes, clinicians will be able to better identify, understand and provide treatment for these individuals.
Ablin JN, Clauw DJ, Lyden AK, Ambrose K, Williams DA, Gracely RH, Glass JM.	Institute of Rheumatology, Sourasky Medical Center, and Tel Aviv University faculty of Medicine, Israel. ajacob@post.tau.ac.il.	Effects of sleep restriction and exercise deprivation on somatic symptoms and mood in healthy adults.	Clin Exp Rheumatol. 2013 Nov-Dec; 31(6 Suppl 79):53-9. Epub 2013 Nov 15.	OBJECTIVES: Exposure to acute 'stressors' (e.g. infections, pain, and trauma) often results in altered sleep habits and reductions in routine activity. In some individuals, these behavioural responses to acute stressors may contribute to the development of chronic somatic symptoms such as widespread pain, fatigue, memory difficulties and mood disturbances, much like those associated with 'functional somatic syndromes' (FSS) such as fibromyalgia or chronic fatigue syndrome. METHODS: Eighty-seven healthy young adults who reported sleeping between 7 and 9 hours nightly and exercising regularly were randomised to one of four groups: exercise cessation, sleep restriction (6 hours nightly), both, or neither. Symptoms of pain, fatigue, cognitive dysfunction and negative mood were measured before and after the 10-day restriction period. RESULTS: Sleep restriction was a potent contributor to the development of somatic symptoms. Exercise cessation was less influential leading only to fatigue. There were no significant interactions between exercise cessation and sleep restriction, except that males were much more likely to develop somatic symptoms when deprived of both sleep and exercise than one or the other. Women were generally much more likely to develop somatic symptoms than men. CONCLUSIONS: This study supports previous research suggesting that both sleep and exercise are critical in 'preventing' somatic symptoms among some individuals. Furthermore, to our knowledge, this is the first time there is data to suggest that women are much more sensitive to decrements in routine sleep and exercise than are men.
Afari N, Ahumada SM, Wright LJ, Mostoufi S, Golnari G, Reis V, Cuneo JG.	VA Center of Excellence for Stress and Mental Health (N.A., S.M.), San Diego, California; VA San Diego Healthcare System (N.A., S.M., J.G.C.), San Diego, California; Department of Psychiatry (N.A., G.G.) University of California, San Diego, San Diego, California; Institute of Child Development (S.M.A.) University of Minnesota,	Psychological Trauma and Functional Somatic Syndromes: A Systematic Review and Meta-Analysis.	Psychosom Med. 2013 Dec 12. [Epub ahead of print]	Objective: This meta-analysis systematically examined the association of reported psychological trauma and posttraumatic stress disorder (PTSD) with functional somatic syndromes including fibromyalgia, chronic widespread pain, chronic fatigue syndrome, temporomandibular disorder, and irritable bowel syndrome. Our goals were to determine the overall effect size of the association and to examine moderators of the relationship.MethodsLiterature searches identified 71 studies with a control or comparison group and examined the association of the syndromes with traumatic events including abuse of a psychological, emotional, sexual, or physical nature sustained during childhood or adulthood, combat exposure, or PTSD. A random-effects model was used to estimate the pooled odds ratio and 95% confidence interval. Planned subgroup analyses and meta-regression examined potential moderators.ResultsIndividuals who reported exposure to trauma were 2.7 (95% confidence interval = 2.27-3.10) times more likely to have a functional somatic syndrome. This association was robust against both publication bias and the generally low quality of the literature. The magnitude of the association with PTSD was significantly larger than that with sexual or physical abuse. Chronic fatigue syndrome had a larger association with reported trauma than did either irritable bowel

	Minneapolis, Minnesota; VA Northern California Health Care System (L.J.W.), Oakland, California; and VA Palo Alto Healthcare System (V.R.), Palo Alto, California.			syndrome or fibromyalgia. Studies using nonvalidated questionnaires or self-report of trauma reported larger associations than did those using validated questionnaires.ConclusionsFindings highlight the limitations of the existing literature and emphasize the importance of conducting prospective studies, further examining the potential similarities and differences of these conditions and pursuing hypothesis-driven studies of the mechanisms underlying the link between trauma, PTSD, and functional somatic syndromes.
Agardy S.	[No address quoted]	Letter to the editor: comments on 'recovery from chronic fatigue syndrome after treatments given in the PACE trial'.	Psychol Med. 2013 Aug; 43(8):1787. doi: 10.1017/S003329171300113X.	Comment in Psychol Med. 2013 Aug; 43(8):1791-2.
Akarsu S, Tekin L, Ay H, Carli AB, Tok F, Simşek K, Kiralp MZ.	Gülhane Military Medical Academy Haydarpasa Training Hospital, Department of Physical Medicine and Rehabilitation, Istanbul, Turkey. selimakarsu@yahoo.com.tr	The efficacy of hyperbaric oxygen therapy in the management of chronic fatigue syndrome.	Undersea Hyperb Med. 2013 Mar-Apr; 40(2):197-200.	OBJECTIVE: Chronic fatigue syndrome (CFS) is a chronic disease with social components that ensue secondary to the incapacity of the person to fulfill work, social and family responsibilities. Currently, there is no consensus regarding its treatment. The aim of this study was to determine the efficacy of hyperbaric oxygen (HBO2) therapy in CFS. DESIGN: Sixteen patients included in the study were diagnosed with CFS according to the Fukuda criteria. Patients received 15 treatment sessions of HBO2 therapy over a period of three consecutive weeks (five days per week). The outcome measures (visual analog fatigue scale (VAFS). Fatigue Severity Scale (FSS) and Fatigue Quality of Life Score (FQLS) were assessed before the treatment and after completion of the 15 sessions. RESULTS: HBO2 therapy was well tolerated, with no complications. After treatment, patients' scores were found to have improved with respect to VAFS, FSS and FQLS (all $p<0.005$). CONCLUSIONS: We may infer that HBO2 therapy decreases the severity of symptoms and increases the life quality of CFS patients. It may be a new treatment modality for the management of CFS. However, further studies with larger sample sizes and control groups are definitely awaited.
Akkaya N, Atalay NS, Selcuk ST, Alkan H, Catalbas N, Sahin F.	Department of Physical Medicine and Rehabilitation, Medicine Faculty, University of Pamukkale, 20070, Kinikli-Denizli, Turkey. nrakkaya@gmail.com	Frequency of fibromyalgia syndrome in breast cancer patients.	Int J Clin Oncol. 2013 Apr;18(2):285-92. doi: 10.1007/s10147-012-0377-9. Epub 2012 Feb 10.	BACKGROUND: We aimed to determine the frequency of fibromyalgia syndrome (FM) in operated breast cancer patients and to research the relationship between FM and the severity of fatigue and quality of life in these breast cancer patients. METHODS: The demographic data of 101 operated breast cancer patients were recorded. The patients who had pain were then classified as having regional pain (RP), widespread pain without FM (WP), and widespread pain with FM (WFM). The FM diagnosis was based on the American College of Rheumatology (ACR) criteria. The severity of fatigue was evaluated with the Brief Fatigue Inventory, the disease impact was evaluated

				with the Fibromyalgia Impact Questionnaire (FIQ), and the quality of life was evaluated with the European Organization for Research on Treatment of Cancer questionnaire Quality of Life-C30 (EORTC-QoL-C30). RESULTS: There was no pain in 38 (37.6%) patients, whereas there was pain in 63 (62.4%) patients (N = 42, 41.6% had RP, N = 21, 20.8% had WP). Ten (9.9%) of the entire patient cohort were diagnosed as having FM according to the ACR criteria. There were no differences among the 3 groups in respect to demographic characteristics when patients were classified as RP (N = 42), WP (N = 11), and WFM (N = 10) groups. While there were negative correlations between the FIQ and EORTC-QoL-C30-function score (r = -0.727) and EORTC-QoL-C30-global score (r = -0.488), there was a positive correlation between the FIQ and EORTC-QoL-C30-symptom score (r = 0.726). CONCLUSION: We note that the frequency of FM in the operated breast cancer patients in this study was higher than that reported in normal populations in the literature. Also, we found that the presence of FM had negative effects on the quality of life of the breast cancer patients. Accordingly, in the evaluation of widespread pain and complaints of fatigue in long-surviving breast cancer patients, after metastatic disease is excluded, the probability of FM should be kept in mind, so that appropriate treatment can be initiated to improve their functional status and quality of life.
Alves Eda S, Ackel-D'Elia C, Luz GP, Cunha TC, Carneiro G, Tufik S, Bittencourt LR, de Mello MT.	Disciplina de Medicina e Biologia do Sono, Departamento de Psicobiologia, Universidade Federal de São Paulo-UNIFESP, São Paulo, CEP: 04020-050, Brazil.	Does physical exercise reduce excessive daytime sleepiness by improving inflammatory profiles in obstructive sleep apnea patients?	Sleep Breath. 2013 May; 17(2):505-10. doi: 10.1007/s11325-012-0729-8. Epub 2012 Jun 20.	INTRODUCTION: Obstructive sleep apnea syndrome (OSAS) is associated with a variety of long-term consequences such as high rates of morbidity and mortality, due to excessive diurnal somnolence as well as cardiovascular and metabolic diseases. Obesity, recurrent episodes of upper airway obstruction, progressive hypoxemia, and sleep fragmentation during sleep cause neural, cardiovascular, and metabolic changes. These changes include activation of peripheral sympathetic nervous system and the hypothalamic-pituitary-adrenal axis, insulin sensitivity, and inflammatory cytokines alterations, which predispose an individual to vascular damage. DISCUSSION: Previous studies proposed that OSAS modulated the expression and secretion of inflammatory cytokines from fat and other tissues. Independent of obesity, patients with OSAS exhibited elevated levels of C-reactive protein, tumor necrosis factor-α and interleukin-6, which are associated with sleepiness, fatigue, and the development of a variety of metabolic and cardiovascular diseases. OSAS and obesity are strongly associated with each other and share many common pathways that induce chronic inflammation. Previous studies suggested that the protective effect of exercise may be partially attributed to the anti-inflammatory effect of regular exercise, and this effect was observed in obese patients. Although some studies assessed the effects of physical exercise on objective and subjective sleep parameters, the quality of life, and mood in patients with OSAS, no study has evaluated the effects of this treatment on inflammatory profiles. In this review, we cited some studies that directed our opinion to believe that since OSAS causes increased inflammation and has excessive daytime sleepiness as a symptom and being

				that physical exercise improves inflammatory profiles and possibly OSAS symptoms, it must be that physical exercise improves excessive daytime sleepiness due to its improvement in inflammatory profiles.
Amr M, Lakhan SE, Sanhan S, Al-Rhaddad D, Hassan M, Thiabh M, Shams T.	Global Neuroscience Initiative Foundation, Beverly Hills, CA, USA. slakhan@gnif.org.	Efficacy and tolerability of quetiapine versus haloperidol in first-episode schizophrenia: a randomized clinical trial.	Int Arch Med. 2013 Dec 5;6 (1):47. doi: 10.1186/1755-7682-6-47.	BACKGROUND: Schizophrenia is a chronic disease of global importance. The second-generation antipsychotic quetiapine has a favorable side-effect profile, however, its clinical effectiveness has been called into question when compared with first-generation antipsychotics such as haloperidol. This study evaluates the efficacy and tolerability of quetiapine versus haloperidol for first-episode schizophrenia in the outpatient setting. METHODS: 156 adult patients with first-episode schizophrenia participated in an outpatient clinical trial and were randomized to quetiapine (200 mg/d; n = 78) or haloperidol (5 mg/d; n = 78). The study medications were titrated to a mean daily dose of 705 mg for quetiapeine and 14 mg for haloperidol. The patients were assessed at baseline, six weeks, and twelve weeks. The primary outcome measures were positive and negative scores of the Positive and Negative Syndrome Scale (PANSS). Secondary measures were Global Assessment of Functioning (GAF) scale for overall psychosocial functioning, and Simpson-Angus Scale (SAS) for extra-pyramidal symptoms. RESULTS: At twelve weeks, the quetiapine group had a greater decrease in PANSS positive (18.9 vs. 15.3, p = 0.013) and negative scores (15.5 vs. 11.6, p = 0.012), however, haloperidol showed a greater decrease in general psychopathology score (23.8 vs. 27.7, p = 0.012). No significant difference between groups were found for total PANSS (58.3 vs. 54.8, p = 0.24) and GAF (45.7 vs. 46.2, p = 0.79).ANOVA identified significant group interactions on PANSS positive (F = 18.72, df = 1.6,52.4, p < 0.0001), negative (F = 5.20, df = 1.1,35.7, p < 0.0001), depression/anxiety (F = 106.49, df = 1.14,37.8, p < 0.0001), and total scores (F = 7.51, df = 1.4,45.6, p = 0.001).SAS (8.62 vs. 0.26, p < 0.0001) and adverse events of akathisia (78% vs. 0%, p = 0.000), parkinsonism (66.6% vs. 0%, p < 0.0001), and fatigue (84.6% vs. 66.6%, p = 0.009) were greater in haloperidol compared to quetiapine, whereas headache was more common in quetiapine treated patients (11.5% vs. 35.9%, p < 0.0001). CONCLUSIONS: Quetiapine has greater efficacy for positive and negative symptoms with less extra-pyramidal symptoms than haloperidol when used for first-episode schizophrenia in the outpatient setting.
Anderson G, Berk M, Maes M.	CRC, Glasgow, UK.	Biological phenotypes underpin the physio-somatic symptoms of somatization, depression, and chronic fatigue syndrome.	Acta Psychiatr Scand. 2013 Aug 17. doi: 10.1111/acps.12182. [Epub ahead of print]	OBJECTIVE: Somatization is a symptom cluster characterized by 'psychosomatic' symptoms, that is, medically unexplained symptoms, and is a common component of other conditions, including depression and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). This article reviews the data regarding the pathophysiological foundations of 'psychosomatic' symptoms and the implications that this has for conceptualization of what may more appropriately be termed physio-somatic symptoms. METHOD: This narrative review used papers published in PubMed, Scopus, and Google Scholar electronic databases using the keywords: depression and chronic fatigue, depression and somatization, somatization and chronic fatigue syndrome,

				each combined with inflammation, inflammatory, tryptophan, and cell-mediated immune (CMI). RESULTS: The physio-somatic symptoms of depression, ME/CFS, and somatization are associated with specific biomarkers of inflammation and CMI activation, which are correlated with, and causally linked to, changes in the tryptophan catabolite (TRYCAT) pathway. Oxidative and nitrosative stress induces damage that increases neoepitopes and autoimmunity that contribute to the immuno-inflammatory processes. These pathways are all known to cause physio-somatic symptoms, including fatigue, malaise, autonomic symptoms, hyperalgesia, intestinal hypermotility, peripheral neuropathy, etc. CONCLUSION: Biological underpinnings, such as immune-inflammatory pathways, may explain, at least in part, the occurrence of physio-somatic symptoms in depression, somatization, or myalgic encephalomyelitis/chronic fatigue syndrome and thus the clinical overlap among these disorders.
Anderson VR, Jason LA, Hlavaty LE.	Department of Psychology, Michigan State University, East Lansing, Michigan, USA.	A Qualitative Natural History Study of ME/CFS in the Community.	Health Care Women Int. 2014 Jan; 35(1):3-26. doi: 10.1080/07399332.2012.684816. Epub 2013 Feb 27.	In previous qualitative research on Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS), researchers have focused on the experiences of patients with ME/CFS in tertiary care samples. This qualitative study examined the natural history of people with ME/CFS (n = 19) from a community-based sample. Findings highlighted multilayered themes involving the illness experience and the physical construction of ME/CFS. In addition, this study further illuminated unique subthemes regarding community response and treatment, which have implications for understanding the progression of ME/CFS as well as experiences of those within patient networks. There is a need for more longitudinal qualitative research on epidemiological samples of patients with ME/CFS.
Angeletti C, Guetti C, Piroli A, Angeletti PM, Paladini A, Ciccozzi A, Marinangeli F, Varrassi G.	Anesthesiology and Pain Medicine, Department of Health Sciences, University of L'Aquila, Italy.	Duloxetine and pregabalin for pain management in multiple rheumatic diseases associated with fibromyalgia.	Pain Pract. 2013 Nov; 13(8):657-62. doi: 10.1111/papr.12009. Epub 2012 Nov 5.	The fibromyalgia syndrome (FMS) is characterized by chronic and widespread musculoskeletal pain and soreness accompanied by sleep disorders, chronic fatigue and affective disorders. FMS is often associated with other forms of immuno-rheumatic diseases. Although FMS pathophysiology is still not fully understood, a number of neuroendocrine, neurotransmission and neurosensitive disorders might generate a mechanism for the elicitation of pain by "central sensitization," which is common to many other painful conditions. The present case describes the success of a therapeutic scheme, which associates two different pharmacological classes, anticonvulsants and new-generation antidepressants, when FMS complicates a rare pathology called Cogan's syndrome. The association of two drugs might noticeably affect the molecular mechanisms of difficult pain, thus solving painful conditions of multifactorial origin.
Antcliff D, Keeley P, Campbell M, Oldham J, Woby S.	Pennine Acute Hospitals NHS Trust, North Manchester General Hospital, Manchester, M8 5RB,	The development of an activity pacing questionnaire for chronic pain and/or fatigue: a Delphi	Physiotherapy. 2013 Sep; 99(3):241-6. doi: 10.1016/j.physio.2012.12.003. Epub 2013 Feb 8.	OBJECTIVE: Activity pacing is frequently advised as a coping strategy for the management of chronic conditions (such as chronic low back pain, chronic widespread pain and chronic fatigue syndrome/myalgic encephalomyelitis). Despite anecdotal support for activity pacing, there is limited and conflicting research evidence into the efficacy of this strategy. There is no consensus on the interpretation

	UK. Deborah.Antcliff@pat.nhs.uk	technique.		of 'pacing' due to diverse descriptions, including strategies that encourage both increasing and decreasing activities. Furthermore, at present, there are few validated scales to measure how patients pace their activities. The aim of this study was to undertake the first stage in the development of a comprehensive tool that assesses the multi-faceted nature of pacing among patients with chronic conditions. DESIGN: Three-round Delphi technique. PARTICIPANTS: Expert panel based in the UK including patients and clinicians. RESULTS: The 42 participants who completed three rounds of Delphi included 4 patients, 3 nurses, 26 physiotherapists and 9 occupational therapists. The 38 questions that reached consensus to be included in the questionnaire encompassed a number of different facets of pacing, for example, breaking down tasks, not over-doing activities, and gradually increasing activities. CONCLUSIONS: To our knowledge, this is the first study that has engaged both patients and clinicians in a Delphi technique to develop an activity pacing questionnaire. In contrast to existing pacing scales, our questionnaire appears to contain a number of distinct facets of pacing. Further study is being undertaken to engage patients in the exploration of the validity, reliability and acceptability of the questionnaire.
Aroniadis OC, Brandt LJ.	Division of Gastroenterology, Montefiore Medical Center, Bronx, New York 10467, USA. oaroniad@montefiore.org	Fecal microbiota transplantation: past, present and future.	Curr Opin Gastroenterol. 2013 Jan;29(1):79-84. doi: 10.1097/MOG.0b013e32835a4b3e.	PURPOSE OF REVIEW: Fecal microbiota transplantation (FMT) re-establishes a balanced intestinal flora with resultant cure of recurrent Clostridium difficile infection (RCDI). FMT has also been used to treat other gastrointestinal (GI) diseases including inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and chronic constipation and a variety of non-GI disorders. The purpose of this review is to discuss the intestinal microbiota and FMT treatment of GI and non-GI diseases. RECENT FINDINGS: It is known that an imbalanced intestinal microbiota predisposes to CDI, IBD and IBS. The complex role of intestinal microbiota to maintain health, however, is a newer concept that is being increasingly studied. The microbiome plays an important role in cellular immunity and energy metabolism and has been implicated in the pathogenesis of non-GI autoimmune diseases, chronic fatigue syndrome, obesity and even some neuropsychiatric disorders. SUMMARY: FMT is a highly effective cure for RCDI, but increased knowledge of the intestinal microbiota in health maintenance, as well as controlled trials of FMT in a wide range of disorders are needed before FMT can be accepted and applied clinically.
Arroll M, Arroll B.	The Optimum Health Clinic, Research Department, London, England. drarroll@theoptimumhealthclinic.com	Chronic fatigue syndrome-a patient centred approach to management.	Aust Fam Physician. 2013 Apr; 42(4):191-3.	BACKGROUND: Chronic fatigue syndrome (myalgic encephalomyelitis) is a diagnosis that can attract feelings of stigma in the patient due to the lack of a definite diagnostic biomarker. To ensure that the patient firstly understands the diagnosis, and subsequently is comfortable with the treatment suggested, a patient centred approach is advised within the consultation. OBJECTIVE: This article presents a hypothetical case and uses this to give guidance on methods for negotiating the diagnosis and treatment of chronic fatigue syndrome. DISCUSSION: It is important to reassure the patient that negative investigation results and the suggestion of

				treatment options that are also used for depressive illness (eg. antidepressants and cognitive behavioural therapy), does not mean that their illness experience is fabricated or that they are being treated for depression. Once red flag features are ruled out and any exclusory illnesses identified, a multidisciplinary pragmatic rehabilitation program can be implemented. This includes strategies for increasing social support, liaising with employers and graded return to activities in a 'What matters to you?' approach.
Arroll MA, Howard A.	The Optimum Health Clinic, London, UK. drarroll@theoptimumhealthclinic.com	'The letting go, the building up, [and] the gradual process of rebuilding': identity change and post-traumatic growth in myalgic encephalomyelitis/chronic fatigue syndrome.	Psychol Health. 2013; 28(3):302-18. doi: 10.1080/08870446.2012.721882. Epub 2012 Sep 11.	The aim of this study was to explore the phenomenon of identity change and subsequent post-traumatic growth (PTG) in individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Ten participants (average illness duration 7.4 years) were interviewed (average length, 79minutes) via a semi-structured interview schedule and verbatim transcriptions were analysed with interpretative phenomenological analysis. The four superordinate themes revealed were 'comparisons of past to present self: "you have to be someone else, and you have to live with that'", 'the effect of social isolation on identity and subsequent insights into others' behaviours', 'contemplation of future and identity: ''where do I go from here?"', and 'PTG: "the letting go, the building up, [and] the gradual process of rebuilding"'. These themes outlined the experiences of those with ME/CFS as they underwent changes in identity due to the limitations the condition imposed on activities and roles, understanding others behaviours after a period of isolation, the comparison of the past self with the present self and finally, the positive growth that was noted by two of the interviewees with regards to a new 'true' self. Despite the distressing and unpredictable nature of ME/CFS, it appears that individuals with this disorder can experience personal growth.
Arroll MA.	The Optimum Health Clinic, Head Office and Training Centre, Bickerton House, 25-27 Bickerton Road, London N19 5JT, United Kingdom. drarroll@theoptimumhealthclinic.com	Allostatic overload in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).	Med Hypotheses. 2013 Sep; 81(3):506-8. doi: 10.1016/j.mehy.2013.06.023. Epub 2013 Jul 11.	Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a debilitating condition characterised by diverse symptoms such as fatigue, pain, sleep disturbance and autonomic dysfunction. There remains to be a singular biomarker identified for this illness, hence numerous theories about its development and perpetuation have been posited in the literature. This brief report presents the model of 'allostasis' as a framework for understanding ME/CFS, specifically the notion that the physiological mechanisms employed in the body to deal with stress termed here as 'allostatic states' (e.g. elevation of inflammatory cytokines), may in and of themselves contribute to the perpetuation of the disorder. This theoretical assertion has important consequences for the understanding of ME/CFS and treatment; rather than searching for a singular pathogen responsible for this condition, ME/CFS can be conceptualised as a maladaptive stress disorder and interventions aimed at addressing the allostatic states may be incorporated into current symptom management programmes.
Asberg M, Nygren A, Nager A.	Stressrehab-FoU, Karolinska institutet,	Distinguishing between depression	Lakartidningen. 2013 Feb 27-Mar 12; 110(9-10):484-6.	[No abstract given]

	Danderyds sjukhus, Stockholm. marie.asberg@ki.se	and chronic fatigue syndrome. [Article in Swedish]		
Bäckström T, Bixo M, Nyberg S, Savic I.	Umeå Neurosteroid Research Centre, Department of Clinical Science, Umeå University, Umeå, Sweden. torbjorn.backstrom@ogbyn.umu.se	Increased neurosteroid sensitivity--an explanation to symptoms associated with chronic work related stress in women?	Psychoneuroendocrinology. 2013 Jul;38(7):1078-89. doi: 10.1016/j.psyneuen.2012.10.014. Epub 2012 Nov 22.	Work related psychosocial stress can be accompanied by so called burnout syndrome with symptoms of mental exhaustion, physical fatigue, and cognitive dysfunction. Underlying mechanisms for acquiring burnout syndrome are not clear. Animal studies show that chronic stress is associated with altered release of GABA-A receptor modulating steroids (GAMS), altered composition of the GABA-A receptor and altered sensitivity to GAMS. In the present study we investigated if such changes occur in women with burnout syndrome. We further asked whether flumazenil (a benzodiazepine antagonist, but with positive modulating effects on GABA-A receptors with altered subunit composition) can block the effect of the GAMS allopregnanolone. Ten women with occupational psychosocial stress and burnout syndrome were compared with twelve healthy controls in an experimental setting. Saccadic eye velocity (SEV) was measured after an injection of allopregnanolone, followed by an injection of flumazenil and a second injection of allopregnanolone. The sensitivity to allopregnanolone was significantly higher in the patients compared to controls after the first injection (p=0.04) and the difference increased when the response per allopregnanolone concentration unit was compared (p=0.006). Following the flumazenil injection the burnout patients (p=0.016), but not controls, showed a decrease in SEV and flumazenil acted like a positive modulator that is agonistic. There was no significant difference between the groups after second allopregnanolone injection. In conclusion, patients with work related psychosocial stress and burnout syndrome show a different response to GABA-A receptor modulators than controls suggesting a changed GABA-A receptor function in these patients. More precisely we hypothesize that the α4 and delta subunits are up-regulated elevating the responsiveness to allopregnanolone and change the effect of flumazenil, which provides a potential explanation to the burnout syndrome. Flumazenil does not block the effect of allopregnanolone.
Badham SP, Hutchinson CV.	School of Psychology, College of Medicine, Biological Sciences and Psychology, University of Leicester, Leicester, UK, s.p.badham@warwick.ac.uk.	Badham SP, Hutchinson CV.	Graefes Arch Clin Exp Ophthalmol. 2013 Dec; 251(12):2769-76. doi: 10.1007/s00417-013-2431-3. Epub 2013 Aug 6.	BACKGROUND: People who suffer from myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) often report that their eye movements are sluggish and that they have difficulties tracking moving objects. However, descriptions of these visual problems are based solely on patients' self-reports of their subjective visual experiences, and there is a distinct lack of empirical evidence to objectively verify their claims. This paper presents the first experimental research to objectively examine eye movements in those suffering from ME/CFS. METHODS: Patients were assessed for ME/CFS symptoms and were compared to age, gender, and education matched controls for their ability to generate saccades and smooth pursuit eye movements. RESULTS: Patients and controls exhibited similar error rates and saccade latencies (response times) on prosaccade and antisaccade tasks. Patients showed

				relatively intact ability to accurately fixate the target (prosaccades), but were impaired when required to focus accurately in a specific position opposite the target (antisaccades). Patients were most markedly impaired when required to direct their gaze as closely as possible to a smoothly moving target (smooth pursuit). CONCLUSIONS: It is hypothesised that the effects of ME/CFS can be overcome briefly for completion of saccades, but that continuous pursuit activity (accurately tracking a moving object), even for a short time period, highlights dysfunctional eye movement behaviour in ME/CFS patients. Future smooth pursuit research may elucidate and improve diagnosis of ME/CFS.
Baraniuk JN, Adewuyi O, Merck SJ, Ali M, Ravindran MK, Timbol CR, Rayhan R, Zheng Y, Le U, Esteitie R, Petrie KN.	Division of Rheumatology, Immunology and Allergy, Georgetown University Washington, DC, USA.	A Chronic Fatigue Syndrome (CFS) severity score based on case designation criteria.	Am J Transl Res. 2013; 5(1):53-68. Epub 2013 Jan 21.	BACKGROUND: Chronic Fatigue Syndrome case designation criteria are scored as physicians' subjective, nominal interpretations of patient fatigue, pain (headaches, myalgia, arthralgia, sore throat and lymph nodes), cognitive dysfunction, sleep and exertional exhaustion. METHODS: Subjects self-reported symptoms using an anchored ordinal scale of 0 (no symptom), 1 (trivial complaints), 2 (mild), 3 (moderate), and 4 (severe). Fatigue of 3 or 4 distinguished "Fatigued" from "Not Fatigued" subjects. The sum of the 8(Sum8) ancillary criteria was tested as a proxy for fatigue. All subjects had history and physical examinations to exclude medical fatigue, and ensure categorization as healthy or CFS subjects. RESULTS: Fatigued subjects were divided into CFS with ≥4 symptoms or Chronic Idiopathic Fatigue (CIF) with ≤3 symptoms. ROC of Sum8 for CFS and Not Fatigued subjects generated a threshold of 14 (specificity=0.934; sensitivity=0.928). CFS (n=256) and CIF (n=55) criteria were refined to include Sum8≥14 and ≤13, respectively. Not Fatigued subjects had highly skewed Sum8 responses. Healthy Controls (HC; n=269) were defined by fatigue≤2 and Sum8≤13. Those with Sum8≥14 were defined as CFS-Like With Insufficient Fatigue Syndrome (CFSLWIFS; n=20). Sum8 and Fatigue were highly correlated (R(2)=0.977; Cronbach's alpha=0.924) indicating an intimate relationship between symptom constructs. Cluster analysis suggested 4 clades each in CFS and HC. Translational utility was inferred from the clustering of proteomics from cerebrospinal fluid. CONCLUSIONS: Plotting Fatigue severity versus Sum8 produced an internally consistent classifying system. This is a necessary step for translating symptom profiles into fatigue phenotypes and their pathophysiological mechanisms.
Baraniuk JN, El-Amin S, Corey R, Rayhan R, Timbol C.	Division of Rheumatology, Immunology and Allergy, Georgetown University, Washington, DC 20007-2197, USA. baraniuj@georgetown.edu	Carnosine treatment for gulf war illness: a randomized controlled trial.	Glob J Health Sci. 2013 Feb 4; 5(3):69-81. doi: 10.5539/gjhs.v5n3p69.	About 25% of 1990-1991 Persian Gulf War veterans experience disabling fatigue, widespread pain, and cognitive dysfunction termed Gulf War illness (GWI) or Chronic Multisymptom Illness (CMI). A leading theory proposes that wartime exposures initiated prolonged production of reactive oxygen species (ROS) and central nervous system injury. The endogenous antioxidant L-carnosine (B-alanyl-L-histidine) is a potential treatment since it is a free radical scavenger in nervous tissue. To determine if nutritional supplementation with L-carnosine would significantly improve pain, cognition and fatigue in GWI, a randomized double blind placebo controlled 12 week dose escalation study involving 25 GWI subjects was employed. L-carnosine was given

				as 500, 1000, and 1500 mg increasing at 4 week intervals. Outcomes included subjective fatigue, pain and psychosocial questionnaires, and instantaneous fatigue and activity levels recorded by ActiWatch Score devices. Cognitive function was evaluated by WAIS-R digit symbol substitution test. Carnosine had 2 potentially beneficial effects: WAIS-R scores increased significantly, and there was a decrease in diarrhea associated with irritable bowel syndrome. No other significant incremental changes were found. Therefore, 12 weeks of carnosine (1500 mg) may have beneficial cognitive effects in GWI. Fatigue, pain, hyperalgesia, activity and other outcomes were resistant to treatment.
Bateman L, Spotila J.	[No address quoted]	Article on CFS does not reflect current best treatment practices.	Am Fam Physician. 2013 Apr 1; 87(7): Online.	Comment on Am Fam Physician. 2012 Oct 15; 86(8):741-6.
Bayliss K, Riste L, Fisher L, Wearden A, Peters S, Lovell K, Chew-Graham C.	1Research Associate, Institute of Population Health, University of Manchester, Manchester, UK.	Diagnosis and management of chronic fatigue syndrome/myalgic encephalitis in black and minority ethnic people: a qualitative study.	Prim Health Care Res Dev. 2013 May 23:1-13. [Epub ahead of print]	Aim This study aims to explore the possible reasons for the lower levels of diagnosis of chronic fatigue syndrome/myalgic encephalitis (CFS/ME) in the black and minority ethnic (BME) population, and the implications for management. BACKGROUND: Population studies suggest CFS/ME is more common in people from BME communities compared with the White British population. However, the diagnosis is made less frequently in BME groups. METHODS: Semi-structured qualitative interviews were conducted with 35 key stakeholders in NW England. Interviews were analysed using open explorative thematic coding. Findings There are barriers at every stage to the diagnosis and management of CFS/ME in people from BME groups. This begins with a lack of awareness of CFS/ME among BME respondents. Religious beliefs and the expectation of roles in the family and community mean that some people in BME groups may choose to manage their symptoms outside primary care using alternative therapies, prayer or spiritual healing. When accessing primary care, all participants recognised the possible influence of language barriers in reducing the likelihood of a diagnosis of CFS/ME. Stereotypical beliefs, including labels such as 'lazy' or 'work shy' were also believed to act as a barrier to diagnosis. Patients highlighted the importance of an on-going relationship with the general practitioner (GP), but perceived a high turnover of GPs in inner city practices, which undermined the holistic approach necessary to achieve a diagnosis. CONCLUSION: Training is required for health professionals to challenge inaccurate assumptions about CFS/ME in BME groups. The focus on the individual in UK primary care may not be appropriate for this group due to the role played by the family and community in how symptoms can be presented and managed. Culturally sensitive, educational resources for patients are also needed to explain symptoms and legitimise consultation.
Beasant L, Mills N, Crawley E.	1 School of Social & Community Medicine, Centre for Child &	Adolescents and mothers value referral to a	Prim Health Care Res Dev. 2013 Apr 25:1-9. [Epub ahead of print]	BACKGROUND: Paediatric chronic fatigue syndrome or myalgic encephalopathy (CFS/ME) is relatively common and disabling. Current guidance recommends referral to specialist services, although some general practitioners believe the label of CFS/ME

	Adolescent Health, University of Bristol, Oakfield Grove, UK.	specialist service for chronic fatigue syndrome or myalgic encephalopathy (CFS/ME).		is harmful and many are not confident about diagnosing CFS/ME. Aim Explore whether or not adolescents and their mothers value referral to a specialist service for young people with CFS/ME. METHODS: A qualitative study nested within a feasibility study of interventions for CFS/ME [Specialist Medical Intervention and Lightning Evaluation (SMILE)]. In-depth interviews were undertaken with 13 mothers and 12 adolescents participating in the SMILE study. Transcripts were systematically assigned codes using the qualitative data organisation package NVivo and analysed thematically using techniques of constant comparison. RESULTS: Gaining access to the specialist service was difficult and took a long time. Mothers felt that they needed to be proactive and persistent, partly because of a lack of knowledge in primary and secondary care. Having gained access, mothers felt the CFS/ME service was useful because it recognised and acknowledged their child's condition and opened channels of dialogue between health-care professionals and education providers. Adolescents reported that specialist medical care resulted in better symptom management, although some adolescents did not like the fact that the treatment approach limited activity. CONCLUSIONS: Adolescents and their mothers value receiving a diagnosis from a specialist service and making progress in managing CFS/ME. General practitioners should support adolescents with CFS/ME in accessing CFS/ME specialist services, consistent with current guidance.
Beatty L, Lambert S.	[No address quoted]	A systematic review of internet-based self-help therapeutic interventions to improve distress and disease-control among adults with chronic health conditions.	Clin Psychol Rev. 2013 Jun; 33(4):609-22.	The evidence base of internet-based self-help interventions has been rapidly growing for mental health conditions over the past decade. However, to date a systematic review of the application of this technology to chronic health conditions has not been reported. The objective of the present review was to therefore critically appraise the research on the efficacy of internet self-help interventions for distress and disease outcomes in adults with physical health complaints. Electronic searches were conducted in Embase, CINAHL, MEDLINE and PsychINFO, and reference lists were examined. Twenty four studies met inclusion criteria, covering 8 health conditions. Across health conditions, consistent evidence was obtained that online therapeutic interventions were efficacious in improving disease-symptoms and control, with the exception of diabetes. Mixed evidence was obtained for distress outcomes: 3 health conditions demonstrated consistent benefit (irritable bowel syndrome, tinnitus, and one heterogeneous chronic illness population); one condition obtained moderate support (chronic pain); while results were not promising for diabetes. The limited research conducted among epilepsy, cancer, and chronic fatigue precluded conclusions from being drawn. Few studies met all methodological quality criteria. This review demonstrates that internet-based self-help interventions hold guarded promise in the amelioration of distress and disease-control, and further research implications are discussed.
Belcaro G, Cornelli U, Luzzi R,	Irvine3 Circulation/Vascular	Improved management of	Panminerva Med. 2013 Nov 14. [Epub ahead of print]	Aim: The aim of this supplement study was to evaluate French oak wood extract (Robuvit®, Horphag Research Ltd) used as a supplement in association with a defined

Cesarone MR, Dugall M, Feragalli B, Hu S, Pellegrini L, Ippolito E.	Labs and San Val. Epidemiology Department of Biomedical Sciences, Chieti−Pescara University, Pescara, Italy - cardres@abol.it.	primary chronic fatigue syndrome with the supplement French oak wood extract (Robuvit®): a pilot, registry evaluation.		management plan for chronic fatigue syndrome (CFS) in healthy subjects with CFS, a condition that has, so far, no specific treatment or management standards. Methods: Robuvit® is a new proprietary and exclusive extract of oak wood with important antoxidant actions. The dosage of the supplementation was 200 mg/day for at least 6 months. The CFS questionnaire and the Brief Mood Introspection Scale (BMIS) questionnaire were used to evaluate mood variations associated with CFS patients. The CFS form includes an analogue scale to record the variations of single symptoms with a score range of 0-10. At inclusion into the registry study, at least 5 symptoms were present. All subjects (age range 35-44; BMI range 24-26) with CFS were tested for oxidative stress: 61 out of 91 subjects had an increased value of oxidative stress. The BMIS scale evaluating mood changes in time was also used. The evaluation was repeated at 3 and 6 months. Results: Out of 91 eligible subjects with CFS, 48 subjects (31 with increased oxidative stress) were accepted as part of the supplement registry study using Robuvit; 43 (30 with increased oxidative stress) were accepted as controls using only the management plan. In the Robuvit® group there were 3 drop outs; also 3 controls were lost. Oxidative stress was increased in 64.58% of subjects that used Robuvit and in 69.7% of controls. The average values of oxidative stress were expressed for the whole group. The average follow up was 199.3; 9.2 days in the Robuvit group and 202.2; 5.5 in the control group with a minimum of 6 months. Considering variations in oxidative stress, there was no significant average change in controls, but a significant decrease from the initial values was observed in Robuvit subjects after 3 and 6 months. The CFS questionnaire variations in score indicated that there was a significant improvement for most symptoms after 3 and 6 months in the Robuvit group. Positive variations were also present in controls, indicating the positive effect of an increased attention to CFS. The improvement in signs/symptoms was significantly more valuable in subjects using the oak wood extract considering the main 8 symptoms and the accessory symptoms. Considering the BMIS variations, the totals for positive and negative items were significantly more favourable for Robuvit subjects. Overall mood evaluation in the oak wood extract group improved from an inclusion average of -6.93;2.1 to +4.32;2.6 at 6 months; in contrast it changed from -6.5;2.5 to -3.4;1.5 in controls. No side effects were observed during the supplementation with Robuvit. The compliance was optimal with 93% of the capsules correctly used. Conclusion: This promising pilot supplement registry study indicates a new opportunity of management for these difficult and often neglected patients. Correlation between oxidative stress and CFS has to be better explored.
Berger JR, Pocoski J, Preblick R, Boklage S.	Department of Neurology, University of Kentucky College of Medicine, Lexington, KY, USA.	Fatigue heralding multiple sclerosis.	Mult Scler. 2013 Oct; 19(11):1526-32. doi: 10.1177/1352458513477924. Epub 2013 Feb 25.	BACKGROUND: Fatigue is a common symptom in multiple sclerosis (MS) and is an important determinant of overall well-being and disability. OBJECTIVE: To assess the frequency with which fatigue precedes the diagnosis of MS using a retrospective database analysis. METHODS: Between January 1, 2003 and September 30, 2008, patients diagnosed with fatigue with and without fatigue-related medications within a

				3-year period prior to newly diagnosed MS were identified from the MarketScan Databases. All statistical analysis was performed using SAS. RESULTS: Of the 16,976 patients with MS in the overall population, 5305 (31.3%) were newly diagnosed with MS and had three years of continuous healthcare coverage prior to MS diagnosis. Of these patients, 1534 (28.9%) were labeled with chronic fatigue syndrome (ICD9-780.71) or malaise or fatigue (ICD9-780.79) prior to the diagnosis of MS. One-third of these patients were labeled with fatigue one to two years before the diagnosis; 30.8% were diagnosed only with fatigue and had no other MS symptoms prior to their MS diagnosis. Among the patients diagnosed with fatigue, 10.4% were also prescribed medication for fatigue. CONCLUSION: This study demonstrates that fatigue may herald MS, often by years. A careful history for transient neurological symptoms and a physical examination is warranted in any patient presenting with fatigue.
Blankfield A.	[No address quoted]	Kynurenine Pathway Pathologies: do Nicotinamide and Other Pathway Co-Factors have a Therapeutic Role in Reduction of Symptom Severity, Including Chronic Fatigue Syndrome (CFS) and Fibromyalgia (FM).	Int J Tryptophan Res. 2013 Jul 21;6 (Suppl 1):39-45. doi: 10.4137/IJTR.S11193. Print 2013.	The definition of dual tryptophan pathways has increased the understanding of the mind-body, body-mind dichotomy. The serotonergic pathway highlights the primary (endogenous) psychiatric disorders. The up-regulation of the kynurenine pathway by physical illnesses can cause neuropathic and immunological disorders1 associated with secondary neuropsychiatric symptoms. Tryptophan and nicotinamide deficiencies fall within the protein energy malnutrition (PEM) spectrum. They can arise if the kynurenine pathway is stressed by primary or secondary inflammatory conditions and the consequent imbalance of available catabolic/anabolic substrates may adversely influence convalescent phase efficiency. The replacement of depleted or reduced NAD+ levels and other cofactors can perhaps improve the clinical management of these disorders. Chronic fatigue syndrome (CFS) and fibromyalgia (FM) appear to meet the criteria of a tryptophan-kynurenine pathway disorder with potential neuroimmunological sequelae. Aspects of some of the putative precipitating factors have been previously outlined.2,3. An analysis of the areas of metabolic dysfunction will focus on future directions for research and management.
Blazquez A, Ruiz E, Aliste L, García-Quintana A, Alegre J.	A Unity of CFS and Fibromyalgia, Vall Hebron Hospital, Internal Medicine, Barcelona, Spain.	The Impact of Fatigue and Fibromyalgia on Sexual Dysfunction in Women with Chronic Fatigue Syndrome.	J Sex Marital Ther. 2013 Nov 25. [Epub ahead of print]	ABSTRACT Sexual dysfunction in patients with chronic fatigue syndrome (CFS) is attracting growing interest but has been analyzed by few studies to date. For this reason we evaluate sexual dysfunction in women with CFS (GRISS) and explore correlations with fatigue and other symptoms. Sexual dysfunction was greater in CFS patients (n = 615) with a higher number of cognitive, neurological, and neurovegetative symptoms, concomitant fibromyalgia, Sjögren's syndrome, or myofascial pain syndrome, and more intense fatigue (P <0.05).
Bloom S, Ablin JN, Lebel D, Rath E, Faran Y, Daphna-Tekoah S, Buskila D.	Orthopedic Surgery Department, Soroka Medical Center, Beersheba, Israel.	Awareness of diagnostic and clinical features of fibromyalgia among orthopedic surgeons.	Rheumatol Int. 2013 Apr; 33(4):927-31. doi: 10.1007/s00296-012-2488-z. Epub 2012 Jul 22.	Fibromyalgia Syndrome (FMS) is a chronic pain syndrome characterized by widespread musculoskeletal pain and fatigue. The current study was designed to evaluate the awareness and skills of orthopedic surgeons (OS) regarding FMS diagnosis and treatment. For the examination of awareness and familiarity of OS in Israel to Fibromyalgia, a questionnaire-based survey was conducted. Two hundred and nineteen OS, residents and specialists, were asked anonymously about

				awareness, knowledge, and treatment of FM. Multivariable statistical analysis was performed. 91 % (199) of responders reported that they recognized the disease. Notwithstanding, the mean knowledge score was 7.6 out of 17. In addition, OS who were trained in the south of Israel were found to have a better degree of knowledge about FM (9.7 vs. 7.4; $p < 0.03$). The awareness and knowledge among OS regarding FM needs to be improved. OS who were trained in the south of Israel were found to have better degree of knowledge regarding FM.
Borsini A, Hepgul N, Mondelli V, Chalder T, Pariante CM.	Section of Stress, Psychiatry and Immunology and Perinatal Psychiatry, Department of Psychological Medicine, Institute of Psychiatry, King's College London, UK.	Childhood stressors in the development of fatigue syndromes: a review of the past 20 years of research.	Psychol Med. 2013 Oct 7:1-15. [Epub ahead of print]	BACKGROUND: Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are both highly prevalent conditions associated with extreme disability and with the development of co-morbid psychiatric disorders, such as depression and anxiety. Childhood stressors have been shown to induce persistent changes in the function of biological systems potentially relevant to the pathogenesis of both CFS and FM, such as the inflammatory system and the hypothalamic-pituitary-adrenal (HPA) axis. In this review, we examined whether multiple forms of childhood stressors are contributing factors to the development of these disorders, and of the associated psychiatric symptoms. METHOD: Using PubMed, we identified 31 papers relevant to this narrative review. We included cohort studies and case-control studies, without any exclusion in terms of age and gender. No study characteristics or publication date restrictions were imposed. RESULTS: Most studies across the literature consistently show that there is a strong association between experiences of childhood stressors and the presence of CFS and FM, with rates of CFS/FM being two- to three-fold higher in exposed than in unexposed subjects. We also found evidence for an increased risk for the development of additional symptoms, such as depression, anxiety and pain, in individuals with CFS and FM with a previous history of childhood stressors, compared with individuals with CFS/FM and no such history. CONCLUSIONS: Our review confirms that exposure to childhood stressors is associated with the subsequent development of fatigue syndromes such as CFS and FM, and related symptoms. Further studies are needed to identify the mechanisms underlying these associations.
Bossuyt X, Cooreman S, De Baere H, Verschueren P, Westhovens R, Blockmans D, Mariën G.	Experimental Laboratory Immunology, Catholic University Leuven, Leuven, Belgium. xavier.bossuyt@uz.kuleuven.ac.be	Detection of antinuclear antibodies by automated indirect immunofluorescence analysis.	Clin Chim Acta. 2013 Jan 16; 415:101-6. doi: 10.1016/j.cca.2012.09.021. Epub 2012 Sep 28. Comment in Clin Chim Acta. 2013 Jun 5; 421:168-9.	BACKGROUND: Testing for antinuclear antibodies is useful for the diagnosis of systemic rheumatic diseases. Automated systems for image acquisition and interpretation of indirect immunofluorescence-based tests are increasingly used. The diagnostic performance of such automated approach in untreated patients has not been reported. METHODS: Antinuclear antibodies were measured by automated indirect immunofluorescence using Zenit G. Sight on HEp2 and HEp2000 substrate in 268 consecutive samples submitted to the laboratory for antinuclear antibody testing, and in 231 patients with a systemic rheumatic disease at the time of diagnosis, 143 blood donors, 134 patients with chronic fatigue syndrome, and 133 diseased controls. RESULTS: Image acquisition by G-Sight was of high quality. The accuracy of pattern assignment was limited. There was a significant correlation between automated estimation of fluorescence intensity (probability index of positivity) and end-point

				titer. Probability index interval specific likelihood ratios for systemic rheumatic disease increased with increasing level of positivity probability. With the HEp-2 substrate, the likelihood ratio for systemic lupus erythematosus was 0.06, 0.4, 6.8, 12.1, and 43.9 for a probability measure of positivity of ≤10, 11-≤30, 31-≤50, 51-≤85, and >85, respectively. CONCLUSION: Quantitative data generated by automated image acquisition facilitates standardized interpretation.
Bould H, Collin SM, Lewis G, Rimes K, Crawley E.	School of Social and Community Medicine, University of Bristol, Bristol, UK.	Depression in paediatric chronic fatigue syndrome.	Arch Dis Child. 2013 Jun; 98(6):425-8. doi: 10.1136/archdischild-2012-303396. Epub 2013 Apr 25.	OBJECTIVE: To describe the prevalence of depression in children with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) and investigate the relationship between depression in CFS/ME and clinical symptoms such as fatigue, disability, pain and school attendance. DESIGN: Cross-sectional survey data using the Hospital Anxiety and Depression Scale (HADS) collected at assessment. SETTING: Specialist paediatric CFS/ME service in the South West. PATIENTS: Children aged 12-18 years with CFS/ME. MAIN OUTCOME MEASURE: Depression was defined as scoring >9 on the HADS depression scale. RESULTS: 542 subjects had complete data for the HADS and 29% (156/542) (95% CI 25% to 33%) had depression. In a univariable analysis, female sex, poorer school attendance, and higher levels of fatigue, disability, pain, and anxiety were associated with higher odds of depression. Age of child and duration of illness were not associated with depression. In a multivariable analysis, the factors most strongly associated with depression were disability, with higher scores on the physical function subscale of the 36 item Short Form (SF-36). CONCLUSIONS: Depression is commonly comorbid with CFS/ME, much more common than in the general population, and is associated with markers of disease severity. It is important to screen for, identify and treat depression in this population.
Bourke JH, Johnson AL, Sharpe M, Chalder T, White PD.	Centre for Psychiatry, Wolfson Institute for Preventive Medicine, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, UK.	Pain in chronic fatigue syndrome: response to rehabilitative treatments in the PACE trial.	Psychol Med. 2013 Aug 23:1-8. [Epub ahead of print]	BACKGROUND: Pain is a common symptom of chronic fatigue syndrome (CFS). We investigated the effects of the treatments used in the PACE trial [cognitive behavioural therapy (CBT), graded exercise therapy (GET), adaptive pacing therapy (APT) and specialist medical care (SMC)] on pain in CFS. METHOD: We compared pain outcomes including individual painful symptoms, taken from the CDC criteria for CFS and co-morbid fibromyalgia. We modelled outcomes adjusting for baseline variables with multiple linear regression. RESULTS: Significantly less frequent muscle pain was reported by patients following treatment with CBT compared to SMC (mean difference = 0.38 unit change in frequency, p = 0.02), GET versus SMC (0.42, p = 0.01) and GET versus APT (0.37, p = 0.01). Significantly less joint pain was reported following CBT versus APT (0.35, p = 0.02) and GET versus APT (0.36, p = 0.02). Co-morbid fibromyalgia was less frequent following GET versus SMC (0.03, p = 0.03). The effect sizes of these differences varied between 0.25 and 0.31 for muscle pain and 0.24 and 0.26 for joint pain. Treatment effects on pain were independent of 'change in fatigue'. CONCLUSIONS: CBT and GET were more effective in reducing the frequency of both muscle and joint pain than APT and SMC. When compared to SMC, GET also reduced the frequency of co-morbid fibromyalgia; the size of this effect on

				pain was small.
Bradley AS, Ford B, Bansal AS.	Department of Immunology, St Helier University Hospital NHS Trust, Carshalton, Surrey, UK.	Altered functional B cell subset populations in patients with chronic fatigue syndrome compared to healthy controls.	Clin Exp Immunol. 2013 Apr; 172(1):73-80. doi: 10.1111/cei.12043.	Chronic fatigue syndrome (CFS) is a heterogeneous disorder of unknown aetiology characterized by disabling fatigue, headaches, sleep disturbance and several other symptoms. The onset of CFS may follow a viral infection or period of stress. Patients with CFS do not have hypogammaglobulinaemia, predisposition to recurrent bacterial infections or symptoms of autoimmunity. To date, defects in B cell numbers or function have not been shown in the literature. However, treatment with anti-B cell therapy using Rituximab has recently shown benefit to CFS patients. We therefore postulated that patients with CFS had a subtle humoral immune dysfunction, and performed extended B cell immunophenotyping. We undertook a detailed characterization of the proportions of the different B cell subsets in 33 patients with CFS fulfilling the Canadian and Fukada criteria for CFS and compared these with 24 age- and gender-matched healthy controls (HC). CFS patients had greater numbers of naive B cells as a percentage of lymphocytes: 6·3 versus 3·9% in HC (P=0·034), greater numbers of naive B cells as a percentage of B cells: 65 versus 47% in controls (P=0·003), greater numbers of transitional B cells: 1·8 versus 0·8% in controls (P=0·025) and reduced numbers of plasmablasts: 0·5 versus 0·9% in controls (P=0·013). While the cause of these changes is unclear, we speculate whether they may suggest a subtle tendency to autoimmunity.
Brenu EW, Huth TK, Hardcastle SL, Fuller K, Kaur M, Johnston S, Ramos SB, Staines DR, Marshall-Gradisnik SM.	School of Medical Science, Griffith University, Gold Coast, Australia.	The Role of Adaptive and Innate Immune Cells in Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis.	Int Immunol. 2013 Dec 16. [Epub ahead of print]	Perturbations in immune processes are a hallmark of a number of autoimmune and inflammatory disorders. Chronic Fatigue Syndrome/ Myalgic Encephalomyelitis (CFS/ME) is an inflammatory disorder with possible autoimmune correlates, characterised by reduced Natural Killer (NK) cell activity, elevations in regulatory T cells (Tregs) and dysregulation in cytokine levels. The purpose of this paper is to examine innate and adaptive immune cell phenotypes and functional characteristics that have not been previously examined in CFS/ME patients. 30 patients with CFS/ME and 25 non-fatigued controls were recruited for this study. Whole blood samples were collected from all participants for the assessment of cell phenotypes, functional properties, receptors, adhesion molecules, antigens and intracellular proteins using flow cytometric protocols. The cells investigated included NK cells, dendritic cells (DCs), neutrophils, B cells, T cells, γδT cells and Tregs. Significant changes were observed in B cell subsets, Tregs, CD4(+)CD73(+)CD39(+) T cells, cytotoxic activity, granzyme B, neutrophil antigens, TNF-α and IFN-γ in the CFS/ME patients in comparison to the non-fatigued controls. Alterations in B cells, Tregs, NK cells and neutrophils suggest significant impairments in immune regulation in CFS/ME and these may have similarities to a number of autoimmune disorders.
Brewer JH, Thrasher JD, Straus DC, Madison RA, Hooper D.	Plaza Infectious Disease and St. Luke's Hospital, 4320 Wornall Road, Suite 440, Kansas	Detection of mycotoxins in patients with chronic fatigue syndrome.	Toxins (Basel). 2013 Apr 11; 5(4):605-17. doi: 10.3390/toxins5040605.	Over the past 20 years, exposure to mycotoxin producing mold has been recognized as a significant health risk. Scientific literature has demonstrated mycotoxins as possible causes of human disease in water-damaged buildings (WDB). This study was conducted to determine if selected mycotoxins could be identified in human urine

	City, MO 64111, USA. jbrewer@plazamedicine.com			from patients suffering from chronic fatigue syndrome (CFS). Patients (n = 112) with a prior diagnosis of CFS were evaluated for mold exposure and the presence of mycotoxins in their urine. Urine was tested for aflatoxins (AT), ochratoxin A (OTA) and macrocyclic trichothecenes (MT) using Enzyme Linked Immunosorbent Assays (ELISA). Urine specimens from 104 of 112 patients (93%) were positive for at least one mycotoxin (one in the equivocal range). Almost 30% of the cases had more than one mycotoxin present. OTA was the most prevalent mycotoxin detected (83%) with MT as the next most common (44%). Exposure histories indicated current and/or past exposure to WDB in over 90% of cases. Environmental testing was performed in the WDB from a subset of these patients. This testing revealed the presence of potentially mycotoxin producing mold species and mycotoxins in the environment of the WDB. Prior testing in a healthy control population with no history of exposure to a WDB or moldy environment (n = 55) by the same laboratory, utilizing the same methods, revealed no positive cases at the limits of detection.
Brimmer DJ, Campbell C, Bonner K, Lin JM.	Chronic Viral Diseases Branch, Division of High-Consequence Pathogens and Pathology,, Centers for Disease Control and Prevention, 1600 Clifton Rd., MS-G41, Atlanta, GA 30333 USA ; McKing Consulting Corporation, 2900 Chamblee Tucker Road Building 10, Suite 100, Atlanta, GA 30341 USA.	News from the CDC: chronic fatigue syndrome (CFS) and standardized patient videos - a novel approach to educating medical students about CFS.	Transl Behav Med. 2013 Dec; 3(4):338-9. doi: 10.1007/s13142-013-0229-9.	[No abstract given]
Brimmer DJ, Maloney E, Devlin R, Jones JF, Boneva R, Nagler C, LeRoy L, Royal S, Tian H, Lin JM, Kasten J, Unger ER.	Division of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, 1600 Clifton Road, MS-G41, Atlanta, GA 30033, USA. dyv4@cdc.gov	A pilot registry of unexplained fatiguing illnesses and chronic fatigue syndrome.	BMC Res Notes. 2013 Aug 2; 6:309. doi: 10.1186/1756-0500-6-309.	BACKGROUND: Chronic fatigue syndrome (CFS) has no diagnostic clinical signs or biomarkers, so diagnosis requires ruling out conditions with similar signs and symptoms. We conducted a pilot registry of unexplained fatiguing illnesses and CFS to determine the feasibility of establishing and operating a registry and implementing an education outreach initiative. The pilot registry was conducted in Bibb County, Georgia. Patient referrals were obtained from healthcare providers who were identified by using various education outreach initiatives. These referrals were later supplemented with self-referrals by members of a local CFS support group. All patients meeting referral criteria were invited to participate in a screening interview to determine eligibility. If patients met registry criteria, they were invited to a one-day clinic for physical and laboratory evaluations. We classified patients based on the 1994 case definition. RESULTS: We registered 827 healthcare providers. Forty-two

				providers referred 88 patients, and 58 patients (66%) completed clinical evaluation. Of the 188 CFS support group members, 53 were self-referred and 46 (87%) completed the clinical evaluation. Of the 104 participants completing evaluation, 36% (n=37) met the criteria for CFS, 17% (n=18) had insufficient fatigue or symptoms (ISF), and 47% (n=49) were found to have exclusionary medical or psychiatric illnesses. Classification varied significantly by type of referral but not by previous history of CFS diagnosis. Healthcare providers referred more patients who were classified as CFS as compared to support group referrals in which more exclusionary conditions were identified. Family practice and internal medicine specialties made the most referrals and had the highest number of CFS cases. We conducted three CME events, held three "Meet and Greet" sessions, visited four large clinical health practices and health departments, mailed five registry newsletters, and conducted in-person office visits as part of education outreach, which contributed to patient referrals. CONCLUSIONS: Referrals from healthcare providers and self-referrals from the patient support group were important to registry enrollment. The number of potentially treatable conditions that were identified highlights the need for continued medical management in this population, as well as the limitations of registries formed without clinical examination. Education initiatives were successful in part because of partnerships with local organizations.
Broadbent S, Coutts R.	School of Health and Human Sciences, Southern Cross University, PO Box 157, Lismore, NSW 2480, Australia. suzanne.broadbent@scu.edu.au	The protocol for a randomised controlled trial comparing intermittent and graded exercise to usual care for chronic fatigue syndrome patients.	BMC Sports Sci Med Rehabil. 2013 Aug 30; 5(1):16. doi: 10.1186/2052-1847-5-16.	BACKGROUND: Chronic Fatigue Syndrome is a debilitating disorder with an unknown aetiology but suspected multifactorial origins. Common "triggers" include severe viral infections and emotional stress. Recent studies have also found evidence of immune dysfunction and elevated inflammatory cytokines in CFS patients, but there has been considerable variation in the outcome measures and magnitude of these studies. Currently, there is no cure for CFS but treatments include rest, specialist medical care, cognitive behavioural therapy, and graded (self-paced) exercise. To date, several studies have examined the efficacy of graded exercise with or without Cognitive Behavioural Therapy, with some success for patients. However, improvements in functional capacity have not necessarily correlated with improvements in immune function, fatigue or other symptoms. This 12-week pilot trial compares graded and intermittent exercise to normal care, measuring physiological outcomes, fatigue levels, immune function and wellness. METHODS/DESIGN: 90 patients aged between 16 to 60 years, who meet the diagnostic criteria for CFS and have been diagnosed by their medical practitioner, will be randomly recruited into groups consisting of Intermitent exercise, Graded exercise and usual care (Control). The outcomes will be measured pre-study (Week 0) and post-study (Week 13). Primary outcomes are VO2peak, anaerobic threshold, peak power, levels of fatigue, immune cell (CD3+CD4+, CD3+CD8+, CD19+, CD 16+CD56+) concentrations and activation. Secondary outcomes include onset of secondary CFS symptoms (e.g. fever, swollen lymph nodes), wellness, mood, and sleep patterns. Primary analysis will be based on intention to treat using

				logistic regression models to compare treatments. Quantitative data will be analysed using repeated measures ANOVA with a linear model, and Cohen's effect size. Qualitative data such as participants' responses (e.g. changes in mood and other reactions) following the exercise modalities will be read and sections demarcated. A code will be applied to each segment. A prevalence of codes will be considered thematically. DISCUSSION: The results of the trial will provide information about the efficacy of intermittent and graded exercise compared to usual care (rest and lifestyle recommendations), contributing to the evidence for best-practice CFS management. TRIAL REGISTRATION: Australia and New Zealand Clinical Trials Registry ACTRN12612001241820.
Broderick G, Ben-Hamo R, Vashishtha S, Efroni S, Nathanson L, Barnes Z, Fletcher MA, Klimas N.	Department of Medicine, University of Alberta, Edmonton, Canada. gordon.broderick@ualberta.ca	Altered immune pathway activity under exercise challenge in Gulf War Illness: an exploratory analysis.	Brain Behav Immun. 2013 Feb; 28: 159-69. doi: 10.1016/j.bbi.2012.11.007. Epub 2012 Nov 29.	Though potentially linked to the basic physiology of stress response we still have no clear understanding of Gulf War Illness (GWI), a debilitating illness presenting with a complex constellation of immune, endocrine and neurological symptoms. Here we compared male GWI (n=20) with healthy veterans (n=22) and subjects with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) (n=7). Blood was drawn during a Graded eXercise Test (GXT) prior to exercise, at peak effort (VO2 max) and 4-h post exercise. Affymetrix HG U133 plus 2.0 microarray gene expression profiling in peripheral blood mononuclear cells (PBMCs) was used to estimate activation of over 500 documented pathways. This was cast against ELISA-based measurement of 16 cytokines in plasma and flow cytometric assessment of lymphocyte populations and cytotoxicity. A 2-way ANOVA corrected for multiple comparisons (q statistic <0.05) indicated significant increases in neuroendocrine-immune signaling and inflammatory activity in GWI, with decreased apoptotic signaling. Conversely, cell cycle progression and immune signaling were broadly subdued in CFS. Partial correlation networks linking pathways with symptom severity via changes in immune cell abundance, function and signaling were constructed. Central to these were changes in IL-10 and CD2+ cell abundance and their link to two pathway clusters. The first consisted of pathways supporting neuronal development and migration whereas the second was related to androgen-mediated activation of NF-κB. These exploratory results suggest an over-expression of known exercise response mechanisms as well as illness-specific changes that may involve an overlapping stress-potentiated neuro-inflammatory response.
Brooks J, King N, Wearden A.	Centre for Applied Psychological Research, University of Huddersfield, UK.	Couples' experiences of interacting with outside others in chronic fatigue syndrome: a qualitative study.	Chronic Illn. 2013 Apr 12. [Epub ahead of print]	OBJECTIVES: Social isolation and stigma are frequently reported by patients with chronic fatigue syndrome/myalgic encephalomyelitis and relationships in the home environment with those close to the patients (their 'significant others') may thus be particularly important. Rather little attention has yet been paid to the beliefs and experiences of 'significant others' themselves in this context. This study sought to explore in-depth the beliefs and experiences of both patients and 'significant others' in relation to chronic fatigue syndrome/myalgic encephalomyelitis. METHODS: In-depth interviews using a semi-structured interview schedule designed around the

				core constructs of the Common-Sense Model of self-regulation were conducted with two patients with chronic fatigue syndrome/myalgic encephalomyelitis and their spouses. Interpretative Phenomenological Analysis was used to analyse interview data. RESULTS: Experiences of social interactions in relation to chronic fatigue syndrome/myalgic encephalomyelitis with others outside of the relationship dyad emerged as a key issue for all participants when reflecting on their experiences of living with the condition. These concerns are presented under two themes: interactions with healthcare professionals and interactions with the social world. CONCLUSIONS: It is evident that significant others play an important role in the lived experience of chronic fatigue syndrome/myalgic encephalomyelitis. For both patients and significant others, the wider social world and interactions with outside others may be important influences on dyadic coping in chronic fatigue syndrome/myalgic encephalomyelitis. Both future research and treatment interventions could usefully include a 'significant other' perspective.
Brooks JM, Daglish J, Wearden AJ.	University of Huddersfield, UK.	Attributions, distress and behavioural responses in the significant others of people with chronic fatigue syndrome.	J Health Psychol. 2013 Oct; 18(10):1288-95. doi: 10.1177/1359105312464670. Epub 2012 Nov 23.	To test an attribution-emotion model of reactions to chronic fatigue syndrome/myalgic encephalomyelitis, 30 significant others of 30 adult patients with chronic fatigue syndrome/myalgic encephalomyelitis were administered a semi-structured interview about their beliefs regarding the patient's illness and completed questionnaire measures of distress and behavioural responses to the patient. Spontaneous causal explanations (attributions) for illness events, symptom exacerbation and negative patient mood were extracted and coded. Significant others' distress and negative behavioural responses towards the chronic fatigue syndrome/myalgic encephalomyelitis patient were associated with attributing illness events to causes personal and internal to the patient. Our findings may inform the future family-based interventions for chronic fatigue syndrome/myalgic encephalomyelitis.
Brooks K, Carter J.	Department of Kinesiology, Texas A&M University, USA.	Overtraining, Exercise, and Adrenal Insufficiency.	J Nov Physiother. 2013 Feb 16;3 (125). pii: 11717.	Running, or any aerobic training in moderation, has a positive effect on health. There is a point of diminishing returns, where chronic stress from overtraining, which is common in runners, may be linked to problems in the adrenal gland. Overtraining Syndrome (OS) has been linked with adrenal insufficiency. There is a direct link between stress and the adrenal glands, and the physical stress of overtraining may cause the hormones produced in these glands to become depleted. Overtraining Syndrome (OS) has been described as chronic fatigue, burnout and staleness, where an imbalance between training/competition, versus recovery occurs. Training alone is seldom the primary cause. In most cases, the total amount of stress on the athlete exceeds their capacity to cope. A triggering stressful event, along with the chronic overtraining, pushes the athlete to start developing symptoms of overtraining syndrome, which is far worse than classic overtraining. Overtraining can be a part of healthy training, if only done for a short period of time. Chronic overtraining is what leads to serious health problems, including adrenal insufficiency. Severe overtraining

				over an extended period can result in adrenal depletion. An Addison-Type overtraining syndrome, where the adrenal glands are no longer able to maintain proper hormone levels and athletic performance is severely compromised has been described by researchers. The purpose of this review is to describe the relationship between overtraining, chronic fatigue, and adrenal insufficiency and to address the overlap in these conditions, as well as examine critical research on the relationship between the dysfunction of the adrenal axis in over trained and stressed athletes.
Brown AA, Evans MA, Jason LA.	Center for Community Research, DePaul University, Chicago, IL, USA.	Examining the energy envelope and associated symptom patterns in chronic fatigue syndrome: does coping matter?	Chronic Illn. 2013 Dec; 9(4):302-11. doi: 10.1177/1742395313478220. Epub 2013 Apr 12.	OBJECTIVE/Hypothesis The objective of this study was to examine sub-types of individuals with chronic fatigue syndrome based on variables that are associated with the energy envelope theory and to examine the role of coping strategies in explaining the differences found between the subtypes. METHODS Cluster analysis was used. Grouping variables included physical functioning, post-exertional malaise severity, and the extent to which an individual was outside of the energy envelope. These clusters were evaluated using discriminant function analysis to determine whether they could be differentiated based on coping styles. RESULTS Cluster analysis identified three groups. Clusters 1 and 2 were consistent with the energy envelope theory. However, Cluster 3 was characterized by patients with the most impairment, but they were to a lesser extent exceeding their energy envelope. Coping strategies explained a small percentage (10%) of the variance in differentiating the clusters. DISCUSSION Energy maintenance may be associated with improved functioning and less severe symptoms for some. However, patients in Cluster 3 were closer to remaining within their energy envelope and also used higher levels of adaptive coping but were more impaired than Cluster 2. This suggests that adaptive coping strategies were not associated with improved health, as members of Cluster 3 were severely limited in functioning.
Bullones Rodríguez MÁ, Afari N, Buchwald DS; National Institute of Diabetes and Digestive and Kidney Diseases Working Group on Urological Chronic Pelvic Pain. Collaborators Afari N, Buchwald DS, Clauw D, Dimitrakov J, Kusek J, Mullins C,	Department of Psychology, University Rey Juan Carlos, Madrid, Spain.	Evidence for overlap between urological and nonurological unexplained clinical conditions.	J Urol. 2013 Jan; 189 (1 Suppl):S66-74. doi: 10.1016/j.juro.2012.11.019.	PURPOSE: Unexplained clinical conditions share common features such as pain, fatigue, disability out of proportion to physical examination findings, inconsistent laboratory abnormalities, and an association with stress and psychosocial factors. We examined the extent of the overlap among urological and nonurological unexplained clinical conditions characterized by pain. We describe the limitations of previous research and suggest several possible explanatory models. MATERIALS AND METHODS: Using hallmark symptoms and syndromes as search terms a search of 12 databases identified a total of 1,037 full-length published articles in 8 languages from 1966 to April 2008. The search focused on the overlap of chronic pelvic pain, interstitial cystitis, painful bladder syndrome, chronic prostatitis/chronic pelvic pain syndrome or vulvodynia with fibromyalgia, chronic fatigue syndrome, temporomandibular joint and muscle disorders or irritable bowel syndrome. We abstracted information on authorship, type of case and control groups, eligibility criteria, case definitions, study methods and major findings. RESULTS: The literature suggests considerable comorbidity between urological and nonurological unexplained

Nyberg L, Payne C, Peñacoba C, Pezzone M, Pontari M, Potts J, Bullones Rodríguez MÁ, Warren J.				clinical conditions. The most robust evidence for overlap was for irritable bowel syndrome and urological unexplained syndromes with some estimates of up to 79% comorbidity between chronic pelvic pain and symptoms of irritable bowel syndrome. However, most studies were limited by methodological problems, such as varying case definitions and selection of controls. CONCLUSIONS: The overlap between urological and selected nonurological unexplained clinical conditions is substantial. Future research should focus on using standardized definitions, and rigorously designed, well controlled studies to further assess comorbidity, clarify the magnitude of the association and examine common pathophysiological mechanisms.
Caccamo D, Cesareo E, Mariani S, Raskovic D, Ientile R, Currò M, Korkina L, De Luca C.	Department of Biomedical Sciences and Morpho-Functional Imaging, Polyclinic University of Messina, 98125 Messina, Italy.	Xenobiotic sensor- and metabolism-related gene variants in environmental sensitivity-related illnesses: a survey on the Italian population.	Oxid Med Cell Longev. 2013; 2013:831969. doi: 10.1155/2013/831969. Epub 2013 Jul 7.	In the environmental sensitivity-related illnesses (SRIs), multiple chemical sensitivity (MCS), chronic fatigue syndrome (FCS), and fibromyalgia (FM), the search for genetic polymorphisms of phase I/II xenobiotic-metabolizing enzymes as suitable diagnostic biomarkers produced so far inconclusive results, due to patient heterogeneity, geographic/ethnic differences in genetic backgrounds, and different methodological approaches. Here, we compared the frequency of gene polymorphisms of selected cytochrome P450 (CYP) metabolizing enzymes and, for the first time, the frequency of the xenobiotic sensor Aryl hydrocarbon receptor (AHR) in the three cohorts of 156 diagnosed MCS, 94 suspected MCS, and 80FM/FCS patients versus 113 healthy controls. We found significantly higher frequency of polymorphisms CYP2C9∗*2, CYP2C9*3, CYP2C19*2, CYP2D6*4 and CYP2D6*41 in patients compared with controls. This confirms that these genetic variants represent a genetic risk factor for SRI. Moreover, the compound heterozygosity for CYP2C9*2 and *3 variants was useful to discriminate between either MCS or FM/CFS versus SMCS, while the PM *41/*41 genotype discriminated between MCS and either SMCS or FM/CFS. The compound heterozygosity for CYP2C9 *1/*3 and CYP2D6 *1/*4 differentiated MCS and SMCS cases from FM/CFS ones. Interestingly, despite the distribution of the AHR Arg554Lys variant did not result significantly different between SRI cases and controls, it resulted useful for the discrimination between MCS and SMCS cases when considered within haplotypes in combination with CYP2C19 *1/*2 and CYP2D6 *1/*4. Results allowed us to propose the genotyping for these specific CYP variants, together with the AHR Arg554Lys variant, as reliable, cost-effective genetic parameters to be included in the still undefined biomarkers' panel for laboratory diagnosis of the main types of environmental-borne SRI.
Cai Y, Tang L.	Department of Nephrology, the Second Affiliated Hospital, Chongqing Medical University, Yuzhong District, Chongqing, China.	Rare acute kidney injury secondary to hypothyroidism-induced rhabdomyolysis.	Yonsei Med J. 2013 Jan 1; 54(1):172-6. doi: 10.3349/ymj.2013.54.1.172.	PURPOSE: Acute kidney injury (AKI) caused by hypothyroidism-induced rhabdomyolysis is a rare and potentially life-threatening syndrome. The aim of this study was to investigate the clinical characteristics of such patients. MATERIALS AND METHODS: We retrospectively analyzed five patients treated at the Second Affiliated Hospital of Chongqing Medical University with AKI secondary to hypothyroidism-induced rhabdomyolysis from January 2006 to December 2010. RESULTS: Of the five cases reviewed (4 males, age range of 37 to 62 years), adult primary hypothyroidism

				was caused by amiodarone (1 case), chronic autoimmune thyroiditis (1 case), and by uncertain etiologies (3 cases). All patients presented with facial and lower extremity edema. Three patients presented with weakness, while two presented with blunted facies and oliguria. Only one patient reported experiencing myalgia and proximal muscle weakness, in addition to fatigue and chills. Creatine kinase, lactate dehydrogenase, and renal function normalized after thyroid hormone replacement, except in two patients who improved through blood purification. CONCLUSION: Hypothyroidism should be considered in patients presenting with renal impairment associated with rhabdomyolysis. Moreover, further investigation into the etiology of the hypothyroidism is warranted.
Carbonario F, Matsutani LA, Yuan SL, Marques AP.	Department of Speech Therapy, Physical Therapy and Occupational Therapy, Faculty of Medicine of the University of São Paulo, SP, Brazil. pasqual@usp.br	Effectiveness of high-frequency transcutaneous electrical nerve stimulation at tender points as adjuvant therapy for patients with fibromyalgia.	Eur J Phys Rehabil Med. 2013 Apr; 49(2):197-204. Epub 2013 Mar 13.	BACKGROUND: Fibromyalgia is a chronic pain syndrome associated with sleep disorders, fatigue and psychological symptoms. Combinations therapies, such as electrotherapy and therapeutic exercises have been used in the clinical practice. AIM: To assess the efficacy of high-frequency transcutaneous electrical nerve stimulation (TENS) as an adjuvant therapy to aerobic and stretching exercises, for the treatment of fibromyalgia. DESIGN: Controlled clinical trial. SETTING: Unit of rehabilitation of a public hospital. POPULATION: Twenty-eight women aged 52.4±7.5 years, with fibromyalgia. METHODS: A visual analogue scale measured pain intensity; tender points pain threshold, by dolorimetry; and quality of life, by the Fibromyalgia Impact Questionnaire. All subjects participated in an eight-week program consisting of aerobic exercises, followed by static stretching of muscle chains. In TENS group, high-frequency (150 Hz) was applied on bilateral tender points of trapezium and supraspinatus. RESULTS: TENS group had a greater pain reduction (mean change score=-2.0±2.9 cm) compared to Without TENS group (-0.7±3.7 cm). There was a difference between mean change scores of each group for pain threshold (right trapezium: 0.2±1 kg/cm² in TENS group and -0.2±1.2 kg/cm² in Without TENS group). In the evaluation of clinically important changes, patients receiving TENS had relevant improvement of pain, work performance, fatigue, stiffness, anxiety and depression compared to those not receiving TENS. CONCLUSION: It has suggested that high-frequency TENS as an adjuvant therapy is effective in relieving pain, anxiety, fatigue, stiffness, and in improving ability to work of patients with fibromyalgia. CLINICAL REHABILITATION IMPACT: High-frequency TENS may be used as a short-term complementary treatment of fibromyalgia.
Carter S.	[No address quoted]	Letter to the editor: 'recovery from chronic fatigue syndrome after treatments given in the PACE trial': recovery or	Psychol Med. 2013 Aug; 43(8):1787-8. doi: 10.1017/S0033291713001268.	Comment in Psychol Med. 2013 Aug; 43(8):1791-2.

		remission?		
Castori M, Morlino S, Celletti C, Ghibellini G, Bruschini M, Grammatico P, Blundo C, Camerota F.	Division of Medical Genetics, Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy.	Re-writing the natural history of pain and related symptoms in the joint hypermobility syndrome/Ehlers-Danlos syndrome, hypermobility type.	Am J Med Genet A. 2013 Dec; 161(12):2989-3004. doi: 10.1002/ajmg.a.36315. Epub 2013 Nov 6.	Joint hypermobility syndrome (JHS) and Ehlers-Danlos syndrome, hypermobility type (EDS-HT) are two clinically overlapping connective tissue disorders characterized by chronic/recurrent pain, joint instability complications, and minor skin changes. Fatigue and headache are also common, although are not yet considered diagnostic criteria. JHS/EDS-HT is a unexpectedly common condition that remains underdiagnosed by most clinicians and pain specialists. This results in interventions limited to symptomatic and non-satisfactory treatments, lacking reasonable pathophysiologic rationale. In this manuscript the fragmented knowledge on pain, fatigue, and headache in JHS/EDS is presented with review of the available published information and a description of the clinical course by symptoms, on the basis of authors' experience. Pathogenic mechanisms are suggested through comparisons with other functional somatic syndromes (e.g., chronic fatigue syndrome, fibromyalgia, and functional gastrointestinal disorders). The re-writing of the natural history of JHS/EDS-HT is aimed to raise awareness among clinical geneticists and specialists treating chronic pain conditions about pain and other complications of JHS/EDS-HT. Symptoms' clustering by disease stage is proposed to investigate both the molecular causes and the symptoms management of JHS/EDS-HT in future studies.
Castro-Marrero J, Cordero MD, Sáez-Francas N, Jimenez-Gutierrez C, Aguilar-Montilla FJ, Aliste L, Alegre-Martin J.	1 CFS Unit, Institut de Recerca Vall d'Hebron, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain .	Could mitochondrial dysfunction be a differentiating marker between chronic fatigue syndrome and fibromyalgia?	Antioxid Redox Signal. 2013 Nov 20; 19(15):1855-60. doi: 10.1089/ars.2013.5346. Epub 2013 May 29.	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are complex and serious illnesses that affect approximately 2.5% and 5% of the general population worldwide, respectively. The etiology is unknown; however, recent studies suggest that mitochondrial dysfunction has been involved in the pathophysiology of both conditions. We have investigated the possible association between mitochondrial biogenesis and oxidative stress in patients with CFS and FM. We studied 23 CFS patients, 20 FM patients, and 15 healthy controls. Peripheral blood mononuclear cell showed decreased levels of Coenzyme Q10 from CFS patients ($p<0.001$ compared with controls) and from FM subjects ($p<0.001$ compared with controls) and ATP levels for CFS patients ($p<0.001$ compared with controls) and for FM subjects ($p<0.001$ compared with controls). On the contrary, CFS/FM patients had significantly increased levels of lipid peroxidation, respectively ($p<0.001$ for both CFS and FM patients with regard to controls) that were indicative of oxidative stress-induced damage. Mitochondrial citrate synthase activity was significantly lower in FM patients ($p<0.001$) and, however, in CFS, it resulted in similar levels than controls. Mitochondrial DNA content (mtDNA/gDNA ratio) was normal in CFS and reduced in FM patients versus healthy controls, respectively ($p<0.001$). Expression levels of peroxisome proliferator-activated receptor gamma-coactivator 1-alpha and transcription factor A, mitochondrial by immunoblotting were significantly lower in FM patients ($p<0.001$) and were normal in CFS subjects compared with healthy controls. These data lead to the hypothesis that mitochondrial dysfunction-dependent

				events could be a marker of differentiation between CFS and FM, indicating the mitochondria as a new potential therapeutic target for these conditions.
Cella M, White PD, Sharpe M, Chalder T.	Institute of Psychiatry, King's College London, UK. matteo.cella@kcl.ac.uk	Cognitions, behaviours and co-morbid psychiatric diagnoses in patients with chronic fatigue syndrome.	Psychol Med. 2013 Feb; 43(2):375-80. doi: 10.1017/S0033291712000979 . Epub 2012 May 9.	BACKGROUND: Specific cognitions and behaviours are hypothesized to be important in maintaining chronic fatigue syndrome (CFS). Previous research has shown that a substantial proportion of CFS patients have co-morbid anxiety and/or depression. This study aims to measure the prevalence of specific cognitions and behaviours in patients with CFS and to determine their association with co-morbid anxiety or depression disorders. METHOD: A total of 640 patients meeting Oxford criteria for CFS were recruited into a treatment trial (i.e. the PACE trial). Measures analysed were: the Cognitive Behavioural Response Questionnaire, the Chalder Fatigue Scale and the Work and Social Adjustment Scale. Anxiety and depression diagnoses were from the Structured Clinical Interview for DSM-IV. Multivariate analysis of variance was used to explore the associations between cognitive-behavioural factors in patients with and without co-morbid anxiety and/or depression. RESULTS: Of the total sample, 54% had a diagnosis of CFS and no depression or anxiety disorder, 14% had CFS and one anxiety disorder, 14% had CFS and depressive disorder and 18% had CFS and both depression and anxiety disorders. Cognitive and behavioural factors were associated with co-morbid diagnoses; however, some of the mean differences between groups were small. Beliefs about damage and symptom focussing were more frequent in patients with anxiety disorders while embarrassment and behavioural avoidance were more common in patients with depressive disorder. CONCLUSIONS: Cognitions and behaviours hypothesized to perpetuate CFS differed in patients with concomitant depression and anxiety. Cognitive behavioural treatments should be tailored appropriately.
Celletti C, Castori M, La Torre G, Camerota F.	Physical Medicine and Rehabilitation, Department of Orthopaedics, Sapienza University, Umberto I Hospital, Rome, Italy. c_celletti@libero.it	Biomed Res Int. 2013;2013: 580460. doi: 10.1155/2013/580460. Epub 2013 Jul 14.	Evaluation of kinesiophobia and its correlations with pain and fatigue in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type.	Ehlers-Danlos syndrome hypermobility type a. k. a. joint hypermobility syndrome (JHS/EDS-HT) is a hereditary musculoskeletal disorder associating generalized joint hypermobility with chronic pain. Anecdotal reports suggest a prominent role for kinesiophobia in disease manifestations, but no study has systematically addressed this point.OBJECTIVE: To investigate the impact of kinesiophobia and its relationship with pain, fatigue, and quality of life in JHS/EDS-HT. DESIGN: Cross-sectional study. SUBJECTS/PATIENTS: 42 patients (40 female and 2 male) with JHS/EDS-HT diagnosis following standardized diagnostic criteria were selected. METHODS: Disease features were analyzed by means of specific questionnaires and scales evaluating kinesiophobia, pain, fatigue, and quality of life. The relationships among variables were investigated using the Spearman bivariate analysis. RESULTS: Kinesiophobia resulted predominantly in the patients' sample. The values of kinesiophobia did not correlate with intensity of pain, quality of life, and (or) the single component of fatigue. A strong correlation was discovered between kinesiophobia and general severity of fatigue. CONCLUSIONS: In JHS/EDS-HT, the onset of pain-avoiding strategies is related to the presence of pain but not to its intensity. The clear-cut

				correlation between kinesiophobia and severity of fatigue suggests a direct link between musculoskeletal pain and fatigue. In JHS/EDS-HT, the underlying mechanism is likely to be facilitated by primary disease characteristics, including hypotonia.
Cha YH, Cui Y, Baloh RW.	Department of Neurology, University of California Los Angeles, Los Angeles, California 90095, USA.	Repetitive transcranial magnetic stimulation for mal de debarquement syndrome.	Otol Neurotol. 2013 Jan; 34(1):175-9. doi: 10.1097/MAO.0b013e318278bf7c.	OBJECTIVE: Mal de debarquement syndrome (MdDS) is a chronic disorder of imbalance characterized by a feeling of rocking and swaying. The disorder starts after prolonged exposure to passive motion such as from a boat or plane. All medical treatment is palliative and symptoms that persist beyond 6 months show low likelihood of remission. This pilot study explored the feasibility and tolerability of repetitive transcranial magnetic stimulation (rTMS) as potential treatment for MdDS. PATIENTS/INTERVENTION: Ten subjects (8 women) with persistent MdDS lasting from 10 to 91 months were given 1 session each of 4 counterbalanced protocols: left 10 Hz (high frequency), left 1 Hz (low frequency), right 10 Hz, and right 1 Hz rTMS over the dorsolateral prefrontal cortex (DLPFC). MAIN OUTCOME MEASURE: Reduction of rocking sensation reported on a visual analogue scale. RESULTS: 1) Right-handers improved most with 10-Hz stimulation over the left DLPFC while left-handers improved most with 10 Hz stimulation over the right DLPFC; 2) low-frequency DLPFC stimulation was associated with symptom worsening in some subjects; 3) duration of symptoms was negatively correlated with treatment response; 4) rTMS was well tolerated in MdDS subjects, showing similar rates of headache (10 of 40 sessions) as for other studies; and 5) fatigue occurred after 6 sessions usually with low-frequency stimulation. CONCLUSION: rTMS was well tolerated in subjects with MdDS with promising short-term symptom improvement. Future studies of rTMS in MdDS may consider sequential days of stimulation, longer post-rTMS observation periods, formal measurement of post-TMS fatigue, and randomization with a sham condition.
Chan JS, Ho RT, Wang CW, Yuen LP, Sham JS, Chan CL.	Centre on Behavioral Health, The University of Hong Kong, Hong Kong.	Effects of qigong exercise on fatigue, anxiety, and depressive symptoms of patients with chronic fatigue syndrome-like illness: a randomized controlled trial.	Evid Based Complement Alternat Med. 2013; 2013:485341. doi: 10.1155/2013/485341. Epub 2013 Jul 31.	Background: Anxiety/depressive symptoms are common in patients with chronic fatigue syndrome- (CFS-) like illness. Qigong as a modality of complementary and alternative therapy has been increasingly applied by patients with chronic illnesses, but little is known about the effect of Qigong on anxiety/depressive symptoms of the patients with CFS-like illness. Purpose: To investigate the effects of Qigong on fatigue, anxiety, and depressive symptoms in patients with CFS-illness. Methods: One hundred and thirty-seven participants who met the diagnostic criteria for CFS-like illness were randomly assigned to either an intervention group or a waitlist control group. Participants in the intervention group received 10 sessions of Qigong training twice a week for 5 consecutive weeks, followed by home-based practice for 12 weeks. Fatigue, anxiety, and depressive symptoms were assessed at baseline and postintervention. Results: Total fatigue score [$F(1,135) = 13.888$, $P < 0.001$], physical fatigue score [$F(1,135) = 20.852$, $P < 0.001$] and depression score [$F(1,135) = 9.918$, $P = 0.002$] were significantly improved and mental fatigue score [$F(1,135) = 3.902$, $P = 0.050$] was marginally significantly improved in the Qigong group compared to controls. The anxiety score was not significantly improved in the Qigong group.

				Conclusion: Qigong may not only reduce the fatigue symptoms, but also has antidepressive effect for patients with CFS-like illness. Trial registration HKCTR-1200.
Chan W, Bosch JA, Jones D, Kaur O, Inston N, Moore S, McClean A, McTernan PG, Harper L, Phillips AC, Borrows R.	1- Department of Nephrology & Kidney Transplantation, Queen Elizabeth Hospital Birmingham, Birmingham, UK. 2 - Department of Nutrition & Dietetics, Queen Elizabeth Hospital Birmingham, Birmingham, UK. 3- School of Sport and Exercise Sciences, The University of Birmingham, Birmingham, UK. 4 - Division of Metabolic and Vascular Health, Clinical Sciences Research Institute, Warwick Medical School, University of Warwick, Coventry, UK. 5 - Centre for Translational Inflammation Research, University of Birmingham Research Laboratories, Queen Elizabeth Hospital Birmingham, Birmingham, UK. 6 - Address correspondence to: Richard Borrows, M.A., Department of Nephrology & Kidney Transplantation,	Predictors and consequences of fatigue in prevalent kidney transplant recipients.	Transplantation. 2013 Dec 15;96 (11):987-94. doi: 10.1097/TP.0b013e3182a2e88b.	BACKGROUND: Fatigue has been underinvestigated in stable kidney transplant recipients (KTRs). The objectives of this study were to investigate the nature, severity, prevalence, and clinical awareness of fatigue in medically stable KTRs, examine the impact of fatigue on quality of life (QoL), and explore the underlying causes of posttransplantation fatigue. METHODS: This single-center cross-sectional study enrolled 106 stable KTRs. Multi-dimensional Fatigue Inventory-20 was used to measure five fatigue dimensions: General Fatigue, Physical Fatigue, Reduced Activity, Reduced Motivation, and Mental Fatigue. Clinical awareness of fatigue was determined by reviewing medical records. QoL was assessed by Medical Outcomes Study Short Form-36 Questionnaire. Demographic, clinical, psychosocial, and behavioral parameters were evaluated as fatigue predictors. RESULTS: Fatigue was found in 59% of KTRs. Only 13% had this symptom documented in medical records. Fatigue in KTRs was in the same range as chronically unwell patients, with Physical Fatigue, Reduced Activity, and Reduced Motivation approached levels observed in chronic fatigue syndrome. All fatigue dimensions significantly and inversely correlated with QoL ($P<0.001$ for all associations). Demographic predictors were male, older age, and non-Caucasian ethnicity ($P\leq0.05$ for all associations). Clinical predictors included elevated highly sensitive C-reactive protein (inflammation), decreased estimated glomerular filtration rate (graft dysfunction), and reduced lean tissue index ($P\leq0.05$ for all associations). Psychosocial and behavioral predictors were inferior sleep quality, anxiety, and depression ($P<0.01$ for all associations). CONCLUSIONS: Fatigue is common and pervasive in clinically stable KTRs. It is strongly associated with reduced QoL. This study identified modifiable fatigue predictors and sets the scene for future interventional studies.

	Queen Elizabeth Hospital Birmingham, Area 5, Level 7 - Mindelsohn Way, Edgbaston, Birmingham, B15 2WB, UK.			
Chang FY, Lu CL.	Environmental Heath and Safety Office, Taipei Veterans General Hospital, National Yang-Ming University School of Medicine, Taipei, Taiwan.	Irritable bowel syndrome and migraine: bystanders or partners?	J Neurogastroenterol Motil. 2013 Jul;19(3):301-11. doi: 10.5056/jnm.2013.19.3.301. Epub 2013 Jul 8.	Irritable bowel syndrome (IBS) and migraine are distinct clinical disorders. Apart from the characteristics of chronic and recurrent pain in nature, these pain-related disorders apparently share many similarities. For example, IBS is female predominant with community prevalence about 5-10%, whereas that of migraine is 1-3% also showing female predominance. They are often associated with many somatic and psychiatric comorbidities in terms of fibromyaglia, chronic fatigue syndrome, interstitial cystitis, insomnia and depression etc., even the IBS subjects may have coexisted migraine with an estimated odds ratio of 2.66. They similarly reduce the quality of life of victims leading to the social, medical and economic burdens. Their pathogeneses have been somewhat addressed in relation to biopsychosocial dysfunction, heredity, genetic polymorphism, central/visceral hypersensitivity, somatic/cutaneous allodynia, neurolimbic pain network, gonadal hormones and abuses etc. Both disorders are diagnosed according to the symptomatically based criteria. Multidisciplinary managements such as receptor target new drugs, melantonin, antispasmodics, and psychological drugs and measures, complementary and alternatives etc. are recommended to treat them although the used agents may not be necessarily the same. Finally, the prognosis of IBS is pretty good, whereas that of migraine is less fair since suicide attempt and stroke are at risk. In conclusion, both distinct chronic pain disorders to share many similarities among various aspects probably suggest that they may locate within the same spectrum of a pain-centered disorder such as central sensitization syndromes. The true pathogenesis to involve these disorders remains to be clarified in the future.
Chen GL, Miller GM.	Harvard Medical School, New England Primate Research Center, Division of Neuroscience, One Pine Hill Drive, Southborough, MA 01772-9102, USA. guo-lin_chen@hms.harvard	Tryptophan hydroxylase-2: an emerging therapeutic target for stress disorders.	Biochem Pharmacol. 2013 May 1; 85(9):1227-33. doi: 10.1016/j.bcp.2013.02.018. Epub 2013 Feb 19.	Serotonin (5-HT) has been long recognized to modulate the stress response, and dysfunction of 5-HT has been implicated in numerous stress disorders. Accordingly, the 5-HT system has been targeted for the treatment of stress disorders. Tryptophan hydroxylase (TPH) is the rate-limiting enzyme in 5-HT synthesis, and the recent identification of a second, neuron-specific TPH isoform (TPH2) opened up a new area of research. With a decade of extensive investigation, it is now recognized that: (1) TPH2 exhibits a highly flexible gene expression that is modulated by an increasing number of internal and external environmental factors including the biological clock, stressors, endogenous hormones, and antidepressant therapies; and (2) genetically determined TPH2 activity is linked to a growing body of stress-related neuronal

	.edu			correlates and behavioral traits. These findings reveal an active role of TPH2 in the stress response and provide new insights into the long recognized but not yet fully understood 5-HT-stress interaction. As a major modulator of 5-HT neurotransmission and the stress response, TPH2 is of both pathophysiological and pharmacological significance, and is emerging as a new therapeutic target for the treatment of stress disorders. Given that numerous antidepressant therapies influence TPH2 gene expression, TPH2 is already inadvertently targeted for the treatment of stress disorders. With increased understanding of the regulation of TPH2 activity we can now purposely utilize TPH2 as a target to develop new or optimize current therapies, which are expected to greatly improve the prevention and treatment of a wide variety of stress disorders.
Chen XQ, Gang ZX, Xu ZP.	chenxiaoqin_cdutcm@163.com	Moxibustion at Yongquan (KI 1) for sleep disorders of chronic fatigue syndrome. [Article in Chinese]	Zhongguo Zhen Jiu. 2013 May; 33(5):450.	[No abstract given]
Chinthapalli K.	[No address quoted]	New research body to look at chronic fatigue syndrome.	BMJ. 2013 Apr 24; 346:f2630. doi: 10.1136/bmj.f2630.	[No abstract given]
Chirilă EL, Postolache P.	Faculty of Medicine, University of Medicine and Pharmacy "Carol Davila"- Bucureşti.	Orthostatic intolerance and chronic fatigue syndrome--possible related conditions.	Rev Med Chir Soc Med Nat Iasi. 2013 Apr-Jun; 117 (2):388-93.	The connection between orthostatic intolerance and chronic fatigue syndrome was first introduced in 1995. It was demonstrated that many patients with chronic fatigue syndrome also had some form of orthostatic intolerance. Some studies suggested that dysautonomia may be the common problem in patients with these syndromes. Although these conditions affect an important number of people, especially younger adults, orthostatic intolerance and chronic fatigue syndrome are among the least understood of the autonomic disorders and sustained research is focused particularly on elucidating their pathogenesis and identifying the most effective methods of treatment.
Christley Y, Duffy T, Everall IP, Martin CR.	School of Health, Nursing and Midwifery, University of the West of Scotland, Ayr Campus, University Avenue, Ayr, KA8 0SX, UK. yvonne.christley@uws.ac.uk	The neuropsychiatric and neuropsychological features of chronic fatigue syndrome: revisiting the enigma.	Curr Psychiatry Rep. 2013 Apr; 15(4):353. doi: 10.1007/s11920-013-0353-8.	The aim of this article is to provide a comprehensive and updated review of the key neuropsychiatric and neuropsychological complaints associated with chronic fatigue syndrome (CFS). Neuropsychiatric and neuropsychological difficulties are common in CFS and are linked primarily to disorders of mood, affect and behaviour. The neuropsychiatric complaint most frequently encountered amongst CFS patients is depression and in particular major depressive disorder (MDD). Despite decades of research, the precise aetiological relationship between CFS and MDD remains poorly understood. This has resulted in the development of a number of interesting and polarised hypotheses regarding the aetiological nature of CFS. Recent scientific advances have however begun to unravel a number of interesting inflammatory and immunological explanations that suggest CFS and MDD are distinct yet interrelated

				conditions. The possibility that the overlap between CFS and MDD might be explained in terms of shared oxidative and nitrosative (IO&NS) pathways is an area of intense research interest and is reviewed in detail in this article. The overlap between CFS and MDD is further differentiated by variations in HPA axis activity between the two disorders. Important immunological differences between MDD and CFS are also reviewed with particular emphasis on antiviral RNase L pathways in CFS. In addition to the presence of neuropsychiatric complaints, CFS is also associated with neuropsychological symptoms such as impaired attention, memory and reaction time. The key neuropsychological problems reported by CFS patients are also included in the review in an effort to understand the significance of cognitive impairment in CFS.
Chung SD, Lin CC, Liu SP, Lin HC.	Division of Urology, Department of Surgery, Far Eastern Memorial Hospital, Ban Ciao, Taipei, Taiwan; School of Health Care Administration, Taipei Medical University, Taipei, Taiwan; Sleep Research Center, Taipei Medical University Hospital, Taipei, Taiwan.	Obstructive Sleep Apnea Increases the Risk of Bladder Pain Syndrome/Interstitial Cystitis: A Population-Based Matched-Cohort Study.	Neurourol Urodyn. 2013 Mar 28. doi: 10.1002/nau.22401. [Epub ahead of print]	AIMS: Previous studies indicated a possible association between bladder pain syndrome/interstitial cystitis (BPS/IC) and sleep disorders including sleep abnormalities with delayed onset of sleep, waking up before needed, and snoring. Nevertheless, no previous study has reported the association between obstructive sleep apnea (OSA) and BPS/IC. In this retrospective cohort study, we examined the risk of BPS/IC among subjects with OSA during a 3-year follow-up in Taiwan using a population-based dataset. METHODS: This study comprised 2,940 study subjects with OSA, and 29,400 randomly selected comparison subjects. We individually followed-up each sampled subject (n=32,340) for a 3-year period to identify those subjects who subsequently received a diagnosis of BPS/IC. A Cox proportional hazards regression model was constructed to estimate the risk of subsequent BPS/IC following a diagnosis of OSA. RESULTS: Incidences of BPS/IC during the 3-year follow-up period were 13.61 (95% confidence interval [CI]=7.37-23.13) and 3.60 (95% CI=2.06-4.39) for subjects with and those without OSA, respectively. After adjusting for diabetes, hypertension, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraines, sicca syndrome, allergies, endometriosis, asthma, tobacco use disorder, and alcohol abuse, the stratified Cox proportional hazards regressions revealed that the hazard ratio for BPS/IC among subjects with OSA was 3.71 (95% CI=1.81-7.62, P<0.001) that of comparison subjects. CONCLUSIONS: This study provides epidemiological evidence of a link between OSA and a subsequent BPS/IC diagnosis. We suggest that clinical practitioners treating subjects with OSA be alert to urinary complaints in this population.
Chung SD, Liu SP, Lin CC, Li HC, Lin HC.	Division of Urology, Department of Surgery, Far Eastern Memorial Hospital, Banciao, Taipei, Taiwan.	Bladder pain syndrome/interstitial cystitis is associated with hyperthyroidism.	PLoS One. 2013 Aug 21; 8(8):e72284. doi: 10.1371/journal.pone.0072284.	BACKGROUND: Although the etiology of bladder pain syndrome/interstitial cystitis (BPS/IC) is still unclear, a common theme with BPS/IC patients is comorbid disorders which are related to the autonomic nervous system that connects the nervous system to end-organs. Nevertheless, no study to date has reported the association between hyperthyroidism and BPS/IC. In this study, we examined the association of IC/BPS with having previously been diagnosed with hyperthyroidism in Taiwan. DESIGN: Data in this study were retrieved from the Longitudinal Health Insurance Database. Our study

				consisted of 736 female cases with BPS/IC and 2208 randomly selected female controls. We performed a conditional logistic regression to calculate the odds ratio (OR) for having previously been diagnosed with hyperthyroidism between cases and controls. RESULTS: Of the 2944 sampled subjects, there was a significant difference in the prevalence of prior hyperthyroidism between cases and controls (3.3% vs. 1.5%, p<0.001). The conditional logistic regression analysis revealed that compared to controls, the OR for prior hyperthyroidism among cases was 2.16 (95% confidence interval (CI): 1.27~3.66). Furthermore, the OR for prior hyperthyroidism among cases was 2.01 (95% CI: 1.15~3.53) compared to controls after adjusting for diabetes, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraines, sicca syndrome, allergies, endometriosis, and asthma. CONCLUSIONS: Our study results indicated an association between hyperthyroidism and BPS/IC. We suggest that clinicians treating female subjects with hyperthyroidism be alert to urinary complaints in this population.
Ciregia F, Giusti L, Da Valle Y, Donadio E, Consensi A, Giacomelli C, Sernissi F, Scarpellini P, Maggi F, Lucacchini A, Bazzichi L.	Department of Pharmacy, University of Pisa, Via Bonanno 6, Pisa, 56126, Italy. lucas@farm.unipi.it.	A multidisciplinary approach to study a couple of monozygotic twins discordant for the chronic fatigue syndrome: a focus on potential salivary biomarkers.	J Transl Med. 2013 Oct 2; 11:243. doi: 10.1186/1479-5876-11-243.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is a severe, systemic illness characterized by persistent, debilitating and medically unexplained fatigue. The etiology and pathophysiology of CFS remains obscure, and diagnosis is formulated through the patient's history and exclusion of other medical causes. Thereby, the availability of biomarkers for CFS could be useful for clinical research. In the present study, we used a proteomic approach to evaluate the global changes in the salivary profile in a couple of monozygotic twins who were discordant for CFS. The aim was to evaluate differences of salivary protein expression in the CFS patient in respect to his healthy twin. METHODS: Saliva samples were submitted to two-dimensional electrophoresis (2DE). The gels were stained with Sypro, and a comparison between CFS subject and the healthy one was performed by the software Progenesis Same Spot including the Analysis of variance (ANOVA test). The proteins spot found with a ≥2-fold spot quantity change and p<0.05 were identified by Nano-liquid chromatography electrospray ionization tandem mass spectrometry. To validate the expression changes found with 2DE of 5 proteins (14-3-3 protein zeta/delta, cyclophilin A, Cystatin-C, Protein S100-A7, and zinc-alpha-2-glycoprotein), we used the western blot analysis. Moreover, proteins differentially expressed were functionally analyzed using the Ingenuity Pathways Analysis software with the aim to determine the predominant canonical pathways and the interaction network involved. RESULTS: The analysis of the protein profiles allowed us to find 13 proteins with a different expression in CFS in respect to control. Nine spots were up-regulated in CFS and 4 down-regulated. These proteins belong to different functional classes, such as inflammatory response, immune system and metabolism. In particular, as shown by the pathway analysis, the network built with our proteins highlights the involvement of inflammatory response in CFS pathogenesis. CONCLUSIONS: This study

				shows the presence of differentially expressed proteins in the saliva of the couple of monozygotic twins discordant for CFS, probably related to the disease. Consequently, we believe the proteomic approach could be useful both to define a panel of potential diagnostic biomarkers and to shed new light on the comprehension of the pathogenetic pathways of CFS.
Cockshell SJ, Mathias JL.	[No address quoted]	Cognitive Functioning in People With Chronic Fatigue Syndrome: A Comparison Between Subjective and Objective Measures.	Neuropsychology. 2013 Dec 23. [Epub ahead of print]	Objective: The purpose of this study was to examine the relationship between subjective and objective assessments of memory and attention in people with chronic fatigue syndrome (CFS), using tests that have previously detected deficits in CFS samples and measures of potential confounds. Method: Fifty people with CFS and 50 healthy controls were compared on subjective (memory and attention symptom severity, Cognitive Failures Questionnaire, Everyday Attention Questionnaires) and objective (California Verbal Learning Test, Rey-Osterreith Complex Figure Test, Paced Auditory Serial Addition Test, Stroop task) measures of memory and attention. Fatigue, sleep, depression, and anxiety were also assessed. Results: The CFS group reported experiencing more cognitive problems than the controls, but the two groups did not differ on the cognitive tests. Scores on the subjective and objective measures were not correlated in either group. Depression was positively correlated with increased severity of cognitive problems in both the CFS and control groups. Conclusions: There is little evidence for a relationship between subjective and objective measures of cognitive functioning for both people with CFS and healthy controls, which suggests that they may be capturing different constructs. Problems with memory and attention in everyday life are a significant part of CFS. Depression appears to be related to subjective problems but does not fully explain them.
Cockshell SJ, Mathias JL.	School of Psychology, The University of Adelaide, South Australia, Australia.	Cognitive deficits in chronic fatigue syndrome and their relationship to psychological status, symptomatology, and everyday functioning.	Neuropsychology. 2013 Mar; 27(2):230-42. doi: 10.1037/a0032084.	OBJECTIVE: To examine cognitive deficits in people with chronic fatigue syndrome (CFS) and their relationship to psychological status, CFS symptoms, and everyday functioning. METHOD: The current study compared the cognitive performance (reaction time, attention, memory, motor functioning, verbal abilities, and visuospatial abilities) of a sample with CFS (n = 50) with that of a sample of healthy controls (n = 50), all of whom had demonstrated high levels of effort and an intention to perform well, and examined the extent to which psychological status, CFS symptoms, and everyday functioning were related to cognitive performance. RESULTS: The CFS group showed impaired information processing speed (reaction time), relative to the controls, but comparable performance on tests of attention, memory, motor functioning, verbal ability, and visuospatial ability. Moreover, information processing speed was not related to psychiatric status, depression, anxiety, the number or severity of CFS symptoms, fatigue, sleep quality, or everyday functioning. CONCLUSION: A slowing in information processing speed appears to be the main cognitive deficit seen in persons with CFS whose performance on effort tests is not compromised. Importantly, this slowing does not appear to be the consequence of other CFS-related variables, such as depression and fatigue, or motor speed.

Collinge W, Yarnold P, Soltysik R.	Collinge and Associates, Eugene, OR, USA.	Fibromyalgia Symptom Reduction by Online Behavioral Self-monitoring, Longitudinal Single Subject Analysis and Automated Delivery of Individualized Guidance.	N Am J Med Sci. 2013 Sep;5 (9):546-53. doi: 10.4103/1947-2714.118920.	BACKGROUND: Fibromyalgia (FM) is a complex chronic pain condition that is difficult to treat. The prevailing approach is an integration of pharmacological, psycho-educational, and behavioral strategies. Information technology offers great potential for FM sufferers to systemically monitor symptoms as well as potential impacts of various management strategies. AIMS: This study aimed to evaluate effects of a web-based, self-monitoring and symptom management system (SMARTLog) that analyzes personal self-monitoring data and delivers data-based feedback over time. MATERIALS AND METHODS: Subjects were self-referred, anonymous, and recruited via publicity on FM advocacy websites. Standardized instruments assessed health status, self-efficacy, and locus of control at baseline and monthly during participation. Subjects were encouraged to complete the SMARTLog several times weekly. Within-subject, univariate, and multivariate analyses were used to derive classification trees for each user associating specific behavior variables with symptom levels over time. RESULTS: Moderate use (3 times weekly x 3 months) increased likelihood of clinically significant improvements in pain, memory, gastrointestinal problems, depression, fatigue, and concentration; heavy use (4.5 times weekly x five months) produced the above plus improvement in stiffness and sleep difficulties. CONCLUSIONS: Individualized, web-based behavioral self-monitoring with personally-tailored feedback can enable FM sufferers to significantly reduce symptom levels over time.
Cordero MD, Alcocer-Gómez E, Culic O, Carrión AM, de Miguel M, Díaz-Parrado E, Pérez-Villegas EM, Bullón P, Battino M, Sánchez-Alcazar JA.	1 Dpto. Citología e Histología Normal y Patológica, Facultad de Medicina, Universidad de Sevilla, Sevilla, Spain.	NLRP3 Inflammasome Is Activated in Fibromyalgia: The Effect of Coenzyme Q10.	Antioxid Redox Signal. 2013 Sep 19. [Epub ahead of print]	Abstract Aims: Fibromyalgia (FM) is a prevalent chronic pain syndrome characterized by generalized hyperalgesia associated with a wide spectrum of symptoms such as fatigue and joint stiffness. Diagnosis of FM is difficult due to the lack of reliable diagnostic biomarkers, while treatment is largely inadequate. We have investigated the role of coenzyme Q10 (CoQ10) deficiency and mitochondrial dysfunction in inflammasome activation in blood cells from FM patients, and in vitro and in vivo CoQ10 deficiency models. Results: Mitochondrial dysfunction was accompanied by increased protein expression of interleukin (IL)-1β, NLRP3 (NOD-like receptor family, pyrin domain containing 3) and caspase-1 activation, and an increase of serum levels of proinflammatory cytokines (IL-1β and IL-18). CoQ10 deficiency induced by p-aminobenzoate treatment in blood mononuclear cells and mice showed NLRP3 inflammasome activation with marked algesia. A placebo-controlled trial of CoQ10 in FM patients has shown a reduced NLRP3 inflammasome activation and IL-1β and IL-18 serum levels. Innovation: These results show an important role for the NLRP3 inflammasome in the pathogenesis of FM, and the capacity of CoQ10 in the control of inflammasome. Conclusion: These findings provide new insights into the pathogenesis of FM and suggest that NLRP3 inflammasome inhibition represents a new therapeutic intervention for the disease. Antioxid. Redox Signal. 00, 000-000.
Cornes O.	Software engineer, London.	Chronic fatigue syndrome: a patient's perspective.	Br J Gen Pract. 2013 Dec;63(617):648. doi: 10.3399/bjgp13X675458.	[No abstract given]

Costantini A, Pala MI.	Department of Neurological Rehabilitation, Villa Immacolata, Viterbo, Italy. carapetata@libero.it	Thiamine and fatigue in inflammatory bowel diseases: an open-label pilot study.	J Altern Complement Med. 2013 Aug; 19(8):704-8. doi: 10.1089/acm.2011.0840. Epub 2013 Feb 4.	OBJECTIVES: To demonstrate that fatigue and other disorders related to ulcerative colitis and Crohn's disease are the manifestation of an intracellular mild thiamine deficiency and not due to malabsorbtion, augmented requirements, or nutritional factors, and that this dysfunction is curable with high doses of thiamine administered orally or parenterally. DESIGN: In this pilot study, we treated fatigue in eight patients with ulcerative colitis and four patients affected by Crohn's disease from January to April 2011. The patients were recruited through general practitioners' surveys and among personnel and affiliated personnel of the clinic Villa Immacolata. Fatigue was measured using the chronic fatigue syndrome scale, and the determination of thiamine and thiamine pyrophosphate levels in the blood was carried out through blood tests. The levels of thiamine and thiamine pyrophosphate in the blood were normal. All patients were assigned to receive high doses of thiamine orally. Depending upon the body weight of each patient, dosage ranged from 600mg/day (60kg) to 1,500mg/day (90kg). The chronic fatigue syndrome scale as well as thiamine and thiamine pyrophosphate levels in the blood were measured 20 days after the beginning of the therapy. RESULTS: Ten patients out of twelve showed complete regression of fatigue, while the remaining two patients showed nearly complete regression of fatigue compared to the chronic fatigue syndrome scale scores before therapy. CONCLUSIONS: The absence of blood thiamine deficiency and the efficacy of high-dose thiamine in our patients suggest that fatigue is the manifestation of a thiamine deficiency, likely due to a dysfunction of the active transport of thiamine inside the cells, or due to structural enzymatic abnormalities. The administration of large quantities of thiamine increases the concentration in the blood to levels in which the passive transport restores the normal glucose metabolism in all cells and leads to a complete regression of fatigue.
Courtney R.	London, United Kingdom, information785@gmail.com.	Improvement rates in adolescent patients with chronic fatigue syndrome after receiving cognitive behavioural therapy.	Eur J Pediatr. 2013 Dec 10. [Epub ahead of print]	[No abstract given]
Courtney R.	[No address quoted]	Letter to the editor: 'recovery from chronic fatigue syndrome after treatments given in the PACE trial': an appropriate threshold for a	Psychol Med. 2013 Aug; 43(8):1788-9. doi: 10.1017/S003329171300127X	Comment in Psychol Med. 2013 Aug; 43(8):1791-2.

		recovery?		
Cox D.	[No address quoted]	Letter to the editor: 'recovery from chronic fatigue syndrome after treatments given in the PACE trial': data on the recovery groups as a whole would be useful.	Psychol Med. 2013 Aug; 43(8):1789. doi: 10.1017/S0033291713001281.	Comment in Psychol Med. 2013 Aug; 43(8):1791-2.
Crawley E, Collin SM, White PD, Rimes K, Sterne JA, May MT; CFS/ME National Outcomes Database.	Centre for Child & Adolescent Health, School of Social & Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol BS8 2BN, UK. esther.crawley@bristol.ac.uk	Treatment outcome in adults with chronic fatigue syndrome: a prospective study in England based on the CFS/ME National Outcomes Database.	QJM. 2013 Jun; 106(6):555-65. doi: 10.1093/qjmed/hct061. Epub 2013 Mar 28. Erratum in QJM. 2013 Jun; 106(6):567.	BACKGROUND: Chronic fatigue syndrome (CFS) is relatively common and disabling. Over 8000 patients attend adult services each year, yet little is known about the outcome of patients attending NHS services. AIM: Investigate the outcome of patients with CFS and what factors predict outcome. DESIGN: Longitudinal patient cohort. METHODS: We used data from six CFS/ME (myalgic encephalomyelitis) specialist services to measure changes in fatigue (Chalder Fatigue Scale), physical function (SF-36), anxiety and depression (Hospital Anxiety and Depression Scale) and pain (visual analogue pain rating scale) between clinical assessment and 8-20 months of follow-up. We used multivariable linear regression to investigate baseline factors associated with outcomes at follow-up. Results: Baseline data obtained at clinical assessment were available for 1643 patients, of whom 834 (51%) had complete follow-up data. There were improvements in fatigue [mean difference from assessment to outcome: -6.8; 95% confidence interval (CI) -7.4 to -6.2; P < 0.001]; physical function (4.4; 95% CI 3.0-5.8; P < 0.001), anxiety (-0.6; 95% CI -0.9 to -0.3; P < 0.001), depression (-1.6; 95% CI -1.9 to -1.4; P < 0.001) and pain (-5.3; 95% CI -7.0 to -3.6; P < 0.001). Worse fatigue, physical function and pain at clinical assessment predicted a worse outcome for fatigue at follow-up. Older age, increased pain and physical function at assessment were associated with poorer physical function at follow-up. CONCLUSION: Patients who attend NHS specialist CFS/ME services can expect similar improvements in fatigue, anxiety and depression to participants receiving cognitive behavioural therapy and graded exercise therapy in a recent trial, but are likely to experience less improvement in physical function. Outcomes were predicted by fatigue, disability and pain at assessment.
Crawley E, Mills N, Beasant L, Johnson D, Collin SM, Deans Z, White K, Montgomery A.	Centre for Child & Adolescent Health, School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Road, BS8	The feasibility and acceptability of conducting a trial of specialist medical care and the Lightning Process in children with chronic	Trials. 2013 Dec 5; 14:415. doi: 10.1186/1745-6215-14-415.	BACKGROUND: Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME) is relatively common in children with limited evidence for treatment. The Phil Parker Lightning Process (LP) is a trademarked intervention, which >250 children use annually. There are no reported studies investigating the effectiveness or possible side effects of LP. METHODS: The trial population was drawn from the Bath and Bristol NHS specialist paediatric CFS or ME service. The study was designed as a pilot randomized trial with children (aged 12 to 18 years) comparing specialist medical care

	2BN, Bristol, UK. esther.crawley@bristol.ac.uk.	fatigue syndrome: feasibility randomized controlled trial (SMILE study).		with specialist medical care plus the Lightning Process. Integrated qualitative methodology was used to explore the feasibility and acceptability of the recruitment, randomization and interventions. RESULTS: A total of 56 children were recruited from 156 eligible children (1 October 2010 to 16 June 2012). Recruitment, randomization and both interventions were feasible and acceptable. Participants suggested changes to improve feasibility and acceptability and we incorporated the following in the trial protocol: stopped collecting 6-week outcomes; introduced a second reminder letter; used phone calls to collect primary outcomes from nonresponders; informed participants about different approaches of each intervention and changed our recommendation for the primary outcome for the full study from school attendance to disability (SF-36 physical function subscale) and fatigue (Chalder Fatigue Scale). CONCLUSIONS: Conducting randomized controlled trials (RCTs) to investigate an alternative treatment such as LP is feasible and acceptable for children with CFS or ME. Feasibility studies that incorporate qualitative methodology enable changes to be made to trial protocols to improve acceptability to participants. This is likely to improve recruitment rate and trial retention. TRIAL REGISTRATION: Feasibility study first randomization: 29 September 2010.Trial registration: Current Controlled Trials ISRCTN81456207 (31 July 2012).Full trial first randomization: 19 September 2012.
Crawley E, Mills N, Hollingworth W, Deans Z, Sterne JA, Donovan JL, Beasant L, Montgomery A.	Centre for Child and Adolescent Health, School of Social and Community Medicine, Oakfield House, Oakfield Grove, Bristol, BS8 2BN, UK. Esther.crawley@bristol.ac.uk.	Comparing specialist medical care with specialist medical care plus the Lightning Process® for chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME): study protocol for a randomised controlled trial (SMILE Trial).	Trials. 2013 Dec 26; 14(1):444.	BACKGROUND: Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is a relatively common and potentially serious condition with a limited evidence base for treatment. Specialist treatment for paediatric CFS/ME uses interventions recommended by National Institute for Health and Clinical Excellence (NICE) including cognitive behavioural therapy, graded exercise therapy and activity management. The Lightning Process® (LP) is a trademarked intervention derived from osteopathy, life-coaching and neuro-linguistic programming, delivered over three consecutive days as group sessions. Although over 250 children with CFS/ME attend LP courses each year, there are no reported studies on the effectiveness or cost-effectiveness. METHODS: This pragmatic randomised controlled trial is set within a specialist paediatric CFS/ME service in the south west of England. Children and young people with CFS/ME (n = 80 to 112), aged 12 to 18 years old will be randomised to specialist medical care (SMC) or SMC plus the LP. The primary outcome will be physical function (SF-36 physical function short form) and fatigue (Chalder Fatigue Scale). DISCUSSION: This study will tell us whether adding the LP to SMC is effective and cost-effective compared to SMC alone. This study will also provide detailed information on the implementation of the LP and SMC.
Crawley E.	[No address quoted]	The epidemiology of chronic fatigue syndrome/myalgic encephalitis in children.	Arch Dis Child. 2013 Oct 21. doi: 10.1136/archdischild-2012-302156. [Epub ahead of print]	Most paediatricians regularly see children with chronic fatigue syndrome or myalgic encephalitis (CFS/ME) in their clinics and yet we know little about how common it is, who is affected, whether there are risk factors and how likely a child is to recover (or what might predict recovery). Recent research suggests that this illness is more complicated than previously thought and that rather than being an illness found in

				middle class families, it is more common in those who are socially deprived. This article reviews what is currently known about this important but little understood condition.
Creed FH, Tomenson B, Chew-Graham C, Macfarlane GJ, Davies I, Jackson J, Littlewood A, McBeth J.	School of Community Based Medicine, University of Manchester, Oxford Road, Manchester, UK. francis.creed@manchester.ac.uk	Multiple somatic symptoms predict impaired health status in functional somatic syndromes.	Int J Behav Med. 2013 Jun; 20(2):194-205. doi: 10.1007/s12529-012-9257-y.	BACKGROUND: The relationship between functional somatic syndromes and multiple somatic symptoms is unclear. PURPOSE: We assessed whether the number of somatic symptoms is a predictor of health status in three functional somatic syndromes (FSS). METHODS: In a population-based study of 990 UK adults we assessed chronic widespread pain (CWP), chronic fatigue (CF) and irritable bowel syndrome (IBS) by questionnaire and medical record data. We assessed health status (Short Form 12 and EQ-5D), number of somatic symptoms (Somatic Symptom Inventory) and anxiety/depression (Hospital Anxiety and Depression Scale) both at baseline and at follow-up 1 year later. RESULTS: The proportion of people with an FSS who also have multiple somatic symptoms (52-55 %) was similar in the three functional syndromes. The presence of multiple somatic symptoms was associated with more impaired health status both at baseline and at follow-up. This finding was not explained by severity of FSS. In the absence of multiple somatic symptoms, the health status of the FSS was fair or good. In multiple regression analysis, the number of somatic symptoms, the presence of a functional syndrome (CWP or CF) and anxiety/depression were predictors of EQ-5D thermometer at follow-up after adjustment for confounders. CONCLUSIONS: Multiple somatic symptoms in people with an FSS are associated with impaired health status and this cannot be explained by more severe functional syndrome or the presence of anxiety and depression.
Crinion SJ, McNicholas WT.	Department of Respiratory and Sleep Medicine, Pulmonary and Sleep Disorders Unit, St. Vincent's University Hospital, Elm Park, Dublin, Ireland.	Sleep-related disorders in chronic obstructive pulmonary disease.	Expert Rev Respir Med. 2013 Dec 30. [Epub ahead of print]	Sleep may have several negative consequences in patients with chronic obstructive pulmonary disease (COPD). Sleep is typically fragmented with diminished slow wave and rapid-eye-movement sleep, which likely represents an important contributing factor to daytime symptoms such as fatigue and lethargy. Furthermore, normal physiological adaptations during sleep, which result in mild hypoventilation in normal subjects, are more pronounced in COPD, which can result in clinically important nocturnal oxygen desaturation. The co-existence of obstructive sleep apnea and COPD is also common, principally because of the high prevalence of each disorder, and there is little convincing evidence that one disorder predisposes to the other. Nonetheless, this co-existence, termed the overlap syndrome, typically results in more pronounced nocturnal oxygen desaturation and there is a high prevalence of pulmonary hypertension in such patients. Management of sleep disorders in patients with COPD should address both sleep quality and disordered gas exchange. Non-invasive pressure support is beneficial in selected cases, particularly during acute exacerbations associated with respiratory failure, and is particularly helpful in patients with the overlap syndrome. There is limited evidence of benefit from pressure support in the chronic setting in COPD patients without obstructive sleep apnea.
Curriu M, Carrillo	Institut de recerca de la	Screening NK-, B- and	J Transl Med. 2013 Mar 20;11:	BACKGROUND: Chronic Fatigue Syndrome (CFS) is a debilitating neuro-immune

J, Massanella M, Rigau J, Alegre J, Puig J, Garcia-Quintana AM, Castro-Marrero J, Negredo E, Clotet B, Cabrera C, Blanco J.	sida, IrsiCaixa-HIVACAT, Institut d'Investigació en Ciències de la Salut Germans Trias I Pujol|, Badalona, Spain.	T-cell phenotype and function in patients suffering from Chronic Fatigue Syndrome.	68. doi: 10.1186/1479-5876-11-68.	disorder of unknown etiology diagnosed by an array of clinical manifestations. Although several immunological abnormalities have been described in CFS, their heterogeneity has limited diagnostic applicability. METHODS: Immunological features of CFS were screened in 22 CFS diagnosed individuals fulfilling Fukuda criteria and 30 control healthy individuals. Peripheral blood T, B and NK cell function and phenotype were analyzed by flow cytometry in both groups. RESULTS: CFS diagnosed individuals showed similar absolute numbers of T, B and NK cells, with minor differences in the percentage of CD4+ and CD8+ T cells. B cells showed similar subset frequencies and proliferative responses between groups. Conversely, significant differences were observed in T cell subsets. CFS individuals showed increased levels of T regulatory cells (CD25+/FOXP3+) CD4 T cells, and lower proliferative responses in vitro and in vivo. Moreover, CD8 T cells from the CFS group showed significantly lower activation and frequency of effector memory cells. No clear signs of T-cell immunosenescence were observed. NK cells from CFS individuals displayed higher expression of NKp46 and CD69 but lower expression of CD25 in all NK subsets defined. Overall, T cell and NK cell features clearly clustered CFS individuals. CONCLUSIONS: Our findings suggest that alterations in T-cell phenotype and proliferative response along with the specific signature of NK cell phenotype may be useful to identify CFS individuals. The striking down modulation of T cell mediated immunity may help to understand intercurrent viral infections in CFS.
Datieva VK, Rosinskaia AV, Levin OS.	[No address quoted]	The use of melatonin in the treatment of chronic fatigue syndrome and circadian rhythm disorders in Parkinson's disease. [Article in Russian]	Zh Nevrol Psikhiatr Im S S Korsakova. 2013;113 (7 Pt 2):77-81.	Chronic fatigue syndrome (CFS), a specific asthenic condition, is identified in a half of patients with Parkinson's disease (PD). An aim of the study was to evaluate an effect of melatonin (melaxen) on the severity of CFS, affective disorders, quality of life and sleep disorders in 30 patients with early and late stages of PD. After treatment, there was a decrease by 21% (p<0,05) on the Parkinson fatigue scale. At the same time, the improvement of sleep, assessed by the PDSS, decrease in the state anxiety on the Spilberger's scale and improvement of quality of life on the PDQ-39 (p<0,05) were found. No significant differences in motor, cognitive autonomic disorders and depression level were noted compared to baseline. Therefore, melatonin, together with optimized antiparkinsonian treatment, can treat CFS improve sleep and quality of life of PD patients.
De Meirleir KL, Khaiboullina SF, Frémont M, Hulstaert J, Rizvanov AA, Palotás A, Lombardi VC.	Whittemore Peterson Institute for Neuro-Immune Disease, University of Nevada, Reno 1664 N Virginia Street MS 0552, Reno, NV 89557 USA.	Plasmacytoid dendritic cells in the duodenum of individuals diagnosed with myalgic encephalomyelitis are uniquely immunoreactive to antibodies to human	In Vivo. 2013 Mar-Apr; 27(2):177-87.	Myalgic encephalomyelitis (ME) is a debilitating illness of unknown etiology characterized by neurocognitive dysfunction, inflammation, immune abnormalities and gastrointestinal distress. An increasing body of evidence suggests that disruptions in the gut may contribute to the induction of neuroinflammation. Therefore, reports of human endogenous retroviral (HERV) expression in association with neuroinflammatory diseases prompted us to investigate the gut of individuals with ME for the presence of HERV proteins. In eight out of 12 individuals with ME, immunoreactivity to HERV proteins was observed in duodenal biopsies. In contrast, no immunoreactivity was detected in any of the eight controls. Immunoreactivity to

		endogenous retroviral proteins.		HERV Gag and Env proteins was uniquely co-localized in hematopoietic cells expressing the C-type lectin receptor CLEC4C (CD303/BDCA2), the co-stimulatory marker CD86 and the class II major histocompatibility complex HLA-DR, consistent with plasmacytoid dendritic cells (pDCs). Although the significance of HERVs present in the pDCs of individuals with ME has yet to be determined, these data raise the possibility of an involvment of pDCs and HERVs in ME pathology. To our knowledge, this report describes the first direct association between pDCs and HERVs in human disease.
Deák M, Szvetnik A, Balog A, Sohár N, Varga R, Pokorny G, Tóth G, Kiss M, Kovács L.	Department of Rheumatology, Faculty of Medicine, Albert Szent-Györgyi Health Centre, University of Szeged, Szeged, Hungary. drdeakmagdi@gmail.com	Neuroimmune interactions in Sjögren's syndrome: relationship of exocrine gland dysfunction with autoantibodies to muscarinic acetylcholine receptor-3 and mental health status parameters.	Neuroimmunomodulation. 2013; 20(2):79-86. doi: 10.1159/000345177. Epub 2012 Dec 12.	OBJECTIVES: Antimuscarinic acetylcholine receptor-3 (m3AChR) autoantibodies have been described in primary Sjögren's syndrome (pSS). The aim of this study was to compare various methods for their detection and to assess the contributions of anti-m3AChR and other immunological and psychosocial factors to the pathomechanism of secondary SS (sSS). METHODS: Sixty-five rheumatoid arthritis (RA) patients, 103 systemic lupus erythematosus (SLE) patients, 76 pSS patients and 50 controls were compared. Three immunodominant epitopes of m3AChR were synthesized and used in ELISA. Two extracellular epitopes were also prepared in fusion with glutathione-S-transferase and one in conjugation with bovine serum albumin. Mental health status was assessed with the 36-item Short-Form Health Survey and Functional Assessment of Chronic Illness Therapy fatigue scale. Correlations were evaluated between glandular function and anti-m3AChR positivities and specificities, features of SLE and RA, and mental health parameters. RESULTS: Fourteen RA and 27 SLE patients had sSS. The autoantibody levels to all epitopes of m3AChR were significantly higher in pSS and SLE patients than in the controls. The fusion protein forms discriminated RA from pSS and SLE; furthermore, the YNIP fusion protein also distinguished pSS from SLE. The prevalence and the mean levels of all autoantibodies did not differ statistically between sicca and non-sicca SLE or RA patients. Glandular dysfunction correlated with higher age in SLE and RA and an impaired health-related quality of life in SLE. CONCLUSIONS: The second and third extracellular loops of m3AChR are antigenic in pSS. Immunoassays with antigens as fusion peptides demonstrate the best performance. Sicca SLE patients have worse mental health status. Anti-m3AChR antibodies represent a peculiar example of neuroimmune interactions.
Dinan TG, Stanton C, Cryan JF.	Alimentary Pharmabiotic Centre, University College Cork and Teagasc Moorepark, Cork, Ireland. Electronic address: t.dinan@ucc.ie.	Psychobiotics: a novel class of psychotropic.	Biol Psychiatry. 2013 Nov 15; 74(10):720-6. doi: 10.1016/j.biopsych.2013.05.001. Epub 2013 Jun 10. Comment in Biol Psychiatry. 2013 Nov 15; 74(10):708-9.	Here, we define a psychobiotic as a live organism that, when ingested in adequate amounts, produces a health benefit in patients suffering from psychiatric illness. As a class of probiotic, these bacteria are capable of producing and delivering neuroactive substances such as gamma-aminobutyric acid and serotonin, which act on the brain-gut axis. Preclinical evaluation in rodents suggests that certain psychobiotics possess antidepressant or anxiolytic activity. Effects may be mediated via the vagus nerve, spinal cord, or neuroendocrine systems. So far, psychobiotics have been most extensively studied in a liaison psychiatric setting in patients with irritable bowel syndrome, where positive benefits have been reported for a number of organisms

				including Bifidobacterium infantis. Evidence is emerging of benefits in alleviating symptoms of depression and in chronic fatigue syndrome. Such benefits may be related to the anti-inflammatory actions of certain psychobiotics and a capacity to reduce hypothalamic-pituitary-adrenal axis activity. Results from large scale placebo-controlled studies are awaited.
Dixit R, Popescu A, Bagić A, Ghearing G, Hendrickson R.	University of Pittsburgh School of Medicine, Pittsburgh, PA, USA.	Medical comorbidities in patients with psychogenic nonepileptic spells (PNES) referred for video-EEG monitoring.	Epilepsy Behav. 2013 Aug; 28(2):137-40. doi: 10.1016/j.yebeh.2013.05.004. Epub 2013 Jun 5.	Differentiating between psychogenic nonepileptic spells (PNES) and epileptic seizures without video-EEG monitoring is difficult. The presence of specific medical comorbidities may discriminate the two, helping physicians suspect PNES over epilepsy earlier. A retrospective analysis comparing the medical comorbidities of patients with PNES with those of patients with epilepsy was performed in 280 patients diagnosed with either PNES (N = 158, 74.7% females) or epilepsy (N = 122, 46.7% females) in the Epilepsy Monitoring Unit (EMU) of the University of Pittsburgh Medical Center over a two-year period. Patients with PNES, compared to those with epilepsy, were mostly female, significantly more likely to have a history of abuse, had more functional somatic syndromes (fibromyalgia, chronic fatigue syndrome, chronic pain syndrome, tension headaches, and irritable bowel syndrome), and had more medical illnesses that are chronic with intermittent attacks (migraines, asthma, and GERD). The presence of at least of one these disorders may lead physicians to suspect PNES over epilepsy and expedite appropriate referral for video-EEG monitoring for diagnosis.
Djamshidian A, Lees AJ.	The National Hospital for Neurology and Neurosurgery, Queen Square and the Reta Lila Weston Institute of Neurological Studies, UCL, London, UK.	Can stress trigger Parkinson's disease?	J Neurol Neurosurg Psychiatry. 2013 Nov 20. doi: 10.1136/jnnp-2013-305911. [Epub ahead of print]	In this manuscript we summarize the role of chronic stress as a potential trigger factor for Parkinson's disease. Underlying mechanisms and stress-induced changes to the neuronal networks have been highlighted. Examples of stress induced reversible symptoms that resemble parkinsonism in humans and in animal models raise the question whether emotional stress can cause striatal degeneration in susceptible patients. A Pubmed literature review searching for the terms 'Stress', 'Distress and Parkinson's disease', 'Emotional Distress and Parkinson's disease', 'Stress and Parkinson's disease', 'Prodromal Parkinson's disease', 'Non motor symptoms and Parkinson's disease', 'Paradoxical kinesia', 'Psychogenic parkinsonism', 'Functional somatic syndromes', 'Chronic fatigue syndrome', 'Irritable bowel syndrome', 'Fibromyalgia', 'Dopamine and fibromyalgia', 'Dopamine and chronic fatigue syndrome' and 'Dopamine and irritable bowel syndrome' was carried out until April 2013. Articles were also identified through searches of the authors' own files. Only papers published in English were reviewed. The final reference list was generated on the basis of originality and relevance to the broad scope of this viewpoint.
Donegan K, Beau-Lejdstrom R, King B, Seabroke S, Thomson A, Bryan P.	Vigilance and Risk Management of Medicines, Medicines and Healthcare products Regulatory	Bivalent human papillomavirus vaccine and the risk of fatigue syndromes in girls in the UK.	Vaccine. 2013 Oct 9;31 (43):4961-7. doi: 10.1016/j.vaccine.2013.08.024. Epub 2013 Sep 1.	INTRODUCTION: Over 70% of cervical cancers are related to human papillomavirus types 16 and 18. In 2008, the vaccine Cervarix, protecting against these two strains, was introduced into the routine UK immunisation programme for girls aged 12-13 years, with a catch-up in girls aged up to 18 years. As part of the risk management planning for this new campaign, the Medicines and Healthcare products Regulatory

	Agency, London, UK.			Agency (MHRA) anticipated a range of conditions, including chronic fatigue syndrome, which might be reported as adverse events in temporal association with the vaccine. METHODS: Near-real time 'observed vs. expected' analyses were conducted comparing the number of reports of fatigue syndromes submitted via the MHRA's Yellow Card passive surveillance scheme to the expected number, using background rates calculated from the Clinical Practice Research Datalink (CPRD) and estimates of vaccination coverage. Subsequently, an ecological analysis and a self-controlled case series (SCCS), both using CPRD, compared the incidence rate of fatigue syndromes in girls before and after the start of the vaccination campaign and the risk in the year post-vaccination compared to other periods. RESULTS: The number of spontaneous reports of chronic fatigue following Cervarix vaccination was consistent with estimated background rates even assuming low reporting. Ecological analyses suggested that there had been no change in the incidence of fatigue syndromes in girls aged 12-20 years after the introduction of the vaccination despite high uptake (IRR: 0.94, 95% CI: 0.78-1.14). The SCCS, including 187 girls, also showed no evidence of an increased risk of fatigue syndromes in the year post first vaccination (IRR: 1.07, 95% CI: 0.57-2.00, p=0.84). DISCUSSION: The successful implementation of an enhanced pharmacovigilance plan provided immediate reassuring evidence that there was no association between vaccination with Cervarix and an increased risk of chronic fatigue syndromes. This has now also been further demonstrated in more comprehensive epidemiological studies.
Dörr J, Nater U.	Psychologie, Universität Marburg.	Fatigue syndromes--an overview of terminology, definitions and classificatory concepts. [Article in German]	Psychother Psychosom Med Psychol. 2013 Feb; 63(2):69-76. doi: 10.1055/s-0032-1327706. Epub 2013 Feb 13.	This article aims at giving a general view of fatigue syndromes, their description, and their differentiation. The syndromes neurasthenia, chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), and burnout are discussed. First, the historical background of fatigue classification is shortly reviewed. Each syndrome is introduced in terms of definition and classification as well as differentiation from each other. The article discusses the differentiation of the syndromes from each other as well as differentiation of CFS/ME and burnout from depression. We conclude that it is difficult to differentiate criteria due to insufficient empirical evidence. More research is needed concerning integration of the diagnoses in classification systems as well as differentiation between syndromes. High comorbidity of depression with CFS and Burnout can be shown, but diagnoses also comprise distinct symptoms.
Dyer C.	[No address quoted]	College was right not to disclose deliberations about chronic fatigue treatment trial, tribunal rules.	BMJ. 2013 Aug 30;347: f5355. doi: 10.1136/bmj.f5355.	Comment in BMJ. 2013;347: f5740.
Efficace F, Baccarani M,	Italian Group for Adult Hematologic Diseases,	Chronic fatigue is the most important	Leukemia. 2013 Jul; 27(7):1511-9. doi:	Health-related quality of life (HRQOL) is an important goal of therapy for chronic myeloid leukemia (CML) patients treated with current molecular-targeted therapies.

Breccia M, Cottone F, Alimena G, Deliliers GL, Baratè C, Specchia G, Di Lorenzo R, Luciano L, Turri D, Martino B, Stagno F, Dabusti M, Bergamaschi M, Leoni P, Simula MP, Levato L, Fava C, Veneri D, Sica S, Rambaldi A, Rosti G, Vignetti M, Mandelli F.	Data Center and Health Outcomes Research Unit, Rome, Italy. f.efficace@gimema.it	factor limiting health-related quality of life of chronic myeloid leukemia patients treated with imatinib.	10.1038/leu.2013.51. Epub 2013 Feb 18.	The main objective of this study was to investigate factors associated with long-term HRQOL outcomes of CML patients receiving imatinib. Analysis was performed on 422 CML patients recruited in an observational multicenter study. HRQOL was assessed with the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). Key socio-demographic and clinical data were investigated for their association with HRQOL outcomes. Chronic fatigue and social support were also investigated. Univariate and multivariate linear regression analyses were used to identify independent factors associated with HRQOL outcomes. Fatigue was the only variable showing an independent and consistent association across all physical and mental HRQOL outcomes ($P<0.01$). Differences between patients reporting low versus high fatigue levels were more than eight and seven times the magnitude of a clinically meaningful difference, respectively, for the role physical ($\Delta=70$ points) and emotional scale ($\Delta=63$ points) of the SF-36. Fatigue did not occur as an isolated symptom and was most highly correlated with musculoskeletal pain ($r=0.511$; $P\leq0.001$) and muscular cramps ($r=0.448$; $P\leq0.001$). Chronic fatigue is the major factor limiting HRQOL of CML patients receiving imatinib.
Elfaitouri A, Herrmann B, Bölin-Wiener A, Wang Y, Gottfries CG, Zachrisson O, Pipkorn R, Rönnblom L, Blomberg J.	Section of Clinical Microbiology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden.	Epitopes of microbial and human heat shock protein 60 and their recognition in myalgic encephalomyelitis.	PLoS One. 2013 Nov 28; 8 (11):e81155. doi: 10.1371/journal.pone.0081155.	Myalgic encephalomyelitis (ME, also called Chronic Fatigue Syndrome), a common disease with chronic fatigability, cognitive dysfunction and myalgia of unknown etiology, often starts with an infection. The chaperonin human heat shock protein 60 (HSP60) occurs in mitochondria and in bacteria, is highly conserved, antigenic and a major autoantigen. The anti-HSP60 humoral (IgG and IgM) immune response was studied in 69 ME patients and 76 blood donors (BD) (the Training set) with recombinant human and E coli HSP60, and 136 30-mer overlapping and targeted peptides from HSP60 of humans, Chlamydia, Mycoplasma and 26 other species in a multiplex suspension array. Peptides from HSP60 helix I had a chaperonin-like activity, but these and other HSP60 peptides also bound IgG and IgM with an ME preference, theoretically indicating a competition between HSP60 function and antibody binding. A HSP60-based panel of 25 antigens was selected. When evaluated with 61 other ME and 399 non-ME samples (331 BD, 20 Multiple Sclerosis and 48 Systemic Lupus Erythematosus patients), a peptide from Chlamydia pneumoniae HSP60 detected IgM in 15 of 61 (24%) of ME, and in 1 of 399 non-ME at a high cutoff ($p<0.0001$). IgM to specific cross-reactive epitopes of human and microbial HSP60 occurs in a subset of ME, compatible with infection-induced autoimmunity.
Elgen I, Hikmat O, Aspevik TN, Hagen EM.	Department of Child and Adolescent Psychiatry, Haukeland University Hospital, 5021 Bergen, Norway; Department of Clinical Medicine, University of	CFS in Children and Adolescent: Ten Years of Retrospective Clinical Evaluation.	Int J Pediatr. 2013; 2013:270373. doi: 10.1155/2013/270373. Epub 2013 Jun 16.	Aim: To estimate number of children being diagnosed with chronic fatigue syndrome (CFS). Methods: For a period of 10 years (2002-2011) data from children being referred for fatigue symptoms were collected retrospectively. Results: Thirty-seven children were referred. Four were excluded due to incorrect coding. Six (18%) patients received other diagnoses at the end of evaluation time. Of the 27 who received the diagnosis G93.3, four had a previous chronic illness, while 23 patients were previously healthy. All patients reported onset of fatigue symptom in relation to

	Bergen, P.O Box 7804, 5020 Bergen, Norway.			an infection, and all tested positive for IgG to either Epstein-Barr virus, cytomegalovirus or borrelia, indicating previous infection. There were 16 (59%) boys among the 27 patients. The mean age at the debut of fatigue symptoms was 141 months (SD 30) for boys and 136 months (SD 31) for girls, respectively. Being underweight, defined as BMI < 17.5, was found in 12 (44%) patients. Conclusion: An increasing number of children and adolescents are evaluated for CFS. The clinical assessment of children and adolescents with possible CFS need systematically evaluation. Nutritional status, possible eating disorder, and psychosocial issues need to be addressed and evaluated carefully. A multidisciplinary approach is essential when assessing CFS in children and adolescents. There is a need for European guidelines.
Enlander D.	Krankenanstalt Rudolfstiftung, Vienna, Austria.	RE: Treatment outcome in adults with chronic fatigue syndrome: a prospective study.	QJM. 2014 Jan; 107(1):87. doi: 10.1093/qjmed/hct169. Epub 2013 Aug 22.	[No abstract given]
Enlander D.	[No address quoted]	Fear of movement and avoidance behaviour toward physical activity in chronic-fatigue syndrome and fibromyalgia: state of the art and implications for clinical practice.	Clin Rheumatol. 2013 Jul; 32(7):1113. doi: 10.1007/s10067-013-2295-2. Epub 2013 May 30.	Comment on Clin Rheumatol. 2013 Aug; 32(8):1121-9.
Eriksen TE, Risør MB.	Department of Occupational and Environmental Medicine, University Hospital of North Norway, Box 6060, 9038, Tromsø, Norway, thor.eirik.eriksen@unn.no.	What is called symptom?	Med Health Care Philos. 2013 Jul 23. [Epub ahead of print]	There is one concept in medicine which is prominent, the symptom. The omnipresence of the symptom seems, however, not to be reflected by an equally prominent curiosity aimed at investigating this concept as a phenomenon. In classic, traditional or conventional medical diagnostics and treatment, the lack of distinction with respect to the symptom represents a minor problem. Faced with enigmatic conditions and their accompanying labels such as chronic fatigue syndrome, fibromyalgia, medically unexplained symptoms, and functional somatic syndromes, the contestation of the symptom and its origin is immediate and obvious and calls for further exploration. Based on a description of the diagnostic framework encompassing medically unexplained conditions and a brief introduction to how such symptoms are managed both within and outside of the medical clinic, we argue on one hand how unexplained conditions invite us to reconsider and re-think the concept we call a "symptom" and on the other hand how the concept "symptom" is no longer an adequate and necessary fulcrum and must be enriched by socio-cultural,

				phenomenological and existential dimensions. Consequently, our main aim is to expand both our interpretative horizon and the linguistic repertoire in the face of those appearances we label medically unexplained symptoms.
Evans M, Jason LA.	[No address quoted]	Effects of Time Frame on the Recall Reliability of CFS Symptoms.	Eval Health Prof. 2013 Sep 23. [Epub ahead of print]	This study serves as an investigation of the reliability of symptom data as reported by individuals with chronic fatigue syndrome (CFS), across three recall time frames (the past week, the past month, and the past 6 months), and at two assessment points (with 1 week in between each assessment). Multilevel model analyses were used to determine the optimal recall time frame, in terms of test -retest reliability, for each of the Fukuda et al. (1994) case defining symptoms. Results suggested that the optimal time frame for reliably reporting CFS symptoms was six months for sore throat, lymph node pain, muscle pain, post-exertional malaise, headaches, memory/concentration difficulties, and unrefreshing sleep. For joint pain, the optimal time frame was one month. Researchers who are interested in the assessment of CFS symptoms need to take recall time frame into account, especially when the intended goal is to standardize and improve the methods used to reliably and accurately diagnose this complex illness.
Finsterer J, Ahting U.	Krankenanstalt Rudolfstiftung, Vienna, Austria.	Mitochondrial depletion syndromes in children and adults.	Can J Neurol Sci. 2013 Sep; 40 (5):635-44.	To highlight differences between early-onset and adult mitochondrial depletion syndromes (MDS) concerning etiology and genetic background, pathogenesis, phenotype, clinical presentation and their outcome. MDSs most frequently occur in neonates, infants, or juveniles and more rarely in adolescents or adults. Mutated genes phenotypically presenting with adult-onset MDS include POLG1, TK2, TyMP, RRM2B, or PEO1/twinkle. Adult MDS manifest similarly to early-onset MDS, as myopathy, encephalo-myopathy, hepato-cerebral syndrome, or with chronic progressive external ophthalmoplegia (CPEO), fatigue, or only minimal muscular manifestations. Diagnostic work-up or treatment is not at variance from early-onset cases. Histological examination of muscle may be normal but biochemical investigations may reveal multiple respiratory chain defects. The outcome appears to be more favorable in adult than in early-onset forms. Mitochondrial depletion syndromes is not only a condition of neonates, infants, or juveniles but rarely also occurs in adults, presenting with minimal manifestations or manifestations like in the early-onset forms. Outcome of adult-onset MDS appears more favorable than early-onset MDS.
Fisher H, Crawley E.	Paediatric CFS/ME Service, Royal National Hospital for Rheumatic Diseases, UK.	Why do young people with CFS/ME feel anxious? A qualitative study.	Clin Child Psychol Psychiatry. 2013 Oct; 18(4):556-73. doi: 10.1177/1359104512460862. Epub 2012 Oct 23.	Young people with chronic fatigue syndrome or myalagic encephalopathy (CFS/ME) (CFS/ME) experience higher levels of psychological distress than healthy controls and young people with other chronic illnesses, and it was recently demonstrated that 38% of this population scored above the clinical cut-off on the Spence Child Anxiety Scale. Subscales of social and separation anxiety were consistently high across gender and age groups. In this study, we used qualitative methods to help us understand more about these two types of anxiety in young people with CFS/ME. Eleven young people (age 12-18) were interviewed. Interviews were self-directed by the participants and

				were wide ranging. The transcripts were analysed using interpretative phenomenological analysis. Five superordinate themes were identified: social loss and adjustment; introduction of uncertainty and unpredictability; the vulnerable self; individual differences; and contributions towards recovery. Many themes were identical to those described in young people coping with other chronic illnesses in adolescence. In addition, young people with CFS/ME describe experiences associated with the perceived illegitimacy of this condition, namely: feeling unable to explain their illness; bullying from peers; disbelief; and distrust from adults around them. This becomes an additional challenge for these young people. Clinicians need to be aware of these problems, and offer appropriate support.
Fitzcharles MA, Ste-Marie PA, Goldenberg DL, Pereira JX, Abbey S, Choinière M, Ko G, Moulin DE, Panopalis P, Proulx J, Shir Y; National Fibromyalgia Guideline Advisory Panel.	Division of Rheumatology, McGill University Health Centre, Montreal, Quebec, Canada. mary-ann.fitzcharles@muhc.mcgill.ca	2012 Canadian Guidelines for the diagnosis and management of fibromyalgia syndrome: executive summary.	Pain Res Manag. 2013 May-Jun; 18(3):119-26.	BACKGROUND: Recent neurophysiological evidence attests to the validity of fibromyalgia (FM), a chronic pain condition that affects >2% of the population. OBJECTIVES: To present the evidence-based guidelines for the diagnosis, management and patient trajectory of individuals with FM. METHODS: A needs assessment following consultation with diverse health care professionals identified questions pertinent to various aspects of FM. A literature search identified the evidence available to address these questions; evidence was graded according to the standards of the Oxford Centre for Evidence-Based Medicine. Drafted recommendations were appraised by an advisory panel to reflect meaningful clinical practice. RESULTS: The present recommendations incorporate the new clinical concepts of FM as a clinical construct without any defining physical abnormality or biological marker, characterized by fluctuating, diffuse body pain and the frequent symptoms of sleep disturbance, fatigue, mood and cognitive changes. In the absence of a defining cause or cure, treatment objectives should be patient-tailored and symptom-based, aimed at reducing global complaints and enhancing function. Healthy lifestyle practices with active patient participation in health care forms the cornerstone of care. Multimodal management may include nonpharmacological and pharmacological strategies, although it must be acknowledged that pharmacological treatments provide only modest benefit. Maintenance of function and retention in the workforce is encouraged. CONCLUSIONS: The new Canadian guidelines for the treatment of FM should provide health professionals with confidence in the complete care of these patients and improve clinical outcomes.
Fjorback LO, Arendt M, Ornbøl E, Walach H, Rehfeld E, Schröder A, Fink P.	The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Denmark. lonefjor@rm.dk	Mindfulness therapy for somatization disorder and functional somatic syndromes: randomized trial with one-year follow-up.	J Psychosom Res. 2013 Jan;74(1):31-40. doi: 10.1016/j.jpsychores.2012.09.006. Epub 2012 Oct 1.	OBJECTIVE: To conduct a feasibility and efficacy trial of mindfulness therapy in somatization disorder and functional somatic syndromes such as fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome, defined as bodily distress syndrome (BDS). METHODS: We randomized 119 patients to either mindfulness therapy (mindfulness-based stress reduction and some cognitive behavioral therapy elements for BDS) or to enhanced treatment as usual (2-hour specialist medical care and brief cognitive behavioral therapy for BDS). The primary outcome measure was change in physical health (SF-36 Physical Component Summary) from baseline to 15-

				month follow-up. RESULTS: The study is negative as we could not demonstrate a different development over time for the two groups (F(3,2674)=1.51, P=.21). However, in the mindfulness therapy group, improvement was obtained toward the end of treatment and it remained present at the 15-month follow-up, whereas the enhanced treatment as usual group achieved no significant change until 15-month follow-up. The change scores averaged half a standard deviation which amounts to a clinically significant change, 29% changed more than 1 standard deviation. Significant between-group differences were observed at treatment cessation. CONCLUSION: Mindfulness therapy is a feasible and acceptable treatment. The study showed that mindfulness therapy was comparable to enhanced treatment as usual in improving quality of life and symptoms. Nevertheless, considering the more rapid improvement following mindfulness, mindfulness therapy may be a potentially useful intervention in BDS patients. Clinically important changes that seem to be comparable to a CBT treatment approach were obtained. Further research is needed to replicate or even expand these findings.
Fjorback LO, Carstensen T, Arendt M, Ornbøl E, Walach H, Rehfeld E, Fink P.	The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Aarhus, Denmark. lonefjor@rm.dk	Mindfulness therapy for somatization disorder and functional somatic syndromes: analysis of economic consequences alongside a randomized trial.	J Psychosom Res. 2013 Jan; 74 (1):41-8. doi: 10.1016/j.jpsychores.2012.09. 010. Epub 2012 Oct 11.	OBJECTIVE: The objective of the present study is to estimate the economic consequences of somatization disorder and functional somatic syndromes such as fibromyalgia and chronic fatigue syndrome, defined as bodily distress syndrome (BDS), when mindfulness therapy is compared with enhanced treatment as usual. METHODS: A total of 119 BDS patients were randomized to mindfulness therapy or enhanced treatment as usual and compared with 5950 matched controls. Register data were analyzed from 10years before their inclusion to 15-month follow-up. The main outcome measures were disability pension at the 15-month follow-up and a reduction in total health care costs. Unemployment and sickness benefit prior to inclusion were tested as possible risk factors. RESULTS: At 15-month follow-up, 25% from the mindfulness therapy group received disability pension compared with 45% from the specialized treatment group (p=.025). The total health care utilization was reduced over time in both groups from the year before inclusion (mean $5325, median $2971) to the year after inclusion (mean $3644, median $1593) (p=.0001). This overall decline was seen in spite of elevated costs due to assessment and mindfulness therapy or enhanced treatment as usual. The BDS patients accumulated significantly more weeks of unemployment and sickness benefit 5 and 10years before inclusion (p<.0001) than the population controls. CONCLUSIONS: Mindfulness therapy may prevent disability pension and it may have a potential to significantly reduce societal costs and increase the effectiveness of care. Accumulated weeks of unemployment and sickness benefit are possible risk factors for BDS.
Flores S, Brown A, Adeoye S, Jason LA, Evans M.	DePaul University, Chicago, IL, USA. S.Flore10@DePaul.Edu	Examining the impact of obesity on individuals with chronic fatigue	Workplace Health Saf. 2013 Jul; 61(7):299-307. doi: 10.3928/21650799-20130617-12. Epub 2013 Jun	Chronic fatigue syndrome (CFS) is a complex disorder affecting multiple body systems. The most commonly used definition of CFS is 6 or more months of fatigue and the presence of at least four of eight minor symptoms. In addition, many health and psychological conditions, including severe obesity-body mass index (BMI) of 40

		syndrome.	24.	kg/m(2) or greater-exclude individuals from a diagnosis of CFS. Obesity has been correlated with fatigue, sleep problems, and less satisfaction with general health, functioning, and vitality. The current study investigated weight trends over time in a community-based sample of individuals with CFS and healthy controls. The study further investigated the impact of comorbid weight issues on several health and disability outcomes in a subset of overweight individuals. Overweight and obese individuals with CFS demonstrated poorer functioning than controls who were similarly weighted. One participant was excluded because she had gained weight at a monitoring visit and her BMI was greater than 40 kg/m(2). The implications of these findings for health care workers are discussed.
Frémont M, Coomans D, Massart S, De Meirleir K.	R.E.D Laboratories NV, Z-1 Researchpark 100, 1731 Zellik, Belgium. mfremont@redlabs.be	High-throughput 16S rRNA gene sequencing reveals alterations of intestinal microbiota in myalgic encephalomyelitis/chronic fatigue syndrome patients.	Anaerobe. 2013 Aug; 22:50-6. doi: 10.1016/j.anaerobe.2013.06.002. Epub 2013 Jun 19.	Human intestinal microbiota plays an important role in the maintenance of host health by providing energy, nutrients, and immunological protection. Intestinal dysfunction is a frequent complaint in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) patients, and previous reports suggest that dysbiosis, i.e. the overgrowth of abnormal populations of bacteria in the gut, is linked to the pathogenesis of the disease. We used high-throughput 16S rRNA gene sequencing to investigate the presence of specific alterations in the gut microbiota of ME/CFS patients from Belgium and Norway. 43 ME/CFS patients and 36 healthy controls were included in the study. Bacterial DNA was extracted from stool samples, PCR amplification was performed on 16S rRNA gene regions, and PCR amplicons were sequenced using Roche FLX 454 sequencer. The composition of the gut microbiota was found to differ between Belgian controls and Norwegian controls: Norwegians showed higher percentages of specific Firmicutes populations (Roseburia, Holdemania) and lower proportions of most Bacteroidetes genera. A highly significant separation could be achieved between Norwegian controls and Norwegian patients: patients presented increased proportions of Lactonifactor and Alistipes, as well as a decrease in several Firmicutes populations. In Belgian subjects the patient/control separation was less pronounced, however some abnormalities observed in Norwegian patients were also found in Belgian patients. These results show that intestinal microbiota is altered in ME/CFS. High-throughput sequencing is a useful tool to diagnose dysbiosis in patients and could help designing treatments based on gut microbiota modulation (antibiotics, pre and probiotics supplementation).
Friedberg F, Napoli A, Coronel J, Adamowicz J, Seva V, Caikauskaite I, Ngan MC, Chang J, Meng H.	Department of Psychiatry and Behavioral Science, Stony Brook University, Stony Brook, NY, USA. fred.friedberg@stonybrookmedicine.edu	Chronic fatigue self-management in primary care: a randomized trial.	Psychosom Med. 2013 Sep; 75(7):650-7. doi: 10.1097/PSY.0b013e31829dbed4. Epub 2013 Aug 6.	OBJECTIVE: To assess the efficacy of brief fatigue self-management (FSM) for medically unexplained chronic fatigue (UCF) and chronic fatigue syndrome (CFS) in primary care. METHODS: A randomized controlled design was used wherein 111 patients with UCF or CFS were randomly assigned to two sessions of FSM, two sessions of symptom monitoring support (attention control; AC), or a usual care control condition (UC). Participants were assessed at baseline and at 3 and 12 months after treatment. The primary outcome, the Fatigue Severity Scale, measured fatigue impact on functioning. Analysis was by intention to treat (multiple imputation) and

				also by per protocol. RESULTS: A group × time interaction across the 15-month trial showed significantly greater reductions in fatigue impact in the FSM group in comparison with the AC group ($p < .023$) and the UC group ($p < .013$). Medium effect sizes for reduced fatigue impact in the FSM group were found in comparison with the AC group ($d = 0.46$) and the UC group ($d = 0.40$). The per-protocol analysis revealed large effect sizes for the same comparisons. Clinically significant decreases in fatigue impact were found for 53% of participants in the FSM condition, 14% in the AC condition, and 17% in the UC condition. Dropout rates at the 12-month follow-up were high (42%-53%), perhaps attributable to the burden of monthly telephone calls to assess health care use. CONCLUSION: A brief self-management intervention for patients with UCF or CFS seemed to be clinically effective for reducing the impact of fatigue on functioning. Trial Registration clinicaltrials.gov Identifier: NCT00997451.
Fuchs CE, van Geelen SM, van Geel R, Sinnema G, van de Putte EM, Hermans HJ, Kuis W.	Division of Paediatric Psychology, University Medical Centre Utrecht, 3584 EA, Lundlaan 6, KE.04.133.1, Utrecht, The Netherlands. c.e.fuchs@umcutrecht.nl	Health and identity: Self-positioning in adolescent chronic fatigue syndrome and juvenile idiopathic arthritis.	Clin Child Psychol Psychiatry. 2013 Jul; 18(3):383-97. doi: 10.1177/1359104512455814. Epub 2012 Oct 11.	The aim of this study is to gain more insight into basic aspects of identity, in relation to adolescent chronic fatigue syndrome (CFS) and juvenile idiopathic arthritis (JIA). In dialogical self theory, identity is regarded as incorporating multiple self-positions, such as 'I as tired', 'I as pessimistic', or 'I as decisive'. Physical and psychosocial impairment might alter the organization of these self-positions. The Personal Position Repertoire procedure, a quantitative method to analyse the prominence of self-positions, the Child Health Questionnaire, assessing health-related functioning, and the Checklist Individual Strength, measuring fatigue, were completed by 42 adolescents with CFS, 37 adolescents with JIA and 23 healthy teenagers. Adolescents with JIA report impaired physical functioning and general health. However, they position themselves very similar to healthy teenagers - i.e. as strong and healthy. While this self-positioning approach might be adequate and sustainable in adolescence, it could prove too strenuous to maintain throughout adult life. Adolescents with CFS, besides indicating severe physical difficulties, also report more psychosocial problems. They position themselves as significantly less strong and more unwell. With this emphasis on positions relating to their illness, there seems to be little room left for stronger positions. It is regarded of clinical importance to address these issues in this crucial developmental period.
Fukuda S, Horiguchi M, Yamaguti K, Nakatomi Y, Kuratsune H, Ichinose H, Watanabe Y.	Department of Medical Science on Fatigue, Osaka City University, Graduate School of Medicine, Osaka, Japan.	Association of monoamine-synthesizing genes with the depression tendency and personality in chronic fatigue syndrome patients.	Life Sci. 2013 Feb 27; 92(3):183-6. doi: 10.1016/j.lfs.2012.11.016. Epub 2012 Dec 13.	AIMS: Tyrosine hydroxylase (TH) and GTP cyclohydrolase I (GCH) are the rate-limiting enzymes for the biosynthesis of catecholamines and tetrahydrobiopterin (BH4), respectively. Since catecholamines and BH4 are thought to be involved in the pathophysiology of CFS, we explored the genetic factors that influence CFS development and examined the possible association between the SNPs of the TH and GCH genes and the various characteristics of CFS patients. MAIN METHODS: After drawing venous blood from CFS patients and controls, genomic DNA was then extracted from whole blood in accordance with standard procedures. Digestion patterns of the PCR products were used for genotyping the SNPs of GCH (rs841; C+243T) and TH (rs10770141; C-824T). We also performed questionnaires consisting

				of fatigue-scale and temperament and character inventory scale (TCI) to CFS patients. KEY FINDINGS: Our results demonstrated that the allele differences for the GCH and TH SNPs were not associated with CFS patients. We did find that the GCH gene with the C+243T polymorphism affected harm avoidance, while the TH gene with the C-824T polymorphism affected persistence in the CFS patients. The concept of persistence has been linked to specific personality, such as perfectionism, in CFS. SIGNIFICANCE: Our results suggest that the biosynthetic pathways of the monoamine neurotransmitters that are mediated by TH and GCH might be associated with the CFS clinical findings, because persistence is one of the typical personality traits observed in CFS and patients with major depressive disorder exhibit a higher harm avoidance score.
Gao J, Gurbaxani BM, Hu J, Heilman KJ, Emanuele Ii VA, Lewis GF, Davila M, Unger ER, Lin JM.	PMB Intelligence LLC West Lafayette, IN, USA; Mechanical and Materials Engineering, Wright State University Dayton, OH, USA.	Multiscale analysis of heart rate variability in non-stationary environments.	Front Physiol. 2013 May 30; 4:119. doi: 10.3389/fphys.2013.00119. eCollection 2013.	Heart rate variability (HRV) is highly non-stationary, even if no perturbing influences can be identified during the recording of the data. The non-stationarity becomes more profound when HRV data are measured in intrinsically non-stationary environments, such as social stress. In general, HRV data measured in such situations are more difficult to analyze than those measured in constant environments. In this paper, we analyze HRV data measured during a social stress test using two multiscale approaches, the adaptive fractal analysis (AFA) and scale-dependent Lyapunov exponent (SDLE), for the purpose of uncovering differences in HRV between chronic fatigue syndrome (CFS) patients and their matched-controls. CFS is a debilitating, heterogeneous illness with no known biomarker. HRV has shown some promise recently as a non-invasive measure of subtle physiological disturbances and trauma that are otherwise difficult to assess. If the HRV in persons with CFS are significantly different from their healthy controls, then certain cardiac irregularities may constitute good candidate biomarkers for CFS. Our multiscale analyses show that there are notable differences in HRV between CFS and their matched controls before a social stress test, but these differences seem to diminish during the test. These analyses illustrate that the two employed multiscale approaches could be useful for the analysis of HRV measured in various environments, both stationary and non-stationary.
Gladwell PW, Pheby D, Rodriguez T, Poland F.	North Bristol NHS Trust, Bristol, UK .	Use of an online survey to explore positive and negative outcomes of rehabilitation for people with CFS/ME.	Disabil Rehabil. 2013 Jun 4. [Epub ahead of print]	Abstract Purpose: First, to explore the experiences of people with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) of rehabilitation therapies so as to build an understanding of reasons for the discrepancy between the notably mixed experiences regarding effectiveness reported in patient surveys and the RCT evidence about the efficacy of Graded Exercise Therapy (GET). GET is a form of structured and supervised activity management that aims for gradual but progressive increases in physical activity. Second, to review patient experiences of two related rehabilitation approaches - Exercise on Prescription (EoP) and Graded Activity Therapy (GAT). Method: An online survey conducted by the charity Action for ME generated qualitative data about 76 patient experiences of rehabilitation undertaken during or

				after 2008, examined using thematic analysis. Results: Both positive and negative experiences of rehabilitation were reported. Positive themes included supportive communication, the benefits of a routine linked with baseline setting and pacing, the value of goal setting, and increasing confidence associated with exercise. Negative themes included poor communication, feeling pushed to exercise beyond a sustainable level, having no setback plan, and patients feeling blamed for rehabilitation not working. Conclusions: The negative themes may help explain the negative outcomes from rehabilitation reported by previous patient surveys. The negative themes indicate rehabilitation processes which contradict the NICE (National Institute for Health and Clinical Excellence) Guideline advice regarding GET, indicating that some clinical encounters were not implementing these. These findings suggest areas for improving therapist training, and for developing quality criteria for rehabilitation in CFS/ME. Implications for Rehabilitation The insensitive delivery of rehabilitation support for people with CFS/ME can explain negative outcomes reported in patient surveys. Therapist-patient collaboration, establishing a sustainable baseline and agreeing a setback plan are all examples of higher quality rehabilitation indicated by this research. Greater awareness of the positive and negative experiences of rehabilitation therapies should enable avoidance of the potential pitfalls identified in this research. Positive experiences of rehabilitation therapies include supportive communication with a therapist, treatment which included routines and goals, and value attached to baselines and controlled pacing. By contrast, factors leading to negative experiences include poor communication and support, conflict in beliefs about CFS/ME and rehabilitation, pressure to comply with treatment, worsening of symptoms, baselines experienced as unsustainable, and feeling blamed for rehabilitation not working.
Goedendorp MM, van der Werf SP, Bleijenberg G, Tummers M, Knoop H.	Department of Health Sciences, University Medical Center Groningen, University of Groningen, The Netherlands. m.m.goedendorp@umcg.nl	Does neuropsychological test performance predict outcome of cognitive behavior therapy for Chronic Fatigue Syndrome and what is the role of underperformance?	J Psychosom Res. 2013 Sep;75(3):242-8. doi: 10.1016/j.jpsychores.2013.07.011. Epub 2013 Jul 26.	OBJECTIVE: A subgroup of patients with Chronic Fatigue Syndrome (CFS) has cognitive impairments, reflected by deviant neuropsychological test performance. However, abnormal test scores can also be caused by suboptimal effort. We hypothesized that worse neuropsychological test performance and underperformance were related to each other and to a smaller reduction in fatigue, functional impairments, physical limitations and higher dropout rates following cognitive behavior therapy (CBT) for CFS. METHODS: Data were drawn from a previous trial, in which CFS patients were randomized to two conditions; 1) guided self-instruction and additional CBT (n=84) or 2) waiting period followed by regular CBT for CFS (n=85). Underperformance was assessed using the Amsterdam Short Term Memory Test (<84). To test neuropsychological test performance, the Symbol Digit Modalities Task, a simple reaction time task and a choice reaction time task were used. Interaction effects were determined between underperformance and neuropsychological test performance on therapy outcomes. RESULTS: Underperformance was associated to worse neuropsychological test performance, but there were no significant interaction effects

				of these two factors by therapy on fatigue severity, functional impairments and physical limitations, but there was a significant main effect of underperformance on functional impairments, physical limitations and dropout rates. CONCLUSION: Underperformance or neuropsychological test performance was not related to the change in fatigue, functional impairments, and physical limitations following CBT for CFS. However, underperforming patients did drop out more often. Therapists should pay attention to beliefs and behavioral or environmental factors that might maintain underperformance and increase the risk of dropout.
Goodwin L, White PD, Hotopf M, Stansfeld SA, Clark C.	Centre for Psychiatry, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, Wolfson Institute of Preventive Medicine, Charterhouse Square, London EC1M 6BQ, UK. l.goodwin@qmul.ac.uk	Life course study of the etiology of self-reported irritable bowel syndrome in the 1958 British birth cohort.	Psychosom Med. 2013 Feb;75(2):202-10. doi: 10.1097/PSY.0b013e31827c351b. Epub 2013 Jan 16.	OBJECTIVE: Irritable bowel syndrome (IBS) is a common gastrointestinal disorder with unknown etiology. This is the first study to use a life course approach to examine premorbid risk markers for self-reported IBS in a UK birth cohort. METHODS: Cohort study using the 1958 British birth cohort, which included 98.7% of births in 1 week in England, Wales, and Scotland. The outcome was self-reported IBS by the age of 42 years, classified with onset after 24 years and onset after 34 years. Childhood psychopathology was assessed by the Rutter scales, and adulthood psychopathology was assessed by the Malaise Inventory. RESULTS: The prevalence of self-reported IBS in this cohort was 8.4% by 42 years (95% confidence interval [CI]=8.2-8.6). In multivariate analyses, being female (odds ratio [OR]=2.00, 95% CI=1.67-2.36), reporting 1 week to 1 month of school absence for ill health at 16 years (OR=1.27, 95% CI=1.03-1.56) and psychopathology at 23 years (OR=1.25, 95% CI=1.01-1.54) and 33 years (OR=2.20, 95% CI=1.74-2.76) were associated with an increased odds for IBS. Prospectively measured childhood adversity showed no significant association. CONCLUSIONS: This is the first study to show a long-term prospective link between premorbid psychopathology and later self-reported IBS, in agreement with previous findings on chronic fatigue syndrome. There is no evidence that prospective measures of childhood adversity are risk markers for IBS, and there is weak evidence that prospective measures of childhood illness at 16 years are risk markers for IBS, differing to results from the same cohort for psychopathology, chronic fatigue syndrome, and chronic widespread pain. This study also does not replicate the findings of retrospective studies examining the etiology of IBS.
Gotts ZM, Deary V, Newton J, Van der Dussen D, De Roy P, Ellis JG.	Northumbria Centre for Sleep Research, Department of Psychology, Northumbria University, Newcastle, UK.	Are there sleep-specific phenotypes in patients with chronic fatigue syndrome? A cross-sectional polysomnography analysis.	BMJ Open. 2013 Jun 20; 3(6). pii: e002999. doi: 10.1136/bmjopen-2013-002999.	OBJECTIVES: Despite sleep disturbances being a central complaint in patients with chronic fatigue syndrome (CFS), evidence of objective sleep abnormalities from over 30 studies is inconsistent. The present study aimed to identify whether sleep-specific phenotypes exist in CFS and explore objective characteristics that could differentiate phenotypes, while also being relevant to routine clinical practice. DESIGN: A cross-sectional, single-site study. SETTING: A fatigue clinic in the Netherlands. PARTICIPANTS: A consecutive series of 343 patients meeting the criteria for CFS, according to the Fukuda definition. MEASURES: Patients underwent a single night of polysomnography (all-night recording of EEG, electromyography, electrooculography, ECG and respiration) that was hand-scored by a researcher blind to diagnosis and

				patient history. RESULTS: Of the 343 patients, 104 (30.3%) were identified with a Primary Sleep Disorder explaining their diagnosis. A hierarchical cluster analysis on the remaining 239 patients resulted in four sleep phenotypes being identified at saturation. Of the 239 patients, 89.1% met quantitative criteria for at least one objective sleep problem. A one-way analysis of variance confirmed distinct sleep profiles for each sleep phenotype. Relatively longer sleep onset latencies, longer Rapid Eye Movement (REM) latencies and smaller percentages of both stage 2 and REM characterised the first phenotype. The second phenotype was characterised by more frequent arousals per hour. The third phenotype was characterised by a longer Total Sleep Time, shorter REM Latencies, and a higher percentage of REM and lower percentage of wake time. The final phenotype had the shortest Total Sleep Time and the highest percentage of wake time and wake after sleep onset. CONCLUSIONS: The results highlight the need to routinely screen for Primary Sleep Disorders in clinical practice and tailor sleep interventions, based on phenotype, to patients presenting with CFS. The results are discussed in terms of matching patients' self-reported sleep to these phenotypes in clinical practice.
Groeger D, O'Mahony L, Murphy EF, Bourke JF, Dinan TG, Kiely B, Shanahan F, Quigley EM.	Alimentary Health Ltd., Cork, Ireland.	Bifidobacterium infantis 35624 modulates host inflammatory processes beyond the gut.	Gut Microbes. 2013 Jul-Aug; 4(4):325-39. doi: 10.4161/gmic.25487. Epub 2013 Jun 21.	Certain therapeutic microbes, including Bifidobacteria infantis (B. infantis) 35624 exert beneficial immunoregulatory effects by mimicking commensal-immune interactions; however, the value of these effects in patients with non-gastrointestinal inflammatory conditions remains unclear. In this study, we assessed the impact of oral administration of B. infantis 35624, for 6-8 weeks on inflammatory biomarker and plasma cytokine levels in patients with ulcerative colitis (UC) (n = 22), chronic fatigue syndrome (CFS) (n = 48) and psoriasis (n = 26) in three separate randomized, double-blind, placebo-controlled interventions. Additionally, the effect of B. infantis 35624 on immunological biomarkers in healthy subjects (n = 22) was assessed. At baseline, both gastrointestinal (UC) and non-gastrointestinal (CFS and psoriasis) patients had significantly increased plasma levels of C-reactive protein (CRP) and the pro-inflammatory cytokines tumor necrosis factor α (TNF-α) and interleukin-6 (IL-6) compared with healthy volunteers. B. infantis 35624 feeding resulted in reduced plasma CRP levels in all three inflammatory disorders compared with placebo. Interestingly, plasma TNF-α was reduced in CFS and psoriasis while IL-6 was reduced in UC and CFS. Furthermore, in healthy subjects, LPS-stimulated TNF-α and IL-6 secretion by peripheral blood mononuclear cells (PBMCs) was significantly reduced in the B. infantis 35624-treated groups compared with placebo following eight weeks of feeding. These results demonstrate the ability of this microbe to reduce systemic pro-inflammatory biomarkers in both gastrointestinal and non-gastrointestinal conditions. In conclusion, these data show that the immunomodulatory effects of the microbiota in humans are not limited to the mucosal immune system but extend to the systemic immune system.
Grover S, Kate N.	Department of	Somatic symptoms in	Int Rev Psychiatry. 2013 Feb;	In medically ill patients the term 'somatic symptoms' is used to understand those

	Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India. drsandeepg2002@yahoo.com	consultation-liaison psychiatry.	25(1):52-64. doi: 10.3109/09540261.2012.727786.	symptoms which cannot be fully understood in the light of existing medical illness(es). These include a number of physical symptoms and also certain clinical syndromes such as irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome among others. However, it is increasingly recognized that such patients have larger degrees of psychological morbidities, especially depressive and anxiety disorders, and have disproportionately elevated rates of medical care utilization, including outpatient visits, hospitalizations and total healthcare costs. In view of this psychological morbidity, significant distress and functional impairment, the role of the consultation-liaison psychiatrist is prominent in the management of these patients. A consultation-liaison (CL) psychiatrist is expected to be part of the primary care team to manage patient with unexplained SS, and at the same time is expected to guide colleagues to practice a patient-centred approach to improve the outcome of patients with such symptoms. The clinical work of a CL psychiatrist involves evaluation of patients with medically unexplained symptoms for probable psychiatric disorders and treatment of psychiatric morbidity and also management of patients without psychiatric morbidity. Management strategies include reattribution, cognitive behaviour therapy and antidepressants, with each strategy showing varying degrees of success.
Haley RW, Charuvastra E, Shell WE, Buhner DM, Marshall WW, Biggs MM, Hopkins SC, Wolfe GI, Vernino S.	Epidemiology Division, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX 75390-8874, USA. robert.haley@UTSouthwestern.edu	Cholinergic autonomic dysfunction in veterans with Gulf War illness: confirmation in a population-based sample.	JAMA Neurol. 2013 Feb; 70(2):191-200. doi: 10.1001/jamaneurol.2013.596. Comment in JAMA Neurol. 2013 Feb; 70(2):158-9.	BACKGROUND: The authors of prior small studies raised the hypothesis that symptoms in veterans of the 1991 Gulf War, such as chronic diarrhea, dizziness, fatigue, and sexual dysfunction, are due to cholinergic autonomic dysfunction. OBJECTIVE: To perform a confirmatory test of this prestated hypothesis in a larger, representative sample of Gulf War veterans. DESIGN: Nested case-control study. SETTING: Clinical and Translational Research Center, University of Texas Southwestern Medical Center, Dallas. PARTICIPANTS: Representative samples of Gulf War veterans meeting a validated case definition of Gulf War illness with 3 variants (called syndromes 1-3) and a control group, all selected randomly from the US Military Health Survey. MAIN OUTCOME MEASURES: Validated domain scales from the Autonomic Symptom Profile questionnaire, the Composite Autonomic Severity Score, and high-frequency heart rate variability from a 24-hour electrocardiogram. RESULTS: The Autonomic Symptom Profile scales were significantly elevated in all 3 syndrome groups (P< .001), primarily due to elevation of the orthostatic intolerance, secretomotor, upper gastrointestinal dysmotility, sleep dysfunction, urinary, and autonomic diarrhea symptom domains. The Composite Autonomic Severity Score was also higher in the 3 syndrome groups (P= .045), especially in syndrome 2, primarily due to a significant reduction in sudomotor function as measured by the Quantitative Sudomotor Axon Reflex Test, most significantly in the foot; the score was intermediate in the ankle and upper leg and was nonsignificant in the arm, indicating a peripheral nerve length-related deficit. The normal increase in high-frequency heart rate variability at night was absent or blunted in all 3 syndrome groups (P< .001). CONCLUSION: Autonomic symptoms are associated with objective, predominantly

				cholinergic autonomic deficits in the population of Gulf War veterans.
Hannan LM, Dominelli GS, Chen YW, Darlene Reid W, Road J.	Institute for Breathing and Sleep, Austin Hospital, Heidelberg, Victoria, Australia; University of Melbourne, Medicine, Dentistry and Health Sciences, Melbourne, Victoria, Australia; University of British Columbia, Respiratory Division and Department of Medicine, Vancouver, British Columbia, Canada. Electronic address: liamhannan1@yahoo.com.au.	Systematic review of non-invasive positive pressure ventilation for chronic respiratory failure.	Respir Med. 2013 Nov 20. Pii: S0954-6111(13)00451-4. doi: 10.1016/j.rmed.2013.11.010. [Epub ahead of print]	BACKGROUND: This systematic review examined the effect of non-invasive positive pressure ventilation (NIPPV) on patient reported outcomes (PROs) and survival for individuals with or at risk of chronic respiratory failure (CRF). METHODS: Randomised controlled trials (RCTs) and prospective non-randomised studies in those treated with NIPPV for CRF were identified from electronic databases, reference lists and grey literature. Diagnostic groups included in the review were amyotrophic lateral sclerosis/motor neuron disease (ALS/MND), Duchenne muscular dystrophy (DMD), restrictive thoracic disease (RTD) and obesity hypoventilation syndrome (OHS). RESULTS: Eighteen studies were included and overall study quality was weak. Those with ALS/MND had improved somnolence and fatigue as well as prolonged survival with NIPPV. For OHS, improvements in somnolence and fatigue, dyspnoea and sleep quality were demonstrated, while for RTD, measures of dyspnoea, sleep quality, physical function and health, mental and emotional health and social function improved. There was insufficient evidence to form conclusions regarding the effect of NIPPV for those with DMD. CONCLUSIONS: This review has demonstrated that NIPPV influences PROs differently depending on the underlying cause of CRF. These findings may provide assistance to patients and clinicians to determine the relative costs and benefits of NIPPV therapy and also highlight areas in need of further research.
Häuser W, Urrútia G, Tort S, Uçeyler N, Walitt B.	Psychosomatic Medicine and Psychotherapy,Technische Universität München, München, Germany.whaeuser@klinikum-saarbruecken.de	Serotonin and noradrenaline reuptake inhibitors (SNRIs) for fibromyalgia syndrome.	Cochrane Database Syst Rev. 2013 Jan 31;1: CD010292. doi: 10.1002/14651858.CD010292.	BACKGROUND: Fibromyalgia syndrome (FMS) is a clinically well-defined chronic condition of unknown etiology characterized by chronic widespread pain that often co-exists with sleep disturbances, cognitive dysfunction and fatigue. Patients often report high disability levels and poor quality of life (QOL). Drug therapy focuses on reducing key symptoms and improving quality of life. OBJECTIVES: To assess the benefits and harms of serotonin and noradrenaline reuptake inhibitors (SNRIs) compared with placebo for treating FMS symptoms in adults. SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), (The Cochrane Library 2012, Issue 9), MEDLINE (1966 to September 2012), EMBASE (1980 to September 2012), www.clinicalstudyresults.org (U.S.-marketed pharmaceuticals) (to September 2012) and www.clinicaltrials.gov (to September 2012) for published and ongoing trials and examined the reference lists of reviewed articles. SELECTION CRITERIA: We selected randomized, controlled trials of any formulation of SNRIs against placebo for the treatment of FMS in adults. DATA COLLECTION AND ANALYSIS: Two review authors independently extracted the data from the included studies, and assessed the risks of bias of the studies. Discrepancies were resolved by discussion. MAIN RESULTS: Ten studies were included with a total of 6038 participants. Five studies investigated duloxetine against placebo, and five investigated milnacipran against placebo. A total of 3611 participants were included into duloxetine or

				milnacipran groups and 2427 participants into placebo groups. The studies had a low risk of bias in general. Duloxetine and milnacipran had a small incremental effect over placebo in reducing pain (standardized mean difference (SMD) -0.23; 95% confidence interval (CI) -0.29 to -0.18; 6.1% relative improvement). One-hundred and ninety-two participants per 1000 on placebo reported an at least 50% pain reduction compared to 280 per 1000 on SNRIs (Risk ratio (RR) 1.49, 95% CI 1.35 to 1.64; number needed to treat to benefit (NNTB) 11, 95% CI 9 to 15). Duloxetine and milnacipran did not reduce fatigue substantially (SMD -0.14; 95% CI -0.19 to -0.08; 2.5% relative improvement; NNTB 17, 95% CI 12 to 29), and did not improve QOL substantially (SMD -0.20; 95% CI -0.25 to -0.14; 4.6% relative improvement; NNTB 12, 95% CI 9 to 17) compared to placebo. There were no statistically significant differences between either duloxetine or milnacipran and placebo in reducing sleep problems (SMD -0.07; 95% CI -0.16 to 0.03; 2.5% relative improvement). One-hundred and seven participants per 1000 on placebo dropped out due to adverse events compared to 196 per 1000 on SNRIs. The dropout rate due to adverse events in the duloxetine and milnacipran groups was statistically significantly higher than in placebo groups (RR 1.83, 95% CI 1.53 to 2.18; number needed to treat to harm (NNTH) 11, 95% CI 9 to 13). There was no statistically significant difference in serious adverse events between either duloxetine or milnacipran and placebo (RR 0.78, 95% CI 0.55 to 1.12). AUTHORS' CONCLUSIONS: The SNRIs duloxetine and milnacipran provided a small incremental benefit over placebo in reducing pain. The superiority of duloxetine and milnacipran over placebo in reducing fatigue and limitations of QOL was not substantial. Duloxetine and milnacipran were not superior to placebo in reducing sleep problems. The dropout rates due to adverse events were higher for duloxetine and milnacipran than for placebo. The most frequently reported symptoms leading to stopping medication were nausea, dry mouth, constipation, headache, somnolence/dizziness and insomnia. Rare complications of both drugs may include suicidality, liver damage, abnormal bleeding, elevated blood pressure and urinary hesitation.
Hawkins RA.	Boonshoft School of Medicine at Wright State University in Dayton, Ohio, USA. bob.hawkins@khnetwork.org	Fibromyalgia: a clinical update.	J Am Osteopath Assoc. 2013 Sep; 113(9):680-9. doi: 10.7556/jaoa.2013.034.	Fibromyalgia is a common chronic syndrome defined by core symptoms of widespread pain, fatigue, and sleep disturbance. Other common symptoms include cognitive difficulty, headache, paresthesia, and morning stiffness. Fibromyalgia is increasingly understood as 1 of several disorders that are referred to as central sensitivity syndromes; these disorders share underlying causes and clinical features. Tender points are often detected in patients with fibromyalgia and were formerly required for diagnosis. Newly proposed criteria, however, rely on patients' reports of widespread pain and other somatic symptoms to establish the diagnosis of fibromyalgia. The management of fibromyalgia requires a multidimensional approach including patient education, cognitive behavioral therapy, exercise, and pharmacologic therapy. The present review provides an update on these various aspects of treating a patient with fibromyalgia.

He J, Hollingsworth KG, Newton JL, Blamire AM.	Institute of Cellular Medicine & Newcastle Magnetic Resonance Centre, Newcastle University, Newcastle upon Tyne, United Kingdom.	Cerebral vascular control is associated with skeletal muscle pH in chronic fatigue syndrome patients both at rest and during dynamic stimulation.	Neuroimage Clin. 2013 Jan 5; 2:168-73. doi: 10.1016/j.nicl.2012.12.006.	Cerebral blood flow (CBF) is maintained despite changing systemic blood pressure through cerebral vascular control, with such tight regulation believed to be under local tissue control. Chronic fatigue syndrome (CFS) associates with a wide range of symptoms, including orthostatic intolerance, skeletal muscle pH abnormalities and cognitive impairment. CFS patients are known to have reduced CBF and orthostatic intolerance associates with abnormal vascular regulation, while skeletal muscle pH abnormalities associate with autonomic dysfunction. These findings point to autonomic dysfunction as the central feature of CFS, and cerebral vascular control being influenced by factors outside of the brain, a macroscopic force affecting the stability of regional regulation. We therefore explored whether there was a physiological link between cerebral vascular control and skeletal muscle pH management in CFS. Seventeen consecutive CFS patients fulfilling the Fukuda criteria were recruited from our local CFS clinical service. To probe the static scenario, CBF and skeletal muscle pH were measured at rest using MRI and (31)P magnetic resonance spectroscopy ((31)P-MRS). To examine dynamic control, brain functional MRI was performed concurrently with Valsalva manoeuvre (VM), a standard autonomic function challenge, while (31) P-MRS was performed during plantar flexion exercise. Significant inverse correlation was seen between CBF and skeletal muscle pH at rest ($r = - 0.67$, $p < 0.01$). Prolonged cerebral vascular constriction during the sympathetic phase of VM was associated with higher pH in skeletal muscle after plantar flexion exercise ($r = 0.69$, $p < 0.008$). In conclusion, cerebral vascular control is closely related to skeletal muscle pH both at rest and after dynamic stimulation in CFS.
Heins M, Knoop H, Nijs J, Feskens R, Meeus M, Moorkens G, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. m.heins@nkcv.umcn.nl	Influence of symptom expectancies on stair-climbing performance in chronic fatigue syndrome: effect of study context.	Int J Behav Med. 2013 Jun; 20(2):213-8. doi: 10.1007/s12529-012-9253-2.	BACKGROUND: In patients with chronic fatigue syndrome (CFS), performance of physical activities may be affected by an anticipated increase in symptoms after these activities. Nijs et al. previously studied the influence of symptom expectancies and related psychological processes on the performance of an isolated physical activity [Nijs J, Meeus M, Heins M, Knoop H, Moorkens G, Bleijenberg G. Kinesiophobia, catastrophizing and anticipated symptoms before stair climbing in chronic fatigue syndrome: an experimental study. Disabil Rehabil 2012. doi: 10.3109/09638288.2011.641661 .]. PURPOSE: We aimed to validate the previous findings in a larger group of patients in a different setting. We also extended the possible underlying psychological processes studied. METHOD: In 49 CFS patients, we measured performance (duration and increase in heart rate) during self-paced climbing and descending of two floors of stairs. Before this task, patients rated experienced fatigue and anticipated fatigue after stair climbing. In addition, kinesiophobia, catastrophising and focusing on bodily symptoms were measured. Using correlational and regression analyses, we tested whether performance during stair climbing could be explained by experienced and anticipated fatigue and psychological factors. RESULTS: Longer duration of stair climbing correlated with

				higher anticipated fatigue, independently of sex, age, body mass index and fatigue before stair climbing. Focusing on bodily symptoms and fatigue-related catastrophising were related to anticipated fatigue. CONCLUSION: Symptom expectations affect the performance of physical activity in CFS patients, possibly through focusing on bodily symptoms and catastrophising. These findings partially contradict the findings of the previous study, which stresses the importance of study context in conducting this type of experiments (i.e., patient characteristics, instructions).
Heins MJ, Knoop H, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, 4628, PO Box 9101, 6500 HB Nijmegen, The Netherlands. m.heins@nkcv.umcn.nl	The role of the therapeutic relationship in cognitive behaviour therapy for chronic fatigue syndrome.	Behav Res Ther. 2013 Jul; 51(7):368-76. doi: 10.1016/j.brat.2013.02.001. Epub 2013 Apr	Cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) can reduce fatigue and impairment. Recently, it was found that changes in fatigue-perpetuating factors, i.e. focusing on symptoms, control over fatigue, perceived activity and physical functioning, are associated with and explain up to half of the variance in fatigue during CBT for CFS. The therapy relationship, e.g. outcome expectations and working alliance, may also contribute to treatment outcome. We aimed to examine the role of the therapy relationship in CBT and determine whether it exerts its effect independently of changes in fatigue-perpetuating factors. We used a cohort of 217 CFS patients in which the pattern of change in fatigue-perpetuating factors was examined previously. Fatigue, therapy relationship and fatigue-perpetuating factors were measured at the start of therapy, three times during CBT and at the end of therapy. Baseline outcome expectations and agreement about the content of therapy predicted post therapy fatigue. A large part of the variance in post-treatment fatigue (25%) was jointly explained by outcome expectations, working alliance and changes in fatigue-perpetuating factors. From this, we conclude that positive outcome expectations and task agreement seem to facilitate changes in fatigue-perpetuating factors during CBT for CFS. It is therefore important to establish a positive therapy relationship early in therapy.
Heins MJ, Knoop H, Burk WJ, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands. m.heins@nkcv.umcn.nl	The process of cognitive behaviour therapy for chronic fatigue syndrome: which changes in perpetuating cognitions and behaviour are related to a reduction in fatigue?	J Psychosom Res. 2013 Sep;75(3):235-41. doi: 10.1016/j.jpsychores.2013.06.034. Epub 2013 Jul 19.	OBJECTIVE: Cognitive behaviour therapy (CBT) can significantly reduce fatigue in chronic fatigue syndrome (CFS), but little is known about the process of change taking place during CBT. Based on a recent treatment model (Wiborg et al. J Psych Res 2012), we examined how (changes in) cognitions and behaviour are related to the decrease in fatigue. METHODS: We included 183 patients meeting the US Centers for Disease Control criteria for CFS, aged 18 to 65 years, starting CBT. We measured fatigue and possible process variables before treatment; after 6, 12 and 18 weeks; and after treatment. Possible process variables were sense of control over fatigue, focusing on symptoms, self-reported physical functioning, perceived physical activity and objective (actigraphic) physical activity. We built multiple regression models, explaining levels of fatigue during therapy by (changes in) proposed process variables. RESULTS: We observed large individual variation in the patterns of change in fatigue and process variables during CBT for CFS. Increases in the sense of control over fatigue, perceived activity and self-reported physical functioning, and decreases in

				focusing on symptoms explained 20 to 46% of the variance in fatigue. An increase in objective activity was not a process variable. CONCLUSION: A change in cognitive factors seems to be related to the decrease in fatigue during CBT for CFS. The pattern of change varies considerably between patients, but changes in process variables and fatigue occur mostly in the same period.
Hempel HA, Burns KH, De Marzo AM, Sfanos KS.	Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA.	Infection of Xenotransplanted Human Cell Lines by Murine Retroviruses: A Lesson Brought Back to Light by XMRV.	Front Oncol. 2013 Jun 17; 3:156. doi: 10.3389/fonc.2013.00156. eCollection 2013.	Infection of xenotransplanted human cells by xenotropic retroviruses is a known phenomenon in the scientific literature, with examples cited since the early 1970s. However, arguably, until recently, the importance of this phenomenon had not been largely recognized. The emergence and subsequent debunking of Xenotropic Murine leukemia virus-Related Virus (XMRV) as a cell culture contaminant as opposed to a potential pathogen in several human diseases, notably prostate cancer and Chronic Fatigue Syndrome, highlighted a potential problem of murine endogenous gammaretroviruses infecting commonly used human cell lines. Subsequent to the discovery of XMRV, many additional cell lines that underwent xenotransplantation in mice have been shown to harbor murine gammaretroviruses. Such retroviral infection poses the threat of not only confounding experiments performed in these cell lines via virus-induced changes in cellular behavior but also the potential infection of other cell lines cultured in the same laboratory. Thus, the possibility of xenotropic retroviral infection of cell lines may warrant additional precautions, such as periodic testing for retroviral sequences in cell lines cultured in the laboratory.
Henningsen P, Martin A.	Klinik für Psychosomatische Medizin und Psychotherapie, Klinikum rechts der Isar der TU München. p.henningsen@tum.de	Chronic fatigue syndrome. [Article in German]	Dtsch Med Wochenschr. 2013 Jan;138(1-2):33-8. doi: 10.1055/s-0032-1327358. Epub 2012 Dec 18.	Enduring and disabling fatigue that cannot be explained by a known disease is the main characteristic of chronic fatigue syndrome. Several definitions do exist, and classification approaches vary regarding supplementary symptoms, time course, and by implicit concepts of aetiology. CFS can be considered as a functional somatic syndrome, e.g. supported by the high rates of comorbid bodily complaints and syndromes that lack clear medical explanation. Accordingly the diagnostic process should not be limited to the thorough physical examination, but also address additional somatic complaints, psychosocial factors (specifically subjective illness beliefs), and impairments. Recently German medical and psychological societies provided treatment guidelines for functional somatic syndromes. Cognitive behavioural therapy and graded activity are evidence based treatment methods for CFS.
Hossenbaccus Z, White PD.	Barts and The London School of Medicine and Dentistry, Queen Mary University London, London, UK.	Views on the nature of chronic fatigue syndrome: content analysis.	JRSM Short Rep. 2013 Jan; 4(1):4. doi: 10.1258/shorts.2012.012051. Epub 2013 Jan 14.	OBJECTIVES: Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME), has provoked much controversy and led to arguments between the medical profession and patient organizations. A particular focus for debate is the categorization of the condition as physical or psychological in its nature. The aim of this study was to compare how the written media, patient organizations and medical authorities regard the illness. DESIGN: Content analysis of newspaper articles, ME patient organization websites, and medical websites and textbooks were assessed by two independent assessors. SETTING: Three national UK newspapers, UK

				ME websites, and UK medical websites and textbooks, were accessed during 2010. PARTICIPANTS: 146 source files were scored from 36 patients' organizations, 72 media articles and 38 medical authorities. MAIN OUTCOME MEASURED: The overall opinion of an article or website was rated using a five point Likert scale, from 'extremely psychological' (scored as 1), 'moderately psychological' (2), 'both psychological and physical' (3), 'moderately physical' (4) or 'extremely physical' (5). RESULTS: Eighty-nine percent (32 of 36) of ME patient organizations considered the illness to be physical, compared with 58% (42/72) of newspaper articles, and 24% (9/38) of medical authorities. Sixty-three percent (24/38) of medical authorities regarded the illness as both physical and psychological. The inter-group differences of the Likert scores were statistically significant ($\chi(2) = 27.37$, 2 df, $P < 0.001$). CONCLUSION: The considerable disagreement, particularly between ME patient organizations and medical authorities, may help to explain the gulf in understanding between doctors and patients and the consequent reluctance of some patients to engage in behavioural treatments.
Hou R (1), Moss-Morris R (2), Risdale A (3), Lynch J(4), Jeevaratnam P (1), Bradley BP(3), Mogg K(3).	(1)Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, United Kingdom. (2) Health Psychology Section, Psychology Department, Institute of Psychiatry, King's College London, London Bridge, London SE1 9RT, United Kingdom. Electronic address: rona.moss-morris@kcl.ac.uk. (3) Psychology, University of Southampton, Southampton, United Kingdom. (4)University of Southampton, Primary Medical Care, Aldermoor Health Centre, Southampton, United Kingdom.	Attention processes in chronic fatigue syndrome: Attentional bias for health-related threat and the role of attentional control.	Behav Res Ther. 2014 Jan; 52:9-16. doi: 10.1016/j.brat.2013.10.005. Epub 2013 Oct 24.	Cognitive behavioural models of chronic fatigue syndrome (CFS) propose that attention processes, specifically, enhanced selective attention to health-threat related cues may play an important role in symptom maintenance. The current study investigated attentional bias towards health-threat stimuli in CFS. It also examined whether individuals with CFS have impaired executive attention, and whether this was related to attentional bias. 27 participants with CFS and 35 healthy controls completed a Visual Probe Task measuring attentional bias, and an Attention Network Test measuring executive attention, alerting and orienting. Participants also completed self-report measures of CFS and mood symptoms. Compared to the control group, the CFS group showed greater attentional bias for health-threat words than pictures; and the CFS group was significantly impaired in executive attention. Furthermore, CFS individuals with poor executive attention showed greater attentional bias to health-threat related words, compared not only to controls but also to CFS individuals with good executive attention. Thus, this study revealed a significant relationship between attentional bias and executive attention in CFS: attentional bias to threat was primarily evident in those with impaired executive attention control. Taking account of individual differences in executive attention control in current intervention models may be beneficial for CFS.

House A.	University of Leeds, Leeds LS2 9LJ, UK.	What's the problem with sharing research committee's discussions?	BMJ. 2013 Sep 25 ;347: f5740. doi: 10.1136/bmj.f5740.	Comment on BMJ. 2013; 347: f5355.
Hughes AM, Lucas RM, McMichael AJ, Dwyer T, Pender MP, van der Mei I, Taylor BV, Valery P, Chapman C, Coulthard A, Dear K, Kilpatrick TJ, Williams D, Ponsonby AL.	National Centre for Epidemiology and Population Health, Australian National University, Canberra, Australia. annmaree.hughes@anu.edu.au	Early-life hygiene-related factors affect risk of central nervous system demyelination and asthma differentially.	Clin Exp Immunol. 2013 Jun; 172(3):466-74. doi: 10.1111/cei.12077.	The increasing prevalence of immune-related diseases, including multiple sclerosis, may be partly explained by reduced microbial burden during childhood. Within a multi-centre case-control study population, we examined: (i) the co-morbid immune diseases profile of adults with a first clinical diagnosis of central nervous system demyelination (FCD) and (ii) sibship structure in relation to an autoimmune (FCD) and an allergic (asthma) disease. FCD cases (n=282) were aged 18-59 years; controls (n=558) were matched on age, sex and region. Measures include: history of doctor-diagnosed asthma; sibling profile (number; dates of birth); and regular childcare attendance. FCD cases did not differ from controls with regard to personal or family history of allergy, but had a greater likelihood of chronic fatigue syndrome [odds ratio (OR) = 3·11; 95% confidence interval (CI) 1·11, 8·71]. Having any younger siblings showed reduced odds of FCD (OR=0·68; 95% CI: 0·49, 0·95) but not asthma (OR = 1·47; 95% CI: 0·91, 2·38). In contrast, an increasing number of older siblings was associated with reduced risk of asthma (P trend = 0·04) but not FCD (P trend=0·66). Allergies were not over-represented among people presenting with FCD. Sibship characteristics influence both FCD and asthma risk but the underlying mechanisms differ, possibly due to the timing of the putative 'sibling effect'.
Hutchinson CV, Badham SP.	College of Medicine, Biological Sciences and Psychology, University of Leicester, Leicester, Leicestershire, United Kingdom. ch190@le.ac.uk	Patterns of abnormal visual attention in myalgic encephalomyelitis.	Optom Vis Sci. 2013 Jun; 90(6):607-14. doi: 10.1097/OPX.0b013e318294c232.	PURPOSE: To experimentally assess visual attention difficulties commonly reported by those with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). METHODS: Twenty-nine ME/CFS patients and 29 controls took part in the study. Performance was assessed using the Useful Field of View (UFOV), a spatial cueing task and visual search. RESULTS: Patients and controls performed similarly on the processing speed subtest of the UFOV. However, patients exhibited marginally worse performance compared with controls on the divided attention subtest and significantly worse performance on the selective attention subtest. In the spatial cueing task, they were slower than controls to respond to the presence of the target, particularly when cues were invalid. They were also impaired, relative to controls, on visual search tasks. CONCLUSIONS: We have provided experimental evidence for ME/CFS-related difficulties in directing visual attention. These findings support the subjective reports of those with ME/CFS and could represent a potential means to improve diagnosis.
Hutchinson CV, Maltby J, Badham SP, Jason LA.	College of Medicine, Biological Sciences and Psychology, School of Psychology, University	Vision-related symptoms as a clinical feature of chronic fatigue	Br J Ophthalmol. 2014 Jan;98(1):144-5. doi: 10.1136/bjophthalmol-2013-304439. Epub 2013 Nov 1.	[No abstract given]

	of Leicester, Leicester, UK.	syndrome/myalgic encephalomyelitis? Evidence from the DePaul Symptom Questionnaire.		
Ickmans K, Clarys P, Nijs J, Meeus M, Aerenhouts D, Zinzen E, Aelbrecht S, Meersdom G, Lambrecht L, Pattyn N.	Pain in Motion Research Group (PIM), Department of Human Physiology, Vrije Universiteit Brussel, Brussels, Belgium	Association between cognitive performance, physical fitness, and physical activity level in women with chronic fatigue syndrome.	J Rehabil Res Dev. 2013;50 (6):795-810. doi: 10.1682/JRRD.2012.08.0156.	Limited scientific evidence suggests that physical activity is directly related to cognitive performance in patients with chronic fatigue syndrome (CFS). To date, no other study has examined the direct relationship between cognitive performance and physical fitness in these patients. This study examined whether cognitive performance and physical fitness are associated in female patients with CFS and investigated the association between cognitive performance and physical activity level (PAL) in the same study sample. We hypothesized that patients who performed better on cognitive tasks would show increased PALs and better performance on physical tests. The study included 31 women with CFS and 13 healthy inactive women. Participants first completed three cognitive tests. Afterward, they undertook a test to determine their maximal handgrip strength, performed a bicycle ergometer test, and were provided with an activity monitor. In patients with CFS, lower peak oxygen uptake and peak heart rate were associated with slower psychomotor speed ($p < 0.05$). Maximal handgrip strength was correlated with working memory performance ($p < 0.05$). Both choice and simple reaction time were lower in patients with CFS relative to healthy controls ($p < 0.05$ and $p < 0.001$, respectively). In conclusion, physical fitness, but not PAL, is associated with cognitive performance in female patients with CFS.
Ickmans K, Meeus M, De Kooning M, Lambrecht L, Nijs J.	Pain in Motion Research Group, Department of Human Physiology and Physiotherapy, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium; Pain in Motion Research Group, Division of Musculoskeletal Physiotherapy, Department of Health Care Sciences, Artesis University College Antwerp, Antwerp, Belgium; Pain in	Recovery of upper limb muscle function in chronic fatigue syndrome with and without fibromyalgia.	Eur J Clin Invest. 2013 Nov 11. doi: 10.1111/eci.12201. [Epub ahead of print]	BACKGROUND: Chronic fatigue syndrome (CFS) patients frequently complain of muscle fatigue and abnormally slow recovery, especially of the upper limb muscles during and after activities of daily living. Furthermore, disease heterogeneity has not yet been studied in relation to recovery of muscle function in CFS. Here, we examine recovery of upper limb muscle function from a fatiguing exercise in CFS patients with (CFS+FM) and without (CFS-only) comorbid fibromyalgia and compare their results with a matched inactive control group. DESIGN: In this case-control study, 18 CFS-only patients, 30 CFS+FM patients and 30 healthy inactive controls performed a fatiguing upper limb exercise test with subsequent recovery measures. RESULTS: There was no significant difference among the three groups for maximal handgrip strength of the non-dominant hand. A significant worse recovery of upper limb muscle function was found in the CFS+FM, but not in de CFS-only group compared with the controls ($P < 0{\cdot}05$). CONCLUSIONS: This study reveals, for the first time, delayed recovery of upper limb muscle function in CFS+FM, but not in CFS-only patients. The results underline that CFS is a heterogeneous disorder suggesting that reducing the heterogeneity of the disorder in future research is important to make progress towards a better understanding and uncovering of mechanisms regarding the nature of divers impairments in these patients.

	Motion Research Group, Department of Physical Medicine and Physiotherapy, University Hospital Brussels, Brussels, Belgium.			
Ickmans K, Meeus M, De Kooning M, Lambrecht L, Pattyn N, Nijs J.	K. Ickmans, PT, MSc, Pain in Motion Research Group, Department of Human Physiology and Physiotherapy, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium; Pain in Motion Research Group, Division of Musculoskeletal Physiotherapy, Department of Health Care Sciences, Artesis University College, Antwerp, Belgium; and Pain in Motion Research Group, Department of Physical Medicine and Physiotherapy, University Hospital Brussels, Brussels, Belgium.	Can Recovery of Peripheral Muscle Function Predict Cognitive Task Performance in Chronic Fatigue Syndrome With and Without Fibromyalgia?	Phys Ther. 2013 Dec 20. [Epub ahead of print]	BACKGROUND: Both good physical and cognitive functioning have a positive influence on the execution of activities of daily living. Patients with chronic fatigue syndrome (CFS) as well as patients with fibromyalgia (FM) have marked cognitive deficits. Furthermore, a good physical and functional health status may have a positive impact on a variety of cognitive skills. A link that has already been observed in young and old healthy individuals, but in patients with CFS evidence is limited. OBJECTIVE: To examine whether recovery of upper limb muscle function could be a significant predictor of cognitive performance in patients with CFS and CFS with comorbid FM. Furthermore, this study determined whether cognitive performance is different in CFS patients with and without comorbid FM. DESIGN: A case-control design. METHODS: Eighteen patients with CFS-only, 30 patients with CFS+FM, and 30 healthy inactive controls were studied. Participants first completed three performance-based cognitive tests designed to assess selective and sustained attention, cognitive inhibition, and working memory capacity. Seven days later, they performed a fatiguing upper limb exercise test with subsequent recovery measures. RESULTS: Recovery of upper limb muscle function was found to be a significant predictor of cognitive performance in patients with CFS. Patients with CFS+FM, but not patients with CFS-only showed significantly decreased cognitive performance compared with the controls. LIMITATIONS: The cross-sectional nature of this study does not allow for inferences of causation. CONCLUSIONS: The results suggest that a better physical health status could predict better mental health in patients with CFS. Furthermore, they underline disease heterogeneity, suggesting that reducing this in future research is important to better understand and uncover mechanisms regarding the nature of diverse impairments in these patients.
Ickmans K, Meeus M, Kos D, Clarys P, Meersdom G, Lambrecht L,	Pain in Motion Research Group (PIM), Department of Human Physiology, Faculty of	Cognitive performance is of clinical importance, but is unrelated to	Clin Rheumatol. 2013 Oct; 32(10):1475-85. doi: 10.1007/s10067-013-2308-1. Epub 2013 Jun 5.	In various chronic pain populations, decreased cognitive performance is known to be related to pain severity. Yet, this relationship has not been investigated in patients with chronic fatigue syndrome (CFS). This study investigated the relationship between cognitive performance and (1) pain severity, (2) level of fatigue, and (3) self-reported

Pattyn N, Nijs J.	Physical Education and Physiotherapy, Vrije Universiteit Brussel, Building L, Pleinlaan 2, 1050, Brussels, Belgium.	pain severity in women with chronic fatigue syndrome.		symptoms and health status in women with CFS. Examining the latter relationships is important for clinical practice, since people with CFS are often suspected to exaggerate their symptoms. A sample of 29 female CFS patients and 17 healthy controls aged 18 to 45 years filled out three questionnaires (Medical Outcomes Study 36-Item Short-Form Health Survey, Checklist Individual Strength (CIS), and CFS Symptom List) and performed three performance-based cognitive tests (psychomotor vigilance task, Stroop task, and operation span task), respectively. In both groups, pain severity was not associated with cognitive performance. In CFS patients, the level of fatigue measured with the CFS Symptom List, but not with the CIS, was significantly correlated with sustained attention. Self-reported mental health was negatively correlated with all investigated cognitive domains in the CFS group. These results provide evidence for the clinical importance of objectively measured cognitive problems in female CFS patients. Furthermore, a state-like measure (CFS Symptom List) appears to be superior over a trait-like measure (CIS) in representing cognitive fatigue in people with CFS. Finally, the lack of a significant relationship between cognitive performance and self-reported pain severity suggests that pain in CFS might be unique.
Ishii A, Tanaka M, Iwamae M, Kim C, Yamano E, Watanabe Y.	Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka, 545-8585, Japan. a.ishii@med.osaka-cu.ac.jp	Fatigue sensation induced by the sounds associated with mental fatigue and its related neural activities: revealed by magnetoencephalography.	Behav Brain Funct. 2013 Jun 13;9:24. doi: 10.1186/1744-9081-9-24.	BACKGROUND: It has been proposed that an inappropriately conditioned fatigue sensation could be one cause of chronic fatigue. Although classical conditioning of the fatigue sensation has been reported in rats, there have been no reports in humans. Our aim was to examine whether classical conditioning of the mental fatigue sensation can take place in humans and to clarify the neural mechanisms of fatigue sensation using magnetoencephalography (MEG). METHODS: Ten and 9 healthy volunteers participated in a conditioning and a control experiment, respectively. In the conditioning experiment, we used metronome sounds as conditioned stimuli and two-back task trials as unconditioned stimuli to cause fatigue sensation. Participants underwent MEG measurement while listening to the metronome sounds for 6 min. Thereafter, fatigue-inducing mental task trials (two-back task trials), which are demanding working-memory task trials, were performed for 60 min; metronome sounds were started 30 min after the start of the task trials (conditioning session). The next day, neural activities while listening to the metronome for 6 min were measured. Levels of fatigue sensation were also assessed using a visual analogue scale. In the control experiment, participants listened to the metronome on the first and second days, but they did not perform conditioning session. MEG was not recorded in the control experiment. RESULTS: The level of fatigue sensation caused by listening to the metronome on the second day was significantly higher relative to that on the first day only when participants performed the conditioning session on the first day. Equivalent current dipoles (ECDs) in the insular cortex, with mean latencies of approximately 190 ms, were observed in six of eight participants after the conditioning session, although ECDs were not identified in any participant before the

				conditioning session. CONCLUSIONS: We demonstrated that the metronome sounds can cause mental fatigue sensation as a result of repeated pairings of the sounds with mental fatigue and that the insular cortex is involved in the neural substrates of this phenomenon.
Iwata K, Shimada T, Kawabata H.	Division of Infectious Diseases, Kobe University Hospital.	A case of lyme disease requiring over 1 year to diagnose at an infectious-disease clinic. [Article in Japanese]	Kansenshogaku Zasshi. 2013 Jan; 87(1):44-8.	A 42-year-old woman presenting with years of fever and vague symptoms could not be satisfactorily diagnosed in physical examination or conventional workups. She was presumptively diagnosed with chronic fatigue syndrome and treated symptomatically. Fourteen months after the initial visit, she developed left facial palsy. Lyme disease serology was positive. Four weeks of oral amoxicillin ameliorated symptoms. Only 5 to 15 cases of Lyme disease are reported annually in Japan, mostly from the northeastern-most island of Hokkaido. It may occur anywhere in Japan, however; probably is underdiagnosed. Lyme disease may cause fevers of unknown origin. Astute clinical suspicion and appropriate workups are thus needed to diagnose this infection.
Jarjour IT.	Department of Pediatrics, Clinic for Autonomic Dysfunction, Texas Children's Hospital, Houston, TX 77030-2399, USA. jarjour@bcm.edu	Postural tachycardia syndrome in children and adolescents.	Semin Pediatr Neurol. 2013 Mar; 20(1):18-26. doi: 10.1016/j.spen.2013.01.001.	Postural tachycardia syndrome is a chronic condition with frequent symptoms of orthostatic intolerance or sympathetic activation and excessive tachycardia while standing, without significant hypotension. Orthostatic symptoms include dizziness, lightheadedness, blurring of vision, near faints, weakness in legs, poor concentration, nausea, and headaches. Somatic symptoms include fatigue, sleep disorder, widespread pain, abdominal pain, and menstrual irregularities. Psychological problems may overlap with physical complaints. This review discusses the normal physiology of orthostatic change, different pathophysiological mechanisms of postural tachycardia syndrome, including hypovolemia, venous pooling, autonomic neuropathy, and hyperadrenergic responses. In addition, an outline for management tailored to the patient's clinical syndrome is presented, along with concluding thoughts on future research needs.
Jason LA, Brown A, Evans M, Sunnquist M, Newton JL.	DePaul University.	Contrasting Chronic Fatigue Syndrome versus Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Fatigue. 2013 Jun 1;1(3):168-183.	BACKGROUND: Much debate is transpiring regarding whether chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) are different illnesses. Several prior studies that compared the Fukuda et al. CFS criteria to the Canadian ME/CFS criteria found that the Canadian criteria identified patients with more functional impairments and greater physical, mental, and cognitive problems than those who met Fukuda et al. criteria.[3,4] These samples were located in the Chicago metropolitan area, so the results could not be generalized to other locations. In addition, past studies used a symptom questionnaire that was not specifically developed to tap the Canadian criteria. PURPOSE: The present comparative study of CFS and ME/CFS criteria was intended to correct the methodological problems of prior studies. METHODS: This article used data from three distinct samples to compare patients who met criteria for the ME/CFS Canadian clinical case definition [1] to those who met the Fukuda et al. CFS case definition.[2]. RESULTS: Findings indicated that fewer individuals met the Canadian criteria than the Fukuda et al.

				criteria. Those who met the Canadian criteria evidenced more severe symptoms and physical functioning impairment. CONCLUSIONS: Future research should continue to compare existing case definitions and determine which criteria best select for this illness.
Jason LA, Brown M, Brown A, Evans M, Flores S, Grant-Holler E, Sunnquist M.	Center for Community Research, DePaul University, Chicago, IL.	Center for Community Research, DePaul University, Chicago, IL.	Fatigue. 2013 Jan 14; 1(1-2):27-42. Epub 2012 Aug 8.	OBJECTIVES: Treatment approaches for patients with Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) have been controversial. This paper provides the theoretical and conceptual background for the Energy Envelope Theory to assist patients with ME/CFS and reviews evidence of its treatment efficacy. METHODS: Over a 15-year period, efforts were directed to develop a non-pharmacologic intervention that endeavored to help patients with ME/CFS self-monitor and self-regulate energy expenditures and learn to pace activities and stay within their energy envelope. CONCLUSIONS: Studies show that the energy envelope approach, which involves rehabilitation methods, helps patients with ME/CFS pace activities and manage symptoms and can significantly improve their quality of life.
Jason LA, Brown MM.	Center for Community Research, DePaul University, Chicago, IL 60614, USA. ljason@depaul.edu	Sub-typing daily fatigue progression in chronic fatigue syndrome.	J Ment Health. 2013 Feb; 22(1):4-11. doi: 10.3109/09638237.2012.670879. Epub 2012 May 1.	BACKGROUND: Activity logs involve patients writing down their activities and symptoms over 1 or more days. Aims This study sought to classify daily fatigue patterns among patients with chronic fatigue syndrome (CFS) using activity logs. METHOD: Fatigue intensity was self-reported every 30 min in a sample of 90 patients with CFS over 1 day. A cluster analysis using fatigue intensity, variability and slope was conducted. RESULTS: Three clusters emerged involving patients with different trajectories. One group evidenced high fatigue intensity, low variability, and fatigue intensity stayed the same over time. A second group had moderate fatigue intensity, high variability, and fatigue intensity decreased over time. A third group had moderate fatigue intensity, high variability, but fatigue intensity increased over time. The three clusters of patients differed on measures of actigraphy, pain and immune functioning. CONCLUSIONS: Activity logs can provide investigators and clinicians with valuable sources of data for understanding patterns of fatigue and activity among patients with CFS.
Jenewein J.	Back pain and somatisation. [Article in German] Abstract available in German from the publisher	Klinik für Psychiatrie und Psychotherapie, Universitätsspital Zürich.	Ther Umsch. 2013 Sep; 70(9):537-41. doi: 10.1024/0040-5930/a000443.	Back pain is frequently found in patients with somatoform disorders, particularly in somatisation and somatoform pain disorders. About 10 % to 20 % of patients suffering from back pain can be diagnosed with somatoform pain disorders. Additionally, up to 50 % of back pain patients suffer from other psychiatric disorders like major depression or anxiety disorders. Diagnostically, somatoform pain disorders must be distinguished from other chronic widespread pain disorders like fibromaylgia and chronic fatigue syndrome. Treatment usually consists of psychological/behavioral interventions in combination with relaxation techniques, physical activation and antidepressants
Jhamb M, Liang K, Yabes J, Steel JL, Dew MA, Shah N,	Renal-Electrolyte Division, Department of Medicine, University	Prevalence and Correlates of Fatigue in Chronic Kidney	Am J Nephrol. 2013 Dec 10; 38 (6):489-495. [Epub ahead of print]	Background: Fatigue is an important symptom to patients with advanced chronic kidney disease (CKD). The aim of this study is to examine the prevalence and severity of fatigue among non-dialysis-dependent CKD and end-stage renal disease (ESRD)

Unruh M.	of Pittsburgh, Pittsburgh, Pa., USA.	Disease and End-Stage Renal Disease: Are Sleep Disorders a Key to Understanding Fatigue?		patients, to examine the association of fatigue with subjective and objective sleep quality, and to identify other modifiable factors associated with fatigue. Methods: A cross-sectional survey of 87 non-dialysis-dependent CKD (eGFR ≤45 ml/min/1.73 m(2)) and 86 ESRD patients was done using the Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) and 36-Item Short-Form (SF-36) vitality scale. Higher FACIT-F score denoted less fatigue. Objective sleep was assessed using in-home polysomnography. Predictors of fatigue were determined using a linear regression model. Results: The mean FACIT-F score among all participants was 34.5 ± 11.0. Mean scores were similar among CKD and ESRD groups (34.25 ± 11.28 vs. 34.73 ± 10.86; p = 0.73). On univariate analyses, patients with higher levels of fatigue were more likely to have cardiovascular disease, benzodiazepine use, depressive symptoms, and slightly lower hemoglobin and serum albumin levels. There was no significant association between severity of sleep apnea and level of fatigue (Apnea Hypopnea Index 20.1 ± 27.6 vs. 20.3 ± 22.0; p = 0.69). Presence of cardiovascular disease, low serum albumin, depressive symptoms, poor subjective sleep quality, excessive daytime sleepiness and restless legs syndrome were independently associated with greater fatigue in multivariable regression models. The FACIT-F score correlated closely with the SF-36 vitality score (r = 0.81, p < 0.0001). Conclusions: Patients with advanced CKD and ESRD experience profound fatigue. Depressive symptoms, restless legs syndrome, excessive daytime sleepiness, and low albumin levels may provide targets for interventions to improve fatigue in patients with advanced CKD.
Johnston S, Brenu EW, Staines D, Marshall-Gradisnik S.	Griffith Health Institute, School of Medical Sciences, National Centre for Neuroimmunology and Emerging Diseases, Griffith University, Parklands, QLD, Australia.	The prevalence of chronic fatigue syndrome/ myalgic encephalomyelitis: a meta-analysis.	Clin Epidemiol. 2013; 5:105-10. doi: 10.2147/CLEP.S39876. Epub 2013 Mar 26.	PURPOSE: To perform a meta-analysis to examine variability among prevalence estimates for CFS/ME, according to the method of assessment used. METHODS: Databases were systematically searched for studies on CFS/ME prevalence in adults that applied the 1994 Centers for Disease Control (CDC) case definition.1 Estimates were categorized into two methods of assessment: self-reporting of symptoms versus clinical assessment of symptoms. Meta-analysis was performed to pool prevalences by assessment using random effects modeling. This was stratified by sample setting (community or primary care) and heterogeneity was examined using the I (2) statistic. RESULTS: Of 216 records found, 14 studies were considered suitable for inclusion. The pooled prevalence for self-reporting assessment was 3.28% (95% CI: 2.24-4.33) and 0.76% (95% CI: 0.23-1.29) for clinical assessment. High variability was observed among self-reported estimates, while clinically assessed estimates showed greater consistency. CONCLUSION: The observed heterogeneity in CFS/ME prevalence may be due to differences in method of assessment. Stakeholders should be cautious of prevalence determined by the self-reporting of symptoms alone. The 1994 CDC case definition appeared to be the most reliable clinical assessment tool available at the time of these studies. Improving clinical case definitions and their adoption internationally will enable better comparisons of findings and inform health systems

				about the true burden of CFS/ME.
Johnston S, Brenu EW, Staines DR, Marshall-Gradisnik S.	Griffith Health Institute, School of Medical Sciences, National Centre for Neuroimmunology and Emerging Diseases, Griffith University, Parklands, QLD, Australia. samantha.johnston3@griffithuni.edu.au	The adoption of chronic fatigue syndrome/myalgic encephalomyelitis case definitions to assess prevalence: a systematic review.	Ann Epidemiol. 2013 Jun; 23(6):371-6. doi: 10.1016/j.annepidem.2013.04.003.	PURPOSE: Prevalence estimates have been based on several case definitions of chronic fatigue syndrome (CFS). The purpose of this work is to provide a rigorous overview of their application in prevalence research. METHODS: A systematic review of primary studies reporting the prevalence of CFS since 1990 was conducted. Studies were summarized according to study design, prevalence estimates, and case definition used to ascertain cases. RESULTS: Thirty-one studies were retrieved, and eight different case definitions were found. Early estimates of CFS prevalence were based on the 1988 Centers for Disease Control and Prevention, Australian, and Oxford. The 1994 Centers for Disease Control and Prevention, however, has been adopted internationally, as a general standard. Only one study has reported prevalence according to the more recent, Canadian Consensus Criteria. Additional estimates were also found according to definitions by Ho-Yen, the 2005 Centers for Disease Control and Prevention empirical definition, and an epidemiological case definition. CONCLUSIONS: Advances in clinical case definitions during the past 10 years such as the Canadian Consensus Criteria have received little attention in prevalence research. Future assessments of prevalence should consider adopting more recent developments, such as the newly available International Consensus Criteria. This move could improve the surveillance of more specific cases found within CFS.
Karabulut GS, Beşer OF, Erginöz E, Kutlu T, Cokuğraş FÇ, Erkan T.	Department of Pediatrics, Cerrahpaşa Medical Faculty, İstanbul University, İstanbul, Turkey.	The Incidence of Irritable Bowel Syndrome in Children Using the Rome III Criteria and the Effect of Trimebutine Treatment.	J Neurogastroenterol Motil. 2013 Jan;19(1):90-3. doi: 10.5056/jnm.2013.19.1.90. Epub 2013 Jan 8.	BACKGROUND/AIMS: Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders and when compared to the vast knowledge pertaining to adults with IBS, very little is known about IBS in children and adolescents. We aimed to explore the prevalence of IBS, identify symptoms and contributing factors and also to examine the efficacy of trimebutine maleate in children and adolescents. METHODS: The study involved 345 children and adolescents (4-18 years) and parents were requested to fill in a questionnaire, Rome III criteria was used to diagnose IBS. To exclude organic disease, all patients underwent medical investigations. Half of the randomly selected IBS patients were treated with trimebutine maleate while the rest of IBS patients were not. The IBS patients were reevaluated at the end of 3 weeks. RESULTS: The prevalence of IBS according to Rome III criteria in children and adolescents was 22.6% and IBS with constipation was the predominant subtype. Back pain (OR, 6.68), headache (OR, 4.72) and chronic fatigue (OR, 3.74) were significantly higher in IBS group. The prevalence of IBS in both parents and depression in mothers was greater for the patient group than the healthy controls ($P < 0.0001$). The prevalence of functional dyspepsia in IBS group was 80.8% and was significantly higher than control group. Clinical recovery was seen in 94.9% of the trimebutine maleate group versus spontaneous recovery in 20.5% of the non-medicated group. The difference was significant ($P < 0.0001$). CONCLUSIONS: IBS is a common disorder in children and adolescents. IBS is closely associated with somatic

				and familial factors. Trimebutine maleate is effective for pediatric IBS patients.
Kartha GK, Kerr H, Shoskes DA.	Glickman Urological and Kidney Institute, Cleveland Clinic, Cleveland, Ohio, USA.	Clinical phenotyping of urologic pain patients.	Curr Opin Urol. 2013 Nov; 23 (6):560-4. doi: 10.1097/MOU.0b013e3283652a9d.	PURPOSE OF REVIEW: Urologic pain conditions such as chronic prostatitis/chronic pelvic pain syndrome, interstitial cystitis/bladder pain syndrome and chronic orchialgia are common, yet diagnosis and treatment are challenging. Current therapies often fail to show efficacy in randomized controlled studies. Lack of efficacy may be due to multifactorial causes and heterogeneity of patient presentation. Efforts have been made to map different phenotypes in patients with urologic pain conditions to tailor more effective therapies. This review will look at current literature on phenotype classification in urologic pain patients and their use in providing effective therapy. RECENT FINDINGS: There has been validation of the 'UPOINT' system (urinary symptoms, psychosocial dysfunction, organ specific findings, infection, neurologic/systemic and tenderness of muscle) to better categorize male chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis/bladder pain syndrome. Refinement of domain systems and recent cluster analysis has suggested possible central processes involved in urologic pain conditions similar to systemic pain syndromes such as fibromyalgia, chronic fatigue and irritable bowel syndrome. SUMMARY: Domain characterization of urologic pain conditions via phenotype mapping can be used to better understand causes of chronic pain and hopefully provide more effective, targeted and multimodal therapy.
Katz BZ, Jason LA.	Division of Infectious Diseases, Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine, Chicago, Illinois 60611, USA. bkatz@northwestern.edu	Chronic fatigue syndrome following infections in adolescents.	Curr Opin Pediatr. 2013 Feb; 25(1):95-102. doi: 10.1097/MOP.0b013e32835c1108.	PURPOSE OF REVIEW: To review the recent epidemiology, pathophysiology, and treatment of postinfectious chronic fatigue syndrome (CFS) in adolescents. RECENT FINDINGS: Thirteen percent of adolescents (mainly women) met the criteria for CFS 6 months following infectious mononucleosis; the figure was 7% at 12 months and 4% at 24 months. Peak work capacity, activity level, orthostatic intolerance, salivary cortisol, and natural killer cell number and function were similar between adolescents with CFS following infectious mononucleosis and recovered controls. Autonomic system, oxygen consumption, peak oxygen pulse, psychological and cytokine network differences were documented between those who recovered and those who did not. SUMMARY: The prognosis of CFS is better in adolescents than in adults. Activity level, exercise tolerance, and orthostatic testing could not distinguish patients with CFS from adolescents who have recovered from infectious mononucleosis (controls), while certain cytokine network analyses, life stress factors, and autonomic symptoms could.
Kawabata M, Ueno T, Tomita J, Kawatani J, Tomoda A, Kume S, Kume K.	[No address quoted]	Temporal organization of rest defined by actigraphy data in healthy and childhood chronic fatigue syndrome	BMC Psychiatry. 2013 Nov 4; 13(1):281. [Epub ahead of print]	BACKGROUND: Accumulating evidence has shown a universality in the temporal organization of activity and rest among animals ranging from mammals to insects. Previous reports in both humans and mice showed that rest bout durations followed long-tailed (i.e., power-law) distributions, whereas activity bouts followed exponential distributions. We confirmed similar results in the fruit fly, Drosophila melanogaster. Conversely, another report showed that the awakening bout durations, which were defined by polysomnography in bed, followed power-law distributions, while sleeping

		children.		periods, which may correspond to rest, followed exponential distributions. This apparent discrepancy has been left to be resolved. METHODS: Actigraphy data from healthy and disordered children were analyzed separately for two periods: time out of bed (UP period) and time in bed (DOWN period). RESULTS: When data over a period of 24 h were analyzed as a whole, rest bouts showed a power law distribution as previously reported. However, when UP and DOWN period data were analyzed separately, neither showed power law properties. Using a newly developed strict method, only 30% of individuals satisfied the power law criteria, even when the 24 h data were analyzed. The human results were in contrast to the Drosophila results, which revealed clear power-law distributions for both day time and night time rest through the use of a strict method. In addition, we analyzed the actigraphy data from patients with childhood type chronic fatigue syndrome (CCFS), and found that they showed differences from healthy controls when their UP and DOWN data were analyzed separately. CONCLUSIONS: These results suggested that the DOWN sleep, the bout distribution of which showed exponential properties, contributes to the production of long-tail distributions in human rest periods. We propose that separate analysis of UP and DOWN period data is important for understanding the temporal organization of activity.
Keijmel SP, Delsing CE, Sprong T, Bleijenberg G, van der Meer JW, Knoop H, Bleeker-Rovers CP.	Radboud Expertise Centre for Q fever, Department of Internal Medicine, Division of Infectious Diseases, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. s.keijmel@aig.umcn.nl	The Qure study: Q fever fatigue syndrome--response to treatment; a randomized placebo-controlled trial.	BMC Infect Dis. 2013 Mar 27; 13:157. doi: 10.1186/1471-2334-13-157.	BACKGROUND: Q fever is a zoonosis that is present in many countries. Q fever fatigue syndrome (QFS) is one of the most frequent sequelae after an acute Q fever infection. QFS is characterized by persistent fatigue following an acute Q fever infection, leading to substantial morbidity and a high socio-economic burden. The occurrence of QFS is well-documented, and has been described in many countries over the past decades. However, a treatment with proven efficacy is not available. Only a few uncontrolled studies have tested the efficacy of treatment with antibiotics on QFS. These studies suggest a positive effect of long-term treatment with a tetracycline on performance state; however, no randomized controlled trials have been performed. Cognitive behavioral therapy (CBT) has been proven to be an effective treatment modality for chronic fatigue in other diseases, but has not yet been tested in QFS. Therefore, we designed a trial to assess the efficacy of long-term treatment with the tetracycline doxycycline and CBT in patients with QFS. METHODS/DESIGN: A randomized placebo-controlled trial will be conducted. One-hundred-eighty adult patients diagnosed with QFS will be recruited and randomized between one of three groups: CBT, long-term doxycycline or placebo. First, participants will be randomized between CBT and medication (ratio 1:2). A second double-blinded randomization between doxycycline and placebo (ratio 1:1) will be performed in the medication condition. Each group will be treated for six months. Outcome measures will be assessed at baseline and post intervention. The primary outcome measure is fatigue severity. Secondary outcome measures are functional impairment, level of psychological distress, and Coxiella burnetii PCR and serology. DISCUSSION: The Qure study is the first randomized

				placebo-controlled trial, which evaluates the efficacy of long-term doxycycline and of cognitive behavioral therapy in patients with QFS. The results of this study will provide knowledge about evidence-based treatment options for adult patients with QFS. TRIAL REGISTRATION: ClinicalTrials.gov: NCT01318356, and Netherlands Trial Register: NTR2797.
Keller J, Chen YK, Lin HC.	School of Public Health, Taipei Medical University, Taipei, Taiwan.	Association of bladder pain syndrome/interstitial cystitis with urinary calculus: a nationwide population-based study.	Int Urogynecol J. 2013 Apr; 24(4):565-71. doi: 10.1007/s00192-012-1917-6. Epub 2012 Aug 16.	INTRODUCTION AND HYPOTHESIS: Although one prior study reported an association between bladder pain syndrome/interstitial cystitis (BPS/IC) and urinary calculi (UC), no population-based study to date has been conducted to explore this relationship. Therefore, using a population-based data set in Taiwan, this study set out to investigate the association between BPS/IC and a prior diagnosis of UC. METHODS: This study included 9,269 cases who had received their first-time diagnosis of BPS/IC between 2006 and 2007 and 46,345 randomly selected controls. We used conditional logistic regression analysis to compute the odds ratio (OR) and its corresponding 95 % confidence interval (CI) for having been previously diagnosed with UC between cases and controls. RESULTS: There was a significant difference in the prevalence of prior UC between cases and controls (8.1 vs 4.3 %, $p < 0.001$). Conditional logistic regression analysis revealed that cases were more likely to have been previously diagnosed with UC than controls (OR = 1.70; 95 % CI = 1.56-1.84) after adjusting for chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraine, sicca syndrome, allergy, endometriosis, and asthma. BPS/IC was found to be significantly associated with prior UC regardless of stone location; the adjusted ORs of kidney calculus, ureter calculus, bladder calculus, and unspecified calculus when compared to controls were 1.58 (95 % CI = 1.38-1.81), 1.73 (95 % CI = 1.45-2.05), 3.80 (95 % CI = 2.18-6.62), and 1.83 (95 % CI = 1.59-2.11), respectively. CONCLUSIONS: This work generates the hypothesis that UC may be associated with BPS/IC.
Keller JJ, Liu SP, Lin HC.	School of Public Health, Taipei Medical University, Taipei, Taiwan.	A case-control study on the association between rheumatoid arthritis and bladder pain syndrome/interstitial cystitis.	Neurourol Urodyn. 2013 Sep; 32(7):980-5. doi: 10.1002/nau.22348. Epub 2012 Nov 5.	AIM: While bladder pain syndrome/interstitial cystitis (BPS/IC) has been suggested by a number of studies to have autoimmune character, no population-based study to date has been conducted investigating its association with rheumatoid arthritis (RA). This study aimed to examine the association between IC/BPS and having previously been diagnosed with RA. METHODS: We conducted this study by using administrative claims data sourced from the Taiwan National Health Insurance Database. Our study included 9,269 cases with BPS/IC and 46,345 randomly selected controls. Conditional logistic regression was performed to calculate the odds ratio (OR) for the association between previously diagnosed RA and IC/BPS. RESULTS: RA was found among 202 (2.2%) cases and 504 (1.12%) controls. Conditional logistic regression analysis suggested that when compared with controls, the OR for prior RA among cases was 1.66 (95% CI=1.47-1.87, P<0.001) after adjusting for diabetes, hypertension, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraine, sicca

				syndrome, allergy, endometriosis, asthma, overactive bladder, tobacco use disorder, and alcohol abuse. Additionally, BPS/IC was consistently and significantly associated with a previous diagnosis of RA regardless of prescription drug use; the OR for prior RA among groups prescribed ≤1 type of disease-modifying antirheumatic drug (DMARD), two types of DMARDs, and ≥3 types of DMARDs or TNF-alpha inhibitor when compared to controls were 1.49 (95% CI=1.28-1.72), 1.91 (95% CI=1.38-2.68), and 2.36 (95% CI=1.77-3.17), respectively. CONCLUSIONS: There is an association between RA and BPS/IC after adjusting for socio-demographic characteristics and medical co-morbidities.
Kempke S, Luyten P, Claes S, Goossens L, Bekaert P, Van Wambeke P, Van Houdenhove B.	Department of Psychology, University of Leuven, Belgium. stefan.kempke@ppw.kuleuven.be	Self-critical perfectionism and its relationship to fatigue and pain in the daily flow of life in patients with chronic fatigue syndrome.	Psychol Med. 2013 May; 43(5):995-1002. doi: 10.1017/S0033291712001936. Epub 2012 Aug 30.	BACKGROUND: Research suggests that the personality factor of self-critical or maladaptive perfectionism may be implicated in chronic fatigue syndrome (CFS). However, it is not clear whether self-critical perfectionism (SCP) also predicts daily symptoms in CFS. Method In the present study we investigated whether SCP predicted fatigue and pain over a 14-day period in a sample of 90 CFS patients using a diary method approach. After completing the Depressive Experiences Questionnaire (DEQ) as a measure of SCP, patients were asked each day for 14 days to complete Visual Analogue Scales (VAS) of fatigue, pain and severity of depression. Data were analysed using multilevel analysis. RESULTS: The results from unconditional models revealed considerable fluctuations in fatigue over the 14 days, suggesting strong temporal variability in fatigue. By contrast, pain was relatively stable over time but showed significant inter-individual differences. Congruent with expectations, fixed-effect models showed that SCP was prospectively associated with higher daily fatigue and pain levels over the 14-day period, even after controlling for levels of depression. CONCLUSIONS: This is the first study to show that SCP predicts both fatigue and pain symptoms in CFS in the daily course of life. Hence, therapeutic interventions aimed at targeting SCP should be considered in the treatment of CFS patients with such features.
Kempke S, Luyten P, Claes S, Van Wambeke P, Bekaert P, Goossens L, Van Houdenhove B.	Department of Psychology, University of Leuven, Leuven, Belgium. stefan.kempke@ppw.kuleuven.be	The prevalence and impact of early childhood trauma in Chronic Fatigue Syndrome.	J Psychiatr Res. 2013 May; 47(5):664-9. doi: 10.1016/j.jpsychires.2013.01.021. Epub 2013 Feb 16.	: Although some studies have found high rates of early childhood trauma in Chronic Fatigue Syndrome (CFS), the role of early trauma in this condition remains controversial. METHODS: This study examined the prevalence of early childhood trauma and its impact on daily fatigue and pain levels over a 14-day period in a sample of 90 carefully screened CFS patients using a diary method approach. Data were analyzed using multilevel analysis. RESULTS: More than half of the patients (54.4%) had experienced at least one type of early trauma, with the majority of these patients reporting multiple traumas. Prevalence rates were particularly high for emotional trauma (i.e., emotional abuse and/or emotional neglect) (46.7%). Moreover, total trauma scores and emotional abuse significantly predicted higher levels of daily fatigue and pain over the 14-day period, even when controlling for demographic features and depressed mood. CONCLUSIONS: This is the first study to demonstrate that early childhood trauma predicts increasing levels of core symptoms

				of CFS in the daily flow of life. Moreover, findings of this study suggest that emotional trauma may be particularly important in CFS.
Kempke S, Van Den Eede F, Schotte C, Claes S, Van Wambeke P, Van Houdenhove B, Luyten P.	Department of Psychology, University of Leuven, Tiensestraat 102, Leuven, Belgium. Stefan.Kempke@ppw.kuleuven.be	Prevalence of DSM-IV personality disorders in patients with chronic fatigue syndrome: a controlled study.	Int J Behav Med. 2013 Jun; 20(2):219-28. doi: 10.1007/s12529-012-9273-y.	BACKGROUND: It is not yet clear whether chronic fatigue syndrome (CFS) is associated with elevated levels of personality disorders. PURPOSE: This study aims to determine the prevalence of DSM-IV axis II personality disorders among patients with CFS. METHODS: We examined the prevalence of personality disorders in a sample of 92 female CFS patients and in two well-matched control groups, i.e., normal community individuals (N=92) and psychiatric patients (N=92). Participants completed the assessment of DSM-IV personality disorders questionnaire (ADP-IV), which yields a categorical and dimensional evaluation of personality disorder features. RESULTS: The prevalence of personality disorders in CFS patients (16.3 %) was significantly lower than in psychiatric patients (58.7 %) and was similar to that in the community sample (16.3 %). Similar results were found for dimensional and pseudodimensional scores, except for the Depressive (DE) and Obsessive-Compulsive Personality Disorder (O-C) subscales. Patients with CFS had significantly higher levels of DE features compared to normal controls and similar dimensional scores on the O-C scale compared to psychiatric controls. CONCLUSIONS: Although the CFS sample was characterized by depressive and obsessive-compulsive personality features, this study provides no evidence for the assumption that these patients generally show a higher prevalence of axis II pathology. Given the conflicting findings in this area, future studies using multiple measures to assess personality disorders in CFS are needed to substantiate these findings.
Kim EH, Pascua PN, Song MS, Baek YH, Kwon HI, Park SJ, Lim GJ, Kim SM, Decano A, Lee KJ, Cho WK, Ma JY, Choi YK.	College of Medicine and Medical Research Institute, Chungbuk National University, 12 Gaeshin-Dong Henugduk-Ku, Cheongju 361-763, Republic of Korea.	Immunomodulaton and attenuation of lethal influenza A virus infection by oral administration with KIOM-C.	Antiviral Res. 2013 Jun; 98(3):386-93. doi: 10.1016/j.antiviral.2013.04.006. Epub 2013 Apr 13.	Herbal medicine is used to treat many conditions such as asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, headaches, menopausal symptoms, chronic fatigue, irritable bowel syndrome, cancer, and viral infections such as influenza. In this study, we investigated the antiviral effect of KIOM-C for the treatment of influenza A virus infection. Our results show that oral administration of KIOM-C conferred a survival benefit to mice infected with the 2009 pandemic H1N1 [A(H1N1)pdm09] virus, and resulted in a 10- to 100-fold attenuation of viral replication in ferrets in a dose-dependent manner. Additionally, oral administration of KIOM-C increased the production of antiviral cytokines, including IFN-γ and TNF-α, and decreased levels of pro-inflammatory cytokines (IL-6) and chemokines (KC, MCP-1) in the Bronchoalveolar lavage fluid (BALF) of A(H1N1)pdm-infected mice. These results indicate that KIOM-C can promote clearance of influenza virus in the respiratory tracts of mice and ferrets by modulating cytokine production in hosts. Taken together, our results suggest that KIOM-C is a potential therapeutic compound mixture for the treatment of influenza virus infection in humans.
Kim JE, Hong KE, Kim HJ, Choi JB, Baek YH, Seo BK,	Department of Medical Research, Korea Institute of Oriental	An open-label study of effects of acupuncture on	Trials. 2013 May 21; 14:147. doi: 10.1186/1745-6215-14-147.	BACKGROUND: Even though chronic fatigue syndrome and idiopathic chronic fatigue are quite common, there are no clearly known causes. Most treatments are therefore symptomatic in nature, and chronic fatigue syndrome and idiopathic chronic fatigue

Lee S, Kang KW, Lee MH, Kim JH, Lee S, Jung SY, Jung HJ, Shin MS, Choi SM.	Medicine, Acupuncture, Moxibustion & Meridian Research Group, 1672 Yuseongdae-ro, Yuseong-gu, Daejeon, South Korea.	chronic fatigue syndrome and idiopathic chronic fatigue: study protocol for a randomized controlled trial.		patients are highly interested in using oriental medicine or complementary and alternative medicine treatment. Acupuncture, one of the major treatments used in oriental medicine, is effective in treating various diseases. This study will attempt to analyze the effectiveness and safety of acupuncture in the treatment of chronic fatigue by comparing the two treatment groups (body acupuncture, Sa-am acupuncture) and the control group (usual care). METHODS/DESIGN: This study consists of a four-center, three-arm, randomized, controlled, and open-label trial. One hundred and fifty participants are randomly divided into treatment groups A and B and a control group. The treatment groups will receive acupuncture treatments either two or three times per week for a total of 10 sessions over a period of 4 weeks. The control group will not receive acupuncture treatments and will continue their usual care during this period. The primary outcome variable is the Fatigue Severity Scale, which will be utilized 5 weeks after randomization. Secondary outcome variables are the Fatigue Severity Scale at 13 weeks, a short form of the Stress Response Inventory, the Beck Depression Inventory, the Numeric Rating Scale, and the EuroQol-5 Dimension at 5 and 13 weeks after randomization. DISCUSSION: This study will provide evidence with high external validity on the effectiveness and safety of acupuncture as a treatment for chronic fatigue syndrome and idiopathic chronic fatigue. TRIAL REGISTRATION: Clinical Research Information Service KCT0000508.
Kindlon T.	Irish ME/CFS Association, PO Box 3075, Dublin 2, Republic of Ireland.	People want to learn as much as possible from the PACE trial for chronic fatigue syndrome.	BMJ. 2013 Sep 25; 347: f5731. doi: 10.1136/bmj.f5731.	Comment in BMJ. 013; 347: f5963.
Kingma EM, Rosmalen JG, White PD, Stansfeld SA, Clark C.	University of Groningen, University Medical Center Groningen, Department of Psychiatry, Interdisciplinary Center Psychopathology and Emotion regulation (ICPE), Groningen, The Netherlands.	The prospective association between childhood cognitive ability and somatic symptoms and syndromes in adulthood: the 1958 British birth cohort.	J Epidemiol Community Health. 2013 Dec 1;67 (12):1047-53. doi: 10.1136/jech-2013-202850. Epub 2013 Sep 10.	BACKGROUND: Cognitive ability is negatively associated with functional somatic symptoms (FSS) in childhood. Lower childhood cognitive ability might also predict FSS and functional somatic syndromes in adulthood. However, it is unknown whether this association would be modified by subjective and objective measures of parental academic expectations. METHODS: 14 068 participants from the 1958 British birth cohort, whose cognitive ability was assessed at 11 years. Outcomes were somatic symptoms at 23, 33 and 42 years. Self-reported irritable bowel syndrome (IBS), chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and operationally defined CFS-like illness were measured at 42 years. RESULTS: Lower cognitive ability at age 11 years was associated with somatic symptoms at ages 23, 33 and 42 years. Adjusting for sex, childhood internalising problems, previous somatic symptoms and concurrent psychological symptoms, childhood cognitive ability remained negatively associated with somatic symptoms at age 23 years (β=-0.060, 95% CI -0.081 to -0.039, p<0.01), 33 years (β= -0.031, 95% CI -0.050 to -0.011, p<0.01), but not with somatic symptoms at 42 years. Overall, we found no clear association between lower childhood cognitive ability and CFS/ME, CFS-like illness and IBS. Associations between

				cognitive ability and somatic symptoms at 23 years were moderated by low parental social class, but not by subjective indicators of parental academic expectations. CONCLUSIONS: Lower childhood cognitive ability predicted somatic symptoms, but not CFS/ME, CFS-like illness and IBS in adulthood. While earlier research indicated an important role for high parental academic expectations in the development of early-life FSS, these expectations do not seem relevant for somatic symptoms or functional somatic syndromes in later adulthood.
Kir'iakov VA, Saarkoppel' LM, Krylova IV, Sukhova AV.	[No address quoted]	Chronic fatigue syndrome in patients with vibration disease. [Article in Russian]	Med Tr Prom Ekol. 2013; (2):28-32.	The article presents study results that demonstrate chronic fatigue syndrome in patients with vibration disease. Clinical manifestations of chronic fatigue syndrome are characterized by changes in the emotional-volitional and cognitive areas. Application of nootropic drug cortexin increases the efficiency of rehabilitation in patients with vibration disease with chronic fatigue syndrome.
Knight S, Harvey A, Lubitz L, Rowe K, Reveley C, Veit F, Hennel S, Scheinberg A.	Clinical Sciences, Murdoch Childrens Research Institute, Melbourne, Victoria, Australia; Victorian Paediatric Rehabilitation Service, Monash Children's, Melbourne, Victoria, Australia; Department of Paediatrics, University of Melbourne, Melbourne, Victoria, Australia; Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, Victoria, Australia.	Paediatric chronic fatigue syndrome: Complex presentations and protracted time to diagnosis.	J Paediatr Child Health. 2013 Nov; 49(11):919-24. doi: 10.1111/jpc.12425. Epub 2013 Oct 31.	AIM: The diagnosis and management of paediatric chronic fatigue syndrome (CFS) remain ongoing challenges for paediatric clinicians, particularly given its unknown aetiology and the little research on effective treatments for this condition. The aim of this study was to describe the presenting features of new patients attending a specialist chronic fatigue clinic at a tertiary-level Australian children's hospital. METHOD: The medical records of all patients with an initial consultation at the chronic fatigue clinic over a 12-month period were reviewed using a standardised data collection template. Functional impact was based on school attendance and classified according to the National Institute of Health and Clinical Excellence guidelines (2007). RESULTS: A total of 99 patients attending the clinic were identified. Of these, 59 were diagnosed with CFS. Median age was 15.4 years with almost two-thirds of patients of female sex. Median time between symptom onset and diagnosis was 15.5 months. There was a high occurrence of fatigue, sleep disturbance, pain, postexertional malaise, and autonomic and cognitive symptoms in the group. The functional impact of CFS was classified as mild for 20%, moderate for 66% and severe for 14% of patients. CONCLUSIONS: Most young people diagnosed with CFS experience symptoms for a protracted period, with considerable functional impact prior to initial tertiary service consultation. This audit has identified important areas for research, practice development and education in relation to the management of patients with CFS.
Knight SJ, Scheinberg A, Harvey AR.	Murdoch Childrens Research Institute, Melbourne, Victoria, Australia. sarah.knight@mcri.edu	Interventions in pediatric chronic fatigue syndrome/myalgic encephalomyelitis: a	J Adolesc Health. 2013 Aug; 53(2):154-65. doi: 10.1016/j.jadohealth.2013.03.009. Epub 2013 May 1.	PURPOSE: A range of interventions have been used for the management of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) in children and adolescents. Currently, debate exists as to the effectiveness of these different management strategies. The objective of this review was to synthesize and critically appraise the literature on interventions for pediatric CFS/ME. METHOD: CINAHL, PsycINFO and

	.au	systematic review.		Medline databases were searched to retrieve relevant studies of intervention outcomes in children and/or adolescents diagnosed with CFS/ME. Two reviewers independently selected articles and appraised the quality on the basis of predefined criteria. RESULTS: A total of 24 articles based on 21 studies met the inclusion criteria. Methodological design and quality were variable. The majority assessed behavioral interventions (10 multidisciplinary rehabilitation; 9 psychological interventions; 1 exercise intervention; 1 immunological intervention). There was marked heterogeneity in participant and intervention characteristics, and outcome measures used across studies. The strongest evidence was for Cognitive Behavioral Therapy (CBT)-based interventions, with weaker evidence for multidisciplinary rehabilitation. Limited information exists on the maintenance of intervention effects. CONCLUSIONS: Evidence for the effectiveness of interventions for children and adolescents with CFS/ME is still emerging. Methodological inadequacies and inconsistent approaches limit interpretation of findings. There is some evidence that children and adolescents with CFS/ME benefit from particular interventions; however, there remain gaps in the current evidence base.
Kossaify A, Kallab K.	Department of Syncope and Electrophysiology, ND Secours/USEK University Hospital, Byblos, Lebanon. antoinekossaify@yahoo.com.	Neurocardiogenic syncope and associated conditions: insight into autonomic nervous system dysfunction.	Turk Kardiyol Dern Ars. 2013 Jan; 41(1):75-83. doi: 10.5543/tkda.2013.44420.	Neurocardiogenic syncope is known to be associated with autonomic nervous system dysfunction, although the mechanism has not been entirely elucidated. In this study, we sought to highlight the pathogenic role of the autonomic nervous system in neurocardiogenic syncope and to review the associated co-morbidities known to have a dysautonomic basis. Herein we discuss migraine, orthostatic hypotension, postural orthostatic tachycardia syndrome, endothelial dysfunction, chronic fatigue syndrome, and carotid sinus hypersensitivity with a focus on the pathogenic role of the autonomic nervous system and any consecutive clinical implications. Other conditions, such as pre-syncopal heart rate acceleration and/or instability and pre-syncopal breathing instability, which occur during a tilt test, are discussed in the same perspective.
Kuemmerle-Deschner JB, Haug I.	Division of Pediatric Rheumatology, Department of Pediatrics, University Children's Hospital Tuebingen, Hoppe-Seyler-Strasse 1, 72076 Tuebingen, Germany.	Canakinumab in patients with cryopyrin-associated periodic syndrome: an update for clinicians.	Ther Adv Musculoskelet Dis. 2013 Dec; 5(6):315-29. doi: 10.1177/1759720X13502629.	The cryopyrin-associated periodic syndrome (CAPS) is a very rare disease. It is estimated that there are 1-2 cases for every 1 million people in the US and 1 in every 360,000 in France. However, many patients are diagnosed very late or not at all, meaning the real prevalence is likely to be higher. CAPS encompasses the three entities of familial cold auto-inflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID)/chronic infantile neurologic, cutaneous and articular (CINCA) syndrome. They have in common a causative mutation in the NLRP3 gene. The altered gene product cryopyrin leads to activation of the inflammasome which in turn is responsible for excessive production of interleukin (IL)-1β. IL-1β causes the inflammatory manifestations in CAPS. These appear as systemic inflammation including fever, headache or fatigue, rash, eye disease, progressive sensorineural hearing loss, musculoskeletal manifestations and central nervous system (CNS) symptoms (NOMID/CINCA only). With the advent of IL-1

				Inhibitors, safe and effective therapeutic options became available for this devastating disease. To prevent severe and possible life-threatening disease sequelae, early and correct diagnosis and immediate initiation of therapy are mandatory in most patients. Canakinumab is a fully human monoclonal IgG1 anti-IL-1β antibody. It provides selective and prolonged IL-1β blockade and has demonstrated a rapid (within hours), complete and sustained response in most CAPS patients without any consistent pattern of side effects. Long-term follow-up trials have demonstrated sustained efficacy, safety and tolerability. Canakinumab is approved by the US Food and Drug Administration for FCAS and MWS and by European Medicines Agency for treatment of all three phenotypes of CAPS.
Kutner NG, Zhang R.	[No address quoted]	Frailty in dialysis-dependent patients with end-stage renal disease.	JAMA Intern Med. 2013 Jan 14; 173(1):78-9. doi: 10.1001/2013.jamainternmed.750.	Comment in JAMA Intern Med. 2013 Jan 14; 173(1):79.
Lakhan SE, Schofield KL.	Global Neuroscience Initiative Foundation, Los Angeles, California, United States of America.	Mindfulness-based therapies in the treatment of somatization disorders: a systematic review and meta-analysis.	PLoS One. 2013 Aug 26;8(8):e71834. doi: 10.1371/journal.pone.0071834.	BACKGROUND: Mindfulness-based therapy (MBT) has been used effectively to treat a variety of physical and psychological disorders, including depression, anxiety, and chronic pain. Recently, several lines of research have explored the potential for mindfulness-therapy in treating somatization disorders, including fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome. METHODS: Thirteen studies were identified as fulfilling the present criteria of employing randomized controlled trials to determine the efficacy of any form of MBT in treating somatization disorders. A meta-analysis of the effects of mindfulness-based therapy on pain, symptom severity, quality of life, depression, and anxiety was performed to determine the potential of this form of treatment. FINDINGS: While limited in power, the meta-analysis indicated a small to moderate positive effect of MBT (compared to wait-list or support group controls) in reducing pain (SMD = -0.21, 95% CI: -0.37, -0.03; p<0.05), symptom severity (SMD = -0.40, 95% CI: -0.54, -0.26; p<0.001), depression (SMD = -0.23, 95% CI: -0.40, -0.07, p<0.01), and anxiety (SMD = -0.20, 95% CI: -0.42, 0.02, p = 0.07) associated with somatization disorders, and improving quality of life (SMD = 0.39, 95% CI: 0.19, 0.59; p<0.001) in patients with this disorder. Subgroup analyses indicated that the efficacy of MBT was most consistent for irritable bowel syndrome (p<0.001 for pain, symptom severity, and quality of life), and that mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MCBT) were more effective than eclectic/unspecified MBT. CONCLUSIONS: Preliminary evidence suggests that MBT may be effective in treating at least some aspects of somatization disorders. Further research is warranted.
Langhorst J, Klose P, Dobos GJ, Bernardy K,	Department of Internal and Integrative Medicine, University of	Efficacy and safety of meditative movement therapies	Rheumatol Int. 2013 Jan; 33(1):193-207. doi: 10.1007/s00296-012-2360-1.	A systematic review with meta-analysis of the efficacy and safety of meditative movement therapies (Qigong, Tai Chi and Yoga) in fibromyalgia syndrome (FMS) was carried out. We screened Clinicaltrials.Gov, Cochrane Library, PsycINFO, PubMed and

Häuser W.	Duisburg-Essen, Kliniken Essen-Mitte, 45276 Essen, Germany. j.langhorst@kliniken-essen-mitte.de	in fibromyalgia syndrome: a systematic review and meta-analysis of randomized controlled trials.	Epub 2012 Feb 15.	Scopus (through December 2010) and the reference sections of original studies for meditative movement therapies (MMT) in FMS. Randomized controlled trials (RCT) comparing MMT to controls were analysed. Outcomes of efficacy were pain, sleep, fatigue, depression and health-related quality of life (HRQOL). Effects were summarized using standardized mean differences (SMD [95% confidence interval]). Outcomes of safety were drop out because of adverse events and serious adverse events. A total of 7 out of 117 studies with 362 subjects and a median of 12 sessions (range 8-24) were included. MMT reduced sleep disturbances (-0.61 [-0.95, -0.27]; 0.0004), fatigue (-0.66 [-0.99, -0.34]; <0.0001), depression (-0.49 [-0.76, -0.22]; 0.0004) and limitations of HRQOL (-0.59 [-0.93, -0.24]; 0.0009), but not pain (-0.35 [-0.80, 0.11]; 0.14) compared to controls at final treatment. The significant effects on sleep disturbances (-0.52 [-0.97, -0.07]; 0.02) and HRQOL (-0.66 [-1.31, -0.01]; 0.05) could be maintained after a median of 4.5 (range 3-6) months. In subgroup analyses, only Yoga yielded significant effects on pain, fatigue, depression and HRQOL at final treatment. Drop out rate because of adverse events was 3.1%. No serious adverse events were reported. MMT are safe. Yoga had short-term beneficial effects on some key domains of FMS. There is a need for high-quality studies with larger sample sizes to confirm the results.
Lattie EG, Antoni MH, Fletcher MA, Czaja S, Perdomo D, Sala A, Nair S, Fu SH, Penedo FJ, Klimas N.	Department of Psychology, University of Miami.	Beyond Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome (ME/CFS) Symptom Severity: Stress Management Skills are Related to Lower Illness Burden.	Fatigue. 2013; 1(4). doi: 10.1080/21641846.2013.843255.	BACKGROUND: The onset of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) typically involves reductions in activities of daily living and social interactions (jointly referred to as "illness burden"). Emotional distress has been linked to increased reported symptoms, and stress management skills have been related to lower fatigue severity in CFS patients. Symptom severity and illness burden are highly correlated. The ability to manage stress may attenuate this relationship, allowing individuals to feel less burdened by the illness independent of the severity of their symptoms. PURPOSE: This study aimed to evaluate if perceived stress management skills affect illness burden via emotional distress, independent of ME/CFS symptom severity. METHODS: A total of 117 adults with ME/CFS completed measures of perceived stress management skills, emotional distress, ME/CFS symptom severity and illness burden. RESULTS: Regression analyses revealed that greater perceived stress management skills related to less social and fatigue-related illness burden, via lower emotional distress. This relationship existed independent of the association of symptom severity on illness burden, and was stronger among those not currently employed. CONCLUSIONS: Ability to manage stress is associated with a lower illness burden for individuals with ME/CFS. Future studies should evaluate the efficacy of psychosocial interventions in lowering illness burden by targeting stress management skills.
Lauche R, Cramer H, Dobos G, Langhorst J,	Department of Internal and Integrative Medicine, Kliniken	A systematic review and meta-analysis of mindfulness-based	J Psychosom Res. 2013 Dec;75(6):500-10. doi: 10.1016/j.jpsychores.2013.10.	OBJECTIVES: This paper presents a systematic review and meta-analysis of the effectiveness of mindfulness-based stress reduction (MBSR) for FMS. METHODS: The PubMed/MEDLINE, Cochrane Library, EMBASE, PsychINFO and CAMBASE databases

Schmidt S.	Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, Essen, Germany. Electronic address: r.lauche@kliniken-essen-mitte.de.	stress reduction for the fibromyalgia syndrome.	010. Epub 2013 Oct 26.	were screened in September 2013 to identify randomized and non-randomized controlled trials comparing MBSR to control interventions. Major outcome measures were quality of life and pain; secondary outcomes included sleep quality, fatigue, depression and safety. Standardized mean differences and 95% confidence intervals were calculated. RESULTS: Six trials were located with a total of 674 FMS patients. Analyses revealed low quality evidence for short-term improvement of quality of life (SMD=-0.35; 95% CI -0.57 to -0.12; P=0.002) and pain (SMD=-0.23; 95% CI -0.46 to -0.01; P=0.04) after MBSR, when compared to usual care; and for short-term improvement of quality of life (SMD=-0.32; 95% CI -0.59 to -0.04; P=0.02) and pain (SMD=-0.44; 95% CI -0.73 to -0.16; P=0.002) after MBSR, when compared to active control interventions. Effects were not robust against bias. No evidence was further found for secondary outcomes or long-term effects of MBSR. Safety data were not reported in any trial. CONCLUSIONS: This systematic review found that MBSR might be a useful approach for FMS patients. According to the quality of evidence only a weak recommendation for MBSR can be made at this point. Further high quality RCTs are required for a conclusive judgment of its effects.
Lauche R, Cramer H, Häuser W, Dobos G, Langhorst J.	Department of Internal and Integrative Medicine, Kliniken Essen-Mitte, Faculty of Medicine, University of Duisburg-Essen, 45276 Essen, Germany.	A systematic review and meta-analysis of qigong for the fibromyalgia syndrome.	Evid Based Complement Alternat Med. 2013;2013:635182. doi: 10.1155/2013/635182. Epub 2013 Oct 31.	Objectives: The fibromyalgia syndrome (FMS) is a chronic condition with only few evidence-based complementary and alternative therapies available. This paper presents a systematic review and meta-analysis of the effectiveness of Qigong for fibromyalgia syndrome. Methods: The PubMed/MEDLINE, Cochrane Library, Embase, PsycINFO, and Cambase databases were screened in December 2012 to identify randomized controlled trials comparing Qigong to control interventions. Major outcome measures were pain and quality of life; and secondary outcomes included sleep quality, fatigue, depression, and safety. Standardized mean differences (SMD) and 95% confidence intervals were calculated. Results: Seven trials were located with a total of 395 FMS patients. Analyses revealed low quality evidence for short-term improvement of pain, quality of life, and sleep quality and very low quality evidence for improvement of fatigue after Qigong for FMS, when compared to usual care. No evidence was found for superiority of Qigong compared to active treatments. No serious adverse events were reported. Discussion: This systematic review found that Qigong may be a useful approach for FMS patients. According to the quality of evidence, only a weak recommendation for Qigong can be made at this point. Further high quality RCTs are required for the conclusive judgment of its long-term effects.
Lehmann S, Milde-Busch A, Straube A, von Kries R, Heinen F.	Institute of Social Paediatrics and Adolescent Medicine, Medical Faculty of Ludwig-Maximilians-University Munich, Munich, Bavaria,	How specific are risk factors for headache in adolescents? Results from a cross-sectional study in Germany.	Neuropediatrics. 2013 Feb; 44(1):46-54. doi: 10.1055/s-0032-1333432. Epub 2013 Jan 10.	BACKGROUND: The identified preventable risk factors for primary headache in adolescents are smoking; consumption of coffee or alcoholic mixed drinks; physical inactivity; muscle pain in the head, neck, or shoulder region; and chronic stress. OBJECTIVE: To investigate the interrelation of headache with other health complaints and the specificity of the above-mentioned risk factors for headache in adolescents. METHODS: A total of 1,260 students (grades 10 and 11) filled in questionnaires on headache, dietary, and lifestyle factors. The type of headache and health complaints

	Germany. steffi.lehmann@med.uni-muenchen.de			such as dizziness, abdominal pain, musculoskeletal pains, symptoms of possible fatigue syndrome, and psychic complaints were assessed. RESULTS: Isolated headache was found in 18% of the headache sufferers; most frequently isolated tension-type headache (78.2%). Only among adolescents with a combination of headache (mainly migraine) and other health complaints, significant associations for almost all analyzed risk factors were found. The strength of the associations with the considered risk factors was very similar in all three analyzed strata except for considerably lower odds ratios for isolated headache. CONCLUSION: All analyzed risk factors are nonspecific for headache in adolescents because they also increase the risk for other health complaints. Interventions, therefore, should consider a holistic approach focusing not only on headache but also on a broader spectrum of health complaints.
Lenert P, Icardi M, Dahmoush L.	Department of Internal Medicine, Carver College of Medicine, The University of Iowa, 200 Hawkins Drive, Iowa City, IA, USA. petar-lenert@uiowa.edu	ANA (+) ANCA (+) systemic vasculitis associated with the use of minocycline: case-based review.	Clin Rheumatol. 2013 Jul; 32(7):1099-106. doi: 10.1007/s10067-013-2245-z. Epub 2013 Apr 21.	Minocycline is a synthetic tetracycline-derived antibiotic with significant anti-inflammatory properties that may benefit patients with rheumatoid arthritis. Surprisingly, chronic exposure to minocycline can also cause a breach in immunologic tolerance resulting in a variety of autoimmune syndromes such as drug-induced lupus or autoimmune hepatitis. Vasculitis, most commonly resembling cutaneous polyarteritis nodosa, has also been seen in patients taking this drug. Herein, we present a case of biopsy-proven systemic vasculitis presenting as an ANA (+) ANCA (+) polyarteritis nodosa-like syndrome in a male patient who was taking minocycline for his acne for approximately 2 years. Patient initially presented with constitutional symptoms such as profound weight loss and fatigue, along with myalgias, oligoarticular arthritis, and livedo reticularis. About 2 months later, he developed a severe left testicular pain. Biopsy showed vasculitis complicated with the infarction of the left testis. Angiography revealed microaneurysms in the renal and splenic circulation. Stopping the offending drug, along with the short course of prednisone and hydroxychloroquine, resulted in prompt resolution of his symptoms. We additionally present a comprehensive review of biopsy-proven cases of vasculitis associated with chronic minocycline treatment focusing on its pathogenesis and clinical manifestations.
Leone C, D Amico E, Cilia S, Nicoletti A, Di Pino L, Patti F.	[No address quoted]	Cognitive impairment and "invisible symptoms" are not associated with CCSVI in MS.	BMC Neurol. 2013 Jul 27; 13(1):97. [Epub ahead of print]	BACKGROUND: We investigated the association between chronic cerebrospinal venous insufficiency (CCSVI) and cognitive impairment (CI) in multiple sclerosis (MS). Moreover, we evaluated the association between CCSVI and other frequent self-reported MS symptoms. METHODS: We looked at the presence of CI in incident MS patients with CCVSI in a population-based cohort of Catania, Italy. All subjects were group-matched by age, sex, disease duration and EDSS score with MS patients without CCSVI, serving as controls. CI was assessed with the Brief Repeatable Battery (BRB) and the Stroop Test (ST) and it was defined by the presence of at least three impaired tests. Fatigue and depressive symptoms were assessed with Fatigue Severity Scale (FSS) and Hamilton Depressive Rating Scale (HDRS), respectively. Bladder and sexual symptoms were assessed with the respective items of the Italian version of

				Guy's Neurological Disability Scale (GNDS). Quality of life was evaluated with Multiple Sclerosis Quality of Life-54 Instrument (MSQOL-54). RESULTS: Out of 61 MS patients enrolled in the study, 27 were CCSVI positive and 34 were CCSVI negative. Of them, 43 were women (70.5%); the mean age was 43.9 +/- 11.8 years; the mean disease duration was 159.7 +/- 113.7 months; mean EDSS was 3.0 +/- 2.6. Of them, 36 (59.0%) were classified relapsing-remitting (RR), 12 (19.7%) secondary progressive (SP), seven (11.5%) primary progressive (PP) and six (9.3%) Clinically Isolated Syndrome (CIS). Overall, CI was detected in 29/61 (47.5%) MS patients; particularly 13/27 (48.1%) in the CCSVI positive group and 16/34 (47.0%) in the CCSVI negative group. Presence of CCSVI was not significantly associated with the presence of CI (OR 1.04; 95%CI 0.37-2.87; p-value = 0.9). Not significant differences were found between the two groups regarding the other MS symptoms investigated. CONCLUSIONS: Our findings suggest a lack of association between CCSVI and CI in MS patients. Fatigue, depressive, bladder/sexual symptoms and self-reported quality of life are not associated with CCSVI.
Lewis I, Pairman J, Spickett G, Newton JL.	Institute for Ageing & Health, Newcastle University, Newcastle upon Tyne, UK.	Is chronic fatigue syndrome in older patients a different disease? - a clinical cohort study.	Eur J Clin Invest. 2013 Mar; 43(3):302-8. doi: 10.1111/eci.12046. Epub 2013 Feb 9.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disabling disorder characterised by persistent fatigue with a typical age of diagnosis of 35-50 years. CFS does present in those aged over 50 but whether this is a different disease in older age groups has not been considered. Therefore, we performed a clinical cohort study to examine and differentiate the clinical and autonomic features in CFS patients aged over 50. DESIGN: A total of 179 Fukuda diagnosed CFS patients were recruited, and 25 older CFS patients (50 + years) were matched case by case for gender and length of history to 25 younger CFS patients (16-29 years). A range of symptomatic-based questionnaires were used in addition to heart rate variability and baroreceptor sensitivity to assess autonomic function. RESULTS: Chronic fatigue syndrome can present for the first time in an older population. Older CFS patients demonstrate increased fatigue (Fatigue impact scale; 85 ± 33 vs. 107 ± 27, P = 0·02) (Chalder fatigue scale; 9 ± 3 vs. 11 ± 1, P = 0·002) and caseness for depression (Hospital Anxiety and Depression scale; 7 ± 3 vs. 10 ± 4; P = 0·005). There is a greater autonomic dysfunction in older CFS patients, with reduced parasympathetic function (HFnu; 49·1 ± 18 vs. 36·2 ± 18, P = 0·01, RR30: 15; ±, P = 0·02) and increased sympathetic function (LFnu; 51·5 ± 17 vs. 63·8 ± 18, P = 0·01). Baroreflex sensitivity was substantially reduced (BRS; 19·7 ± 12 vs. 9·9 ± 5, P = 0·0004), and left ventricular ejection time prolonged (LVET; 274·6 ± 16 vs. 285·8 ± 9, P = 0·004). CONCLUSIONS: Older CFS patients demonstrate a disease phenotype very different from younger patients. The combination of differing underlying pathogenic mechanisms and the physiological aspects of ageing result in a greater disease impact in older CFS patients.
Lewis I, Pairman J, Spickett G, Newton JL.	Institute for Ageing & Health, Newcastle University, Newcastle,	Clinical characteristics of a novel subgroup of	J Intern Med. 2013 May; 273(5):501-10. doi: 10.1111/joim.12022. Epub	OBJECTIVES: A significant proportion of patients with chronic fatigue syndrome (CFS) also have postural orthostatic tachycardia syndrome (POTS). We aimed to characterize these patients and differentiate them from CFS patients without POTS in

	UK.	chronic fatigue syndrome patients with postural orthostatic tachycardia syndrome.	2013 Jan 7. Comment in J Intern Med. 2013 May; 273(5):498-500.	terms of clinical and autonomic features. METHODS: A total of 179 patients with CFS (1994 Centers for Disease Control and Prevention criteria) attending one of the largest Department of Health-funded CFS clinical services were included in this study. Outcome measures were as follows: (i) symptom assessment tools including the fatigue impact scale, Chalder fatigue scale, Epworth sleepiness scale (ESS), orthostatic grading scale (OGS) and hospital anxiety and depression scale (HADS-A and -D, respectively), (ii) autonomic function analysis including heart rate variability and (iii) haemodynamic responses including left ventricular ejection time and systolic blood pressure drop upon standing. RESULTS: CFS patients with POTS (13%, n = 24) were younger (29 ± 12 vs. 42 ± 13 years, P < 0.0001), less fatigued (Chalder fatigue scale, 8 ± 4 vs. 10 ± 2, P = 0.002), less depressed (HADS-D, 6 ± 4 vs. 9 ± 4, P = 0.01) and had reduced daytime hypersomnolence (ESS, 7 ± 6 vs. 10 ± 5, P = 0.02), compared with patients without POTS. In addition, they exhibited greater orthostatic intolerance (OGS, 11 ± 5; P < 0.0001) and autonomic dysfunction. A combined clinical assessment tool of ESS ≤9 and OGS ≥9 identifies accurately CFS patients with POTS with 100% positive and negative predictive values. CONCLUSIONS: The presence of POTS marks a distinct clinical group of CFS patents, with phenotypic features differentiating them from those without POTS. A combination of validated clinical assessment tools can determine which CFS patients have POTS with a high degree of accuracy, and thus potentially identify those who require further investigation and consideration for therapy to control heart rate.
Light KC, Agarwal N, Iacob E, White AT, Kinney AY, Vanhaitsma TA, Aizad H, Hughen RW, Bateman L, Light AR.	Department of Anesthesiology, University of Utah Health Sciences Center, Salt Lake City, UT, USA. Electronic address: kathleen.c.light@hsc.utah.edu.	Differing leukocyte gene expression profiles associated with fatigue in patients with prostate cancer versus chronic fatigue syndrome.	Psychoneuroendocrinology. 2013 Dec;38(12):2983-95. doi: 10.1016/j.psyneuen.2013.08.008 Epub 2013 Sep 6.	BACKGROUND: Androgen deprivation therapy (ADT) often worsens fatigue in patients with prostate cancer, producing symptoms similar to chronic fatigue syndrome (CFS). Comparing expression (mRNA) of many fatigue-related genes in patients with ADT-treated prostate cancer versus with CFS versus healthy controls, and correlating mRNA with fatigue severity may clarify the differing pathways underlying fatigue in these conditions. METHODS: Quantitative real-time PCR was performed on leukocytes from 30 fatigued, ADT-treated prostate cancer patients (PCF), 39 patients with CFS and 22 controls aged 40-79, together with ratings of fatigue and pain severity. 46 genes from these pathways were included: (1) adrenergic/monoamine/neuropeptides, (2) immune, (3) metabolite-detecting, (4) mitochondrial/energy, (5) transcription factors. RESULTS: PCF patients showed higher expression than controls or CFS of 2 immune transcription genes (NR3C1 and TLR4), chemokine CXCR4, and mitochondrial gene SOD2. They showed lower expression of 2 vasodilation-related genes (ADRB2 and VIPR2), 2 cytokines (TNF and LTA), and 2 metabolite-detecting receptors (ASIC3 and P2RX7). CFS patients showed higher P2RX7 and lower HSPA2 versus controls and PCF. Correlations with fatigue severity were similar in PCF and CFS for only DBI, the GABA-A receptor modulator (r=-0.50, p<0.005 and r=-0.34, p<0.05). Purinergic P2RY1 was correlated only with PCF fatigue and pain severity (r=+0.43 and +0.59, p=0.025 and p=0.001). CONCLUSIONS: PCF patients

				differed from controls and CFS in mean expression of 10 genes from all 5 pathways. Correlations with fatigue severity implicated DBI for both patient groups and P2RY1 for PCF only. These pathways may provide new targets for interventions to reduce fatigue.
Lillestøl K, Bondevik H.	Avdeling for samfunnsmedisin, Institutt for helse og samfunn, Universitetet i Oslo, Norway. kristine.lillestol@medisin.uio.no	Neurasthenia in Norway 1880-1920. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2013 Mar 19; 133(6):661-5. doi: 10.4045/tidsskr.12.1221.	Neurasthenia was introduced as a diagnostic category in America in 1869, and rapidly spread to Europe. Many have drawn parallels between the historical disease entity of neurasthenia and contemporary conditions such as chronic fatigue syndrome/myalgic encephalopathy and burn-out, but we have little knowledge about the early history of neurasthenia in Norway. On the basis of Norwegian medical journals from the period 1880-1920, we have sought to study the introduction, understanding and application of the concept of neurasthenia in Norwegian medical practice, with particular emphasis on symptoms, causes, treatment, prognosis and prevalence. Results show that the term was probably used in a Norwegian medical journal for the first time in 1876, and during the 1880s there followed an increasing number of reports of people who had been diagnosed with neurasthenia. The condition was defined as a weakness of the nervous system. The symptom picture was extensive, with exhaustion as the main symptom. The causes of the symptoms could not be objectively verified or located, and theories abounded. Overexertion was a common explanation, although traumas, infections, malnutrition, heredity and sexual excesses were also assumed to be causes. The recommended treatment focused on strengthening the nervous system, for example through rest and electrotherapy. The condition was described as typical of its time, as a response to the «Zeitgeist» and modern life.
Lind R, Berstad A, Hatlebakk J, Valeur J.	Department of Medicine, Haukeland University Hospital, Bergen.	Chronic fatigue in patients with unexplained self-reported food hypersensitivity and irritable bowel syndrome: validation of a Norwegian translation of the Fatigue Impact Scale.	Clin Exp Gastroenterol. 2013 Jul 4;6:101-7. doi: 10.2147/CEG.S45760. Print 2013.	BACKGROUND: Patients with unexplained self-reported food hypersensitivity and irritable bowel syndrome (IBS) suffer from several health complaints, including fatigue. The aim of the present study was to validate a Norwegian translation of the Fatigue Impact Scale (FIS), and to assess the impact of fatigue in patients with self-reported food hypersensitivity and IBS, as compared with healthy controls. METHODS: Thirty-eight patients with unexplained self-reported food hypersensitivity and IBS, who participated in the validation of the FIS completed the following additional questionnaires: the Short Form of Nepean Dyspepsia Index for assessment of quality of life, the Subjective Health Complaint Inventory, and questionnaires for diagnosis and severity of IBS. Impact of fatigue was studied in 43 patients with unexplained self-reported food hypersensitivity, 70% diagnosed with IBS, and 42 healthy controls. RESULTS: Cronbach's α for the FIS was 0.98, indicating excellent agreement between individual items. Scores on the FIS correlated with scores on the Short Form of Nepean Dyspepsia Index ($r = 0.50$, $P = 0.001$), indicating good convergent validity, and were higher in patients (median 85.0, interquartile range 36.8-105.3) than in controls (median 14.0, interquartile range 3.0-29.0, $P \leq 0.0001$). CONCLUSION: The Norwegian translation of the FIS performed excellently in patients with unexplained self-reported

				food hypersensitivity and IBS, with patients reporting significantly more impact of chronic fatigue than healthy controls.
Ljøstad U, Mygland Å.	Department of Neurology, Sørlandet Hospital, Kristiansand, Norway. unn.ljostad@sshf.no	Chronic Lyme; diagnostic and therapeutic challenges.	Acta Neurol Scand Suppl. 2013; (196):38-47. doi: 10.1111/ane.12048.	In this review, we aim to discuss the definition, clinical and laboratory features, diagnostics, and management of chronic Lyme. Chronic Lyme is a rare condition caused by long-lasting and ongoing infection with the spirochete Borrelia burgdorferi (Bb). The most common manifestations are progressive encephalitis, myelitis, acrodermatitis chronica atrophicans with or without neuropathy, and arthritis. Chronic Lyme is not considered to present with isolated subjective symptoms. Direct detection of Bb has low yield in most manifestations of chronic Lyme, while almost 100% of the cases are seropositive, that is, have detectable Bb IgG antibodies in serum. Detection of Bb antibodies only with Western blot technique and not with ELISA and detection of Bb IgM antibodies without simultaneous detection of Bb IgG antibodies should be considered as seronegativity in patients with long-lasting symptoms. Patients with chronic Lyme in the nervous system (neuroborreliosis) have, with few exceptions, pleocytosis and production of Bb antibodies in their cerebrospinal fluid. Strict guidelines should be applied in diagnostics of chronic Lyme, and several differential diagnoses, including neurological disease, rheumatologic disease, post-Lyme disease syndrome, chronic fatigue syndrome, and psychiatric disease, should be considered in the diagnostic workup. Antibiotic treatment with administration route and dosages according to current guidelines are recommended. Combination antimicrobial therapy or antibiotic courses longer than 4 weeks are not recommended. Patients who attribute their symptoms to chronic Lyme on doubtful basis should be offered a thorough and systematic diagnostic approach, and an open and respectful dialogue.
Lloyd AR.	[No address quoted]	Apology.	J Intern Med. 2013 Jun; 273(6):628. doi: 10.1111/joim.12074. Epub 2013 May 6.	Comment on J Intern Med. 2012 Jan; 271(1):29-31.
Lu Y (1), Liu Y(2), Li Y(1).	(1)Laboratory of Oral Biomedical Science and Translational Medicine, Department of Orthodontics, School of Stomatology, Tongji University, Shanghai, China. (2)Laboratory of Oral Biomedical Science and Translational Medicine, Department of	Comparison of natural estrogens and synthetic derivative on genioglossus function and estrogen receptors expression in rats with chronic intermittent hypoxia.	J Steroid Biochem Mol Biol. 2013 Dec 12; 140 C: 71-79. doi: 10.1016/j.jsbmb.2013.12.006. [Epub ahead of print]	The pathogenesis of obstructive sleep apnea-hypopnea syndrome (OSAHS) is summarized as the narrow anatomic structure of upper airway (UA) and the defective function of UA dilator muscles. Up to now, there have been no specific treatments for the UA dilator muscle deficiency. We previously found that some estrogen-like compounds exert protective effects on genioglossus, but this protection tends to be less satisfactory. A novel phytoestrogen derivative was synthesized in recent years and was verified to have some cytoprotective activity. This study was designed to compare the effects of natural estrogens and the synthetic resveratrol dimer on genioglossus contraction and expression of estrogen receptors (ERs) under chronic intermittent hypoxia (CIH) condition. Genioglossus myoblasts of rat were isolated and cultured in a culture medium with different agents (estradiol, genistein, resveratrol, and resveratrol dimer, respectively) under hypoxia condition, and ERs expressions

	Orthodontics, School of Stomatology, Tongji University, Shanghai, China. Electronic address: liuyuehua@tongji.edu.cn.			were detected. In vivo study, 48 ovariectomized female rats were randomized into six groups. After CIH exposure and agents injection, rats were tested for genioglossus contractile properties and further analysis of ERs expression. Estradiol up-regulated ERα level and exerted the best protective effect of fatigue resistance. Genistein, resveratrol and resveratrol dimer primarily up-regulated the expression of ERβ. Resveratrol dimer exhibited better protection of fatigue resistance than genistein and resveratrol, and expressed higher binding affinity for ERβ than for ERα. Besides estrogenic effects, there may be some other mechanisms for the fatigue resistance improvement contributed by phytoestrogens and their derivatives.
Lucas K, Maes M.	Sportzenkoppel 54, 22359, Hamburg, Germany.	Role of the Toll Like receptor (TLR) radical cycle in chronic inflammation: possible treatments targeting the TLR4 Pathway.	Mol Neurobiol. 2013 Aug; 48(1):190-204. doi: 10.1007/s12035-013-8425-7. Epub 2013 Feb 26.	Activation of the Toll-like receptor 4 (TLR4) complex, a receptor of the innate immune system, may underpin the pathophysiology of many human diseases, including asthma, cardiovascular disorder, diabetes, obesity, metabolic syndrome, autoimmune disorders, neuroinflammatory disorders, schizophrenia, bipolar disorder, autism, clinical depression, chronic fatigue syndrome, alcohol abuse, and toluene inhalation. TLRs are pattern recognition receptors that recognize damage-associated molecular patterns and pathogen-associated molecular patterns, including lipopolysaccharide (LPS) from gram-negative bacteria. Here we focus on the environmental factors, which are known to trigger TLR4, e.g., ozone, atmosphere particulate matter, long-lived reactive oxygen intermediate, pentachlorophenol, ionizing radiation, and toluene. Activation of the TLR4 pathways may cause chronic inflammation and increased production of reactive oxygen and nitrogen species (ROS/RNS) and oxidative and nitrosative stress and therefore TLR-related diseases. This implies that drugs or substances that modify these pathways may prevent or improve the abovementioned diseases. Here we review some of the most promising drugs and agents that have the potential to attenuate TLR-mediated inflammation, e.g., anti-LPS strategies that aim to neutralize LPS (synthetic anti-LPS peptides and recombinant factor C) and TLR4/MyD88 antagonists, including eritoran, CyP, EM-163, epigallocatechin-3-gallate, 6-shogaol, cinnamon extract, N-acetylcysteine, melatonin, and molecular hydrogen. The authors posit that activation of the TLR radical (ROS/RNS) cycle is a common pathway underpinning many "civilization" disorders and that targeting the TLR radical cycle may be an effective method to treat many inflammatory disorders.
Lukkahatai N, Saligan LN.	National Institute of Nursing Research, National Institutes of Health, Bethesda, MD 20892, USA. nada.lukkahatai@nih.gov	Association of catastrophizing and fatigue: a systematic review.	J Psychosom Res. 2013 Feb;74(2):100-9. doi: 10.1016/j.jpsychores.2012.11.006. Epub 2012 Dec 2.	OBJECTIVE: Catastrophizing is an exaggerated negative evaluation and attention to specific symptoms such as pain or fatigue. A number of studies consistently support the significant role of catastrophizing in pain. However, the role of catastrophizing in fatigue is less frequently investigated. This article provides a critical review of published studies investigating this association. METHODS: Using the keyword "Fatigue AND Catastrophizing", we performed a search in PubMed, SCOPUS, PsycINFO, and EMBASE. RESULTS: Fourteen studies were reviewed and all except one were found to provide empirical support for an association between high

				catastrophizing and high fatigue. Most of these reviewed articles also show the large impact of catastrophizing on fatigue severity. Two longitudinal studies found that fatigue catastrophizing level before cancer treatment is a significant predictor of post-treatment fatigue. Studies also demonstrated that persons who had higher scores for catastrophizing recalled fatigue more accurately than those with lower scores. CONCLUSION: In spite the differences of its definition and the measurements used, a similar significant association between catastrophizing and fatigue was reported. Because this observation was based on 14 studies with limited types of patients, further studies are recommended to examine the role of catastrophizing in fatigue from other clinical populations and to investigate its utility as a behavioral marker for central fatigue.
Maas ML, Wever PC, Plat AW, Hoogeveen EK.	Department of Internal Medicine, Jeroen Bosch Hospital's-Hertogenbosch, The Netherlands. martjemaas@hotmail.com	An uncommon cause of Staphylococcus aureus sepsis.	Scand J Infect Dis. 2013 Sep;45(9):722-4. doi: 10.3109/00365548.2013.795658. Epub 2013 Jun 9.	We describe a case of Staphylococcus aureus sepsis after acupuncture for chronic fatigue syndrome (CFS). Sepsis is a rare, but potentially fatal complication of acupuncture. The most common cause of bacterial infection after acupuncture is S. aureus. The effectiveness of acupuncture for the treatment of CFS is not proven, therefore the potential benefits should be weighed against the risks.
Maes M, Anderson G, Morris G, Berk M.	[No address quoted]	Diagnosis of myalgic encephalomyelitis: where are we now?	Expert Opin Med Diagn. 2013 May; 7(3):221-5. doi: 10.1517/17530059.2013.776039. Epub 2013 Feb 27.	INTRODUCTION: The World Health Organization has classified myalgic encephalomyelitis (ME) as a neurological disease since 1969 considering chronic fatigue syndrome (CFS) as a synonym used interchangeably for ME since 1969. ME and CFS are considered to be neuro-immune disorders, characterized by specific symptom profiles and a neuro-immune pathophysiology. However, there is controversy as to which criteria should be used to classify patients with "chronic fatigue syndrome." AREAS COVERED: The Centers for Disease Control and Prevention (CDC) criteria consider chronic fatigue (CF) to be distinctive for CFS, whereas the International Consensus Criteria (ICC) stresses the presence of post-exertion malaise (PEM) as the hallmark feature of ME. These case definitions have not been subjected to rigorous external validation methods, for example, pattern recognition analyses, instead being based on clinical insights and consensus. EXPERT OPINION: Pattern recognition methods showed the existence of three qualitatively different categories: (a) CF, where CF evident, but not satisfying full CDC syndrome criteria. (b) CFS, satisfying CDC criteria but without PEM. (c) ME, where PEM is evident in CFS. Future research on this "chronic fatigue spectrum" should, therefore, use the above-mentioned validated categories and novel tailored algorithms to classify patients into ME, CFS, or CF.
Maes M, Ringel K, Kubera M,	Maes Clinics @ TRIA, Bangkok, Thailand.	In myalgic encephalomyelitis/ch	J Affect Disord. 2013 Sep 5; 150 (2):223-30. doi:	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is accompanied by activation of immuno-inflammatory pathways, increased bacterial

Anderson G, Morris G, Galecki P, Geffard M.	dr.michaelmaes@hotmail.com	ronic fatigue syndrome, increased autoimmune activity against 5-HT is associated with immuno-inflammatory pathways and bacterial translocation.	10.1016/j.jad.2013.03.029. Epub 2013 May 10.	translocation and autoimmune responses to serotonin (5-HT). Inflammation is known to damage 5-HT neurons while bacterial translocation may drive autoimmune responses. This study has been carried out to examine the autoimmune responses to 5-HT in ME/CFS in relation to inflammation and bacterial translocation. METHODS: We examined 5-HT antibodies in 117 patients with ME/CFS (diagnosed according to the centers for disease control and prevention criteria, CDC) as compared with 43 patients suffering from chronic fatigue (CF) but not fulfilling the CDC criteria and 35 normal controls. Plasma interleukin-1 (IL-1), tumor necrosis factor (TNF) α, neopterin and the IgA responses to Gram-negative bacteria were measured. Severity of physio-somatic symptoms was measured using the fibromyalgia and chronic fatigue syndrome rating scale (FF scale). RESULTS: The incidence of positive autoimmune activity against 5-HT was significantly higher ($p<0.001$) in ME/CFS (61.5%) than in patients with CF (13.9%) and controls (5.7%). ME/CFS patients with 5-HT autoimmune activity displayed higher TNFα, IL-1 and neopterin and increased IgA responses against LPS of commensal bacteria than those without 5-HT autoimmune activity. Anti-5-HT antibody positivity was significantly associated with increased scores on hyperalgesia, fatigue, neurocognitive and autonomic symptoms, sadness and a flu-like malaise. DISCUSSION: The results show that, in ME/CFS, increased 5-HT autoimmune activity is associated with activation of immuno-inflammatory pathways and increased bacterial translocation, factors which are known to play a role in the onset of autoimmune reactions. 5-HT autoimmune activity could play a role in the pathophysiology of ME/CFS and the onset of physio-somatic symptoms. These results provide mechanistic support for the notion that ME/CFS is a neuro-immune disorder.
Maestú C, Blanco M, Nevado A, Romero J, Rodríguez-Rubio P, Galindo J, Bautista Lorite J, de Las Morenas F, Fernández-Argüelles P.	[No address quoted]	Reduction of pain thresholds in fibromyalgia after very low-intensity magnetic stimulation: A double-blinded, randomized placebo-controlled clinical trial.	Pain Res Manag. 2013 Nov-Dec; 18 (6):e101-6.	BACKGROUND: Exposure to electromagnetic fields has been reported to have analgesic and antinociceptive effects in several organisms. Objective: To test the effect of very low-intensity transcranial magnetic stimulation on symptoms associated with fibromyalgia syndrome. METHODS: A double-blinded, placebo-controlled clinical trial was performed in the Sagrado Corazón Hospital, Seville, Spain. Female fibromyalgia patients (22 to 50 years of age) were randomly assigned to either a stimulation group or a sham group. The stimulation group (n=28) was stimulated using 8 Hz pulsed magnetic fields of very low intensity, while the sham group (n=26) underwent the same protocol without stimulation. Pressure pain thresholds before and after stimulation were determined using an algometer during the eight consecutive weekly sessions of the trial. In addition, blood serotonin levels were measured and patients completed questionnaires to monitor symptom evolution. RESULTS: A repeated-measures ANOVA indicated statistically significant improvement in the stimulation group compared with the control group with respect to somatosensory pain thresholds, ability to perform daily activities, perceived chronic pain and sleep quality. While improvement in pain thresholds was apparent after the first stimulation session, improvement in the other three measures occurred after the

				sixth week. No significant between-group differences were observed in scores of depression, fatigue, severity of headaches or serotonin levels. No adverse side effects were reported in any of the patients. CONCLUSIONS: Very low-intensity magnetic stimulation may represent a safe and effective treatment for chronic pain and other symptoms associated with fibromyalgia.
Mantovani G, Madeddu C, Macciò A.	Department of Medical Oncology, University of Cagliari, Monserrato, Cagliari, Italy. mantovan@medicina.unica.it	Drugs in development for treatment of patients with cancer-related anorexia and cachexia syndrome.	Drug Des Devel Ther. 2013 Aug 12; 7:645-56. doi: 10.2147/DDDT.S39771. **Retraction** in Drug Des Devel Ther. 2013; 7:1385.	Cancer-related anorexia and cachexia syndrome (CACS) is a complex multifactorial condition, with loss of lean body mass, chronic inflammation, severe metabolic derangements, reduced food intake, reduced physical activity, and poor quality of life as key symptoms. Cachexia recognizes different phases or stages, moving from precachexia through overt cachexia to advanced or refractory cachexia. The purpose of this review is to describe currently effective approaches for the treatment of cachexia, moving forward to drugs and treatments already shown to be effective but needing further clinical trials to confirm their efficacy. We then introduce novel promising investigational drugs and approaches which, based on a strong rationale from the most recent data on the molecular targets/pathways driving the pathophysiology of cachexia, need to be tested either in currently ongoing or appropriate future clinical trials to confirm their clinical potential. Although different drugs and treatments have been tested, we can speculate that a single therapy may not be completely successful. Indeed, considering the complex clinical picture and the multifactorial pathogenesis of CACS, we believe that its clinical management requires a multidisciplinary and multitargeted approach. In our opinion, appropriate treatment for cachexia should target the following conditions: inflammatory status, oxidative stress, nutritional disorders, muscle catabolism, immunosuppression, quality of life, and above all, fatigue. A comprehensive list of the most interesting and effective multitargeted treatments is reported and discussed, with the aim of suggesting the most promising with regard to clinical outcome. A critical issue is that of testing therapies at the earliest stages of cachexia, possibly at the precachexia stage, with the aim of preventing or delaying the development of overt cachexia and thereby obtaining the best possible clinical outcome for patients.
Maresca T, Covini E, Márquez López Mato A.	Instituto de Psiquiatría Biológica Integral (IPBI). ipbi@ipbi.com.ar.	Conditions, controversies and contradictions between central sensitivity syndrome and depressive disorders. [Article in Spanish]	Vertex. 2013 Sep; 24 (111):373-91.	We present a description of the Central Sensitivity Syndrome (CSS) and some of its main components such as Multiple Chemical Sensitivity Syndrome, Chronic Fatigue Syndrome and Fibromyalgia. We review the changes in pain perception, describing the physiology and pathophysiology of the painful experience from the medulla horn to the CNS. We explain the theory of central sensitization as the basis to the syndrome. We refer to the differences between fibromyalgia and depressive disorders, is spite of their frequent presentation in comorbidity. We state the main clinical and neurobiological differences. We point out the main psychoneuroimmunoendocrinologic differences such as adrenal activity (hypoactivity vs. hyperactivity, DST hypersuppressive response vs. DST non suppression, hypersensitivity of central glucocorticoid receptors vs. desensitization of these,

				among others), thyroid (probable reverse T3 vs. flat stimuli TSH response curve) and growth hormone secretion (probable increase vs. disruption of normal circadian rhythm) that makes CSS resemble PTSD. We describe differential changes in sleep patterns (alpha-delta intrusion vs. altered sleep time, REM latency, and stage 3/4) and immunological disturbances almost opposite in each pathological entity. We finally argue which medical specialty should treat these complex syndromes.
Mariman A, Delesie L, Tobback E, Hanoulle I, Sermijn E, Vermeir P, Pevernagie D, Vogelaers D.	Department of General Internal Medicine, Infectious Diseases and Psychosomatic Medicine, University Hospital Ghent, Belgium; Center for Neurophysiologic Monitoring, University Hospital Ghent, Belgium. Electronic address: an.mariman@ugent.be.	Undiagnosed and comorbid disorders in patients with presumed chronic fatigue syndrome.	J Psychosom Res. 2013 Nov;75(5):491-6. doi: 10.1016/j.jpsychores.2013.07.010. Epub 2013 Aug 20.	OBJECTIVE: To assess undiagnosed and comorbid disorders in patients referred to a tertiary care center with a presumed diagnosis of chronic fatigue syndrome (CFS). METHODS: Patients referred for chronic unexplained fatigue entered an integrated diagnostic pathway, including internal medicine assessment, psychodiagnostic screening, physiotherapeutic assessment and polysomnography+multiple sleep latency testing. Final diagnosis resulted from a multidisciplinary team discussion. Fukuda criteria were used for the diagnosis of CFS, DSM-IV-TR criteria for psychiatric disorders, ICSD-2 criteria for sleep disorders. RESULTS: Out of 377 patients referred, 279 (74.0%) were included in the study [84.9% female; mean age 38.8years (SD 10.3)]. A diagnosis of unequivocal CFS was made in 23.3%. In 21.1%, CFS was associated with a sleep disorder and/or psychiatric disorder, not invalidating the diagnosis of CFS. A predominant sleep disorder was found in 9.7%, 19.0% had a psychiatric disorder and 20.8% a combination of both. Only 2.2% was diagnosed with a classical internal disease. In the total sample, a sleep disorder was found in 49.8%, especially obstructive sleep apnea syndrome, followed by psychophysiologic insomnia and periodic limb movement disorder. A psychiatric disorder was diagnosed in 45.2%; mostly mood and anxiety disorder. CONCLUSIONS: A multidisciplinary approach to presumed CFS yields unequivocal CFS in only a minority of patients, and reveals a broad spectrum of exclusionary or comorbid conditions within the domains of sleep medicine and psychiatry. These findings favor a systematic diagnostic approach to CFS, suitable to identify a wide range of diagnostic categories that may be subject to dedicated care.
Mariman AN, Vogelaers DP, Tobback E, Delesie LM, Hanoulle IP, Pevernagie DA.	Ghent University Hospital, Department of Internal Diseases, Infectious Diseases and Psychosomatic Medicine, 185 De Pintelaan, 9000 Ghent, Belgium. An.mariman@ugent.be	Sleep in the chronic fatigue syndrome.	Sleep Med Rev. 2013 Jun; 17(3):193-9. doi: 10.1016/j.smrv.2012.06.003. Epub 2012 Oct 6.	Chronic fatigue syndrome (CFS) is a disabling condition characterized by severe fatigue lasting for more than six months and the presence of at least four out of eight minor criteria. Sleep disturbance presenting as unrefreshing or nonrestorative sleep is one of these criteria and is very common in CFS patients. Biologically disturbed sleep is a known cause of fatigue and could play a role in the pathogenesis of CFS. However, the nature of presumed sleep impairment in CFS remains unclear. Whilst complaints of NRS persist over time, there is no demonstrable neurophysiological correlate to substantiate a basic deficit in sleep function in CFS. Polysomnographic findings have not shown to be significantly different between subjects with CFS and normal controls. Discrepancies between subjectively poor and objectively normal sleep suggest a role for psychosocial factors negatively affecting perception of sleep quality. Primary sleep disorders are often detected in patients who otherwise qualify for a CFS

				diagnosis. These disorders could contribute to the presence of daytime dysfunctioning. There is currently insufficient evidence to indicate that treatment of primary sleep disorders sufficiently improves the fatigue associated with CFS. Therefore, primary sleep disorders may be a comorbid rather than an exclusionary condition with respect to CFS.
Marković I, Culo MI, Gudelj-Gracanin A, Morović-Vergles J.	Opća bolnica Dr. Ivo Pedisić, Sisak. imarkoviczg@gmail.com	Gluten-sensitive enteropathy: a disease to take into consideration - a case report. [Article in Croatian]	Reumatizam. 2013; 60(1):32-6.	Gluten-sensitive enteropathy or celiac disease is a chronic small intestinal immune-mediated enteropathy precipitated by exposure to dietary gluten in genetically predisposed individuals. Although the disease may manifest itself at any age, it occurs mostly in either early childhood or in the third or fourth decade of life. Malabsorption syndrome as a typical clinical feature is commonly absent. Patients may exhibit minor gastrointestinal complaints, as well as numerous extraintestinal manifestations. We report a 43-year-old female patient with mi gratory arthralgias as the leading symptom, fatigue, sideropenic anemia and mild intermittent diarrhoea, who was diagnosed with gluten-sensitive enteropathy. Four months after introduction of gluten-free diet the patient reported no arthralgias, and complete clinical response was achieved. The aim of our case-report was to show that migratory arthralgias can be an extraintestinal manifestation of gluten-sensitive enteropathy. Unexplained articular complaints should raise clinical suspicion of celiac disease.
Marques M, De Gucht V, Leal I, Maes S.	Health Psychology, Leiden University, Wassenaarseweg 52, Leiden, The Netherlands. mmarques@ispa.pt	A cross-cultural perspective on psychological determinants of chronic fatigue syndrome: a comparison between a Portuguese and a Dutch patient sample.	Int J Behav Med. 2013 Jun; 20(2):229-38. doi: 10.1007/s12529-012-9265-y.	BACKGROUND: Few studies focus on cross-cultural differences in Chronic fatigue syndrome (CFS). PURPOSE: This study aimed to (1) compare fatigue severity and impairment, somatic complaints, psychological distress, and quality of life (QoL) in a population of Portuguese and Dutch patients; (2) explore the differential contribution of behavioral and cognitive determinants of fatigue severity; and (3) investigate the relation between fatigue severity and somatic complaints on one hand and QoL on the other in both populations. METHOD: Eighty-five female patients from Portugal (Mean age=47.54) and 167 female CFS patients from The Netherlands (Mean age=44.93) participated in the study. All participants were surveyed for demographic and clinical characteristics, fatigue severity, somatic symptoms, psychological distress, (physical and psychological) QoL, physical activity, behavior regulation patterns, and illness representations. RESULTS: Cross-cultural differences were found in relation to working status, duration of fatigue symptoms, psychological distress, somatic complaints, and psychological QoL. Although behavioral characteristics and illness representations were significantly associated with fatigue severity in both Portuguese and Dutch patients, there were important differences in the determinants of CFS. Moreover, higher levels of fatigue and severity of other somatic complaints were related to poor QoL. CONCLUSIONS: These findings show cross-cultural similarities and differences in clinical characteristics and psychological determinants of CFS that are important in view of diagnosis and treatment.
Maryhew C.	[No address quoted]	Letter to the editor: comments on	Psychol Med. 2013 Aug; 43 (8):1789-90. doi:	Comment in Psychol Med. 2013 Aug; 43(8):1791-2.

		'recovery from chronic fatigue syndrome after treatments given in the PACE trial'.	10.1017/S0033291713001293 .	
Mascarelli PE, Maggi RG, Hopkins S, Mozayeni BR, Trull CL, Bradley JM, Hegarty BC, Breitschwerdt EB.	Intracellular Pathogens Research Laboratory, Center for Comparative Medicine and Translational Research, College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27607, USA.	Bartonella henselae infection in a family experiencing neurological and neurocognitive abnormalities after woodlouse hunter spider bites.	Parasit Vectors. 2013 Apr 15; 6:98. doi: 10.1186/1756-3305-6-98.	BACKGROUND: Bartonella species comprise a group of zoonotic pathogens that are usually acquired by vector transmission or by animal bites or scratches. METHODS: PCR targeting the Bartonella 16S-23S intergenic spacer (ITS) region was used in conjunction with BAPGM (Bartonella alpha Proteobacteria growth medium) enrichment blood culture to determine the infection status of the family members and to amplify DNA from spiders and woodlice. Antibody titers to B. vinsonii subsp. berkhoffii (Bvb) genotypes I-III, B. henselae (Bh) and B. koehlerae (Bk) were determined using an IFA test. Management of the medical problems reported by these patients was provided by their respective physicians. RESULTS: In this investigation, immediately prior to the onset of symptoms two children in a family experienced puncture-like skin lesions after exposure to and presumptive bites from woodlouse hunter spiders. Shortly thereafter, the mother and both children developed hive-like lesions. Over the ensuing months, the youngest son was diagnosed with Guillain-Barre (GBS) syndrome followed by Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP). The older son developed intermittent disorientation and irritability, and the mother experienced fatigue, headaches, joint pain and memory loss. When tested approximately three years after the woodlouse hunter spider infestation, all three family members were Bartonella henselae seroreactive and B. henselae DNA was amplified and sequenced from blood, serum or Bartonella alpha-proteobacteria (BAPGM) enrichment blood cultures from the mother and oldest son. Also, B. henselae DNA was PCR amplified and sequenced from a woodlouse and from woodlouse hunter spiders collected adjacent to the family's home. CONCLUSIONS: Although it was not possible to determine whether the family's B. henselae infections were acquired by spider bites or whether the spiders and woodlice were merely accidental hosts, physicians should consider the possibility that B. henselae represents an antecedent infection for GBS, CIDP, and non-specific neurocognitive abnormalities.
Mascarelli PE, Maggi RG, Hopkins S, Mozayeni BR, Trull CL, Bradley JM, Hegarty BC, Breitschwerdt EB.	Intracellular Pathogens Research Laboratory, Center for Comparative Medicine and Translational Research, College of Veterinary Medicine, North Carolina State	Bartonella henselae infection in a family experiencing neurological and neurocognitive abnormalities after woodlouse hunter spider bites.	Bartonella henselae infection in a family experiencing neurological and neurocognitive abnormalities after woodlouse hunter spider bites.	BACKGROUND: Bartonella species comprise a group of zoonotic pathogens that are usually acquired by vector transmission or by animal bites or scratches. METHODS: PCR targeting the Bartonella 16S-23S intergenic spacer (ITS) region was used in conjunction with BAPGM (Bartonella alpha Proteobacteria growth medium) enrichment blood culture to determine the infection status of the family members and to amplify DNA from spiders and woodlice. Antibody titers to B. vinsonii subsp. berkhoffii (Bvb) genotypes I-III, B. henselae (Bh) and B. koehlerae (Bk) were determined using an IFA test. Management of the medical problems reported by

	University, Raleigh, NC 27607, USA.			these patients was provided by their respective physicians. RESULTS: In this investigation, immediately prior to the onset of symptoms two children in a family experienced puncture-like skin lesions after exposure to and presumptive bites from woodlouse hunter spiders. Shortly thereafter, the mother and both children developed hive-like lesions. Over the ensuing months, the youngest son was diagnosed with Guillain-Barre (GBS) syndrome followed by Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP). The older son developed intermittent disorientation and irritability, and the mother experienced fatigue, headaches, joint pain and memory loss. When tested approximately three years after the woodlouse hunter spider infestation, all three family members were Bartonella henselae seroreactive and B. henselae DNA was amplified and sequenced from blood, serum or Bartonella alpha-proteobacteria (BAPGM) enrichment blood cultures from the mother and oldest son. Also, B. henselae DNA was PCR amplified and sequenced from a woodlouse and from woodlouse hunter spiders collected adjacent to the family's home. CONCLUSIONS: Although it was not possible to determine whether the family's B. henselae infections were acquired by spider bites or whether the spiders and woodlice were merely accidental hosts, physicians should consider the possibility that B. henselae represents an antecedent infection for GBS, CIDP, and non-specific neurocognitive abnormalities.
Matsuo K, Saburi M, Ishikawa H, Tei K, Hosokawa Y, Fujii C, Mizuno T, Nakagawa M.	Division of Neurology, Ohmihachiman Community Medical Center, Japan. matsuo@pb4.so-net.ne.jp	Sjögren syndrome presenting with encephalopathy mimicking Creutzfeldt-Jakob disease.	J Neurol Sci. 2013 Mar 15;326(1-2):100-3. doi: 10.1016/j.jns.2013.01.005. Epub 2013 Jan 18.	A 61-year-old man developed subacute progressive dementia, general fatigue, a tonic-clonic seizure, and a decreased level of consciousness. He had a past history of chronic hepatitis type C and was diagnosed as having hepatic encephalopathy due to hyperammonemia. His level of consciousness did not improve even though the serum ammonia level improved. In addition, he had repeated general myoclonic seizures. Head MRI (diffusion-weighted imaging) showed high signal intensities in the right thalamus and the cerebral cortices in the frontal, temporal and parietal lobes (predominantly on the right side). An electroencephalogram (EEG) showed periodic lateralized epileptic discharges (PLEDs). Cerebrospinal fluid analysis revealed high total tau protein and 14-3-3 protein levels. This case was diagnosed as Creutzfeldt-Jakob disease (CJD) based on these clinical data. However, the patient gradually improved without specific treatment. The differential diagnosis was reconsidered, and an increased erythrocyte sedimentation rate and positive serum anti-SS-A and anti-SS-B antibodies were noted. A diagnosis of Sjögren syndrome (SjS) was finally made based on a biopsy of a minor salivary gland showing infiltration of lymphocytes around the gland ducts. Steroid therapy (prednisolone 40mg/day orally) was given, and his clinical condition improved. The lesions on the head MRI decreased, and the EEG findings normalized. This case suggests that SjS has a wide spectrum, including neurological disorders, and that SjS should be considered in the differential diagnosis of CJD.
Medow MS,	Department of	Modulation of the	J Appl Physiol (1985). 2013	Local cutaneous heating causes vasodilation as an initial first peak, a nadir, and

Aggarwal A, Baugham I, Messer Z, Stewart JM.	Pediatrics, New York Medical College and The Center for Pediatric Hypotension, Hawthorne, New York 10532, USA. Marvin_Medow@NYMC.edu	axon-reflex response to local heat by reactive oxygen species in subjects with chronic fatigue syndrome.	Jan 1; 114(1):45-51. doi: 10.1152/japplphysiol.00821.2012. Epub 2012 Nov 8.	increase to plateau. Reactive oxygen species (ROS) modulate the heat plateau in healthy controls. The initial peak, due to C-fiber nociceptor-mediated axon reflexes, is blunted with local anesthetics and may serve as a surrogate for the cutaneous response to peripheral heat. Chronic fatigue syndrome (CFS) subjects report increased perception of pain. To determine the role of ROS in this neurally mediated response, we evaluated changes in cutaneous blood flow from local heat in nine CFS subjects (16-22 yr) compared with eight healthy controls (18-26 yr). We heated skin to 42°C and measured local blood flow as a percentage of maximum cutaneous vascular conductance (%CVC(max)). Although CFS subjects had significantly lower baseline flow [8.75 ± 0.56 vs. 12.27 ± 1.07 (%CVC(max), CFS vs. control)], there were no differences between groups to local heat. We then remeasured this with apocynin to inhibit NADPH oxidase, allopurinol to inhibit xanthine oxidase, tempol to inhibit superoxide, and ebselen to reduce H(2)O(2). Apocynin significantly increased baseline blood flow (before heat, 14.91 ± 2.21 vs. 8.75 ± 1.66) and the first heat peak (69.33 ± 3.36 vs. 59.75 ± 2.75). Allopurinol and ebselen only enhanced the first heat peaks (71.55 ± 2.48 vs. 61.72 ± 2.01 and 76.55 ± 5.21 vs. 58.56 ± 3.66, respectively). Tempol had no effect on local heating. None of these agents changed the response to local heat in control subjects. Thus the response to heat may be altered by local levels of ROS, particularly H(2)O(2) in CFS subjects, and may be related to their hyperesthesia/hyperalgesia.
Meeus M, Goubert D, De Backer F, Struyf F, Hermans L, Coppieters I, De Wandele I, Da Silva H, Calders P.	Department of Rehabilitation Sciences and Physiotherapy, Ghent University and Artevelde University College, Ghent Campus Heymans (UZ) 3 B3, De Pintelaan 185, Ghent, Belgium; "Pain in Motion" Research Group, Department of Rehabilitation Sciences and Physiotherapy, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium. Electronic address: mira.meeus@artesis.be.	Heart rate variability in patients with fibromyalgia and patients with chronic fatigue syndrome: a systematic review.	Semin Arthritis Rheum. 2013 Oct; 43(2):279-87. doi: 10.1016/j.semarthrit.2013.03.004. Epub 2013 Jul 6.	OBJECTIVE: The goal of this systematic literature review is to determine whether there are differences and similarities in heart rate variability (HRV) between adult patients with fibromyalgia (FM), chronic fatigue syndrome (CFS), and healthy pain-free control subjects. METHODS: To obtain relevant articles, PubMed and Web of Knowledge were searched for case-control studies. Selection of the literature was based on selection criteria ascertaining studies with adult human patient groups comparing HRV. Risk of bias and levels of evidence were determined. RESULTS: Sixteen case-control studies were included, 10 comparing FM patients to controls and 6 comparing CFS patients to controls. Methodological quality was moderate to good. Both time domain and frequency domain measurements were used. The majority of the researchers observed lower HRV in FM patients compared to healthy control persons, as well as increased sympathetic activity and a blunted autonomic response to stressors. Resistance training improved HRV in FM patients. In CFS patients HRV was only reduced during sleep. CONCLUSION: FM patients show more HRV aberrances and indices of increased sympathetic activity. Increased sympathetic activity is only present in CFS patients at night. Since direct comparisons are lacking and some confounders have to be taken into account, further research is warranted. The role of pain and causality can be subject of further research, as well as therapy studies directed to reduced HRV.

Meeus M, Ickmans K, Struyf F, Hermans L, Van Noesel K, Oderkerk J, Declerck LS, Moorkens G, Hans G, Grosemans S, Nijs J.	Department of Human Physiology and Rehabilitation Sciences, Vrije Universiteit Brussels, Belgium. Mira.Meeus@artesis.be	Does acetaminophen activate endogenous pain inhibition in chronic fatigue syndrome/fibromyalgia and rheumatoid arthritis? A double-blind randomized controlled cross-over trial.	Pain Physician. 2013 Mar-Apr; 16(2):E61-70.	BACKGROUND: Although enhanced temporal summation (TS) and conditioned pain modulation (CPM), as characteristic for central sensitization, has been proved to be impaired in different chronic pain populations, the exact nature is still unknown. OBJECTIVES: We examined differences in TS and CPM in 2 chronic pain populations, patients with both chronic fatigue syndrome (CFS) and comorbid fibromyalgia (FM) and patients with rheumatoid arthritis (RA), and in sedentary, healthy controls, and evaluated whether activation of serotonergic descending pathways by acetaminophen improves central pain processing. STUDY DESIGN: Double-blind randomized controlled trial with cross-over design. METHODS: Fifty-three women (19 CFS/FM patients, 16 RA patients, and 18 healthy women) were randomly allocated to the experimental group (1 g acetaminophen) or the placebo group (1 g dextrose). Participants underwent an assessment of endogenous pain inhibition, consisting of an evaluation of temporal summation with and without conditioned pain modulation (CPM). Seven days later groups were crossed-over. Patients and assessors were blinded for the allocation. RESULTS: After intake of acetaminophen, pain thresholds increased slightly in CFS/FM patients, and decreased in the RA and the control group. Temporal summation was reduced in the 3 groups and CPM at the shoulder was better overall, however only statistically significant for the RA group. Healthy controls showed improved CPM for both finger and shoulder after acetaminophen, although not significant. LIMITATIONS: The influence of acetaminophen on pain processing is inconsistent, especially in the patient groups examined. CONCLUSION: This is the first study comparing the influence of acetaminophen on central pain processing in healthy controls and patients with CFS/FM and RA. It seems that CFS/FM patients present more central pain processing abnormalities than RA patients, and that acetaminophen may have a limited positive effect on central pain inhibition, but other contributors have to be identified and evaluated.
Meeus M, Nijs J, Hermans L, Goubert D, Calders P.	University of Antwerp, Faculty of Medicine and Health Sciences, Department of Rehabilitation Sciences and Physiotherapy, Pain in Motion Research Group, Antwerp, Belgium. mira.meeus@ugent.be	The role of mitochondrial dysfunctions due to oxidative and nitrosative stress in the chronic pain or chronic fatigue syndromes and fibromyalgia patients: peripheral and central mechanisms as therapeutic targets?	Expert Opin Ther Targets. 2013 Sep; 17(9):1081-9. doi: 10.1517/14728222.2013.818657. Epub 2013 Jul 9.	INTRODUCTION: Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are characterized by persistent pain and fatigue. It is hypothesized that reactive oxygen species (ROS), caused by oxidative and nitrosative stress, by inhibiting mitochondrial function can be involved in muscle pain and central sensitization as typically seen in these patients. AREAS COVERED: The current evidence regarding oxidative and nitrosative stress and mitochondrial dysfunction in CFS and FM is presented in relation to chronic widespread pain. Mitochondrial dysfunction has been shown in leukocytes of CFS patients and in muscle cells of FM patients, which could explain the muscle pain. Additionally, if mitochondrial dysfunction is also present in central neural cells, this could result in lowered ATP pools in neural cells, leading to generalized hypersensitivity and chronic widespread pain. EXPERT OPINION: Increased ROS in CFS and FM, resulting in impaired mitochondrial function and reduced ATP in muscle and neural cells, might lead to chronic widespread pain in these patients. Therefore,

				targeting increased ROS by antioxidants and targeting the mitochondrial biogenesis could offer a solution for the chronic pain in these patients. The role of exercise therapy in restoring mitochondrial dysfunction remains to be explored, and provides important avenues for future research in this area.
Melikoglu M, Melikoglu MA.	Department of Dermatology, Ministry of Health Erzurum Regional Training and Research Hospital, Erzurum, Turkey. mmelikoglu@gmail.com	The prevalence of fibromyalgia in patients with Behçet's disease and its relation with disease activity.	Rheumatol Int. 2013 May; 33(5):1219-22. doi: 10.1007/s00296-012-2530-1. Epub 2012 Sep 28.	Behçet's disease (BD) is a chronic disorder characterized by mucocutaneous and multisystem manifestations. Fibromyalgia (FM) is characterized by widespread musculoskeletal pain and may be present concomitantly with several rheumatic diseases. Our aims were to investigate the prevalence of FM in patients with BD and to evaluate the possible relation of FM presence with BD disease activity. A total of 104 Behcet patients were included in this study. Age, sex, disease durations and the BD Current Activity Form (BDCAF) scores as disease activity evaluation were recorded. Presence of FM and the Fibromyalgia Impact Questionnaire (FIQ) scores was investigated. Also, ESR and CRP concentrations were determined in all patients. Mann-Whitney U test and Pearson's correlation tests were used for the statistical analysis. There were 60 female and 40 male patients with an age range of 19-51 years. Eighteen of 100 BD patients were diagnosed as FM. Although ages, disease duration and laboratory parameters did not differ between BD patients with and without FM, BD patients with FM were more frequently female ($p < 0.000$). The presence of FM did not differ significantly between patients with and without systemic manifestations. Also, oral-genital ulcers, erythema nodosum, thrombophlebitis, pustular lesions and doctor's impression of disease activity scores were not found to be different in BD patients with or without FM. However, there were significant differences in fatigue, headache, arthralgia and patient impression of disease activity (today and last 28 days) between these groups ($p < 0.000$; $p < 0.01$; $p < 0.01$; $p = 0.021$ and $p = 0.027$, respectively). Also, there were significant correlations between BDCAF and FIQ items that refer pain and fatigue ($p < 0.01$). FM is a common and important clinical problem that may represent an additional factor that worsens pain and physical limitations in patients with BD. The higher prevalence of FM in patients with BD seems to be affected by BD itself, rather than its severity.
Miller RR, Gardy JL, Tang P, Patrick DM.	School of Population and Public Health, University of British Columbia, Vancouver, Canada. Email: ruth.miller@bccdc.ca.	A metagenomic approach to investigate the microbial causes of myalgic encephalomyelitis/ chronic fatigue syndrome: moving beyond XMRV.	Fatigue. 2013 Oct; 1 (4):185-189.	[No abstract given]
Minton O, Stone PC.	Division of Population Health Sciences and	A comparison of cognitive function,	BMJ Support Palliat Care. 2013 Sep; 2(3):231-238. Epub	BACKGROUND: Chronic fatigue is a feature in a subset of women successfully treated for breast cancer but is not well characterised. This study examines differences in

	Education, St George's, University of London, London, UK.	sleep and activity levels in disease-free breast cancer patients with or without cancer-related fatigue syndrome.	2012 May 31.	objective cognitive function, activity levels and sleep in disease-free women who do and do not meet criteria for cancer-related fatigue syndrome (CRFS). METHODS: Women between 3 months and 2 years after completion of any primary therapy were recruited from a cancer centre follow-up clinic. On the basis of a diagnostic semi-structured interview they were classified as being CRFS cases or non-fatigued controls. Participants underwent objective cognitive testing using a computerised battery, wore an activity monitor for 1 week and completed quality of life and fatigue questionnaires. RESULTS: 114 women were recruited (69 controls and 45 CRFS cases). There were significant differences between groups on fatigue, mood, sleep and quality of life scores, and in objective cognitive testing (tests of sustained attention, reaction time and verbal memory all $p<0.03$). There was an overall difference in daytime activity ($p=0.03$) from actigraphy recordings. There were no differences on objective measures of sleep or in routine laboratory measures. CONCLUSIONS: Our preliminary results suggest that disease-free women with CRFS after successful breast cancer treatment have significantly lower subjective quality of life and mood. Additionally, objective cognitive impairment in certain domains may play an important role in the subjective manifestation of these symptoms. There is also objective evidence on actigraphy of differing levels of activity. The subjective sleep disturbance and higher prevalence of insomnia do not correlate with objective measures.
Mizuno K, Watanabe Y.	Pathophysiological and Health Science Team, RIKEN Center for Life Science Technologies Kobe City, Hyogo, Japan ; Department of Physiology, Osaka City University Graduate School of Medicine Osaka, Japan ; Department of Medical Science on Fatigue, Osaka City University Graduate School of Medicine Osaka, Japan.	Neurocognitive impairment in childhood chronic fatigue syndrome.	Front Physiol. 2013 Apr 19; 4:87. doi: 10.3389/fphys.2013.00087. eCollection 2013.	Neurocognitive impairment is a feature of childhood chronic fatigue syndrome (CCFS). Several studies have demonstrated reduced attention control in CCFS patients in switching and divided attention tasks. In students, the extent of deterioration in task performance depends on the level of fatigue. Poor performance in switching and divided attention is common in both fatigued students and CCFS patients. Additionally, attentional functions show dramatic development from childhood to adolescence, suggesting that abnormal development of switching and divided attention may be induced by chronic fatigue. The brain structures associated with attentional control are situated in the frontal and parietal cortices, which are the last to mature, suggesting that severe fatigue in CCFS patients and students may inhibit normal structural and functional development in these regions. A combination of treatment with cognitive behavioral therapy and antidepressant medication is effective to improve attentional control processing in CCFS patients. Studies identifying the features of neurocognitive impairment in CCFS have improved our current understanding of the neurophysiological mechanisms of CCFS.
Moerman RV, Bootsma H, Kroese FG, Vissink A.	Servei de Malalties Autoimmunes, Hospital Clínic, Barcelona, Spain.	Primary Sjögren syndrome: an update on current pharmacotherapy	Expert Opin Pharmacother. 2013 Feb; 14(3):279-89. doi: 10.1517/14656566.2013.767333. Epub 2013 Jan 25.	INTRODUCTION: Primary Sjögren syndrome (SS) is a chronic systemic autoimmune disease characterized by sicca features and systemic manifestations, and requires a multidisciplinary therapeutic approach. AREAS COVERED: Treatment of sicca manifestations is symptomatic and is based on the administration of topical therapies

		options and future directions.		(saliva substitutes and preservative-free artificial tears). In severe cases of keratoconjunctivitis sicca, topical cyclosporine A may be used. For patients with residual salivary gland function, stimulation of salivary flow with a sialogogue (pilocarpine or cevimeline) is the treatment of choice. The management of extraglandular features must be tailored to the specific organ(s) involved. Hydroxychloroquine may be appropriate for patients with fatigue, arthralgia and myalgia, while glucocorticoids and immunosuppressive agents should be reserved for severe systemic involvement (although no controlled trials in primary SS guide their use). RCTs have demonstrated the lack of efficacy of antitumor necrosis factor agents and promising results for B-cell depleting agents. EXPERT OPINION: The overall low level of evidence in therapeutic studies in primary SS suggests that much larger trials of the most promising therapies are necessary. The use of drugs targeting molecules and receptors involved in the etiopathogenesis of primary SS may open up a new era in the therapeutic management of the disease, but the potential risks and benefits of these agents must be weighed carefully.
Moerman RV, Bootsma H, Kroese FG, Vissink A.	Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.	Sjögren's syndrome in older patients: aetiology, diagnosis and management.	Drugs Aging. 2013 Mar; 30(3):137-53. doi: 10.1007/s40266-013-0050-7.	Sjögren's syndrome (SS) is a systemic autoimmune disease, characterized by chronic inflammation of exocrine glands that results in development of xerostomia and keratoconjunctivitis sicca. The disease activity of SS is not restricted to exocrine glands, and many other organs and organ systems can be involved. Diagnosis of SS in the elderly population can be challenging because xerostomia, dry eyes, symptoms of fatigue, weight loss and muscle pain are also common features of old age. Delay between clinical onset and diagnosis of SS in the elderly may be due to the shared features of SS and old age. The 2002 revised American-European Consensus Group (AECG) classification criteria for SS are the preferred tool used to confirm diagnosis of SS, but recently alternative criteria have been put forward by the American College of Rheumatology (ACR). The AECG criteria set combines subjective symptoms of dry eyes and dry mouth with objective signs of keratoconjunctivitis sicca, salivary gland dysfunction and histopathological (salivary gland biopsy) and serological (autoantibodies against SSA/Ro and SSB/La antigens) features. Treatment of SS in the elderly does not differ from that in younger patients. The aims of the treatment of SS are to control glandular and extraglandular manifestations, to prevent damage to organ systems and loss of function, and to decrease morbidity and mortality. Treatment of the elderly can be complicated by co-morbidities, an increased rate of adverse events related to therapeutic agents, and polypharmacy. Therefore, careful follow-up of the treatment is required.
Montoya JG, Kogelnik AM, Bhangoo M, Lunn MR, Flamand L, Merrihew LE, Watt	Department of Medicine, Stanford University School of Medicine, Stanford, California; Division of	Randomized clinical trial to evaluate the efficacy and safety of valganciclovir in a subset of patients	J Med Virol. 2013 Dec; 85(12):2101-9. doi: 10.1002/jmv.23713. Epub 2013 Aug 19	There is no known treatment for chronic fatigue syndrome (CFS). Little is known about its pathogenesis. Human herpesvirus 6 (HHV-6) and Epstein-Barr virus (EBV) have been proposed as infectious triggers. Thirty CFS patients with elevated IgG antibody titers against HHV-6 and EBV were randomized 2:1 to receive valganciclovir (VGCV) or placebo for 6 months in a double-blind, placebo-controlled trial. Clinical

T, Kubo JT, Paik J, Desai M.	Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California.	with chronic fatigue syndrome.		endpoints aimed at measuring physical and mental fatigue included the Multidimensional Fatigue Inventory (MFI-20) and Fatigue Severity Scale (FSS) scores, self-reported cognitive function, and physician-determined responder status. Biological endpoints included monocyte and neutrophil counts and cytokine levels. VGCV patients experienced a greater improvement by MFI-20 at 9 months from baseline compared to placebo patients but this difference was not statistically significant. However, statistically significant differences in trajectories between groups were observed in MFI-20 mental fatigue subscore (P=0.039), FSS score (P=0.006), and cognitive function (P=0.025). VGCV patients experienced these improvements within the first 3 months and maintained that benefit over the remaining 9 months. Patients in the VGCV arm were 7.4 times more likely to be classified as responders (P=0.029). In the VGCV arm, monocyte counts decreased (P<0.001), neutrophil counts increased (P=0.037) and cytokines were more likely to evolve towards a Th1-profile (P<0.001). Viral IgG antibody titers did not differ between arms. VGCV may have clinical benefit in a subset of CFS patients independent of placebo effect, possibly mediated by immunomodulation and/or antiviral effect. Further investigation with longer treatment duration and a larger sample size is warranted.
Mørch K, Hanevik K, Rivenes AC, Bødtker JE, Næss H, Stubhaug B, Wensaas KA, Rortveit G, Eide GE, Hausken T, Langeland N.	National Centre for Tropical Infectious Diseases, Department of Medicine, Haukeland University Hospital, Bergen, Norway. kristine.morch@helse-bergen.no	Chronic fatigue syndrome 5 years after giardiasis: differential diagnoses, characteristics and natural course.	BMC Gastroenterol. 2013 Feb 12;13:28. doi: 10.1186/1471-230X-13-28.	BACKGROUND: A high prevalence of chronic fatigue has previously been reported following giardiasis after a large waterborne outbreak in Bergen, Norway in 2004. The aim of this study was to describe and evaluate differential diagnoses and natural course of fatigue five years after giardiasis among patients who reported chronic fatigue three years after the infection. METHODS: Patients who three years after Giardia infection met Chalder's criteria for chronic fatigue (n=347) in a questionnaire study among all patients who had laboratory confirmed giardiasis during the Bergen outbreak (n=1252) were invited to participate in this study five years after the infection (n=253). Structured interviews and clinical examination were performed by specialists in psychiatry, neurology and internal medicine/infectious diseases. Fukuda et al's 1994 criteria were used to diagnose chronic fatigue syndrome (CFS) and idiopathic chronic fatigue (ICF). Self-reported fatigue recorded with Chalder Fatigue Questionnaire three and five years after infection were compared. RESULTS: 53 patients were included. CFS was diagnosed in 41.5% (22/53) and ICF in 13.2% (7/53). Chronic fatigue caused by other aetiology was diagnosed in 24.5% (13/53); five of these patients had sleep apnoea/hypopnoea syndrome, six had depression and five anxiety disorder, and among these two had more than one diagnosis. Fatigue had resolved in 20.8% (11/53). Self-reported fatigue score in the cohort was significantly reduced at five years compared to three years (p<0.001). CONCLUSION: The study shows that Giardia duodenalis may induce CFS persisting as long as five years after the infection. Obstructive sleep apnoea/hypopnoea syndrome, depression and anxiety were important differential diagnoses, or possibly comorbidities, to post-

				infectious fatigue in this study. Improvement of chronic fatigue in the period from three to five years after giardiasis was found.
Morris G, Anderson G, Berk M, Maes M.	Tir Na Nog, Bryn Road Seaside 87, Llanelli, SA152LW, Wales, UK.	Coenzyme Q10 depletion in medical and neuropsychiatric disorders: potential repercussions and therapeutic implications	Mol Neurobiol. 2013 Dec; 48(3):883-903. doi: 10.1007/s12035-013-8477-8. Epub 2013 Jun 13.	Coenzyme Q10 (CoQ10) is an antioxidant, a membrane stabilizer, and a vital cofactor in the mitochondrial electron transport chain, enabling the generation of adenosine triphosphate. It additionally regulates gene expression and apoptosis; is an essential cofactor of uncoupling proteins; and has anti-inflammatory, redox modulatory, and neuroprotective effects. This paper reviews the known physiological role of CoQ10 in cellular metabolism, cell death, differentiation and gene regulation, and examines the potential repercussions of CoQ10 depletion including its role in illnesses such as Parkinson's disease, depression, myalgic encephalomyelitis/chronic fatigue syndrome, and fibromyalgia. CoQ10 depletion may play a role in the pathophysiology of these disorders by modulating cellular processes including hydrogen peroxide formation, gene regulation, cytoprotection, bioenegetic performance, and regulation of cellular metabolism. CoQ10 treatment improves quality of life in patients with Parkinson's disease and may play a role in delaying the progression of that disorder. Administration of CoQ10 has antidepressive effects. CoQ10 treatment significantly reduces fatigue and improves ergonomic performance during exercise and thus may have potential in alleviating the exercise intolerance and exhaustion displayed by people with myalgic encepholamyletis/chronic fatigue syndrome. Administration of CoQ10 improves hyperalgesia and quality of life in patients with fibromyalgia. The evidence base for the effectiveness of treatment with CoQ10 may be explained via its ability to ameliorate oxidative stress and protect mitochondria.
Morris G, Anderson G, Galecki P, Berk M, Maes M.	Tir Na Nog, Bryn Road Seaside 87, Llanelli SA152LW, UK.	A narrative review on the similarities and dissimilarities between myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and sickness behavior.	BMC Med. 2013 Mar 8; 11:64. doi: 10.1186/1741-7015-11-64.	It is of importance whether myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a variant of sickness behavior. The latter is induced by acute infections/injury being principally mediated through proinflammatory cytokines. Sickness is a beneficial behavioral response that serves to enhance recovery, conserves energy and plays a role in the resolution of inflammation. There are behavioral/symptomatic similarities (for example, fatigue, malaise, hyperalgesia) and dissimilarities (gastrointestinal symptoms, anorexia and weight loss) between sickness and ME/CFS. While sickness is an adaptive response induced by proinflammatory cytokines, ME/CFS is a chronic, disabling disorder, where the pathophysiology is related to activation of immunoinflammatory and oxidative pathways and autoimmune responses. While sickness behavior is a state of energy conservation, which plays a role in combating pathogens, ME/CFS is a chronic disease underpinned by a state of energy depletion. While sickness is an acute response to infection/injury, the trigger factors in ME/CFS are less well defined and encompass acute and chronic infections, as well as inflammatory or autoimmune diseases. It is concluded that sickness behavior and ME/CFS are two different conditions.
Morris G, Berk M,	Mumbles Head,	The Emerging Role of	Mol Neurobiol. 2013 Sep 26.	The World Health Organization classifies myalgic encephalomyelitis/chronic fatigue

Galecki P, Maes M.	Pembrey, Llanelli, UK.	Autoimmunity in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/cfs).	[Epub ahead of print]	syndrome (ME/cfs) as a nervous system disease. Together with other diseases under the G93 heading, ME/cfs shares a triad of abnormalities involving elevated oxidative and nitrosative stress (O&NS), activation of immuno-inflammatory pathways, and mitochondrial dysfunctions with depleted levels of adenosine triphosphate (ATP) synthesis. There is also abundant evidence that many patients with ME/cfs (up to around 60 %) may suffer from autoimmune responses. A wide range of reported abnormalities in ME/cfs are highly pertinent to the generation of autoimmunity. Here we review the potential sources of autoimmunity which are observed in people with ME/cfs. The increased levels of pro-inflammatory cytokines, e.g., interleukin-1 and tumor necrosis factor-α, and increased levels of nuclear factor-κB predispose to an autoimmune environment. Many cytokine abnormalities conspire to produce a predominance of effector B cells and autoreactive T cells. The common observation of reduced natural killer cell function in ME/cfs is a source of disrupted homeostasis and prolonged effector T cell survival. B cells may be pathogenic by playing a role in autoimmunity independent of their ability to produce antibodies. The chronic or recurrent viral infections seen in many patients with ME/cfs can induce autoimmunity by mechanisms involving molecular mimicry and bystander activation. Increased bacterial translocation, as observed in ME/cfs, is known to induce chronic inflammation and autoimmunity. Low ATP production and mitochondrial dysfunction is a source of autoimmunity by inhibiting apoptosis and stimulating necrotic cell death. Self-epitopes may be damaged by exposure to prolonged O&NS, altering their immunogenic profile and become a target for the host's immune system. Nitric oxide may induce many faces of autoimmunity stemming from elevated mitochondrial membrane hyperpolarization and blockade of the methionine cycle with subsequent hypomethylation of DNA. Here we also outline options for treatment involving rituximab and endotherapia.
Morris G, Maes M.	Tir Na Nog, Pembrey, Llanelli, UK. activatedmicroglia@gmail.com.	Myalgic encephalomyelitis/ chronic fatigue syndrome and encephalomyelitis disseminata/multiple sclerosis show remarkable levels of similarity in phenomenology and neuroimmune characteristics.	BMC Med. 2013 Sep 17;11:205. doi: 10.1186/1741-7015-11-205.	BACKGROUND: 'Encephalomyelitis disseminata' (multiple sclerosis) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) are both classified as diseases of the central nervous system by the World Health Organization. This review aims to compare the phenomenological and neuroimmune characteristics of MS with those of ME/CFS. DISCUSSION: There are remarkable phenomenological and neuroimmune overlaps between both disorders. Patients with ME/CFS and MS both experience severe levels of disabling fatigue and a worsening of symptoms following exercise and resort to energy conservation strategies in an attempt to meet the energy demands of day-to-day living. Debilitating autonomic symptoms, diminished cardiac responses to exercise, orthostatic intolerance and postural hypotension are experienced by patients with both illnesses. Both disorders show a relapsing-remitting or progressive course, while infections and psychosocial stress play a large part in worsening of fatigue symptoms. Activated immunoinflammatory, oxidative and nitrosative (O+NS) pathways and autoimmunity occur in both illnesses. The consequences of O+NS

				damage to self-epitopes is evidenced by the almost bewildering and almost identical array of autoantibodies formed against damaged epitopes seen in both illnesses. Mitochondrial dysfunctions, including lowered levels of ATP, decreased phosphocreatine synthesis and impaired oxidative phosphorylation, are heavily involved in the pathophysiology of both MS and ME/CFS. The findings produced by neuroimaging techniques are quite similar in both illnesses and show decreased cerebral blood flow, atrophy, gray matter reduction, white matter hyperintensities, increased cerebral lactate and choline signaling and lowered acetyl-aspartate levels. SUMMARY: This review shows that there are neuroimmune similarities between MS and ME/CFS. This further substantiates the view that ME/CFS is a neuroimmune illness and that patients with MS are immunologically primed to develop symptoms of ME/CFS
Morris G, Maes M.	Mumbles Head, Pembrey llanelli, UK.	Case definitions and diagnostic criteria for Myalgic Encephalomyelitis and Chronic fatigue Syndrome: from clinical-consensus to evidence-based case definitions.	Neuro Endocrinol Lett. 2013; 34(3):185-99.	The symptom spectrum of Myalgic Encephalomyelitis (ME) was first detailed in 1959 and later operationalised into a diagnostic protocol (Melvin Ramsey). In 1988 the Holmes case definition coined the term chronic fatigue syndrome (CFS). Fukuda's Centers for Disease Control and Prevention criteria are very heterogeneous and comprise patients with milder symptoms than the Holmes case definition. The CDC Empirical Criteria for CFS lack sensitivity and/or specificity. Other CFS definitions, e.g. the Oxford criteria, delineate people with idiopathic fatigue. Some authors make the clinical CFS diagnosis when slightly increased self-rated fatigue scores are present. In 2011, Carruthers' International Consensus Criteria attempted to restore the focus on selecting people who suffer from ME. Cognitive bias in criteria construction, patient selection, data collection and interpretation has led to the current state of epistemological chaos with ME, CFS, CFS/ME and ME/CFS, and CF being used interchangeably. Moreover, none of the above mentioned classifications meet statistically based criteria for validation. Diagnostic criteria should be based on statistical methods rather than consensus declarations. Ongoing discussions about which case definition to employ miss the point that the criteria did not pass appropriate external validation. In 2012, Maes et al. performed pattern recognition methods and concluded that CFS patients (according to Fukuda's criteria) should be divided into those with CFS or ME, on the basis that people with ME display a worsening of their illness following increases in physical or cognitive activity. Both ME and CFS are complex disorders that share neuro-immune disturbances, which are more severe in ME than in CFS. This paper expands on that strategy and details a range of objective tests, which confirm that a person with ME or CFS has a neuro-immune disease. By means of pattern recognition methods future research should refine the Maes' case definitions for ME and CFS by including well-scaled symptoms, staging characteristics and neuro-immune biomarkers, including immune-inflammatory assays, bioenergetic markers and brain imaging.
Morris G, Maes M.	Tir Na Nog, Pembrey,	A neuro-immune	Metab Brain Dis. 2013 Dec;	This paper proposes a neuro-immune model for Myalgic Encephalomyelitis/Chronic

	Llanelli, UK.	model of Myalgic Encephalomyelitis/Chronic fatigue syndrome.	28(4):523-40. doi: 10.1007/s11011-012-9324-8. Epub 2012 Jun 21.	fatigue syndrome (ME/CFS). A wide range of immunological and neurological abnormalities have been reported in people suffering from ME/CFS. They include abnormalities in proinflammatory cytokines, raised production of nuclear factor-κB, mitochondrial dysfunctions, autoimmune responses, autonomic disturbances and brain pathology. Raised levels of oxidative and nitrosative stress (O&NS), together with reduced levels of antioxidants are indicative of an immuno-inflammatory pathology. A number of different pathogens have been reported either as triggering or maintaining factors. Our model proposes that initial infection and immune activation caused by a number of possible pathogens leads to a state of chronic peripheral immune activation driven by activated O&NS pathways that lead to progressive damage of self epitopes even when the initial infection has been cleared. Subsequent activation of autoreactive T cells conspiring with O&NS pathways cause further damage and provoke chronic activation of immuno-inflammatory pathways. The subsequent upregulation of proinflammatory compounds may activate microglia via the vagus nerve. Elevated proinflammatory cytokines together with raised O&NS conspire to produce mitochondrial damage. The subsequent ATP deficit together with inflammation and O&NS are responsible for the landmark symptoms of ME/CFS, including post-exertional malaise. Raised levels of O&NS subsequently cause progressive elevation of autoimmune activity facilitated by molecular mimicry, bystander activation or epitope spreading. These processes provoke central nervous system (CNS) activation in an attempt to restore immune homeostatsis. This model proposes that the antagonistic activities of the CNS response to peripheral inflammation, O&NS and chronic immune activation are responsible for the remitting-relapsing nature of ME/CFS. Leads for future research are suggested based on this neuro-immune model.
Morriss R.	[No address quoted]	Chronic fatigue syndrome/myalgic encephalomyelitis: more heat, some light--directions for research and clinical practice.	J Neurol Neurosurg Psychiatry. 2013 Feb 13. [Epub ahead of print]	[No abstract given]
Moss-Morris R, Deary V, Castell B.	Psychology Department, King's College London, London, UK. rona.moss-morris@kcl.ac.uk	Chronic fatigue syndrome.	Handb Clin Neurol. 2013; 110:303-14. doi: 10.1016/B978-0-444-52901-5.00025-3.	Chronic fatigue syndrome (CFS) is an illness characterized by disabling fatigue of at least 6 months. The aetiology of the condition has been hotly debated. In this chapter the evidence for CFS as a post viral condition and/or a neurological condition is reviewed. Although there is evidence that CFS is triggered by certain viruses in some patients and that neurobiological changes such as hypocortisolism are associated with the syndrome, neither mechanism is sufficient to explain the extent of the symptoms or disability experienced by patients. It is unlikely that CFS can be understood through one aetiological mechanism. Rather it is a complex illness which is best explained in

				terms of a multifactorial cognitive behavioural model. This model proposes that CFS is precipitated by life events and/or viral illness in vulnerable individuals, such as those who are genetically predisposed, prone to distress, high achievement, and over or under activity. A self perpetuating cycle where physiological changes, illness beliefs, reduced and inconsistent activity, sleep disturbance, medical uncertainty and lack of guidance interact to maintain symptoms. Treatments based on this model including cognitive behavioural therapy and graded exercise therapy are effective at significantly reducing fatigue and disability in CFS. This chapter provides a description of these approaches and details of the trials conducted in the area.
Mostafalou S, Abdollahi M.	Department of Toxicology and Pharmacology, Faculty of Pharmacy and Pharmaceutical Sciences Research Center, Tehran University of Medical Sciences, Tehran, Iran.	Pesticides and human chronic diseases: evidences, mechanisms, and perspectives.	Toxicol Appl Pharmacol. 2013 Apr 15; 268(2):157-77. doi: 10.1016/j.taap.2013.01.025. Epub 2013 Feb 9.	Along with the wide use of pesticides in the world, the concerns over their health impacts are rapidly growing. There is a huge body of evidence on the relation between exposure to pesticides and elevated rate of chronic diseases such as different types of cancers, diabetes, neurodegenerative disorders like Parkinson, Alzheimer, and amyotrophic lateral sclerosis (ALS), birth defects, and reproductive disorders. There is also circumstantial evidence on the association of exposure to pesticides with some other chronic diseases like respiratory problems, particularly asthma and chronic obstructive pulmonary disease (COPD), cardiovascular disease such as atherosclerosis and coronary artery disease, chronic nephropathies, autoimmune diseases like systemic lupus erythematous and rheumatoid arthritis, chronic fatigue syndrome, and aging. The common feature of chronic disorders is a disturbance in cellular homeostasis, which can be induced via pesticides' primary action like perturbation of ion channels, enzymes, receptors, etc., or can as well be mediated via pathways other than the main mechanism. In this review, we present the highlighted evidence on the association of pesticide's exposure with the incidence of chronic diseases and introduce genetic damages, epigenetic modifications, endocrine disruption, mitochondrial dysfunction, oxidative stress, endoplasmic reticulum stress and unfolded protein response (UPR), impairment of ubiquitin proteasome system, and defective autophagy as the effective mechanisms of action.
Murgai M, Thomas J, Cherepanova O, Delviks-Frankenberry K, Deeble P, Pathak VK, Rekosh D, Owens G.	Robert M, Berne Cardiovascular Research Center, University of Virginia, School of Medicine Charlottesville, Charlottesville, VA 22908, USA.	Xenotropic MLV envelope proteins induce tumor cells to secrete factors that promote the formation of immature blood vessels.	Retrovirology. 2013 Mar 27; 10:34. doi: 10.1186/1742-4690-10-34.	BACKGROUND: Xenotropic Murine leukemia virus-Related Virus (XMRV) is a γ-retrovirus initially reported to be present within familial human prostate tumors and the blood of patients with chronic fatigue syndrome. Subsequent studies however were unable to replicate these findings, and there is now compelling evidence that the virus evolved through rare retroviral recombination events in human tumor cell lines established through murine xenograft experiments. There is also no direct evidence that XMRV infection has any functional effects that contribute to tumor pathogenesis. RESULTS: Herein we describe an additional xenotropic MLV, "B4rv", found in a cell line derived from xenograft experiments with the human prostate cancer LNCaP cell line. When injected subcutaneously in nude mice, LNCaP cells infected with XMRV or B4rv formed larger tumors that were highly hemorrhagic and displayed poor pericyte/smooth muscle cell (SMC) investment, markers of increased

				metastatic potential. Conditioned media derived from XMRV- or B4rv-infected LNCaPs, but not an amphotropic MLV control virus infected LNCaPs, profoundly decreased expression of marker genes in cultured SMC, consistent with inhibition of SMC differentiation/maturation. Similar effects were seen with a chimeric virus of the amphotropic MLV control virus containing the XMRV env gene, but not with an XMRV chimeric virus containing the amphotropic MLV env gene. UV-inactivated XMRV and pseudovirions that were pseudotyped with XMRV envelope protein also produce conditioned media that down-regulated SMC marker gene expression in vitro. CONCLUSIONS: Together these results indicate that xenotropic MLV envelope proteins are sufficient to induce the production of factors by tumor cells that suppress vascular SMC differentiation, providing evidence for a novel mechanism by which xenotropic MLVs might alter tumor pathogenesis by disrupting tumor vascular maturation. Although it is highly unlikely that either XMRV or B4Rv themselves infect humans and are pathogenic, the results suggest that xenograft approaches commonly used in the study of human cancer promote the evolution of novel retroviruses with pathogenic properties.
Murray B, Yashar BM, Uhlmann WR, Clauw DJ, Petty EM.	Division of Cardiology, Johns Hopkins Hospital, Baltimore, Maryland.	Ehlers-Danlos syndrome, hypermobility type: A characterization of the patients' lived experience.	Am J Med Genet A. 2013 Dec; 161(12):2981-8. doi: 10.1002/ajmg.a.36293. Epub 2013 Nov 6.	Hypermobility type Ehlers-Danlos syndrome (EDS-HT) is an inherited connective tissue disorder clinically diagnosed by the presence of significant joint hypermobility and associated skin manifestations. This article presents a large-scale study that reports the lived experience of EDS-HT patients, the broad range of symptoms that individuals with EDS-HT experience, and the impact these symptoms have on daily functioning. A 237-item online survey, including validated questions regarding pain and depression, was developed. Four hundred sixty-six (466) adults (90% female, 52% college or higher degree) with a self-reported diagnosis of EDS-HT made in a clinic or hospital were included. The most frequently reported symptoms were joint pain (99%), hypermobility (99%), and limb pain (91%). They also reported a high frequency of other conditions including chronic fatigue (82%), anxiety (73%), depression (69%), and fibromyalgia (42%). Forty-six percent of respondents reported constant pain often described as aching and tiring/exhausting. Despite multiple interventions and therapies, many individuals (53%) indicated that their diagnosis negatively affected their ability to work or attend school. Our results show that individuals with EDS-HT can experience a wide array of symptoms and co-morbid conditions. The degree of constant pain and disability experienced by the majority of EDS-HT respondents is striking and illustrates the impact this disorder has on quality of life as well as the clinical challenges inherent in managing this complex connective tissue disorder.
Myhill S, Booth NE, McLaren-Howard J.	Sarah Myhill Ltd Llangunllo, Powys UK.	Targeting mitochondrial dysfunction in the treatment of Myalgic Encephalomyelitis/C	Int J Clin Exp Med. 2013; 6(1):1-15. Epub 2012 Nov 20.	We report on an audit of 138 ME/CFS patients who attended a private practice and took the ATP Profile biomedical test. The results revealed that all of these patients had measureable mitochondrial dysfunction. A basic treatment regime, based on 1) eating the evolutionary correct stone-age diet, 2) ensuring optimum hours of good quality sleep, 3) taking a standard package of nutritional supplements, and 4) getting

		hronic Fatigue Syndrome (ME/CFS) - a clinical audit.		the right balance between work and rest, was recommended for all patients. Additions to the basic regime were tailored for each patient according to the results of the ATP Profile and additional nutritional tests and clues from the clinical history. Mitochondrial function is typically impaired in two ways: substrate or co-factor deficiency, and inhibition by chemicals, exogenous or endogenous. For the former, additional nutrients are recommended where there is a deficiency, and for the latter, improvement of anti-oxidant status and selective chelation therapy or far-infrared saunas are appropriate. We show case histories of nine patients who have taken the ATP Profile on three or four occasions, and a before-and-after treatment summary of the 34 patients who have had at least two ATP Profile tests separated by some months. Finally, we summarize the results for the 30 patients who followed all aspects of the treatment regime and compare them with the 4 patients who were lax on two or more aspects of the treatment regime. All patients who followed the treatment regime improved in mitochondrial function by on average a factor of 4.
Nakamura T, Schwander S, Donnelly R, Cook DB, Ortega F, Togo F, Yamamoto Y, Cherniack NS, Klapholz M, Rapoport D, Natelson BH.	Pain & Fatigue Study Center.	Exercise and sleep deprivation do not change cytokine expression levels in patients with chronic fatigue syndrome.	Clin Vaccine Immunol. 2013 Nov; 20 (11):1736-42. doi: 10.1128/CVI.00527-13. Epub 2013 Sep 11.	A major hypothesis regarding the cause of chronic fatigue syndrome (CFS) is immune dysregulation, thought to be reflected in upregulated proinflammatory cytokines leading to the symptoms that are characteristic of this illness. Because the symptoms worsen with physical exertion or sleep loss, we hypothesized that we could use these stressors to magnify the underlying potential pathogenic abnormalities in the cytokine systems of people with CFS. We conducted repeat blood sampling for cytokine levels from healthy subjects and CFS patients during both postexercise and total sleep deprivation nights and assayed for protein levels in the blood samples, mRNA activity in peripheral blood lymphocytes (PBLs), and function in resting and stimulated PBLs. We found that these environmental manipulations did not produce clinically significant upregulation of proinflammatory cytokines. These data do not support an important role of immune dysregulation in the genesis of stress-induced worsening of CFS.
Nam KJ, Kim YJ, Lee SY, Lee JG, Cho YH, Lee YH, Choi EJ, Tak YJ, Yi DW, Park SW, Jeong DW.	Department of Family Medicine, Pusan National University Yangsan Hospital, Yangsan, Korea.	A case of incidentally discovered subclinical Cushing syndrome in a patient with chronic fatigue and anxiety.	Korean J Fam Med. 2013 Jul;34(4):289-92. doi: 10.4082/kjfm.2013.34.4.289. Epub 2013 Jul 24.	Subclinical Cushing syndrome (SCS) is a hypothalamic-pituitary-adrenal axis abnormality characterized by autonomous cortisol secretion in patients with no typical signs or symptoms of Cushing syndrome. SCS patients may have adverse metabolic and cardiovascular effects due to slight, but continuous glucocorticoid secretion. Glucocorticoids also affect behavior, mood, neural activity, and a number of specific biochemical processes in the central nervous system. Here, we report a case of SCS due to an adrenal incidentaloma in a hypertensive diabetic patient who presented with chronic fatigue and anxiety that disappeared after the removal of the adrenal adenoma.
Natelson BH.	Director, Pain and Fatigue Study Center, Department of Pain Medicine and Palliative	Brain dysfunction as one cause of CFS symptoms including difficulty with	Front Physiol. 2013 May 20; 4:109. doi: 10.3389/fphys.2013.00109. eCollection 2013.	We have been able to reduce substantially patient pool heterogeneity by identifying phenotypic markers that allow the researcher to stratify chronic fatigue syndrome (CFS) patients into subgroups. To date, we have shown that stratifying based on the presence or absence of comorbid psychiatric diagnosis leads to a group with evidence

	Care, Beth Israel Medical Center, Manhattan New York, NY, USA; Professor of Neurology, Albert Einstein College of Medicine, Bronx New York, NY, USA.	attention and concentration.		of neurological dysfunction across a number of spheres. We have also found that stratifying based on the presence or absence of comorbid fibromyalgia leads to information that would not have been found on analyzing the entire, unstratified patient group. Objective evidence of orthostatic intolerance (OI) may be another important variable for stratification and may define a group with episodic cerebral hypoxia leading to symptoms. We hope that this review will encourage other researchers to collect data on discrete phenotypes in CFS to allow this work to continue more broadly. Finding subgroups of CFS suggests different underlying pathophysiological processes responsible for the symptoms seen. Understanding those processes is the first step toward developing discrete treatments for each.
Neblett R, Cohen H, Choi Y, Hartzell MM, Williams M, Mayer TG, Gatchel RJ.	PRIDE Research Foundation, Dallas, Texas, USA.	The Central Sensitization Inventory (CSI): establishing clinically significant values for identifying central sensitivity syndromes in an outpatient chronic pain sample.	J Pain. 2013 May; 14(5):438-45. doi: 10.1016/j.jpain.2012.11.012. Epub 2013 Mar 13.	Central sensitization (CS) is a proposed physiological phenomenon in which central nervous system neurons become hyperexcitable, resulting in hypersensitivity to both noxious and non-noxious stimuli. The term central sensitivity syndrome (CSS) describes a group of medically indistinct (or nonspecific) disorders, such as fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome, for which CS may be a common etiology. In a previous study, the Central Sensitization Inventory (CSI) was introduced as a screening instrument for clinicians to help identify patients with a CSS. It was found to have high reliability and validity (test-retest reliability = .82; Cronbach's alpha = .88). The present study investigated a cohort of 121 patients who were referred to a multidisciplinary pain center, which specializes in the assessment and treatment of complex pain and psychophysiological disorders, including CSSs. A large percentage of patients (n = 89, 74%) met clinical criteria for one or more CSSs, and CSI scores were positively correlated with the number of diagnosed CSSs. A receiver operating characteristic analysis determined that a CSI score of 40 out of 100 best distinguished between the CSS patient group and a nonpatient comparison sample (N = 129) (area under the curve = .86, sensitivity = 81%, specificity = 75%).PERSPECTIVE: The CSI is a new self-report screening instrument to help identify patients with CSSs, including fibromyalgia. The present study investigated CSI scores in a heterogeneous pain population with a large percentage of CSSs, and a normative nonclinical sample to determine a clinically relevant cutoff value.
Nes LS, Ehlers SL, Whipple MO, Vincent A.	Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA ; Center for Shared Decision Making and Collaborative Care Research, Oslo University Hospital,	Self-regulatory fatigue in chronic multisymptom illnesses: scale development, fatigue, and self-control.	J Pain Res. 2013; 6:181-8. doi: 10.2147/JPR.S40014. Epub 2013 Mar 6.	BACKGROUND: Self-regulatory capacity involves ability to regulate thoughts, emotions, and behavior. Chronic multisymptom illnesses such as fibromyalgia and chronic fatigue syndrome are accompanied by numerous challenges, and have recently been associated with self-regulatory fatigue (SRF). Chronic multisymptom illnesses are also frequently associated with physical fatigue, and through development of a scale measuring SRF, the current study aimed to examine how SRF can be distinguished from physical fatigue. The study also sought to distinguish SRF from self-control. METHODS: Two self-regulation researchers developed 30 items related to self-regulatory capacity. These items were distributed to patients (n = 296)

	Oslo, Norway.			diagnosed with chronic multisymptom illness together with validated measures of physical fatigue and self-control. A principal factor analysis was employed to examine factor structures, identify inter-item relationships, and aid in scale development. RESULTS: The final proposed scale consisted of 18 items measuring self-regulatory capacity (SRF-18) with cognitive, emotional, and behavioral SRF components. Internal consistency and reliability was acceptable (Cronbach's á = 0.81). The final scale was moderately correlated with self-control (r = -0.48) and highly correlated with physical fatigue (r = 0.75), although more so with emotional (r = 0.72) and mental (r = 0.65) than physical (r = 0.46) fatigue components. CONCLUSION: The current study suggests a new scale for measurement of SRF in chronic multisymptom illness. Although cross-validation studies are necessary, such a scale may contribute to a better understanding of the concept of self-regulation and the role of SRF in chronic illness. Although related to physical fatigue and self-control, the results point to SRF as a distinct construct.
Ng SM, Yiu YM.	Department of Social Work and Social Administration, University of Hong Kong, Hong Kong, China. ngsiuman@hku.hk	Acupuncture for chronic fatigue syndrome: a randomized, sham-controlled trial with single-blinded design.	Altern Ther Health Med. 2013 Jul-Aug;19 (4):21-6.	CONTEXT: Given that the etiology of chronic fatigue syndrome (CFS) is believed to be multidimensional, interventions generally have been nonspecific and typically produce only mild to moderate effects. In medical practice, treatment for CFS remains largely symptomatic. Preliminary evidence of the efficacy of acupuncture for CFS is available, but the field has lacked high-quality trials. OBJECTIVE: The research team conducted the study to determine the efficacy of acupuncture for CFS. DESIGN: A two-arm, randomized, controlled, singleblinded design was adopted. SETTING: The study took place in a teaching laboratory at the School of Chinese Medicine at the University of Hong Kong, Hong Kong, China. PARTICIPANTS: Recruited through press publicity in Hong Kong, 127 individuals--40 men and 87 women--participated in the study. Intervention Through careful implementation of sham acupuncture in the control group (CG), the study blinded all participants with regard to their experimental or control status. The treatment regime was 2 sessions/wk for 4 consecutive wk. OUTCOME MEASURES: Measures of fatigue (Chalder's Fatigue Scale), health-related quality of life (SF-12), and general mental health (GH Q-12) were taken at baseline and upon completion of treatment. RESULTS: Ninety-nine participants completed the interventions, with 50 and 49 participants in the experimental group (EG) and CG respectively. Repeated measures ANOVA revealed a significant decrease in physical (F (1,93) = 4.327; P = .040) and mental fatigue (F(1,96) = 10.451; P = .002) and improvement in the physical component score of SF-12 (F(1,93) = 4.774; P = .031). Considerable effects with Cohen's d were observed in the sham-control group: 0.92, 0.78, and 0.38 for the three scores, respectively. These positive effects could have included some therapeutic effects due to pressure on the acupuncture points from the sham needles in addition to normal placebo effects. The EG showed moderate net effect sizes with Cohen's d: 0.52, 0.63, and 0.54 for the three outcome measures, respectively. CONCLUSION: Despite considerable positive effects for the

				CG, the EG demonstrated significant net-effect sizes at a moderate magnitude in physical and mental fatigue and in the physical component of health-related quality of life. The impacts on general mental health outcomes appeared to be smaller.
Nguyen RH, Veasley C, Smolenski D.	Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN.	Latent class analysis of comorbidity patterns among women with generalized and localized vulvodynia: preliminary findings.	J Pain Res. 2013 Apr 18; 6:303-9. doi: 10.2147/JPR.S42940. Print 2013.	BACKGROUND: The pattern and extent of clustering of comorbid pain conditions with vulvodynia is largely unknown. However, elucidating such patterns may improve our understanding of the underlying mechanisms involved in these common causes of chronic pain. We sought to describe the pattern of comorbid pain clustering in a population-based sample of women with diagnosed vulvodynia. METHODS: A total of 1457 women with diagnosed vulvodynia self-reported their type of vulvar pain as localized, generalized, or both. Respondents were also surveyed about the presence of comorbid pain conditions, including temporomandibular joint and muscle disorders, interstitial cystitis, fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, endometriosis, and chronic headache. Age-adjusted latent class analysis modeled extant patterns of comorbidity by vulvar pain type, and a multigroup model was used to test for the equality of comorbidity patterns using a comparison of prevalence. A two-class model (no/single comorbidity versus multiple comorbidities) had the best fit in individual and multigroup models. RESULTS: For the no/single comorbidity class, the posterior probability prevalence of item endorsement ranged from 0.9% to 24.4%, indicating a low probability of presence. Conversely, the multiple comorbidity class showed that at least two comorbid conditions were likely to be endorsed by at least 50% of women in that class, and irritable bowel syndrome and fibromyalgia were the most common comorbidities regardless of type of vulvar pain. Prevalence of the multiple comorbidity class differed by type of vulvar pain: both (37.6% prevalence, referent), generalized (21.6% prevalence, adjusted odds ratio 0.41, 95% confidence interval 0.27-0.61), or localized (12.5% prevalence, adjusted odds ratio 0.31, 95% confidence interval 0.21-0.47). CONCLUSION: This novel work provides insight into potential shared mechanisms of vulvodynia by describing that a prominent comorbidity pattern involves having both irritable bowel syndrome and fibromyalgia. In addition, the prevalence of a multiple comorbidity class pattern increases with increasing severity of vulvar pain.
Nijhof SL, Priesterbach LP, Bleijenberg G, Engelbert RH, van de Putte EM.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht.	Functional improvement is accompanied by reduced pain in adolescent chronic fatigue syndrome.	Pain Med. 2013 Sep; 14(9):1435-8. doi: 10.1111/pme.12181. Epub 2013 Jun 26.	[No abstract given]
Nijhof SL, Priesterbach LP, Uiterwaal CS,	Department of Pediatrics, University Medical Center	Internet-based therapy for adolescents with	Pediatrics. 2013 Jun; 131(6):e1788-95. doi: 10.1542/peds.2012-2007.	OBJECTIVE: Cognitive behavioral therapy (CBT) is known to be an effective treatment of adolescents with chronic fatigue syndrome (CFS), but its availability is limited. Fatigue in Teenagers on the Internet (FITNET), an Internet-based CBT program for

Bleijenberg G, Kimpen JL, van de Putte EM.	Utrecht, Utrecht, Netherlands. s.l.nijhof@umcutrecht.nl	chronic fatigue syndrome: long-term follow-up.	Epub 2013 May 13.	adolescents with CFS, has been developed as an alternative to face-to-face CBT. Recently, its short-term effectiveness has been proven in a randomized clinical trial. Here we aimed to assess the long-term outcome of CFS in adolescents after FITNET treatment and after usual care. In addition, factors related to recovery at long-term follow-up (LTFU) for adolescents treated with the FITNET program were investigated. METHODS: The study was an LTFU of participants of the FITNET trial. Data were completed for 112 (88.2%) of 127 approached FITNET study participants. Primary outcomes were fatigue severity (Checklist Individual Strength-20), physical functioning (87-item Child Health Questionnaire), and school/work attendance. RESULTS: After a mean follow-up of 2.7 years, 66 (58.9%) adolescents had recovered from CFS. Most adolescents who recovered directly after treatment with FITNET were still recovered at LTFU. At LTFU there was no difference between the recovery rates for the different treatment strategies (original randomization: FITNET [64%] versus any form of usual care [52.8%]). Per additional month of "pretreatment disease duration," the odds for recovery were 4% lower (odds ratio: 0.96; 95% confidence interval: 0.93-0.99; P = .016), and per added point on "focus on bodily symptoms" (Body Consciousness Scale) of the mother (0-20 points) the odds for recovery were 11% lower (odds ratio: 0.89; 95% confidence interval: 0.80-0.99; P = .029). CONCLUSIONS: The short-term effectiveness of Internet-based CBT on adolescent CFS is maintained at LTFU. At LTFU, usual care led to similar recovery rates, although these rates were achieved at a slower pace.
Nijhof SL, Werker CL, van de Putte EM.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Office KE 04.133.1, Postbox 85090, 3508 AB, Utrecht, The Netherlands, s.l.nijhof@umcutrecht.nl.	Improvement rates in adolescent patients with chronic fatigue syndrome after receiving cognitive behavioural therapy. Correspondence in response to: Clinical Practice: Chronic fatigue syndrome-Author's reply.	Eur J Pediatr. 2013 Dec 10. [Epub ahead of print]	[No abstract given]
Nijs J, Ickmans K.	[No address quoted]	Postural orthostatic tachycardia syndrome as a clinically important subgroup of chronic fatigue syndrome: further evidence for	J Intern Med. 2013 May; 273(5):498-500. doi: 10.1111/joim.12034. Epub 2013 Feb 8.	Comment on J Intern Med. 2013 May; 273(5):501-10.

		central nervous system dysfunctioning.		
Nijs J, Lundberg M.	Pain in Motion Research Group, Departments of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium, Jo.Nijs@vub.ac.be.	Avoidance behavior towards physical activity in chronic fatigue syndrome and fibromyalgia: the fear for post-exertional malaise.	Clin Rheumatol. 2013 Nov 7. [Epub ahead of print]	[No abstract given]
Nijs J, Roussel N, Van Oosterwijck J, De Kooning M, Ickmans K, Struyf F, Meeus M, Lundberg M.	Pain in Motion research group, Department of Human Physiology and Rehabilitation Sciences, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Building L-Mfys, Pleinlaan 2, 1050 Brussels, Belgium. Jo.Nijs@vub.ac.be	Fear of movement and avoidance behaviour toward physical activity in chronic-fatigue syndrome and fibromyalgia: state of the art and implications for clinical practice.	Clin Rheumatol. 2013 Aug; 32(8):1121-9. doi: 10.1007/s10067-013-2277-4. Epub 2013 May 3.	Severe exacerbation of symptoms following physical activity is characteristic for chronic-fatigue syndrome (CFS) and fibromyalgia (FM). These exacerbations make it understandable for people with CFS and FM to develop fear of performing body movement or physical activity and consequently avoidance behaviour toward physical activity. The aims of this article were to review what measures are available for measuring fear of movement and avoidance behaviour, the prevalence fear of movement and avoidance behaviour toward physical activity and the therapeutic options with fear of movement and avoidance behaviour toward physical activity in patients with CFS and FM. The review revealed that fear of movement and avoidance behaviour toward physical activity is highly prevalent in both the CFS and FM population, and it is related to various clinical characteristics of CFS and FM, including symptom severity and self-reported quality of life and disability. It appears to be crucial for treatment (success) to identify CFS and FM patients displaying fear of movement and avoidance behaviour toward physical activity. Individually tailored cognitive behavioural therapy plus exercise training, depending on the patient's classification as avoiding or persisting, appears to be the most promising strategy for treating fear of movement and avoidance behaviour toward physical activity in patients with CFS and FM.
Nirenberg MJ.	Department of Neurology, NYU School of Medicine, New York, NY, USA. melissa.nirenberg@nyumc.org	Dopamine agonist withdrawal syndrome: implications for patient care.	Drugs Aging. 2013 Aug; 30(8):587-92. doi: 10.1007/s40266-013-0090-z.	Dopamine agonists are effective treatments for a variety of indications, including Parkinson's disease and restless legs syndrome, but may have serious side effects, such as orthostatic hypotension, hallucinations, and impulse control disorders (including pathological gambling, compulsive eating, compulsive shopping/buying, and hypersexuality). The most effective way to alleviate these side effects is to taper or discontinue dopamine agonist therapy. A subset of patients who taper a dopamine agonist, however, develop dopamine agonist withdrawal syndrome (DAWS), which has been defined as a severe, stereotyped cluster of physical and psychological

				symptoms that correlate with dopamine agonist withdrawal in a dose-dependent manner, cause clinically significant distress or social/occupational dysfunction, are refractory to levodopa and other dopaminergic medications, and cannot be accounted for by other clinical factors. The symptoms of DAWS include anxiety, panic attacks, dysphoria, depression, agitation, irritability, suicidal ideation, fatigue, orthostatic hypotension, nausea, vomiting, diaphoresis, generalized pain, and drug cravings. The severity and prognosis of DAWS is highly variable. While some patients have transient symptoms and make a full recovery, others have a protracted withdrawal syndrome lasting for months to years, and therefore may be unwilling or unable to discontinue DA therapy. Impulse control disorders appear to be a major risk factor for DAWS, and are present in virtually all affected patients. Thus, patients who are unable to discontinue dopamine agonist therapy may experience chronic impulse control disorders. At the current time, there are no known effective treatments for DAWS. For this reason, providers are urged to use dopamine agonists judiciously, warn patients about the risks of DAWS prior to the initiation of dopamine agonist therapy, and follow patients closely for withdrawal symptoms during dopamine agonist taper.
Norheim KB, Le Hellard S, Nordmark G, Harboe E, Gøransson L, Brun JG, Wahren-Herlenius M, Jonsson R, Omdal R.	Clinical Immunology Unit, Department of Internal Medicine, Stavanger University Hospital, Pb. 8100 Forus, 4068, Stavanger, Norway, katnorheim@gmail.com.	A possible genetic association with chronic fatigue in primary Sjögren's syndrome: a candidate gene study.	Rheumatol Int. 2013 Sep 3. [Epub ahead of print]	Fatigue is prevalent and disabling in primary Sjögren's syndrome (pSS). Results from studies in chronic fatigue syndrome (CFS) indicate that genetic variation may influence fatigue. The aim of this study was to investigate single nucleotide polymorphism (SNP) variations in pSS patients with high and low fatigue. A panel of 85 SNPs in 12 genes was selected based on previous studies in CFS. A total of 207 pSS patients and 376 healthy controls were genotyped. One-hundred and ninety-three patients and 70 SNPs in 11 genes were available for analysis after quality control. Patients were dichotomized based on fatigue visual analogue scale (VAS) scores, with VAS <50 denominated "low fatigue" (n = 53) and VAS ≥50 denominated "high fatigue" (n = 140). We detected signals of association with pSS for one SNP in SLC25A40 (unadjusted p = 0.007) and two SNPs in PKN1 (both p = 0.03) in our pSS case versus control analysis. The association with SLC25A40 was stronger when only pSS high fatigue patients were analysed versus controls (p = 0.002). One SNP in PKN1 displayed an association in the case-only analysis of pSS high fatigue versus pSS low fatigue (p = 0.005). This candidate gene study in pSS did reveal a trend for associations between genetic variation in candidate genes and fatigue. The results will need to be replicated. More research on genetic associations with fatigue is warranted, and future trials should include larger cohorts and multicentre collaborations with sharing of genetic material to increase the statistical power.
Oakes B, Hoagland-Henefield M, Komaroff AL,	Graduate Program in Pharmacology and Experimental Therapeutics, Sackler	Human endogenous retrovirus-K18 superantigen expression and	Clin Infect Dis. 2013 May; 56(10):1394-400. doi: 10.1093/cid/cit086. Epub 2013 Feb 13.	BACKGROUND: Chronic fatigue syndrome (CFS) is a complex, heterogeneous disease characterized by debilitating fatigue that is not improved with bed rest and worsens after physical activity or mental exertion. Despite extensive research into a cause of CFS, no definitive etiology has been determined; however, a large percentage of CFS

Erickson JL, Huber BT.	School of Graduate Biomedical Sciences, Tufts University, Boston, MA, USA.	human herpesvirus-6 and human herpesvirus-7 viral loads in chronic fatigue patients.		patients note an acute infectious event that triggers their fatigue. METHODS: Blood and saliva were collected from 39 CFS cases and 9 healthy control subjects. Peripheral blood mononuclear cells (PBMCs) were tested for human endogenous retrovirus-K18 (HERV-K18) env transcripts using a TaqMan quantitative polymerase chain reaction (qPCR). In addition, viral copy number of human herpesvirus-6 (HHV-6) and human herpesvirus-7 (HHV-7) were measured in both saliva and PBMCs using TaqMan qPCRs. Transcript levels and viral copy number were compared to patient CFS symptom severity. RESULTS: HERV-K18 env transcripts were not significantly different between healthy control subjects and CFS patients. Also, HERV-K18 env transcripts did not correlate with HHV-6 viral copy number or HHV-7 viral copy number in either PBMCs or saliva. HHV-6 viral copy number and HHV-7 viral copy number in both PBMCs and saliva were not significantly different between healthy control subjects and CFS patients. HERV-K18 env transcripts, HHV-6 viral copy number, and HHV-7 viral copy number did not correlate with CFS symptom severity. CONCLUSIONS: We fail to demonstrate a difference in HERV-K18 env transcripts, HHV-6 viral copy number, and HHV-7 viral copy number between CFS patients and healthy controls. Our data do not support the hypothesis of reactivation of HHV-6 or HHV-7 in CFS.
Ocon AJ.	Departments of Physiology/Medicine, Center for Hypotension, New York Medical College Valhalla, NY, USA.	Caught in the thickness of brain fog: exploring the cognitive symptoms of Chronic Fatigue Syndrome.	Front Physiol. 2013 Apr 5; 4:63. doi: 10.3389/fphys.2013.00063. eCollection 2013.	Chronic Fatigue Syndrome (CFS) is defined as greater than 6 months of persistent fatigue that is experienced physically and cognitively. The cognitive symptoms are generally thought to be a mild cognitive impairment, but individuals with CFS subjectively describe them as "brain fog." The impairment is not fully understood and often is described as slow thinking, difficulty focusing, confusion, lack of concentration, forgetfulness, or haziness in thought processes. Causes of "brain fog" and mild cognitive impairment have been investigated. Possible physiological correlates may be due to the effects of chronic orthostatic intolerance (OI) in the form of the Postural Tachycardia Syndrome (POTS) and decreases in cerebral blood flow (CBF). In addition, fMRI studies suggest that individuals with CFS may require increased cortical and subcortical brain activation to complete difficult mental tasks. Furthermore, neurocognitive testing in CFS has demonstrated deficits in speed and efficiency of information processing, attention, concentration, and working memory. The cognitive impairments are then perceived as an exaggerated mental fatigue. As a whole, this is experienced by those with CFS as "brain fog" and may be viewed as the interaction of physiological, cognitive, and perceptual factors. Thus, the cognitive symptoms of CFS may be due to altered CBF activation and regulation that are exacerbated by a stressor, such as orthostasis or a difficult mental task, resulting in the decreased ability to readily process information, which is then perceived as fatiguing and experienced as "brain fog." Future research looks to further explore these interactions, how they produce cognitive impairments, and explain the perception of "brain fog" from a mechanistic standpoint.
Oka T, Kanemitsu	Department of	Psychological stress	Biopsychosoc Med. 2013 Mar	BACKGROUND: Low-grade fever is a common symptom in patients with chronic

Y, Sudo N, Hayashi H, Oka K.	Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka 812-8582, Japan. oka-t@cephal.med.kyushu-u.ac.jp.	contributed to the development of low-grade fever in a patient with chronic fatigue syndrome: a case report.	8; 7(1):7. doi: 10.1186/1751-0759-7-7.	fatigue syndrome (CFS), but the mechanisms responsible for its development are poorly understood. We submit this case report that suggests that psychological stress contributes to low-grade fever in CFS. CASE PRESENTATION: A 26-year-old female nurse with CFS was admitted to our hospital. She had been recording her axillary temperature regularly and found that it was especially high when she felt stress at work. To assess how psychological stress affects temperature and to investigate the possible mechanisms for this hyperthermia, we conducted a 60-minute stress interview and observed the changes in the following parameters: axillary temperature, fingertip temperature, systolic blood pressure, diastolic blood pressure, heart rate, plasma catecholamine levels, and serum levels of interleukin (IL)-1β and IL-6 (pyretic cytokines), tumor necrosis factor-α and IL-10 (antipyretic cytokines). The stress interview consisted of recalling and talking about stressful events. Her axillary temperature at baseline was 37.2°C, increasing to 38.2°C by the end of the interview. In contrast, her fingertip temperature decreased during the interview. Her heart rate, systolic and diastolic blood pressures, and plasma levels of noradrenaline and adrenaline increased during the interview; there were no significant changes in either pyretic or antipyretic cytokines during or after the interview. CONCLUSIONS: A stress interview induced a 1.0°C increase in axillary temperature in a CFS patient. Negative emotion-associated sympathetic activation, rather than pyretic cytokine production, contributed to the increase in temperature induced by the stress interview. This suggests that psychological stress may contribute to the development or the exacerbation of low-grade fever in some CFS patients.
Oltra E, García-Escudero M, Mena-Durán AV, Monsalve V, Cerdá-Olmedo G.	Facultad de Medicina, C/Quevedo, 2, 46001 Valencia, Spain. elisa.oltra@ucv.es.	Lack of evidence for retroviral infections formerly related to chronic fatigue in Spanish Fibromyalgia patients.	Virol J. 2013 Nov 11; 10 (1):332. doi: 10.1186/1743-422X-10-332.	BACKGROUND: The etiology of fibromyalgia and chronic fatigue syndrome (FM/CFS) is currently unknown. A recurrent viral infection is an attractive hypothesis repeatedly found in the literature since it would explain the persistent pain and tiredness these patients suffer from. The initial striking link of two distinct orphan retroviruses: the gamma retroviruses murine leukemia virus (MLV)-related virus and the delta retrovirus T-lymphotropic virus type 2 (HTLV-2) to chronic fatigue have not been confirmed to date. RESULTS: Genomic DNA (gDNA) from 75 fibromyalgia patients suffering from chronic fatigue and 79 age-matched local healthy controls were screened for the presence of MLV-related and HTLV-2 related proviral sequences. The XMRV env gene was amplified in 20% of samples tested (24% patients/15% healthy controls). Unexpectedly, no PCR amplifications from independent gDNA preparations of the same individuals were obtained. None of the positive samples showed presence of contaminating murine sequences previously reported by other investigators, neither contained additional regions of the virus making us conclude that the initial env amplification came from spurious air-driven amplicon contaminants. No specific HTLV-2 sequences were obtained at any time from any of the 154 quality-controlled gDNA preparations screened. CONCLUSIONS: Previous associations between MLV-related or HTLV-2 retrovirus infection with chronic fatigue

				must be discarded. Thus, studies showing positive amplification of HTLV-2 sequences from chronic fatigue participants should be revised for possible undetected technical problems.To avoid false positives of viral infection, not only extreme precautions should be taken when nested-PCR reactions are prepared and exhaustive foreign DNA contamination controls performed, but also consistent amplification of diverse regions of the virus in independent preparations from the same individual must be demanded.The fact that our cohort of patients did not present evidence of any of the two types of retroviral infection formerly associated to chronic fatigue does not rule out the possibility that other viruses are involved in inciting or maintaining fibromyalgia and/or chronic fatigue conditions.
Oral A, Ilieva EM, Küçükdeveci AA, Varela E, Valero R, Berteanu M, Christodoulou N.	Member, Board Committee, UEMS Board of PRM, Department of Physical Medicine and RehabilitationIstanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey - aydanoral@yahoo.com .	Generalised and regional soft tissue pain syndromes. The role of physical and rehabilitation medicine physicians. The European perspective based on the best evidence. A paper by the UEMS-PRM Section Professional Practice Committee.	Eur J Phys Rehabil Med. 2013 Aug; 49 (4):535-49.	One of the objectives of the Professional Practice Committee (PPC) of the Physical and Rehabilitation Medicine (PRM) Section of the Union of European Medical Specialists (UEMS) is the development of the field of competence of PRM physicians in Europe. To achieve this objective, UEMS PRM Section PPC has adopted a systematic action plan of preparing a series of papers describing the role of PRM physicians in a number of disabling health conditions, based on the evidence of effectiveness of PRM interventions. Generalised and regional soft tissue pain syndromes constitute a major problem leading to loss of function and disability, resulting in enormous societal burden. The aim of this paper is to describe the unique role of PRM physicians in the management of these disabling conditions that require not only pharmacological interventions but also a holistic approach including the consideration of body functions, activities and participation as well as contextual factors as described in the ICF. Evidence-based effective PRM interventions include exercise and multicomponent treatment including a psychotherapeutic intervention such as cognitive behavioural therapy (CBT) in addition to exercise, the latter based on strong evidence for reducing pain and improving quality of life in fibromyalgia syndrome (FMS). Balneotherapy, meditative movement therapies, and acupuncture have also been shown as efficacious in improving symptoms in FMS. Emerging evidence suggests the use of transcranial magnetic or direct current stimulation (rTMS or tDCS) in FMS patients with intractable pain not alleviated by other interventions. Graded exercise therapy and CBT are evidence-based options for chronic fatigue syndrome. The use of some physical modalities and manipulation for myofascial pain syndrome is also supported by evidence. As for complex regional pain syndrome (CRPS), strong evidence exists for rTMS and graded motor imagery as well as moderate evidence for mirror therapy. Interventional techniques such as blocks and spinal cord stimulation may also be considered for CRPS based on varying levels of evidence. PRM physicians' functioning oriented approaches on the assessment and management, adopting the ICF as a reference, may well meet the needs of patients with soft tissue pain syndromes, the common problems for whom are loss of function and impaired quality of life. Available evidence for the effectiveness of PRM interventions serves as the

				basis for the explicit role of PRM specialists in the management of these health conditions
Osnes LT, Nakken B, Bodolay E, Szodoray P.	Institute of Immunology, Rikshospitalet, Oslo University Hospital, Norway.	Assessment of intracellular cytokines and regulatory cells in patients with autoimmune diseases and primary immunodeficiencies - novel tool for diagnostics and patient follow-up.	Autoimmun Rev. 2013 Aug; 12(10):967-71. doi: 10.1016/j.autrev.2013.02.003. Epub 2013 Mar 26.	Serum and intracytoplasmic cytokines are mandatory in host defense against microbes, but also play a pivotal role in the pathogenesis of autoimmune diseases by initiating and perpetuating various cellular and humoral autoimmune processes. The intricate interplay and fine balance of pro- and anti-inflammatory processes drive, whether inflammation and eventually organ damage will occur, or the inflammatory cascade quenches. In the early and late, as well as inactive and active stages of autoimmune diseases, different cellular and molecular patterns can dominate in these patients. However, the simultaneous assessment of pro- and anti-inflammatory biomarkers aids to define the immunological state of a patient. A group of the most useful inflammatory biomarkers are cytokines, and with increasing knowledge during the last decade their role have been well-defined in patients with autoimmune diseases and immunodeficiencies. Multiple pathological processes drive the development of autoimmunity and immunodeficiencies, most of which involve quantitative and qualitative disturbances in regulatory cells, cytokine synthesis and signaling pathways. The assessment of these biomarkers does not aid only in the mechanistic description of autoimmune diseases and immunodeficiencies, but further helps to subcategorize diseases and to evaluate therapy responses. Here, we provide an overview, how monitoring of cytokines and regulatory cells aid in the diagnosis and follow-up of patients with autoimmune diseases and immunodeficiencies furthermore, we pinpoint novel cellular and molecular diagnostic possibilities in these diseases.
Ozsahin M, Gonen I, Ermis F, Oktay M, Besir FH, Kutlucan A, Sahin A, Ataoglu S.	Department of Physical Medicine and Rehabilitation, Medical School of Duzce University Duzce, Turkey.	The prevalence of fibromyalgia among patients with hepatitis B virus infection.	Int J Clin Exp Med. 2013 Sep 25;6(9):804-8.	Fibromyalgia (FM) is a syndrome characterized by widespread and chronic musculoskeletal pain, fatigue, morning stiffness, and sleep disturbance. However, the etiopathogenesis of FM remains unclear. Various etiological factors have been suggested to trigger FM. These include systemic rheumatismal disease, physical trauma, psychological disorders, and chronic infections. We determined the prevalence of FM in patients with chronic active hepatitis B virus (HBV) and inactive hepatitis B carriers, compared with matched healthy controls. Seventy-seven HBV patients (39 HBV carriers and 38 with chronic active hepatitis), were evaluated for FM syndrome. Seventy-seven HBsAg-negative healthy subjects were enrolled as a control group. We found that FM was very prevalent in patients with HBV infections (22% of the total). We found no difference in FM prevalence when patients with chronic active hepatitis B infections (21% FM prevalence) and those who were inactive hepatitis B carriers (23% FM prevalence) were compared. FM was not associated with the levels of HBV-DNA, ALT, or AST. Recognition and management of FM in HBsAg-positive patients will aid in improvement of quality-of-life. We fully accept that our preliminary results require confirmation in studies including larger numbers of patients. More work is needed to allow us to understand the role played by, and the

				relevance of, infections (including HBV) in FM syndrome pathogenesis.
Pantry SN, Medveczky MM, Arbuckle JH, Luka J, Montoya JG, Hu J, Renne R, Peterson D, Pritchett JC, Ablashi DV, Medveczky PG.	Department of Molecular Medicine, University of South Florida, Morsani College of Medicine, Tampa, Florida 33612, USA.	Persistent human herpesvirus-6 infection in patients with an inherited form of the virus.	J Med Virol. 2013 Nov; 85(11):1940-6. doi: 10.1002/jmv.23685. Epub 2013 Jul 25.	Human herpesvirus-6 (HHV-6) A and 6B are ubiquitous betaherpesviruses viruses with lymphotropic and neurotropic potential. As reported earlier, these viruses establish latency by integration into the telomeres of host chromosomes. Chromosomally integrated HHV-6 (CIHHV-6) can be transmitted vertically from parent to child. Some CIHHV-6 patients are suffering from neurological symptoms, while others remain asymptomatic. Four patients with CIHHV-6 and CNS dysfunction were treated with valganciclovir or foscarnet. HHV-6 replication was detected by reverse transcriptase polymerase chain reaction amplification of a late envelope glycoprotein. In this study we also compared the inherited and persistent HHV-6 viruses by DNA sequencing. The prevalence of CIHHV-6 in this cohort of adult patients from the USA suffering from a wide range of neurological symptoms including long-term fatigue were found significantly greater than the reported 0.8% in the general population. Long-term antiviral therapy inhibited HHV-6 replication as documented by loss of viral mRNA production. Sequence comparison of the mRNA and the inherited viral genome revealed that the transcript is produced by an exogenous virus. In conclusion, the data presented here document that some individuals with CIHHV-6 are infected persistently with exogenous HHV-6 strains that lead to a wide range of neurological symptoms; the proposed name for this condition is inherited herpesvirus 6 syndrome or IHS.
Parkman HP, Yates K, Hasler WL, Nguyen L, Pasricha PJ, Snape WJ, Farrugia G, Koch KL, Calles J, Abell TL, Sarosiek I, McCallum RW, Lee L, Unalp-Arida A, Tonascia J, Hamilton F.	Gastroenterology Section, Parkinson Pavilion, School of Medicine, Temple University, 8th Floor 3401 North Broad Street, Philadelphia, PA 19140, USA. henry.parkman@temple.edu	Cholecystectomy and clinical presentations of gastroparesis.	Dig Dis Sci. 2013 Apr; 58(4):1062-73. doi: 10.1007/s10620-013-2596-y. Epub 2013 Mar 2.	BACKGROUND: Many patients with gastroparesis have had their gallbladders removed. AIM: To determine if clinical presentations of patients with gastroparesis differ in those with prior cholecystectomy compared to patients who have not had their gallbladder removed. METHODS: Gastroparetic patients were prospectively enrolled in the NIDDK Gastroparesis Registry. Detailed history and physical examinations were performed; patients filled out questionnaires including patient assessment of GI symptoms. RESULTS: Of 391 subjects with diabetic or idiopathic gastroparesis (IG), 142 (36 %) had a prior cholecystectomy at the time of enrollment. Patients with prior cholecystectomy were more often female, older, married, and overweight or obese. Cholecystectomy had been performed in 27/59 (46 %) of T2DM compared to 19/78 (24 %) T1DM and 96/254 IG (38 %) ($p = 0.03$). Patients with cholecystectomy had more comorbidities, particularly chronic fatigue syndrome, fibromyalgia, depression, and anxiety. Postcholecystectomy gastroparesis patients had increased health care utilization, and had a worse quality of life. Independent characteristics associated with prior cholecystectomy included insidious onset (OR = 2.06; $p = 0.01$), more comorbidities (OR = 1.26; $p < 0.001$), less severe gastric retention (OR(severe) = 0.68; overall $p = 0.03$) and more severe symptoms of retching (OR = 1.19; $p = 0.02$) and upper abdominal pain (OR = 1.21; $p = 0.02$), less severe constipation symptoms (OR = 0.84; $p = 0.02$), and not classified as having irritable bowel syndrome (OR = 0.51; $p = 0.02$). Etiology was not independently associated

				with a prior cholecystectomy. CONCLUSIONS: Symptom profiles in patients with and without cholecystectomy differ: postcholecystectomy gastroparesis patients had more severe upper abdominal pain and retching and less severe constipation. These data suggest that prior cholecystectomy is associated with selected manifestations of gastroparesis.
Payne BA, Hateley CL, Ong EL, Premchand N, Schmid ML, Schwab U, Newton JL, Price DA.	Department of Infection and Tropical Medicine, Royal Victoria Infirmary, Newcastle-upon-Tyne, UK. brendan.payne@ncl.ac.uk	HIV-associated fatigue in the era of highly active antiretroviral therapy: novel biological mechanisms?	HIV Med. 2013 Apr; 14(4):247-51. doi: 10.1111/j.1468-1293.2012.01050.x. Epub 2012 Sep 23.	OBJECTIVE: The aim of the study was to determine the prevalence and risk factors for HIV-associated fatigue in the era of highly active antiretroviral therapy (HAART). METHODS: A cross-sectional survey of 100 stable HIV-infected out-patients was carried out. Severity of fatigue was measured using the Fatigue Impact Scale (FIS). Symptoms of orthostatic intolerance (dysautonomia) were evaluated using the Orthostatic Grading Scale (OGS). Data for HIV-infected patients were compared with those for 166 uninfected controls and 74 patients with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (encephalopathy) (ME). RESULTS: Ninety-one per cent of HIV-infected patients were on HAART and 78% had suppressed plasma HIV viral load (≤40 HIV-1 RNA copies/mL). Fifty-one per cent of HIV-infected patients reported excessive symptomatic fatigue (FIS≥40), and 28% reported severe fatigue symptoms (FIS≥80). The mean FIS score among HIV-infected patients was 50.8 [standard deviation (SD) 41.9] compared with 13.0 (SD 17.6) in uninfected control subjects, and 92.9 (SD 29.0) in CFS patients ($P < 0.001$ for comparison of HIV-infected patients and uninfected controls). Among HIV-infected patients, fatigue severity was not significantly associated with current or nadir CD4 lymphocyte count, HIV plasma viral load, or whether on HAART. Prior dideoxynucleoside analogue (d-drug) exposure ($P = 0.016$) and the presence of clinical lipodystrophy syndrome ($P = 0.011$) were associated with fatigue. Additionally, fatigue severity correlated strongly with symptomatic orthostatic intolerance ($r = 0.65$; $P < 0.001$). CONCLUSIONS: Fatigue is very common and often severe in HIV-infected out-patients, despite viral suppression and good immune function. In a subgroup of patients, prior d-drug exposure may contribute to fatigue, suggesting a metabolic basis. Dysautonomia may also drive fatigue associated with HIV infection, as in other chronic diseases, and CFS/ME, and should be further evaluated with the potential for a shared therapeutic approach.
Pemberton S, Cox DL.	Yorkshire Fatigue Clinic, Forsyth Business Centre , York, North Yorkshire , UK	Experiences of daily activity in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and their implications for rehabilitation programmes.	Disabil Rehabil. 2013 Dec 27. [Epub ahead of print]	Abstract Purpose: Chronic Fatigue Syndrome, also known as Myalgic Encephalomyelitis (CFS/ME), has a significant impact upon daily functioning. Most recommended treatments aim to alter activity patterns based upon assumptions of activity avoidance. However, as there is limited research on the experience of activity and occupational beliefs in people with CFS/ME, this study took a qualitative approach to understand the meaning of activity in people with this disabling condition. Method: This study applied a social constructivist grounded theory methodology. Semi-structured interviews took place with 14 participants attending a Specialist CFS/ME Service in England. Findings: The emergent themes described a premorbid state of constant action with difficulty stopping an activity once it had

				commenced. When this pattern was interrupted by illness, participants attempted to maintain their previous level of occupational engagement. Negative associations and emotions were described in response to the concept of doing nothing or limited activity. A recurring cycle was reported of increasing activity levels when symptoms improved, followed by post-exertional symptoms. Conclusions: Consequently, participants' beliefs about concepts of both activity and inactivity need to be considered within the application of rehabilitation programmes for CFS/ME that aim to modify activity related behaviours. Implications for Rehabilitation Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is commonly treated in the UK using activity modification. In this small qualitative study, patients expressed negative feelings and beliefs towards the concept of doing nothing and therefore sought to push their activity levels when this was available, leading to recurring cycles of symptoms and activity. Rehabilitation programmes need to consider how people with CFS/ME engaged with activity and inactivity before the condition and how this may impact upon engagement with activity-based rehabilitation programmes.
Pinquart M.	Department of Psychology, Philipps University, Marburg, Germany. pinquart@staff.uni-marburg.de	Self-esteem of children and adolescents with chronic illness: a meta-analysis.	Child Care Health Dev. 2013 Mar; 39(2):153-61. doi: 10.1111/j.1365-2214.2012.01397.x. Epub 2012 Jun 19.	Chronic illness may be a risk factor for low self-esteem; however, previous meta-analyses are inconclusive whether children with a chronic illness have lower self-esteem than their healthy peers. The goal of the present study was to summarize available research in order to compare the self-esteem of children and adolescents with a chronic illness with that of healthy children. Random-effects meta-analysis was used to integrate the results of 621 empirical studies that compare levels of self-esteem of children with a chronic physical illness with healthy peers or general test norms. Studies were identified via the electronic databases Adolesc, Embase, Google Scholar, MEDLINE, PSNYDEX, PSYCINFO, and cross-referencing. Children with chronic illnesses have lower self-esteem than healthy peers or test norms (g = -0.18 standard deviation units). The lowest levels of self-esteem were observed in children with chronic fatigue syndrome and chronic headaches. Lower levels of self-esteem in children with a chronic illness were found in girls than in boys, in adolescents than in children, in children from developing or threshold countries, when results were collected from observer ratings rather than child reports, in studies published in the 1990s, and when children with chronic illnesses were directly compared with healthy children instead of test norms. Paediatricians, parents, and teachers should promote experiences of success and positive peer-relations, which are important sources of self-esteem. In addition, psychosocial interventions for children with chronic illnesses should be offered for children with reduced self-esteem.
Pirón M, Alegre J, Ribera E, Sauleda S.	[No address quoted]	Absence of xenotropic murine leukaemia virus-related virus sequences in healthy	Enferm Infecc Microbiol Clin. 2013 Aug-Sep; 31(7):491-2. doi: 10.1016/j.eimc.2012.11.016. Epub 2013 Jan 17.	[No abstract given]

		blood donors and chronic fatigue syndrome patients in Catalonia, Spain. [Article in Spanish]		
Poeschla B, Strachan E, Dansie E, Buchwald DS, Afari N.	Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, Seattle, WA 98104-2499, USA. bpoeschl@u.washington.edu	Chronic fatigue and personality: a twin study of causal pathways and shared liabilities.	Ann Behav Med. 2013 Jun; 45(3):289-98. doi: 10.1007/s12160-012-9463-5. Comment in Ann Behav Med. 2013 Jun; 45(3):271-2.	BACKGROUND: The etiology of chronic fatigue syndrome (CFS) remains unknown. Personality traits influence well-being and may play a role in CFS and unexplained chronic fatigue. PURPOSE: This study aimed to examine the association of emotional instability and extraversion with chronic fatigue and CFS in a genetically informative sample. METHODS: We evaluated 245 twin pairs for two definitions of chronic fatigue. They completed the Neuroticism and Extraversion subscales of the NEO Five Factor Inventory. Using a co-twin control design, we examined the association between personality and chronic fatigue. RESULTS: Higher emotional instability was associated with both definitions of chronic fatigue and was confounded by shared genetics. Lower extraversion was also associated with both definitions of fatigue, but was not confounded by familial factors. CONCLUSIONS: Both emotional instability and extraversion are related to chronic fatigue and CFS. Whereas emotional instability and chronic fatigue are linked by shared genetic mechanisms, the relationship with extraversion may be causal and bidirectional.
Pontari M, Giusto L.	Temple University Hospital, Department of Urology, Philadelphia, Pennsylvania, USA.	New developments in the diagnosis and treatment of chronic prostatitis/chronic pelvic pain syndrome.	Curr Opin Urol. 2013 Nov; 23 (6):565-9. doi: 10.1097/MOU.0b013e3283656a55.	PURPOSE OF REVIEW: To describe new developments in the diagnosis and treatment of chronic prostatitis/chronic pelvic pain syndrome (CPPS). RECENT FINDINGS: Symptoms in men with chronic prostatitis/CPPS appear to cluster into a group with primarily pelvic or localized disease, and a group with more systemic symptoms. Several other chronic pain conditions can be associated with chronic prostatitis/CPPS, including irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome. Markers of neurologic inflammation and autoimmune disease parallel changes in symptoms after treatment. Treatment options include new alpha-blockers, psychological intervention, and prostate-directed therapy. The areas of acupuncture and pelvic floor physical therapy/myofascial release have received increased recent attention and appear to be good options in these patients. Future therapy may include antibodies to mediators of neurogenic inflammation and even treatment of bacteria in the bowel. SUMMARY: The diagnosis of chronic prostatitis/CPPS must include conditions traditionally outside the scope of urologic practice but important for the care of men with chronic pelvic pain. The treatment is best done using multiple simultaneous therapies aimed at the different aspects of the condition.
Poppe C, Petrovic M, Vogelaers D, Crombez G.	Department of General Internal Medicine, Ghent University Hospital, Belgium.	Cognitive behavior therapy in patients with chronic fatigue syndrome: the role	J Psychosom Res. 2013 May; 74(5):367-72. doi: 10.1016/j.jpsychores.2013.02.011. Epub 2013 Mar 25.	OBJECTIVE: Increasing the quality of life (QoL) of patients with chronic fatigue is challenging because recovery is seldom achieved. Therefore, it is important to identify processes that improve QoL. This study examined the extent of improvement related to cognitive behavior group therapy (CBT), and whether improvement is affected by

	Carine.Poppe@ugent.be	of illness acceptance and neuroticism.		initial levels of acceptance and neuroticism. METHODS: Eighty CFS patients followed CBT, and self-reported (pre-post design) on mental and physical QoL (MQoL and PQoL), fatigue, acceptance, and neuroticism. The extent of improvement was analyzed using t-tests, effect sizes, and clinically significant change criteria. Whether acceptance and neuroticism at baseline predicted changes were analyzed by means of correlation and regression analyses. RESULTS: Significant improvement was found for all variables. The effect size for MQoL and PQoL was small; for acceptance and fatigue, effect size was moderate. About 20% (MQoL) to 40% (fatigue) of the participants clinically improved. Pre-treatment level of acceptance was negatively correlated with changes in MQoL, not with PQoL changes. Neuroticism pre-treatment was positively related with MQoL changes. Regression analysis showed an effect of acceptance on changes in MQoL beyond the effect of neuroticism. CONCLUSIONS: Although CBT is an evidence-based treatment, the sizes of the effects are often small regarding QoL. Our study also revealed small effect sizes. Our study showed that patient characteristics at baseline were significantly associated with MQoL outcome; indicating that CFS patients with high neuroticism or with a low acceptance show more improvement in MQoL. We propose to specifically target acceptance and neuroticism before treatment in order to maximize clinical relevance.
Post RM, Altshuler LL, Leverich GS, Frye MA, Suppes T, McElroy SL, Keck PE Jr, Nolen WA, Kupka RW, Grunze H, Rowe M.	Bipolar Collaborative Network, 5415 West Cedar Lane Suite 201B, Bethesda, MD 20814, USA. robert.post@speakeasy.net	Role of childhood adversity in the development of medical co-morbidities associated with bipolar disorder.	J Affect Disord. 2013 May; 147(1-3):288-94. doi: 10.1016/j.jad.2012.11.020. Epub 2013 Jan 18.	OBJECTIVE: A role for childhood adversity in the development of numerous medical conditions in adults has been described in the general population, but has not been examined in patients with bipolar disorder who have multiple medical comorbidities which contribute to their premature mortality. METHODS: More than 900 outpatients (average age 41) with bipolar disorder completed questionnaires that included information about the occurrence of verbal, physical, or sexual abuse in childhood and whether their parents had a mood or substance abuse disorder, or a history of suicidality. These factors were combined to form a total childhood adversity score, which was then related to one or more of 30 medical conditions patients rated as present or absent. RESULTS: The child adversity score was significantly related to the total number of medical comorbidities a patient had ($p<.001$), as well as to 11 specific medical conditions that could be modeled in a logistic regression ($p<.03$). These included: asthma, arthritis, allergies, chronic fatigue syndrome, chronic menstrual irregularities, fibromyalgia, head injury (without loss of consciousness), hypertension, hypotension, irritable bowel syndrome, and migraine headaches. LIMITATIONS: The contribution of parental diagnosis to childhood adversity is highly inferential. CONCLUSIONS: These data link childhood adversity to the later occurrence of multiple medical conditions in adult outpatients with bipolar disorder. Recognition of these relationships and early treatment intervention may help avert a more severe course of not only bipolar disorder but also of its prominent medical comorbidities and their combined adverse effects on patients'health, wellbeing, and longevity.
Powell DJ, Liossi C,	Faculty of Social and	Unstimulated cortisol	Psychoneuroendocrinology.	The hypothalamic-pituitary-adrenal (HPA) axis is a psychoneuroendocrine regulator of

Moss-Morris R, Schlotz W.	Human Sciences, University of Southampton, Southampton, UK. Electronic address: daniel.powell@soton.ac.uk.	secretory activity in everyday life and its relationship with fatigue and chronic fatigue syndrome: a systematic review and subset meta-analysis.	2013 Nov;38(11):2405-22. doi: 10.1016/j.psyneuen.2013.07.004. Epub 2013 Aug 2.	the stress response and immune system, and dysfunctions have been associated with outcomes in several physical health conditions. Its end product, cortisol, is relevant to fatigue due to its role in energy metabolism. The systematic review examined the relationship between different markers of unstimulated salivary cortisol activity in everyday life in chronic fatigue syndrome (CFS) and fatigue assessed in other clinical and general populations. Search terms for the review related to salivary cortisol assessments, everyday life contexts, and fatigue. All eligible studies (n=19) were reviewed narratively in terms of associations between fatigue and assessed cortisol markers, including the cortisol awakening response (CAR), circadian profile (CP) output, and diurnal cortisol slope (DCS). Subset meta-analyses were conducted of case-control CFS studies examining group differences in three cortisol outcomes: CAR output; CAR increase; and CP output. Meta-analyses revealed an attenuation of the CAR increase within CFS compared to controls (d=-.34) but no statistically significant differences between groups for other markers. In the narrative review, total cortisol output (CAR or CP) was rarely associated with fatigue in any population; CAR increase and DCS were most relevant. Outcomes reflecting within-day change in cortisol levels (CAR increase; DCS) may be the most relevant to fatigue experience, and future research in this area should report at least one such marker. Results should be considered with caution due to heterogeneity in one meta-analysis and the small number of studies.
Prados G, Miró E, Martínez MP, Sánchez AI, López S, Sáez G.	Department of Personality, Assessment and Psychological Treatment, School of Psychology, University of Granada, Granada, Spain/ Internal Medicine Service, Virgen de las Nieves University Hospital, Granada, Spain. germanprados@ugr.es.	Fibromyalgia: gender differences and sleep-disordered breathing.	Clin Exp Rheumatol. 2013 Nov-Dec; 31 (6 Suppl 79):102-10. Epub 2013 Dec 2.	OBJECTIVES: The prevalence of fibromyalgia (FM) is much lower in men than in women. Therefore, current knowledge about this chronic pain syndrome emerged mainly from research on women. The aim of the present study was to compare clinical symptoms and sleep parameters between male and female FM patients. METHODS: Forty FM patients (18 men and 22 women) aged 48.00±8.45 years were evaluated with questionnaires on pain, sleep, fatigue, depression, anxiety and functional impact, and polysomnography (PSG). RESULTS: 61% of male FM patients had an apnea-hypopnea index (AHI) greater than 15, compared to 31.8% of women, and a desaturation index (DI) above five, which was twice more prevalent in men than in women. In addition, males had poorer sleep quality (16.05±2.92% vs. 13.08±3.88%; p=0.01) and slow wave sleep (SWS) (stage 3 duration: 9.02±7.84% vs. 14.44±7.32%; p=0.03) than women. No differences were found between the two groups in the level of pain, emotional distress, or daily functioning. However, pain in men, fatigue in women, and functional impact in both sexes seemed to be related to worse sleep quality. Also in women, alterations in total sleep time (TST) and rapid eye movement (REM) sleep features appeared to be related to emotional status. CONCLUSIONS: Alterations in sleep respiratory patterns were more highly prevalent in male than in female FM patients. More so in male FM patients, the alterations in sleep patterns, non-refreshing sleep, and other FM-related symptoms observed in this population might be part of a primary sleep-disordered breathing.

Prinsen H, Heerschap A, Bleijenberg G, Zwarts MJ, Leer JW, van Asten JJ, van der Graaf M, Rijpkema M, van Laarhoven HW.	Department of Medical Oncology, Radboud University Nijmegen Medical Centre, Nijmegen, Gelderland, The Netherlands.	PLoS One. 2013 Sep 11;8 (9):e74638. doi: 10.1371/journal.pone.0074638.	Magnetic resonance spectroscopic imaging and volumetric measurements of the brain in patients with postcancer fatigue: a randomized controlled trial.	BACKGROUND: Postcancer fatigue is a frequently occurring problem, impairing quality of life. Until now, little is known about (neuro) physiological factors determining postcancer fatigue. For non-cancer patients with chronic fatigue syndrome, certain characteristics of brain morphology and metabolism have been identified in previous studies. We investigated whether these volumetric and metabolic traits are a reflection of fatigue in general and thus also of importance for postcancer fatigue. METHODS: Fatigued patients were randomly assigned to either the intervention condition (cognitive behavior therapy) or the waiting list condition. Twenty-five patients in the intervention condition and fourteen patients in the waiting list condition were assessed twice, at baseline and six months later. Baseline measurements of 20 fatigued patients were compared with 20 matched non-fatigued controls. All participants had completed treatment of a malignant, solid tumor minimal one year earlier. Global brain volumes, subcortical brain volumes, metabolite tissue concentrations, and metabolite ratios were primary outcome measures. RESULTS: Volumetric and metabolic parameters were not significantly different between fatigued and non-fatigued patients. Change scores of volumetric and metabolic parameters from baseline to follow-up were not significantly different between patients in the therapy and the waiting list group. Patients in the therapy group reported a significant larger decrease in fatigue scores than patients in the waiting list group. CONCLUSIONS: No relation was found between postcancer fatigue and the studied volumetric and metabolic markers. This may suggest that, although postcancer fatigue and chronic fatigue syndrome show strong resemblances as a clinical syndrome, the underlying physiology is different. TRIAL REGISTRATION: ClinicalTrials.gov NCT01096641.
Prior KN, Bond MJ.	General Practice, School of Medicine, Flinders University, Adelaide, Australia.	Construct validity and temporal stability of the abridged 31-item Illness Behaviour Questionnaire.	Psychol Health. 2013 Dec 16. [Epub ahead of print]	Objective: Key psychometric information was sought for three newly derived dimensions from an abridged Illness Behaviour Questionnaire (IBQ-31): Affirmation of Illness (AI), Concern for Health (CH) and General Affective State (GAS). The construct validity of these scales was examined along with their test-retest reliability and long-term stability. Design: A longitudinal, observational study was conducted with 675 participants (general community members and those with eitherasthma, diabetes and chronic pain or chronic fatigue syndrome) providing self-report questionnaire data at baseline, with additional information sought at three (n = 483; 71.6%) and 12 months (n = 517, 76.6%). Main outcome measures: Construct validity of the IBQ-31 was explored using well-validated psychological measures of Symptom Attributions and Symptom Experience, Cognitive Distortion of Somatic Information and Illness Likelihood. Results: In general, AI, CH and GAS shared predictable empirical overlap with related psychological indices across the five samples. Adequate three-month test-retest reliability was evident, with greater score variability over 12 months. Conclusion: The IBQ-31 comprises three theoretically relevant dimensions which demonstrate relative short- and long-term stability for individuals with diverse illness

				experiences. Future investigations should explore the predictive validity of AI, CH and GAS, along with the potential value of 'cut-off' scores for clinical use.
Proal AD, Albert PJ, Marshall TG, Blaney GP, Lindseth IA.	Autoimmunity Research Foundation, 3423 Hill Canyon Ave, Thousand Oaks, CA 91360, USA.	Immunostimulation in the treatment for chronic fatigue syndrome/myalgic encephalomyelitis.	Immunol Res. 2013 Jul; 56(2-3):398-412. doi: 10.1007/s12026-013-8413-z.	Chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) has long been associated with the presence of infectious agents, but no single pathogen has been reliably identified in all patients with the disease. Recent studies using metagenomic techniques have demonstrated the presence of thousands of microbes in the human body that were previously undetected and unknown to science. More importantly, such species interact together by sharing genes and genetic function within communities. It follows that searching for a singular pathogen may greatly underestimate the microbial complexity potentially driving a complex disease like CFS/ME. Intracellular microbes alter the expression of human genes in order to facilitate their survival. We have put forth a model describing how multiple species-bacterial, viral, and fungal-can cumulatively dysregulate expression by the VDR nuclear receptor in order to survive and thus drive a disease process. Based on this model, we have developed an immunostimulatory therapy that is showing promise inducing both subjective and objective improvement in patients suffering from CFS/ME.
Qanneta R (1), Fontova R(2), Pàmies A(2).	(1)Chronic Fatigue Unit, Department of Rheumatology, Hospital Universitari Joan XXIII, Tarragona, Spain. E-mail address: rami_kanita229@hotmail.com. (2)Department of Rheumatology, Hospital Universitari Joan XXIII, Tarragona, Spain.	Etiology of sicca syndrome in a consecutive series of 199 patients with chronic fatigue syndrome. [Article in English, Spanish]	Reumatol Clin. 2013 Dec 16. pii: S1699-258X(13)00217-9. doi: 0.1016/j.reuma.2013.11.002. [Epub ahead of print]	[No abstract given]
Qanneta R, Fontova R, Poveda MJ, Castro S.	Unidad de Fatiga Crónica, Departamento de Reumatología, Hospital Universitari Joan XXIII, Tarragona, España. Electronic address: rami_kanita229@hotmail.com.	Clinical typology of chronic fatigue syndrome: Classificatory hypothesis. [Article in English, Spanish]	Reumatol Clin. 2013 Jul 9. pii: S1699-258X(13)00097-1. doi: 10.1016/j.reuma.2013.04.004. [Epub ahead of print]	[No abstract given]
Qanneta R.	Chronic Fatigue Unit, Department of	Obstructive sleep apnea syndrome	Rheumatol Int. 2013 Apr 18. [Epub ahead of print]	[No abstract given]

	Rheumatology, Hospital Universitari Joan XXIII, Tarragona, Spain, rami_kanita229@hotmail.com.	manifested as a subset of chronic fatigue syndrome: a comorbidity or an exclusion criterion?		
Rayhan RU, Raksit MP, Timbol CR, Adewuyi O, Vanmeter JW, Baraniuk JN.	Division of Rheumatology, Immunology and Allergy; Department of Medicine, Georgetown University Medical Center Room 3004F 3rd Floor PHC Building, 3800 Reservoir Road, NW, Washington, DC 20007, USA.	Prefrontal lactate predicts exercise-induced cognitive dysfunction in Gulf War Illness.	Am J Transl Res. 2013; 5(2):212-23. Epub 2013 Mar 28.	BACKGROUND: 25% to 30% of Veterans deployed to the 1990 to 1991 Persian Gulf War exhibit an idiopathic syndrome of chronic fatigue, exertional exhaustion, pain, hyperalgesia, cognitive and affective dysfunction known as Gulf War Illness (GWI). METHODS: Gulf War veterans (n=15) and sedentary veteran and civilian controls (n=11) completed a 2-back working memory test in an fMRI before and after two bicycle exercise stress test. We performed single voxel (1)H MRS to evaluate brain metabolic differences in the left anterior cingulate cortex and the changes associated with exercise. RESULTS: Eight GWI subjects increased their 2-back scores after exercise (labelled increasers) and seven GWI subjects decreased their 2-back scores after exercise (labelled decreasers). These phenotypic responses were absent for controls. Decreasers had significantly elevated prefrontal lactate levels compared to Increasers prior to completion of the exercise stress tests. Evaluation of prefrontal lactate levels prior to exercise demonstrated predictability (ROC analysis) of the two diametrically opposed subgroups. CONCLUSION: Prefrontal lactate levels may be a potential biomarker for exercise-induced subgroups in GWI. The alterations in brain energetics may be in part responsible for a subgroup of GWI and underlie some of the symptoms present in the patient population.
Rayhan RU, Ravindran MK, Baraniuk JN.	Division of Rheumatology, Immunology and Allergy, Department of Medicine, Georgetown University Washington, DC, USA.	Migraine in gulf war illness and chronic fatigue syndrome: prevalence, potential mechanisms, and evaluation.	Front Physiol. 2013 Jul 24; 4:181. doi: 10.3389/fphys.2013.00181. eCollection 2013.	Objective: To assess the prevalence of headache subtypes in Gulf War Illness (GWI) and Chronic Fatigue Syndrome (CFS) compared to controls. Background: Approximately, 25% of the military personnel who served in the 1990-1991 Persian Gulf War have developed GWI. Symptoms of GWI and CFS have considerable overlap, including headache complaints. Migraines are reported in CFS. The type and prevalence of headaches in GWI have not been adequately assessed. Methods: 50 GWI, 39 CFS and 45 controls had structured headache evaluations based on the 2004 International Headache Society criteria. All subjects had history and physical examinations, fatigue and symptom related questionnaires, measurements of systemic hyperalgesia (dolorimetry), and assessments for exclusionary conditions. Results: Migraines were detected in 64% of GWI (odds ratio = 11.6 [4.1-32.5]) (mean [±95% CI]) and 82% of CFS subjects (odds ratio = 22.5 [7.8-64.8]) compared to only 13% of controls. There was a predominance of females in the CFS compared to GWI and controls. However, migraine status was independent of gender in GWI and CFS groups (x (2) = 2.7; P = 0.101). Measures of fatigue, pain, and other ancillary criteria were comparable between GWI and CFS subjects with and without headache. Conclusion: The high prevalence of migraine in CFS was confirmed and extended to

				GWI subjects. GWI and CFS may share dysfunctional central pathophysiological pathways that contribute to migraine and subjective symptoms. The high migraine prevalence warrants the inclusion of a structured headache evaluation in GWI and CFS subjects, and treatment when present.
Rayhan RU, Stevens BW, Timbol CR, Adewuyi O, Walitt B, VanMeter JW, Baraniuk JN.	Georgetown University Medical Center, Department of Medicine, Division of Rheumatology, Immunology and Allergy, Washington, DC, United States of America. rur@georgetown.edu	Increased brain white matter axial diffusivity associated with fatigue, pain and hyperalgesia in Gulf War illness.	PLoS One. 2013; 8(3):e58493. doi: 10.1371/journal.pone.0058493Epub 2013 Mar 20.	BACKGROUND: Gulf War exposures in 1990 and 1991 have caused 25% to 30% of deployed personnel to develop a syndrome of chronic fatigue, pain, hyperalgesia, cognitive and affective dysfunction. METHODS: Gulf War veterans (n=31) and sedentary veteran and civilian controls (n=20) completed fMRI scans for diffusion tensor imaging. A combination of dolorimetry, subjective reports of pain and fatigue were correlated to white matter diffusivity properties to identify tracts associated with symptom constructs. RESULTS: Gulf War Illness subjects had significantly correlated fatigue, pain, hyperalgesia, and increased axial diffusivity in the right inferior fronto-occipital fasciculus. ROC generated thresholds and subsequent binary regression analysis predicted CMI classification based upon axial diffusivity in the right inferior fronto-occipital fasciculus. These correlates were absent for controls in dichotomous regression analysis. CONCLUSION: The right inferior fronto-occipital fasciculus may be a potential biomarker for Gulf War Illness. This tract links cortical regions involved in fatigue, pain, emotional and reward processing, and the right ventral attention network in cognition. The axonal neuropathological mechanism(s) explaining increased axial diffusivity may account for the most prominent symptoms of Gulf War Illness.
Reeves WC, Lin JM, Nater UM.	Public Health Surveillance and Informatics Program Office, Mail Stop E-33, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, GA 30333, USA.	Mental illness in metropolitan, urban and rural Georgia populations.	BMC Public Health. 2013 Apr 30; 13:414. doi: 10.1186/1471-2458-13-414.	BACKGROUND: Mental illness represents an important public health problem. Local-level data concerning mental illness in different populations (e.g., socio-demographics and residence--metropolitan/urban/rural) provides the evidence-base for public health authorities to plan, implement and evaluate control programs. This paper describes prevalence and covariates of psychiatric conditions in Georgia populations in three defined geographic areas. METHODS: Data came from the Georgia population-based random-digit-dialing study investigating unwellness and chronic fatigue syndrome (CFS) in Georgia populations of three defined geographic areas (metropolitan, urban, and rural). Respondents were screened for symptoms of fatigue, sleep, cognition, and pain at household screening interviews, and a randomly selected sample completed detailed individual phone interviews. Based on the detailed phone interviews, we conducted one-day clinical evaluations of 292 detailed interview participants classified as unwell with a probable CFS (i.e. CFS-like; a functional somatic syndrome), 268 classified as other unwell, and 223 well (matched to CFS-like). Clinical evaluation included psychiatric classification by means of the Structured Clinical Interview for DSM (SCID). To derive prevalence estimates we used sample weighting to account for the complexity of the multistage sampling design. We used 2- and 3-way table analyses to examine socio-demographic and urbanicity specific associations and multiple logistic regression to calculate adjusted odds ratios.

				RESULTS: Anxiety and mood disorders were the most common psychiatric conditions. Nineteen percent of participants suffered a current anxiety disorder, 18% a mood disorder and 10% had two or more conditions. There was a significant linear trend in occurrence of anxiety or mood disorders from well to CFS-like. The most common anxiety disorders were post-traumatic stress disorder (PTSD) (6.6%) and generalized anxiety disorder (GAD) (5.8%). Logistic regression showed that lower education and female sex contributed significantly to risk for both PTSD and GAD. In addition, rural/urban residence and Hispanic ethnicity were associated with PTSD. We defined moderate to severe depression as Major Depressive Disorder or a Zung score>60 and logistic regression found lower education to be significantly associated but sex, age and urbanicity were not. CONCLUSIONS: Overall occurrence of anxiety and mood disorders in Georgia mirrored national findings. However, PTSD and GAD occurred at twice the published national rates (3.6 and 2.7%, respectively). State and local prevalence and associations with education, sex and urbanicity comprise important considerations for developing control programs. The increased prevalence of anxiety and mood disorders in people with a functional somatic syndrome (or CFS-like illness) is important for primary care providers, who should consider additional psychiatric screening or referral of individuals presenting with somatoform symptoms.
Reme SE, Archer N, Chalder T.	Harvard School of Public Health, Harvard University, Boston, Massachusetts, USA. sreme@hsph.harvard.edu	Experiences of young people who have undergone the Lightning Process to treat chronic fatigue syndrome/myalgic encephalomyelitis--a qualitative study.	Br J Health Psychol. 2013 Sep; 18(3):508-25. doi: 10.1111/j.2044-8287.2012.02093.x. Epub 2012 Sep 19.	OBJECTIVES: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a serious condition characterized by debilitating but unexplained fatigue. Treatment alternatives are few, and especially so for young people. The aetiology of CFS/ME is still unclear and controversial, but rehabilitative interventions seem so far most promising. The Lightning Process is a 3-day training programme that has recently become available, but no outcome studies have yet been published. It is a non-medical training programme that combines concepts from Neuro-Linguistic Programming, Life Coaching and Osteopathy. The aim of this study was to explore the experiences of young people with CFS/ME after they had undergone the Lightning Process. DESIGN: Qualitative research study. METHODS: Semi-structured interviews were conducted with an opportunistic sample recruited through open advertisements of nine young people, aged 14-26, who had undergone the treatment, and three of their parents. Inductive thematic analysis was used to evaluate the content of the interviews. RESULTS: Mostly positive experiences were reported of the Lightning Process. Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved. Particular helpful aspects were the theoretical rationale, practical exercises, and the technique they learned. Less helpful aspects were the intensity and short duration of the treatment with little follow-up, the secrecy surrounding it, and feelings of being blamed if the treatment did not work. CONCLUSIONS: As this is the first report of young people's experiences with the Lightning Process, it will be important to consider the helpful and unhelpful treatment components for future refinement of interventions for CFS/ME.

Reynolds GK, Lewis DP, Richardson AM, Lidbury BA.	Department of Genome Biology, The John Curtin School of Medical Research, The Australian National University, Canberra, Australian Capital Territory, Australia.	Comorbidity of postural orthostatic tachycardia syndrome and chronic fatigue syndrome in an Australian cohort.	J Intern Med. 2013 Nov 9. doi: 10.1111/joim.12161. [Epub ahead of print]	OBJECTIVE: Patients with chronic fatigue syndrome (CFS) are frequently diagnosed with comorbid postural orthostatic tachycardia syndrome (POTS), suggesting a shared pathogenesis. The aim of this study was to examine the relationship between demographic characteristics, autonomic functioning and fatigue levels amongst CFS patients with and without comorbid POTS. DESIGN AND SETTING: All patients presenting to the CFS Discovery Clinic between 2009 and 2012 completed a 20-min standing task as part of their initial assessment. Heart rate and pulse pressure were recorded at baseline, at 2-min intervals poststanding, at the end of the task and following a recovery period. Average heart rate and pulse pressure variability were calculated from this data. Age, gender, length of illness and self-reported fatigue scores were also recorded. POTS patients were diagnosed by an orthostatic increase in heart rate >30 beats per min, concomitant symptoms of orthostatic intolerance and no orthostatic hypotension. Differences in autonomic functioning between POTS and CFS patients were compared using independent samples t-tests, whilst logistic and linear regressions were performed to examine the contribution of autonomic functioning to task completion and perceived fatigue, respectively. RESULTS: Comorbidity of CFS and POTS (CFS-POTS) was observed in 11% (33/306) of patients. CFS-POTS patients were significantly younger ($P < 0.001$), had a shorter length of illness ($P = 0.034$), experienced greater task difficulty ($P = 0.002$) and were able to stand for significantly shorter periods compared to the CFS-only patients ($P < 0.001$). CFS-POTS patients experienced significantly lower baseline diastolic blood pressure ($P = 0.002$), significantly higher heart rate and lower pulse pressures at each standing measurement. Early heart rate changes ($P = 0.002$) and overall heart rate change ($P < 0.001$) were significant predictors of completion status, whereas heart rate variability ($P < 0.001$) and female gender ($P < 0.001$) were significant predictors of increased perceived task difficulty. CONCLUSIONS: Haemodynamic and demographic differences between CFS-POTS and CFS-only patients suggest that the former group reflects a distinct subgroup of the CFS population. The findings highlight the utility of screening younger patients with fatigue for POTS, and identified heart rate variability as an important marker of fatigue for CFS patients in general.
Rezaei SD, Hearps AC, Mills J, Pedersen J, Tachedjian G.	Retroviral Biology and Antivirals Laboratory, Centre for Virology, Burnet Institute, 85 Commercial Road, Melbourne, Victoria 3004, Australia.	No association between XMRV or related gammaretroviruses in Australian prostate cancer patients.	Virol J. 2013 Jan 10; 10:20. doi: 10.1186/1743-422X-10-20.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus reported to be associated with prostate cancer (PC) and chronic fatigue syndrome (CFS). While the association of XMRV with CFS and PC has recently been discredited, no studies have been performed in Australian patients to investigate the association between PC and XMRV or related murine leukemia virus (MLV) in matched PC and normal tissue. METHODS: Genomic DNA (gDNA) was purified from matched normal and cancer formalin-fixed paraffin-embedded (FFPE) prostate tissue from 35 Australian PC patients with Gleason scores ranging from 7 - 10. The presence of the ribonuclease L (RNase L) polymorphism R462Q was determined by allele specific PCR. Samples were screened for XMRV and related

				murine leukemia virus (MLV) variants by qPCR. Contaminating mouse DNA was detected using qPCR targeting mouse intracisternal A particle long terminal repeat DNA. RESULTS: gDNA was successfully purified from 94% (66/70) of normal and cancer FFPE prostate tissues. RNase L typing revealed 8% were homozygous (QQ), 60% were heterozygous (RQ) and 32% were wild-type (RR) for the RNase L mutation. None of the 66 samples tested were positive for XMRV or related MLV sequences using broad MLV or XMRV specific primers with detection sensitivities of 1 viral copy of MLV/XMRV and XMRV DNA, respectively. CONCLUSIONS: Using highly sensitive qPCR we found no evidence of XMRV or related gammaretroviruses in prostate tissues from 35 Australian PC patients. Our findings are consistent with other studies demonstrating that XMRV is a laboratory contaminant that has no role in the aetiology of PC.
Richardson G, Epstein D, Chew-Graham C, Dowrick C, Bentall RP, Morriss RK, Peters S, Riste L, Lovell K, Dunn G, Wearden AJ; FINE Trial Writing group on behalf of the FINE Trial group. **Collaborators Bennett C, Bentall R, Booth L, Brocki J, Cahill G, Chapman A, Chew-Graham C, Connell S, Dowrick C, Dunn G, Fleetwood D, Ibbotson L, Jerman D, Lovell K, Mann J, Morriss R, Peters S, Powell P, Quarmby D, Richardson G, Riste L, Wearden A, Williams J.**	Centre for Health Economics, University of York, Hull/York Medical School, York YO10 5DD, United Kingdom.	Cost-effectiveness of supported self-management for CFS/ME patients in primary care.	BMC Fam Pract. 2013 Jan 18; 14:12. doi: 10.1186/1471-2296-14-12.	BACKGROUND: Nurse led self-help treatments for people with chronic fatigue syndrome/myalgic encephalitis (CFS/ME) have been shown to be effective in reducing fatigue but their cost-effectiveness is unknown. METHODS: Cost-effectiveness analysis conducted alongside a single blind randomised controlled trial comparing pragmatic rehabilitation (PR) and supportive listening (SL) delivered by primary care nurses, and treatment as usual (TAU) delivered by the general practitioner (GP) in North West England. A within trial analysis was conducted comparing the costs and quality adjusted life years (QALYs) measured within the time frame of the trial. 296 patients aged 18 and over with CFS/ME diagnosed using the Oxford criteria were included in the cost-effectiveness analysis. RESULTS: Treatment as usual is less expensive and leads to better patient outcomes compared with Supportive Listening. Treatment as usual is also less expensive than Pragmatic Rehabilitation. PR was effective at reducing fatigue in the short term, but the impact of the intervention on QALYs was uncertain. However, based on the results of this trial, PR is unlikely to be cost-effective in this patient population. CONCLUSIONS: This analysis does not support the introduction of SL. Any benefits generated by PR are unlikely to be of sufficient magnitude to warrant recommending PR for this patient group on cost-effectiveness grounds alone. However, dissatisfaction with current treatment options means simply continuing with 'treatment as usual' in primary care is unlikely to be acceptable to patients and practitioners. TRIAL REGISTRATION: The trial registration number is IRCTN74156610.

Rimes KA, Wingrove J.	University of Bath, Department of Psychology, Claverton Down, Bath, UK. K.A.Rimes@bath.ac.uk	Mindfulness-based cognitive therapy for people with chronic fatigue syndrome still experiencing excessive fatigue after cognitive behaviour therapy: a pilot randomized study.	Clin Psychol Psychother. 2013 Mar-Apr;20(2):107-17. doi: 10.1002/cpp.793. Epub 2011 Oct 9.	Cognitive behaviour therapy (CBT) is an effective treatment for chronic fatigue syndrome (CFS; sometimes known as myalgic encephalomyelitis). However, only a minority of patients fully recover after CBT; thus, methods for improving treatment outcomes are required. This pilot study concerned a mindfulness-based cognitive therapy (MBCT) intervention adapted for people with CFS who were still experiencing excessive fatigue after CBT. The study aimed to investigate the acceptability of this new intervention and the feasibility of conducting a larger-scale randomized trial in the future. Preliminary efficacy analyses were also undertaken. Participants were randomly allocated to MBCT or waiting list. Sixteen MBCT participants and 19 waiting-list participants completed the study, with the intervention being delivered in two separate groups. Acceptability, engagement and participant-rated helpfulness of the intervention were high. Analysis of covariance controlling for pre-treatment scores indicated that, at post-treatment, MBCT participants reported lower levels of fatigue (the primary clinical outcome) than the waiting-list group. Similarly, there were significant group differences in fatigue at 2-month follow-up, and when the MBCT group was followed up to 6 months post-treatment, these improvements were maintained. The MBCT group also had superior outcomes on measures of impairment, depressed mood, catastrophic thinking about fatigue, all-or-nothing behavioural responses, unhelpful beliefs about emotions, mindfulness and self-compassion. In conclusion, MBCT is a promising and acceptable additional intervention for people still experiencing excessive fatigue after CBT for CFS, which should be investigated in a larger randomized controlled trial.KEY PRACTITIONER MESSAGE: Only about 30% of people with chronic fatigue syndrome (CFS) recover after cognitive behaviour therapy (CBT); thus, methods for improving treatment outcomes are needed. This is the first pilot randomized study to demonstrate that a mindfulness-based intervention was associated with reduced fatigue and other benefits for people with CFS who were still experiencing excessive fatigue after a course of CBT. Levels of acceptability, engagement in the intervention and rated helpfulness were high. A larger-scale randomized controlled trial is required.
Roca M, Verduri A, Corbetta L, Clini E, Fabbri LM, Beghé B.	Section of Respiratory Diseases, Department of Oncology, Haematology and Respiratory Diseases, University of Modena and Reggio Emilia, Modena, Italy.	Mechanisms of acute exacerbation of respiratory symptoms in chronic obstructive pulmonary disease.	Eur J Clin Invest. 2013 May; 43(5):510-21. doi: 10.1111/eci.12064. Epub 2013 Mar 12.	Exacerbations of chronic obstructive respiratory disease (ECOPD) are acute events characterized by worsening of the patient's respiratory symptoms, particularly dyspnoea, leading to change in medical treatment and/or hospitalisation. AECOP are considered respiratory diseases, with reference to the respiratory nature of symptoms and to the involvement of airways and lung. Indeed respiratory infections and/or air pollution are the main causes of ECOPD. They cause an acute inflammation of the airways and the lung on top of the chronic inflammation that is associated with COPD. This acute inflammation is responsible of the development of acute respiratory symptoms (in these cases the term ECOPD is appropriate). However, the acute

				inflammation caused by infections/pollutants is almost associated with systemic inflammation, that may cause acute respiratory symptoms through decompensation of concomitant chronic diseases (eg acute heart failure, thromboembolism, etc) almost invariably associated with COPD. Most concomitant chronic diseases share with COPD not only the underlying chronic inflammation of the target organs (i.e. lungs, myocardium, vessels, adipose tissue), but also clinical manifestations like fatigue and dyspnoea. For this reason, in patients with multi-morbidity (eg COPD with chronic heart failure and hypertension, etc), the exacerbation of respiratory symptoms may be particularly difficult to investigate, as it may be caused by exacerbation of COPD and/or ≥ comorbidity, (e.g. decompensated heart failure, arrhythmias, thromboembolisms) without necessarily involving the airways and lung. In these cases the term ECOPD is inappropriate and misleading.
Rodgers CC, Hooke MC, Hockenberry MJ.	Baylor College of Medicine/Texas Children's Hospital, Houston, Texas 77030, USA.	Symptom clusters in children.	Curr Opin Support Palliat Care. 2013 Mar; 7(1):67-72. doi: 10.1097/SPC.0b013e32835ad551.	PURPOSE OF REVIEW: Researchers have focused on identifying and describing symptom experiences among children with various diseases but symptoms can have a synergistic and/or an antecedent effect that must be evaluated. This review reports the current knowledge of symptoms among various pediatric diseases and highlights symptom cluster research. RECENT FINDINGS: Symptoms of depression and anxiety are the most prevalent variables studied across pediatric disease studies followed by pain, fatigue, and quality of life. Although previous pediatric symptom research provides a foundation for understanding the complexities of these symptoms, there is limited evidence on symptom cluster research in pediatrics. Pain and fatigue are the most common symptoms analyzed for correlations, and relationships among symptoms that have been evaluated in children with juvenile idiopathic arthritis, HIV, cancer, cardiac disease requiring an implantable cardioverter defibrillator, and at end of life. Pain and fatigue have been associated with sleep disturbances, anxiety, depression, anorexia, and nausea/vomiting. SUMMARY: Pediatric oncology researchers are leading the way with symptom cluster studies; however, this work remains in the early stages. There is great potential to advance the state of the science with cluster analysis. Future research work should focus on evaluating symptoms and their interactions.
Roest HI, Bossers A, van Zijderveld FG, Rebel JM.	Department of Bacteriology and TSEs, Central Veterinary Institute, Wageningen University and Research Centre, Lelystad, The Netherlands.	Clinical microbiology of Coxiella burnetii and relevant aspects for the diagnosis and control of the zoonotic disease Q fever.	Vet Q. 2013 Sep; 33(3):148-60. doi: 10.1080/01652176.2013.843809. Epub 2013 Oct 28.	Coxiella burnetii is the causative agent of the zoonotic disease Q fever. Since its first recognition as a disease in the 1930s, the knowledge about the agent and the disease itself has increased. This review summarizes the current knowledge on C. burnetii and Q fever, its pathogenesis, diagnosis and control. C. burnetii is a bacterium which naturally replicates inside human or animal host cells. The clinical presentation of Q fever varies per host species. C. burnetii infection in animals is mainly asymptomatic except for pregnant ruminants in which abortions and stillbirth can occur. In humans, the disease is also mainly asymptomatic, but clinical presentations include acute and chronic Q fever and the post-Q fever fatigue syndrome. Knowledge of the pathogenesis of Q fever in animals and excretion of C. burnetii in infected animals is

				crucial in understanding the transmission routes and risks of human infection. Our studies indicated that infected pregnant animals only excrete C. burnetii during and after parturition, independent of abortion, and that C. burnetii phase specific serology can be a useful tool in the early detection of infection. Domestic ruminants are the main reservoir for human Q fever, which has a major public health impact when outbreaks occur. In outbreaks, epidemiological source identification can only be refined by genotypic analysis of the strains involved. To control outbreaks and Q fever in domestic ruminants, vaccination with a phase 1 vaccine is effective. Future challenges are to identify factors for virulence, host susceptibility and protection.
Roggenbuck D, Hiemann R, Bogdanos D, Reinhold D, Conrad K.	[No address quoted]	Standardization of automated interpretation of immunofluorescence tests.	Clin Chim Acta. 2013 Jun 5; 421:168-9. doi: 10.1016/j.cca.2013.03.019. Epub 2013 Mar 26.	Comment on Clin Chim Acta. 2013 Jan 16; 415:101-6.
Rowe PC, Fontaine KR, Violand RL.	Division of General Pediatrics and Adolescent Medicine, Department of Pediatrics, Johns Hopkins University School of Medicine Baltimore, MD, USA.	Neuromuscular strain as a contributor to cognitive and other symptoms in chronic fatigue syndrome: hypothesis and conceptual model.	Front Physiol. 2013 May 16; 4:115. doi: 10.3389/fphys.2013.00115. eCollection 2013.	Individuals with chronic fatigue syndrome (CFS) have heightened sensitivity and increased symptoms following various physiologic challenges, such as orthostatic stress, physical exercise, and cognitive challenges. Similar heightened sensitivity to the same stressors in fibromyalgia (FM) has led investigators to propose that these findings reflect a state of central sensitivity. A large body of evidence supports the concept of central sensitivity in FM. A more modest literature provides partial support for this model in CFS, particularly with regard to pain. Nonetheless, fatigue and cognitive dysfunction have not been explained by the central sensitivity data thus far. Peripheral factors have attracted attention recently as contributors to central sensitivity. Work by Brieg, Sunderland, and others has emphasized the ability of the nervous system to undergo accommodative changes in length in response to the range of limb and trunk movements carried out during daily activity. If that ability to elongate is impaired-due to movement restrictions in tissues adjacent to nerves, or due to swelling or adhesions within the nerve itself-the result is an increase in mechanical tension within the nerve. This adverse neural tension, also termed neurodynamic dysfunction, is thought to contribute to pain and other symptoms through a variety of mechanisms. These include mechanical sensitization and altered nociceptive signaling, altered proprioception, adverse patterns of muscle recruitment and force of muscle contraction, reduced intra-neural blood flow, and release of inflammatory neuropeptides. Because it is not possible to differentiate completely between adverse neural tension and strain in muscles, fascia, and other soft tissues, we use the more general term "neuromuscular strain." In our clinical work, we have found that neuromuscular restrictions are common in CFS, and that many symptoms of CFS can be reproduced by selectively adding neuromuscular strain during the examination. In this paper we submit that neuromuscular strain is a previously

				unappreciated peripheral source of sensitizing input to the nervous system, and that it contributes to the pathogenesis of CFS symptoms, including cognitive dysfunction.
Sarkisiants NK, Grigorian ÉG.	[No address quoted]	Predicting side effects of the treatment of chronic hepatitis with peginterferon alpha-2A with ribaverin. [Article in Russian]	Klin Med (Mosk). 2013; 91(5):46-9.	The aim of the study was to monitor the commonest side effects of the treatment of chronic hepatitis with peginterferon alpha-2A (PEG-IFN) and ribaverin (RBV) and the influence of various factors on their development. The work was done in the Department of Infectious Disease, Erevan State Medical University. Monitoring 16 adverse reactions was carried out with the use of special tables within 1, 2, 4 and 6 months after the onset of therapy in patients with genotypes 2 and 3 and in addition after 8, 10 and 12 months in patients with genotype 1. The influence of independent prognostic factors was estimated by logistic regression analysis. The commonest side effects of PEG-IFN plus RBV therapy were leukopenia, thrombocytopenia, weight loss, depression, fatigue, and insomnia that occurred at one time or another in more than half of the patients. Weight loss during therapy amounted to 8.36 kg (95% CI 6.7-10) (maximum 21 kg). Myalgia, anorexia, arthralgia, headache, alopecia, and vomiting were documented in 20-50% of the cases. Anemia, pruritis, eruption, erythema, and hair shedding at injection sites occurred in 1/4 of the patients. It is concluded that logistic regression analysis with matching selected prognostic factors permits to estimate the probability of such side effects as weight loss, flu-like syndrome, and myalgia.
Schouwers S, Bonnet M, Verschueren P, Westhovens R, Blockmans D, Mariën G, Bossuyt X.	[No address quoted]	Value-added reporting of antinuclear antibody testing by automated indirect immunofluorescence analysis.	Clin Chem Lab Med. 2013 Nov 13:1-5. doi: 10.1515/cclm-2013-0610. [Epub ahead of print]	Abstract Background: Automated systems for antinuclear antibody analysis are being introduced. The aim was to evaluate whether automated quantitative reading of fluorescence intensity is clinically relevant and allows for value-added reporting of test results. Methods: Consecutive samples (n=260) were used to correlate fluorescence intensity with end-point titer. Moreover, 434 samples from controls (150 healthy blood donors, 150 chronic fatigue syndrome, and 134 diseased controls) and 252 samples (obtained at diagnosis) from patients with systemic rheumatic diseases were screened for antinuclear antibodies (1:80) on HEp-2 cells using NOVA View®, and likelihood ratios were calculated for fluorescence intensity result intervals. Results: There was a significant correlation between end-point titer and fluorescence intensity. Likelihood ratios for a systemic rheumatic disease increased with increasing fluorescence intensity. The likelihood ratio for a systemic rheumatic disease was 0.06, 0.18, 0.51, 5.3, and 37.5 for a fluorescence intensity of ≤66, 67-150, 151-300, 301-1000, >1000, respectively. A range of 31%-37% of the patients with Sjögren's syndrome, systemic sclerosis or systemic lupus erythematosus had fluorescence intensities >1000. Conclusions: Estimation of fluorescence intensity by automated antinuclear antibody analysis offers clinically useful information. Likelihood ratios based on fluorescence intensity test result intervals aid with the interpretation of automated antinuclear antibody analysis and allow value-added reporting.
Schüttrumpf J, Hourfar MK, Alesci	Institut für Transfusionsmedizin	No detection of the retrovirus xenotropic	Transfus Med Hemother. 2013 Feb; 40(1):32-5. doi:	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) is a retrovirus that has recently been related to prostate cancers and chronic fatigue syndrome.

S, Miesbach W, Seifried E, Schmidt M.	und Immunhämatologie, Klinikum der Johann Wolfgang Goethe Universität, DRK-Blutspendedienst Baden-Württemberg - Hessen, Frankfurt/M., Germany ; Chemotherapeutisches Forschungsinstitut Georg-Speyer-Haus, Frankfurt/M., Germany.	murine leukemia virus-related virus in individuals with hemophilia.	10.1159/000345661. Epub 2013 Jan 3.	Since other human-pathogenic retroviruses, such as HIV, human T-lymphotropic virus type I (HTLV-I) and -II, are known blood-transmitted pathogens, XMRV might present another hazard associated with products derived from in vitro cultures of human or animal origin, or blood component-based therapeutics. Here, we investigated whether XMRV was transmitted to individuals with hemophilia and frequent exposure to plasma-derived or recombinant clotting factors. METHODS: We used highly sensitive real-time PCR to test plasma samples from 127 consecutive individuals with hemophilia who consulted our hemophilia center either for treatment or for a standard check-up. RESULTS: From the 127 hemophiliacs, 80 had prior contact to persons with either hepatitis B (n = 30), hepatitis C (n = 74) and/or HIV (n = 21), and 30 were currently being treated with plasma-derived and 97 with recombinant factor concentrates. None of the individuals tested positive for XMRV. CONCLUSIONS: Independent of the ongoing discussion on whether the positive XMRV testing in initial reports was a result of reagent, sample, or tissue contamination, and whether XMRV is a real threat or a testing artifact, our data suggest that XMRV might not play an important role for hemophiliacs.
Senel K, Baygutalp F, Baykal T, Erdal A, Ugur M.	Department of Physical Medicine and Rehabilitation, Atatürk University Medical Faculty, Erzurum, Turkey. kazimsenel@gmail.com	Melatonin levels in premenopausal women with fibromyalgia syndrome.	Rheumatol Int. 2013 Jun; 33(6):1609-10. doi: 10.1007/s00296-011-2315-y. Epub 2011 Dec 23.	The fibromyalgia syndrome (FMS) is a chronic, widespread pain disorder of unknown etiology. It has been suggest that familial component, environmental factors, endocrine and neurotransmitter alterations, and psychological factors may contribute to the development of FMS. The role of melatonin in FMS is unclear. Some studies describe a lower nocturnal peak and a decreased secretion of melatonin in women with FMS when compared with healthy matched controls. The aim of the present study was to determine the possible role of melatonin in FMS patients. We examined the characteristics and levels of melatonin in 25 consecutive premenopausal women with FMS. Serum blood samples were collected from 25 patients and 20 the age and gender matched healthy controls. Melatonin levels were measured by enzyme-linked immunosorbent assay. Then, the results were compared with those from healthy subjects. Serum melatonin levels of FMS patients were not statistically different from those of controls ($P > 0.05$). No association was observed between melatonin levels of patients with FMS and disease duration, sleep disturbances, fatigue, and pain scores. Our results demonstrate that melatonin levels were similar in patients with FMS and healthy controls. Further studies are needed to determine the possible role of melatonin.
Shanks L, Jason LA, Evans M, Brown A.	Center for Community Research, DePaul University Chicago, IL, USA.	Cognitive impairments associated with CFS and POTS.	Front Physiol. 2013 May 16; 4:113. doi: 10.3389/fphys.2013.00113. eCollection 2013.	Chronic fatigue syndrome (CFS) is characterized by fatigue, sleep dysfunction, and cognitive deficits (Fukuda et al., 1994). Research surrounding cognitive functioning among patients with CFS has found difficulty with memory, attention, and information processing. A similar disorder, postural tachycardia syndrome (POTS), is characterized by increased heart rate, fatigue, and mental cloudiness (Raj et al., 2009). Potential implications of cognitive deficits for patients with CFS and/or POTS are discussed, including difficulties with school and/or employment. A few biological

				theories (i.e., kindling, impairments in the central nervous system, and difficulty with blood flow) have emerged as potential explanations for the cognitive deficits reported in both CFS and POTS Future research should continue to examine possible explanations for cognitive impairments in CFS and POTS, and ultimately use this information to try and reduce cognitive impairments for these patients.
Shepherd C.	[No address quoted]	Letter to the editor: comments on 'recovery from chronic fatigue syndrome after treatments given in the PACE trial'.	Psychol Med. 2013 Aug;43(8):1790-1. doi: 10.1017/S003329171300130X	[No abstract given]
Shreevathsa M, Ravishankar B, Dwivedi R.	Professor and Head, Department of Post Graduate Studies in Ayurveda Siddhanta, Government Ayurveda Medical College, Mysore, India.	Anti depressant activity of Mamsyadi Kwatha: An Ayurvedic compound formulation.	Ayu. 2013 Jan; 34(1):113-7. doi: 10.4103/0974-8520.115448.	Depression is a psychiatric condition in which there is loss of interest in all pleasurable outlets, viz. food, sex, work, friends, hobbies and entertainment. The prevalence rate of the disease is 6-8% in women and 3-5% in men. Ayurveda, the science of life, provides systematic management principles for depression. Mamsyadi Kwatha is one such formulation stated by Yadavji Trikamji Acharya in Siddha Yoga Sangraha and Bheshaja Samhita, which is said to be effective in psychiatric conditions. The ingredients are Jatamansi (Nardostachys jatamansi), Ashwagandh (Withania somnifera) and Parasika Yavani (Hyocymus niger) in an 8:4:1 ratio, respectively. The test drug was subjected for antidepressant activity in experimental models. The models selected for anti depressant activity were behavioral despair test, anti-reserpine test and Chronic Fatigue Syndrome (CFS) test in albino mice. The test formulation showed significant inhibition of behavioural despair ($P < 0.05$), weak to moderate anti-reserpine activity - ptosis ($P < 0.001$), catatonia ($P < 0.01$), sedation ($P < 0.01$) and moderate effect in CFS test ($P < 0.050$). These effects clearly show that Mamsyadi Kwatha has an anti-depressant activity.
Shultz E, Malone DA Jr.	Department of Psychiatry and Psychology, Cleveland Clinic; Clinical Instructor, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH.	A practical approach to prescribing antidepressants.	Cleve Clin J Med. 2013 Oct; 80 (10):625-31. doi: 10.3949/ccjm.80a.12133.	Although antidepressant drugs do not differ much in their efficacy rates, the particular characteristics of one drug may make it a better choice in a given patient. This article provides insight into the art of prescribing antidepressants in primary care, with recommendations for prescribing for patients with chronic pain, sexual dysfunction, anxiety, chronic fatigue syndrome, fibromyalgia, severe insomnia, old age, diabetes, and heart problems.
Skalova S, Neuman D, Lnenicka P,	Department of Pediatrics, Faculty of	Gitelman syndrome as a cause of	Arab J Nephrol Transplant. 2013 Jan; 6(1):37-9.	INTRODUCTION: Gitelman syndrome (GS) is a very rare autosomal recessive tubulopathy due to loss-of-function or mutation in solute carrier family12, member 3

Stekrova J.	Medicine in Hradec Kralove, Charles University, Prague, Czech Republic. skalovasylva@seznam.cz	psychomotor retardation in a toddler.		gene (SLC12A3 gene) encoding thiazide-sensitive NaCl co-transporter in the distal convoluted tubule, leading to hypokalemia, metabolic alkalosis, hypomagnesemia, hypocalciuria and low-to-normal blood pressure. Clinical signs are mostly secondary to chronic hypokalemia and include dizziness, fatigue, constipation and weakness. Patients can also present with muscle cramps, tetany, fatigue and convulsions due to severe metabolic alkalosis or hypomagnesemia. Manifestations of GS are rarely apparent before the age of five, and the syndrome is usually diagnosed during adolescence or adulthood. Here we describe a case of GS presenting in infancy with hypokalemia and psychomotor retardation. CASE REPORT: We present an 18-month-old boy who presented with psychomotor retardation and failure to thrive. Investigations revealed hypokalemia at 2.7 mmol/L, metabolic alkalosis, hypocalciuria and normal serum magnesium level. The diagnoses of Barter syndrome (BS) and Gitelman syndrome (GS) were considered. Genetic studies confirmed the diagnosis of GS and three different mutations of in SLC12A3 gene were detected. Two mutations (c.2576T>C and c.2929C>Ty) were considered as causal ones, with the patient´s parents being the heterozygous carriers. Oral potassium supplementation resulted in normalisation of the hypokalemia and psychomotor improvement. CONCLUSION: We report a rare case of psychomotor retardation occurring at an early age in genetically confirmed GS. In spite of being a rare disorder, GS has to be considered in children with developmental delay and muscle weakness. With adequate treatment, GS patients have an excellent prognosis.
Smith SN, Crawley E.	School of Medicine, Swansea University, Swansea, UK. 630443@swansea.ac.uk	Is there effective behavioural treatment for children with chronic fatigue syndrome/myalgic encephalomyelitis?	Arch Dis Child. 2013 Jul; 98(7):561-3. doi: 10.1136/archdischild-2013-304307.	[No abstract given]
Smorgick N, Marsh CA, As-Sanie S, Smith YR, Quint EH.	Department of Obstetrics and Gynecology, University of Michigan Health System, Ann Arbor, Michigan 48109, USA. noam_yossi@yahoo.com	Prevalence of pain syndromes, mood conditions, and asthma in adolescents and young women with endometriosis.	J Pediatr Adolesc Gynecol. 2013 Jun; 26(3):171-5. doi: 10.1016/j.jpag.2012.12.006. Epub 2013 Mar 16.	STUDY OBJECTIVE: Adult women with endometriosis are often diagnosed with comorbid pain, mood, and autoimmune conditions. This study aims to describe the occurrence of pain syndromes, mood conditions, and asthma in adolescents and young women with endometriosis evaluated at our medical center. DESIGN: Retrospective review of medical records. SETTING: Department of Obstetrics and Gynecology at a tertiary referral center. PARTICIPANTS: 138 adolescents/young women who were less than age 24 years at the time of their initial visit at our medical center, and whose surgical diagnosis of endometriosis was made at our institution or by outside institutions by the age of 21. INTERVENTIONS: None. MAIN OUTCOME MEASURES: Prevalence of comorbid pain syndromes (defined as interstitial cystitis, irritable bowel syndrome, chronic headaches, chronic low back pain, vulvodynia, fibromyalgia, temporomandibular joint disease, and chronic fatigue syndrome), mood

				conditions (defined as depression and anxiety), and asthma. RESULTS: Comorbid pain syndromes were found in 77 (56%) women, mood conditions in 66 (48%) women, and asthma in 31 (26%) women. Comparing endometriosis patients with and without comorbid pain syndromes, no differences were found in age at time of diagnosis, endometriosis symptoms, and endometriosis stage. Patients with comorbid pain syndromes were more likely to report mood conditions (62% vs 30% respectively, P < .001) and smoking (31% vs 10% respectively, P = .003), underwent more surgeries for endometriosis (median of 2 [range, 1-7] vs 1 [range, 1-5], P < .005), and were more likely to undergo appendectomy or cholecystectomy (30% vs 13%, P = .02). CONCLUSIONS: Comorbid pain syndromes, mood conditions and asthma are common in adolescents and young women with endometriosis.
Smylie AL, Broderick G, Fernandes H, Razdan S, Barnes Z, Collado F, Sol C, Fletcher MA, Klimas N.	Department of Medicine, University of Alberta, Edmonton, AB, Canada.	A comparison of sex-specific immune signatures in Gulf War illness and chronic fatigue syndrome.	BMC Immunol. 2013 Jun 25; 14:29. doi: 10.1186/1471-2172-14-29.	BACKGROUND: Though potentially linked to the basic physiology of stress response we still have no clear understanding of Gulf War Illness (GWI), a debilitating condition presenting complex immune, endocrine and neurological symptoms. Here we compared male (n = 20) and female (n = 10) veterans with GWI separately against their healthy counterparts (n = 21 male, n = 9 female) as well as subjects with chronic fatigue syndrome/ myalgic encephalomyelitis (CFS/ME) (n = 12 male, n = 10 female). METHODS: Subjects were assessed using a Graded eXercise Test (GXT) with blood drawn prior to exercise, at peak effort (VO2 max) and 4-hours post exercise. Using chemiluminescent imaging we measured the concentrations of IL-1a, 1b, 2, 4, 5, 6, 8, 10, 12 (p70), 13, 15, 17 and 23, IFNγ, TNFα and TNFβ in plasma samples from each phase of exercise. Linear classification models were constructed using stepwise variable selection to identify cytokine co-expression patterns characteristic of each subject group. RESULTS: Classification accuracies in excess of 80% were obtained using between 2 and 5 cytokine markers. Common to both GWI and CFS, IL-10 and IL-23 expression contributed in an illness and time-dependent manner, accompanied in male subjects by NK and Th1 markers IL-12, IL-15, IL-2 and IFNγ. In female GWI and CFS subjects IL-10 was again identified as a delineator but this time in the context of IL-17 and Th2 markers IL-4 and IL-5. Exercise response also differed between sexes: male GWI subjects presented characteristic cytokine signatures at rest but not at peak effort whereas the opposite was true for female subjects. CONCLUSIONS: Though individual markers varied, results collectively supported involvement of the IL-23/Th17/IL-17 axis in the delineation of GWI and CFS in a sex-specific way.
Snell CR, Stevens SR, Davenport TE, Van Ness JM.	C.R. Snell, PhD, Department of Sport Sciences, University of the Pacific, Stockton, California, and Workwell Foundation, Ripon, California.	Discriminative validity of metabolic and workload measurements for identifying people with chronic fatigue syndrome.	Phys Ther. 2013 Nov; 93(11):1484-92. doi: 10.2522/ptj.20110368. Epub 2013 Jun 27.	BACKGROUND: Reduced functional capacity and postexertion fatigue after physical activity are hallmark symptoms of chronic fatigue syndrome (CFS) and may even qualify for biomarker status. That these symptoms are often delayed may explain the equivocal results for clinical cardiopulmonary exercise testing in people with CFS. Test reproducibility in people who are healthy is well documented. Test reproducibility may not be achievable in people with CFS because of delayed symptoms. OBJECTIVE: The objective of this study was to determine the discriminative validity of objective

				measurements obtained during cardiopulmonary exercise testing to distinguish participants with CFS from participants who did not have a disability but were sedentary. DESIGN: A prospective cohort study was conducted. METHODS: Gas exchange data, workloads, and related physiological parameters were compared in 51 participants with CFS and 10 control participants, all women, for 2 maximal exercise tests separated by 24 hours. RESULTS: Multivariate analysis showed no significant differences between control participants and participants with CFS for test 1. However, for test 2, participants with CFS achieved significantly lower values for oxygen consumption and workload at peak exercise and at the ventilatory or anaerobic threshold. Follow-up classification analysis differentiated between groups with an overall accuracy of 95.1%. LIMITATIONS: Only individuals with CFS who were able to undergo exercise testing were included in this study. Individuals who were unable to meet the criteria for maximal effort during both tests, were unable to complete the 2-day protocol, or displayed overt cardiovascular abnormalities were excluded from the analysis. CONCLUSIONS: The lack of any significant differences between groups for the first exercise test would appear to support a deconditioning hypothesis for CFS symptoms. However, the results from the second test indicated the presence of CFS-related postexertion fatigue. It might be concluded that a single exercise test is insufficient to reliably demonstrate functional impairment in people with CFS. A second test might be necessary to document the atypical recovery response and protracted fatigue possibly unique to CFS, which can severely limit productivity in the home and workplace.
Stahl D, Rimes KA, Chalder T.	Department of Biostatistics, Institute of Psychiatry, King's College London, UK.	Mechanisms of change underlying the efficacy of cognitive behaviour therapy for chronic fatigue syndrome in a specialist clinic: a mediation analysis.	Psychol Med. 2013 Aug 12:1-14. [Epub ahead of print]	BACKGROUND: Several randomized controlled trials (RCTs) have shown that cognitive behavioural psychotherapy (CBT) is an efficacious treatment for chronic fatigue syndrome (CFS). However, little is known about the mechanisms by which the treatment has its effect. The aim of this study was to investigate potential mechanisms of change underlying the efficacy of CBT for CFS. We applied path analysis and introduce novel model comparison approaches to assess a theoretical CBT model that suggests that fearful cognitions will mediate the relationship between avoidance behaviour and illness outcomes (fatigue and social adjustment). Method Data from 389 patients with CFS who received CBT in a specialist service in the UK were collected at baseline, at discharge from treatment, and at 3-, 6- and 12-month follow-ups. Path analyses were used to assess possible mediating effects. Model selection using information criteria was used to compare support for competing mediational models. RESULTS: Path analyses were consistent with the hypothesized model in which fear avoidance beliefs at the 3-month follow-up partially mediate the relationship between avoidance behaviour at discharge and fatigue and social adjustment respectively at 6 months. CONCLUSIONS: The results strengthen the validity of a theoretical model of CBT by confirming the role of cognitive and behavioural factors in CFS.

Stenhoff AL, Sadreddini S, Peters S, Wearden A.	University of Manchester, UK.	Understanding medical students' views of Chronic Fatigue Syndrome: A qualitative study.	J Health Psychol. 2013 Sep 20. [Epub ahead of print]	Chronic fatigue syndrome receives little attention in the medical curriculum. This study explores UK medical students' knowledge of and attitudes towards chronic fatigue syndrome. Semi-structured interviews (average length 22 minutes) were conducted with 21 participants (7 females and 14 males) in years 3 (n = 4), 4 (n = 11) and 5 (n = 6) of their studies. Inductive thematic analysis taking a realist perspective produced three themes: limited knowledge, influences on attitudes and training needs. Students acquired their knowledge and attitudes largely from informal sources and expressed difficulty understanding chronic fatigue syndrome within a traditional biomedical framework. Incorporating teaching about chronic fatigue syndrome into the medical curriculum within the context of a biopsychosocial understanding of illness could encourage more positive attitudes towards chronic fatigue syndrome.
Strahler J, Fischer S, Nater UM, Ehlert U, Gaab J.	Clinical Biopsychology, Department of Psychology, University of Marburg, Gutenbergstrasse 18, 35032 Marburg, Germany. jana.strahler@gmail.com	Norepinephrine and epinephrine responses to physiological and pharmacological stimulation in chronic fatigue syndrome.	Biol Psychol. 2013 Sep;94(1):160-6. doi: 10.1016/j.biopsycho.2013.06.002. Epub 2013 Jun 13.	Chronic fatigue syndrome (CFS) is characterized by fatigue lasting 6 months or longer. CFS has been associated with a disturbed (re-)activity of the autonomic nervous system. However, the sympathetic adrenomedulla (SAM) remains under-examined in CFS. To investigate SAM reactivity, we implemented a submaximal cycle ergometry (ERGO) and a pharmacological test (Insulin Tolerance Test, ITT) in 21 CFS patients and 20 age-, sex-, and BMI-matched controls. Plasma norepinephrine and epinephrine were collected once before and twice after the tests (+10/+20, and +30 min). Lower baseline levels and attenuated responses of epinephrine to the ERGO were found in CFS patients compared to controls, while the groups did not differ in their responses to the ITT. To conclude, we found evidence of altered sympathetic-neural and SAM reactivity in CFS. Exercise stress revealed a subtle catecholaminergic hyporeactivity in CFS patients. It is conceivable that inadequate catecholaminergic responses to physical exertion might contribute to CFS symptoms.
Stringer EA, Baker KS, Carroll IR, Montoya JG, Chu L, Maecker HT, Younger JW.	Department of Anesthesiology, Stanford University School of Medicine, Stanford, CA 94304, USA.	Daily cytokine fluctuations, driven by leptin, are associated with fatigue severity in chronic fatigue syndrome: evidence of inflammatory pathology.	J Transl Med. 2013 Apr 9; 11:93. doi: 10.1186/1479-5876-11-93.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating disorder characterized by persistent fatigue that is not alleviated by rest. The lack of a clearly identified underlying mechanism has hindered the development of effective treatments. Studies have demonstrated elevated levels of inflammatory factors in patients with CFS, but findings are contradictory across studies and no biomarkers have been consistently supported. Single time-point approaches potentially overlook important features of CFS, such as fluctuations in fatigue severity. We have observed that individuals with CFS demonstrate significant day-to-day variability in their fatigue severity. METHODS: Therefore, to complement previous studies, we implemented a novel longitudinal study design to investigate the role of cytokines in CFS pathophysiology. Ten women meeting the Fukuda diagnostic criteria for CFS and ten healthy age- and body mass index (BMI)-matched women underwent 25 consecutive days of blood draws and self-reporting of symptom severity. A 51-plex cytokine panel via Luminex was performed for each of the 500 serum samples collected. Our primary hypothesis was that daily fatigue severity would be significantly correlated with the inflammatory adipokine

				leptin, in the women with CFS and not in the healthy control women. As a post-hoc analysis, a machine learning algorithm using all 51 cytokines was implemented to determine whether immune factors could distinguish high from low fatigue days. RESULTS: Self-reported fatigue severity was significantly correlated with leptin levels in six of the participants with CFS and one healthy control, supporting our primary hypothesis. The machine learning algorithm distinguished high from low fatigue days in the CFS group with 78.3% accuracy. CONCLUSIONS: Our results support the role of cytokines in the pathophysiology of CFS.
Stürzel CM, Palesch D, Khalid M, Wissing S, Fischer N, Münch J.	Institute of Molecular Virology, Ulm University Medical Centre, Ulm, Germany.	Utilization of replication-competent XMRV reporter-viruses reveals severe viral restriction in primary human cells.	PLoS One. 2013 Sep 13; 8(9):e74427. doi: 10.1371/journal.pone.0074427.	The gammaretrovirus termed xenotropic murine leukemia virus-related virus (XMRV) was described to be isolated from prostate cancer tissue biopsies and from blood of patients suffering from chronic fatigue syndrome. However, many studies failed to detect XMRV and to verify these disease associations. Data suggesting the contamination of specimens in particular by PCR-based methods and recent reports demonstrating XMRV generation via recombination of two murine leukemia virus precursors raised serious doubts about XMRV being a genuine human pathogen. To elucidate cell tropism of XMRV, we generated replication competent XMRV reporter viruses encoding a green fluorescent protein or a secretable luciferase as tools to analyze virus infection of human cell lines or primary human cells. Transfection of proviral DNAs into LNCaP prostate cancer cells resulted in readily detectably reporter gene expression and production of progeny virus. Inoculation of known XMRV susceptible target cells revealed that these virions were infectious and expressed the reporter gene, allowing for a fast and highly sensitive quantification of XMRV infection. Both reporter viruses were capable of establishing a spreading infection in LNCaP and Raji B cells and could be easily passaged. However, after inoculation of primary human blood cells such as CD4 T cells, macrophages or dendritic cells, infection rates were very low, and a spreading infection was never established. In line with these results we found that supernatants derived from these XMRV infected primary cell types did not contain infectious virus. Thus, although XMRV efficiently replicated in some human cell lines, all tested primary cells were largely refractory to XMRV infection and did not support viral spread. Our results provide further evidence that XMRV is not a human pathogen.
Suskind AM, Berry SH, Suttorp MJ, Elliott MN, Hays RD, Ewing BA, Clemens JQ.	Department of Urology, University of Michigan Health System, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109, USA.	Health-related quality of life in patients with interstitial cystitis/bladder pain syndrome and frequently associated comorbidities.	Qual Life Res. 2013 Sep; 22(7):1537-41. doi: 10.1007/s11136-012-0285-5. Epub 2012 Oct 7.	PURPOSE: To estimate the association of chronic non-urologic conditions [i.e., fibromyalgia (FM), chronic fatigue syndrome (CFS), and irritable bowel syndrome (IBS)] with health-related quality of life (HRQOL) in patients with interstitial cystitis/bladder pain syndrome (IC/BPS). METHODS: A total of 276 women with established diagnoses of IC/BPS completed a telephone interview which included demographics, self-reported medical conditions, the SF-36 health survey, and the interstitial cystitis symptom index (ICSI). Multivariate linear regression analysis was used to identify correlates of SF-36 physical and mental component summary scores. RESULTS: Mean patient age was 45.1 (SD 15.9) years, and 83% of the subjects were

				white. Mean values for the SF-36 Physical Component Score (PCS) and Mental Component Score (MCS) means were 39 (SD 14) and 45 (SD 12), respectively, indicating significant HRQOL reductions. Mean ICSI score was 11.27 (SD = 4.86). FM and IBS were significantly associated with worse SF-36 scores: -8 points on the PCS ($p < 0.001$) and -6 points on the MCS ($p < 0.001$). CFS and the presence of other pelvic conditions (overactive bladder, vulvodynia, endometriosis) were not significantly associated with SF-36 PCS and MCS scores. CONCLUSIONS: In patients with IC/BPS, the presence of FM, CFS, and IBS has a significant association with HRQOL, equivalent in impact to the bladder symptoms themselves. These results emphasize the importance of a multidisciplinary approach to treating patients with IC/BPS and other conditions.
Tak LM, Rosmalen JG.	Dimence Institute of Mental Health, Nico Bolkesteinlaan 1, 7416 SB Deventer, The Netherlands. Electronic address: L.Tak@dimence.nl.	Potential bias in research of heart rate variability in fibromyalgia and chronic fatigue syndrome.	Semin Arthritis Rheum. 2013 Oct 11. pii: S0049-0172(13)00198-4. doi: 10.1016/j.semarthrit.2013.09.002. [Epub ahead of print]	[No abstract given]
Teixeira F, Moreira I, Silva AM, Vasconcelos C, Farinha F, Santos E.	[No address quoted]	Neurological involvement in Primary Sjögren Syndrome.	Acta Reumatol Port. 2013 Jan-Mar;38(1):29-36.	OBJECTIVES: To perform an observational retrospective cross-sectional case-control study to evaluate prevalence, clinical patterns and outcomes of neurological involvement in a cohort of Primary Sjögren Syndrome (pSS) patients followed up in a single center. MATERIAL AND METHODS: From a total of 93 pSS patients, diagnosed according to the 2002 criteria proposed by the American-European Consensus Group, we reviewed the clinical data of those with neurological complaints that were referred to observation by Neuroimmunology doctors. Demographic, clinical, seroimmunological data were compared between patients with and without neurological involvement. RESULTS: Neurological involvement was detected in 26 (28%) of the 93 patients. Neurological symptoms preceded the diagnosis of pSS in 12 (46%) patients. They were all females. The mean age at disease onset and neurological onset were 41,2 and 47,9 years, respectively. Twelve patients (46%) had peripheral system involvement (PNS), 13 (50%) patients had central nervous involvement (CNS) disorders and one (4%) patient had both PNS and CNS involvement. In patients with PNS, pure sensory neuropathy (small fiber neuropathy confirmed by quantitative sensory testing and sural neuropathy) occurred most frequently (n =5), followed by cranial nerve involvement affecting trigeminal, facial, or trochlear nerves (n = 4). Multiple mononeuropathy (n = 1), sensorimotor polyneuropathy (n=1), autonomic neuropathy (n=1) and myasthenia gravis (n = 1), were also observed. In patients with CNS disorders, headache (n=3) occurred most frequently, in two patients with MRI abnormalities compatible with inflammatory

				disease. Spinal cord involvement (n=2), seizures (n = 2), motor and sensory deficit (n=2), movement disorders (n=2), neuromyelitis optica (n=2), aseptic meningitis (n=1) were others manifestations observed. Cognitive dysfunction was observed in 3 of these patients. The frequency of constitutional symptoms (such as fever and fatigue) and lung involvement was significantly higher (p< 0,05) and the articular symptoms were significantly less frequent (p< 0,05) in pSS with neurological involvement. The neurologic outcome was good in 77% of the patients. CONCLUSION: The current study underlines the diversity of neurologic complications of pSS. The frequency of neurologic manifestations as first manifestation of pSS, especially in the event of CNS involvement, could explain why SS is frequently under diagnosed or late diagnosed. Screening for SS should be systematically performed in cases of acute or chronic myelopathy, axonal sensorimotor neuropathy, or cranial nerve involvement.
Tirelli U, Lleshi A, Berretta M, Spina M, Talamini R, Giacalone A.	Department of Medical Oncology, Division of Medical Oncology A, National Cancer Institute of Aviano, Pordenone, Italy. oma@cro.it	Treatment of 741 Italian patients with chronic fatigue syndrome.	Eur Rev Med Pharmacol Sci. 2013 Nov; 17(21):2847-52.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is a distinctive syndrome characterized by specific symptoms cluster. CFS mostly affects women and often results in severe functional limitation. Its prevalence varies from 0.4 to 2.5% in the general population. In our prior studies on the clinical features of 205 CFS patients we founded immunological and brain abnormalities. In this paper we illustrate our caseload on CFS treatment. PATIENTS AND METHODS: From January 2000 to December 2005, we evaluated all the patients admitted at the CFS Unit of the Aviano National Cancer Institute, for staging procedures and treatments. Patients not meeting the Fukuda diagnostic criteria were excluded. RESULTS: 250 male and 491 female (median age 35.5 and 39.3 years, respectively) were enrolled and treated for CFS. As expected, CFS resulted from previous infectious disease in all patients. Female patients showed to be more affected by symptoms than male patients. The treatment schedules followed by the patients included nutritional supplements alone, corticosteroids, antidepressant/sedative drugs, and antiviral/immunoglobulin drugs. Antiviral/ immunoglobulin drugs achieved the best response (15.3% positive responses vs. 8.3% negative responses; OR 0.44, CI 0.26-0.74, p = 0.002). The carrying out of 4 or more treatments showed a protective effect (OR 0.46, CI 0.28-0.77, p = 0.003). This finding was confirmed in the multivariate analysis, adjusted by type of drugs (OR 0.49, CI 0.28-0.84, p = 0.009) and number of treatments carried out (OR 0.51, CI 0.30-0.86, p = 0.01); these two variables were independent. CONCLUSIONS: These findings show that the antiviral/immunoglobulin approach has a longer positive disease free survival in comparison with other approaches. However, CSF still remains a difficult disease to be effectively treated.
Tjensvoll AB, Harboe E, Gøransson LG, Beyer MK, Greve OJ, Kvaløy JT,	Department of Neurology, Stavanger University Hospital, Stavanger, Norway.	Headache in primary Sjøgren's syndrome: a population-based retrospective cohort study.	Eur J Neurol. 2013 Mar;20(3):558-63. doi: 10.1111/ene.12033. Epub 2012 Nov 28.	BACKGROUND: We investigated whether the prevalence of primary headaches was higher in patients with primary Sjøgren's syndrome (PSS) than in healthy individuals. METHODS: This retrospective cohort study included 71 patients with PSS (patients) based on the American European Consensus Classification criteria, and 71 age- and gender-matched healthy subjects (controls). Headaches were classified according to

Omdal R.				the International Classification of Headache Disorders. We measured depression with the Beck Depression Inventory, and fatigue with the Fatigue Severity Scale. RESULTS: Fifty-one patients and 42 controls had headaches in the previous 12 months (71.8% vs. 59.2%, P = 0.10). Thirty-eight patients and 28 controls had tension type headaches (TTHs) (53.5% vs. 39.4%, P = 0.12). Eight patients (11.3%) and one control had chronic TTHs (P = 0.05). Migraines and migraines with aura were equally prevalent in patients (26.8% and 11.3%, respectively) and controls (28.2% and 15.5%, respectively; P = 0.61). CONCLUSIONS: In general, patients did not have more migraines or headaches than controls. However, patients had more chronic TTHs than controls. Chronic TTHs were not associated with PSS-related autoantibodies, fatigue, depression, abnormalities on magnetic resonance imaging or abnormalities in the cerebrospinal fluid. Patients with PSS did, however, have higher depression and fatigue scores than controls.
Togo F, Lange G, Natelson BH, Quigley KS.	Educational Physiology Laboratory, Graduate School of Education, University of Tokyo, Japan.	Attention network test: Assessment of cognitive function in chronic fatigue syndrome.	J Neuropsychol. 2013 Sep 24. doi: 10.1111/jnp.12030. [Epub ahead of print]	Information processing difficulties are common in patients with chronic fatigue syndrome (CFS). It has been shown that the time it takes to process a complex cognitive task, rather than error rate, may be the critical variable underlying CFS patients' cognitive complaints. The Attention Network Task (ANT) developed by Fan and colleagues may be of clinical utility to assess cognitive function in CFS, because it allows for simultaneous assessment of mental response speed, also called information processing speed, and error rate under three conditions challenging the attention system. Comparison of data from two groups of CFS patients (those with and without comorbid major depressive disorder; n = 19 and 22, respectively) to controls (n = 29) consistently showed that error rates did not differ among groups across conditions, but speed of information processing did. Processing time was prolonged in both CFS groups and most significantly affected in response to the most complex task conditions. For simpler tasks, processing time was only prolonged in CFS participants with depression. The data suggest that the ANT may be a task that could be used clinically to assess information processing deficits in individuals with CFS.
Togo F, Natelson BH.	Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, Tokyo, Japan. tougou@p.u-tokyo.ac.jp	Heart rate variability during sleep and subsequent sleepiness in patients with chronic fatigue syndrome.	Auton Neurosci. 2013 Jun;176(1-2):85-90. doi: 10.1016/j.autneu.2013.02.015 . Epub 2013 Mar 15.	We determined whether alterations in heart rate dynamics during sleep in patients with chronic fatigue syndrome (CFS) differed from controls and/or correlated with changes of sleepiness before and after a night in the sleep laboratory. We compared beat-to-beat RR intervals (RRI) during nocturnal sleep, sleep structure, and subjective scores on visual analog scale for sleepiness in 18 CFS patients with 19 healthy controls aged 25-55 after excluding subjects with sleep disorders. A short-term fractal scaling exponent (α1) of RRI dynamics, analyzed by the detrended fluctuation analysis (DFA) method, was assessed after stratifying patients into those who reported more or less sleepiness after the night's sleep (a.m. sleepier or a.m. less sleepy, respectively). Patients in the a.m. sleepier group showed significantly ($p<0.05$) higher fractal scaling index α1 during non-rapid eye movement (non-REM) sleep (Stages 1, 2, and 3 sleep) than healthy controls, although standard polysomnographic measures did not differ

				between the groups. The fractal scaling index α1 during non-REM sleep was significantly ($p<0.05$) higher than that during awake periods after sleep onset for healthy controls and patients in the a.m. less sleepy group, but did not differ between sleep stages for patients in the a.m. sleepier group. For patients, changes in self-reported sleepiness before and after the night correlated positively with the fractal scaling index α1 during non-REM sleep ($p<0.05$). These results suggest that RRI dynamics or autonomic nervous system activity during non-REM sleep might be associated with disrupted sleep in patients with CFS.
Tokizane K, Konishi H, Yasui M, Ogawa T, Sasaki K, Minamino N, Kiyama H.	Department of Functional Anatomy and Neuroscience, Nagoya University, Graduate School of Medicine, Nagoya, Aichi 466-8550, Japan.	Continuous stress promotes expression of VGF in melanotroph via suppression of dopamine.	Mol Cell Endocrinol. 2013 Jun 15; 372(1-2):49-56. doi: 10.1016/j.mce.2013.03.012. Epub 2013 Mar 26.	Prolonged exposure to stress elicits profound effects on homeostasis that may lead to cryptogenic disorders such as chronic fatigue syndrome. To investigate the pathophysiology associated with the syndrome, we used a rat continuous stress (CS) model where the pituitary represents one of the most affected organs. Here we found that mRNA for VGF (non-acronymic), a member of the granin family, was induced specifically in the intermediate lobe (IL). This was matched by a concomitant increase at the peptide/protein level assessed by C-terminal antibody. Furthermore, the up-regulation of VGF was confirmed by immunohistochemistry in a subset of melanotrophs. VGF expression was altered in the IL of rats receiving the dopamine D2 receptor agonist bromocriptine or the antagonist sulpiride. In vitro, dopamine dose-dependently decreased the mRNA levels in cultured melanotrophs. These findings suggest that VGF expression under CS is negatively regulated by dopaminergic neurons projecting from the hypothalamus.
Tschudi-Madsen H, Kjeldsberg M, Natvig B, Ihlebaek C, Straand J, Bruusgaard D.	Department of General Practice, Institute of Health and Society, Faculty of Medicine, University of Oslo, PO Box 1130, Blindern, N-0318 Oslo	Medically unexplained conditions considered by patients in general practice.	Fam Pract. 2013 Dec 24. [Epub ahead of print]	BACKGROUND: Patients frequently present with multiple and 'unexplained' symptoms, often resulting in complex consultations. To better understand these patients is a challenge to health care professionals, in general, and GPs, in particular. OBJECTIVES: In our research on symptom reporting, we wanted to explore whether patients consider that they may suffer from conditions commonly regarded as unexplained, and we explored associations between these concerns and symptom load, life stressors and socio-demographic factors. METHODS: Consecutive, unselected patients in general practice completed questionnaires addressing eight conditions commonly regarded as unexplained (amalgam poisoning, Candida syndrome, fibromyalgia, food intolerance, electromagnetic hypersensitivity, burnout syndrome, chronic fatigue syndrome and irritable bowel syndrome). With logistic regression, we analysed associations with symptom load, burden of life stressors with negative impact on present health and socio-demographic variables. RESULTS: Out of the 909 respondents (response rate = 88.8%), 863 had complete data. In total, 39.6% of patients had considered that they may suffer from one or more unexplained conditions (UCs). These concerns were strongly and positively associated with recent symptom load and number of life stressors. If we excluded burnout and food intolerance, corresponding associations were found. CONCLUSION: Patients frequently considered that they may suffer from UCs. The likelihood of such concerns

				strongly increased with an increasing symptom load and with the number of life stressors with negative impact on present health. Hence, the number of symptoms may be a strong indicator of whether patients consider their symptoms part of such often controversial multi-symptom conditions.
Tummers M, Knoop H, van Dam A, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. m.tummers@nkcv.umcn.nl	Moderators of the treatment response to guided self-instruction for chronic fatigue syndrome.	J Psychosom Res. 2013 May; 74(5):373-7. doi: 10.1016/j.jpsychores.2013.01.007. Epub 2013 Mar 5.	OBJECTIVE: The efficiency and efficacy of guided self-instruction for chronic fatigue syndrome (CFS) can be enhanced if it is known which patients will benefit from the intervention. This study aimed to identify moderators of treatment response. METHODS: This study is a secondary analysis of two randomized controlled trials evaluating the efficacy of guided self-instruction for CFS. A sample of 261 patients fulfilling US Center for Disease Control and Prevention criteria for CFS was randomly allocated to guided self-instruction or a wait list. The following potential treatment moderators were selected from the literature: age, fatigue severity, level of physical functioning, pain, level of depressive symptoms, self-efficacy with respect to fatigue, somatic attributions, avoidance of activity, and focus on bodily symptoms. Logistic and linear regression analyses were used with interaction term between treatment response and the potential moderator. RESULTS: Age, level of depression, and avoidance of activity moderated the response to guided self-instruction. Patients who were young, had low levels of depressive symptoms, and who had a low tendency to avoid activity benefited more from the intervention than older patients and patients with high levels of depressive symptoms and a strong tendency to avoid activity. CONCLUSION: Guided self-instruction is exclusively aimed at cognitions and behaviours that perpetuate fatigue. Patients with severe depressive symptom may need more specific interventions aimed at the reduction of depressive symptoms to profit from the intervention. Therefore we suggest that patients with substantial depressive symptoms be directly referred to regular cognitive behaviour therapy.
Tummers M, Lucassen PL, Wiborg JF, Bleijenberg G.	[No address quoted]	The challenge of diagnosing CFS in primary care.	Int J Clin Pract. 2013 May; 67(5):489. doi: 10.1111/ijcp.12139.	[No abstract given]
Twisk F.	[No address quoted]	Reaction on 'Chronic fatigue syndrome; the closing of the treatment centres for CFS in Belgium: quo vadis?' [Article in Dutch]	Tijdschr Psychiatr. 2013; 55(4):314-6.	Comment in Tijdschr Psychiatr. 2013; 55(4):316-7. Comment on Tijdschr Psychiatr. 2013; 55(2):79-81.
Tzanis G, Dimopoulos S, Agapitou V, Nanas S.	1st Critical Care Medicine Department, Cardiopulmonary Exercise Testing and	Exercise Intolerance in Chronic Heart Failure: The Role of Cortisol and the	Curr Heart Fail Rep. 2013 Nov 30. [Epub ahead of print]	Chronic heart failure (CHF) is a complex clinical syndrome leading to exercise intolerance due to muscular fatigue and dyspnea. Hemodynamics fail to explain the reduced exercise capacity, while a significant skeletal muscular pathology seems to constitute the main underlying mechanism for exercise intolerance in CHF patients.

	Rehabilitation Laboratory, "Evgenidio Hospital", National & Kapodestrian University of Athens, Papadiamantopoulou str., 20, Athens, 11528, Greece.	Catabolic State.		There have been proposed several metabolic, neurohormonal and immune system abnormalities leading to an anabolic/catabolic imbalance that plays a central role in the pathogenesis of the wasting process of skeletal muscle myopathy. The impairment of the anabolic axes is associated with the severity of symptoms and the poor outcome in CHF, whereas increased cortisol levels are predictive of exercise intolerance, ventilatory inefficiency and chronotropic incompetence, suggesting a significant contributing mechanism to the limited functional status. Exercise training and device therapy could have beneficial effects in preventing and treating muscle wasting in CHF. However, specific anabolic treatment needs more investigation to prove possible beneficial effects.
Valero S, Sáez-Francàs N, Calvo N, Alegre J, Casas M.	Department of Psychiatry, Hospital Universitari Vall d'Hebron, CIBERSAM, Universitat Autònoma de Barcelona, Passeig de la Vall d'Hebron 119-129, 08035 Barcelona, Catalonia, Spain. Electronic address: svalero@vhebron.net.	The role of neuroticism, perfectionism and depression in chronic fatigue syndrome. A structural equation modeling approach.	Compr Psychiatry. 2013 Oct; 54(7):1061-7. doi: 10.1016/j.comppsych.2013.04.015. Epub 2013 Jun 5.	OBJECTIVE: Previous studies have reported consistent associations between Neuroticism, maladaptive perfectionism and depression with severity of fatigue in Chronic Fatigue Syndrome (CFS). Depression has been considered a mediator factor between maladaptive perfectionism and fatigue severity, but no studies have explored the role of neuroticism in a comparable theoretical framework. This study aims to examine for the first time, the role of neuroticism, maladaptive perfectionism and depression on the severity of CFS, analyzing several explanation models. METHODS: A sample of 229 CFS patients were studied comparing four structural equation models, testing the role of mediation effect of depression severity in the association of Neuroticism and/or Maladaptive perfectionism on fatigue severity. RESULTS: The model considering depression severity as mediator factor between Neuroticism and fatigue severity is the only one of the explored models where all the structural modeling indexes have fitted satisfactorily (Chi square=27.01, p=0.079; RMSE=0.047, CFI=0.994; SRMR=0.033). Neuroticism is associated with CFS by the mediation effect of depression severity. This personality variable constitutes a more consistent factor than maladaptive perfectionism in the conceptualization of CFS severity.
Valle LA, Gorodeski Baskin RL, Porter K, Sipos JA, Khawaja R, Ringel MD, Kloos RT.	Department of Internal Medicine, The Ohio State University, Columbus, Ohio, USA.	In thyroidectomized patients with thyroid cancer, a serum thyrotropin of 30μU/mL after thyroxine withdrawal is not always adequate for detecting an elevated stimulated serum thyroglobulin.	Thyroid. 2013 Feb; 23(2):185-93. doi: 10.1089/thy.2012.0327.	BACKGROUND: The thyrotropin (TSH) level or duration of thyroid hormone withdrawal (THW) required to detect stimulated thyroglobulin (Tg) in differentiated thyroid cancer (DTC) monitoring is unknown. The objective of this study was to evaluate the TSH cutoff of >30μU/mL as a means to detect stimulated Tg ≥2ng/mL after THW (THW-Tg≥2), and sensitivity of the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) questionnaire for detecting hypothyroid symptoms. METHODS: This was a prospective longitudinal cohort study done at a tertiary academic medical center. Forty-seven patients with DTC undergoing their first Tg stimulation or after previously abnormal Tg stimulation had weekly measurements of TSH and Tg during the 4 weeks THW, and repeated questionnaire assessments. RESULTS: TSH did not reach a plateau in any patient, and in those whose Tg did not remain undetectable, Tg continued to rise. Seventy-five percent of patients had an undetectable Tg <0.2ng/mL at baseline (95% were <0.5mg/mL) with 16% remaining

				undetectable throughout THW. The majority of patients (72.7% and 97.8%) achieved TSH >30 µU/mL by 3 and 4 weeks THW, respectively. Of the 15 patients with maximum stimulated THW-Tg≥2, 38% were detected before the minimal TSH >30µU/mL cutoff. At 2 weeks THW, 3 had a TSH>30µU/mL, and none of them had Tg ≥2ng/mL. At 3 weeks THW, 11 had a TSH >30µU/mL, and 64% of them had Tg ≥2ng/mL. Only 60% were detected at 3-week THW regardless of their TSH level. Eighty-six percent were detected by TSH 60-<80µU/mL. Conversely, all patients whose serum Tg was <0.2ng/mL when their serum TSH was >20µU/mL did not achieve a THW-Tg≥2. CONCLUSION: The minimal TSH cutoff of >30µU/mL was inadequate to detect many patients with final stimulated THW-Tg≥2 during complete THW. TSH >80-100µU/mL was a better cutoff, achieved in only 53% after 4-week THW. Conversely, we propose a preliminary THW-stopping rule for ending THW early in selected patients. In patients with a Tg <0.2ng/mL when TSH >20µU/mL, all had a final stimulated Tg ≤2ng/mL, potentially saving qualifying patients 40% of THW duration compared to 4-week THW. FACIT-F correlated with TSH, but was not sensitive to detect mild hypothyroidism.
Van Den Eede F, Moorkens G.	[No address quoted]	Reaction on 'Chronic fatigue syndrome; the closing of the treatment centres for CFS in Belgium: quo vadis?' Reply to Twisk. [Article in Dutch]	Tijdschr Psychiatr. 2013; 55(4):316-7.	Comment on Tijdschr Psychiatr. 2013;55(2):79-81.Tijdschr Psychiatr. 2013; 55(4):314-6.
Van Den Eede F, Moorkens G.	[No address quoted]	Chronic fatigue syndrome; the closing of the treatment centres for CFS in Belgium: quo vadis? [Article in Dutch]	Tijdschr Psychiatr. 2013; 55(2):79-81.	Comment in Tijdschr Psychiatr. 2013;55(4):316-7. Tijdschr Psychiatr. 2013; 55(4):314-6.
van Doorn PA.	Department of Neurology, Erasmus MC, Rotterdam, The Netherlands. p.a.vandoorn@erasmusmc.nl	Diagnosis, treatment and prognosis of Guillain-Barré syndrome (GBS).	Presse Med. 2013 Jun; 42(6 Pt 2):e193-201. doi: 10.1016/j.lpm.2013.02.328. Epub 2013 Apr 28.	Guillain-Barré syndrome (GBS) is an acute polyneuropathy with a variable degree of weakness that reaches its maximal severity within 4 weeks. The disease is mostly preceded by an infection and generally runs a monophasic course. Both intravenous immunoglobulin (IVIg) and plasma exchange (PE) are effective in GBS. Rather surprisingly, steroids alone are ineffective. Mainly for practical reasons, IVIg usually is the preferred treatment. GBS can be subdivided in the acute inflammatory demyelinating polyneuropathy (AIDP), the most frequent form in the western world; acute motor axonal neuropathy (AMAN), most frequent in Asia and Japan; and in Miller-Fisher syndrome (MFS). Additionally, overlap syndromes exist (GBS-MFS

				overlap). About 10% of GBS patients have a secondary deterioration within the first 8 weeks after start of IVIg. Such a treatment-related fluctuation (TRF) requires repeated IVIg treatment. About 5% of patients initially diagnosed with GBS turn out to have chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) with acute onset (A-CIDP). It is yet unknown whether GBS patients who remain able to walk ('mildly affected GBS patients'), or patients with MFS, also benefit from IVIg. Despite current treatment, GBS remains a severe disease, as about 25% of patients require artificial ventilation during a period of days to months, about 20% of patients are still unable to walk after 6 months and 3-10% of patients die. Additionally, many patients have pain, fatigue or other residual complaints that may persist for months or years. Pain can also be very confusing in making the diagnosis, especially when it precedes the onset of weakness. Advances in prognostic modelling resulted in the development of a simple prognostic scale that predicts the chance for artificial ventilation, already at admission; and in an outcome scale that can be used to determine the chance to be able to walk unaided after 1, 3 or 6 months. GBS patients with a poor prognosis potentially might benefit from a more intensified treatment. A larger increase in serum IgG levels after standard IVIg treatment (0.4 g/kg/day for 5 consecutive days) seems to be related with an improved outcome after GBS. This was one of the reasons to start the second course IVIg trial (SID-GBS trial) in GBS patients with a poor prognosis. This study is currently going on. The international GBS outcome study (IGOS) is a new worldwide prognostic study that aims to get further insight in the (immune) pathophysiology and outcome of GBS, both in children and adults. Hopefully these and other studies will further help to improve the understanding and especially the outcome in patients with GBS.
van Geelen SM.	University Medical Center Utrecht, Utrecht, The Netherlands. S.M.vanGeelen@umcutrecht.nl	Getting closer - advancing the study of persons with chronic fatigue syndrome: a comment on Poeschla et al.	Ann Behav Med. 2013 Jun; 45(3):271-2. doi: 10.1007/s12160-013-9467-9.	Comment on Ann Behav Med. 2013 Jun; 45(3):289-98.
VanElzakker MB.	Tufts University Psychology, Massachusetts General Hospital Psychiatric Neuroscience, 490 Boston Avenue, Medford, MA 02155, USA.	Chronic fatigue syndrome from vagus nerve infection: a psychoneuroimmunological hypothesis.	Med Hypotheses. 2013 Sep; 81(3):414-23. doi: 10.1016/j.mehy.2013.05.034. Epub 2013 Jun 19.	Chronic fatigue syndrome (CFS) is an often-debilitating condition of unknown origin. There is a general consensus among CFS researchers that the symptoms seem to reflect an ongoing immune response, perhaps due to viral infection. Thus, most CFS research has focused upon trying to uncover that putative immune system dysfunction or specific pathogenic agent. However, no single causative agent has been found. In this speculative article, I describe a new hypothesis for the etiology of CFS: infection of the vagus nerve. When immune cells of otherwise healthy individuals detect any peripheral infection, they release proinflammatory cytokines.

	michael.vanelzakker@gmail.com			Chemoreceptors of the sensory vagus nerve detect these localized proinflammatory cytokines, and send a signal to the brain to initiate sickness behavior. Sickness behavior is an involuntary response that includes fatigue, fever, myalgia, depression, and other symptoms that overlap with CFS. The vagus nerve infection hypothesis of CFS contends that CFS symptoms are a pathologically exaggerated version of normal sickness behavior that can occur when sensory vagal ganglia or paraganglia are themselves infected with any virus or bacteria. Drawing upon relevant findings from the neuropathic pain literature, I explain how pathogen-activated glial cells can bombard the sensory vagus nerve with proinflammatory cytokines and other neuroexcitatory substances, initiating an exaggerated and intractable sickness behavior signal. According to this hypothesis, any pathogenic infection of the vagus nerve can cause CFS, which resolves the ongoing controversy about finding a single pathogen. The vagus nerve infection hypothesis offers testable hypotheses for researchers, animal models, and specific treatment strategies.
Vieira da Motta M, Vieira da Motta E.	University of Sao Paulo, Medical School, Pinheiros, Sao Paulo Brazil.	Levonorgestrel-releasing intrauterine system and iron overload syndrome.	Clin Med Insights Case Rep. 2013 Jun 3;6: 93-7. doi: 10.4137/CCRep.S11888. Print 2013.	Severe fatigue is a common complaint among patients. This report presents a clinical case of a woman complaining of fatigue associated with diarrhea and myalgia that were first attributed to emotional stress and depression. Initially, the patient was diagnosed with chronic fatigue and irritable bowel syndrome. The patient followed nutritional and physical exercise programs without any improvement. Other clinical conditions, such as nutritional deficiencies, endocrine dysfunctions, autoimmune diseases and neoplasias, were then assessed. During clinical investigation, serum ferritin and iron levels were abnormally elevated despite normal hemoglobin levels, which pointed to an iron overload syndrome later diagnosed as hemochromatosis. It is possible that the symptoms were triggered by the amenorrhea caused by the levonorgestrel-releasing intrauterine system used for contraception.
Vishnu VY, Modi M, Prabhakar S, Bhansali A, Goyal MK.	Department of Neurology, Post Graduate Institute of Medical Education and Research, Chandigarh 160012, India. Electronic address: vishnuvy16@yahoo.com.	"A" motor neuron disease.	Department of Neurology, Post Graduate Institute of Medical Education and Research, Chandigarh 160012, India. Electronic address: vishnuvy16@yahoo.com.	Importance: Allgrove syndrome is a rare autosomal recessive disorder characterised by achalasia, alacrima, adrenal insufficiency, autonomic dysfunction and amyotrophy. The syndrome has been described in childhood and adult presentation, as in our case, is very rare. There is a considerable delay in diagnosis due to lack of awareness about the syndrome. Observations: We report a single case of a 36year old man who was initially diagnosed and treated for achalasia cardia in our institute 14years before. After 8years he presented again with weakness and wasting predominantly distally. He had tongue fasciculations, brisk reflexes and extensor plantar. After supportive electrophysiological studies he was diagnosed as Amyotrophic lateral sclerosis. After 5years he presented with generalised fatigue without any significant worsening of his neurological status. On reevaluation he had alacrimia, autonomic dysfunction and mild ACTH resistance. Conclusions and relevance: Allgrove syndrome may be an underdiagnosed cause of multisystem neurological disease due to the heterogeneous clinical presentation as well as for ignorance of clinician about the syndrome. Based on our case, we also believe that there does exist a subgroup of patients who follow a

				less severe and chronic course. Recognition of syndrome allows for treatment of autonomic dysfunction, adrenal insufficiency and dysphagia.
Vos-Vromans DC, Huijnen IP, Köke AJ, Seelen HA, Knottnerus JA, Smeets RJ.	Revant Rehabilitation Centre Breda, Brabantlaan 1, 4817 JW Breda, The Netherlands. d.vos@revant.nl	Differences in physical functioning between relatively active and passive patients with Chronic Fatigue Syndrome.	J Psychosom Res. 2013 Sep;75(3):249-54. doi: 10.1016/j.jpsychores.2013.05.001. Epub 2013 Jun 2.	OBJECTIVE: According to the Cognitive behavioral therapy (CBT) protocol for patients with Chronic Fatigue Syndrome (CFS), therapists are advised to categorize patients in relatively active and passive patients. However, evidence to support the differences in physical functioning between these subgroups is limited. Using the baseline data from a multicentre randomized controlled trial (FatiGo), the differences in actual and perceived physical functioning between active and passive patients with CFS were evaluated. METHODS: Sixty patients, who received CBT during the FatiGo trial were included. Based on the expert opinion and using the definitions of subgroups defined in the CBT protocols, the therapist categorized the patient. Data from an activity monitor was used to calculate actual physical functioning, physical activity, daily uptime, activity fluctuations and duration of rest during daily life. Perceived physical functioning was assessed by measuring physical activity, physical functioning and functional impairment with the Checklist Individual Strength, Short Form-36 and Sickness-Impact Profile 8. RESULTS: Relatively active patients have a significantly higher daily uptime and show significantly less fluctuations in activities between days. Passive patients experience a significantly lower level of physical functioning and feel more functionally impaired in their mobility. However, no significant differences were found in the other actual or perceived physical functioning indices. CONCLUSIONS: A clear difference in actual and perceived physical functioning between relatively active and passive patients with CFS as judged by their therapists could not be found. Future research is needed to form a consensus on how to categorize subgroups of patients with CFS.
Walwyn R, Potts L, McCrone P, Johnson AL, Decesare JC, Baber H, Goldsmith K, Sharpe M, Chalder T, White PD.	MH&N Clinical Trials Unit, Institute of Psychiatry, King's College London, DeCrespigny Park, London, SE5 8AF, UK. R.E.A.Walwyn@leeds.ac.uk.	A randomised trial of adaptive pacing therapy, cognitive behaviour therapy, graded exercise, and specialist medical care for chronic fatigue syndrome (PACE): statistical analysis plan.	Trials. 2013 Nov 13;14:386. doi: 10.1186/1745-6215-14-386.	BACKGROUND: The publication of protocols by medical journals is increasingly becoming an accepted means for promoting good quality research and maximising transparency. Recently, Finfer and Bellomo have suggested the publication of statistical analysis plans (SAPs).The aim of this paper is to make public and to report in detail the planned analyses that were approved by the Trial Steering Committee in May 2010 for the principal papers of the PACE (Pacing, graded Activity, and Cognitive behaviour therapy: a randomised Evaluation) trial, a treatment trial for chronic fatigue syndrome. It illustrates planned analyses of a complex intervention trial that allows for the impact of clustering by care providers, where multiple care-providers are present for each patient in some but not all arms of the trial. RESULTS: The trial design, objectives and data collection are reported. Considerations relating to blinding, samples, adherence to the protocol, stratification, centre and other clustering effects, missing data, multiplicity and compliance are described. Descriptive, interim and final analyses of the primary and secondary outcomes are then outlined. CONCLUSIONS: This SAP maximises transparency, providing a record of all planned analyses, and it may be a resource for those who are developing SAPs,

				acting as an illustrative example for teaching and methodological research. It is not the sum of the statistical analysis sections of the principal papers, being completed well before individual papers were drafted. TRIAL REGISTRATION: ISRCTN54285094 assigned 22 May 2003; First participant was randomised on 18 March 2005.
Wang J, Sun C, Zheng Y, Pan H, Zhou Y, Fan Y.	Jilin Province Key Laboratory on Chemistry and Biology of Changbai Mountain Natural Drugs School of Life Sciences, Northeast Normal University, Changchun, 130024, People's Republic of China.	The effective mechanism of the polysaccharides from Panax ginseng on chronic fatigue syndrome.	Arch Pharm Res. 2013 Aug 21. [Epub ahead of print]	Ginseng acidic polysaccharide WGPA isolated from the root of Panax ginseng C. A. Meyer was fractionated into WGPA-A and WGPA-N by anion-exchange chromatography. The antifatigue activity of ginseng acidic polysaccharide WGPA has been reported in our previous research. This present study was designed to identify its active component and elucidate the mechanism for preventing chronic fatigue syndrome (CFS). WGPA, WGPA-A and WGPA-N were orally administered to mice once daily for 15 days. The effects of these compounds on physiological biomarkers of oxidative stress and on the morphology of the mitochondria in striated skeletal muscle were assessed. The results of forced swimming test-induced indicated that WGPA and WGPA-A could lengthen the swimming time, while WGPA-N could not. In addition, malondialdehyde and lactate dehydrogenase levels in serum were enhanced; while those of superoxide dismutase and glutathione peroxidase were lowered. Interestingly, the structural degeneration of mitochondria were all ameliorated. These findings suggested that WGPA-A is the active component of WGPA, it might have potential therapeutic effects for CFS and the oxidative stress might be involved in the pathogenesis. Our results also provided essential data for a better understanding of the antifatigue effects of P. ginseng extracts.
Wang WJ, Lu G, Ding N, Huang HP, Ding WX, Zhang XL.	Department of Respiratory Medicine, Nanjing Hospital Affiliated to Nanjing Medical University, Nanjing, Jiangsu 210001, China.	Adiponectin alleviates contractile dysfunction of genioglossus in rats exposed to chronic intermittent hypoxia.	Chin Med J (Engl). 2013; 126 (17):3259-63.	BACKGROUND: Genioglossal dysfuntion takes an important role in pathogenesis of obstructive sleep apnea hypopnea syndrome (OSAHS) in which chronic intermittent hypoxia (CIH) is the major pathological origin. Recent studies have suggested genioglossal injury induced by CIH might be improved by adiponectin. The aim of this study was to investigate the effects of adiponectin on genioglossus contractile properties in rats exposed to CIH. METHODS: Thirty-nine healthy male Wistar rats were randomly divided into three groups: normal control (NC), CIH and adiponectin supplement (CIH+Ad) with 13 rats in each. Rats in NC were kept breathing normal air, while rats in CIH and CIH+Ad experienced the same CIH environment eight hours per day for 35 successive days. Rats in CIH+Ad were given intravenous adiponectin of 10 μg twice a week for 30 successive days. Rats in the NC and CIH were injected with normal saline as a control. After 35 days' CIH exposure, the levels of serum adiponectin and genioglossus contractile properties were compared. RESULTS: Serum adiponectin level was significantly lower in CIH than in NC (1210 ng/ml vs. 2236 ng/ml). Serum adiponectin level in CIH+Ad (1844 ng/ml) was significantly higher than CIH but lower than NC. Twitch tension, time to peak tension, half relaxation time and tetanic tension were significantly lower in CIH than NC and improved in CIH+Ad. All mean tetanic fatigue indices decreased more rapidly in the first 20 seconds than during the subsequent 100 seconds. Tetanic fatigue indices in NC and CIH+Ad were

				significantly higher compared to CIH. CONCLUSIONS: CIH could lead to hypoadiponectinaemia, impaired genioglossus contractile properties and decreased fatigue resistance in rats. Such changes could be partially offset by supplementation of adiponectin.
Warren JW, Clauw DJ, Langenberg P.	Department of Medicine, University of Maryland School of Medicine, Baltimore, MD 21201, USA. jwarren@medicine.umaryland.edu	Prognostic factors for recent-onset interstitial cystitis/painful bladder syndrome.	Comment in J Urol. 2013 Aug; 190(2):551.	Study Type - Prognosis (case series) Level of Evidence 4 What's known on the subject? and What does the study add? Interstitial cystitis/painful bladder syndrome (IC/PBS) comprises pain perceived to be from the bladder, urinary urgency and frequency, and nocturia. As diagnosed at present, it is primarily identified in adult women. It is a chronic disease yet its natural history has not been well studied. In a prospective study of 304 incident female IC/PBS cases followed for a median of 33 months after onset, women with baseline chronic fatigue syndrome had a worse prognosis for IC/PBS. Mild IC/PBS at baseline was the only variable that was directly associated with a good prognosis.OBJECTIVE: To identify baseline variables that predict the prognosis of interstitial cystitis/painful bladder syndrome (IC/PBS) in women seeking medical care for recent onset of this syndrome. SUBJECTS AND METHODS: In a prospective study of women with incident IC/PBS (≤12 months of symptoms), we contacted patients at intervals and asked standardized questions about IC/PBS symptoms in the previous week. Logistic regression analyses assessed baseline variables as predictors of mild vs more severe IC/PBS at the last follow-up. RESULTS: Median length of follow-up was 33 months after onset of IC/PBS; 304 (97%) patients had at least one follow-up assessment. Mild IC/PBS at baseline was the only variable that was directly associated with a mild IC/PBS endpoint. Conversely, a history of chronic fatigue syndrome (CFS) was inversely associated with a mild endpoint of IC/PBS (i.e. individuals with CFS had a worse prognosis for their IC/PBS symptoms). CONCLUSIONS: At a median of nearly 3 years after onset, baseline mild IC/PBS was directly associated with a milder disease severity. Baseline co-morbid CFS was associated with more severe disease. Whether CFS was uniquely associated or represented several co-morbid non-bladder syndromes (NBSs) could not be determined.
Warren JW, Langenberg P, Clauw DJ.	Department of Medicine, University of Maryland School of Medicine, Baltimore, MD 21201, USA. jwarren@medicine.umaryland.edu	The number of existing functional somatic syndromes (FSSs) is an important risk factor for new, different FSSs.	J Psychosom Res. 2013 Jan; 74(1):12-7. doi: 10.1016/j.jpsychores.2012.09.002. Epub 2012 Sep 26. J Psychosom Res. 2013 Aug; (2):190. J Psychosom Res. 2013 Aug; 5(2):191.	OBJECTIVE: The objective of this study is to test the hypothesis that the number of functional somatic syndromes (FSSs) predicts new, additional FSSs. METHODS: In a recent case-control study of interstitial cystitis/painful bladder syndrome (IC/PBS), we used symptom-based consensus definitions to identify these FSSs: fibromyalgia (FM), chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), chronic pelvic pain, migraine, sicca syndrome and panic disorder. Those present before the incidence year were called antecedent FSSs; those with onset during the incidence year were called incident FSSs. In each of two groups, 312 IC/PBS cases and 313 controls, rates of incident FSSs were compared among those with 0, 1, 2, or ≥3 antecedent FSSs. Confounding was assessed using logistic regression analyses that included the individual antecedent FSSs, published correlates of these FSSs, and demographic variables. RESULTS: The incidence of a new FSS increased with the number of

				antecedent FSSs, as did that of incident FM, CFS and IBS studied separately. These findings were not confounded by other variables. The presence of multiple antecedent FSSs generally had the highest odds ratio for new, different, incident FSSs. CONCLUSIONS: This study revealed that the number of antecedent FSSs was among the strongest risk factors for other FSSs, especially incident FM, CFS and IBS. This suggests that the FSSs are linked through a polysyndromic phenotype. If each FSS is heterogeneous, to seek a pathogenesis common to all FSSs, individuals with multiple FSSs should be sought; to seek a pathogenesis unique to a specific FSS, mature persons who have only that FSS should be studied.
Wearden AJ, Emsley R.	School of Psychological Sciences, University of Manchester.	Mediators of the effects on fatigue of pragmatic rehabilitation for chronic fatigue syndrome.	J Consult Clin Psychol. 2013 Oct; 81(5):831-8. doi: 10.1037/a0033561. Epub 2013 Jun 24.	OBJECTIVE: To examine potential mediators of the effect of pragmatic rehabilitation on improvements in fatigue following a randomized controlled trial for patients with chronic fatigue syndrome (CFS/ME) in primary care (IRCTN 74156610). METHOD: Patients fulfilled the Oxford criteria for CFS. Ninety-five patients were randomized to pragmatic rehabilitation and 100 to general practitioner (GP) treatment as usual. The outcome was the Chalder fatigue scale score (0123 scoring) at end of treatment (20 weeks) and 1-year follow up (70 weeks). First, the effect of treatment on potential mediators was assessed. Then fatigue was regressed on significant mediators, treatment allocation, and baseline measures of fatigue and significant mediators. RESULTS: Reduction in limiting activities at 20 weeks mediated the positive effect of pragmatic rehabilitation on fatigue at 70 weeks (mediated effect size = -2.64, SE = 0.81, p = .001, proportion of effect mediated = 82.0%). Reduction in catastrophizing at 20 weeks mediated the positive effect of pragmatic rehabilitation on fatigue at 70 weeks (mediated effect size = -1.39, SE = 0.61, p = .023, proportion of effect mediated = 43.2%). Reductions in 70-week measures of fear avoidance, embarrassment avoidance, limiting activities, and all-or-nothing behavior all mediated improvement in fatigue at 70 weeks, although the causal direction of these cross-sectional effects cannot be determined. There were no between-group differences on measures of exercise capacity (a timed step test). CONCLUSIONS: Improvements in fatigue following pragmatic rehabilitation are related to changes in behavioral responses to and beliefs about fatigue.
Werker CL, Nijhof SL, van de Putte EM.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht, The Netherlands, c.l.werker@students.uu.nl.	Clinical Practice: Chronic fatigue syndrome.	Eur J Pediatr. 2013 Oct; 172(10):1293-8. doi: 10.1007/s00431-013-2058-8. Epub 2013 Jun 12.	The diagnosis chronic fatigue syndrome (CFS) was conceptualized in the mid-1980s. It is a clinically defined condition characterized by severe and disabling new onset fatigue with at least four additional symptoms: impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, multi-joint pain, new headaches, unrefreshing sleep or post-exertion malaise. Chronic fatigue syndrome in adolescents is a rare condition compared to symptomatic fatigue. The estimated prevalence of adolescent CFS ranges between 0.11 and 1.29 % in Dutch, British, and US populations. Diagnosis of the chronic fatigue syndrome is established through exclusion of other medical and psychiatric causes of chronic fatiguing illness. Taking a full clinical history and a full physical examination are therefore vital. In adolescence,

				CFS is associated with considerable school absence with long-term detrimental effects on academic and social development. One of the most successful potential treatments for adolescents with CFS is cognitive behavioural therapy, which has been shown to be effective after 6 months in two thirds of the adolescents with CFS. This treatment effect sustains at 2-3-year follow-up. In conclusion, the diagnosis CFS should be considered in any adolescent patient with severe disabling long-lasting fatigue. Cognitive behavioural therapy is effective in 60-70 % of the patients. Prompt diagnosis favours the prognosis.
White PD, Chalder T, Sharpe M, Johnson T, Goldsmith K.	Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK.	PACE trial authors' reply to letter by Kindlon.	BMJ. 2013 Oct 15; 347: f5963. doi: 10.1136/bmj.f5963.	Comment on BMJ. 013;347:f5731.
White PD, Goldsmith K, Johnson AL, Chalder T, Sharpe M.	[No address quoted]	Letter to the editor: response to correspondence concerning 'recovery from chronic fatigue syndrome after treatments in the PACE trial'.	Psychol Med. 2013 Aug;43(8):1791-2. doi: 10.1017/S0033291713001311.	Comment on Psychol Med. 2013 Aug; 43(8):1788-9. Psychol Med. 2013 Aug;43(8):1787. Psychol Med. 2013 Aug;43(8):1787-8. Psychol Med. 2013 Aug;43(8):1789. Psychol Med. 2013 Aug;43(8):1789-90. Psychol Med. 2013 Aug;43(8):1790-1.
White PD, Goldsmith K, Johnson AL, Chalder T, Sharpe M.	Wolfson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, UK. p.d.white@qmul.ac.uk	Recovery from chronic fatigue syndrome after treatments given in the PACE trial.	Psychol Med. 2013 Oct; 43(10):2227-35. doi: 10.1017/S0033291713000020.	BACKGROUND: A multi-centre, four-arm trial (the PACE trial) found that rehabilitative cognitive behaviour therapy (CBT) and graded exercise therapy (GET) were more effective treatments for chronic fatigue syndrome (CFS) than specialist medical care (SMC) alone, when each was added to SMC, and more effective than adaptive pacing therapy (APT) when added to SMC. In this study we compared how many participants recovered after each treatment. METHOD: We defined recovery operationally using multiple criteria, and compared the proportions of participants meeting each individual criterion along with two composite criteria, defined as (a) recovery in the context of the trial and (b) clinical recovery from the current episode of the illness, however defined, 52 weeks after randomization. We used logistic regression modelling to compare treatments. RESULTS: The percentages (number/total) meeting trial criteria for recovery were 22% (32/143) after CBT, 22% (32/143) after GET, 8% (12/149) after APT and 7% (11/150) after SMC. Similar proportions met criteria for clinical recovery. The odds ratio (OR) for trial recovery after CBT was 3.36 [95% confidence interval (CI) 1.64–6.88] and for GET 3.38 (95% CI 1.65–6.93), when compared to APT, and after CBT 3.69 (95% CI 1.77–7.69) and GET 3.71 (95% CI 1.78–

				7.74), when compared to SMC (p values < or =0.001 for all comparisons). There was no significant difference between APT and SMC. Similar proportions recovered in trial subgroups meeting different definitions of the illness. CONCLUSIONS: This study confirms that recovery from CFS is possible, and that CBT and GET are the therapies most likely to lead to recovery.
Winger A, Ekstedt M, Wyller VB, Helseth S.	Faculty of Nursing, Oslo and Akershus University College of Applied Sciences, Oslo, Norway; Medical Faculty, Institute of Clinical Medicine, University of Oslo, Oslo, Norway.	'Sometimes it feels as if the world goes on without me': adolescents' experiences of living with chronic fatigue syndrome.	J Clin Nurs. 2013 Dec 20. Doi : 10.1111/jocn.12522. [Epub ahead of print]	AIMS AND OBJECTIVES: To explore the experience of being an adolescent with chronic fatigue syndrome. BACKGROUND: Despite ample research, chronic fatigue syndrome is still poorly understood, and there are still controversies related to the illness. Adolescents with chronic fatigue syndrome are often unable to attend school and lose social relations with friends. The challenges they face will affect their quality of life. DESIGN: A qualitative, phenomenological hermeneutical design. METHOD: Six boys and twelve girls, aged 12-18, were interviewed, emphasising their own experiences living with chronic fatigue syndrome. Analyses were performed using a phenomenological hermeneutical method. RESULTS: The core theme, 'Sometimes it feels as if the world goes on without me', encompasses the feelings an adolescent living with chronic fatigue syndrome might have about life. The core theme was supported by four subthemes: 'On the side of life - locked in and shut out'; 'the body, the illness and me'; 'if the illness is not visible to others, does it exist? '; and 'handling life while hoping for a better future'. The subthemes reflect the experience of social isolation, their own and others' understanding of the illness and hope for the future. CONCLUSIONS: Not being able to be with friends, or attend school, made the adolescents feel different and forgotten. They felt alienated in their own bodies and were struggling to be visible to themselves and to their surroundings. Spending less time with friends and more time with their parents constituted a threat to independence and development. Yet they managed to envision a better future despite all the difficulties. RELEVANCE FOR CLINICAL PRACTICE: To provide effective support and constructive relations to adolescents with chronic fatigue syndrome, all health professions involved need insight from the persons who are themselves ill. Health centres could function as resource centres for patients and healthcare professionals.
Witsch J, Galldiks N, Bender A, Kollmar R, Bösel J, Hobohm C, Günther A, Schirotzek I, Fuchs K, Jüttler E.	Center for Stroke Research Berlin (CSB), Charité University Medicine Berlin, Charitéplatz 1, 10117 Berlin, Germany. Jens.Witsch@charite.de	Long-term outcome in patients with Guillain-Barré syndrome requiring mechanical ventilation.	J Neurol. 2013 May; 260(5):1367-74. doi: 10.1007/s00415-012-6806-x. Epub 2013 Jan 9.	We aimed to determine long-term disability and quality of life in patients with Guillain-Barré syndrome (GBS) who required mechanical ventilation (MV) in the acute phase. Our retrospective cohort study included 110 GBS patients admitted to an intensive care unit and requiring MV (01/1999-08/2010) in nine German tertiary academic medical centers. Outcome was determined 1 year or longer after hospital admission using the GBS disability scale, Barthel index (BI), EuroQuol-5D (EQ-5D) and Fatigue Severity Scale. Linear/multivariate regression analysis was used to analyze predicting factors for outcome. Mean time to follow up was 52.6 months. Hospital mortality was 5.5 % and long-term mortality 13.6 %. Overall 53.8 % had a favorable outcome (GBS disability score 0-1) and 73.7 % of survivors had no or mild disability (BI

				90-100). In the five dimensions of the EQ-5D "mobility", "self-care", "usual activities", "pain" and "anxiety/depression" no impairments were stated by 50.6, 58.4, 36.4, 36.4 and 50.6 % of patients, respectively. A severe fatigue syndrome was present in 30.4 % of patients. Outcome was statistically significantly correlated with age, type of therapy and number of immunoglobulin courses. In GBS-patients requiring MV in the acute phase in-hospital, and long-term mortality are lower than that in previous studies, while long-term quality of life is compromised in a large fraction of patients, foremost by immobility and chronic pain. Efforts towards improved treatment approaches should address autonomic dysfunction to further reduce hospital mortality while improved rehabilitation concepts might ameliorate long-term disability.
Wyller VB, Helland IB.	Department of Paediatrics, Oslo University Hospital and University of Oslo, Oslo, Norway. brwylle@online.no.	Relationship between autonomic cardiovascular control, case definition, clinical symptoms, and functional disability in adolescent chronic fatigue syndrome: an exploratory study.	Biopsychosoc Med. 2013 Feb 7; 7(1):5. doi: 10.1186/1751-0759-7-5.	Chronic Fatigue Syndrome (CFS) is characterized by severe impairment and multiple symptoms. Autonomic dysregulation has been demonstrated in several studies. We aimed at exploring the relationship between indices of autonomic cardiovascular control, the case definition from Centers for Disease Control and Prevention (CDC criteria), important clinical symptoms, and disability in adolescent chronic fatigue syndrome. 38 CFS patients aged 12-18 years were recruited according to a wide case definition (ie. not requiring accompanying symptoms) and subjected to head-up tilt test (HUT) and a questionnaire. The relationships between variables were explored with multiple linear regression analyses. In the final models, disability was positively associated with symptoms of cognitive impairments ($p<0.001$), hypersensitivity ($p<0.001$), fatigue ($p=0.003$) and age ($p=0.007$). Symptoms of cognitive impairments were associated with age ($p=0.002$), heart-rate (HR) at baseline ($p=0.01$), and HR response during HUT ($p=0.02$). Hypersensitivity was associated with HR response during HUT ($p=0.001$), high-frequency variability of heart rate (HF-RRI) at baseline ($p=0.05$), and adherence to the CDC criteria ($p=0.005$). Fatigue was associated with gender ($p=0.007$) and adherence to the CDC criteria ($p=0.04$). In conclusion, a) The disability of CFS patients is not only related to fatigue but to other symptoms as well; b) Altered cardiovascular autonomic control is associated with certain symptoms; c) The CDC criteria are poorly associated with disability, symptoms, and indices of altered autonomic nervous activity.
Young JL.	Wayne State University School of Medicine, Detroit, MI 48307, USA. jyoung@rcbm.net	Chronic fatigue syndrome: 3 cases and a discussion of the natural history of attention-deficit/hyperactivity disorder.	Postgrad Med. 2013 Jan; 125(1):162-8. doi: 10.3810/pgm.2013.01.2631.	Fatigue is commonly reported in the primary care setting; however, its cause is often unclear. This article presents 3 cases involving patients with chronic fatigue syndrome who responded poorly to treatment. After clinical evaluation, all patients were found to meet criteria for attention-deficit/hyperactivity disorder (ADHD) and underwent a standard regimen of a psychostimulant medication. After treatment with psychostimulants, the 3 patients reported improved symptoms of fatigue and pain, and cognitive and core ADHD symptoms. These cases suggest that ADHD and chronic fatigue syndrome (and possibly fibromyalgia) share a common underlying mechanism. This article presents a model suggesting that over time, ADHD (predominantly

				inattentive type) develops into a syndrome of chronic fatigue and pain. These cases indicate that fatigue may be an important presenting symptom of adult ADHD. These cases also suggest the need for additional research to determine the prevalence of ADHD in patients who present with fatigue, and, in those meeting criteria for ADHD, the responsiveness of fatigue to psychostimulant treatment.
Young JL.	Wayne State University School of Medicine, Detroit, MI, USA. jyoung@rcbm.net	Use of lisdexamfetamine dimesylate in treatment of executive functioning deficits and chronic fatigue syndrome: a double blind, placebo-controlled study.	Psychiatry Res. 2013 May 15; 207(1-2):127-33. doi: 10.1016/j.psychres.2012.09.007. Epub 2012 Oct 9.	The purpose of this study was to assess the efficacy of lisdexamfetamine dimesylate (LDX) for the treatment of executive functioning deficits in adults (ages 18-60) with chronic fatigue syndrome (CFS). The study's primary outcome measure was the Behavior Rating Inventory of Executive Function-Adult (BRIEF-A). Secondary outcome measures were standardized assessments of fatigue, pain and global functioning. Twenty-six adults who met criteria for CFS and had clinically significant executive functioning deficits were randomly assigned to a flexible morning dose (30, 50, 70 mg/day) of either placebo or LDX for a 6-week trial. The data were analyzed with standard analysis of variance (ANOVA) procedures. Participants in the LDX group showed significantly more positive change in BRIEF-A scores (Mchange=21.38, SD=15.85) than those in the placebo group (Mchange=3.36, SD=7.26). Participants in the active group also reported significantly less fatigue and generalized pain relative to the placebo group. Although future studies with LDX should examine whether these benefits generalize to larger, more diverse samples of patients, these results suggest that LDX could be a safe and efficacious treatment for the executive functioning deficits often associated with CFS. The possibility that dopaminergic medications could play an important role addressing the symptoms of CFS is also discussed.
Zhang L, Xu MM, Zeng L, Liu S, Liu X, Wang X, Li D, Huang RZ, Zhao LB, Zhan QL, Zhu D, Zhang YY, Xu P, Xie P.	Department of Neurology, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuzhong District, 400016, Chongqing, People's Republic of China.	Evidence for Borna disease virus infection in neuropsychiatric patients in three western China provinces.	Eur J Clin Microbiol Infect Dis. 2013 Oct 30. [Epub ahead of print]	Borna disease virus (BDV) is a non-cytolytic, neurotropic RNA virus that can infect a wide variety of vertebrate species from birds and primates to humans. Several studies have been carried out to investigate whether BDV is associated with neuropsychiatric diseases. However, this association is still inconclusive. Two panels of subjects consisting of 1,679 various neuropsychiatric patients and healthy people from three western China provinces were enrolled in this study. BDV p24 or p40 RNA in peripheral blood mononuclear cells (PBMCs) were detected in the first panel of 1,481 subjects using reverse transcription quantitative polymerase chain reaction (RT-qPCR) and cerebrospinal fluid (CSF) samples from the BDV RNA-positive individuals were subjected to BDV p24 antibodies testing by enzyme-linked immunosorbent assay (ELISA). BDV p24 or p40 RNA in PBMCs and p24 antibodies in plasma were detected in the second panel of 198 subjects by RT-qPCR and Western blot. A higher prevalence for BDV RNA was demonstrated in patients with viral encephalitis (6.70 %), Guillain-Barré syndrome (6.70 %), schizophrenia (9.90 %) and chronic fatigue syndrome (CFS) (12.70 %) compared to healthy controls

				in the first panel. CSF p24 antibodies were demonstrated in three viral encephalitis patients, two schizophrenia patients and two major depressive disorder (MDD) patients. The prevalences of p24 antibodies in plasma from patients with viral encephalitis (13.24 %), multiple sclerosis (25.00 %) and Parkinson's disease (22.73 %) were significantly higher than healthy controls. This study demonstrates that BDV infection also exists in humans from three western China provinces, and suggests the involvement of the contribution of BDV in the aetiology of Chinese patients with some neuropsychiatric disorders, including viral encephalitis, schizophrenia, CFS, multiple sclerosis and Parkinson's disease.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No authors listed]	[No address quoted]	Information from your family doctor. Chronic fatigue syndrome.	Am Fam Physician. 2012 Oct 15;86(8):1-1.	[No abstract given]
Abbi B, Natelson BH.	MD, Pain and Fatigue Study Center, Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, 120 East 16th Street, 12th Floor, New York, NY 10003, USA. bnatelson@chpnet.org.	Is chronic fatigue syndrome the same illness as fibromyalgia: evaluating the 'single syndrome' hypothesis.	QJM. 2013 Jan;106(1):3-9. doi: 10.1093/qjmed/hcs156. Epub 2012	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained syndromes that can and often do co-occur. For this reason, some have posited that the two are part of the same somatic syndrome-examples of symptom amplification. This hypothesis would suggest that few differences exist between the two syndromes. To evaluate this interpretation, we have searched the literature for articles comparing CFS to FM, reviewing only those articles which report differences between the two. This review presents data showing differences across a number of parameters-implying that the underlying pathophysiology in CFS may differ from that of FM. We hope that our review encourages other groups to look for additional differences between CFS and FM. By continuing to preserve the unique illness definitions of the two syndromes, clinicians will be able to better identify, understand and provide treatment for these individuals.
Ablin JN, Buskila D, Van Houdenhove B, Luyten P, Atzeni F, Sarzi-Puttini P.	Institute of Rheumatology and Internal Medicine F, Tel Aviv Sourasky Medical Center, Israel.	Is fibromyalgia a discrete entity?	Autoimmun Rev. 2012 Jun;11(8):585-8. doi: 10.1016/j.autrev.2011.10.018.	Fibromyalgia (FM) is defined as chronic widespread pain (CWP) with allodynia or hyperalgesia to pressure pain, and is classified as one of the largest group of soft tissue pain syndromes. Its pathogenesis is not entirely understood, although it is currently believed to be the result of a central nervous system (CNS) malfunction that increases pain transmission and perception. There are no instrumental tests to confirm the diagnosis, but many of the differential diagnoses can be excluded by means of an extensive clinical examination and patient history. Although fibromyalgia is a recognisable clinical entity, it would seem appropriate to consider the entire range of tenderness and distress in clinic patients in order to tailor treatment on an individual basis.
Agliari E, Barra A, Vidal KG, Guerra F.	Dipartimento di Fisica, Università degli Studi di Parma, viale G.P. Usberti 7/A, 43100, Parma, Italy. elena.agliari@fis.unipr.it	Can persistent Epstein-Barr virus infection induce chronic fatigue syndrome as a Pavlov reflex of the immune response?	J Biol Dyn. 2012;6(2):740-62. doi: 10.1080/17513758.2012.704083.	Chronic fatigue syndrome is a protracted illness condition (lasting even years) appearing with strong flu symptoms and systemic defiances by the immune system. Here, by means of statistical mechanics techniques, we study the most widely accepted picture for its genesis, namely a persistent acute mononucleosis infection, and we show how such infection may drive the immune system towards an out-of-equilibrium metastable state displaying chronic activation of both humoral and cellular responses (a state of full inflammation without a direct 'causes-effect' reason). By exploiting a bridge with a neural scenario, we mirror killer lymphocytes T(K) and B cells to neurons and helper lymphocytes [Formula: see text] and [Formula: see text] to synapses, hence showing that the immune system may experience the Pavlov conditional reflex phenomenon: if the exposition to a stimulus (Epstein-Barr virus antigens) lasts for too long, strong internal correlations among B,T(K) and T(H)

				may develop ultimately resulting in a persistent activation even though the stimulus itself is removed. These outcomes are corroborated by several experimental findings.
Alberts B.	[No address quoted]	Retraction.	Science. 2011 Dec 23;334(6063):1636. doi: 10.1126/science.334.6063.1636-a.	Retraction of Lombardi VC, Ruscetti FW, Das Gupta J, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA. Science. 2009 Oct 23;326(5952):585-9. Science is fully retracting the report "Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome" (V. C. Lombardi et al., Science 326, 585 (2009); 10.1126/science.1179052)
Allen J, Murray A, Di Maria C, Newton JL.	Microvascular Diagnostics, Regional Medical Physics Department, Freeman Hospital, Newcastle upon Tyne NE7 7DN, UK.	Chronic fatigue syndrome and impaired peripheral pulse characteristics on orthostasis--a new potential diagnostic biomarker.	Physiol Meas. 2012 Feb;33(2):231-41. doi: 10.1088/0967-3334/33/2/231.	Autonomic nervous system dysfunction is frequently reported in chronic fatigue syndrome (CFS) with orthostatic intolerance, a common symptom that can be objectively assessed. The frequent finding of autonomic dysfunction and symptoms on standing has the potential to provide a diagnostic biomarker in chronic fatigue. In this study we explored the clinical value of non-invasive optical multi-site photoplethysmography (PPG) technology to assess cardiovascular responses to standing. Multi-site PPG pulses were collected from tissue pads of the ears, fingers and toes of 14 patients with CFS and 14 age-matched sedentary subjects using a measurement protocol of a 10 min baseline (subject supine) followed by 3 min of tilting on a tilt table (head-up to 70°). Percentage change in pulse timing (pulse transit time, PTTf) and pulse amplitude (AMP) at each site were calculated using beat-to-beat pulse wave analysis. A significant reduction in the overall pulse timing response to controlled standing was found for the CFS group (using summed absolute percentage change in PTTf for ear, finger and toe sites, median change of 26% for CFS and 37% for control with $p = 0.002$). There were no significant differences between subject groups for the AMP measure at any site. Changes in AMP with tilt were, however, weakly significantly and negatively correlated with fatigue severity ($p < 0.05$). Receiver operating characteristic (ROC) analysis of timing measures produced an area under the curve of 0.81. Experimental linear discriminant classification analysis comparing both timing and amplitude measures produced an overall diagnostic accuracy of 82%. Pulse wave abnormalities have been observed in CFS and represent a potential objective measure to help differentiate between CFS patients and healthy controls.
Alter HJ, Mikovits JA, Switzer WM, Ruscetti FW, Lo SC, Klimas N, Komaroff AL, Montoya JG, Bateman L, Levine S, Peterson D, Levin B, Hanson	Department of Transfusion Medicine, Warren G. Magnuson Clinical Center, National Institutes of Health, Bethesda, Maryland, USA.	A multicenter blinded analysis indicates no association between chronic fatigue syndrome/myalgic encephalomyelitis and either xenotropic murine	MBio. 2012 Sep 18;3(5). pii: e00266-12. doi: 10.1128/mBio.00266-12. Print 2012.	The disabling disorder known as chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) has been linked in two independent studies to infection with xenotropic murine leukemia virus-related virus (XMRV) and polytropic murine leukemia virus (pMLV). Although the associations were not confirmed in subsequent studies by other investigators, patients continue to question the consensus of the scientific community in rejecting the validity of the association. Here we report blinded analysis of peripheral blood from a rigorously characterized, geographically diverse population of 147 patients with CFS/ME and 146 healthy subjects by the investigators describing the original association. This analysis reveals no evidence of

MR, Genfi A, Bhat M, Zheng H, Wang R, Li B, Hung GC, Lee LL, Sameroff S, Heneine W, Coffin J, Hornig M, Lipkin WI.		leukemia virus-related virus or polytropic murine leukemia virus.		either XMRV or pMLV infection. IMPORTANCE Chronic fatigue syndrome/myalgic encephalomyelitis has an estimated prevalence of 42/10,000 in the United States, with annual direct medical costs of $7 billion. Here, the original investigators who found XMRV and pMLV (polytropic murine leukemia virus) in blood of subjects with this disorder report that this association is not confirmed in a blinded analysis of samples from rigorously characterized subjects. The increasing frequency with which molecular methods are used for pathogen discovery poses new challenges to public health and support of science. It is imperative that strategies be developed to rapidly and coherently address discoveries so that they can be carried forward for translation to clinical medicine or abandoned to focus resource investment more productively. Our study provides a paradigm for pathogen dediscovery that may be helpful to others working in this field.
Alves ED, Ackel-D'Elia C, Luz GP, Cunha TC, Carneiro G, Tufik S, Bittencourt LR, de Mello MT.	Disciplina de Medicina e Biologia do Sono, Departamento de Psicobiologia, Universidade Federal de São Paulo-UNIFESP, São Paulo, CEP: 04020-050, Brazil.	Does physical exercise reduce excessive daytime sleepiness by improving inflammatory profiles in obstructive sleep apnea patients?	Sleep Breath. 2012 Jun 20.	INTRODUCTION: Obstructive sleep apnea syndrome (OSAS) is associated with a variety of long-term consequences such as high rates of morbidity and mortality, due to excessive diurnal somnolence as well as cardiovascular and metabolic diseases. Obesity, recurrent episodes of upper airway obstruction, progressive hypoxemia, and sleep fragmentation during sleep cause neural, cardiovascular, and metabolic changes. These changes include activation of peripheral sympathetic nervous system and the hypothalamic-pituitary-adrenal axis, insulin sensitivity, and inflammatory cytokines alterations, which predispose an individual to vascular damage. DISCUSSION: Previous studies proposed that OSAS modulated the expression and secretion of inflammatory cytokines from fat and other tissues. Independent of obesity, patients with OSAS exhibited elevated levels of C-reactive protein, tumor necrosis factor-α and interleukin-6, which are associated with sleepiness, fatigue, and the development of a variety of metabolic and cardiovascular diseases. OSAS and obesity are strongly associated with each other and share many common pathways that induce chronic inflammation. Previous studies suggested that the protective effect of exercise may be partially attributed to the anti-inflammatory effect of regular exercise, and this effect was observed in obese patients. Although some studies assessed the effects of physical exercise on objective and subjective sleep parameters, the quality of life, and mood in patients with OSAS, no study has evaluated the effects of this treatment on inflammatory profiles. In this review, we cited some studies that directed our opinion to believe that since OSAS causes increased inflammation and has excessive daytime sleepiness as a symptom and being that physical exercise improves inflammatory profiles and possibly OSAS symptoms, it must be that physical exercise improves excessive daytime sleepiness due to its improvement in inflammatory profiles.
Anderson G, Maes M, Berk M.	CRC, Rm 30, 57 Laurel St., Glasgow, G11 7QT Scotland, United	Biological underpinnings of the commonalities in	Med Hypotheses. 2012 Jun;78(6):752-6. doi: 10.1016/j.mehy.2012.02.023.	BACKGROUND: Somatization is a multisomatoform disorder characterized by medically unexplained, functional or psychosomatic symptoms. Similar somatic symptoms are key components of depression and Myalgic Encephalomyelitis/Chronic

	Kingdom. anderson.george@rocketmail.com	depression, somatization, and Chronic Fatigue Syndrome.		Fatigue Syndrome (ME/CFS). METHODS: This paper reviews the evidence that such symptoms are organically based. We use the term "physio-somatic" to describe these symptoms. RESULTS: Inflammation, cell-mediated immune (CMI) activation and alterations in the tryptophan catabolite (TRYCAT) pathway are associated with the physio-somatic symptoms of depression, ME/CFS and/or somatization. Proinflammatory cytokines, decreased tryptophan and aberrations in TRYCATs may cause physio-somatic symptoms, such as fatigue, autonomic symptoms, hyperalgesia and somatic presentations. CONCLUSIONS: The data suggest co-ordinated and interacting biological pathways driving the occurrence of physio-somatic symptoms across these three disorders, giving a biologically validated "pathway phenotype". These data have far-reaching implications for DSM-IV diagnostic conceptualizations of somatization (and ME/CFS) suggesting the presence of an emerging organic explanation. Future research should focus on the role of immune regulation, and co-ordination, of neuronal activity and, through larger data sets, ultimately creating new, biologically validated classification rules. These data have implications for the development of novel therapies utilizing these insights, buttressing the role of psychotherapy in psychosomatic presentations.
Anderson VR, Jason LA, Hlavaty LE, Porter N, Cudia J.	Department of Psychology, Michigan State University, East Lansing, MI 48824, USA. ande1538@msu.edu	A review and meta-synthesis of qualitative studies on myalgic encephalomyelitis/chronic fatigue syndrome.	Patient Educ Couns. 2012 Feb;86(2):147-55. doi: 10.1016/j.pec.2011.04.016.	OBJECTIVE: To review and synthesize findings across qualitative studies on Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS). METHODS: Articles were systematically reviewed and analyzed within a meta-analytic framework. Analyses included a multi-perspective examination of ME/CFS, as well as a comparative analysis of ME/CFS versus other chronic conditions. RESULTS: Thirty-four qualitative studies on ME/CFS were included. Findings include three substantive thematic areas that focus on: (1) experiences of people with ME/CFS, (2) experiences of physicians, and (3) themes that intersect both of these groups. For patients, illness development influenced identity, reductions in functioning, and coping. Physician-specific themes described lack of awareness about ME/CFS and recommended improvement in educational resources. Intersecting themes expressed issues with diagnosis creating tensions and fueling the stigmatization of ME/CFS. CONCLUSIONS: Findings indicate multilayered, context-specific experiences and ways in which both people with ME/CFS, as well as those involved in their lives (e.g., family or the medical community), interpret this illness. Future qualitative studies should recognize the various facets of the ME/CFS experience, the network members of people with ME/CFS, and the sociocultural environment through which the illness is understood. PRACTICE IMPLICATIONS: Health care professionals can gain unique insight from patient experiences, allowing for more accurate diagnoses and treatment recommendations.
Andersson G.	Department of Behavioural Sciences and Learning,	Internet-based CBT improves fatigue severity, physical	Evid Based Ment Health. 2012 Aug;15(3):81. doi: 10.1136/ebmental-2012-	Comment on Lancet. 2012 Apr 14;379(9824):1412-8.

	Linköping University, Karolinska Institute, Sweden.	function and school attendance in adolescents with chronic fatigue syndrome.	100818.	
Angeletti C, Guetti C, Piroli A, Angeletti PM, Paladini A, Ciccozzi A, Marinangeli F, Varrassi G.	Anesthesiology and Pain Medicine, Department of Health Sciences, University of L'Aquila, Italy.	Duloxetine and Pregabalin for Pain Management in Multiple Rheumatic Diseases Associated with Fibromyalgia.	Pain Pract. 2012 Nov 5. doi: 10.1111/papr.12009.	The fibromyalgia syndrome (FMS) is characterized by chronic and widespread musculoskeletal pain and soreness accompanied by sleep disorders, chronic fatigue and affective disorders. FMS is often associated with other forms of immuno-rheumatic diseases. Although FMS pathophysiology is still not fully understood, a number of neuroendocrine, neurotransmission and neurosensitive disorders might generate a mechanism for the elicitation of pain by "central sensitization," which is common to many other painful conditions. The present case describes the success of a therapeutic scheme, which associates two different pharmacological classes, anticonvulsants and new-generation antidepressants, when FMS complicates a rare pathology called Cogan's syndrome. The association of two drugs might noticeably affect the molecular mechanisms of difficult pain, thus solving painful conditions of multifactorial origin.
Aparicio VA, Carbonell-Baeza A, Ortega FB, Estevez F, Ruiz JR, Delgado-Fernández M.	Department of Physical Education and Sport, School of Sports Sciences, University of Granada, Spain. virginiaparicio@ugr.es	Usefulness of tenderness to characterise fibromyalgia severity in women.	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S28-33.	OBJECTIVES: To investigate the usefulness of tenderness (tender points count (TPC) and algometer score) to characterise fibromyalgia (FM) severity and symptomatology in women. METHODS: The study sample comprised 174 women aged 51±7 years. We ossesse tenderness using pressure algometry; quality of life by means of the Short-Form 36 Health Survey (SF-36) and the Hospital Anxiety and Depression Scale (HADS). We used the FM impact questionnaire (FIQ) to assess FM severity and symptomatology. Patients were categorised according to three FIQ-derived categories: FIQ<70 vs. ≥70; FIQ<59 vs. ≥59; and FM-type I and II. RESULTS: TPC was significantly higher in the group of patients with FIQ≥59 (16.9±2 vs. 15.6±4, p=0.02), whereas no differences between groups were observed according to FIQ≥70 (17.0±2 vs. 16.2±3, p=0.12) or FM type (16.8±3 for type II vs. 15.9±4 for type I, p=0.13). We observed a significant association between TPC and FIQ-job difficulty, pain, morning tiredness and stiffness dimensions (all p<0.05), yet it was not correlated with total score of FIQ, FIQ-anxiety, fatigue and depression dimensions (all p>0.05). Algometer score was lower in the FIQ≥70 (45.7±12 vs. 51.1±14, p=0.05) and FIQ≥59 (46.7±13 vs. 52.7±14, p=0.05) groups, and there were no difference between FM types (48.7±13 vs. 49.5±14 for type II and I respectively, p=0.81). Algometer score was not associated with total score of FIQ or FIQ dimensions (all p≥0.1). CONCLUSIONS: Widespread pain and pain hypersensitivity, as measured by TPC and algometer score, do not seem to be useful to characterise FM severity and symptomatology (measured by FIQ) in women.
Armstrong CW, McGregor NR,	Department of Biochemistry and	NMR metabolic profiling of serum	Clin Chim Acta. 2012 Oct 9;413(19-20):1525-31. doi:	Chronic fatigue syndrome (CFS) is a debilitating multisystem disorder characterised by long-term fatigue with a variety of other symptoms including cognitive dysfunction,

Sheedy JR, Buttfield I, Butt HL, Gooley PR.	Molecular Biology, University of Melbourne, Parkville, Victoria 3010, Australia.	identifies amino acid disturbances in chronic fatigue syndrome.	10.1016/j.cca.2012.06.022.	unrefreshing sleep, muscle pain, and post-exertional malaise. It is a poorly understood condition that occurs in ~5 in every 1000 individuals. We present here a preliminary study on the analysis of blood samples from 11 CFS and 10 control subjects through NMR metabolic profiling. Identified metabolites that were found to be significantly altered between the groups were subjected to correlation analysis to potentially elucidate disturbed metabolic pathways. Our results showed a significant reduction of glutamine ($P=0.002$) and ornithine ($P<0.05$) in the blood of the CFS samples. Correlation analysis of glutamine and ornithine with other metabolites in the CFS sera showed relationships with glucogenic amino acids and metabolites that participate in the urea cycle. This indicates a possible disturbance to amino acid and nitrogen metabolism. It would be beneficial to identify any potential biomarkers of CFS for accurate diagnosis of the disorder.
Arnett SV, Clark IA.	Research School of Biology, Australian National University, Australia. simon.arnett@anu.edu.au	Inflammatory fatigue and sickness behaviour - lessons for the diagnosis and management of chronic fatigue syndrome.	J Affect Disord. 2012 Dec 10;141(2-3):130-42. doi: 10.1016/j.jad.2012.04.004.	Persistent and severe fatigue is a common part of the presentation of a diverse range of disease processes. There is a growing body of evidence indicating a common inflammatory pathophysiology underlying many conditions where fatigue is a primary patient concern, including chronic fatigue syndrome. This review explores current models of how inflammatory mediators act on the central nervous system to produce fatigue and sickness behaviour, and the commonality of these processes in conditions as diverse as surgical trauma, infection, various cancers, inflammatory bowel disease, connective tissue diseases and autoimmune diseases. We also discuss evidence indicating chronic fatigue syndrome may have important pathophysiological similarities with cytokine mediated sickness behaviour, and what lessons can be applied from sickness behaviour to chronic fatigue syndrome with regards to the diagnosis and management.
Arredondo M, de Bethencourt F, Treviño A, Collado A, Torres P, Barbolla L, Soriano V, de Mendoza C.	Infectious Diseases Department, Hospital Carlos III, Madrid, Spain.	Short communication: RNASEL alleles and susceptibility to infection by human retroviruses and hepatitis viruses.	AIDS Res Hum Retroviruses. 2012 Oct;28(10):1259-61.	RNASEL seems to function as an intracellular restriction factor blocking the establishment of infections caused by viral agents. Herein, we investigated whether allelic variants at the RNASEL gene might influence the susceptibility to viral infections or conditions potentially linked to viral agents. The allelic distribution at codon 462 was 139 (33.9%), 204 (49.8%), and 67 (16.3%) for RR, RQ, and QQ, respectively, in 410 individuals in Spain. There were no significant differences comparing 105 blood donors and 71 patients with HIV-1 infection, 27 with chronic hepatitis C, 67 with prostate cancer, and 107 with chronic fatigue syndrome. In contrast, two-thirds of 18 patients with HTLV-1 infection and 15 with chronic hepatitis B harbored RR. Thus, polymorphisms at the RNASEL gene do not seem to influence the susceptibility to common viral infections or conditions potentially of viral etiology. The role in influencing the susceptibility to HTLV-1 or HBV chronic infection warrants further examination in larger patient populations.
Arredondo M, Hackett J Jr, de Bethencourt FR,	Infectious Diseases Department, Hospital Carlos III, Madrid,	Prevalence of xenotropic murine leukemia virus-	AIDS Res Hum Retroviruses. 2012 Sep;28(9):1089-94. doi: 10.1089/AID.2011.0149.	Human infection with the xenotropic murine leukemia virus-related virus (XMRV) has been associated controversially with prostate cancer and chronic fatigue syndrome. Information is lacking about the mechanisms of transmission and potential risk groups

Treviño A, Escudero D, Collado A, Qiu X, Swanson P, Soriano V, de Mendoza C.	Spain.	related virus infection in different risk populations in Spain.		for XMRV infection. Plasma and peripheral blood mononuclear cells (PBMCs) from individuals with retroviral infections, chronic viral hepatitis, autoimmune diseases, prostate cancer, chronic fatigue syndrome, and blood donors were tested for XMRV markers. Antibodies to XMRV proteins p15E and gp70 were examined using research assays. DNA extracted from PBMCs was tested for the presence of XMRV gag and env sequences. A total of 1103 specimens belonging to individuals with chronic fatigue syndrome and/or fibromyalgia (437), prostate cancer (69), HIV-1 (149), HTLV-1/2 (31), chronic hepatitis B (81), chronic hepatitis C (72), autoimmune diseases (18), and blood donors (246) were examined. Overall, three samples (0.3%) were p15E seroreactive (two HTLV-1 and one HCV patient). Another 15 (1.4%) were gp70 seroreactive (six chronic fatigue syndrome-fibromyalgia, four blood donors, two HIV-1, one prostate cancer, one HBV, and one HCV). Four specimens were initially positive for XMRV gag sequences, but none could be confirmed by repeated testing. In summary, no evidence of XMRV infection was found in populations with retroviral and viral hepatitis infections in Spain. Likewise, XMRV was not recognized in patients with autoimmune diseases, chronic fatigue syndrome-fibromyalgia, prostate cancer, or healthy blood donors.
Arroll MA, Howard A	The Optimum Health Clinic , London , UK.	'The letting go, the building up, (and) the gradual process of rebuilding': Identity change and post-traumatic growth in myalgic encephalomyelitis/chronic fatigue syndrome.	Psychol Health. 2012 Sep 11	The aim of this study was to explore the phenomenon of identity change and subsequent post-traumatic growth (PTG) in individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Ten participants (average illness duration 7.4 years) were interviewed (average length, 79 minutes) via a semi-structured interview schedule and verbatim transcriptions were analysed with interpretative phenomenological analysis. The four superordinate themes revealed were 'comparisons of past to present self: "you have to be someone else, and you have to live with that"', 'the effect of social isolation on identity and subsequent insights into others' behaviours', 'contemplation of future and identity: ''where do I go from here?"', and 'PTG: "the letting go, the building up, [and] the gradual process of rebuilding"'. These themes outlined the experiences of those with ME/CFS as they underwent changes in identity due to the limitations the condition imposed on activities and roles, understanding others' behaviours after a period of isolation, the comparison of the past self with the present self and finally, the positive growth that was noted by two of the interviewees with regards to a new 'true' self. Despite the distressing and unpredictable nature of ME/CFS, it appears that individuals with this disorder can experience personal growth.
Arroll MA, Howard A.	Department of Research, The Optimum Health Clinic, London, UK.	A preliminary prospective study of nutritional, psychological and combined therapies for myalgic	BMJ Open. 2012 Nov 19;2(6). pii: e001079. doi: 10.1136/bmjopen-2012-001079. Print 2012.	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a condition characterised by severe and persistent fatigue, neurological disturbances, autonomic and endocrine dysfunctions and sleep difficulties that have a pronounced and significant impact on individuals' lives. Current National Institute for Health and Clinical Excellence guidelines within the UK suggest that this condition should be treated with cognitive behavioural therapy and/or graded exercise therapy, where

		encephalomyelitis/chronic fatigue syndrome (ME/CFS) in a private care setting.		appropriate. There is currently a lack of an evidence base concerning alternative techniques that may be beneficial to those with ME/CFS. OBJECTIVES: This study aimed to investigate whether three modalities of psychology, nutrition and combined treatment influenced symptom report measures in those with ME/CFS over a 3-month time period and whether there were significant differences in these changes between groups. DESIGN AND SETTING: This is a preliminary prospective study with one follow-up point conducted at a private secondary healthcare facility in London, UK. PARTICIPANTS: 138 individuals (110 females, 79.7%; 42 participants in psychology, 44 in nutrition and 52 in combined) participated at baseline and 72 participants completed the battery of measures at follow-up (52.17% response rate; 14, 27 and 31 participants in each group, respectively). OUTCOME MEASURES: Self-reported measures of ME/CFS symptoms, functional ability, multidimensional fatigue and perceived control. RESULTS: Baseline comparisons showed those in the combined group had higher levels of fatigue. At follow-up, all groups saw improvements in fatigue, functional ability and symptomatology; those within the psychology group also experienced a shift in perceived control over time. CONCLUSIONS: This study provides early evidence that psychological, nutritional and combined techniques for the treatment of ME/CFS may influence symptomatology, fatigue, function and perceived control. However, these results must be viewed with caution as the allocation to groups was not randomised, there was no control group and the study suffered from high drop-out rates.
Aschbacher K, Adam EK, Crofford LJ, Kemeny ME, Demitrack MA, Ben-Zvi A.	Department of Psychiatry, University of California, San Francisco, CA, United States. kirstin.aschbacher@ucsf.edu	Linking disease symptoms and subtypes with personalized systems-based phenotypes: a proof of concept study.	Brain Behav Immun. 2012 Oct;26(7):1047-56. doi: 10.1016/j.bbi.2012.06.002. Comment in Brain Behav Immun. 2012 Oct;26(7):1045-6.	A dynamic systems model was used to generate parameters describing a phenotype of Hypothalamic-Pituitary-Adrenal (HPA) behavior in a sample of 36 patients with chronic fatigue syndrome (CFS) and/or fibromyalgia (FM) and 36 case-matched healthy controls. Altered neuroendocrine function, particularly in relation to somatic symptoms and poor sleep quality, may contribute to the pathophysiology of these disorders. Blood plasma was assayed for cortisol and ACTH every 10 min for 24h. The dynamic model was specified with an ordinary differential equation using three parameters: (1) ACTH-adrenal signaling, (2) inhibitory feedback, and (3) non-ACTH influences. The model was "personalized" by estimating an individualized set of parameters from each participant's data. Day and nighttime parameters were assessed separately. Two nocturnal parameters (ACTH-adrenal signaling and inhibitory feedback) significantly differentiated the two patient subgroups ("fatigue-predominant" patients with CFS only versus "pain-predominant" patients with FM and comorbid chronic fatigue) from controls (all p's<.05), whereas daytime parameters and diurnal/nocturnal slopes did not. The same nocturnal parameters were significantly associated with somatic symptoms among patients (p's<.05). There was a significantly different pattern of association between nocturnal non-ACTH influences and sleep quality among patients versus controls (p<.05). Although speculative, the finding that patient somatic symptoms decreased when more cortisol

				was produced per unit ACTH, is consistent with cortisol's anti-inflammatory and sleep-modulatory effects. Patients' HPA systems may compensate by promoting more rapid or sustained cortisol production. Mapping "behavioral phenotypes" of stress-arousal systems onto symptom clusters may help disentangle the pathophysiology of complex disorders with frequent comorbidity.
Aslakson E, Szekely S, Vernon SD, Bateman L, Baumbach J, Setty Y.	Department of Computer Science and Applied Mathematics, Weizmann Institute of Science, Rehovot, 76100, Israel. yaki.setty@gmail.com.	Live sequence charts to model medical information.	Theor Biol Med Model. 2012 Jun 15;9:22. doi: 10.1186/1742-4682-9-22.	ABSTRACT:BACKGROUND: Medical records accumulate data concerning patient health and the natural history of disease progression. However, methods to mine information systematically in a form other than an electronic health record are not yet available. The purpose of this study was to develop an object modeling technique as a first step towards a formal database of medical records. METHOD: Live Sequence Charts (LSC) were used to formalize the narrative text obtained during a patient interview. LSCs utilize a visual scenario-based programming language to build object models. LSC extends the classical language of UML message sequence charts (MSC), predominantly through addition of modalities and providing executable semantics. Inter-object scenarios were defined to specify natural history event interactions and different scenarios in the narrative text. RESULT: A simulated medical record was specified into LSC formalism by translating the text into an object model that comprised a set of entities and events. The entities described the participating components (i.e., doctor, patient and record) and the events described the interactions between elements. A conceptual model is presented to illustrate the approach. An object model was generated from data extracted from an actual new patient interview, where the individual was eventually diagnosed as suffering from Chronic Fatigue Syndrome (CFS). This yielded a preliminary formal designated vocabulary for CFS development that provided a basis for future formalism of these records. CONCLUSIONS: Translation of medical records into object models created the basis for a formal database of the patient narrative that temporally depicts the events preceding disease, the diagnosis and treatment approach. The LSCs object model of the medical narrative provided an intuitive, visual representation of the natural history of the patient's disease.
Atzeni F, Sallì S, Benucci M, Di Franco M, Alciati A, Sarzi-Puttini P.	sarzi@tiscalinet.it	Fibromyalgia and arthritides.	Reumatismo. 2012 Sep 28;64(4):286-92. doi: 10.4081/reumatismo.2012.286.	Fibromyalgia (FM) is a chronic pain syndrome that affects at least 2% of the adult population. It is characterised by widespread pain, fatigue, sleep alterations and distress, and emerging evidence suggests a central nervous system (CNS) malfunction that increases pain transmission and perception. FM is often associated with other diseases that act as confounding and aggravating factors, such as rheumatoid arthritis (RA), spondyloarthritides (SpA), osteoarthritis (OA) and thyroid disease. Mechanism-based FM management should consider both peripheral and central pain, including effects due to cerebral input and that come from the descending inhibitory pathways. Rheumatologists should be able to distinguish primary and secondary FM, and need new guidelines and instruments to avoid making mistakes, bearing in mind that the diffuse pain of arthritides compromises the patients' quality of life.

Bäckström T, Bixo M, Nyberg S, Savic I.	Umeå Neurosteroid Research Centre, Department of Clinical Science, Umeå University, SE-901 85 Umeå, Sweden. Electronic address: torbjorn.backstrom@ogbyn.umu.se.	Increased neurosteroid sensitivity - An explanation to symptoms associated with chronic work related stress in women?	Psychoneuroendocrinology. 2012 Nov 21. pii: S0306-4530(12)00349-6. doi: 10.1016/j.psyneuen.2012.10.014.	Work related psychosocial stress can be accompanied by so called burnout syndrome with symptoms of mental exhaustion, physical fatigue, and cognitive dysfunction. Underlying mechanisms for acquiring burnout syndrome are not clear. Animal studies show that chronic stress is associated with altered release of GABA-A receptor modulating steroids (GAMS), altered composition of the GABA-A receptor and altered sensitivity to GAMS. In the present study we investigated if such changes occur in women with burnout syndrome. We further asked whether flumazenil (a benzodiazepine antagonist, but with positive modulating effects on GABA-A receptors with altered subunit composition) can block the effect of the GAMS allopregnanolone. Ten women with occupational psychosocial stress and burnout syndrome were compared with twelve healthy controls in an experimental setting. Saccadic eye velocity (SEV) was measured after an injection of allopregnanolone, followed by an injection of flumazenil and a second injection of allopregnanolone. The sensitivity to allopregnanolone was significantly higher in the patients compared to controls after the first injection (p=0.04) and the difference increased when the response per allopregnanolone concentration unit was compared (p=0.006). Following the flumazenil injection the burnout patients (p=0.016), but not controls, showed a decrease in SEV and flumazenil acted like a positive modulator that is agonistic. There was no significant difference between the groups after second allopregnanolone injection. In conclusion, patients with work related psychosocial stress and burnout syndrome show a different response to GABA-A receptor modulators than controls suggesting a changed GABA-A receptor function in these patients. More precisely we hypothesize that the α4 and delta subunits are up-regulated elevating the responsiveness to allopregnanolone and change the effect of flumazenil, which provides a potential explanation to the burnout syndrome. Flumazenil does not block the effect of allopregnanolone.
Bansal AS, Bradley AS, Bishop KN, Kiani-Alikhan S, Ford B.	Dept. of Immunology, Epsom and St. Helier University Hospitals NHS Trust, Carshalton, Surrey, SM5 1AA and Chronic Illness Research Team, Stratford Campus, University of East London, London E15 4LZ, UK. Amolak.Bansal@ESTH.nhs.uk	Chronic fatigue syndrome, the immune system and viral infection.	Brain Behav Immun. 2012 Jan;26(1):24-31. doi: 10.1016/j.bbi.2011.06.016.	The chronic fatigue syndrome (CFS), as defined by recent criteria, is a heterogeneous disorder with a common set of symptoms that often either follows a viral infection or a period of stress. Despite many years of intense investigation there is little consensus on the presence, nature and degree of immune dysfunction in this condition. However, slightly increased parameters of inflammation and pro-inflammatory cytokines such as interleukin (IL) 1, IL6 and tumour necrosis factor (TNF) α are likely present. Additionally, impaired natural killer cell function appears evident. Alterations in T cell numbers have been described by some and not others. While the prevalence of positive serology for the common herpes viruses appears no different from healthy controls, there is some evidence of viral persistence and inadequate containment of viral replication. The ability of certain herpes viruses to impair the development of T cell memory may explain this viral persistence and the continuation of symptoms. New therapies based on this understanding are more likely to produce benefit than current methods.

Barnden LR, Crouch B, Kwiatek R, Burnet R, Mernone A, Chryssidis S, Scroop G, Del Fante P.	Department of Nuclear Medicine, The Queen Elizabeth Hospital, Adelaide, South Australia. Leighton.Barnden@health.sa.gov.au	A brain MRI study of chronic fatigue syndrome: evidence of brainstem dysfunction and altered homeostasis.	NMR Biomed. 2011 Dec;24(10):1302-12. doi: 10.1002/nbm.1692.	To explore brain involvement in chronic fatigue syndrome (CFS), the statistical parametric mapping of brain MR images has been extended to voxel-based regressions against clinical scores. Using SPM5 we performed voxel-based morphometry (VBM) and analysed T(1) - and T(2) -weighted spin-echo MR signal levels in 25 CFS subjects and 25 normal controls (NC). Clinical scores included CFS fatigue duration, a score based on the 10 most common CFS symptoms, the Bell score, the hospital anxiety and depression scale (HADS) anxiety and depression, and hemodynamic parameters from 24-h blood pressure monitoring. We also performed group × hemodynamic score interaction regressions to detect locations where MR regressions were opposite for CFS and NC, thereby indicating abnormality in the CFS group. In the midbrain, white matter volume was observed to decrease with increasing fatigue duration. For T(1) -weighted MR and white matter volume, group × hemodynamic score interactions were detected in the brainstem [strongest in midbrain grey matter (GM)], deep prefrontal white matter (WM), the caudal basal pons and hypothalamus. A strong correlation in CFS between brainstem GM volume and pulse pressure suggested impaired cerebrovascular autoregulation. It can be argued that at least some of these changes could arise from astrocyte dysfunction. These results are consistent with an insult to the midbrain at fatigue onset that affects multiple feedback control loops to suppress cerebral motor and cognitive activity and disrupt local CNS homeostasis, including resetting of some elements of the autonomic nervous system (ANS).
Barrioluengo V, Wang Y, Le Grice SF, Menéndez-Arias L.	Centro de Biología Molecular Severo Ochoa (Consejo Superior de Investigaciones Científicas and Universidad Autónoma de Madrid), Madrid, Spain.	Intrinsic DNA synthesis fidelity of xenotropic murine leukemia virus-related virus reverse transcriptase.	FEBS J. 2012 Apr;279(8):1433-44. doi: 10.1111/j.1742-4658.2012.08532.x.	Although recent reports have provided strong evidence to suggest that xenotropic murine leukemia virus-related virus (XMRV) is unlikely to be the causative agent of prostate cancer and chronic fatigue syndrome, this recombinant retrovirus can nonetheless infect human cells in vitro and induce a chronic infection in macaques. In the present study, we determined the accuracy of DNA synthesis of the reverse transcriptases (RTs) of XMRV and Moloney murine leukemia virus (MoMLV) using a combination of pre-steady-state kinetics of nucleotide incorporation and an M13mp2-based forward mutation assay. The results obtained were compared with those previously reported for the HIV type 1 BH10 strain (HIV-1(BH10)) RT. MoMLV and XMRV RTs were 13.9 and 110 times less efficient [as determined by the catalytic rate constant of the nucleotide incorporation reaction ((pol))/equilibrium constant (K(d))] than the HIV-1(BH10) RT in incorporating correct nucleotides. Misinsertion and mispair extension kinetic studies demonstrated that MoMLV RT was more accurate than the HIV-1(BH10) RT. In comparison with the MoMLV RT, the XMRV RT showed decreased mispair extension fidelity and was less faithful when misincorporating C or A opposite A. However, the XMRV RT showed stronger selectivity against G in misinsertion fidelity assays. Forward mutation assays revealed that XMRV and MoMLV RTs had similar accuracy of DNA-dependent DNA synthesis, but were > 13 times more faithful than the HIV-1(BH10) enzyme. The mutational spectra of XMRV

				and MoMLV RTs were similar in having a relatively higher proportion of frameshifts and transversions compared with the HIV-1(BH10) RT. However, the XMRV polymerase was less prone to introduce large deletions and one-nucleotide insertions.
Bazzichi L, Sernissi F, Consensi A, Giacomelli C, Sarzi-Puttini P.	Division of Rheumatology, Department of Internal Medicine, University of Pisa, Piza, Italy. l.bazzichi@gmail.com	Fibromyalgia: a critical digest of the recent literature.	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S1-11.	Fibromyalgia is a common syndrome characterised by widespread pain and a constellation of other symptoms and overlapping conditions that contribute to complicate the diagnosis, the assessment and the treatment. Furthermore, the etiological causes for the moment only consist of assumptions, and the underlying pathogenetic mechanisms still remain to be clarified. For the above-mentioned reasons, with the present review we sought to provide an overview of the literature on fibromyalgia from both the pre-clinical and clinical studies indexed in PubMed during the last year, classifying original articles and reviews into etiopathogenesis, assessment and therapy.
Beaumont A, Burton AR, Lemon J, Bennett BK, Lloyd A, Vollmer-Conna U.	School of Psychiatry, University of New South Wales, Sydney, New South Wales, Australia.	Reduced cardiac vagal modulation impacts on cognitive performance in chronic fatigue syndrome.	PLoS One. 2012;7(11):e49518. doi: 10.1371/journal.pone.0049518.	BACKGROUND: Cognitive difficulties and autonomic dysfunction have been reported separately in patients with chronic fatigue syndrome (CFS). A role for heart rate variability (HRV) in cognitive flexibility has been demonstrated in healthy individuals, but this relationship has not as yet been examined in CFS. The objective of this study was to examine the relationship between HRV and cognitive performance in patients with CFS. METHODS: Participants were 30 patients with CFS and 40 healthy controls; the groups were matched for age, sex, education, body mass index, and hours of moderate exercise/week. Questionnaires were used to obtain relevant medical and demographic information, and assess current symptoms and functional impairment. Electrocardiograms, perceived fatigue/effort and performance data were recorded during cognitive tasks. Between-group differences in autonomic reactivity and associations with cognitive performance were analysed. RESULTS: Patients with CFS showed no deficits in performance accuracy, but were significantly slower than healthy controls. CFS was further characterized by low and unresponsive HRV; greater heart rate (HR) reactivity and prolonged HR-recovery after cognitive challenge. Fatigue levels, perceived effort and distress did not affect cognitive performance. HRV was consistently associated with performance indices and significantly predicted variance in cognitive outcomes. CONCLUSIONS: These findings reveal for the first time an association between reduced cardiac vagal tone and cognitive impairment in CFS and confirm previous reports of diminished vagal activity.
Benarroch EE.	Department of Neurology, Mayo Clinic, Rochester, MN. Electronic address: benarroch.eduardo@mayo.edu.	Postural tachycardia syndrome: a heterogeneous and multifactorial disorder.	Mayo Clin Proc. 2012 Dec;87(12):1214-25. doi: 10.1016/j.mayocp.2012.08.013.	Postural tachycardia syndrome (POTS) is defined by a heart rate increment of 30 beats/min or more within 10 minutes of standing or head-up tilt in the absence of orthostatic hypotension; the standing heart rate is often 120 beats/min or higher. POTS manifests with symptoms of cerebral hypoperfusion and excessive sympathoexcitation. The pathophysiology of POTS is heterogeneous and includes impaired sympathetically mediated vasoconstriction, excessive sympathetic drive, volume dysregulation, and deconditioning. POTS is frequently included in the

				differential diagnosis of chronic unexplained symptoms, such as inappropriate sinus tachycardia, chronic fatigue, chronic dizziness, or unexplained spells in otherwise healthy young individuals. Many patients with POTS also report symptoms not attributable to orthostatic intolerance, including those of functional gastrointestinal or bladder disorders, chronic headache, fibromyalgia, and sleep disturbances. In many of these cases, cognitive and behavioral factors, somatic hypervigilance associated with anxiety, depression, and behavioral amplification contribute to symptom chronicity. The aims of evaluation in patients with POTS are to exclude cardiac causes of inappropriate tachycardia; elucidate, if possible, the most likely pathophysiologic basis of postural intolerance; assess for the presence of treatable autonomic neuropathies; exclude endocrine causes of a hyperadrenergic state; evaluate for cardiovascular deconditioning; and determine the contribution of emotional and behavioral factors to the patient's symptoms. Management of POTS includes avoidance of precipitating factors, volume expansion, physical countermaneuvers, exercise training, pharmacotherapy (fludrocortisone, midodrine, β-blockers, and/or pyridostigmine), and behavioral-cognitive therapy. A literature search of PubMed for articles published from January 1, 1990, to June 15, 2012, was performed using the following terms (or combination of terms): POTS; postural tachycardia syndrome, orthostatic; orthostatic; syncope; sympathetic; baroreceptors; vestibulosympathetic; hypovolemia; visceral pain; chronic fatigue; deconditioning; headache; Chiari malformation; Ehlers-Danlos; emotion; amygdala; insula; anterior cingulate; periaqueductal gray; fludrocortisone; midodrine; propranolol; β-adrenergic; and pyridostigmine. Studies were limited to those published in English. Other articles were identified from bibliographies of the retrieved articles.
Bercea R, Bercea B, Mihăescu T.	Universitatea de Medicină şi Farmacie "Grigore T. Popa" Iaşi, România. ralbercea@yahoo.com	Association between the serum level of testosterone and other comorbidities in obstructive sleep apnea]. [Article in Romanian]	Pneumologia. 2012 Apr-Jun;61(2):98-101.	Testosterone seems to play a role in the pathophysiology of OSAS but the mechanisms are not yet well defined. Research of this relationship has focused on two main assumptions: first case support the emergence of OSAS or augmentation of OSAS severity in men treated with testosterone for symptomatic hypogonadism; the second hypothesis suggest that serum testosterone deficiency is due to hypoxia and microarousals generated by OSAS with direct impact on hypothalamic-pituitary-gonadal axis. The correlation between sleep apnea and androgenic disorders should be considered in the light of the intervention of many other factors which can act as confounding factors: age, obesity and other associated pathologies (chronic lung disease, smoking status). Many studies conducted so far on this interrelation (sleep apnea, endocrine system) have ignored these factors. In most cases CPAP (continuous positive airway pressure) therapy revert low serum testosterone levels to normal levels. Depressive status and fatigue, as OSAS consequences associated with hypogonadism have been reported in the literature and may have clinically significant aspects due to summary effect, with notable improvement after CPAP therapy avoiding adverse effects of hormonal or antidepressant treatment. The clinical

				implications and major consequences of association between androgen dysfunction and sleep apnea syndrome require a correct management in the recognition and treatment of obstructive sleep apnea syndrome associated with comorbidities.
Bernstein CN.	John Buhler Research Centre, University of Manitoba, 804F-175 McDermot Avenue, Winnipeg, MB, Canada. cbernst@cc.umanitoba.ca	Summing up: quality of life in chronic immune-mediated inflammatory diseases.	J Rheumatol Suppl. 2011 Nov;88:62-5. doi: 10.3899/jrheum.110908.	A series of reports is summarized in which measurement of quality of life (QOL) in various immune-mediated inflammatory diseases (IMID), the parameters that contribute to QOL, and the interrelationship between inflammatory diseases in specific organ systems and psychosocial domains are explored. Current treatment trials in IMID include QOL measures, particularly clinical trials of biologic therapy. There is increasing evidence that several available therapies benefit QOL. Among the factors that contribute to QOL, fatigue, depression, and stress are common and deserve attention from clinicians managing these patients.
Berstad A, Undseth R, Lind R, Valeur J.	Department of Medicine, Unger-Vetlesen's Institute, Lovisenberg Diakonale Hospital, Oslo, 0440, Norway. Arnold.Berstad@med.uib.no	Functional bowel symptoms, fibromyalgia and fatigue: a food-induced triad?	Scand J Gastroenterol. 2012 Sep;8-9(47):914-9. doi: 10.3109/00365521.2012.690045.	OBJECTIVE: Patients with perceived food hypersensitivity typically present with multiple health complaints. We aimed to assess the severity of their intestinal and extra-intestinal symptoms. MATERIALS AND METHODS: In a prospective study, 84 patients referred to our outpatient clinic for investigation of perceived food hypersensitivity were enrolled consecutively. Irritable bowel syndrome (IBS) was diagnosed according to the Rome III criteria. Severity and impact of bowel symptoms, fatigue and musculoskeletal pain were evaluated by using the following questionnaires: The IBS Severity Scoring System (IBS-SSS), the Fatigue Impact Scale (FIS), the FibroFatigue Scale (FFS), and visual analogue scales (VAS) for scoring of musculoskeletal pain. RESULTS: All but one patient were diagnosed with IBS, 58% with severe symptoms. Extra-intestinal symptoms suggestive of chronic fatigue and fibromyalgia were demonstrated in 85% and 71%, respectively. Neither IgE-mediated food allergy nor organic pathology could explain the patients' symptoms. Nevertheless, malabsorption of fat was demonstrated in 10 of 38 subjects. CONCLUSIONS: Perceived food hypersensitivity may be associated with severe, debilitating illness. The comorbid triad of IBS, chronic fatigue, and musculoskeletal pain is striking and may point to a common underlying cause.
Bjerkestrand S.	[No address quoted]	Power shift.[Article in English & Norwegian]	Tidsskr Nor Laegeforen. 2012 Jan 24;132(2):125. doi: 10.4045/tidsskr.12.02E1.	Comment in Tidsskr Nor Laegeforen. 2012 Mar 27;132(6):619. Tidsskr Nor Laegeforen. 2012 Feb 21;132(4):389-90. Tidsskr Nor Laegeforen. 2012 Mar 6;132(5):510. Tidsskr Nor Laegeforen. 2012 Mar 6;132(5):509-10. Tidsskr Nor Laegeforen. 2012 Feb 21;132(4):388-9. Tidsskr Nor Laegeforen. 2012 Apr 30;132(8):927. Tidsskr Nor Laegeforen. 2012 Feb 21;132(4):388-9. Tidsskr Nor Laegeforen. 2012 Feb 21;132(4):389.
Blankfield A.	Kew, Australia.	A Brief Historic Overview of Clinical Disorders Associated with Tryptophan: The Relevance to Chronic Fatigue Syndrome	Int J Tryptophan Res. 2012;5:27-32. doi: 10.4137/IJTR.S10085	Last century there was a short burst of interest in the tryptophan related disorders of pellagra and related abnormalities that are usually presented in infancy.1,2 Nutritional physiologists recognized that a severe human dietary deficiency of either tryptophan or the B group vitamins could result in central nervous system (CNS) sequelae such as ataxia, cognitive dysfunction and dysphoria, accompanied by skin hyperpigmentation.3,4 The current paper will focus on the emerging role of

		(CFS) and Fibromyalgia (FM).		tryptophan in chronic fatigue syndrome (CFS) and fibromyalgia (FM).
Blazquez A, Guillamó E, Alegre J, Ruiz E, Javierre C.	Faculty of Medicine, Department of Physiological Sciences II, Medical School, University of Barcelona, IDIBELL. L'Hospitalet, Barcelona, Spain.ablazquez@ub.edu	Psycho-physiological impact on women with chronic fatigue syndrome in the context of their couple relationship.	Psychol Health Med. 2012;17(2):150-63. doi: 10.1080/13548506.2011.582124.	The quality of dyadic adjustment is likely to play an important role in patients' relational problems and may also be associated with the clinical presentation of chronic fatigue syndrome (CFS) symptoms. The objective of this study was (1) to determine whether CFS patients and their partners have similar perceptions of their dyadic adjustment and (2) to evaluate whether the influence of dyadic satisfaction in women with CFS, as well as common psychological parameters such as anxiety, may correlate with physiological responses at rest and/or when performing very low intensity exercise. Forty females with CFS and their partners completed the Dyadic Adjustment Scale, the State-Trait Anxiety Inventory, and the Hospital Anxiety and Depression scale. The cardiovascular adaptation of patients was evaluated during resting conditions and on a precalibrated cycle ergometer while performing very low intensity exercise. Patients and partners had similar perceptions of their marital relationship. Both at rest and during very low workload, various physiological parameters in the patient group showed statistical correlations with certain psychological parameters. Several psychological variables, such as anxiety and dyadic adjustment, were associated with the cardioventilatory response monitored at rest and during very low intensity exercise. Further studies are needed to determine the nature of this association.
Blomberg J, Blomberg F, Sjösten A, Sheikholvaezin A, Bölin-Wiener A, Elfaitouri A, Hessel S, Gottfries CG, Zachrisson O, Ohrmalm C, Jobs M, Pipkorn R.	Section of Clinical Microbiology, Department of Medical Sciences, Uppsala University, Uppsala, Sweden. Jonas.Blomberg@medsci.uu.se	No evidence for xenotropic murine leukemia-related virus infection in Sweden using internally controlled multiepitope suspension array serology.	Clin Vaccine Immunol. 2012 Sep;19(9):1399-410. doi: 10.1128/CVI.00391-12	Many syndromes have a large number of differential diagnoses, a situation which calls for multiplex diagnostic systems. Myalgic encephalomyelitis (ME), also named chronic fatigue syndrome (CFS), is a common disease of unknown etiology. A mouse retrovirus, xenotropic murine leukemia-related virus (XMRV), was found in ME/CFS patients and blood donors, but this was not corroborated. However, the paucity of serological investigations on XMRV in humans prompted us to develop a serological assay which cover many aspects of XMRV antigenicity. It is a novel suspension array method, using a multiplex IgG assay with nine recombinant proteins from the env and gag genes of XMRV and 38 peptides based on known epitopes of vertebrate gammaretroviruses. IgG antibodies were sought in 520 blood donors and 85 ME/CFS patients and in positive- and negative-control sera from animals. We found no differences in seroreactivity between blood donors and ME/CFS patients for any of the antigens. This did not support an association between ME/CFS and XMRV infection. The multiplex serological system had several advantages: (i) biotinylated protein G allowed us to run both human and animal sera, which is essential because of a lack of XMRV-positive humans; (ii) a novel quality control was a pan-peptide positive-control rabbit serum; and (iii) synthetic XMRV Gag peptides with degenerate positions covering most of the variation of murine leukemia-like viruses did not give higher background than nondegenerate analogs. The principle may be used for creation of variant tolerant peptide serologies. Thus, our system allows rational large-

				scale serological assays with built-in quality control.
Bloom S, Ablin JN, Lebel D, Rath E, Faran Y, Daphna-Tekoah S, Buskila D.	Orthopedic Surgery Department, Soroka Medical Center, Beersheba, Israel	Awareness of diagnostic and clinical features of fibromyalgia among orthopedic surgeons.	Rheumatol Int. 2012 Jul 22.	Fibromyalgia Syndrome (FMS) is a chronic pain syndrome characterized by widespread musculoskeletal pain and fatigue. The current study was designed to evaluate the awareness and skills of orthopedic surgeons (OS) regarding FMS diagnosis and treatment. For the examination of awareness and familiarity of OS in Israel to Fibromyalgia, a questionnaire-based survey was conducted. Two hundred and nineteen OS, residents and specialists, were asked anonymously about awareness, knowledge, and treatment of FM. Multivariable statistical analysis was performed. 91 % (199) of responders reported that they recognized the disease. Notwithstanding, the mean knowledge score was 7.6 out of 17. In addition, OS who were trained in the south of Israel were found to have a better degree of knowledge about FM (9.7 vs. 7.4; $p < 0.03$). The awareness and knowledge among OS regarding FM needs to be improved. OS who were trained in the south of Israel were found to have better degree of knowledge regarding FM.
Bodei L, Cremonesi M, Grana CM, Chinol M, Baio SM, Severi S, Paganelli G.	Division of Nuclear Medicine, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy.	Yttrium-labelled peptides for therapy of NET.	Eur J Nucl Med Mol Imaging. 2012 Feb;39 Suppl 1:S93-102. doi: 10.1007/s00259-011-2002-y.	Peptide receptor radionuclide therapy (PRRT) consists in the systemic administration of a synthetic peptide, labelled with a suitable beta-emitting radionuclide, able to irradiate tumours and their metastases via the internalization through a specific receptor, overexpressed on the cell membrane. After 15 years of experience, we can state that PRRT with (90)Y-labelled peptides is generally well tolerated. Acute side effects are usually mild, some of which are related to the co-administration of amino acids, such as nausea. Others are related to the radiopeptide, such as fatigue or the exacerbation of an endocrine syndrome, which rarely occurs in functioning tumours. Chronic and permanent effects on target organs, particularly the kidneys and the bone marrow, are generally mild if the necessary precautions are taken. Currently, the potential risk to kidney and red marrow limits the amount of radioactivity that may be administered. However, when tumour masses are irradiated with adequate doses, volume reduction may be observed. (90)Y-octreotide has been the most widely used radiopeptide in the first 8-10 years of experience. Unfortunately, all of the published results derive from different and inhomogeneous phase I/II studies. Hence, a direct comparison is virtually impossible to date. Nevertheless, even with these limitations, objective responses are registered in 10-34% of patients. The optimal timing of (90)Y-DOTATOC in the management of somatostatin receptor (SSTR)-positive tumours and the way in which it should be integrated with other treatments have yet to be defined, and prospective phase II/III trials comparing the efficacy and toxicity of different schemes of (90)Y-DOTATOC administration are still warranted.
Booth NE, Myhill S, McLaren-Howard J.	[No address quoted]	Mitochondrial dysfunction and the pathophysiology of Myalgic Encephalomyelitis/C	Int J Clin Exp Med. 2012;5(3):208-20.	The objectives of this study are to test the hypothesis that the fatigue and accompanying symptoms of Chronic Myalgic Encephalomyelitis/Fatigue Syndrome are in part due to defects in energy provision at the cellular level, and to understand the pathophysiology of the defects so that effective medical intervention can be implemented. We performed an audit of 138 patients (ages 18-65) diagnosed with

		hronic Fatigue Syndrome (ME/CFS).		ME/CFS and attending a private practice. The patients and 53 normal, healthy controls had the ATP Profile test carried out on neutrophils from a 3-ml venous blood sample. This test yields 6 numerical factors that describe the availability of ATP and the efficiency of oxidative phosphorylation in mitochondria. Other biomedical measurements, including the concentration of cell-free DNA in plasma, were made. The results of the audit are compared with the controls and a previous cohort of 61 patients. We find that all patients tested have measureable mitochondrial dysfunction which correlates with the severity of the illness. The patients divide into two main groups differentiated by how cellular metabolism attempts to compensate for the dysfunction. Comparisons with exercise studies suggest that the dysfunction in neutrophils also occurs in other cells. This is confirmed by the cell-free DNA measurements which indicate levels of tissue damage up to 3.5 times the normal reference range. The major immediate causes of the dysfunction are lack of essential substrates and partial blocking of the translocator protein sites in mitochondria. The ATP Profile is a valuable diagnostic tool for the clinical management of ME/CFS.
Bossuyt X, Cooreman S, De Baere H, Verschueren P, Westhovens R, Blockmans D, Mariën G.	Experimental Laboratory Immunology, Catholic University Leuven, Leuven, Belgium; Department of Laboratory Medicine, Immunology, University Hospitals Leuven, Leuven, Belgium. Electronic address: xavier.bossuyt@uz.kuleuven.ac.be.	Detection of antinuclear antibodies by automated indirect immunofluorescence analysis.	Clin Chim Acta. 2013 Jan 16;415:101-6. doi: 10.1016/j.cca.2012.09.021.	BACKGROUND: Testing for antinuclear antibodies is useful for the diagnosis of systemic rheumatic diseases. Automated systems for image acquisition and interpretation of indirect immunofluorescence-based tests are increasingly used. The diagnostic performance of such automated approach in untreated patients has not been reported. METHODS: Antinuclear antibodies were measured by automated indirect immunofluorescence using Zenit G. Sight on HEp2 and HEp2000 substrate in 268 consecutive samples submitted to the laboratory for antinuclear antibody testing, and in 231 patients with a systemic rheumatic disease at the time of diagnosis, 143 blood donors, 134 patients with chronic fatigue syndrome, and 133 diseased controls. RESULTS: Image acquisition by G-Sight was of high quality. The accuracy of pattern assignment was limited. There was a significant correlation between automated estimation of fluorescence intensity (probability index of positivity) and end-point titer. Probability index interval specific likelihood ratios for systemic rheumatic disease increased with increasing level of positivity probability. With the HEp-2 substrate, the likelihood ratio for systemic lupus erythematosus was 0.06, 0.4, 6.8, 12.1, and 43.9 for a probability measure of positivity of ≤10, 11-≤30, 31-≤50, 51-≤85, and >85, respectively. CONCLUSION: Quantitative data generated by automated image acquisition facilitates standardized interpretation.
Bower JE.	UCLA Department of Psychology, 1285 Franz Hall, Los Angeles, CA 90095-1563, USA. jbower@ucla.edu	Fatigue, brain, behavior, and immunity: summary of the 2012 Named Series on fatigue.	Brain Behav Immun. 2012 Nov;26(8):1220-3. doi: 10.1016/j.bbi.2012.08.009.	The focus on fatigue for the 2012 Named Series in brain, behavior, and immunity reflects the growing wave of research examining immune underpinnings of fatigue in healthy and clinical populations. Fatigue is prevalent in the general population and in patients with a variety of medical conditions. However, the etiology of fatigue remains elusive. Psychoneuroimmunological approaches to fatigue have yielded important advances in our understanding of this complex symptom and are represented in the twelve articles included in the Named Series. These articles

				include animal and human models of fatigue and cross a variety of different medical conditions, including cancer, chronic fatigue syndrome, and diabetes. This review briefly summarizes the articles included in the series and highlights the themes that have emerged from this body of work.
Brenu EW, Ashton KJ, van Driel M, Staines DR, Peterson D, Atkinson GM, Marshall-Gradisnik SM.	Faculty of Health Science and Medicine, Population Health and Neuroimmunology Unit, Bond University, Robina, Queensland, Australia. ekbrenu@bond.edu.au	Cytotoxic lymphocyte microRNAs as prospective biomarkers for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.	J Affect Disord. 2012 Dec 10;141(2-3):261-9. doi: 10.1016/j.jad.2012.03.037.	BACKGROUND: Immune dysfunction associated with a disease often has a molecular basis. A novel group of molecules known as microRNAs (miRNAs) have been associated with suppression of translational processes involved in cellular development and proliferation, protein secretion, apoptosis, immune function and inflammatory processes. MicroRNAs may be implicated in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME), where immune function is impaired. The objective of this study was to determine the association between miRNAs in cytotoxic cells and CFS/ME. METHODS: Natural Killer (NK) and CD8(+)T cells were preferentially isolated from peripheral blood mononuclear cells from all participants (CFS/ME, n=28; mean age=41.8±9.6 years and controls, n=28; mean age=45.3±11.7 years), via negative cell enrichment. Following total RNA extraction and subsequent synthesis of cDNA, reverse transcriptase-quantitative polymerase chain reaction (RT-qPCR) was used to determine the expression levels of nineteen miRNAs. RESULTS: There was a significant reduction in the expression levels of miR-21, in both the NK and CD8(+)T cells in the CFS/ME sufferers. Additionally, the expression of miR-17-5p, miR-10a, miR-103, miR-152, miR-146a, miR-106, miR-223 and miR-191 was significantly decreased in NK cells of CFS/ME patients in comparison to the non-fatigued controls. LIMITATIONS: The results from these investigations are not yet transferable into the clinical setting, further validatory studies are now required. CONCLUSIONS: Collectively these miRNAs have been associated with apoptosis, cell cycle, development and immune function. Changes in miRNAs in cytotoxic cells may reduce the functional capacity of these cells and disrupt effective cytotoxic activity along with other immune functions in CFS/ME patients.
Brenu EW, van Driel ML, Staines DR, Ashton KJ, Hardcastle SL, Keane J, Tajouri L, Peterson D, Ramos SB, Marshall-Gradisnik SM.	Population Health and Neuroimmunology Unit, Bond University, Robina, QLD, Australia. ekbrenu@bond.edu.au	Longitudinal investigation of natural killer cells and cytokines in chronic fatigue syndrome/myalgic encephalomyelitis.	J Transl Med. 2012 May 9;10:88. doi: 10.1186/1479-5876-10-88.	BACKGROUND: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is an etiologically unexplained disorder characterised by irregularities in various aspects of the immunological function. Presently, it is unknown whether these immunological changes remain consistent over time. This study investigates Natural Killer (NK) cell cytotoxic activity, NK cell subsets (CD56brightCD16- and CD56dimCD16+) and cytokines, over the course of a12 month period in patients with CFS/ME. METHODS: The participants in the study comprised 65 (47.2 ± 11.5 years) CFS/ME participants and 21 (45.2 ± 9.3 years) non-fatigued controls. Flow cytometry protocols were used to assess NK subsets and NK cytotoxic activity at various time points that included baseline (T1), 6 (T2) and 12 months (T3). Cytokine secretions were measured following mitogenic stimulation of peripheral blood mononuclear cells. RESULTS: NK cytotoxic activity was significantly decreased in the CFS/ME patients at T1, T2 and T3 compared to the non-fatigued group. Additionally, in comparison to the non-fatigued

				controls, the CFS/ME group had significantly lower numbers of CD56brightCD16- NK cells at both T1 and T2. Interestingly, following mitogenic stimulation, cytokine secretion revealed significant increases in IL-10, IFN-γ and TNF-α at T1 in the CFS/ME group. A significant decrease was observed at T2 in the CFS/ME group for IL-10 and IL-17A while at T3, IL-2 was increased in the CFS/ME group in comparison to the non-fatigued controls. Overall cytotoxic activity was significantly decreased at T3 compared to T1 and T2. CD56brightCD16- NK cells were much lower at T2 compared to T1 and T3. IL-10 and IL-17A secretion was elevated at T2 in comparison to T1 and T3. CONCLUSION: These results confirm decreases in immune function in CFS/ME patients, suggesting an increased susceptibility to viral and other infections. Furthermore, NK cytotoxic activity may be a suitable biomarker for diagnosing CFS/ME as it was consistently decreased during the course of the 12 months study.
Broderick G, Ben Hamo R, Vashishtha S, Efroni S, Nathanson L, Barnes Z, Fletcher MA, Klimas N.	Department of Medicine, University of Alberta, Edmonton, Canada. Electronic address: gordon.broderick@ualberta.ca.	Altered immune pathway activity under exercise challenge in Gulf War Illness: An exploratory analysis.	Brain Behav Immun. 2012 Nov 29. pii: S0889-1591(12)00493-X. doi: 10.1016/j.bbi.2012.11.007.	Though potentially linked to the basic physiology of stress response we still have no clear understanding of Gulf War Illness (GWI), a debilitating illness presenting with a complex constellation of immune, endocrine and neurological symptoms. Here we compared male GWI (n=20) with healthy veterans (n=22) and subjects with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) (n=7). Blood was drawn during a Graded eXercise Test (GXT) prior to exercise, at peak effort (VO2 max) and 4-h post exercise. Affymetrix HG U133 plus 2.0 microarray gene expression profiling in peripheral blood mononuclear cells (PBMCs) was used to estimate activation of over 500 documented pathways. This was cast against ELISA-based measurement of 16 cytokines in plasma and flow cytometric assessment of lymphocyte populations and cytotoxicity. A 2-way ANOVA corrected for multiple comparisons (q statistic <0.05) indicated significant increases in neuroendocrine-immune signaling and inflammatory activity in GWI, with decreased apoptotic signaling. Conversely, cell cycle progression and immune signaling were broadly subdued in CFS. Partial correlation networks linking pathways with symptom severity via changes in immune cell abundance, function and signaling were constructed. Central to these were changes in IL-10 and CD2+ cell abundance and their link to two pathway clusters. The first consisted of pathways supporting neuronal development and migration whereas the second was related to androgen-mediated activation of NF-κB. These exploratory results suggest an over-expression of known exercise response mechanisms as well as illness-specific changes that may involve an overlapping stress-potentiated neuro-inflammatory response.
Broderick G, Fletcher MA, Gallagher M, Barnes Z, Vernon SD, Klimas NG.	Department of Medicine, Division of Pulmonary Medicine, University of Alberta, Edmonton, AB, Canada. gordon.broderick@ual	Exploring the diagnostic potential of immune biomarker coexpression in Gulf War Illness.	Methods Mol Biol. 2012;934:145-64. doi: 10.1007/978-1-62703-071-7_8.	Complex disorders like Gulf War Illness (GWI) often defy diagnosis on the basis of a single biomarker and may only be distinguishable by considering the coexpression of multiple markers measured in response to a challenge. We demonstrate the practical application of such an approach using an example where blood was collected from 26 GWI, 13 healthy control subjects, and 9 unhealthy controls with Chronic Fatigue at three points during a graded exercise challenge. A 3-way multivariate projection

	berta.ca			model based on 12 markers of endocrine and immune function was constructed using a training set of n = 10 GWI and n = 11 healthy controls. These groups were separated almost completely on the basis of two coexpression patterns. In a separate test set these same features allowed for discrimination of new GWI subjects (n = 16) from unhealthy (n = 9) and healthy control subjects with a sensitivity of 70% and a specificity of 90%.
Broderick G, Katz BZ, Fernandes H, Fletcher MA, Klimas N, Smith FA, O'Gorman MR, Vernon SD, Taylor R.	Division of Pulmonary Medicine, Department of Medicine, University of Alberta, WMC 2E4.41 WC Mackenzie Health Sciences Centre, 8440 112 Street, Edmonton, AB T6G 2R7, Canada. gordon.broderick@ualberta.ca	Cytokine expression profiles of immune imbalance in post-mononucleosis chronic fatigue.	J Transl Med. 2012 Sep 13;10:191. doi: 10.1186/1479-5876-10-191.	BACKGROUND: As Chronic Fatigue Syndrome (CFS) has been known to follow Epstein-Bar virus (EBV) and other systemic infections; our objective was to describe differences in immune activation in post-infective CFS (PI-CFS) patients and recovered controls. We studied 301 adolescents prospectively over 24 months following the diagnosis of monospot-positive infectious mononucleosis (IM). We found an incidence of CFS at 6, 12 and 24 months of 13%, 7% and 4% respectively. METHODS: Using chemiluminescent imaging we measured the concentrations of IL-1a, 1b, 2, 4, 5, 6, 8, 10, 12 (p70), 13, 15, 17 and 23, IFN-γ, TNF-α and TNF-β in duplicate plasma samples available in bio-bank from 9 PI-CFS subjects and 12 recovered controls at 24 months post-infection. RESULTS: Standard comparative analysis indicated significant differences in IL-8 and 23 across subject groups. In constructing a linear classification model IL-6, 8 and 23 were selected by two different statistical approaches as discriminating features, with IL-1a, IL-2 and IFN-γ also selected in one model or the other. This supported an assignment accuracy of better than 80% at a confidence level of 0.95 into PI-CFS versus recovered controls. CONCLUSION: These results suggest that co-expression patterns in as few as 5 cytokines associated with Th17 function may hold promise as a tool for the diagnosis of post-infectious CFS.
Broderick G.	[No address quoted]	Response to 'A controversial consensus'; by the International Consensus Panel.	J Intern Med. 2012 Feb;271(2):213-7. doi: 10.1111/j.1365-2796.2011.02499.x.	Comment on J Intern Med. 2012 Jan;271(1):29-31.
Brooks J, Daglish J, Wearden A.	University of Huddersfield, UK.	Attributions, distress and behavioural responses in the significant others of people with Chronic Fatigue Syndrome.	J Health Psychol. 2012 Nov 23.	To test an attribution-emotion model of reactions to chronic fatigue syndrome/myalgic encephalomyelitis, 30 significant others of 30 adult patients with chronic fatigue syndrome/myalgic encephalomyelitis were administered a semi-structured interview about their beliefs regarding the patient's illness and completed questionnaire measures of distress and behavioural responses to the patient. Spontaneous causal explanations (attributions) for illness events, symptom exacerbation and negative patient mood were extracted and coded. Significant others' distress and negative behavioural responses towards the chronic fatigue syndrome/myalgic encephalomyelitis patient were associated with attributing illness events to causes personal and internal to the patient. Our findings may inform the future family-based interventions for chronic fatigue syndrome/myalgic encephalomyelitis.

Brooks J, Lycett-Lambert K, Caminiti K, Merks H, McMillan R, Sandstrom P.	National HIV & Retrovirology Laboratories, National Microbiology Laboratory, Public Health Agency of Canada, Ottawa, Canada. james.brooks@phac-aspc.gc.ca	No evidence of cross-species transmission of mouse retroviruses to animal workers exposed to mice.	Transfusion. 2012 Feb;52(2):317-25. doi: 10.1111/j.1537-2995.2011.03463.x	BACKGROUND: Although recent data have brought into question the association between xenotropic murine leukemia virus-related virus (XMRV) and chronic fatigue syndrome, one group has reported evidence of human infection with distinct polytropic murine leukemia viruses (MLVs). Occult retroviral infection among humans poses a significant public health risk should it be introduced into the blood supply. To explore the possibility of cross-species transmission of MLVs to humans, we sought molecular and serologic evidence of XRMV/MLV infection among a cohort of animal workers highly exposed to mice. STUDY DESIGN AND METHODS: Before the commencement of the study, the laboratory and equipment were demonstrated to be free of XMRV/MLV DNA sequences. DNA extracted from 43 animal workers was tested using nested polymerase chain reaction (PCR) with published primer sets, targeting regions of XMRV and MLV gag. Negative controls were assayed in a 1:1 ratio with specimens. Serum specimens were tested using a validated immunoblot assay containing cross-reactive XMRV antigens. RESULTS: Initial molecular assays demonstrated that the physical space and laboratory equipment were free of MLV and XMRV DNA sequences. Nested PCR assays using multiple primer sets successfully amplified XMRV and MLV sequences from positive controls with high sensitivity. A single, nonreproducible, false-positive result from one specimen was shown to be the result of subsequent contamination. Immunoblotting of all subjects' sera failed to demonstrate any evidence of seroreactivity to XMRV proteins. CONCLUSIONS: There was no evidence of human infection with XMRV/MLV among a cohort of individuals highly exposed to mice. These data suggest that the likelihood of cross-species transmission events of MLV from mice to humans is low.
Brooks SK, Rimes KA, Chalder T.	Department of Psychological Medicine, King's College London, UK.	The role of acceptance in chronic fatigue syndrome.	J Psychosom Res. 2011 Dec;71(6):411-5. doi: 10.1016/j.jpsychores.2011.08.001.	OBJECTIVE: In this paper we consider the role that acceptance plays in fatigue and physical and social functioning. We predicted that lack of acceptance would be positively correlated with fatigue and impairment in functioning; that there would be a significant relationship between perfectionism and acceptance; and cognitive behavioural therapy (CBT) would increase acceptance. METHODS: Two hundred and fifty nine patients with chronic fatigue syndrome (CFS) completed questionnaires measuring fatigue, physical functioning, work and social adjustment, lack of acceptance, perfectionism and depression. Ninety consecutive attenders received a course of CBT and completed further questionnaires at discharge and 3months post-treatment. Correlations and multiple hierarchical regressions were used to determine relationships between acceptance, perfectionism and clinical outcome variables. RESULTS: At baseline, lack of acceptance was the key factor associated with impaired physical functioning and work and social adjustment. Lack of acceptance and doubts about actions were associated with fatigue in a multiple regression analysis. At discharge and follow-up patients showed significantly increased acceptance, as well as reduced Concern over Mistakes, less fatigue and impairment of physical functioning, and improved work and social adjustment. CONCLUSION: This is the first

				study to our knowledge which shows a change in acceptance after CBT and a relationship between acceptance and perfectionism. Acceptance may be an important factor to consider within treatments for CFS.
Brown M, Kaplan C, Jason L.	DePaul University, Chicago 60618, USA. mbrown59@depaul.edu	Factor analysis of the Beck Depression Inventory-II with patients with chronic fatigue syndrome. Brown M, Kaplan C, Jason L.	J Health Psychol. 2012 Sep;17(6):799-808. doi: 10.1177/1359105311424470.	This study examined the properties of the Beck Depression Inventory-II (BDI-II) in a sample of 111 patients with chronic fatigue syndrome (CFS). Exploratory factor analysis identified two factors. The mean score for the Somatic-Affective factor was significantly higher than the Cognitive factor. Convergent and discriminant validity were assessed for BDI-II total score, the two factor scores, and the BDI for Primary Care (BDI-PC). The BDI-PC and Cognitive factor demonstrated superior validity. Results suggest patients endorse BDI-II somatic items that overlap with CFS symptoms at a high rate. Factor scores should be evaluated separately, or the BDI-PC should be utilized with this population.
Brown MM, Bell DS, Jason LA, Christos C, Bell DE.	DePaul University, Chicago, IL 60614, USA. mbrown59@depaul.edu	Understanding long-term outcomes of chronic fatigue syndrome.	J Clin Psychol. 2012 Sep;68(9):1028-35. doi: 10.1002/jclp.21880.	OBJECTIVE: This study sought to examine long-term health, symptom, and disability outcomes among patients with chronic fatigue syndrome (CFS) by comparing those diagnosed with CFS 25 years ago with healthy controls. METHOD: Of the 25 participants diagnosed with CFS 25 years ago, 5 self-reported that they maintained a diagnosis of CFS, while 20 reported no longer having a diagnosis. These two groups were compared with healthy controls on outcomes related to functioning and symptom severity. RESULTS: Those who remitted from CFS showed significantly more impairment on 21 out of 23 outcomes compared with controls. On 17 outcomes, those who remitted had nonsignificant differences in impairment compared to those who maintained a CFS diagnosis. CONCLUSIONS: Findings from this study suggest that over time many individuals will not maintain a CFS diagnosis but will not return to their premorbid level of functioning.
Brubakk O.	[No address quoted]	Two sub editorials. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2012 Apr 30;132(8):927. doi: 10.4045/tidsskr.12.0202.	Comment on Tidsskr Nor Laegeforen. 2012 Jan 24;132(2):125. Tidsskr Nor Laegeforen. 2012 Feb 7;132(3):261-2.
Burbelo PD, Bayat A, Wagner J, Nutman TB, Baraniuk JN, Iadarola MJ.	Neurobiology and Pain Therapeutics Section, Laboratory of Sensory Biology, National Institute of Dental and Craniofacial Research, National Institutes of Health Bethesda, MD.	No serological evidence for a role of HHV-6 infection in chronic fatigue syndrome	Am J Transl Res. 2012;4(4):443-51.	Human herpesvirus 6A (HHV-6A) and human herpesvirus 6B (HHV-6B) are associated with a variety of conditions including rash, fever, and encephalitis and may play a role in several neurological diseases. Here luciferase immunoprecipitation systems (LIPS) was used to develop HHV-6 serologic diagnostic tests using antigens encoded by the U11 gene from HHV-6A (p100) and HHV-6B (p101). Analysis of the antibody responses against Renilla luciferase fusions with different HHV-6B p101 fragments identified an antigenic fragment (amino acids 389 to 858) that demonstrated ~86% seropositivity in serum samples from healthy US blood donors. Additional experiments detected a HHV-6A antigenic fragment (amino acids 751-870) that showed ~48% antibody seropositivity in samples from Mali, Africa, a known HHV-6A endemic region. In contrast to the high levels of HHV-6A immunoreactivity seen in the African samples, testing of US blood donors with the HHV-6A p100 antigenic fragment revealed little immunoreactivity. To potentially explore the role of HHV-6 infection in human

				disease, a blinded cohort of controls (n=59) and chronic fatigue syndrome (CFS) patients (n=72) from the US was examined for serum antibodies. While only a few of the controls and CFS patients showed high level immunoreactivity with HHV-6A, a majority of both the controls and CFS patients showed significant immunoreactivity with HHV-6B. However, no statistically significant differences in antibody levels or frequency of HHV-6A or HHV-6B infection were detected between the controls and CFS patients. These findings highlight the utility of LIPS for exploring the seroepidemiology of HHV-6A and HHV-6B infection, but suggest that these viruses are unlikely to play a role in the pathogenesis of CFS.
Burgess M, Andiappan M, Chalder T.	South London & Maudsley Trust, London, UK. mary.burgess@slam.nhs.uk	Cognitive behaviour therapy for chronic fatigue syndrome in adults: face to face versus telephone treatment: a randomized controlled trial.	Behav Cogn Psychother. 2012 Mar;40(2):175-91. doi: 10.1017/S1352465811000543.	BACKGROUND: Previous research has shown that face to face cognitive behaviour therapy (CBT) is an effective treatment for chronic fatigue syndrome (CFS)/Myalgic Encephalomyelitis (ME). However, some patients are unable to travel to the hospital for a number of reasons. AIMS: The aim of this study was to assess whether face to face CBT was more effective than telephone CBT (with face to face assessment and discharge appointment) for patients with CFS. METHOD: Patients aged 18-65 were recruited from consecutive referrals to the Chronic Fatigue Syndrome (CFS) Research and Treatment Unit at The South London and Maudsley NHS Trust in London. Participants were randomly allocated to either face to face CBT or telephone CBT by a departmental administrator. Blinding of participants and care givers was inappropriate for this trial. A parallel-groups randomised controlled trial was used to compare the two treatments. The primary outcomes were physical functioning and fatigue. RESULTS: Significant improvements in the primary outcomes of physical functioning and fatigue occurred and were maintained to one year follow-up after discharge from treatment. Improvements in social adjustment and global outcome were noted and patient satisfaction was similar in both groups. CONCLUSIONS: Results from this study indicate that telephone CBT with two face to face appointments is a mild to moderately effective treatment for CFS and may be offered to patients where face to face treatment is not a viable option. Despite these encouraging conclusions, dropout was relatively high and therapists should be aware of this potential problem.
Burns D.	School of Nursing, Midwifery and Social Work, University of Manchester. dianne.burns@manchester.ac.uk	Chronic fatigue syndrome or myalgic encephalomyelitis.	Nurs Stand. 2012 Feb 22-28;26(25):48-56; quiz 58.	Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is a debilitating illness that affects many systems of the body, particularly the nervous and immune systems. The condition affects all age, racial, ethnic and socioeconomic groups. This article focuses on the knowledge, understanding and skills necessary to recognise, assess, manage and support patients with CFS/ME. The principles of management and rehabilitation can be applied by nurses and other healthcare professionals irrespective of the clinical setting and context.
Calandre EP, Rico-Villademoros F.	Institute of Neuroscience and Center for Biomedical	The role of antipsychotics in the management of	CNS Drugs. 2012 Feb 1;26(2):135-53. doi: 10.2165/11597130-	Fibromyalgia is a syndrome characterized by chronic generalized pain associated with different somatic symptoms, such as sleep disturbances, fatigue, stiffness, balance problems, hypersensitivity to physical and psychological environmental stimuli,

	Investigations, University of Granada, Granada, Spain. calandre@gmail.com	fibromyalgia.	000000000-00000.	depression and anxiety. It has been estimated to affect roughly the 2-4% of the general population in most countries studied, and it has been shown to be much more prevalent in women than in men. Although its pathophysiology is not yet fully understood, it is known that both genetic and environmental factors are involved in its development. Fibromyalgia shares a high degree of co-morbidity with other conditions, including chronic headache, temporomandibular disorder, irritable bowel syndrome, major depression, anxiety disorders and chronic fatigue syndrome. Therefore, this is a syndrome difficult to treat for which multimodal treatments including physical exercise, psychological therapies and pharmacological treatment are recommended. Although different kinds of drugs have been studied for the treatment of fibromyalgia, the most widely used drugs that have the higher degree of evidence for efficacy include the α(2)δ ligands pregabalin and gabapentin, and the tricyclic antidepressants (TCAs) and serotonin noradrenaline (norepinephrine) reuptake inhibitors (SNRIs). However, there is a need to look for newer additional therapeutic pharmacological options for the treatment of this complex and disabling disease. First- and second-generation antipsychotics have shown analgesic properties both in an experimental setting and in humans, although most of the available evidence for the treatment of human pain concerns older antipsychotics and involves clinical trials performed several decades ago. In addition, several second-generation antipsychotics, risperidone, olanzapine and quetiapine, have shown efficacy in the treatment of some anxiety disorders. Some second-generation antipsychotics, mainly quetiapine, aripiprazole and amisulpride, have demonstrated antidepressant activity, with quetiapine approved for the treatment of bipolar depression and refractory major depression, and aripiprazole approved as an adjunctive treatment for major depressive disorder. Finally, several old and new antipsychotics, including promethazine, levopromazine, olanzapine, quetiapine and ziprasidone, have been shown to improve sleep parameters in healthy subjects. Each of these properties suggests that antipsychotics could represent a new potential alternative for the treatment of fibromyalgia syndrome. To date, most of the published studies on the use of antipsychotics in the treatment of fibromyalgia syndrome have been uncontrolled, either case reports or case series, dealing with olanzapine, quetiapine, ziprasidone, levopromazine and amisulpride. The studies on olanzapine and quetiapine have suggested therapeutic efficacy although, in the case of olanzapine, hampered by tolerability problems. A double-blind controlled trial, published in 1980, showed that chlorpromazine increased slow-wave sleep and improved pain and mood disturbances. More recently, four double-blind controlled studies have explored the efficacy of quetiapine, either alone or as an add-on treatment, in fibromyalgia management. None of these trials has yet been published, although two of them have been presented as congress communications, both of them suggesting that quetiapine could be a potential alternative treatment for fibromyalgia. In summary,

				the current available evidence suggests that at least some antipsychotics, specifically quetiapine, could be useful for the treatment of fibromyalgia and that further studies on the efficacy of these compounds are worth pursuing.
Callaway E.	[No address quoted]	Embattled scientist in theft probe.	Nature. 2011 Nov 29;480(7375):13-4. doi: 10.1038/480013a.	[No abstract given]
Cao Y, Hu Y, Liu P, Zhao HX, Zhou XJ, Wei YM.	Department of Clinical Pharmacology, Chinese PLA General Hospital, Beijing 100853, China.	Effects of a Chinese traditional formula Kai Xin San (KXS) on chronic fatigue syndrome mice induced by forced wheel running.	J Ethnopharmacol. 2012 Jan 6;139(1):19-25. doi: 10.1016/j.jep.2011.08.030.	ETHNOPHARMACOLOGICAL RELEVANCE: In traditional medicine, Kai Xin San (KXS), composed of ginseng (Panax ginseng), hoelen (Wolfiporia cocos), polygala (Polygala tenuifolia) and Acorus gramineus, is famous for the treatment of emotion-thought disease, such as settling fright, quieting the spirit and nourishing the heart. AIM OF THE STUDY: The present study investigated the effect of KXS on chronic fatigue syndrome (CFS) mice induced by forced wheel running. MATERIALS AND METHODS: Seventy two healthy adult male Kunming mice were randomly divided into six groups: home cage control group, CFS group, CFS group with Modafinil treatment at 13 mg/kg/d doge, KXS treatment at 175 mg/kg/d, 350 mg/kg/d and 700 mg/kg/d doge. CFS mice were induced by forced wheel running with higher speed for 4 weeks and then taken an exhausted exercise. The biochemical parameters including serum lactate dehydrogenase (LDH), serum urea nitrogen (SUN), serum testosterone (T), liver glycogen (LG), muscle glycogen (MG) and muscle lactic acid (MLA) were determined by using commercially available kits. The splenocytes proliferation from mice was examined by MTT method. The levels of interleukin-2 (IL-2) and interleukin-4 (IL-4) secreted by splenocytes were determined by ELISA. RESULTS: CFS mice with KXS administration exhibited less electric shock time when compared with CFS group without drug treatment. The effect of KXS has after demonstrated reduction in SUN, LDH and MLA levels and an increase in T, LG and MG levels. CFS mice with KXS could improve the proliferation of splenocytes compared with CFS group without drug treatment. The cultured splenocytes from CFS mice without KXS supplementation produced more interleukin-2 (IL-2) but less interleukin-4 (IL-4) when compared with home cage control mice. The cultured splenocytes of CFS mice with KXS supplementation produced more interleukin-2 (IL-2) but less interleukin-4 (IL-4) when compared with CFS group without drug treatment. CONCLUSIONS: The results of this preliminary study provide evidence that KXS could ameliorate CFS by affecting the physiological markers for fatigue. This study also supported the use of KXS against CFS by improving the proliferation of splenocytes from CFS mice and modulating the disturbance of cytokines induced by CFS.
Carbonell-Baeza A, Aparicio VA, Chillón P, Femia P, Delgado-Fernandez M, Ruiz	Department of Physical Education and Sport, University of Granada, Granada, Spain. anellba@ugr.es	Effectiveness of multidisciplinary therapy on symptomatology and quality of life in	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S97-103.	OBJECTIVES: To study the effects of a 3-month multidisciplinary intervention based on exercise and psychological therapy on symptomatology and quality of life in women with fibromyalgia. METHODS: Seventy-five women with fibromyalgia volunteered to participate and were allocated to a 3-month (3-times/week) multidisciplinary (pool, land-based and psychological session based on the Acceptance and Commitment

JR.		women with fibromyalgia.		Therapy) intervention (n=41), or to a usual care group (n=34). Sixty-five women with fibromyalgia completed the study protocol (n=33 multidisciplinary intervention, aged 51.4±7.4 years and n=32 usual care group, aged 50.0±7.3 years). The outcomes variables were Fibromyalgia Impact Questionnaire (FIQ), Short Form Health Survey 36 (SF-36), Hospital Anxiety and Depression Scale, Vanderbilt Pain Management Inventory and Rosenberg Self-Esteem Scale. RESULTS: We observed a significant interaction effect (group*time) for the FIQ total score, the subscales fatigue, stiffness, anxiety and depression, and the subscales of SF-36 physical role, bodily pain, vitality and social functioning. Post-hoc analysis revealed significant improvements in total score of FIQ ($p<0.001$), fatigue ($p=0.001$), stiffness ($p<0.001$), anxiety ($p=0.011$), depression ($p=0.008$), physical role ($p=0.002$), bodily pain ($p<0.001$), vitality ($p<0.001$) and social functioning ($p<0.001$) in the intervention group, whereas in the control group, there was a significant worsening in the subscale depression ($p=0.006$) and social functioning ($p=0.019$). CONCLUSIONS: A 3-month low-moderate intensity multidisciplinary intervention improved fibromyalgia symptomatology and quality of life in women with fibromyalgia.
Castori M, Morlino S, Celletti C, Celli M, Morrone A, Colombi M, Camerota F, Grammatico P.	Division of Medical Genetics, Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy. mcastori@scamilloforlanini.rm.it	Management of pain and fatigue in the joint hypermobility syndrome (a.k.a. Ehlers-Danlos syndrome, hypermobility type): principles and proposal for a multidisciplinary approach.	Am J Med Genet A. 2012 Aug;158A(8):2055-70. doi: 10.1002/ajmg.a.35483.	Joint hypermobility syndrome (JHS), or Ehlers-Danlos syndrome (EDS) hypermobility type (EDS-HT), is a underdiagnosed heritable connective tissue disorder characterized by generalized joint hypermobility and a wide range of visceral, pelvic, neurologic, and cognitive dysfunctions. Deterioration of quality of life is mainly associated with pain and fatigue. Except for the recognized effectiveness of physiotherapy for some musculoskeletal features, there are no standardized guidelines for the assessment and treatment of pain and fatigue. In this work, a practical classification of pain presentations and factors contributing in generating painful sensations in JHS/EDS-HT is proposed. Pain can be topographically classified in articular limb (acute/subacute and chronic), muscular limb (myofascial and fibromyalgia), neuropathic limb, back/neck, abdominal and pelvic pain, and headache. For selected forms of pain, specific predisposing characteristics are outlined. Fatigue appears as the result of multiple factors, including muscle weakness, respiratory insufficiency, unrefreshing sleep, dysautonomia, intestinal malabsorption, reactive depression/anxiety, and excessive use of analgesics. A set of lifestyle recommendations to instruct patients as well as specific investigations aimed at characterizing pain and fatigue are identified. Available treatment options are discussed in the set of a structured multidisciplinary approach based on reliable outcome tools.
Castori M, Ritelli M, Zoppi N, Molisso L, Chiarelli N, Zaccagna F, Grammatico P, Colombi M.	Medical Genetics, Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy.	Adult presentation of arterial tortuosity syndrome in a 51-year-old woman with a novel homozygous c.1411+1G>A	Am J Med Genet A. 2012 May;158A(5):1164-9. doi: 10.1002/ajmg.a.35266.	Arterial tortuosity syndrome (ATS) is an autosomal recessive connective tissue disorder, mainly characterized by tortuosity and elongation of the large- and medium-sized arteries with predisposition to stenoses and aneurysms. ATS is caused by mutations in the SLC2A10 gene, encoding for the facilitative glucose transporter 10 (GLUT10) and is described typically in pediatric patients. We report on a 51-year-old woman, originally ascertained because of unexplained widespread chronic pain and

	mcastori@scamilloforlanini.rm.it	mutation in the SLC2A10 gene.		positive family history of aortic malformation. The main findings included aged appearance, congenital joint hypermobility, joint instability complications, chronic fatigue syndrome, progressive painful joint stiffness, abdominal hernias, pelvic prolapses, multiple cardiac valve prolapses, varicose veins, easy bruising, and gingival recession. Vascular imaging revealed kinking and anomalous origin of the aortic arch branches, marked tortuosity of the aorta, pulmonary and most middle arteries, and a small aneurysm of the splenic artery. SLC2A10 analysis disclosed homozygosity for the novel c.1411+1G>A splice mutation, leading to a 41 amino acids GLUT10 internal deletion. Expression study by immunofluorescence using healthy control cells showed lack of membrane internalization of GLUT10 in patient's skin fibroblasts. This report describes the first splice-site SLC2A10 mutation and increases to 19 the repertoire of known mutations in this gene. Comparison with the few previously published adult patients with ATS contributes to the natural history of this condition, which is probably under diagnosed within the expanding family of inherited connective tissue disorders.
Castori M, Sperduti I, Celletti C, Camerota F, Grammatico P.	Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy. mcastori@scamilloforlanini.rm.it	Symptom and joint mobility progression in the joint hypermobility syndrome (Ehlers-Danlos syndrome, hypermobility type).	Clin Exp Rheumatol. 2011 Nov-Dec;29(6):998-1005.	OBJECTIVES: To evaluate progression of symptoms and joint mobility in the joint hypermobility syndrome (JHS) in order to identify specific disease pictures by age at presentation. METHODS: Fifty JHS patients (44 females, 6 males) were evaluated by Beighton score (BS) calculation, and presence/absence and age at onset of 20 key symptoms. Incidence and prevalence rates by age at onset and sex were calculated and compared by chi-square, Fisher's exact test and Mann-Whitney U-test. Relationship between BS and age at examination was evaluated by the Spearman rho correlation. The existence of an age cut-off separating patients with or without a positive BS was analysed by the receiver operating characteristic analysis. Influence of age on the single components of the BS was also investigated. RESULTS: Except for isolated features, the overall clinical presentation was the same between sexes. In the whole sample, statistically significant differences by age at presentation were registered for fatigue, myalgias, muscle cramps, strains/sprains, dislocations, tendon ruptures, tendonitis, gastroesophageal reflux, chronic gastritis, constipation/diarrhoea and abdominal hernias. A clear inverse correlation between age at examination and BS was demonstrated with an age cut-off fixed at 33 years. Among the components of the BS, spine and elbow joints were not significantly influenced by age. CONCLUSIONS: This study confirmed the existence of a protean clinical history of JHS which may be exemplified in different phases with distinguishable presentations. The knowledge of the peculiarities of each of them will help the practitioner in recognising and, hopefully, treating this condition.
Castori M, Sperduti I, Celletti C, Camerota F, Grammatico P.	Medical Genetics, Department of Molecular Medicine, Sapienza University,	Symptom and joint mobility progression in the joint hypermobility	Clin Exp Rheumatol. 2011 Nov 30.	OBJECTIVES: To evaluate progression of symptoms and joint mobility in the joint hypermobility syndrome (JHS) in order to identify specific disease pictures by age at presentation. METHODS: Fifty JHS patients (44 females, 6 males) were evaluated by Beighton score (BS) calculation, and presence/absence and age at onset of 20 key

	San Camillo-Forlanini Hospital, Rome, Italy. mcastori@scamilloforlanini.rm.it.	syndrome		symptoms. Incidence and prevalence rates by age at onset and sex were calculated and compared by chi-square, Fisher's exact test and Mann-Whitney U-test. Relationship between BS and age at examination was evaluated by the Spearman rho correlation. The existence of an age cut-off separating patients with or without a positive BS was analysed by the receiver operating characteristic analysis. Influence of age on the single components of the BS was also investigated. RESULTS: Except for isolated features, the overall clinical presentation was the same between sexes. In the whole sample, statistically significant differences by age at presentation were registered for fatigue, myalgias, muscle cramps, strains/sprains, dislocations, tendon ruptures, tendonitis, gastroesophageal reflux, chronic gastritis, constipation/diarrhoea and abdominal hernias. A clear inverse correlation between age at examination and BS was demonstrated with an age cut-off fixed at 33 years. Among the components of the BS, spine and elbow joints were not significantly influenced by age. CONCLUSIONS: This study confirmed the existence of a protean clinical history of JHS which may be exemplified in different phases with distinguishable presentations. The knowledge of the peculiarities of each of them will help the practitioner in recognising and, hopefully, treating this condition.
Cavalcante AG, de Bruin PF, de Bruin VM, Pereira ED, Cavalcante MM, Nunes DM, Viana CS.	Faculdade de Medicina, Universidade Federal do Ceará, Brazil.	Restless legs syndrome, sleep impairment, and fatigue in chronic obstructive pulmonary disease.	Sleep Med. 2012 Aug;13(7):842-7. doi: 10.1016/j.sleep.2012.03.017.	OBJECTIVE: To investigate the frequency of factors associated with restless legs syndrome (RLS) in patients with chronic obstructive pulmonary disease (COPD). METHODS: RLS diagnosis was investigated (International RLS Study Group, IRLSSG) and severity was assessed (IRLS rating scale) in 104 consecutive COPD patients (age 69.1±8). Other measures were dyspnea severity (Modified Medical Research Council, MMRC), sleep quality (Pittsburgh Sleep Quality Index, PSQI), daytime somnolence (Epworth Sleepiness Scale, ESS), depressive symptoms (Beck Depression Inventory, BDI-II), and fatigue (Fatigue Severity Scale, FSS). Laboratory values included hemoglobin, ferritin, creatinine, and fibrinogen. RESULTS: Thirty-two patients (30.8%) were diagnosed with RLS (65.6% women), which was moderate/severe (IRLS >11) in 26 (81.3%). RLS symptoms started after age 40 in most patients (93.3%). RLS patients had poorer sleep quality (PSQI >5=59.6%; p=0.002), worse fatigue (FSS >27=51%; p=0.005), and more depressive symptoms (BDI-II >10=14.4%; p=0.005). Patients with RLS also presented more severe dyspnea (p=0.009) and lower creatinine levels (p=0.005). Overall, fatigue severity was correlated with older age (p=0.001); level of dyspnea was positively correlated with PSQI and FSS (p<0.005) and negatively correlated with ferritin (p=0.03) and creatinine (p=0.005), and PSQI scores correlated positively with FSS (p<0.005) and negatively with ferritin (p=0.005) and creatinine (p=0.02). Quality of sleep was independently predicted by dyspnea severity and creatinine and fatigue by age and depression. CONCLUSION: RLS is common in COPD. Patients with RLS have low creatinine, poorer quality of sleep, and more fatigue and depressive symptoms. RLS symptom severity is correlated to lower ferritin and severity of dyspnea.

Cella M, White PD, Sharpe M, Chalder T.	Institute of Psychiatry, King's College London, UK.	Cognitions, behaviours and co-morbid psychiatric diagnoses in patients with chronic fatigue syndrome.	Psychol Med. 2013 Feb;43(2):375-80. doi: 10.1017/S0033291712000979.	BACKGROUND: Specific cognitions and behaviours are hypothesized to be important in maintaining chronic fatigue syndrome (CFS). Previous research has shown that a substantial proportion of CFS patients have co-morbid anxiety and/or depression. This study aims to measure the prevalence of specific cognitions and behaviours in patients with CFS and to determine their association with co-morbid anxiety or depression disorders. Method A total of 640 patients meeting Oxford criteria for CFS were recruited into a treatment trial (i.e. the PACE trial). Measures analysed were: the Cognitive Behavioural Response Questionnaire, the Chalder Fatigue Scale and the Work and Social Adjustment Scale. Anxiety and depression diagnoses were from the Structured Clinical Interview for DSM-IV. Multivariate analysis of variance was used to explore the associations between cognitive-behavioural factors in patients with and without co-morbid anxiety and/or depression. RESULTS: Of the total sample, 54% had a diagnosis of CFS and no depression or anxiety disorder, 14% had CFS and one anxiety disorder, 14% had CFS and depressive disorder and 18% had CFS and both depression and anxiety disorders. Cognitive and behavioural factors were associated with co-morbid diagnoses; however, some of the mean differences between groups were small. Beliefs about damage and symptom focussing were more frequent in patients with anxiety disorders while embarrassment and behavioural avoidance were more common in patients with depressive disorder. CONCLUSIONS: Cognitions and behaviours hypothesized to perpetuate CFS differed in patients with concomitant depression and anxiety. Cognitive behavioural treatments should be tailored appropriately.
Chalder T, Sharpe M, White PD.	[No address quoted]	PACE trial clarification.	Lancet. 2012 Feb 18;379(9816):616. doi: 10.1016/S0140-6736(12)60267-0.	Comment on Lancet. 2011 Mar 5;377(9768):823-36.
Chandran V, Pal PK, Reddy JY, Thennarasu K, Yadav R, Shivashankar N.	Department of Neurology, National Institute of Mental Health & Neurosciences, Bangalore, India.	Non-motor features in essential tremor.	Acta Neurol Scand. 2012 May;125(5):332-7. doi: 10.1111/j.1600-0404.2011.01573.x.	INTRODUCTION: Essential tremor (ET) is increasingly recognized to have several non-motor manifestations. The aim of this study was to determine the prevalence of non-motor manifestations in ET and its impact on the quality of life (QOL). METHODS: This was a cross-sectional case-control questionnaire-based study. The subjects were 50 patients with ET and 50 matched healthy controls. All subjects were assessed by Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, Parkinson Fatigue Scale, Brief Pain Inventory, Hamilton Anxiety Rating Scale, and Hamilton Depression Rating Scale. In addition, QOL in Essential Tremor questionnaire was administered to patients with ET. RESULTS: Patients with ET, when compared with controls, had significantly higher prevalence and higher mean scores of sleep disturbances (46% vs 8%, $P < 0.001$; 5.9 ± 4.6 vs 2.6 ± 2.3, $P < 0.001$), fatigue (30% vs 8%, $P = 0.009$; 5.8 ± 0.8 vs 2.5 ± 0.4, $P < 0.001$), anxiety (66% vs 18%, $P = 0.009$; 7.4 ± 9.0 vs 0.7 ± 2.6, $P < 0.001$), depression (44% vs 8%, $P = 0.009$; 7.8 ± 7.9 vs 1.7 ± 3.3, $P < 0.001$) as well as higher mean score of pain severity (1.9 ± 2.3 vs 0.6 ± 1.2, $P = 0.001$) and interference

				owing to pain (2.0 ± 2.9 vs 0.5 ± 1.2, P = 0.001). Following hierarchical regression analysis, depression was the only non-motor feature that affected the QOL. CONCLUSION: There was a significantly higher prevalence and greater severity of sleep disturbances, fatigue, pain, anxiety, and depression in patients with ET and depression significantly affected the QOL.
Chang CM, Warren JL, Engels EA.	Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, Maryland.	Chronic fatigue syndrome and subsequent risk of cancer among elderly US adults	Cancer. 2012 Dec 1;118(23):5929-36. doi: 10.1002/cncr.27612.	BACKGROUND: The cause of chronic fatigue syndrome (CFS) is unknown but is thought to be associated with immune abnormalities or infection. Because cancer can arise from similar conditions, associations between CFS and cancer were examined in a population-based case-control study among the US elderly. METHODS: Using linked Surveillance, Epidemiology, and End Results (SEER)-Medicare registry data, approximately 1.2 million cancer cases and 100,000 controls (age range, 66-99 years; 1992-2005) were evaluated. CFS was identified in the period more than 1 year prior to selection, using linked Medicare claims. Unconditional logistic regression was used to estimate the odds ratios (ORs) comparing the CFS prevalence in cases and controls, adjusting for age, sex, and selection year. All statistical tests were 2-sided. RESULTS: CFS was present in 0.5% of cancer cases overall and 0.5% of controls. CFS was associated with an increased risk of non-Hodgkin lymphoma (NHL) (OR = 1.29, 95% confidence interval [CI] = 1.16-1.43, P = 1.7 × 10(-6)). Among NHL subtypes, CFS was associated with diffuse large B cell lymphoma (OR = 1.34, 95% CI = 1.12-1.61), marginal zone lymphoma (OR = 1.88, 95% CI = 1.38-2.57), and B cell NHL not otherwise specified (OR = 1.51, 95% CI = 1.03-2.23). CFS associations with NHL overall and NHL subtypes remained elevated after excluding patients with medical conditions related to CFS or NHL, such as autoimmune conditions. CFS was also associated, although not after multiple comparison adjustment, with cancers of the pancreas (OR = 1.25, 95% CI = 1.07-1.47), kidney (OR = 1.27, 95% CI = 1.07-1.49), breast (OR = 0.85, 95% CI = 0.74-0.98), and oral cavity and pharynx (OR = 0.70, 95% CI = 0.49-1.00). CONCLUSIONS: Chronic immune activation or an infection associated with CFS may play a role in explaining the increased risk of NHL.
Chapenko S, Krumina A, Logina I, Rasa S, Chistjakovs M, Sultanova A, Viksna L, Murovska M.	August Kirchenstein Institute of Microbiology and Virology, Riga Stradins University, Ratsupites Street 5, LV-1067 Riga, Latvia.	Association of active human herpesvirus-6, -7 and parvovirus b19 infection with clinical outcomes in patients with myalgic encephalomyelitis/chronic fatigue syndrome.	Adv Virol. 2012;2012:205085. doi: 10.1155/2012/205085.	Frequency of active human herpesvirus-6, -7 (HHV-6, HHV-7) and parvovirus B19 (B19) infection/coinfection and its association with clinical course of ME/CFS was evaluated. 108 ME/CFS patients and 90 practically healthy persons were enrolled in the study. Viral genomic sequences were detected by PCR, virus-specific antibodies and cytokine levels-by ELISA, HHV-6 variants-by restriction analysis. Active viral infection including concurrent infection was found in 64.8% (70/108) of patients and in 13.3% (12/90) of practically healthy persons. Increase in peripheral blood leukocyte DNA HHV-6 load as well as in proinflammatory cytokines' levels was detected in patients during active viral infection. Definite relationship was observed between active betaherpesvirus infection and subfebrility, lymphadenopathy and malaise after exertion, and between active B19 infection and multijoint pain. Neuropsychological disturbances were detected in all patients. The manifestation of symptoms was of

				more frequent occurrence in patients with concurrent infection. The high rate of active HHV-6, HHV-7 and B19 infection/coinfection with the simultaneous increase in plasma proinflammatory cytokines' level as well as the association between active viral infection and distinctive types of clinical symptoms shows necessity of simultaneous study of these viral infections for identification of possible subsets of ME/CFS.
Chelimsky G, Heller E, Buffington CA, Rackley R, Zhang D, Chelimsky T.	Department of Pediatric Gastroenterology, Medical College of Wisconsin Milwaukee, WI, USA.	Co-morbidities of interstitial cystitis.	Front Neurosci. 2012;6:114. doi: 10.3389/fnins.2012.00114.	Introduction: This study aimed to estimate the proportion of patients with interstitial cystitis/painful bladder syndrome (IC/BPS) with systemic dysfunction associated co-morbidities such as irritable bowel syndrome (IBS) and fibromyalgia (FM). Materials and Methods: Two groups of subjects with IC/BPS were included: (1) physician diagnosed patients with IC/BPS and (2) subjects meeting NIDDK IC/PBS criteria based on a questionnaire (ODYSA). These groups were compared to healthy controls matched for age and socio-economic status. NIDDK criteria required: pain with bladder filling that improves with emptying, urinary urgency due to discomfort or pain, polyuria >11 times/24 h, and nocturia >2 times/night. The ODYSA instrument evaluates symptoms pertaining to a range of disorders including chronic fatigue, orthostatic intolerance, syncope, IBS, dyspepsia, cyclic vomiting syndrome, headaches and migraines, sleep, Raynaud's syndrome, and chronic aches and pains. Results: IC/BPS was diagnosed in 26 subjects (mean age 47 ± 16 years, 92% females), 58 had symptoms of IC/BPS by NIDDK criteria (mean age 40 ± 17 years, 79% females) and 48 were healthy controls (mean age 31 ± 14 years, mean age 77%). Co-morbid complaints in the IC/BPS groups included gastrointestinal symptoms suggestive of IBS and dyspepsia, sleep abnormalities with delayed onset of sleep, feeling poorly refreshed in the morning, waking up before needed, snoring, severe chronic fatigue and chronic generalized pain, migraines, and syncope. Discussion: Patients with IC/BPS had co-morbid central and autonomic nervous system disorders. Our findings mirror those of others in regard to IBS, symptoms suggestive of FM, chronic pain, and migraine. High rates of syncope and functional dyspepsia found in the IC/BPS groups merit further study to determine if IC/BPS is part of a diffuse disorder of central, autonomic, and sensory processing affecting multiple organs outside the bladder.
Chen M, Cheung FW, Chan MH, Hui PK, Ip SP, Ling YH, Che CT, Liu WK.	School of Chinese Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong.	Protective roles of Cordyceps on lung fibrosis in cellular and rat models.	J Ethnopharmacol. 2012 Sep 28;143(2):448-54. doi: 10.1016/j.jep.2012.06.033	ETHNOPHARMACOLOGICAL RELEVANCE: Cordyceps sinensis is a fungus used in traditional Chinese medicine as a tonic to soothe the lung for the treatment of fatigue and respiratory diseases. Idiopathic pulmonary fibrosis is a chronic, irreversible and debilitating lung disease showing fibroblast/myofibroblast expansion and excessive deposition of extracellular matrix in the interstitium leading to breathing difficulty. Our previous observation revealed a partial relief of lung fibrosis in patients suffering from severe acute respiratory syndrome (SARS). We hypothesize that Cordyceps has beneficial effects on lung fibrosis and the objective of this study is to explore the target(s) of Cordyceps in the relief of lung fibrosis in animal and cell models and to gain insight into its underlying mechanisms. MATERIAL AND METHODS: A rat model of

				bleomycin (BLM)-induced lung fibrosis and a fibrotic cell model with transforming growth factor beta-1 induction were employed in the studies. RESULTS: Reduction of infiltration of inflammatory cells, deposition of fibroblastic loci and collagen, formation of reactive oxygen species, and production of cytokines, as well as recovery from imbalance of MMP-9/TIMP-1, were observed in fibrotic rats after treatment with Cordyceps in preventive (from the day of BLM administration) and therapeutic (from 14 days after BLM) regimens. In a fibrotic cell model with transforming growth factor beta-1 induction, the human lung epithelial A549 acquired a mesenchymal phenotype and an increase of vimentin expression with a concomitant decrease of E-cadherin. This epithelial-mesenchymal transition could be partially reverted by cordycepin, a major component of Cordyceps. CONCLUSION: The findings provide an insight into the preventive and therapeutic potentials of Cordyceps for the treatment of lung fibrosis.
Christley Y, Duffy T, Martin CR.	School of Health, Nursing and Midwifery, University of the West of Scotland, Ayr Campus, UK.	A review of the definitional criteria for chronic fatigue syndrome.	J Eval Clin Pract. 2012 Feb;18(1):25-31. doi: 10.1111/j.1365-2753.2010.01512.x.	RATIONALE, AIMS AND OBJECTIVES: The research community has for more than three decades tried to unravel the diagnostic mystery that is Chronic Fatigue Syndrome (CFS). This has resulted in considerable amounts of time and money being invested in attempts aimed at establishing the aetiology and pathogenesis of CFS. All of this investment has produced evidence of an interesting variety of endocrine, immune, infectious, muscular and neurological abnormalities in CFS; however, the cause remains elusive. The absence of a known causative agent or diagnostic test for CFS has resulted in the development of a number of CFS case definitions. As such, the main objectives of this paper are to provide a critical review of the similarities and differences between the varying approaches to CFS case definition. The conflicts and controversies that have emerged as a result of the differing definitional criterion for CFS are highlighted and the potential impact on future research is identified. METHODS, RESULTS AND CONCLUSIONS: This paper presents a critical review of the most frequently used case definitions in CFS. There are currently five case definitions of CFS; however, the most prominent and widely used of these definitions is the 1994 Centre for Disease Control and Prevention Case Definitions. However, the pre-eminence of this definition over the others has never been substantiated and it has been widely criticized for its lack of specificity. Furthermore, none of the above case definitions have produced evidence to demonstrate their accuracy or precision at defining cases of CFS. A summary description of the symptom profile included in each of the case definitions is provided. The inconsistencies that have emerged in CFS research as a consequence of differing approaches to case definition are also highlighted and discussed.
Chu L, Friedberg F, Friedman KJ, Littrell N, Stevens S, Vallings R.	International Association for CFS/ME, Chicago, IL, USA Department of	Exercise and chronic fatigue syndrome: maximize function, minimize post-	Eur J Clin Invest. 2012 Dec;42(12):1362. doi: 10.1111/j.1365-2362.2012.02723.x.	[No abstract given]

	Psychiatry and Behavioral Sciences, Stony Brook University, Stony Brook, NY, USA Department of Natural Sciences, Castleton State College, Castleton, VT, USA Workwell Foundation, Ripon, CA, USA.	exertional malaise.		
Cingöz O, Paprotka T, Delviks-Frankenberry KA, Wildt S, Hu WS, Pathak VK, Coffin JM.	Department of Molecular Biology and Microbiology, Genetics Program, Sackler School of Graduate Biomedical Sciences, Tufts University, Boston, Massachusetts, USA.	Characterization, mapping, and distribution of the two XMRV parental proviruses.	J Virol. 2012 Jan;86(1):328-38. doi: 10.1128/JVI.06022-11.	Xenotropic murine leukemia virus-related virus (XMRV) was previously reported to be associated with human prostate cancer and chronic fatigue syndrome. Our groups recently showed that XMRV was created through recombination between two endogenous murine retroviruses, PreXMRV-1 and PreXMRV-2, during the passaging of a prostate tumor xenograft in nude mice. Here, multiple approaches that led to the identification of PreXMRV-2, as well as the distribution of both parental proviruses among different mouse species, are described. The chromosomal loci of both proviruses were determined in the mouse genome, and integration site information was used to analyze the distribution of both proviruses in 48 laboratory mouse strains and 46 wild-derived strains. The strain distributions of PreXMRV-1 and PreXMRV-2 are quite different, the former being found predominantly in Asian mice and the latter in European mice, making it unlikely that the two XMRV ancestors could have recombined independently in the wild to generate an infectious virus. XMRV was not present in any of the mouse strains tested, and among the wild-derived mouse strains analyzed, not a single mouse carried both parental proviruses. Interestingly, PreXMRV-1 and PreXMRV-2 were found together in three laboratory strains, Hsd nude, NU/NU, and C57BR/cd, consistent with previous data that the recombination event that led to the generation of XMRV could have occurred only in the laboratory. The three laboratory strains carried the Xpr1(n) receptor variant nonpermissive to XMRV and xenotropic murine leukemia virus (X-MLV) infection, suggesting that the xenografted human tumor cells were required for the resulting XMRV recombinant to infect and propagate.
Clemens JQ, Elliott MN, Suttorp M, Berry SH.	Department of Urology, University of Michigan Medical Center, Ann Arbor, Michigan. Electronic address: qclemens@umich.edu.	Temporal Ordering of Interstitial Cystitis/Bladder Pain Syndrome and Non-bladder Conditions.	Urology. 2012 Dec;80(6):1227-32. doi: 10.1016/j.urology.2012.06.059.	OBJECTIVE: To examine the prevalence and timing of nonbladder conditions in a community cohort of women with symptoms of interstitial cystitis/bladder pain syndrome (IC/BPS). METHODS: As part of the Rand Interstitial Cystitis Epidemiology (RICE) study, we identified 3397 community women who met a validated case definition for IC/BPS symptoms. Each completed a survey asking if they had a physician diagnose them as having irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, migraines, panic attacks, or depression. If a positive response was received, subjects were asked to provide the age of symptom onset. All subjects were

				also asked to provide the date of IC/BPS symptom onset. RESULTS: A total of 2185 women reported a diagnosis of at least one of the nonbladder conditions. Onset of bladder symptoms was not consistently earlier or later than the onset of nonbladder symptoms. Depression tended to occur earlier (P < .05), whereas fibromyalgia generally occurred later (P < .05). Mean age of onset was lowest for migraine symptoms, depression symptoms, and panic attacks symptoms, and greatest for fibromyalgia and chronic fatigue syndrome symptoms. Mean age of irritable bowel syndrome and IC/BPS symptom onset was between these other conditions. CONCLUSION: These findings confirm the common co-occurrence of IC/BPS with chronic nonbladder conditions. In women with IC/BPS symptoms and coexistent nonbladder conditions, bladder symptoms do not uniformly predate the nonbladder symptoms. These observations suggest that phenotypic progression from isolated bladder symptoms to regional/systemic symptoms is not a predominant pattern in IC/BPS, although such a pattern may occur in a subset of individuals.
Cockshell SJ, Mathias JL.	School of Psychology, The University of Adelaide, Adelaide, SA, Australia.	Test effort in persons with Chronic Fatigue Syndrome when assessed using the Validity Indicator Profile.	J Clin Exp Neuropsychol. 2012;34(7):679-87. doi: 10.1080/13803395.2012.668176.	The current study examined the potential contribution of suboptimal effort to the cognitive deficits that are associated with Chronic Fatigue Syndrome (CFS) using the Validity Indicator Profile (VIP). Unlike most tests of effort, the VIP distinguishes between intentional and unintentional poor performance and does not assess cognitive functions that are affected by CFS, thereby reducing the risk of mistakenly attributing genuinely poor performance to reduced effort. The VIP was administered to 54 persons with CFS and 54 matched healthy community controls, and performance categorized into 1 of 4 response styles (valid: compliant; invalid: suppressed, irrelevant, inconsistent), based on the level of effort expended (high or low) and the intention to perform well or not. VIP performance was classified as valid for the majority of participants (CFS and controls), indicating high levels of effort and an intention to perform well. Three participants in the CFS group and four in the control group showed low levels of effort but an intention to do well (invalid: inconsistent). No participant performed in a manner indicative of an intent to perform poorly (invalid: suppressed, inconsistent). These findings suggest that poor effort is unlikely to contribute to cognitive test performance of persons with CFS.
Cohen J.	[No address quoted]	Intellectual property. Dispute over lab notebooks lands researcher in jail.	Science. 2011 Dec 2;334(6060):1189-90. doi: 10.1126/science.334.6060.1189.	[No abstract given]
Collin SM, Sterne JA, Hollingworth W, May MT, Crawley E.	School of Social and Community Medicine, University of Bristol, Bristol, UK.	Equity of access to specialist chronic fatigue syndrome (CFS/ME) services in England (2008-2010): a national survey and	BMJ Open. 2012 Aug 16;2(4). pii: e001417. doi: 10.1136/bmjopen-2012-001417. Print 2012.	OBJECTIVES: Provision of National Health Service (NHS) specialist chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) services in England has been deemed patchy and inconsistent. Our objective was to explore variation in the provision of NHS specialist CFS/ME services and to investigate whether access is related to measures of deprivation and inequality. DESIGN: Survey of all CFS/ME clinical teams in England, plus cross-sectional data from a subset of teams. SETTING:

		cross-sectional study.		Secondary care. OUTCOME MEASURES: We used clinic activity data from CFS/ME clinical teams in England to describe provision of specialist CFS/ME services (referral, assessment and diagnosis rates per 1000 adults per year) during 2008-2011 according to Primary Care Trust (PCT) population estimates, and to investigate whether use of services was related to PCT-level measures of deprivation and inequality. We used postcode data from seven services to investigate variation in provision by deprivation. RESULTS: Clinic activity data were obtained from 93.9% (46/49) of clinical teams in England which between them received referrals from 84.9% (129/152) of PCTs. 12 PCTs, covering a population of 2.08 million adults, provided no specialist CFS/ME service. There was a six-fold variation in referral and assessment rates between services which could not be explained by PCT-level measures of deprivation and inequality. The median assessment rate in 2010 was 0.25 (IQR 0.17, 0.35) per 1000 adults per year. 91.9% (IQR 76.5%, 100.0%) of adults assessed were diagnosed with CFS/ME. Postcode data from seven clinical teams showed that assessment rates were equal across deprivation quartiles for four teams but were 40-50% lower in the most deprived compared with the most affluent areas for three teams. CONCLUSIONS: Two million adults in England do not have access to a specialist CFS/ME service. In some areas which do have a specialist service, access is inequitable. This inequity may worsen with the impending fragmentation of NHS commissioning across England.
Cook DB, Stegner AJ, Nagelkirk PR, Meyer JD, Togo F, Natelson BH.	Department of Kinesiology, University of Wisconsin - Madison, Madison, WI 53706, USA. dcook@education.wisc.edu	Responses to exercise differ for chronic fatigue syndrome patients with fibromyalgia.	Med Sci Sports Exerc. 2012 Jun;44(6):1186-93. doi: 10.1249/MSS.0b013e3182417b9a.	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are chronic multisymptom illnesses with substantial clinical and diagnostic overlap. We have previously shown that, when controlling for aerobic fitness and accounting for comorbid FM, CFS patients do not exhibit abnormal cardiorespiratory responses during maximal aerobic exercise compared with healthy controls, despite differences in pain and exertion.PURPOSE: The purpose of the present study was to examine cardiac and perceptual responses to steady-state submaximal exercise in CFS patients and healthy controls. METHODS: Twenty-one CFS patients (13 CFS with comorbid FM (CFS + FM)) and 14 controls completed 20 min of submaximal cycling exercise. Impedance cardiography was used to determine cardiac responses during exercise. Systolic blood pressure (SBP), RPE, and leg muscle pain were also measured. Data were analyzed using a doubly multivariate, repeated-measures MANOVA to model the exercise response. RESULTS: There was a significant multivariate time-by-group interaction ($P < 0.05$). The CFS + FM group exhibited an exercise response characterized by higher stroke index, ventilatory equivalents for oxygen and carbon dioxide and RPE, lower SBP, and similar HR responses compared to controls. CONCLUSIONS: The present results extend on our previous work with maximal exercise and show that CFS and CFS + FM differ in their responses to steady-state exercise. These results highlight the importance of accounting for comorbid conditions when conducting CFS research, particularly when examining psychophysiological responses to exercise.
Cool M, Bouchard	Laboratory of	No detectable XMRV	Virology. 2011 Nov	We investigated the presence of XMRV in a cohort of Quebec patients with chronic

N, Massé G, Laganière B, Dumont A, Hanna Z, Phaneuf D, Morisset R, Jolicoeur P.	Molecular Biology, Clinical Research Institute of Montreal, Montreal, Quebec, Canada H2W 1R7.	in subjects with chronic fatigue syndrome from Quebec.	10;420(1):66-72. doi: 10.1016/j.virol.2011.08.018.	fatigue syndrome (CFS). DNA was purified from activated peripheral blood mononuclear cells (PBMCs) and PCR was used to detect XMRV gag and env in 72 patients. Anti-XMRV antibodies were searched in sera of 62 patients by Western blot analysis. Attempts to detect XMRV antigens was made, using immunofluorescence with Gag anti-p30 antiserum on activated PBMC from 50 patients. Plasma viremia was measured by RT-PCR on 9 subjects. Finally, detection of infectious virus in 113 CFS subjects was made by co-culture of PHA+IL-2 activated PBMC with human LNCaP carcinoma cells, and by infecting the same susceptible cells with plasma, using a reverse transcriptase (RT) assay as a readout in both experiments. No detection of XMRV footprints nor infectious virus was detected with any of the approaches, in any of the tested individuals.
Cordero MD, Cano-García FJ, Alcocer-Gómez E, De Miguel M, Sánchez-Alcázar JA.	Centro Andaluz de Biología del Desarrollo, Universidad Pablo de Olavide-CSIC-Junta de Andalucía and Centro de Investigación Biomédica en Red de Enfermedades Raras, ISCIII, Sevilla, Spain. mdcormor@upo.es	Oxidative stress correlates with headache symptoms in fibromyalgia: coenzyme Q_{10} effect on clinical improvement.	PLoS One. 2012;7(4):e35677. doi: 10.1371/journal.pone.0035677.	BACKGROUND: Fibromyalgia (FM) is a chronic pain syndrome with unknown etiology and a wide spectrum of symptoms such as allodynia, debilitating fatigue, joint stiffness and migraine. Recent studies have shown some evidences demonstrating that oxidative stress is associated to clinical symptoms in FM of fibromyalgia. We examined oxidative stress and bioenergetic status in blood mononuclear cells (BMCs) and its association to headache symptoms in FM patients. The effects of oral coenzyme Q(10) (CoQ(10)) supplementation on biochemical markers and clinical improvement were also evaluated. METHODS: We studied 20 FM patients and 15 healthy controls. Clinical parameters were evaluated using the Fibromyalgia Impact Questionnaire (FIQ), visual analogues scales (VAS), and the Headache Impact Test (HIT-6). Oxidative stress was determined by measuring CoQ(10), catalase and lipid peroxidation (LPO) levels in BMCs. Bioenergetic status was assessed by measuring ATP levels in BMCs. RESULTS: We found decreased CoQ(10), catalase and ATP levels in BMCs from FM patients as compared to normal control ($P < 0.05$ and $P < 0.001$, respectively) We also found increased level of LPO in BMCs from FM patients as compared to normal control ($P < 0.001$). Significant negative correlations between CoQ(10) or catalase levels in BMCs and headache parameters were observed ($r = -0.59$, $P < 0.05$; $r = -0.68$, $P < 0.05$, respectively). Furthermore, LPO levels showed a significant positive correlation with HIT-6 ($r = 0.33$, $P<0.05$). Oral CoQ(10) supplementation restored biochemical parameters and induced a significant improvement in clinical and headache symptoms ($P < 0.001$). DISCUSSION: The results of this study suggest a role for mitochondrial dysfunction and oxidative stress in the headache symptoms associated with FM. CoQ10 supplementation should be examined in a larger placebo controlled trial as a possible treatment in FM.
Côté M, Zheng YM, Liu SL.	Department of Microbiology and Immunology, McGill University, Montreal, Quebec, Canada.	Membrane fusion and cell entry of XMRV are pH-independent and modulated by the	PLoS One. 2012;7(3):e33734. doi: 10.1371/journal.pone.0033734.	Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus that was originally identified from human prostate cancer patients and subsequently linked to chronic fatigue syndrome. Recent studies showed that XMRV is a recombinant mouse retrovirus; hence, its association with human diseases has become questionable. Here, we demonstrated that XMRV envelope (Env)-mediated pseudoviral infection is

		envelope glycoprotein's cytoplasmic tail.		not blocked by lysosomotropic agents and cellular protease inhibitors, suggesting that XMRV entry is not pH-dependent. The full length XMRV Env was unable to induce syncytia formation and cell-cell fusion, even in cells overexpressing the viral receptor, XPR1. However, truncation of the C-terminal 21 or 33 amino acid residues in the cytoplasmic tail (CT) of XMRV Env induced substantial membrane fusion, not only in the permissive 293 cells but also in the nonpermissive CHO cells that lack a functional XPR1 receptor. The increased fusion activities of these truncations correlated with their enhanced SU shedding into culture media, suggesting conformational changes in the ectodomain of XMRV Env. Noticeably, further truncation of the CT of XMRV Env proximal to the membrane-spanning domain severely impaired the Env fusogenicity, as well as dramatically decreased the Env incorporations into MoMLV oncoretroviral and HIV-1 lentiviral vectors resulting in greatly reduced viral transductions. Collectively, our studies reveal that XMRV entry does not require a low pH or low pH-dependent host proteases, and that the cytoplasmic tail of XMRV Env critically modulates membrane fusion and cell entry. Our data also imply that additional cellular factors besides XPR1 are likely to be involved in XMRV entry.
Cottle LE, Mekonnen E, Beadsworth MB, Miller AR, Beeching NJ.	Tropical and Infectious Disease Unit, Royal Liverpool University Hospital, Prescot Street, Liverpool L7 8XP, UK.	Lyme disease in a British referral clinic.	QJM. 2012 Jun;105(6):537-43. doi: 10.1093/qjmed/hcs003.	BACKGROUND: Concerns about over-diagnosis and inappropriate management of Lyme disease (LD) are well documented in North America and supported by clinical data. There are few parallel data on the situation in the UK. AIM: To describe the patterns of referral, investigation, diagnosis and treatment of patients with suspected LD referred to an infectious disease unit in Liverpool, UK. Previous management by National Health Service (NHS) and non-NHS practitioners was reviewed. DESIGN: Descriptive study conducted by retrospective casenotes review. METHODS: Retrospective casenotes review of adults referred with possible LD to an infectious disease unit in Liverpool, UK, over 5 years (2006-2010). RESULTS: Of 115 patients, 27 (23%) were diagnosed with LD, 38 (33%) with chronic fatigue syndrome (CFS) and 13 (11%) with other medical conditions. No specific diagnosis could be made in 38 (33%). At least 53 unnecessary antibiotic courses had been given by non-NHS practitioners; 21 unnecessary courses had been prescribed by NHS practitioners. Among 38 patients, 17 (45%) with CFS had been misdiagnosed as having LD by non-NHS practitioners. CONCLUSION: A minority of referred patients had LD, while a third had CFS. LD is over-diagnosed by non-specialists, reflecting the complexities of clinical and/or laboratory diagnosis. Patients with CFS were susceptible to misdiagnosis in non-NHS settings, reinforcing concerns about missed opportunities for appropriate treatment for this group and about the use of inappropriate diagnostic modalities and anti-microbials in non-NHS settings.
Crawford BK, Piault EC, Lai C, Bennett RM.	Mapi Values, Tokyo, Japan. bruce.crawford@mapivalues.com	Assessing fibromyalgia-related fatigue: content validity and	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S34-43.	OBJECTIVES: To document 1) the content validity and 2) measure improvements in fatigue, using the Fatigue Visual Analogue Scale (VAS) assessment tool in patients with fibromyalgia. METHODS: The relevance and comprehensiveness of the Fatigue VAS were tested through a qualitative analysis of 20 subjects' verbatim transcripts from

		psychometric performance of the Fatigue Visual Analog Scale in adult patients with fibromyalgia.		semi-structured qualitative interviews. Data from two randomised, controller trials in fibromyalgia (n=1121) were used to conduct correlation analyses with the Fatigue and Tiredness items from the Fibromyalgia Impact Questionnaire (FIQ) and the Short Form-36 Vitality scale. Known-groups and cross classification analyses were conducted to demonstrate the ability to measure improvement in fatigue using the Fatigue VAS. RESULTS: All subjects spontaneously reported that fatigue was an important symptom to capture in fibromyalgia. The Fatigue VAS was well understood by most subjects (n=18/20). High correlations (Pearson r>0.75) and good agreement (k>0.66) were found between the Fatigue VAS and the FIQ tiredness items no. 16 and 17 and SF-36™ Vitality scale. In both clinical trials there was a substantial separation of approximately 20 points on the mean change in the Fatigue VAS score between responders (>30% improvement in pain VAS) and non-responders. CONCLUSIONS: Previous studies have confirmed that fatigue is a major component of the fibromyalgia experience. This current study reports that fibromyalgia patients spontaneously rated fatigue as a highly significant feature of their illness, and supports the use of the Fatigue VAS as a valid questionnaire in fibromyalgia clinical trials.
Crawford J.	[No address quoted]	Internet-based CBT for adolescents with chronic fatigue syndrome.	Lancet. 2012 Aug 11;380(9841):561-2; author reply 562. doi: 10.1016/S0140-6736(12)61325-7.	Comment on Lancet. 2012 Apr 14;379(9824):1412-8.
Crawley EM, Emond AM, Sterne JA.	Centre for Child and Adolescent Health, School of Social and Community Medicine, Bristol, UK.	Unidentified Chronic Fatigue Syndrome/myalgic encephalomyelitis (CFS/ME) is a major cause of school absence: surveillance outcomes from school-based clinics.	BMJ Open. 2011 Dec 12;1(2):e000252. doi: 10.1136/bmjopen-2011-000252. Print 2011.	Objective To investigate the feasibility of conducting clinics for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in schools. Design School-based clinical project. Participants Children aged 11-16 years were enrolled in three state secondary schools in England. Main outcome measures Number of children newly diagnosed as having CFS/ME. Methods Attendance officers identified children missing ≥20% of school in a 6-week term without a known cause, excluding those with a single episode off school, a known medical illness explaining the absence or known to be truanting. Children with fatigue were referred to a specialist CFS/ME service for further assessment. The authors compared children with CFS/ME identified through school-based clinics with those referred via health services. Outcomes of CFS/ME were evaluated at 6 weeks and 6 months. Results 461 of the 2855 enrolled children had missed ≥20% school over a 6-week period. In 315, of whom three had CFS/ME, the reason for absence was known. 112 of the 146 children with unexplained absence attended clinical review at school; two had been previously diagnosed as having CFS/ME and 42 were referred on to a specialist clinic, where 23 were newly diagnosed as having CFS/ME. Therefore, 28 of the 2855 (1.0%) children had CFS/ME. Children with CFS/ME identified through surveillance had been ill for an amount of time comparable to those referred via health services but had less fatigue (mean difference

				4.4, 95% CI 2.2 to 6.6), less disability (mean difference -5.7, 95% CI -7.9 to -3.5) and fewer symptoms (mean difference 1.86, 95% CI 0.8 to 2.93). Of 19 children followed up, six had fully recovered at 6 weeks and a further six at 6 months. Conclusions Chronic fatigue is an important cause of unexplained absence from school. Children diagnosed through school-based clinics are less severely affected than those referred to specialist services and appear to make rapid progress when they access treatment.
Crawley EM.	Centre for Child and Adolescent Health, School of Social and Community Medicine, Oakfield House, Oakfield Grove Bristol BS8 2BN, UK; esther.crawley@bristol.ac.uk.	Internet-based cognitive behavioural therapy (FITNET) is an effective treatment for adolescents with chronic fatigue syndrome.	Arch Dis Child Educ Pract Ed. 2012 Dec;97(6):238. doi: 10.1136/archdischild-2012-302484.	[No abstract given]
Creed FH, Tomenson B, Chew-Graham C, Macfarlane GJ, Davies I, Jackson J, Littlewood A, McBeth J.	School of Community Based Medicine, University of Manchester, Jean Macfarlane Building (3rd floor), Oxford Road, Manchester, M13 9PL, UK, francis.creed@manchester.ac.uk.	Multiple Somatic Symptoms Predict Impaired Health Status in Functional Somatic Syndromes.	Int J Behav Med. 2012 Aug 30.	BACKGROUND: The relationship between functional somatic syndromes and multiple somatic symptoms is unclear. PURPOSE: We assessed whether the number of somatic symptoms is a predictor of health status in three functional somatic syndromes (FSS). METHODS: In a population-based study of 990 UK adults we assessed chronic widespread pain (CWP), chronic fatigue (CF) and irritable bowel syndrome (IBS) by questionnaire and medical record data. We assessed health status (Short Form 12 and EQ-5D), number of somatic symptoms (Somatic Symptom Inventory) and anxiety/depression (Hospital Anxiety and Depression Scale) both at baseline and at follow-up 1 year later. RESULTS: The proportion of people with an FSS who also have multiple somatic symptoms (52-55 %) was similar in the three functional syndromes. The presence of multiple somatic symptoms was associated with more impaired health status both at baseline and at follow-up. This finding was not explained by severity of FSS. In the absence of multiple somatic symptoms, the health status of the FSS was fair or good. In multiple regression analysis, the number of somatic symptoms, the presence of a functional syndrome (CWP or CF) and anxiety/depression were predictors of EQ-5D thermometer at follow-up after adjustment for confounders. CONCLUSIONS: Multiple somatic symptoms in people with an FSS are associated with impaired health status and this cannot be explained by more severe functional syndrome or the presence of anxiety and depression.
Dansie EJ, Furberg H, Afari N, Buchwald D, Edwards K, Goldberg J, Schur E, Sullivan PF.	Center for Clinical and Epidemiological Research, University of Washington, Seattle, WA 98101, USA. Edansie@uw.edu	Conditions comorbid with chronic fatigue in a population-based sample.	Psychosomatics. 2012 Jan-Feb;53(1):44-50. doi: 10.1016/j.psym.2011.04.001.	BACKGROUND: Chronic fatigue syndrome (CFS) has been found to be comorbid with various medical conditions in clinical samples, but little research has investigated CFS comorbidity in population-based samples. OBJECTIVE: This study investigated conditions concurrent with a CFS-like illness among twins in the population-based Mid-Atlantic Twin Registry (MATR), including chronic widespread pain (CWP), irritable bowel syndrome (IBS), and major depressive disorder (MDD). METHOD: A survey was

				mailed to participants in the MATR in 1999. Generalized estimating equations were used to estimate odds ratios to assess associations between CFS-like illness and each comorbid condition. RESULTS: A total of 4590 completed surveys were collected. Most participants were female (86.3%); mean age was 44.7 years. Among participants with a CFS-like illness, lifetime prevalences of CWP, IBS, and MDD were 41%, 16%, and 57% respectively. Participants reporting at least one of the three comorbid conditions were about 14 times more likely to have CFS-like illness than those without CWP, IBS, or MDD (95% confidence interval 8.1%-21.3%). Only MDD showed a temporal pattern of presentation during the same year as diagnosis of CFS-like illness. Age, gender, body mass index, age at illness onset, exercise level, self-reported health status, fatigue symptoms, and personality measures did not differ between those reporting CFS-like illness with and without comorbidity. CONCLUSION: These results support findings in clinically based samples that CFS-like illness is frequently cormorbid with CWP, IBS, and/or MDD. We found no evidence that CFS-like illnesses with comorbidities are clinically distinct from those without comorbidities.
Dansie EJ, Heppner P, Furberg H, Goldberg J, Buchwald D, Afari N.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA.	The comorbidity of self-reported chronic fatigue syndrome, post-traumatic stress disorder, and traumatic symptoms.	Psychosomatics. 2012 May;53(3):250-7. doi: 10.1016/j.psym.2011.08.007.	BACKGROUND: Data from primary care and community samples suggest higher rates of post-traumatic stress disorder (PTSD) among individuals with chronic fatigue syndrome (CFS). OBJECTIVE: This study investigated the co-occurrence of CFS, PTSD, and trauma symptoms and assessed the contribution of familial factors to the association of CFS with lifetime PTSD and current traumatic symptoms. METHOD: Data on lifetime CFS and PTSD, as measured by self-report of a doctor's diagnosis of the disorder, and standardized questionnaire data on traumatic symptoms, using the Impact of Events Scale (IES), were obtained from 8544 female and male twins from the community-based University of Washington Twin Registry. RESULTS: Lifetime prevalence of CFS was 2% and lifetime prevalence of PTSD was 4%. Participants who reported a history of PTSD were over eight times more likely to report a history of CFS. Participants with scores ≥ 26 on the IES were over four times more likely to report CFS than those who had scores ≤ 25. These associations were attenuated but remained significant after adjusting for familial factors through within-twin pair analyses. CONCLUSION: These results support similar findings that a lifetime diagnosis of CFS is strongly associated with both lifetime PTSD and current traumatic symptoms, although familial factors, such as shared genetic and environmental contributions, played a limited role in the relationship between CFS, PTSD, and traumatic symptoms. These findings suggest that future research should investigate both the familial and the unique environmental factors that may give rise to both CFS and PTSD.
de Carvalho Leite JC, de L Drachler M, Killett A, Kale S, Nacul L, McArthur M, Hong CS,	School of Allied Health Professions, University of East Anglia, Norwich, England, United Kingdom, NR4	Social support needs for equity in health and social care: a thematic analysis of experiences of	Int J Equity Health. 2011 Nov 2;10(1):46. doi: 10.1186/1475-9276-10-46.	BACKGROUND: Needs-based resource allocation is fundamental to equitable care provision, which can meet the often-complex, fluctuating needs of people with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). This has posed challenges both for those providing and those seeking support providers, in building shared understanding of the condition and of actions to address it. This qualitative

O'Driscoll L, Pheby D, Campion P, Lacerda E, Poland F.	7TJ, UK. f.poland@uea.ac.uk.	people with chronic fatigue syndrome/myalgic encephalomyelitis.		study reports on needs for equity in health and social care expressed by adults living with CFS/ME. METHODS: The participants were 35 adults with CFS/ME in England, purposively selected to provide variation in clinical presentations, social backgrounds and illness experiences. Accounts of experienced needs and needs-related encounters with health and social services were obtained through a focus group (n = 6) and semi-structured interviews (n = 35). These were transcribed and needs related topics identified through data-led thematic analysis. FINDINGS: Participants emphasised needs for personalised, timely and sustained support to alleviate CFS/ME impacts and regain life control, in three thematic areas: (1) Illness symptoms, functional limitations and illness management; (2) practical support and social care; (3) financial support. Access of people with CFS/ME to support from health and social services was seen to be constrained by barriers stemming from social, cultural, organisational and professional norms and practices, further heightened for disadvantaged groups including some ethnic minorities. These reduced opportunities for their illness to be explained or associated functional limitations and social disadvantages to be addressed through social support. Participants sought more understanding of bio-psycho-social aspects of CFS/ME, of felt needs of people with CFS/ME and of human rights and disability rights, for providing person-centred, equitable care. CONCLUSIONS: Changes in attitudes of health practitioners, policy makers and general public and more flexibly organised health and social care provision are needed to address equity issues in support needs expressed by people with CFS/ME, to be underpinned by research-based knowledge and communication, for public and professional education. Policy development should include shared decision-making and coordinated action across organizations working for people with CFS/ME, human rights and disadvantaged groups. Experiences of people with CFS/ME can usefully inform an understanding of equity in their health and social care.
de Souza PA, Matheus SM, Castan EP, Campos DH, Cicogna AC, Carvalho RF, Dal-Pai-Silva M.	Department of Morphology, Institute of Biosciences, UNESP, Botucatu, São Paulo, Brazil. pats_souza@yahoo.com.br	Morphological aspects of neuromuscular junctions and gene expression of nicotinic acetylcholine receptors (nAChRs) in skeletal muscle of rats with heart failure.	J Mol Histol. 2011 Dec;42(6):557-65. doi: 10.1007/s10735-011-9354-2.	HF is syndrome initiated by a reduction in cardiac function and it is characterized by the activation of compensatory mechanisms. Muscular fatigue and dyspnoea are the more common symptoms in HF; these may be due in part to specific skeletal muscle myopathy characterized by reduced oxidative capacity, a shift from slow fatigue resistant type I to fast less fatigue resistant type II fibers and downregulation of myogenic regulatory factors (MRFs) gene expression that can regulate gene expression of nicotinic acetylcholine receptors (nAChRs). In chronic heart failure, skeletal muscle phenotypic changes could influence the maintenance of the neuromuscular junction morphology and nAChRs gene expression during this syndrome. Two groups of rats were studied: control (CT) and Heart Failure (HF), induced by a single intraperitoneal injection of monocrotaline (MCT). At the end of the experiment, HF was evaluated by clinical signs and animals were sacrificed. Soleus (SOL) muscles were removed and processed for morphological, morphometric and molecular NMJ analyses. Our major finding was an up-regulation in the gene

				expression of the alpha1 and epsilon subunits of nAChR and a spot pattern of nAChR in SOL skeletal muscle in this acute monocrotaline induced HF. Our results suggest a remodeling of nAChR alpha1 and epsilon subunit during heart failure and may provide valuable information for understanding the skeletal muscle myopathy that occurs during this syndrome.
de Tommaso M, Federici A, Serpino C, Vecchio E, Franco G, Sardaro M, Delussi M, Livrea P.	Neurophysiopathology of Pain Unit, Neurological and Psychiatric Sciences Department, Medical Faculty, Policlinico General Hospital, Aldo Moro University, Neurological Building, Piazza Giulio Cesare 11, 70124, Bari, Italy. m.detommaso@neurol.uniba.it	Clinical features of headache patients with fibromyalgia comorbidity.	J Headache Pain. 2011 Dec;12(6):629-38. doi: 10.1007/s10194-011-0377-6.	Our previous study assessed the prevalence of fibromyalgia (FM) syndrome in migraine and tension-type headache. We aimed to update our previous results, considering a larger cohort of primary headache patients who came for the first time at our tertiary headache ambulatory. A consecutive sample of 1,123 patients was screened. Frequency of FM in the main groups and types of primary headaches; discriminating factor for FM comorbidity derived from headache frequency and duration, age, anxiety, depression, headache disability, allodynia, pericranial tenderness, fatigue, quality of life and sleep, and probability of FM membership in groups; and types of primary headaches were assessed. FM was present in 174 among a total of 889 included patients. It prevailed in the tension-type headache main group (35%, $p < 0.0001$) and chronic tension-type headache subtype (44.3%, $p < 0.0001$). Headache frequency, anxiety, pericranial tenderness, poor sleep quality, and physical disability were the best discriminating variables for FM comorbidity, with 81.2% sensitivity. Patients presenting with chronic migraine and chronic tension-type headache had a higher probability of sharing the FM profile (Bonferroni test, $p < 0.01$). A phenotypic profile where headache frequency concurs with anxiety, sleep disturbance, and pericranial tenderness should be individuated to detect the development of diffuse pain in headache patients.
Deák M, Szvetnik A, Balog A, Sohár N, Varga R, Pokorny G, Tóth G, Kiss M, Kovács L.	Department of Rheumatology, Faculty of Medicine, Albert Szent-Györgyi Health Centre, University of Szeged, Szeged, Hungary.	Neuroimmune Interactions in Sjögren's Syndrome: Relationship of Exocrine Gland Dysfunction with Autoantibodies to Muscarinic Acetylcholine Receptor-3 and Mental Health Status Parameters.	Neuroimmunomodulation. 2012 Dec 12;20(2):79-86.	Objectives: Antimuscarinic acetylcholine receptor-3 (m3AChR) autoantibodies have been described in primary Sjögren's syndrome (pSS). The aim of this study was to compare various methods for their detection and to assess the contributions of anti-m3AChR and other immunological and psychosocial factors to the pathomechanism of secondary SS (sSS). Methods: Sixty-five rheumatoid arthritis (RA) patients, 103 systemic lupus erythematosus (SLE) patients, 76 pSS patients and 50 controls were compared. Three immunodominant epitopes of m3AChR were synthesized and used in ELISA. Two extracellular epitopes were also prepared in fusion with glutathione-S-transferase and one in conjugation with bovine serum albumin. Mental health status was assessed with the 36-item Short-Form Health Survey and Functional Assessment of Chronic Illness Therapy fatigue scale. Correlations were evaluated between glandular function and anti-m3AChR positivities and specificities, features of SLE and RA, and mental health parameters. Results: Fourteen RA and 27 SLE patients had sSS. The autoantibody levels to all epitopes of m3AChR were significantly higher in pSS and SLE patients than in the controls. The fusion protein forms discriminated RA from pSS and SLE; furthermore, the YNIP fusion protein also distinguished pSS from SLE. The prevalence and the mean levels of all autoantibodies did not differ statistically

				between sicca and non-sicca SLE or RA patients. Glandular dysfunction correlated with higher age in SLE and RA and an impaired health-related quality of life in SLE. Conclusions: The second and third extracellular loops of m3AChR are antigenic in pSS. Immunoassays with antigens as fusion peptides demonstrate the best performance. Sicca SLE patients have worse mental health status. Anti-m3AChR antibodies represent a peculiar example of neuroimmune interactions.
Dean ME, Karsandas R, Bland JM, Gooch D, Macpherson H.	Dept, of Health Sciences, University of York, York YO10 5DD, UK. hugh.macpherson@york.ac.uk.	Homeopathy for mental fatigue: lessons from a randomized, triple blind, placebo-controlled cross-over clinical trial.	BMC Complement Altern Med. 2012 Oct 1;12(1):167. doi: 10.1186/1472-6882-12-167.	ABSTRACT:BACKGROUND: Difficulty in controlling attention can lead to mental fatigue in the healthy population. We identified one trial reporting a benefit in patients' attention using a homeopathic formula preparation. One component of the preparation was potassium phosphate, widely available off the shelf as Kali phos 6x for cognitive problems. The aim of this exploratory trial was to assess the effectiveness of Kali phos 6x for attention problems associated with mental fatigue. METHODS: We recruited student and staff volunteers (University of York) with self-reported mental fatigue, excluding any using homeopathy or prescribed stimulants, or with a diagnosis of chronic fatigue syndrome. In a triple blind, cross-over, placebo-controlled clinical trial, 86 volunteers were randomized to receive Kali phos 6x or identical placebo 10 minutes before taking a psychological test of attention (Stroop Colour-Word Test). One week later they were crossed over and took the other preparation before repeating the test. RESULTS: We found no evidence of a treatment effect in a comparison of Kali phos 6x with placebo (Kali phos minus placebo = -1.1 (95% CI -3.0 to 0.9, P = 0.3) Stroop score units, Cohen effect size = -0.17) even when allowing for a weak period effect with accuracy scores in the second period being higher than those in the first (P = 0.05). We observed a ceiling effect in the Stroop test which undermined our ability to interpret this result. CONCLUSIONS: Kali phos 6x was not found to be effective in reducing mental fatigue. A ceiling effect in our primary outcome measure meant that we could not rule out a type II error. Thorough piloting of an adequate outcome measure could have led to an unequivocal result. CURRENT CONTROLLED TRIALS: ISRCTN16521161.
Del Prete GQ, Kearney MF, Spindler J, Wiegand A, Chertova E, Roser JD, Estes JD, Hao XP, Trubey CM, Lara A, Lee K, Chaipan C, Bess JW Jr, Nagashima K, Keele BF, Macallister R,	AIDS and Cancer Virus Program, National Cancer Institute, Frederick, Maryland, USA.	Restricted replication of xenotropic murine leukemia virus-related virus in pigtailed macaques.	J Virol. 2012 Mar;86(6):3152-66. doi: 10.1128/JVI.06886-11.	Although xenotropic murine leukemia virus-related virus (XMRV) has been previously linked to prostate cancer and myalgic encephalomyelitis/chronic fatigue syndrome, recent data indicate that results interpreted as evidence of human XMRV infection reflect laboratory contamination rather than authentic in vivo infection. Nevertheless, XMRV is a retrovirus of undefined pathogenic potential that is able to replicate in human cells. Here we describe a comprehensive analysis of two male pigtailed macaques (Macaca nemestrina) experimentally infected with XMRV. Following intravenous inoculation with >10(10) RNA copy equivalents of XMRV, viral replication was limited and transient, peaking at ≤2,200 viral RNA (vRNA) copies/ml plasma and becoming undetectable by 4 weeks postinfection, though viral DNA (vDNA) in peripheral blood mononuclear cells remained detectable through 119 days of follow-up. Similarly, vRNA was not detectable in lymph nodes by in situ hybridization despite

Smedley J, Pathak VK, Kewalramani VN, Coffin JM, Lifson JD.				detectable vDNA. Sequencing of cell-associated vDNA revealed extensive G-to-A hypermutation, suggestive of APOBEC-mediated viral restriction. Consistent with limited viral replication, we found transient upregulation of type I interferon responses that returned to baseline by 2 weeks postinfection, no detectable cellular immune responses, and limited or no spread to prostate tissue. Antibody responses, including neutralizing antibodies, however, were detectable by 2 weeks postinfection and maintained throughout the study. Both animals were healthy for the duration of follow-up. These findings indicate that XMRV replication and spread were limited in pigtailed macaques, predominantly by APOBEC-mediated hypermutation. Given that human APOBEC proteins restrict XMRV infection in vitro, human XMRV infection, if it occurred, would be expected to be characterized by similarly limited viral replication and spread.
Dell'Osso L, Carmassi C, Consoli G, Conversano C, Ramacciotti CE, Musetti L, Massimetti E, Pergentini I, Corsi M, Ciapparelli A, Bazzichi L.	Department of Psychiatry, Neurobiology, Pharmacology and Biotecnology, University of Pisa, Pisa, Italy.	Lifetime post-traumatic stress symptoms are related to the health-related quality of life and severity of pain/fatigue in patients with fibromyalgia.	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S73-8.	OBJECTIVES: The aim of the present study was to investigate the impact of lifetime potentially traumatic events, including losses, and of post-traumatic stress symptoms on the severity of illness and health-related quality of life in patients with fibromyalgia (FM). METHODS: Seventy patients with FM, diagnosed according to the American College of Rheumatology criteria, were consecutively enrolled at the Unit of Rheumatology of the University of Pisa, Italy. Assessments included: SCID-I/P; the Fibromyalgia Impact Questionnaire (FIQ) and the Medical Outcomes Study Short Form-36 Health Survey (MOS SF-36), for the severity of pain; the Health-Related Quality of Life (HRQoL); the Trauma and Loss Spectrum Self-Report (TALS-SR) life-time version. RESULTS: The FIQ total score was related to the number of loss events (Domain I) and to symptoms of grief reactions (Domain II) and re-experiencing (Domain V) of the TALS-SR. The 'VAS fatigue' scores (FIQ) were significantly related to the TALS-SR symptoms of grief reactions (Domain II) and re-experiencing (Domain V). The Mental Component Summary and Bodily Pain scores of the MOS SF-36 were significantly related to all TALS-SR domains, the latter with the exception of the VIII (Arousal). CONCLUSIONS: Our results corroborate the presence of a relationship between the lifetime exposure to potentially traumatic events, in particular loss events, and lifetime post-traumatic stress symptoms and the severity of illness and HRQoL in patients with FM.
Delviks-Frankenberry K, Cingöz O, Coffin JM, Pathak VK.	Viral Mutation Section, NCI, HIV DRP, Frederick National Laboratory for Cancer Research, Frederick, MD, United States.	Recombinant origin, contamination, and de-discovery of XMRV.	Curr Opin Virol. 2012 Aug;2(4):499-507. doi: 10.1016/j.coviro.2012.06.009	The discovery and de-discovery of the xenotropic murine leukemia virus-related virus (XMRV) has been a tumultuous roller-coaster ride for scientists and patients. The initial associations of XMRV with chronic fatigue syndrome and prostate cancer, while providing much hope and optimism, have now been discredited and/or retracted following overwhelming evidence that (1) numerous patient cohorts from around the world are XMRV-negative, (2) the initial reports of XMRV-positive patients were due to contamination with mouse DNA, XMRV plasmid DNA, or virus from the 22Rv1 cell line and (3) XMRV is a laboratory-derived virus generated in the mid 1990s through recombination during passage of a prostate tumor xenograft in immuno-

				compromised mice. While these developments are disappointing to scientists and patients, they provide a valuable road map of potential pitfalls to the would-be microbe hunters.
Devasahayam A, Lawn T, Murphy M, White PD.	NHS Greater Glasgow and Clyde, Yorkhill Hospital , Glasgow , UK.	Alternative diagnoses to chronic fatigue syndrome in referrals to a specialist service: service evaluation survey.	JRSM Short Rep. 2012 Jan;3(1):4. doi: 10.1258/shorts.2011.011127.	OBJECTIVE: To assess the accuracy of diagnoses made by referrers to a chronic fatigue syndrome (CFS) service. DESIGN: Retrospective service evaluation surveys of both rejected referral letters and medical case-notes after full clinical assessment. SETTING: A specialist CFS clinic in London, UK. PARTICIPANTS: In the first survey, we assessed rejected referral letters between March 2007 and September 2008. In the second survey, we ascertained the primary diagnosis made in case-notes of 250 consecutive new patients assessed between April 2007 and November 2008. MAIN OUTCOME MEASURES: Reasons for rejection of referrals and primary diagnosis in those assessed. RESULTS: In the first survey, 154 out of 418 referrals (37%) were rejected. Of these, 77 out of the available 127 referrals (61%) had a likely alternative diagnosis. In the second survey of clinically assessed patients, 107 (43%) had alternative medical/psychiatric diagnoses, while 137 out of 250 (54%) patients received a diagnosis of CFS. The commonest alternative medical diagnoses of those assessed were sleep disorders and the commonest alternative psychiatric diagnosis was depressive illness. Altogether 184 of 377 (49%) patients had alternative diagnoses to CFS. CONCLUSIONS: Half of all the referred patients to a specialist CFS clinic had alternative medical and psychiatric diagnoses. Specialist medical assessment for patients with unexplained, disabling, chronic fatigue needs to incorporate both medical and psychiatric assessments.
Dodd RY, Hackett J Jr, Linnen JM, Dorsey K, Wu Y, Zou S, Qiu X, Swanson P, Schochetman G, Gao K, Carrick JM, Krysztof DE, Stramer SL.	American Red Cross Holland Laboratory, Rockville, Maryland 20855, USA. dodd@usa.redcross.org	Xenotropic murine leukemia virus-related virus does not pose a risk to blood recipient safety.	Transfusion. 2012 Feb;52(2):298-306. doi: 10.1111/j.1537-2995.2011.03450.x.	BACKGROUND: When xenotropic murine leukemia virus-related virus (XMRV) was first reported in association with chronic fatigue syndrome, it was suggested that it might offer a risk to blood safety. Thus, the prevalence of the virus among blood donors and, if present, its transmissibility by transfusion need to be defined. STUDY DESIGN AND METHODS: Two populations of routine blood donor samples (1435 and 13,399) were obtained for prevalence evaluations; samples from a linked donor-recipient repository were also evaluated. Samples were tested for the presence of antibodies to XMRV-related recombinant antigens and/or for XMRV RNA, using validated, high-throughput systems. RESULTS: The presence of antibodies to XMRV could not be confirmed among a total of 17,249 blood donors or recipients (0%; 95% confidence interval [CI], 0%-0.017%); 1763 tested samples were nonreactive for XMRV RNA (0%; 95% CI, 0%-0.17%). Evidence of infection was absent from 109 recipients and 830 evaluable blood samples tested after transfusion of a total of 3741 blood components. CONCLUSIONS: XMRV and related murine leukemia virus (MLV) markers are not present among a large population of blood donors and evidence of transfusion transmission could not be detected. Thus, these viruses do not currently pose a threat to blood recipient safety and further actions relating to XMRV and MLV are not justified.

Dörr J, Ohlraun S, Skarabis H, Paul F.	NeuroCure Clinical Research Center, Charité - Universitätsmedizin Berlin, Berlin, Germany. jan-markus.doerr@charite.de	Efficacy of vitamin D supplementation in multiple sclerosis (EVIDIMS Trial): study protocol for a randomized controlled trial.	Trials. 2012 Feb 8;13:15. doi: 10.1186/1745-6215-13-15.	BACKGROUND: Multiple sclerosis is the most common chronic inflammatory disease of the central nervous system in young adults. Despite the fact that numerous lines of evidence link both the risk of disease development and the disease course to the serum level of 25-hydroxyvitamin D it still remains elusive whether multiple sclerosis patients benefit from boosting the serum level of 25-hydroxyvitamin D, mainly because interventional clinical trials that directly address the therapeutic effects of vitamin D in multiple sclerosis are sparse. We here present the protocol of an interventional clinical phase II study to test the hypothesis, that high-dose vitamin D supplementation of multiple sclerosis patients is safe and superior to low-dose supplementation with respect to beneficial therapeutic effects. METHODS/DESIGN: The EVIDIMS trial is a German multi-center, stratified, randomized, controlled and double-blind clinical phase II pilot study. Eighty patients with the diagnosis of definite multiple sclerosis or clinically isolated syndrome who are on a stable immunomodulatory treatment with interferon-β1b will be randomized to additionally receive either high-dose (average daily dose 10.200 IU) or low-dose (average daily dose 200 IU) cholecalciferol for a total period of 18 months. The primary outcome measure is the number of new lesions detected on T2-weighted cranial MRI at 3 tesla. Secondary endpoints include additional magnetic resonance imaging and optical coherence tomography parameters for neuroinflammation and -degeneration, clinical parameters for disease activity, as well as cognition, fatigue, depression, and quality of life. Safety and tolerability of high-dose vitamin D supplementation are further outcome parameters. DISCUSSION: In light of the discrepancy between existing epidemiological and preclinical data on the one hand and available clinical data on the other the EVIDIMS trial will substantially contribute to the evaluation of the efficacy of high-dose vitamin D supplementation in MS patients. The study design presented here fulfills the criteria of a high-quality clinical phase II trial in MS. TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT01440062.
Dyer C.	[No address quoted]	Researcher into chronic fatigue syndrome is released on bail.	BMJ. 2011 Nov 25;343:d7683. doi: 10.1136/bmj.d7683.	[No abstract given]
Dyer C.	[No address quoted]	GMC rules against doctor who used unconventional tests and treatments for chronic fatigue syndrome.	BMJ. 2011 Nov 7;343:d7220. doi: 10.1136/bmj.d7220.	[No abstract given]
Enserink M.	[No address quoted]	Infectious diseases. New XMRV studies bring closure--and	Science. 2012 Sep 21;337(6101):1441-2.	[No abstract given]

		fresh dispute		
Erdur FM, Soyoral YU, Emre H, Begenik H, Canbaz ET, Erkoc R.	Yuzuncu Yil University, Medical Faculty, Department of Internal Medicine, Van, Turkey. drfme@yahoo.com	Fenofibrate-induced rhabdomyolysis in a patient with chronic renal failure due to nephrotic syndrome: a rare case report.	Clin Biochem. 2012 Jan;45(1-2):162-4. doi: 10.1016/j.clinbiochem.2011.09.025.	OBJECTIVES: Fenofibrate is a fibric acid derivative that is used alone or combination with statins in the treatment of hyperlipidemia. These drugs have potential risks, including rhabdomyolysis and acute renal failure. Despite reports of rhabdomyolysis with the use of fenofibrate alone or with statin-fibrate combinations, there have been no cases of rhabdomyolysis described when fenofibrate was used alone to treat patients with chronic renal failure owing to nephrotic syndrome. DESIGN AND METHODS: We report on a 26-year-old male who presented with fenofibrate-induced rhabdomyolysis with chronic renal failure due to nephrotic syndrome. RESULTS: After the discontinuation of fenofibrate, the patient was treated with intravenous fluid replacement and urine alkalization. Subsequently, his clinical and biochemical findings improved. CONCLUSIONS: Before starting fenofibrate therapy, the causes of secondary hyperlipidemia, especially nephrotic syndrome, should be investigated. In the presence of chronic renal failure and hypoalbuminemia, the fenofibrate dose should be adjusted. Physicians should be aware of the potential toxicities of fenofibrate, and patients should be informed about its potential side effects.
Erueti C, Glasziou P, Mar CD, van Driel ML.	Faculty of Health Sciences and Medicine, Bond University, Gold Coast, Queensland, Australia. cerueti@bond.edu.au	Do you think it's a disease? a survey of medical students.	BMC Med Educ. 2012 Apr 3;12:19. doi: 10.1186/1472-6920-12-19.	BACKGROUND: The management of medical conditions is influenced by whether clinicians regard them as "disease" or "not a disease". The aim of the survey was to determine how medical students classify a range of conditions they might encounter in their professional lives and whether a different name for a condition would influence their decision in the categorisation of the condition as a 'disease' or 'not a disease'. METHODS: We surveyed 3 concurrent years of medical students to classify 36 candidate conditions into "disease" and "non-disease". The conditions were given a 'medical' label and a (lay) label and positioned where possible in alternate columns of the survey. RESULTS: The response rate was 96% (183 of 190 students attending a lecture): 80% of students concurred on 16 conditions as "disease" (eg diabetes, tuberculosis), and 4 as "non-disease" (eg baldness, menopause, fractured skull and heat stroke). The remaining 16 conditions (with 21-79% agreement) were more contentious (especially obesity, infertility, hay fever, alcoholism, and restless leg syndrome). Three pairs of conditions had both a more, and a less, medical label: the more medical labels (myalgic encephalomyelitis, hypertension, and erectile dysfunction) were more frequently classified as 'disease' than the less medical (chronic fatigue syndrome, high blood pressure, and impotence), respectively, significantly different for the first two pairs. CONCLUSIONS: Some conditions excluded from the classification of "disease" were unexpected (eg fractured skull and heat stroke). Students were mostly concordant on what conditions should be classified as "disease". They were more likely to classify synonyms as 'disease' if the label was medical. The findings indicate there is still a problem 30 years on in the concept of 'what is a disease'. Our findings suggest that we should be addressing such concepts to medical students.

Etzioni A	[No address quoted]	Chronic fatigue syndrome: still a long way to go.	Isr Med Assoc J. 2011 Dec;13(12):761.	[No abstract given]
Fagermoen E, Sulheim D, Winger A, Andersen AM, Vethe NT, Saul JP, Thaulow E, Wyller VB.	Department of Pediatrics, Oslo University Hospital and University of Oslo, Oslo, Norway.	Clonidine in the treatment of adolescent chronic fatigue syndrome: a pilot study for the NorCAPITAL trial.	BMC Res Notes. 2012 Aug 7;5:418. doi: 10.1186/1756-0500-5-418.	BACKGROUND: This pilot study (ClinicalTrials.gov ID: NCT01507701) assessed the feasibility and safety of clonidine in adolescent chronic fatigue syndrome (CFS). Specifically, we assessed clonidine dosage in relation to a) plasma concentration levels, b) orthostatic cardiovascular responses, and c) possible adverse effects. FINDINGS: Five adolescent CFS patients (14-19 years old) received 50 µg clonidine twice per day during 14 days in an open, uncontrolled design. Plasma concentration of clonidine was assayed by standard laboratory methods. Changes in orthostatic cardiovascular responses were assessed by a 20o head-up tilt-test (HUT). Adverse effects were mapped by a questionnaire.After 14 days, C0 median (range) of clonidine was 0.21 (0.18-0.36) µg/L, and Cmax median (range) of clonidine was 0.41 (0.38-0.56) µg/L. Also, supine blood pressures and heart rate were lower during clonidine treatment, and the HUT response was closer to the normal response. No serious adverse effects were registered. CONCLUSION: Clonidine 50 µg BID seems to be safe enough to proceed from a pilot study to a controlled trial in a select group of adolescents with CFS (ClinicalTrials.gov ID: NCT01040429).
Felger JC, Cole SW, Pace TW, Hu F, Woolwine BJ, Doho GH, Raison CL, Miller AH.	Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA 30322, USA. jfelger@gmail.com	Molecular signatures of peripheral blood mononuclear cells during chronic interferon-α treatment: relationship with depression and fatigue.	Psychol Med. 2012 Aug;42(8):1591-603. doi: 10.1017/S0033291711002868.	BACKGROUND: Interferon-alpha (IFN-α) treatment for infectious disease and cancer causes high rates of depression and fatigue, and has been used to investigate the impact of inflammatory cytokines on brain and behavior. However, little is known about the transcriptional impact of chronic IFN-α on immune cells in vivo and its relationship to IFN-α-induced behavioral changes. METHOD: Genome-wide transcriptional profiling was performed on peripheral blood mononuclear cells (PBMCs) from 21 patients with chronic hepatitis C virus (HCV) either awaiting IFN-α therapy (n=10) or at 12 weeks of IFN-α treatment (n=11). RESULTS: Significance analysis of microarray data identified 252 up-regulated and 116 down-regulated gene transcripts. Of the up-regulated genes, 2'-5'-oligoadenylate synthetase 2 (OAS2), a gene linked to chronic fatigue syndrome (CFS), was the only gene that was differentially expressed in patients with IFN-α-induced depression/fatigue, and correlated with depression and fatigue scores at 12 weeks (r=0.80, p=0.003 and r=0.70, p=0.017 respectively). Promoter-based bioinformatic analyses linked IFN-α-related transcriptional alterations to transcription factors involved in myeloid differentiation, IFN-α signaling, activator protein-1 (AP1) and cAMP responsive element binding protein/activation transcription factor (CREB/ATF) pathways, which were derived primarily from monocytes and plasmacytoid dendritic cells. IFN-α-treated patients with high depression/fatigue scores demonstrated up-regulation of genes bearing promoter motifs for transcription factors involved in myeloid differentiation, IFN-α and AP1 signaling, and reduced prevalence of motifs for CREB/ATF, which has been implicated in major depression. CONCLUSIONS: Depression

				and fatigue during chronic IFN-α administration were associated with alterations in the expression (OAS2) and transcriptional control (CREB/ATF) of genes linked to behavioral disorders including CFS and major depression, further supporting an immune contribution to these diseases.
Fisher H, Crawley E.	Paediatric CFS/ME Service, Royal National Hospital for Rheumatic Diseases, UK.	Why do young people with CFS/ME feel anxious? A qualitative study.	Clin Child Psychol Psychiatry. 2012 Oct 23	Young people with chronic fatigue syndrome or myalagic encephalopathy (CFS/ME) (CFS/ME) experience higher levels of psychological distress than healthy controls and young people with other chronic illnesses, and it was recently demonstrated that 38% of this population scored above the clinical cut-off on the Spence Child Anxiety Scale. Subscales of social and separation anxiety were consistently high across gender and age groups. In this study, we used qualitative methods to help us understand more about these two types of anxiety in young people with CFS/ME. Eleven young people (age 12-18) were interviewed. Interviews were self-directed by the participants and were wide ranging. The transcripts were analysed using interpretative phenomenological analysis. Five superordinate themes were identified: social loss and adjustment; introduction of uncertainty and unpredictability; the vulnerable self; individual differences; and contributions towards recovery. Many themes were identical to those described in young people coping with other chronic illnesses in adolescence. In addition, young people with CFS/ME describe experiences associated with the perceived illegitimacy of this condition, namely: feeling unable to explain their illness; bullying from peers; disbelief; and distrust from adults around them. This becomes an additional challenge for these young people. Clinicians need to be aware of these problems, and offer appropriate support.
Fjorback LO, Arendt M, Ornbøl E, Walach H, Rehfeld E, Schröder A, Fink P	The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Denmark. Electronic address: lonefjor@rm.dk	Mindfulness therapy for somatization disorder and functional somatic syndromes - Randomized trial with one-year follow-up	J Psychosom Res. 2013 Jan;74(1):31-40. doi: 10.1016/j.jpsychores.2012.09.006. Epub 2012 Oct 1	OBJECTIVE: To conduct a feasibility and efficacy trial of mindfulness therapy in somatization disorder and functional somatic syndromes such as fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome, defined as bodily distress syndrome (BDS). METHODS: We randomized 119 patients to either mindfulness therapy (mindfulness-based stress reduction and some cognitive behavioral therapy elements for BDS) or to enhanced treatment as usual (2-hour specialist medical care and brief cognitive behavioral therapy for BDS). The primary outcome measure was change in physical health (SF-36 Physical Component Summary) from baseline to 15-month follow-up. RESULTS: The study is negative as we could not demonstrate a different development over time for the two groups ($F(3,2674)=1.51$, $P=.21$). However, in the mindfulness therapy group, improvement was obtained toward the end of treatment and it remained present at the 15-month follow-up, whereas the enhanced treatment as usual group achieved no significant change until 15-month follow-up. The change scores averaged half a standard deviation which amounts to a clinically significant change, 29% changed more than 1 standard deviation. Significant between-group differences were observed at treatment cessation. CONCLUSION: Mindfulness therapy is a feasible and acceptable treatment. The study showed that mindfulness therapy was comparable to enhanced treatment as usual in improving

				quality of life and symptoms. Nevertheless, considering the more rapid improvement following mindfulness, mindfulness therapy may be a potentially
Fjorback LO, Carstensen T, Arendt M, Ornbøl E, Walach H, Rehfeld E, Fink P.	The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 4, Aarhus, Denmark. Electronic address: lonefjor@rm.dk.	Mindfulness therapy for somatization disorder and functional somatic syndromes: Analysis of economic consequences alongside a randomized trial.	J Psychosom Res. 2013 Jan;74(1):41-8. doi: 10.1016/j.jpsychores.2012.09.010.	OBJECTIVE: The objective of the present study is to estimate the economic consequences of somatization disorder and functional somatic syndromes such as fibromyalgia and chronic fatigue syndrome, defined as bodily distress syndrome (BDS), when mindfulness therapy is compared with enhanced treatment as usual. METHODS: A total of 119 BDS patients were randomized to mindfulness therapy or enhanced treatment as usual and compared with 5950 matched controls. Register data were analyzed from 10years before their inclusion to 15-month follow-up. The main outcome measures were disability pension at the 15-month follow-up and a reduction in total health care costs. Unemployment and sickness benefit prior to inclusion were tested as possible risk factors. RESULTS: At 15-month follow-up, 25% from the mindfulness therapy group received disability pension compared with 45% from the specialized treatment group (p=.025). The total health care utilization was reduced over time in both groups from the year before inclusion (mean $5325, median $2971) to the year after inclusion (mean $3644, median $1593) (p=.0001). This overall decline was seen in spite of elevated costs due to assessment and mindfulness therapy or enhanced treatment as usual. The BDS patients accumulated significantly more weeks of unemployment and sickness benefit 5 and 10years before inclusion (p<.0001) than the population controls. CONCLUSIONS: Mindfulness therapy may prevent disability pension and it may have a potential to significantly reduce societal costs and increase the effectiveness of care. Accumulated weeks of unemployment and sickness benefit are possible risk factors for BDS.
Fjorback LO.	The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, Nørrebrogade 44, 8000 Aarhus C, Denmark. lonefjor@rm.dk.	Mindfulness and bodily distress.	Dan Med J. 2012 Nov;59(11):B4547.	We have created a mindfulness approach to treat patients who experience multiple, persistent, and disabling physical symptoms that cannot be explained by a well-defined medical or surgical condition. Randomized controlled trials in this area are few, and research is hampered by the lack of clear definitions. Bodily distress syndrome (BDS) or bodily stress is an empirically defined definition unifying various conditions such as fibromyalgia, chronic fatigue syndrome, and somatization disorder. In the present PhD, we explored whether patients suffering from BDS may be committed to mental training in the form of mindfulness therapy, which is a mindfulness program specifically targeted patients suffering from BDS. The theoretical model for including mindfulness training in the treatment of BDS is based on identified neurobiological impairments in these patients and the neurobiological improvements that mindfulness training may offer. BDS is a major public health issue possibly associated with the pathology of the immuno-endocrine and autonomic nervous system. BDS patients are often stigmatized, and effective treatment is rarely delivered, which leaves these patients isolated, left by themselves, vulnerable to potentially harming medical and/or alternative treatments. Accordingly, there is a need for non-harming practical tools that patients can learn to master so that they

				can improve the ability to take responsibility for their own health and wellbeing. Mindfulness-Based Stress Reduction (MBSR) is a group program that employs mindfulness practice to alleviate suffering associated with physical, psychosomatic, and psychiatric disorders. Mindfulness-Based Cognitive Therapy (MBCT) is designed to prevent depressive relapse. Paper I and II present systematic literature reviews only of randomized controlled trials on MBSR and MBCT. The effect of MBSR has been explored on fibromyalgia in three studies, none of them showed convincing results, but gave some indications as to improvement. The reviews recommended MBSR as a useful method for improving mental health; however, lack of long-term follow-up and active control groups are limitations in most studies. MBCT was recommended as a tool for preventing depressive relapse in recovered, recurrently depressed patients, but the implication of MBSR and MBCT is problematic, especially due to the lack of well educated mindfulness teachers. We combined MBSR with cognitive behavioral therapy, CBT, specifically targeted BDS. Paper III provides original data from 119 patients enrolled in a randomized clinical trial, mindfulness therapy for BDS. The randomized controlled trial indicates that BDS patients are capable of and willing to engage in mindfulness therapy. This thesis showed that mindfulness therapy can safely and successfully engage BDS patients in mindfulness practice. Since individual CBT and psychiatric consultation have previously been found to have positive outcomes for BDS patients, we compared mindfulness therapy to an active control group entitled specialized treatment in which an individual treatment was planned in collaboration between the patient and an MD specialized in BDS, CBT, and psychiatry. Mindfulness therapy was comparable to specialized treatment in improving the quality of life and the symptoms of the patients with BDS at 15-month follow-up. For primary outcome physical health (PCS) at 15-month follow-up, different developments over time for the two treatment groups could not be established ($F(3,2674) = 1.51$, $p = 0.21$). However, in the mindfulness therapy group, PCS significant changed at the end of treatment and this change remained at 15-month follow-up, whereas no significantly change was seen in the specialized treatment group until at the 15-month follow-up. In the mindfulness therapy group, 26%; CI: 14-38 reported a marked improvement (> 1 SD) at the end of treatment compared with 10%; CI: 2-18 in the specialized treatment group. This amounts to a statistically significant difference between the groups (OR = 3.21; CI 1.05-9.78, $p = 0.04$). The results are indicating that mindfulness therapy produced greater and more rapid improvements than specialized treatment. Mindfulness therapy appears to produce improvements within the range of those reported in the STreSS-1 trial, where CBT was compared with enhanced usual care, and no improvements on the SF-36 scale were observed in the enhanced usual care group. This indicates that the changes accomplished with the two treatments mindfulness therapy and specialized treatment reflect real changes attributable to the interventions. The economic effects

				of mindfulness therapy are evaluated in paper IV by the use of original register data from the 119 enrolled patients and a matched control group of 5,950 individuals. Mindfulness therapy had substantial socioeconomic benefits over specialized treatment. The costs incurred to cover permanent health-related benefits, especially disability pension, were significantly lower in the mindfulness therapy group than in the specialized treatment group over a 15-month follow-up period; 25% from the mindfulness therapy group received disability pension compared with 45% from the specialized treatment group (p = 0.025). The total health care utilization was reduced over time in both groups from the year before inclusion (mean $ 5,325, median $ 2,971) to the year after inclusion (mean $ 3,644, median $ 1,593) (p = 0.0001). There was no difference between the two groups. Five and ten years before their inclusion, the BDS patients were less self-supporting than an age-, gender- and ethnicity-matched population control group; the BDS patients accumulated more weeks of sickness benefit and unemployment. Thus, the included BDS patients may have been ill and in high risk for a social decline five and ten years before they received a proper diagnosis and treatment. In conclusion, the social and economic consequences of BDS are significant and mindfulness therapy may have a potential to significantly improve function, quality of life and symptoms, prevent a social decline, and reduce societal costs.
Friedlander JI, Shorter B, Moldwin RM.	The Arthur Smith Institute for Urology, Department of Nutrition, New Hyde Park, NY, USA. justinfriedlander@gmail.com	Diet and its role in interstitial cystitis/bladder pain syndrome (IC/BPS) and comorbid conditions.	BJU Int. 2012 Jun;109(11):1584-91. doi: 10.1111/j.1464-410X.2011.10860.x. Epub 2012 Jan 11.	What's known on the subject? and What does the study add? Nearly 90% of patients with interstitial cystitis/bladder pain syndrome (IC/BPS) report sensitivities to a wide variety of dietary comestibles. Current questionnaire-based literature suggests that citrus fruits, tomatoes, vitamin C, artificial sweeteners, coffee, tea, carbonated and alcoholic beverages, and spicy foods tend to exacerbate symptoms, while calcium glycerophosphate and sodium bicarbonate tend to improve symptoms. At present we recommend employing a controlled method to determine dietary sensitivities, such as an elimination diet, in order to identify sensitivities while at the same time maintain optimal nutritional intake. We review current literature with regard to diet's effect upon IC/BPS and common comorbidities (irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, neuropathic pain, vulvodynia, and headache) with a focus upon questionnaire-based investigations. We discuss the pathologic mechanisms that may link diet and IC/BPS related-pain, concentrating upon specific comestibles such as acidic foods, foods high in potassium, caffeine, and alcohol. Up to 90% of patients with interstitial cystitis/bladder pain syndrome (IC/BPS) report sensitivities to a wide variety of comestibles. Pathological mechanisms suggested to be responsible for the relationship between dietary intake and symptom exacerbation include peripheral and/or central neural upregulation, bladder epithelial dysfunction, and organ 'cross-talk', amongst others. Current questionnaire-based data suggests that citrus fruits, tomatoes, vitamin C, artificial sweeteners, coffee, tea, carbonated and alcoholic beverages, and spicy foods tend to exacerbate symptoms, while calcium

				glycerophosphate and sodium bicarbonate tend to improve symptoms. Specific comestible sensitivities varied between patients and may have been influenced by comorbid conditions. This suggests that a controlled method to determine dietary sensitivities, such as an elimination diet, may play an important role in patient management.
Frith J, Zalewski P, Klawe JJ, Pairman J, Bitner A, Tafil-Klawe M, Newton JL.	UK NIHR Biomedical Research Centre in Ageing, Newcastle, UK.	Impaired blood pressure variability in chronic fatigue syndrome--a potential biomarker.	QJM. 2012 Sep;105(9):831-8. doi: 10.1093/qjmed/hcs085.	INTRODUCTION: Autonomic dysfunction is common in chronic fatigue syndrome (CFS). This study set out to derive an autonomic biomarker using a comprehensive assessment of heart rate and blood pressure variability. METHODS: Heart rate and non-invasive continuous blood pressure measurements (task force monitor) at rest and on standing were performed in CFS (Fukuda n = 68) and matched controls (n = 68) to derive high frequency (HF; parasympathetic) and low frequency (LF; sympathetic) heart rate variability (HRV), systolic (SBPV) and diastolic (DBPV) blood pressure variability. Variables of significance were combined using receiver operator curves to explore the diagnostic utility of parameters particularly at rest. RESULTS: At rest, LF-HRV (sympathetic) was significantly increased in CFS compared to controls, while parasympathetic markers were significantly reduced (P = 0.006). Total DBP spectral power was increased (P = 0.0003) across all domains, with a shift towards sympathetic and away from parasympathetic SBPV (P = 0.05). On standing, overall SBPV response was significantly reduced with reductions in both sympathetic and parasympathetic components of SBPV (all P < 0.0001). Change in LF-DBP and relative balance of LF/HF DBP on standing differed between CFS and controls (P < 0.0001). Using the 85% sensitivity levels, we determined a threshold for three chosen resting BPV parameters of LF DBP >3.185, rest HF DBP >0.86, rest total DBP >7.05. Achieving all of these differentiated between CFS and controls with 77% sensitivity and 53% specificity. CONCLUSION: This study has shown that there are objectively measured abnormalities of blood pressure variability in CFS and that these abnormalities have the potential to be a bedside diagnostic tool.
Fuchs CE, van Geelen SM, van Geel R, Sinnema G, van de Putte EM, Hermans HJ, Kuis W.	Division of Paediatric Psychology, University Medical Centre Utrecht, The Netherlands.	Health and identity: Self-positioning in adolescent chronic fatigue syndrome and juvenile idiopathic arthritis.	Clin Child Psychol Psychiatry. 2012 Oct 11.	The aim of this study is to gain more insight into basic aspects of identity, in relation to adolescent chronic fatigue syndrome (CFS) and juvenile idiopathic arthritis (JIA). In dialogical self theory, identity is regarded as incorporating multiple self-positions, such as 'I as tired', 'I as pessimistic', or 'I as decisive'. Physical and psychosocial impairment might alter the organization of these self-positions. The Personal Position Repertoire procedure, a quantitative method to analyse the prominence of self-positions, the Child Health Questionnaire, assessing health-related functioning, and the Checklist Individual Strength, measuring fatigue, were completed by 42 adolescents with CFS, 37 adolescents with JIA and 23 healthy teenagers. Adolescents with JIA report impaired physical functioning and general health. However, they position themselves very similar to healthy teenagers - i.e. as strong and healthy. While this self-positioning approach might be adequate and sustainable in adolescence, it could prove too strenuous to maintain throughout adult life.

				Adolescents with CFS, besides indicating severe physical difficulties, also report more psychosocial problems. They position themselves as significantly less strong and more unwell. With this emphasis on positions relating to their illness, there seems to be little room left for stronger positions. It is regarded of clinical importance to address these issues in this crucial developmental period.
Fukuda S, Horiguchi M, Yamaguti K, Nakatomi Y, Kuratsune H, Ichinose H, Watanabe Y.	Department of Medical Science on Fatigue, Osaka City University, Graduate School of Medicine, Osaka, Japan; Center for Molecular Imaging Science, RIKEN, Kobe, Hyogo, Japan.	Association of monoamine-synthesizing genes with the depression tendency in chronic fatigue syndrome patients.	Life Sci. 2012 Dec 13. pii: S0024-3205(12)00711-4. doi: 10.1016/j.lfs.2012.11.016.	AIMS: Tyrosine hydroxylase (TH) and GTP cyclohydrolase I (GCH) are the rate-limiting enzymes for the biosynthesis of catecholamines and tetrahydrobiopterin (BH4), respectively. Since catecholamines and BH4 are thought to be involved in the pathophysiology of CFS, we explored the genetic factors that influence CFS development and examined the possible association between the SNPs of the TH and GCH genes and the various characteristics of CFS patients. MAIN METHODS: After drawing venous blood from CFS patients and controls, genomic DNA was then extracted from whole blood in accordance with standard procedures. Digestion patterns of the PCR products were used for genotyping the SNPs of GCH (rs841; C+243T) and TH (rs10770141; C-824T). We also performed questionnaires consisting of fatigue-scale and temperament and character inventory scale (TCI) to CFS patients. KEY FINDINGS: Our results demonstrated that the allele differences for the GCH and TH SNPs were not associated with CFS patients. We did find that the GCH gene with the C+243T polymorphism affected harm avoidance, while the TH gene with the C-824T polymorphism affected persistence in the CFS patients. SIGNIFICANCE: Our results suggest that the biosynthetic pathways of the monoamine neurotransmitters that are mediated by TH and GCH might be associated with the CFS clinical findings, because persistence is one of the typical personality traits observed in CFS and patients with major depressive disorder exhibit a higher harm avoidance score.
Galbraith S, Cameron B, Li H, Lau D, Vollmer-Conna U, Lloyd AR.	School of Mathematics and Statistics, Faculty of Science, University of New South Wales, Sydney, Australia.	Peripheral blood gene expression in postinfective fatigue syndrome following from three different triggering infections.	J Infect Dis. 2011 Nov 15;204(10):1632-40. doi: 10.1093/infdis/jir612.	BACKGROUND: Several infections trigger postinfective fatigue syndromes, which share key illness characteristics with each other and with chronic fatigue syndrome (CFS). Previous cross-sectional case-control studies of CFS have suggested that unique gene expression signatures are evident in peripheral blood samples. METHODS: Peripheral blood transcriptomes in samples collected longitudinally, in 18 subjects with a fatigue syndrome lasting ≥ 6 months after acute infection due to Epstein-Barr virus, Ross River virus, or Coxiella burnetii (Q fever), and 18 matched control subjects who had recovered promptly, were studied by microarray (n = 127) and confirmatory quantitative polymerase chain reaction (PCR). Gene expression patterns associated with CFS were sought by univariate statistics and regression modeling. RESULTS: There were 23 genes with modest differential expression (0.6-2.3-fold change) in within-subject comparisons of early, symptomatic time points with late, recovered time points. There were modest differences found in 63 genes, either in cross-sectional comparison of cases and controls at 6 months after infection onset or in the regression model. There were 223 genes significantly correlated with individual symptom domains. Quantitative PCR confirmed 33 (73%) of 45 genes-none were

				consistent across cohorts. CONCLUSIONS: Although the illness characteristics of patients with postinfective fatigue syndromes have more similarities than differences, no reliable peripheral blood gene expression correlate is evident.
Gherardi RK, Authier FJ.	AP-HP, Hôpital H. Mondor, France.	Macrophagic myofasciitis: characterization and pathophysiology.	Lupus. 2012 Feb;21(2):184-9. doi: 10.1177/0961203311429557.	Aluminium oxyhydroxide (alum), a nanocrystalline compound forming agglomerates, has been used in vaccines for its immunological adjuvant effect since 1927. Alum is the most commonly used adjuvant in human and veterinary vaccines, but the mechanisms by which it stimulates immune responses remain incompletely understood. Although generally well tolerated, alum may occasionally cause disabling health problems in presumably susceptible individuals. A small proportion of vaccinated people present with delayed onset of diffuse myalgia, chronic fatigue and cognitive dysfunction, and exhibit very long-term persistence of alum-loaded macrophages at the site of previous intramuscular (i.m.) immunization, forming a granulomatous lesion called macrophagic myofasciitis (MMF). Clinical symptoms associated with MMF are paradigmatic of the recently delineated 'autoimmune/inflammatory syndrome induced by adjuvants' (ASIA). The stereotyped cognitive dysfunction is reminiscent of cognitive deficits described in foundry workers exposed to inhaled Al particles. Alum safety concerns will largely depend on whether the compound remains localized at the site of injection or diffuses and accumulates in distant organs. Animal experiments indicate that biopersistent nanomaterials taken up by monocyte-lineage cells in tissues, such as fluorescent alum surrogates, can first translocate to draining lymph nodes, and thereafter circulate in blood within phagocytes and reach the spleen, and, eventually, slowly accumulate in the brain.
Gibson PR, Morrison G.	Eastern Health Clinical School, Monash University, Melbourne, Victoria, Australia. peter.gibson@monash.edu	Effects of methylnaltrexone in patients with narcotic bowel syndrome: a pilot observational study.	Intern Med J. 2012 Aug;42(8):907-12. doi: 10.1111/j.1445-5994.2012.02726.x.	BACKGROUND: Narcotic bowel syndrome (NBS) describes disabling chronic severe abdominal pain that worsens despite continuing or escalating doses of opiates. Therapy is very limited. AIM: To examine effects of blocking peripheral μ-opioid receptors on the symptomatology of patients with NBS and its safety. METHODS: An open-label observational study was performed in four women with NBS. After a 2-week run-in period, patients were treated for 12 weeks with 8-12 mg methylnaltrexone bromide subcutaneously every other day, increasing to daily if there was poor response. Patient and physician assessment was documented, and patients completed an eight-symptom visual analogue scale weekly and the Functional Assessment of Chronic Illnesses Therapy-Fatigue questionnaire for fatigue. Patients were observed for 4 weeks following withdrawal of the drug. RESULTS: One patient was unable to tolerate the study medication because of worsening pain after injection, and withdrew. Two showed clear benefit with reduction of symptoms overall, pain, bloating, distension, nausea and tiredness, with improved satisfaction and consistency of bowel actions and fatigue scores. Both reduced analgesic usage. The third had improved ileostomy output and had no episodes of severe bloating, but pain scores remained high. All three worsened after drug withdrawal and requested retreatment. Three experienced abdominal pains of moderate severity for 30-60 min

				consistently within 5 min of each injection. No other adverse events were experienced. CONCLUSIONS: Methylnaltrexone has a positive impact on symptoms in women with NBS, although treatment does induce transient pain following its administration. Larger studies are required to examine its efficacy and longer term safety in this patient group.
Gingaras C, Danielson BP, Vigil KJ, Vey E, Arduino RC, Kimata JT.	Section of Retrovirology, Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA.	Absence of XMRV in peripheral blood mononuclear cells of ARV-treatment naïve HIV-1 infected and HIV-1/HCV coinfected individuals and blood donors.	PLoS One. 2012;7(2):e31398. doi: 10.1371/journal.pone.0031398.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) has been found in the prostatic tissue of prostate cancer patients and in the blood of chronic fatigue syndrome patients. However, numerous studies have found little to no trace of XMRV in different human cohorts. Based on evidence suggesting common transmission routes between XMRV and HIV-1, HIV-1 infected individuals may represent a high-risk group for XMRV infection and spread. METHODOLOGY/PRINCIPAL FINDINGS: DNA was isolated from the peripheral blood mononuclear cells (PBMCs) of 179 HIV-1 infected treatment naïve patients, 86 of which were coinfected with HCV, and 54 healthy blood donors. DNA was screened for XMRV provirus with two sensitive, published PCR assays targeting XMRV gag and env and one sensitive, published nested PCR assay targeting env. Detection of XMRV was confirmed by DNA sequencing. One of the 179 HIV-1 infected patients tested positive for gag by non-nested PCR whereas the two other assays did not detect XMRV in any specimen. All healthy blood donors were negative for XMRV proviral sequences. Sera from 23 HIV-1 infected patients (15 HCV(+)) and 12 healthy donors were screened for the presence of XMRV-reactive antibodies by Western blot. Thirteen sera (57%) from HIV-1(+) patients and 6 sera (50%) from healthy donors showed reactivity to XMRV-infected cell lysate. CONCLUSIONS/SIGNIFICANCE: The virtual absence of XMRV in PBMCs suggests that XMRV is not associated with HIV-1 infected or HIV-1/HCV coinfected patients, or blood donors. Although we noted isolated incidents of serum reactivity to XMRV, we are unable to verify the antibodies as XMRV specific.
Gonzalez M, Fisher M.	Division of Adolescent Medicine, Steven and Alexandra Cohen Children's Medical Center of New York, North Shore-Long Island Jewish Health System, Hofstra-North Shore LIJ School of Medicine, Hempstead, New York, USA. Mgonzalez52@NSHS.edu	An adolescent evaluated for chronic fatigue: does she have a sleep disorder?	Adolesc Med State Art Rev. 2012 Aug;23(2):277-84.	A 13-year-old girl presented to our Division of Adolescent Medicine for evaluation of ongoing fatigue. She and her mother reported that 15 months earlier, when the patient was in the 7th grade, she started to be tired and "sleep all the time." They do not remember her being ill at that time; a test for mononucleosis was reportedly positive, but Epstein-Barr virus titers showed "old disease." She remained fatigued throughout 7th grade but attended school without falling asleep; however, she was too tired to do her work and had to attend summer school. The patient received home instruction in 8th grade and reported that on weekdays she slept from 1 AM to 11 AM with a nap from 4 to 8 PM and on weekends she slept from 3 AM to 1 PM without a nap.
Goudsmit EM, Nijs	School of Psychology,	Pacing as a strategy	Disabil Rehabil.	PURPOSE: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a

J, Jason LA, Wallman KE.	University of East London, Stratford, London, E15 4LZ, UK. ellengoudsmit@hotmail.com	to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: a consensus document.	2012;34(13):1140-7. doi: 10.3109/09638288.2011.635746.	debilitating condition characterized by a number of symptoms which typically worsen following minimal exertion. Various strategies to manage the limited energy levels have been proposed. Of these, pacing has been consistently rated as one of the most helpful in surveys conducted by patient groups. This review is a response to the paucity of the information on pacing in the scientific literature. METHOD: We describe the principle of pacing and how this can be adapted to meet individual abilities and preferences. A critical evaluation of the research was conducted to ascertain the benefits and limitations of this strategy. RESULTS: Based on various studies, it is proposed that pacing can help to stabilize the condition and avoid post-exertional malaise. CONCLUSION: Pacing offers practitioners an additional therapeutic option which is acceptable to the majority of patients and can reduce the severity of the exertion-related symptoms of ME/CFS.
Graff LA, Walker JR, Russell AS, Bissonnette R, Bernstein CN.	Department of Clinical Health Psychology, University of Manitoba, 771 Bannatyne Avenue, Winnipeg, Manitoba, Canada. lgraff@hsc.mb.ca	Fatigue and quality of sleep in patients with immune-mediated inflammatory disease.	Int J Equity Health. 2011 Nov 2;10(1):46. doi: 10.1186/1475-9276-10-46.	Fatigue, a systemic feeling of exhaustion, is a common symptom of many chronic illnesses, including immune-mediated inflammatory diseases (IMID). IMID-related fatigue is associated with disease activity and pain and has detrimental effects on patient quality of life and overall well-being. Thus, routine assessment and management of fatigue in clinical practice is important. This article provides an overview of the prevalence, correlates, and predictors of fatigue in IMID. There is also discussion of the effects of different treatments on fatigue outcomes, as well as management recommendations.
Groom HC, Bishop KN.	Division of Virology, MRC National Institute for Medical Research, London NW7 1AA, UK.	The tale of xenotropic murine leukemia virus-related virus.	J Gen Virol. 2012 May;93(Pt 5):915-24. doi: 10.1099/vir.0.041038-0.	In 2006, a new retrovirus was isolated from prostate cancer patient tissue. Named xenotropic murine leukemia virus-related virus (XMRV), this was potentially the third class of retrovirus to be pathogenic in humans. XMRV made a more dramatic impact on the wider scientific community, and indeed the media, in 2009 when it was reported to be present in a remarkably high proportion of patients with chronic fatigue syndrome as well as a significant, albeit smaller, proportion of healthy controls. The apparent strong link to disease and the fear of a previously unknown retrovirus circulating in the general population lead to a surge in XMRV research. Subsequent studies failed to find an association of XMRV with disease and, in most cases, failed to find the virus in human samples. In 2011, the case against XMRV and human disease strengthened, ending with several decisive publications revealing the origin of the virus and demonstrating contamination of samples. In this review, we outline the passage of research on XMRV and its potential association with disease from its isolation to the present day, where we find ourselves at the end of a turbulent story.
Guidelli GM, Tenti S, De Nobili E, Fioravanti A.	Rheumatology Unit, Department of Clinical Medicine and Immunological Sciences, University of	Fibromyalgia syndrome and spa therapy: myth or reality?	Clin Med Insights Arthritis Musculoskelet Disord. 2012;5:19-26. doi: 10.4137/CMAMD.S8797.	Fibromyalgia syndrome (FS) is a common musculoskeletal disorder characterized by otherwise unexplained chronic widespread pain, a lowered pain threshold, high tender point counts, sleep disturbances, fatigue, headache, irritable bowel syndrome, morning stiffness, paraesthesias in the extremities, often psychological distress and depressed mood. Consequently, FS has a negative impact on working capacity, family

	Siena, Italy.			life, social functioning and quality of life. Because of unknown etiology and not clearly understood pathogenesis, there is no standard therapy regime for FS. A variety of medical treatments, including antidepressants, opioids, analgesic or non-steroidal anti-inflammatory drugs, sedatives, muscle relaxants and antiepileptics, have been used to treat FS. Currently, no pharmacological treatment for FS is consistently successful. According to recent guidelines, the optimal treatment of FS requires a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment modalities. Spa therapy is a popular treatment for FS in many European countries, as well as in Japan and Israel. However, despite their long history and popularity spa treatments are still the subject of debate and their role in modern medicine is still not clear. The objective of this review is to summarize the currently available information on clinical effects and mechanism of action of spa therapy in FS. We also provide some suggestions for further development in this area.
Guillard O, Fauconneau B, Pineau A, Marrauld A, Bellocq JP, Chenard MP.	CHU Poitiers, Department of Biochemistry, Poitiers, France. olivier.guillard@univ-poitiers.fr	Aluminium overload after 5 years in skin biopsy following post-vaccination with subcutaneous pseudolymphoma.	J Trace Elem Med Biol. 2012 Oct;26(4):291-3. doi: 10.1016/j.jtemb.2012.02.005.	Aluminium hydroxide is used as an effective adjuvant in a wide range of vaccines for enhancing immune response to the antigen. The pathogenic role of aluminium hydroxide is now recognized by the presence of chronic fatigue syndrome, macrophagic myofasciitis and subcutaneous pseudolymphoma, linked to intramuscular injection of aluminium hydroxide-containing vaccines. The aim of this study is to verify if the subcutaneous pseudolymphoma observed in this patient in the site of vaccine injection is linked to an aluminium overload. Many years after vaccination, a subcutaneous nodule was discovered in a 45-year-old woman with subcutaneous pseudolymphoma. In skin biopsy at the injection site for vaccines, aluminium (Al) deposits are assessed by Morin stain and quantification of Al is performed by Zeeman Electrothermal Atomic Absorption Spectrophotometry. Morin stain shows Al deposits in the macrophages, and Al assays (in µg/g, dry weight) were 768.10±18 for the patient compared with the two control patients, 5.61±0.59 and 9.13±0.057. Given the pathology of this patient and the high Al concentration in skin biopsy, the authors wish to draw attention when using the Al salts known to be particularly effective as adjuvants in single or repeated vaccinations. The possible release of Al may induce other pathologies ascribed to the well-known toxicity of this metal.
Güthlin C, Anton A, Kruse J, Walach H.	Johann Wolfgang Goethe University, Frankfurt/Main, Germany. guethlin@allgemeinmedizin.uni-frankfurt.de	Subjective concepts of chronically ill patients using distant healing.	Qual Health Res. 2012 Mar;22(3):320-31. doi: 10.1177/1049732311421914.	Distant healing procedures consist of benevolent intentions, often taking the form of prayers for a patient. Despite inconclusive evidence regarding distant healing, prayers are a widespread health-related technique. We studied subjective concepts of distant healing in 17 patients suffering from chronic fatigue syndrome and multiple chemical sensitivity who were given distant healing during a randomized controlled trial. We applied reconstructive interview analysis when analyzing the results. The overall theme was the tension between mainstream medicine and the immaterial healing procedure. Several components highlighted this tension: (a) patterns of legitimizing the use of distant healing, (b) distant healing and the social setting, (c) integrating

				distant healing into their belief system, and (d) reconstruction of effects by means of hindsight. The interviews showed that patients felt the need to legitimize having tried distant healing. They had to bear the full ambiguity of biomedicine being in competition with distant healing, though also experiencing distant healing as giving support.
Haba-Rubio J, de Seigneux S, Heinzer R.	Centre d'investigation et de recherche sur le sommeil, CHU Vaudois (CHUV), BH 06-204, 1011 Lausanne, Suisse.	Sleep disorders in chronic renal failure. [Article in French]	Nephrol Ther. 2012 Apr;8(2):74-80. doi: 10.1016/j.nephro.2011.07.408.	Sleep disorders are common in patients with chronic renal failure (CRF), especially in those receiving hemodialysis. Sleep-related complaints in this patient population may include insomnia, daytime sleepiness or fatigue and depression. In addition to causing impairment of daytime function and quality of life, sleep apnea may also increase the cardiovascular morbidity and mortality, especially in dialysis patients. In CRF patients, an increased prevalence of sleep apnea, restless legs syndrome and periodic limb movement during sleep has been reported. Epidemiology, pathophysiology and treatment of sleep disorders in CRF and dialysis patients are still unclear and require further research.
Hanevik K, Kristoffersen EK, Sørnes S, Mørch K, Næss H, Rivenes AC, Bødtker JE, Hausken T, Langeland N.	[No address quoted]	Immunophenotyping in post-giardiasis functional gastrointestinal disease and chronic fatigue syndrome.	BMC Infect Dis. 2012 Oct 14;12(1):258.	ABSTRACT: BACKGROUND: A Giardia outbreak was associated with development of post-infectious functional gastrointestinal disorders (PI-FGID) and chronic fatigue syndrome (PI-CFS). Markers of immune dysfunction have given conflicting results in CFS and FGID patient populations. The aim of this study was to evaluate a wide selection of markers of immune dysfunction in these two co-occurring post-infectious syndromes. METHODS: 48 patients, reporting chronic fatigue in a questionnaire study, were clinically evaluated five years after the outbreak and grouped according to Fukuda criteria for CFS (n=19) and idiopathic chronic fatigue (n=5) and Rome II criteria for FGIDs (n=54). 22 Giardia exposed non-fatigued individuals and 10 healthy unexposed individuals were recruited as controls. Peripheral blood lymphocyte subsets were analyzed by flow cytometry. RESULTS: In peripheral blood we found significantly higher CD8 T-cell levels in PI-FGID, and significantly lower NK-cell levels in PI-CFS patients. Severity of abdominal and fatigue symptoms correlated negatively with NK-cell levels. A tendency towards lower T-cell CD26 expression in FGID was seen. CONCLUSION: Patients with PI-CFS and/or PI-FGID 5 years after Giardia lamblia infection showed alterations in NK-cell and CD8-cell populations suggesting a possible immunological abnormality in these conditions. We found no significant changes in other markers examined in this well-defined group of PI-CFS and PI-FGID elicited by a gastrointestinal infection. Controlling for co-morbid conditions is important in evaluation of CFS-biomarkers.
Hannon KL, Peters S, Fisher L, Riste L, Wearden A, Lovell K, Turner P, Leech Y, Chew-Graham C.	[No address quoted]	Developing resources to support the diagnosis and management of Chronic Fatigue Syndrome/Myalgic	BMC Fam Pract. 2012 Sep 21;13(1):93	ABSTRACT: BACKGROUND: NICE guidelines emphasise the need for a confident, early diagnosis of Chronic Fatigue Syndrome/ Myalgic Encephalitis (CFS/ME) in Primary Care with management tailored to the needs of the patient. Research suggests that GPs are reluctant to make the diagnosis and resources for management are currently inadequate. This study aimed to develop resources for practitioners and patients to support the diagnosis and management of CFS/ME in primary care. METHODS: Semi

		Encephalitis (CFS/ME) in primary care. A qualitative study.		structured interviews were conducted with patients, carers, GPs, practice nurses and CFS/ME specialists in North West England. All interviews were audio recorded, transcribed and analysed qualitatively using open explorative thematic coding. Two patient involvement groups were consulted at each stage of the development of resources to ensure that the resources reflect everyday issues faced by people living with CFS/ME. RESULTS: Patients and carers stressed the importance of recognising CFS/ME as a legitimate condition, and the need to be believed by health care professionals. GPs and practice nurses stated that they do not always have the knowledge or skills to diagnose and manage the condition. They expressed a preference for an online training package. For patients, information on getting the most out of a consultation and the role of carers was thought to be important. Patients did not want to be overloaded with information at diagnosis, and suggested information should be given in steps. A DVD was suggested, to enable information sharing with carers and family, and also for those whose symptoms act as a barrier to reading. CONCLUSION: Rather than use a top-down approach to the development of training for health care practitioners and information for patients and carers, we have used data from key stakeholders to develop a patient DVD, patient leaflets to guide symptom management and a modular e-learning resource which should equip GPs to diagnose and manage CFS/ME effectively, meet NICE guidelines and give patients acceptable, evidence-based information.
Haug C.	[No address quoted]	The guardians of opinion. [Article in English & Norwegian]	Tidsskr Nor Laegeforen. 2012 Feb 7;132(3):261-2. doi: 10.4045/tidsskr.12.03E1.	Comment in Tidsskr Nor Laegeforen. 2012 Apr 30;132(8):927.
Hawkes N.	[No address quoted]	Researcher who linked chronic fatigue syndrome to mouse virus is arrested.	BMJ. 2011 Nov 22;343:d7573. doi: 10.1136/bmj.d7573.	[No abstract given]
Haywood KL, Staniszewska S, Chapman S.	Royal College of Nursing Research Institute, School of Health and Social Studies, University of Warwick, Coventry CV4 7AL, UK. k.l.haywood@warwick.ac.uk	Quality and acceptability of patient-reported outcome measures used in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review.	Qual Life Res. 2012 Feb;21(1):35-52. doi: 10.1007/s11136-011-9921-8.	PURPOSE: To review the quality and acceptability of condition-specific, domain-specific and generic multi-item patient-reported outcome measures (PROMs) used in the assessment of adults with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). METHODS: Systematic literature searches were made to identify PROMs. Quality and acceptability was assessed against an appraisal framework, which captured evidence of both the thoroughness and results of evaluations: evidence of measurement (reliability, validity, responsiveness, interpretability, data quality/precision) and practical properties (feasibility, patient acceptability), and the extent of active patient involvement was sought. RESULTS: A total of 11 CFS/ME-specific, 55 domain-specific and 11 generic measures were reviewed. With the exception of the generic SF-36, all measures had mostly limited evidence of measurement and/or practical properties. Patient involvement was poorly reported and often cursory. CONCLUSIONS: The quality and acceptability of reviewed PROMs is

				limited, and recommendations for patient-reported assessment are difficult. Significant methodological and quality issues in PROM development/evaluation were identified by the appraisal framework, which must be addressed in future research. Clear discrepancies exist between what is measured in research and how patients define their experience of CFS/ME. Future PROM development/evaluation must seek to involve patients more collaboratively to measure outcomes of importance using relevant and credible methods of assessment.
He X, Walker TD, Maranga IO, Oliver AW, Hampson L, Hampson IN.	Viral Oncology Laboratories, University of Manchester School of Cancer & Enabling Sciences, St Mary's Hospital, Manchester, United Kingdom.	No biological evidence of XMRV infection in cervical smears from HIV/ HPV positive and negative Kenyan women.	PLoS One. 2012;7(10):e47208. doi: 10.1371/journal.pone.0047208.	BACKGROUND: XMRV (xenotropic murine leukaemia virus-related virus) is a gammaretrovirus first discovered in human prostate carcinomas and later linked to chronic fatigue syndrome (CFS). Emerging conflicting data and lack of reproducibility of results within the scientific community has now led to the association of XMRV with CFS being discounted. Indeed the case for an involvement with any human disease has been questioned with the suggestion that XMRV is a laboratory generated recombinant virus. The fact that not all published positive findings can be easily explained as contamination artefacts coupled with the observation that XMRV may have a sexually transmitted mode of infectivity and can be infectious for primates, where it preferential resides in cells of the reproductive tract, prompted us to look for evidence of XMRV in the cervical cells of a cohort of Kenyan women both with and without pre-existing HIV/HPV infections. RESULTS: Using a highly sensitive and selective triplex PCR approach we analysed DNA from the liquid based cytology (LBC) cervical smears of 224 Kenyan women. There was no evidence of XMRV expression in any of the sample population irrespective of HPV and/or HIV status. CONCLUSIONS: The data presented show no indication of XMRV infection in any of the cervical samples screened in this study. Approximately 50% of the women were HIV positive but this did not influence the findings signifying that XMRV does not act as an opportunistic infection in this cohort nor is it related to HPV status. Our results therefore support the findings that XMRV is confined to the laboratory and does not currently represent an infectious agent for humans, with a cautionary adage that such potential zoonotic viruses should be carefully monitored in the future.
Heins M, Knoop H, Nijs J, Feskens R, Meeus M, Moorkens G, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, 4628, PO Box 9101, 6500, HB, Nijmegen, The Netherlands, m.heins@nkcv.umcn.nl.	Influence of Symptom Expectancies on Stair-Climbing Performance in Chronic Fatigue Syndrome: Effect of Study Context	Int J Behav Med. 2012 Aug 4.	BACKGROUND: In patients with chronic fatigue syndrome (CFS), performance of physical activities may be affected by an anticipated increase in symptoms after these activities. Nijs et al. previously studied the influence of symptom expectancies and related psychological processes on the performance of an isolated physical activity [Nijs J, Meeus M, Heins M, Knoop H, Moorkens G, Bleijenberg G. Kinesiophobia, catastrophizing and anticipated symptoms before stair climbing in chronic fatigue syndrome: an experimental study. Disabil Rehabil 2012. doi: 10.3109/09638288.2011.641661 .]. PURPOSE: We aimed to validate the previous findings in a larger group of patients in a different setting. We also extended the possible underlying psychological processes studied. METHOD: In 49 CFS patients, we measured performance (duration and increase in heart rate) during self-paced

				climbing and descending of two floors of stairs. Before this task, patients rated experienced fatigue and anticipated fatigue after stair climbing. In addition, kinesiophobia, catastrophising and focusing on bodily symptoms were measured. Using correlational and regression analyses, we tested whether performance during stair climbing could be explained by experienced and anticipated fatigue and psychological factors. RESULTS: Longer duration of stair climbing correlated with higher anticipated fatigue, independently of sex, age, body mass index and fatigue before stair climbing. Focusing on bodily symptoms and fatigue-related catastrophising were related to anticipated fatigue. CONCLUSION: Symptom expectations affect the performance of physical activity in CFS patients, possibly through focusing on bodily symptoms and catastrophising. These findings partially contradict the findings of the previous study, which stresses the importance of study context in conducting this type of experiments (i.e., patient characteristics, instructions).
Heins MJ, Knoop H, Lobbestael J, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands. m.heins@nkcv.umcn.nl	Childhood maltreatment and the response to cognitive behavior therapy for chronic fatigue syndrome.	J Psychosom Res. 2011 Dec;71(6):404-10. doi: 10.1016/j.jpsychores.2011.05.005.	OBJECTIVE: To examine the relationship between a history of childhood maltreatment and the treatment response to cognitive behavior therapy for chronic fatigue syndrome (CFS). METHODS: A cohort study in a tertiary care clinic with a referred sample of 216 adult patients meeting the Centers for Disease Control and Prevention criteria for CFS, and starting cognitive behavior therapy. Main outcome measures changes between pre- and post therapy in fatigue (Checklist Individual Strength fatigue subscale), disabilities (Sickness Impact Profile total score), physical functioning (short form 36 health survey subscale) and psychological distress (Symptom checklist 90 total score). RESULTS: At baseline, patients with a history of childhood maltreatment had significantly more limitations and a higher level of psychological distress, but were not more severely fatigued. Change scores on the outcome measures after cognitive behavior therapy did not differ significantly between patients with or without a history of childhood maltreatment, or between the different types of childhood maltreatment. However, patients with a history of childhood maltreatment still experienced more limitations and a higher level of psychological distress after CBT. CONCLUSIONS: A history of childhood maltreatment was not related to the treatment response of cognitive behavior therapy for CFS. In patients with a history of childhood maltreatment CFS symptoms can be treated with CBT just as well as those without.
Helfenstein M Jr, Goldenfum MA, Siena CA.	Universidade Federal de São Paulo, São Paulo, SP, Brazil. m.helfen@terra.com.br	Fibromyalgia: clinical and occupational aspects. [Article in English & Portuguese]	Rev Assoc Med Bras. 2012 Jun;58(3):358-65.	Fibromyalgia (FM) is a clinical syndrome commonly observed in daily medical practice and its etiopathogenesis is still unclear. As it is characterized by chronic musculoskeletal pain associated with several symptoms, FM may be confused with several other rheumatic and nonrheumatic diseases when they course with pictures of diffuse pain and chronic fatigue. FM treatment should be multidisciplinary, individualized, count on active participation of the patient, and based on combined pharmacological and nonpharmacological modalities. It is found both in work and

				non-work settings, and there is no scientific evidence in the literature showing that FM might be caused by occupation. FM seldom leads to incapacity to work. In cases where pain or fatigue do not respond to appropriate treatment, reaching significant levels, a short period away from work can be considered. As FM is a relevant subject, this review article was based on exploratory, qualitative, and bibliographic investigation, aiming to study the main clinical and occupational aspects of FM, emphasizing the theoretical-conceptual background and the experience of specialists.
Henningsen P, Martin A.	Klinik für Psychosomatische Medizin und Psychotherapie, Klinikum rechts der Isar der TU München	Chronic fatigue syndrome [Article in German]	Dtsch Med Wochenschr. 2013 Jan;138(1-2):33-8. doi: 10.1055/s-0032-1327358.	Enduring and disabling fatigue that cannot be explained by a known disease is the main characteristic of chronic fatigue syndrome. Several definitions do exist, and classification approaches vary regarding supplementary symptoms, time course, and by implicit concepts of aetiology. CFS can be considered as a functional somatic syndrome, e.g. supported by the high rates of comorbid bodily complaints and syndromes that lack clear medical explanation. Accordingly the diagnostic process should not be limited to the thorough physical examination, but also address additional somatic complaints, psychosocial factors (specifically subjective illness beliefs), and impairments. Recently German medical and psychological societies provided treatment guidelines for functional somatic syndromes. Cognitive behavioural therapy and graded activity are evidence based treatment methods for CFS.
Ho RT, Chan JS, Wang CW, Lau BW, So KF, Yuen LP, Sham JS, Chan CL.	Centre on Behavioral Health, The University of Hong Kong, China. tinho@hku.hk	A randomized controlled trial of qigong exercise on fatigue symptoms, functioning, and telomerase activity in persons with chronic fatigue or chronic fatigue syndrome.	Ann Behav Med. 2012 Oct;44(2):160-70. doi: 10.1007/s12160-012-9381-6. Comment in Ann Behav Med. 2012 Oct;44(2):145-6.	BACKGROUND: Chronic fatigue is common in the general population. Complementary therapies are often used by patients with chronic fatigue or chronic fatigue syndrome to manage their symptoms. PURPOSE: This study aimed to assess the effect of a 4-month qigong intervention program among patients with chronic fatigue or chronic fatigue syndrome. METHODS: Sixty-four participants were randomly assigned to either an intervention group or a wait list control group. Outcome measures included fatigue symptoms, physical functioning, mental functioning, and telomerase activity. RESULTS: Fatigue symptoms and mental functioning were significantly improved in the qigong group compared to controls. Telomerase activity increased in the qigong group from 0.102 to 0.178 arbitrary units ($p < 0.05$). The change was statistically significant when compared to the control group ($p < 0.05$). CONCLUSION: Qigong exercise may be used as an alternative and complementary therapy or rehabilitative program for chronic fatigue and chronic fatigue syndrome.
Hollingsworth KG, Hodgson T, Macgowan GA, Blamire AM, Newton JL.	Newcastle Magnetic Resonance Centre, Institute of Cellular Medicine, Newcastle University, NE4 5PL, Newcastle upon Tyne, UK. k.g.hollingsworth@ncl.	Impaired cardiac function in chronic fatigue syndrome measured using magnetic resonance cardiac tagging.	J Intern Med. 2012 Mar;271(3):264-70. doi: 10.1111/j.1365-2796.2011.02429.x.	OBJECTIVES: Impaired cardiac function has been confirmed in patients with chronic fatigue syndrome (CFS). Magnetic resonance cardiac tagging is a novel technique that assesses myocardial wall function in vivo. We hypothesized that patients with CFS may have impaired development and release of myocardial torsion and strain. METHODS: Cardiac morphology and function were assessed using magnetic resonance imaging and cardiac tagging methodology in 12 CFS patients (Fukuda) and 10 matched controls. RESULTS: Compared to controls, the CFS group had substantially reduced left ventricular mass (reduced by 23%), end-diastolic volume (30%), stroke

	ac.uk			volume (29%) and cardiac output (25%). Residual torsion at 150% of the end-systolic time was found to be significantly higher in the patients with CFS (5.3 ± 1.6°) compared to the control group (1.7 ± 0.7°, P = 0.0001). End-diastolic volume index correlated negatively with both torsion-to-endocardial-strain ratio (TSR) (r = -0.65, P = 0.02) and the residual torsion at 150% end-systolic time (r = -0.76, P = 0.004), so decreased end-diastolic volume is associated with raised TSR and torsion persisting longer into diastole. Reduced end-diastolic volume index also correlated significantly with increased radial thickening (r = -0.65, P = 0.03) and impaired diastolic function represented by the ratio of early to late ventricular filling velocity (E/A ratio, r = 0.71, P = 0.009) and early filling percentage (r = 0.73, P = 0.008). CONCLUSION: Patients with CFS have markedly reduced cardiac mass and blood pool volumes, particularly end-diastolic volume: this results in significant impairments in stroke volume and cardiac output compared to controls. The CFS group appeared to have a delay in the release of torsion.
Hong P, Li J.	National Center for Clinical Laboratories, Beijing Hospital of the Ministry of Health, Beijing, People's Republic of China. Pinghong98@yahoo.com	Lack of evidence for a role of xenotropic murine leukemia virus-related virus in the pathogenesis of prostate cancer and/or chronic fatigue syndrome.	Virus Res. 2012 Jul;167(1):1-7. doi: 10.1016/j.virusres.2012.04.004.	Since the discovery of xenotropic murine leukemia virus-related virus (XMRV) in 2006, one of the most controversial topics is whether it contributes to the pathogenesis of prostate cancer (PCa) and/or chronic fatigue syndrome (CFS). The debate began with the failure to detect XMRV in clinical PCa samples. Concerns about the potential health risk of XMRV exposure were reinforced by a study demonstrating the presence of XMRV in patients with CFS. However, serious concerns on whether XMRV plays a role in the development of PCa and/or CFS have been raised. However, inconsistent reports linking XMRV with PCa and/or CFS have led to conflicting views about the potential of XMRV as a human pathogen. Several recent studies suggest that contamination could account for the positive correlations between XMRV and PCa and/or CFS to date. At present, evidence does not indicate that XMRV plays any role in the pathogenesis of PCa or CFS.
Hooper PL, Hightower LE, Hooper PL.	Division of Endocrinology, Metabolism, and Diabetes, School of Medicine, University of Colorado, Anschutz Medical Campus, Aurora, CO 80045, USA. phoopermd@gmail.com	Loss of stress response as a consequence of viral infection: implications for disease and therapy.	Cell Stress Chaperones. 2012 Nov;17(6):647-55. doi: 10.1007/s12192-012-0352-4.	Herein, we propose that viral infection can induce a deficient cell stress response and thereby impairs stress tolerance and makes tissues vulnerable to damage. Having a valid paradigm to address the pathological impacts of viral infections could lead to effective new therapies for diseases that have previously been unresponsive to intervention. Host response to viral infections can also lead to autoimmune diseases like type 1 diabetes. In the case of Newcastle disease virus, the effects of viral infection on heat shock proteins may be leveraged as a therapy for cancer. Finally, the search for a specific virus being responsible for a condition like chronic fatigue syndrome may not be worthwhile if the disease is simply a nonspecific response to viral infection.
Hornig M, Briese T, Licinio J, Khabbaz RF, Altshuler LL,	Center for Infection and Immunity, Columbia University	Absence of evidence for bornavirus infection in	Mol Psychiatry. 2012 May;17(5):486-93. doi: 10.1038/mp.2011.179.	In 1983, reports of antibodies in subjects with major depressive disorder (MDD) to an as-yet uncharacterized infectious agent associated with meningoencephalitis in horses and sheep led to molecular cloning of the genome of a novel, negative-

Potkin SG, Schwemmle M, Siemetzki U, Mintz J, Honkavuori K, Kraemer HC, Egan MF, Whybrow PC, Bunney WE, Lipkin WI.	Mailman School of Public Health, New York, NY 10032, USA. mady.hornig@columbia.edu	schizophrenia, bipolar disorder and major depressive disorder.	Comment in Mol Psychiatry. 2012 May;17(5):472-3.	stranded neurotropic virus, Borna disease virus (BDV). This advance has enabled the development of new diagnostic assays, including in situ hybridization, PCR and serology based on recombinant proteins. Since these assays were first implemented in 1990, more than 80 studies have reported an association between BDV and a wide range of human illnesses that include MDD, bipolar disorder (BD), schizophrenia (SZ), anxiety disorder, chronic fatigue syndrome, multiple sclerosis, amyotrophic lateral sclerosis, dementia and glioblastoma multiforme. However, to date there has been no blinded case-control study of the epidemiology of BDV infection. Here, in a United States-based, multi-center, yoked case-control study with standardized methods for clinical assessment and blinded serological and molecular analysis, we report the absence of association of psychiatric illness with antibodies to BDV or with BDV nucleic acids in serially collected serum and white blood cell samples from 396 subjects, a study population comprised of 198 matched pairs of patients and healthy controls (52 SZ/control pairs, 66 BD/control pairs and 80 MDD/control pairs). Our results argue strongly against a role for BDV in the pathogenesis of these psychiatric disorders.
Hsu ES.	Department of Anesthesiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. ehsu@mednet.ucla.edu	Acute and chronic pain management in fibromyalgia: updates on pharmacotherapy.	Am J Ther. 2011 Nov;18(6):487-509. doi: 10.1097/MJT.0b013e3181d6b6d4.	Fibromyalgia (FM) is a mysterious pain syndrome with progressive and widespread pain, explicit areas of tender points, stiffness, sleep disturbance, fatigue, and psychological distress without any obvious disease. FM is commonly perceived as a condition of central pain and sensory augmentation. There are documented functional abnormalities in pain and sensory processing in FM. Central sensitization and lack of descending analgesic activity are the 2 leading mechanisms that have been demonstrated by advance in both basic and clinical research. The pathogenesis of FM may also be attributed to the genetic polymorphisms involving serotoninergic, dopaminergic, and catecholaminergic systems. Any psychiatric disorders and psychosocial influences in FM may also affect the severity of pain. The various external stimuli or trigger such as infection, trauma, and stress may all contribute to proceed to presentation of FM. The recent launches of 3 US Food and Drug Administration-approved pharmacotherapy for FM namely pregabalin, duloxetine, and milnacipran have certainly raised the profile of optimal chronic pain management. However, appropriate evaluation and efficacious management of acute pain has not been as well publicized as chronic pain in FM. Acute pain or flare up caused by any trauma or surgery certainly may present a real challenge for patients with FM and their health care providers. Pre-emptive analgesia and pro-active treatment may offer the momentum for acute pain control based on model of central sensitization and pain in FM. This review article on FM appraises the modern practice of multimodal therapy focus on both acute and chronic pain management. Meanwhile, the evolving nonpharmacological approach is summarized and stressed as an essential component of integrated care in FM.
Hunskar GS,	Department of Public	The impact of atopic	Scand J Gastroenterol. 2012	OBJECTIVE: To investigate whether atopic disease influences the prevalence of

Langeland N, Wensaas KA, Hanevik K, Eide GE, Mørch K, Rortveit G.	Health and Primary Health Care, University of Bergen, Norway. gunnhild.hunskar@student.uib.no	disease on the risk of post-infectious fatigue and irritable bowel syndrome 3 years after Giardia infection. A historic cohort study.	Sep;8-9(47):956-61. doi: 10.3109/00365521.2012.696681.	irritable bowel syndrome (IBS) and chronic fatigue (CF) after giardiasis. METHODS: A questionnaire was sent to all confirmed cases of giardiasis after a Norwegian outbreak, with response rate of 65.3% (817/1252). Controls were randomly selected matched on age and sex, with response rate of 31.4% (1128/3598). Associations were evaluated by use of logistic regression analyses. RESULTS: In the Giardia exposed group, 47.8% of those with asthma had IBS compared with 45.3% in those without asthma (p = 0.662). For controls, corresponding percentages were 23.9% and 12.2% (p < 0.001). Among those with asthma, the adjusted relative risk (RR) for IBS was 2.03 (95% confidence interval (CI): 1.45, 2.62) for the exposed group compared with controls. In those without asthma, the corresponding RR was 3.80 (95% CI: 3.30, 4.32). In the exposed group, 51.5% of those with asthma had CF compared with 44.9% in those without asthma (p = 0.218). For controls, corresponding percentages were 19.3% and 10.7% (p = 0.004). Among those with asthma, the adjusted RR for CF was 2.73 (95% CI: 1.98, 3.45) for the exposed compared with controls. In those without asthma, the corresponding RR for CF was 4.25 (95% CI: 3.66, 4.85). CONCLUSION: For the exposed, having asthma or allergy did not increase the outcome of IBS or CF. For the control group, having an atopic disease made a substantial risk difference, with significantly more IBS and CF.
Iannuccelli C, Sarzi-Puttini P, Atzeni F, Cazzola M, di Franco M, Guzzo MP, Bazzichi L, Cassisi GA, Marsico A, Stisi S, Salaffi F.	La Sapienza University, Rome, Italy.	Psychometric properties of the Fibromyalgia Assessment Status (FAS) index: a national web-based study of fibromyalgia.	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S49-54.	Fibromyalgia (FM) is a generalized chronic pain condition that is often accompanied by symptoms such as fatigue, sleep disturbances, psychological and cognitive alterations, headache, migraine, variable bowel habits, diffuse abdominal pain, and urinary frequency. Its key assessment domains include pain, fatigue, disturbed sleep, physical and emotional functioning, and patient global satisfaction and health-related quality of life (HRQL). A number of evaluation measures have been adapted from the fields of rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, and others such as the Fibromyalgia Assessment Status (FAS) index and the Fibromyalgia Impact Questionnaire (FIQ) have been specifically developed. The aim of this study was to assess the impact of FM on HRQL by comparing the performance of the FAS index, the FIQ and the Health Assessment Questionnaire [HAQ] in 541 female and 31 male FM patients (mean age 50 years; mean disease duration 7.7 years) entered in the database of a web-based survey registry developed by the Italian Fibromyalgia Network (IFINET). Tests of convergent validity showed that the FAS index and FIQ significantly correlated with each other (rho=0.608, p<0.0001), but there were also significant correlations between the FAS index and other clinical measures of disability, including the HAQ (rho=0.423, p<0.0001), anxiety (rho=0.138, p=0.0009), depression (rho=0.174, p<0.0001) and, especially, the number of comorbidities (rho=0.147, p=0.0004). The FAS index revealed a statistically significant difference between males and females (p=0.048), analysed using the Mann-Whitney U-test for all pair wise comparisons. The FAS index is a valid three-item instrument (pain, fatigue and sleep disturbances) that performs at least as well as the FIQ in FM patients, and

				is simpler to administer and score. Both questionnaires may be useful when screening FM patients, with the choice of the most appropriate instrument depending on the setting.
Israeli E.	The Zabludowicz Center for Autoimmune Diseases, Chaim Sheba Medical Center, Tel-Hashomer, Israel. eitanister@gmail.com	Gulf War syndrome as a part of the autoimmune (autoinflammatory) syndrome induced by adjuvant (ASIA).	Lupus. 2012 Feb;21(2):190-4. doi: 10.1177/0961203311429552.	Gulf War syndrome (GWS) is a multi-symptom condition comprising a variety of signs and symptoms described in the literature, which not been fully resolved. The various symptoms of the condition include muscle fatigue and tiredness, malaise, myalgia, impaired cognition, ataxia, diarrhoea, bladder dysfunction, sweating disturbances, headaches, fever, arthralgia, skin rashes, and gastrointestinal and sleep disturbances. In addition, excessive chemical sensitivity and odour intolerance is reported. The aetiology of the condition is unclear, but many reviews and epidemiological analyses suggest association with pyridostigmine bromide (PB), certain vaccination regimes, a variety of possible chemical exposures, including smoke from oil-well fires or depleted uranium from shells, as well as physical and psychological stress. Recently, Shoenfeld et al. suggested that four conditions--siliconosis, macrophagic myofaciitis (MMF), GWS and post-vaccination phenomena--that share clinical and pathogenic resemblances, may be incorporated into common syndrome called 'Autoimmune (Autoinflammatory) Syndrome induced by Adjuvants' (ASIA). Symptoms and signs of the four conditions described by Shoenfeld et al. show that at least eight out of ten main symptoms are in correlation in all four conditions. Namely, myalgia, arthralgias, chronic fatigue, neurological cognitive impairment, gastrointestinal symptoms, respiratory symptoms, skin manifestations and appearance of autoantibodies. Regardless of the aetiology of GWS, be it exposure to environmental factors or chemical drugs, vaccinations or the adjuvants in them, GWS fits well with the definition of ASIA and is included as part of 'Shoenfeld's syndrome'.
Itoh Y, Shigemori T, Igarashi T, Fukunaga Y.	Department of Pediatrics, Nippon Medical School, Sendagi, Bukyo City, Tokyo, Japan. yasuhiko@nms.ac.jp	Fibromyalgia and chronic fatigue syndrome in children.	Pediatr Int. 2012 Apr;54(2):266-71. doi: 10.1111/j.1442-200X.2011.03514.x	BACKGROUND: Fibromyalgia (FM) is characterized by widespread persistent pain and the presence of multiple discrete tender points. Chronic fatigue syndrome (CFS) is a syndrome characterized by debilitating fatigue associated with a variable number of non-specific complaints. Because neither condition had necessarily been recognized in children until recently, those patients have been treated as having school refusal without being diagnosed as having either syndrome. There is a considerable overlap of clinical symptoms between these two syndromes. It is therefore controversial as to whether these syndromes have the same pathogenesis or not. The aim of the present study was to clarify the relationship between these syndromes in children. METHODS: Fifteen patients with FM and 21 patients with CFS were investigated both clinically and immunologically. Immunological assessments included thorough analysis of autoantibodies using several techniques. RESULTS: Anti-nuclear antibody titers were higher and the prevalence of anti-Sa antibody was far more frequent in CFS patients than in FM patients. CONCLUSION: CFS and FM are different from each other at least in childhood, from an immunological aspect, although some patients could have both conditions.

Jackson ML, Bruck D.	School of Social Sciences and Psychology, Victoria University, Victoria, Australia.	Sleep abnormalities in chronic fatigue syndrome/myalgic encephalomyelitis: a review.	J Clin Sleep Med. 2012 Dec 15;8(6):719-28. doi: 10.5664/jcsm.2276.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a chronic, disabling illness that affects approximately 0.2% of the population. Non-restorative sleep despite sufficient or extended total sleep time is one of the major clinical diagnostic criteria; however, the underlying cause of this symptom is unknown. This review aims to provide a comprehensive overview of the literature examining sleep in CFS/ME and the issues surrounding the current research findings. Polysomnographic and other objective measures of sleep have observed few differences in sleep parameters between CFS/ME patients and healthy controls, although some discrepancies do exist. This lack of significant objective differences contrasts with the common subjective complaints of disturbed and unrefreshed sleep by CFS/ME patients. The emergence of new, more sensitive techniques that examine the microstructure of sleep are showing promise for detecting differences in sleep between patients and healthy individuals. There is preliminary evidence that alterations in sleep stage transitions and sleep instability, and other physiological mechanisms, such as heart rate variability and altered cortisol profiles, may be evident.Future research investigating the etiology of non-restorative sleep in CFS/ME may also help us to undercover the causes of non-restorative sleep and fatigue in other medical conditions
Jahan F, Nanji K, Qidwai W, Qasim R.	[No address quoted]	Fibromyalgia syndrome: an overview of pathophysiology, diagnosis and management.	Oman Med J. 2012 May;27(3):192-5. doi: 10.5001/omj.2012.44.	Fibromyalgia Syndrome (FMS) is a chronic condition causing pain, stiffness, and tenderness of the muscles, tendons, and joints. It is also characterized by restless sleep, tiredness, fatigue, anxiety, depression, and disturbances in bowel functions. The etiology of fibromyalgia remains unknown, but recent advances and discoveries have helped to unravel some of the mysteries of this disease. Research highlights some of the biochemical, metabolic, and immunoregulatory abnormalities associated with fibromyalgia. Management of FMS at the present time is very difficult as it has multiple etiological factors and psychological predispositions; however, a patient centered approach is essential to handle this problem.
Jammes Y, Steinberg JG, Delliaux S.	UMR MD2 P2COE, Faculty of Medicine, Aix-Marseille University and Clinical Respiratory Physiology and Exercise Testing Laboratory, Thorax Pole, National Assistance - Hospitals in Marseille, Marseille, France. yves.jammes@univmed.fr	Chronic fatigue syndrome: acute infection and history of physical activity affect resting levels and response to exercise of plasma oxidant/antioxidant status and heat shock proteins.	J Intern Med. 2012 Jul;272(1):74-84. doi: 10.1111/j.1365-2796.2011.02488.x	OBJECTIVES: A history of high-level physical activity and/or acute infection might constitute stress factors affecting the plasma oxidant-antioxidant status and levels of heat shock proteins (HSPs) in patients with chronic fatigue syndrome (CFS). DESIGN: This case-control study compared data from 43 CFS patients to results from a matched control group of 23 healthy sedentary subjects. SETTING AND SUBJECTS: Five patients had no relevant previous history (group I). Eighteen had practised high-level sport (group II), and severe acute infection had been diagnosed in nine patients (group III). A combination of sport practice and infection was noted in 11 patients (group IV). INTERVENTIONS: After examination at rest, all subjects performed a maximal cycling exercise test. Plasma levels of two markers of oxidative stress [thiobarbituric acid reactive substances (TBARS) and reduced ascorbic acid (RAA)] and both HSP27 and HSP70 were measured. RESULTS: At rest, compared with the control group, the TBARS level was higher in groups II, III and IV patients, and the RAA level

				was lower in groups III and IV. In addition, HSP70 levels were significantly lower in all CFS groups, compared with controls, but negative correlations were found between resting HSP27 and HSP70 levels and the history of physical activity. After exercise, the peak level of TBARS significantly increased in groups II, III and IV, and the variations in HSP27 and HSP70 were attenuated or suppressed, with the greatest effects in groups III and IV. CONCLUSION: The presence of stress factors in the history of CFS patients is associated with severe oxidative stress and the suppression of protective HSP27 and HSP70 responses to exercise.
Jason L, Sorenson M, Sebally K, Alkazemi D, Lerch A, Porter N, Kubow S.	Department of Psychology, DePaul University, Chicago, IL 60614, United States.	Increased HDAC in association with decreased plasma cortisol in older adults with chronic fatigue syndrome.	Brain Behav Immun. 2011 Nov;25(8):1544-7. doi: 10.1016/j.bbi.2011.04.007.	Hypocortisolism is a frequent finding in individuals with chronic fatigue syndrome (CFS) with other research findings implying potential dysregulation of glucocorticoid signaling. Glucocorticoid signaling is under the influence of several pathways, several of which are of interest in the study of CFS. Oxidative stress and decreased antioxidant capacity are known to disrupt the hypothalamic-pituitary-adrenal (HPA) axis (Epel et al., 2004) and the presence of histone deacetylases (HDAC) could also impact glucocorticoid signaling. The intent of this pilot study was to investigate the relationship among oxidative stress elements, select HDAC's (2/3) and glucocorticoid receptor signaling in an elderly sample with CFS. Findings suggest increased histone deacetylase activity, lower total antioxidant power, in the context of decreased plasma cortisol and increased plasma dehydroepiandrosterone concomitant with decreased expression of the encoding gene for the glucocorticoid receptor. These findings support the presence of HPA axis dysregulation in elderly individuals with CFS.
Jason LA, Brown A, Clyne E, Bartgis L, Evans M, Brown M.	DePaul University, Chicago, IL 60614, USA.	Contrasting case definitions for chronic fatigue syndrome, Myalgic Encephalomyelitis/chronic fatigue syndrome and myalgic encephalomyelitis.	Eval Health Prof. 2012 Sep;35(3):280-304. doi: 10.1177/0163278711424281.	This article uses data from patients recruited using the 1994 case definition of chronic fatigue syndrome (CFS) to contrast those meeting criteria for the Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) Canadian case definition with those that did not meet these criteria. The study also contrasts those meeting criteria for Myalgic Encephalomyelitis (ME) based on criteria from Ramsay and other theorists with those that did not meet the ME criteria. The ME/CFS case definition criteria identified a subset of patients with more functional impairments and physical, mental, and cognitive problems than the subset not meeting these criteria. The ME subset had more functional impairments, and more severe physical and cognitive symptoms than the subset not meeting ME criteria. When applied to a population meeting the 1994 CFS case definition, both ME/CFS and ME criteria appear to select a more severe subset of patients.
Jason LA, Brown MM.	Center for Community Research , DePaul University , Chicago, IL , USA.	Sub-typing daily fatigue progression in chronic fatigue syndrome.	J Ment Health. 2012 May 1.	Background Activity logs involve patients writing down their activities and symptoms over 1 or more days. Aims This study sought to classify daily fatigue patterns among patients with chronic fatigue syndrome (CFS) using activity logs. Method Fatigue intensity was self-reported every 30 min in a sample of 90 patients with CFS over 1 day. A cluster analysis using fatigue intensity, variability and slope was conducted. Results Three clusters emerged involving patients with different trajectories. One

				group evidenced high fatigue intensity, low variability, and fatigue intensity stayed the same over time. A second group had moderate fatigue intensity, high variability, and fatigue intensity decreased over time. A third group had moderate fatigue intensity, high variability, but fatigue intensity increased over time. The three clusters of patients differed on measures of actigraphy, pain and immune functioning. Conclusions Activity logs can provide investigators and clinicians with valuable sources of data for understanding patterns of fatigue and activity among patients with CFS.
Jason LA, Skendrovic B, Furst J, Brown A, Weng A, Bronikowski C.	DePaul University, USA. Ljason@depaul.edu	Data mining: comparing the empiric CFS to the Canadian ME/CFS case definition.	J Clin Psychol. 2012 Jan;68(1):41-9. doi: 10.1002/jclp.20827.	This article contrasts two case definitions for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). We compared the empiric CFS case definition (Reeves et al., 2005) and the Canadian ME/CFS clinical case definition (Carruthers et al., 2003) with a sample of individuals with CFS versus those without. Data mining with decision trees was used to identify the best items to identify patients with CFS. Data mining is a statistical technique that was used to help determine which of the survey questions were most effective for accurately classifying cases. The empiric criteria identified about 79% of patients with CFS and the Canadian criteria identified 87% of patients. Items identified by the Canadian criteria had more construct validity. The implications of these findings are discussed.
Jason LA, Unger ER, Dimitrakoff JD, Fagin AP, Houghton M, Cook DB, Marshall GD Jr, Klimas N, Snell C.	DePaul University, United States. LJason@DePaul.edu	Minimum data elements for research reports on CFS.	Brain Behav Immun. 2012 Mar;26(3):401-6. doi: 10.1016/j.bbi.2012.01.014.	Chronic fatigue syndrome (CFS) is a debilitating condition that has received increasing attention from researchers in the past decade. However, it has become difficult to compare data collected in different laboratories due to the variability in basic information regarding descriptions of sampling methods, patient characteristics, and clinical assessments. The issue of variability in CFS research was recently highlighted at the NIH's 2011 State of the Knowledge of CFS meeting prompting researchers to consider the critical information that should be included in CFS research reports. To address this problem, we present our consensus on the minimum data elements that should be included in all CFS research reports, along with additional elements that are currently being evaluated in specific research studies that show promise as important patient descriptors for subgrouping of CFS. These recommendations are intended to improve the consistency of reported methods and the interpretability of reported results. Adherence to minimum standards and increased reporting consistency will allow for better comparisons among published CFS articles, provide guidance for future research and foster the generation of knowledge that can directly benefit the patient.
Jason LA.	DePaul University, Chicago, IL, USA. ljason@depaul.edu	Small wins matter in advocacy movements: giving voice to patients.	Am J Community Psychol. 2012 Jun;49(3-4):307-16. doi: 10.1007/s10464-011-9457-7.	In this article, the various players are delineated in a story of a contested illness and patient advocacy, played out within the corridors of federal power. It is suggested that the mistreatment and negative attitudes that health care providers and others have towards those with chronic fatigue syndrome (CFS) is possibly due to the social construction of this illness as being a "Yuppie flu" disease. Institutional factors are identified that created these norms and attributions, as well as the multiple stakeholders and constituent groups invested in exerting pressure on policy makers to

				effect systemic change. This article also provides examples of how the field of Community Psychology, which is fundamentally committed to/based on listening to and giving voice to patients, is broadly relevant to patient activism communities. This approach focused, over time, on epidemiological studies, the name, the case definition, and ultimately the change in CFS leadership at the Centers for Disease Control and Prevention. Keys to this "small wins" approach were coalition building, use of "oppositional experts" (professionals in the scientific community who support patient advocacy goals) to challenge federal research, and taking advantage of developing events/shifts in power. Ultimately, this approach can result in significant scientific and policy gains, and changes in medical and public perception of an illness.
Jelsness-Jørgensen LP, Bernklev T, Henriksen M, Torp R, Moum B.	Department of Gastroenterology, Oslo University Hospital Aker and Østfold Hospital Trust, 1603 Fredrikstad, Norway. l.p.jelsness-jorgensen@medisin.uio.no	Chronic fatigue is associated with increased disease-related worries and concerns in inflammatory bowel disease.	World J Gastroenterol. 2012 Feb 7;18(5):445-52. doi: 10.3748/wjg.v18.i5.445.	AIM: To investigate the impact of chronic fatigue on disease-related worries in inflammatory bowel disease (IBD) and the potential multicolinearity between subjective questionnaires. METHODS: Patients in remission or with mild-to-moderate disease activity completed the fatigue questionnaire (FQ), the rating form of IBD patient concerns (RFIPC), the Short-Form 36 (SF-36), and IBD questionnaire (N-IBDQ). In addition, clinical and epidemiological data were obtained. RESULTS: In total, 140 patients were included; of which 92 were diagnosed with ulcerative colitis and 48 with Crohn's disease. The mean age of patients with chronic fatigue was 44.2 years (SD = 15.8) and for non-fatigued patients was 44.7 years (SD = 16.0). Chronic fatigued patients had clinically significantly increased levels of disease-related worries, as measured by Cohen's d effect size. Worries about having an ostomy bag, loss of bowel control, and energy levels were most prominent in both chronic fatigued and non-chronic fatigued IBD patients. Variance inflation factor (VIF) and tolerance indicated that there were no problematic multicolinearity among the FQ, RFIPC, SF-36 and N-IBDQ responses (VIF < 5 and tolerance > 2). CONCLUSION: Chronic fatigue is associated with increased levels of disease-related worries and concerns in IBD. Increased levels of worries were also associated with impaired health-related quality of life.
Jones DE, Hollingsworth KG, Jakovljevic DG, Fattakhova G, Pairman J, Blamire AM, Trenell MI, Newton JL.	Institute of Cellular Medicine Newcastle, Newcastle University, Newcastle, UK.	Loss of capacity to recover from acidosis on repeat exercise in chronic fatigue syndrome: a case-control study.	Eur J Clin Invest. 2012 Feb;42(2):186-94. doi: 10.1111/j.1365-2362.2011.02567.x.	BACKGROUND: Chronic fatigue syndrome (CFS) patients frequently describe difficulties with repeat exercise. Here, we explore muscle bioenergetic function in response to three bouts of exercise. METHODS: A total of 18 CFS (CDC 1994) patients and 12 sedentary controls underwent assessment of maximal voluntary contraction (MVC), repeat exercise with magnetic resonance spectroscopy and cardio-respiratory fitness test to determine anaerobic threshold. RESULT: Chronic fatigue syndrome patients undertaking MVC fell into two distinct groups: 8 (45%) showed normal PCr depletion in response to exercise at 35% of MVC (PCr depletion >33%; lower 95% CI for controls); 10 CFS patients had low PCr depletion (generating abnormally low MVC values). The CFS whole group exhibited significantly reduced anaerobic threshold, heart rate, VO(2) , VO(2) peak and peak work compared to controls. Resting muscle pH was similar in controls and both CFS patient groups. However, the CFS group

				achieving normal PCr depletion values showed increased intramuscular acidosis compared to controls after similar work after each of the three exercise periods with no apparent reduction in acidosis with repeat exercise of the type reported in normal subjects. This CFS group also exhibited significant prolongation (almost 4-fold) of the time taken for pH to recover to baseline. CONCLUSION: When exercising to comparable levels to normal controls, CFS patients exhibit profound abnormality in bioenergetic function and response to it. Although exercise intervention is the logical treatment for patients showing acidosis, any trial must exclude subjects who do not initiate exercise as they will not benefit. This potentially explains previous mixed results in CFS exercise trials.
Julkunen H.	HYKS, medisiininen tulosyksikkö, Peijaksen sairaala.	Systemic lupus erythematosus]. [Article in Finnish]	Duodecim. 2012;128(1):51-61.	Systemic lupus erythematosus (SLE) is a chronic syndrome with unknown etiology and polymorphic clinical picture occurring mainly in women. The patients have immunological abnormalities such as autoantibodies against nuclear structures. The prognosis has improved due to active early diagnostics and more efficient treatment of the disease. Mild forms of the disease are associated with fatigue, articular and muscular symptoms, skin rashes, pleuritis or pericarditis and minor changes in the blood. Severe SLE involves glomerulonephritis, complications in the central nervous system, cardiac and pulmonary complications and major changes in the blood.
Kahraman H, Ozkan F, Altınoluk B, Koksal N.	Department of Chest Diseases, Kahramanmaras Sutcuimam University, Turkey.	Scimitar syndrome with renal agenesis.	N Am J Med Sci. 2012 Apr;4(4):193-5. doi: 10.4103/1947-2714.94948.	Partial pulmonary venous connection anomaly is relatively uncommon form of congenital heart diseases. The quite rare combination of this anomaly with hypoplasia of the right lung and dextroposition of the heart is designated as scimitar syndrome. Most cases are presented in infantile period and adult presentation is exceedingly rare. Our patient, a 38-year-old man, was admitted to a doctor with flu-like complaint and because of abnormalities on chest X-ray he was sent to our clinic. He did not have any chronic complaints such as shortness of breath and fatigue. After investigation, scimitar syndrome was diagnosed. Left renal agenesis was determined with abdominal examination. Best of our knowledge in literature we did not detect any case both with Scimitar syndrome and renal agenesis, and we wanted to report the asymptomatic adult Scimitar syndrome case with left renal agenesis.
Kano O, Iwamoto K, Cridebring D, Ikeda K, Iwasaki Y.	[No address quoted]	Relationship between vitamin D and depression in multiple sclerosis.	Acta Neurol Scand. 2012 May;125(5):e25; author reply e26-7. doi: 10.1111/j.1600-0404.2011.01641.x.	Comment on Acta Neurol Scand. 2011 Sep;124(3):171-5.
Kapfhammer HP.	Klinik für Psychiatrie, Medizinische Universität Graz, Auenbruggerplatz 31, 8036 Graz, Österreich. Hans-peter.kapfhammer@kli	Psychopharmacological treatment in patients with somatoform disorders and functional body syndromes. [Article	Nervenarzt. 2012 Sep;83(9):1128-41. doi: 10.1007/s00115-011-3446-9.	Somatoform disorders and functional body syndromes define a major, diagnostically heterogeneous group of patients with medically unexplained physical symptoms. Psychopharmacological approaches can be derived from the conceptualization of somatoform symptoms and syndromes within a biopsychosocial model. The survey presented focuses on randomized, double-blind and placebo-controlled studies. Antidepressants show a statistically and clinically relevant impact on many somatoform symptoms. In special reference to pain symptoms serotonergic and

	nikum-graz.at	in German]		noradrenergic antidepressants seem to mediate a more favorable effect than selective serotonin reuptake inhibitors. For some functional body syndromes, e.g. irritable bowel syndrome and fibromyalgia, a major analgesic effect of antidepressants can be underlined as well. The empirical data for fibromyalgia, however, seem to be more convincing than for irritable bowel syndrome. Pregabalin holds an empirically well established position in the treatment of fibromyalgia. As yet there is no convincing psychopharmacological strategy for chronic fatigue syndrome. Probably due to the inherent relationships to anxiety, obsessive-compulsive and depressive disorders, both hypochondria and body dysmorphic disorder can be positively treated by serotonergic antidepressants as well.
Karafin MS, Stramer SL.	Department of Pathology, Johns Hopkins University, Baltimore, Maryland, USA.	The scientific method at work: xenotropic murine leukemia virus-related virus is neither a cause of chronic fatigue syndrome nor a threat to the blood supply.	Transfusion. 2012 Feb;52(2):222-5. doi: 10.1111/j.1537-2995.2011.03518.x.	[No abstract given]
Karakus N, Yigit S, Inanir A, Inanir S, Toprak H, Okan S.	Ondokuz Mayis University, Faculty of Medicine, Department of Medical Biology, Samsun, Turkey; Gaziosmanpasa University, Faculty of Medicine, Department of Medical Biology, Tokat, Turkey.	Association between sequence variations of the Mediterranean fever gene and fibromyalgia syndrome in a cohort of Turkish patients.	Clin Chim Acta. 2012 Dec 24;414:36-40. doi: 10.1016/j.cca.2012.07.019.	OBJECTIVE: Fibromyalgia syndrome (FMS) is a common chronic widespread pain syndrome mainly affecting women. Genetic risk factors are known to contribute to the etiology of the syndrome. Clinical features show that FMS and familial Mediterranean fever (FMF) have some overlapping symptoms. Mediterranean fever (MEFV) gene has already been identified as being responsible for FMF. The aim of this study was to explore the frequency and clinical significance of missense mutations and a common polymorphism of MEFV gene in a cohort of Turkish patients with FMS. METHODS: The study included 187 patients with FMS and 190 healthy controls. Genomic DNA was isolated and genotyped using polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analyses for the five MEFV gene mutations (M694V, M680I, V726A, E148Q and P369S) and one polymorphism (R202Q). RESULTS: There were statistically significant differences of the MEFV gene mutation carrier rates and allele frequencies between FMS patients and healthy controls (p=0.002, OR: 2.3, 95% CI: 1.35-4.16 and p=0.003, OR: 2.2, 95% CI: 1.28-3.75, respectively). There was also a significant difference between MEFV mutation carriers and non-carriers with respect to the clinical characteristic of morning fatigue (p=0.045). The genotype and allele frequencies of R202Q polymorphism of MEFV gene showed statistically significant differences between FMS patients and healthy controls (p<0.0001 and p<0.0001, respectively) and especially the homozygous AA genotype was significantly higher in FMS patients than in healthy controls (p=0.0003; OR: 7.43, 95% CI: 2.14-39.75). While 13 of the 44 FMS patients with MEFV mutation

				had R202Q polymorphism, none of the 22 controls with MEFV mutation had R202Q polymorphism. Stratification analysis according to clinical features for this disease reveals that morning fatigue and irritable bowel syndrome had associations with R202Q polymorphism (p=0.022 and p=0.031 respectively). CONCLUSION: The results of this study suggest that MEFV gene mutations and polymorphism are positively associated with predisposition to develop FMS. Further studies with larger populations will be required to confirm these findings.
Karlson R.	[No address quoted]	Chronic fatigue syndrome and evolutionary adaptation. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2012 Jun 12;132(11):1317. doi:10.4045/tidsskr.12.0538.	Comment on Tidsskr Nor Laegeforen. 2012 May 15;132(9):1060.
Karlson R.	Psykologisk-pedagogisk tjeneste, for videregående skoler, Rogaland fylkeskommune, Stavanger, Norway. rune.karlson@ppt.rogfk.no	An evolutionary understanding of chronic fatigue syndrome. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2012 Feb 21;132(4):400-1. doi: 10.4045/tidsskr.11.1335.	Comment in Tidsskr Nor Laegeforen. 2012 May 15;132(9):1060.
Karthikeyan P, Ramalingam KP.	Department of Physiotherapy, Divine Word University, Madang, Papua New Guinea. pkarthi@dwu.ac.pg	Meningitis: is a major cause of disability amongst Papua New Guinea children?	Disabil Rehabil. 2012;34(18):1585-8. doi: 10.3109/09638288.2011.651190.	PURPOSE: This article is intended to focus on the need for the use of rehabilitation services, for children with meningitis in Papua New Guinea, which is one of largest developing country in The Pacific with diverse culture and landscape. Meningitis is the fifth leading disease that results in disability in the country. The first line of treatment is usually antibiotics, administration of vaccination is also recommended. Currently community based rehabilitation workers and Physiotherapist offer the rehabilitation services. There is a need for the other rehabilitation professionals and appropriate education to the CBR workers, caregivers for providing effective Rehabilitation. METHOD: Articles related to meningitis were recruited through various electronic database such as Ovid SP, MEDLINE, CINHAL, Google Scholar and HINARI and EBSCOhost for full text. The search includes journal articles, editorials, research reports, systematic reviews and books. RESULTS: The neurological sequelae resulting from meningitis are increasing. There is a need for Hib vaccination to reduce the rate of mortality. Physiotherapists are new professionals that emerged since 2006 and are assisting in reducing the motor and neurological disability. CONCLUSIONS: A multidisciplinary approach is required to manage the child with meningitis. Adequate knowledge, resources and assistance about the condition among the health professionals, carers and teachers would enable the children to achieve the quality of life.
Katz BZ, Jason LA	Division of Infectious	Chronic fatigue	Curr Opin Pediatr. 2012 Dec	PURPOSE OF REVIEW: To review the recent epidemiology, pathophysiology, and

	Diseases, Ann and Robert H. Lurie Children's Hospital of Chicago, Northwestern University Feinberg School of Medicine & Center for Community Research, DePaul University, Chicago, Illinois, USA.	syndrome following infections in adolescents	19	treatment of postinfectious chronic fatigue syndrome (CFS) in adolescents. RECENT FINDINGS: Thirteen percent of adolescents (mainly women) met the criteria for CFS 6 months following infectious mononucleosis; the figure was 7% at 12 months and 4% at 24 months. Peak work capacity, activity level, orthostatic intolerance, salivary cortisol, and natural killer cell number and function were similar between adolescents with CFS following infectious mononucleosis and recovered controls. Autonomic system, oxygen consumption, peak oxygen pulse, psychological and cytokine network differences were documented between those who recovered and those who did not. SUMMARY: The prognosis of CFS is better in adolescents than in adults. Activity level, exercise tolerance, and orthostatic testing could not distinguish patients with CFS from adolescents who have recovered from infectious mononucleosis (controls), while certain cytokine network analyses, life stress factors, and autonomic symptoms could.
Katz BZ, Stewart JM, Shiraishi Y, Mears CJ, Taylor R.	Northwestern University, Chicago, IL 60611, USA. bkatz@northwestern.edu	Orthostatic tolerance testing in a prospective cohort of adolescents with chronic fatigue syndrome and recovered controls following infectious mononucleosis.	Clin Pediatr (Phila). 2012 Sep;51(9):835-9. doi: 10.1177/0009922812455094	Chronic fatigue syndrome (CFS) is a complex condition responsible for marked functional impairment. The authors recently reported that 6 months following acute infectious mononucleosis (IM), 13%, of adolescents met criteria for CFS. The authors' objective was to assess standing orthostatic tolerance (SOT) in adolescents with CFS and in controls 6 months following IM. In all, 36 of 39 adolescents diagnosed with CFS 6 months following IM and 43 of 50 recovered controls had SOT testing (SOTT) performed. χ(2) Analysis was performed to study the relationships between SOTT and the diagnosis of CFS. Adolescents diagnosed with CFS and recovered controls did not differ significantly in age, weight, or body mass index. The authors found that 9 of 36 adolescents with CFS (25%) versus 9 of 43 recovered controls (21%) had an abnormal SOTT, which was not a statistically significant difference. Adolescents who meet criteria for CFS 6 months following IM do not have, as a group, more standing orthostatic intolerance than recovered controls.
Kawatani J, Mizuno K, Shiraishi S, Takao M, Joudoi T, Fukuda S, Watanabe Y, Tomoda A.	Department of Child Development, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan.	Cognitive dysfunction and mental fatigue in childhood chronic fatigue syndrome--a 6-month follow-up study.	Brain Dev. 2011 Nov;33(10):832-41. doi: 10.1016/j.braindev.2010.12.009.	OBJECTIVES: Cognitive function was investigated in patients with childhood type chronic fatigue syndrome (CCFS) using the modified advanced trail making test (mATMT). METHODS: mATMT was performed on 19 patients with CCFS and 25 healthy controls of comparable age and sex. The effectiveness of combined treatment with cognitive behavioral therapy (CBT) and pharmacotherapy and its relationship to cognitive function was investigated by evaluation of Chalder's fatigue scale and behavior state before and after treatment for 6 consecutive months. RESULTS: All three tasks (motor skill, selective and alternative attention, and spatial working memory) of the mATMT, especially the difference in reaction time of the alternative attention task, could discriminate CCFS patients from control subjects with 70.5% accuracy (P=0.007). CCFS patients showed significantly lower alternative attention and Chalder's fatigue score before treatment (P=0.037 and 0.002, respectively). A significant improvement in performance status scores was found during the 6 months follow-up period with combined treatment with CBT and

				medication (P<0.001). Improvement of their cognitive symptoms was significantly correlated with improvement of alternative attention (r=0.653, P=0.002). CONCLUSIONS: Higher-order level cognitive dysfunction affects CCFS pathogenesis. Alternative attention performance evaluated by the mATMT may be used to monitor improvement in patients with CCFS. Combined treatment with CBT and medication may be effective to improve poor attention characteristics associated with CCFS.
Kearney MF, Lee K, Bagni RK, Wiegand A, Spindler J, Maldarelli F, Pinto PA, Linehan WM, Vocke CD, Delviks-Frankenberry KA, Devere White RW, Del Prete GQ, Mellors JW, Lifson JD, Kewalramani VN, Pathak VK, Coffin JM, Le Grice SF.	HIV Drug Resistance Program, National Cancer Institute at Frederick, Frederick, MD 21702-1201, USA.	Nucleic Acid, Antibody, and Virus Culture Methods to Detect Xenotropic MLV-Related Virus in Human Blood Samples.	Adv Virol. 2011;2011:272193. doi: 10.1155/2011/272193.	The MLV-related retrovirus, XMRV, was recently identified and reported to be associated with both prostate cancer and chronic fatigue syndrome. At the National Cancer Institute-Frederick, MD (NCI-Frederick), we developed highly sensitive methods to detect XMRV nucleic acids, antibodies, and replication competent virus. Analysis of XMRV-spiked samples and/or specimens from two pigtail macaques experimentally inoculated with 22Rv1 cell-derived XMRV confirmed the ability of the assays used to detect XMRV RNA and DNA, and culture isolatable virus when present, along with XMRV reactive antibody responses. Using these assays, we did not detect evidence of XMRV in blood samples (N = 134) or prostate specimens (N = 19) from two independent cohorts of patients with prostate cancer. Previous studies detected XMRV in prostate tissues. In the present study, we primarily investigated the levels of XMRV in blood plasma samples collected from patients with prostate cancer. These results demonstrate that while XMRV-related assays developed at the NCI-Frederick can readily measure XMRV nucleic acids, antibodies, and replication competent virus, no evidence of XMRV was found in the blood of patients with prostate cancer.
Kearney MF, Spindler J, Wiegand A, Shao W, Anderson EM, Maldarelli F, Ruscetti FW, Mellors JW, Hughes SH, Le Grice SF, Coffin JM.	HIV Drug Resistance Program, National Cancer Institute, Frederick, Maryland, United States of America. kearneym@mail.nih.gov	Multiple sources of contamination in samples from patients reported to have XMRV infection.	PLoS One. 2012;7(2):e30889. doi: 10.1371/journal.pone.0030889.	Xenotropic murine leukemia virus (MLV)-related retrovirus (XMRV) was reported to be associated with prostate cancer by Urisman, et al. in 2006 and chronic fatigue syndrome (CFS) by Lombardi, et al. in 2009. To investigate this association, we independently evaluated plasma samples from 4 patients with CFS reported by Lombardi, et al. to have XMRV infection and from 5 healthy controls reported to be XMRV uninfected. We also analyzed viral sequences obtained from supernatants of cell cultures found to contain XMRV after coculture with 9 clinical samples from 8 patients. A qPCR assay capable of distinguishing XMRV from endogenous MLVs showed that the viral sequences detected in the CFS patient plasma behaved like endogenous MLVs and not XMRV. Single-genome sequences (N = 89) from CFS patient plasma were indistinguishable from endogenous MLVs found in the mouse genome that are distinct from XMRV. By contrast, XMRV sequences were detected by qPCR in 2 of the 5 plasma samples from healthy controls (sequencing of the qPCR product confirmed XMRV not MLV). Single-genome sequences (N = 234) from the 9 culture supernatants reportedly positive for XMRV were indistinguishable from XMRV sequences obtained from 22Rv1 and XMRV-contaminated 293T cell-lines. These results indicate that MLV DNA detected in the plasma samples from CFS patients evaluated in this study was from contaminating mouse genomic DNA and that XMRV detected in plasma samples from healthy controls and in cultures of patient samples

				was due to cross-contamination with XMRV (virus or nucleic acid).
Keller J, Chen YK, Lin HC.	School of Public Health, Taipei Medical University, Taipei, Taiwan.	Association of bladder pain syndrome/interstitial cystitis with urinary calculus: a nationwide population-based study.	Int Urogynecol J. 2012 Aug 16.	INTRODUCTION AND HYPOTHESIS: Although one prior study reported an association between bladder pain syndrome/interstitial cystitis (BPS/IC) and urinary calculi (UC), no population-based study to date has been conducted to explore this relationship. Therefore, using a population-based data set in Taiwan, this study set out to investigate the association between BPS/IC and a prior diagnosis of UC. METHODS: This study included 9,269 cases who had received their first-time diagnosis of BPS/IC between 2006 and 2007 and 46,345 randomly selected controls. We used conditional logistic regression analysis to compute the odds ratio (OR) and its corresponding 95 % confidence interval (CI) for having been previously diagnosed with UC between cases and controls. RESULTS: There was a significant difference in the prevalence of prior UC between cases and controls (8.1 vs 4.3 %, $p < 0.001$). Conditional logistic regression analysis revealed that cases were more likely to have been previously diagnosed with UC than controls (OR = 1.70; 95 % CI = 1.56-1.84) after adjusting for chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraine, sicca syndrome, allergy, endometriosis, and asthma. BPS/IC was found to be significantly associated with prior UC regardless of stone location; the adjusted ORs of kidney calculus, ureter calculus, bladder calculus, and unspecified calculus when compared to controls were 1.58 (95 % CI = 1.38-1.81), 1.73 (95 % CI = 1.45-2.05), 3.80 (95 % CI = 2.18-6.62), and 1.83 (95 % CI = 1.59-2.11), respectively. CONCLUSIONS: This work generates the hypothesis that UC may be associated with BPS/IC.
Keller JJ, Liu SP, Lin HC.	School of Public Health, Taipei Medical University, Taipei, Taiwan.	A case-control study on the association between rheumatoid arthritis and bladder pain syndrome/interstitial cystitis.	Neurourol Urodyn. 2012 Nov 5. doi: 10.1002/nau.22348.	AIM: While bladder pain syndrome/interstitial cystitis (BPS/IC) has been suggested by a number of studies to have autoimmune character, no population-based study to date has been conducted investigating its association with rheumatoid arthritis (RA). This study aimed to examine the association between IC/BPS and having previously been diagnosed with RA. METHODS: We conducted this study by using administrative claims data sourced from the Taiwan National Health Insurance Database. Our study included 9,269 cases with BPS/IC and 46,345 randomly selected controls. Conditional logistic regression was performed to calculate the odds ratio (OR) for the association between previously diagnosed RA and IC/BPS. RESULTS: RA was found among 202 (2.2%) cases and 504 (1.12%) controls. Conditional logistic regression analysis suggested that when compared with controls, the OR for prior RA among cases was 1.66 (95% CI = 1.47-1.87, $P < 0.001$) after adjusting for diabetes, hypertension, coronary heart disease, obesity, hyperlipidemia, chronic pelvic pain, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, depression, panic disorder, migraine, sicca syndrome, allergy, endometriosis, asthma, overactive bladder, tobacco use disorder, and alcohol abuse. Additionally, BPS/IC was consistently and significantly associated with a previous diagnosis of RA regardless of prescription drug use; the OR for prior RA among groups prescribed ≤1 type of disease-modifying antirheumatic

				drug (DMARD), two types of DMARDs, and ≥3 types of DMARDs or TNF-alpha inhibitor when compared to controls were 1.49 (95% CI = 1.28-1.72), 1.91 (95% CI = 1.38-2.68), and 2.36 (95% CI = 1.77-3.17), respectively. CONCLUSIONS: There is an association between RA and BPS/IC after adjusting for socio-demographic characteristics and medical co-morbidities.
Kempke S, Luyten P, Claes S, Goossens L, Bekaert P, Van Wambeke P, Van Houdenhove B.	Department of Psychology, University of Leuven, Belgium.	Self-critical perfectionism and its relationship to fatigue and pain in the daily flow of life in patients with chronic fatigue syndrome.	Psychol Med. 2012 Aug 30:1-8	BACKGROUND: Research suggests that the personality factor of self-critical or maladaptive perfectionism may be implicated in chronic fatigue syndrome (CFS). However, it is not clear whether self-critical perfectionism (SCP) also predicts daily symptoms in CFS. Method In the present study we investigated whether SCP predicted fatigue and pain over a 14-day period in a sample of 90 CFS patients using a diary method approach. After completing the Depressive Experiences Questionnaire (DEQ) as a measure of SCP, patients were asked each day for 14 days to complete Visual Analogue Scales (VAS) of fatigue, pain and severity of depression. Data were analysed using multilevel analysis. RESULTS: The results from unconditional models revealed considerable fluctuations in fatigue over the 14 days, suggesting strong temporal variability in fatigue. By contrast, pain was relatively stable over time but showed significant inter-individual differences. Congruent with expectations, fixed-effect models showed that SCP was prospectively associated with higher daily fatigue and pain levels over the 14-day period, even after controlling for levels of depression. CONCLUSIONS: This is the first study to show that SCP predicts both fatigue and pain symptoms in CFS in the daily course of life. Hence, therapeutic interventions aimed at targeting SCP should be considered in the treatment of CFS patients with such features.
Kempke S, Luyten P, Van Houdenhove B, Goossens L, Bekaert P, Van Wambeke P.	Department of Psychology, University of Leuven, Tiensestraat 102, 3000 Leuven, Belgium. stefan.kempke@psy.kuleuven.be	Self-esteem mediates the relationship between maladaptive perfectionism and depression in chronic fatigue syndrome.	Clin Rheumatol. 2011 Dec;30(12):1543-8. doi: 10.1007/s10067-011-1772-8.	Patients with chronic fatigue syndrome (CFS) often experience depression which may negatively affect prognosis and treatment outcome. Research has shown that depression in CFS is associated with maladaptive or self-critical perfectionism. However, currently, little is known about factors that may explain this relationship, but studies in nonclinical samples suggest that low self-esteem may be an important mediator of this relationship. The present study therefore examined whether self-esteem mediated the cross-sectional association between maladaptive perfectionism and severity of depression in 192 patients meeting Centres for Disease Control and Prevention criteria for CFS. Patients completed self-report measures of maladaptive perfectionism, self-esteem, depression, and fatigue. Regression analyses and more direct tests of indirect effects (i.e., the Sobel test and bootstrapping) were used to test for mediation. Congruent with expectations, we found that self-esteem fully mediated the relationship between maladaptive perfectionism and depression in CFS. Findings from this study suggest that self-esteem may explain the link between maladaptive perfectionism and depression in CFS, which may have important implications for the treatment and prevention of depression in these patients.
Kempke S, Van	Department of	Prevalence of DSM-	Int J Behav Med. 2012 Oct 13.	BACKGROUND: It is not yet clear whether chronic fatigue syndrome (CFS) is associated

Den Eede F, Schotte C, Claes S, Van Wambeke P, Van Houdenhove B, Luyten P.	Psychology, University of Leuven, Tiensestraat 102, 3000, Leuven, Belgium, Stefan.Kempke@ppw.kuleuven.be.	IV Personality Disorders in Patients with Chronic Fatigue Syndrome: A Controlled Study.		with elevated levels of personality disorders. PURPOSE: This study aims to determine the prevalence of DSM-IV axis II personality disorders among patients with CFS. METHODS: We examined the prevalence of personality disorders in a sample of 92 female CFS patients and in two well-matched control groups, i.e., normal community individuals (N = 92) and psychiatric patients (N = 92). Participants completed the assessment of DSM-IV personality disorders questionnaire (ADP-IV), which yields a categorical and dimensional evaluation of personality disorder features. RESULTS: The prevalence of personality disorders in CFS patients (16.3 %) was significantly lower than in psychiatric patients (58.7 %) and was similar to that in the community sample (16.3 %). Similar results were found for dimensional and pseudodimensional scores, except for the Depressive (DE) and Obsessive-Compulsive Personality Disorder (O-C) subscales. Patients with CFS had significantly higher levels of DE features compared to normal controls and similar dimensional scores on the O-C scale compared to psychiatric controls. CONCLUSIONS: Although the CFS sample was characterized by depressive and obsessive-compulsive personality features, this study provides no evidence for the assumption that these patients generally show a higher prevalence of axis II pathology. Given the conflicting findings in this area, future studies using multiple measures to assess personality disorders in CFS are needed to substantiate these findings.
Kim SE, Chang L.	Oppenheimer Family Center of Neurobiology of Stress, Los Angeles, CA, USA.	Overlap between functional GI disorders and other functional syndromes: what are the underlying mechanisms?	Neurogastroenterol Motil. 2012 Oct;24(10):895-913. doi: 10.1111/j.1365-2982.2012.01993.x.	BACKGROUND: Irritable bowel syndrome and other gastrointestinal (GI) and non-GI disorders such as functional dyspepsia, fibromyalgia, temporomandibular joint disorder, interstitial cystitis/painful bladder syndrome, and chronic fatigue syndrome are known as functional pain syndromes. They commonly coexist within the same individual. The pathophysiologic mechanisms of these disorders are not well understood, but it has been hypothesized that they share a common pathogenesis. PURPOSE: The objective of this review is to discuss the proposed pathophysiologic mechanisms, which have been similarly studied in these conditions. These mechanisms include enhanced pain perception, altered regional brain activation, infectious etiologies, dysregulations in immune and neuroendocrine function, and genetic susceptibility. Studies suggest that these functional disorders are multifactorial, but factors which increase the vulnerability of developing these conditions are shared.
Kindlon T	[No address quoted]	Internet-based CBT for adolescents with chronic fatigue syndrome.	Lancet. 2012 Aug 11;380(9841):561; author reply 562. doi: 10.1016/S0140-6736(12)61324-5.	Comment on Lancet. 2012 Apr 14;379(9824):1412-8.
Kindlon T.	Irish ME/CFS Association, Dublin, Ireland.	Objective compliance and outcome measures should be	Eur J Clin Invest. 2012 Dec;42(12):1360-1. doi: 10.1111/j.1365-	[No abstract given]

		used in trials of exercise interventions for Chronic Fatigue Syndrome.	2362.2012.02724.x.	
King M, Kingery J, Casey B.	Department of Family and Community Medicine, University of Kentucky College of Medicine, Lexington, KY 40536, USA. mrking02@uky.edu	Diagnosis and evaluation of heart failure.	Am Fam Physician. 2012 Jun 15;85(12):1161-8.	Heart failure is a common clinical syndrome characterized by dyspnea, fatigue, and signs of volume overload, which may include peripheral edema and pulmonary rales. Heart failure has high morbidity and mortality rates, especially in older persons. Many conditions, such as coronary artery disease, hypertension, valvular heart disease, and diabetes mellitus, can cause or lead to decompensation of chronic heart failure. Up to 40 to 50 percent of patients with heart failure have diastolic heart failure with preserved left ventricular function, and the overall mortality is similar to that of systolic heart failure. The initial evaluation includes a history and physical examination, chest radiography, electrocardiography, and laboratory assessment to identify causes or precipitating factors. A displaced cardiac apex, a third heart sound, and chest radiography findings of venous congestion or interstitial edema are useful in identifying heart failure. Systolic heart failure is unlikely when the Framingham criteria are not met or when B-type natriuretic peptide level is normal. Echocardiography is the diagnostic standard to confirm systolic or diastolic heart failure through assessment of left ventricular ejection fraction. Evaluation for ischemic heart disease is warranted in patients with heart failure, especially if angina is present, given that coronary artery disease is the most common cause of heart failure.
Kingma EM, Moddejonge R, Rosmalen J.	Rijksuniversiteit Groningen, Universitair Medisch Centrum Groningen, Interdisciplinair Centrum Psychopathologie en Emotieregulatie (ICPE), Groningen, the Netherlands. e.m.kingma@umcg.nl	How do patients interpret terms for medically unexplained symptoms? [Article in Dutch]	Ned Tijdschr Geneeskd. 2012;156(37):A4541.	OBJECTIVE: To investigate how primary care patients interpret the existing terminology used to describe medically unexplained symptoms; to contribute to the current academic discussion on unequivocal terminology. DESIGN: Descriptive cohort study. METHODS: We approached patients in the waiting rooms of two general medical practices in the city of Groningen and in the province of Drenthe. Based on a fictitious case, the patients were asked to assign connotations to a number of possible diagnoses for medically unexplained tiredness. The patients could choose from seven predetermined connotations. Among the diagnoses for medically unexplained tiredness were 'functional fatigue', 'chronic fatigue syndrome', 'psychosomatic tiredness', and 'medically unexplained tiredness'. From the seven connotations, we labeled three connotations as being negative. When patients gave at least one negative connotation to a possible diagnosis, the diagnosis was labeled as 'offensive'. RESULTS: A total of 184 patients participated in the study. From the alternative diagnoses for medically unexplained tiredness, 'psychosomatic tiredness' had the most negative connotations: at least one negative connotation for 65 (35%) patients. 'Chronic fatigue syndrome' and 'functional fatigue' had the fewest negative connotations: at least one negative connotation for respectively 17 (9%) and 24 (13%)

				patients. CONCLUSION: The terms 'chronic fatigue syndrome' and 'functional fatigue' were less offensive. Our results could imply that terms for medically unexplained tiredness that refer less to a psychological basis are most acceptable for the patient.
Kishi A, Natelson BH, Togo F, Struzik ZR, Rapoport DM, Yamamoto Y.	Educational Physiology Laboratory, Graduate School of Education, University of Tokyo, Tokyo, Japan.	Sleep-stage dynamics in patients with chronic fatigue syndrome with or without fibromyalgia.	Sleep. 2011 Nov 1;34(11):1551-60. doi: 10.5665/sleep.1396.	STUDY OBJECTIVES: Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained conditions that often have overlapping symptoms, including sleep-related complaints. However, differences between the 2 conditions have been reported, and we hypothesized that dynamic aspects of sleep would be different in the 2 groups of patients. PARTICIPANTS: Subjects were 26 healthy control subjects, 14 patients with CFS but without FM (CFS alone), and 12 patients with CFS and FM (CFS+FM)-all women. MEASUREMENTS AND RESULTS: We studied transition probabilities and rates between sleep stages (waking, rapid eye movement [REM] sleep, stage 1 [S1], stage 2 [S2], and slow-wave sleep [SWS]) and duration distributions of each sleep stage. We found that the probability of transition from REM sleep to waking was significantly greater in subjects with CFS alone than in control subjects, which may be the specific sleep problem for people with CFS alone. Probabilities of (a) transitions from waking, REM sleep, and S1 to S2 and (b) those from SWS to waking and S1 were significantly greater in subjects with CFS+FM than in control subjects; in addition, rates of these transitions were also significantly increased in subjects with CFS+FM. Result (a) might indicate increased sleep pressure in subjects with CFS+FM whereas result (b) may be the specific sleep problem of subjects with CFS+FM. We also found that shorter durations of S2 sleep are specific to patients with CFS+FM, not to CFS alone. CONCLUSIONS: These results suggest that CFS and FM may be different illnesses associated with different problems of sleep regulation.
Klimas NG, Broderick G, Fletcher MA.	Miami Veterans Affairs Medical Center, Miami, FL, USA. Nancy.Klimas@va.gov	Biomarkers for chronic fatigue.	Brain Behav Immun. 2012 Nov;26(8):1202-10. doi: 10.1016/j.bbi.2012.06.006.	Fatigue that persists for 6 months or more is termed chronic fatigue. Chronic fatigue (CF) in combination with a minimum of 4 of 8 symptoms and the absence of diseases that could explain these symptoms, constitute the case definition for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). Inflammation, immune system activation, autonomic dysfunction, impaired functioning in the hypothalamic-pituitary-adrenal axis, and neuroendocrine dysregulation have all been suggested as root causes of fatigue. The identification of objective markers consistently associated with CFS/ME is an important goal in relation to diagnosis and treatment, as the current case definitions are based entirely on physical signs and symptoms. This review is focused on the recent literature related to biomarkers for fatigue associated with CFS/ME and, for comparison, those associated with other diseases. These markers are distributed across several of the body's core regulatory systems. A complex construct of symptoms emerges from alterations and/or dysfunctions in the nervous, endocrine and immune systems. We propose that new insight will depend on our ability to develop and deploy an integrative profiling of CFS/ME pathogenesis at the molecular level. Until such a molecular signature is obtained efforts to develop

				effective treatments will continue to be severely limited.
Kmietowicz Z.	[No address quoted]	Researchers get 1.6m pound to look at scientific basis of chronic fatigue syndrome.	BMJ. 2011 Dec 21;343:d8281. doi: 10.1136/bmj.d8281.	[No abstract given]
Knudsen A, Lervik L, Harvey S, Løvvik C, Omenås A, Mykletun A.	Department of Health Promotion and Development, Faculty of Psychology, University of Bergen , Bergen , Norway.	Comparison of chronic fatigue syndrome/myalgic encephalopathy with other disorders: an observational study.	JRSM Short Rep. 2012 May;3(5):32. doi: 10.1258/shorts.2011.011167.	OBJECTIVES: To examine the level of activity in online discussion forums for chronic fatigue syndrome/myalgic encephalopathy (CFS/ME) compared to other disorders. We hypothesized the level of activity to be higher in CFS/ME online discussion forums. DESIGN: Observational study SETTING: Norway, which has more than 80% household coverage in internet access, September 2009 PARTICIPANTS: Twelve Norwegian disorder-related online discussion forums MAIN OUTCOME MEASURES: Number of registered users and number of posted messages on each discussion forum RESULTS: Two forums were targeted towards individuals with CFS/ME. These forums had the highest number of registered users per estimated 1,000 cases in the population (50.5 per 1,000 and 29.7 per 1,000), followed by a site for drug dependency (5.4 per 1,000). Counting the number of posted messages per 1,000 cases gave similar indications of high online activity in the CFS/ME discussion forums. CONCLUSIONS: CFS/ME online forums had more than ten times the relative activity of any other disorder or condition related forum. This high level of activity may have multiple explanations. Individuals suffering from a stigmatized condition of unknown aetiology may use the internet to look for explanations of symptoms or to seek out alternative treatments. Internet forum activity may also be reinforced by the creation of in-group identity and pre-morbid personality traits. More knowledge on the type and quality of information provided in online forums is urgently needed.
Knudsen AK, Henderson M, Harvey SB, Chalder T.	Research Section of Mental Health Epidemiology, Department of Health Promotion and Development, Faculty of Psychology, University of Bergen, Christiesgt. 13, N-5020 Bergen, Norway. Ann.Knudsen@psych.uib.no	Long-term sickness absence among patients with chronic fatigue syndrome	Br J Psychiatry. 2011 Nov;199(5):430-1. doi: 10.1192/bjp.bp.110.082974.	Chronic fatigue syndrome is associated with high levels of occupational disability. Consecutive out-patients at a chronic fatigue syndrome treatment service were studied for associations between occupational status, symptom severity and cognitive and behavioural responses to symptoms. All patients had high symptom levels; however, those on long-term sickness absence had significantly more physical fatigue ($\beta = 0.098$, $P<0.05$) and worse sleep ($\beta = 0.075$, $P<0.05$). Patients with long-term sickness absence also demonstrated more embarrassment avoidance cognitions ($\beta = 0.086$, $P<0.05$) and avoidance resting behavioural responses ($\beta = 0.078$, $P<0.05$). Identifying and addressing avoidance behaviours and cognitions regarding embarrassment in interventions may enhance the chances of individuals returning to work.
Korenromp IH, Meeus M, Bleijenberg G.	St. Antonius Ziekenhuis, centrum Interstitiële	Dutch language area definition of chronic fatigue. [Article in	Ned Tijdschr Geneeskd. 2012;156(16):A4403.	Chronic fatigue is a frequent but unspecific characteristic of many diseases. However, a clear definition of 'chronic fatigue' is still lacking. The Flemish-Dutch Research Group - Chronic Fatigue (VNO-CHROVER) has taken the opportunity to formulate such a

	Longziekten, Nieuwegein, the Netherlands. i.korenromp@antoniusziekenhuis.nl	Dutch]		definition that can be widely applied. This definition is not only beneficial to researchers conducting, reporting and comparing scientific studies on chronic fatigue in diverse patient populations, but also to clinicians of various disciplines in order to improve patient care. VNO-CHROVER proposes to define chronic fatigue as 'a self-reported reduction of physical and/or mental well-being that persists longer than 6 months and is manifested as exhaustion by which one fails to function at the desired level.'
Korn K, Reil H, Ensser A, Knöll A.	Institute of Clinical and Molecular Virology, Friedrich-Alexander-University Erlangen-Nuremberg, Erlangen, Germany.	No evidence of XMRV infection in immunocompromised patients and HIV-positive individuals from Germany.	Infection. 2012 Apr;40(2):181-4. doi: 10.1007/s15010-012-0249-2.	BACKGROUND: Xenotropic murine leukaemia virus-related virus (XMRV) has been detected in patients with prostate cancer and chronic fatigue syndrome (CFS). The detection of XMRV in healthy individuals has raised concern about a possible virus transmission by blood products. However, recent studies challenge the association between XMRV and human disease. This study investigated whether or not XMRV is present in patients with altered immune function and individuals at increased risk of blood-borne viral infections in Germany. METHODS: We investigated 503 peripheral blood mononuclear cell (PBMC) samples from 240 patients with iatrogenic immune suppression (71 haematopoietic stem cell recipients, 132 solid organ transplant recipients, 37 others) and 311 PBMC samples from 302 patients with HIV-1 infection for the presence of proviral XMRV by real-time polymerase chain reaction (PCR). RESULTS: All 814 PBMC samples from 542 patients tested negative for XMRV DNA and positive for an internal herpesvirus saimiri (HVS) control. Human genomic DNA was detected in all samples, and 90% of the samples contained >10,000 cell equivalents per XMRV PCR reaction. CONCLUSIONS: Our failure to detect proviral XMRV provides evidence against the presence of XMRV in patients at increased risk of viral infections in Ge
Koshimichi M, Sugimoto K, Yanagida H, Fujita S, Miyazawa T, Sakata N, Okada M, Takemura T.	Department of Pediatrics, Kinki University School of Medicine, Osaka, Japan.	Newly-identified symptoms of left renal vein entrapment syndrome mimicking orthostatic disturbance.	World J Pediatr. 2012 May;8(2):116-22. doi: 10.1007/s12519-012-0349-1.	BACKGROUND: In addition to the urinary abnormalities, symptoms of left renal vein entrapment between the aorta and superior mesenteric artery (left renal vein entrapment syndrome, LRVES) may include abdominal and flank pain as well as chronic fatigue. We investigated various LRVES symptoms in this study. METHODS: In 53 pediatric LRVES patients treated at our department, 22 had a score of 5 points or higher on orthostasis. Initial evaluation of LRVES by abdominal ultrasonography showed a stenotic-to-prestenotic vein diameter ratio of 0.2 or less. Definitive diagnosis was made by computed tomography and magnetic resonance angiography. Cortisol, catecholamine (CA), and brain natriuretic peptide (BNP) were also measured. RESULTS: The frequency of LRVES was 2.5 times higher in girls than in boys. Low or very low body mass indexes were seen in both sexes. The most common initial finding was urine abnormalities, followed by dizziness and malaise. In 6 patients, orthostasis precluded school attendance. Ten patients had orthostasis scores above 12. Patients unable to attend school had either low levels of plasma or urinary cortisol. Midodrine significantly decreased orthostasis scores. Some patients required treatment with fludrocortisone. Plasma CA, renin, and BNP levels were all normal. CONCLUSIONS:

				Locally excessive venous pressure may cause reversible adrenal dysfunction with transitory Addisonian symptoms. Children with cryptogenic malaise or severe orthostasis should be evaluated for LRVES.
Krause K, Grattan CE, Bindslev-Jensen C, Gattorno M, Kallinich T, de Koning HD, Lachmann HJ, Lipsker D, Navarini AA, Simon A, Traidl-Hoffmann C, Maurer M.	Autoinflammation Reference Center Charité, Charité-Universitätsmedizin Berlin, Berlin, Germany.	How not to miss autoinflammatory diseases masquerading as urticaria.	Allergy. 2012 Dec;67(12):1465-74. doi: 10.1111/all.12030.	Urticarial skin reactions are one of the most frequent problems seen by allergists and clinical immunologists in daily practice. The most common reason for recurrent wheals is spontaneous urticaria. There are, however, several less common diseases that present with urticarial rash, such as urticarial vasculitis and autoinflammatory disorders. The latter include cryopyrin-associated periodic syndrome and Schnitzler's syndrome, both rare and disabling conditions mediated by increased interleukin-1 secretion. Apart from the urticarial rash, patients are suffering from a variety of systemic symptoms including recurrent fever attacks, arthralgia or arthritis and fatigue. Autoinflammatory diseases are often associated with a diagnostic delay of many years and do not respond to antihistamines and other treatments of urticaria. Also, the chronic inflammation may lead to long-term complications such as amyloidosis. It is therefore important not to miss these diseases when diagnosing and treating patients with chronic recurrent urticarial rash. Here, we present clinical clues and tips that can help to identify autoinflammatory disorders in patients presenting with chronic urticarial rash and discuss their clinical picture and management.
Kreijkamp-Kaspers S, Brenu EW, Marshall S, Staines D, Van Driel ML.	Academic General Practice, Faculty of Health Sciences & Medicine, Bond University, Gold Coast, Queensland. skreijka@bond.edu.au	Treating chronic fatigue syndrome - a study into the scientific evidence for pharmacological treatments.	Aust Fam Physician. 2011 Nov;40(11):907-12.	BACKGROUND: Chronic fatigue syndrome, or myalgic encephalomyelitis (CFS), is a severe disabling condition. Patients with CFS usually trial many different medicines, both conventional and complementary. An overview of the pharmacological treatments used by CFS patients and the available evidence underpinning the use of these treatments would be of great value to both patients and their healthcare providers. METHODS: Ninety-four CFS patients recruited into an Australian study investigating immunological biomarkers filled out a questionnaire assessing the medicines they were taking. Evidence from randomised clinical trials was sought in biomedical databases. RESULTS: The 94 CFS patients used 474 different medicines and supplements. The most commonly used medicines were antidepressants, analgesics, sedatives, and B vitamins. We identified 20 randomised controlled trials studying these medicines in CFS patients. DISCUSSION: While conventional and complementary medicines are widely used by CFS patients, the evidence for effectiveness in CFS is very limited.
Kümmerle-Deschner JB	Klinik für Kinder- und Jugendmedizin, Abteilung für pädiatrische Rheumatologie, Autoinflammation Reference Center Tübingen,	Cryopyrin-associated periodic syndrome. [Article in German]	Z Rheumatol. 2012 Apr;71(3):199-208. doi: 10.1007/s00393-011-0856-9.	The cryopyrin-associated periodic syndrome is a very rare disease. It is estimated that there are 1-2 cases out of 1 million inhabitants in the USA and 1/360,000 in France. However, many patients are diagnosed very late or not at all. Therefore the real prevalence is likely to be higher. CAPS encompasses the three entities familial cold autoinflammatory syndrome (FCAS), the Muckle-Wells syndrome and the neonatal-onset multisystem inflammatory disease (NOMID)/chronic infantile neurologic cutaneous and articular (CINCA) syndrome. They have in common a causative mutation in the NLRP3-gene. The altered gene product cryopyrin leads to activation of

	Universitätsklinikum Tübingen, Hoppe-Seyler-Str. 1, 72076, Tübingen, Deutschland. kuemmerle.deschner@uni-tuebingen.de			the inflammasome which in turn is responsible for excessive production of IL-1β. IL-1β causes the inflammatory manifestations in CAPS. These appear as systemic inflammation including fever, headache or fatigue, rash, eye disease, progressive sensorineural hearing loss, musculoskeletal manifestations and CNS symptoms (NOMID/CINCA only). With the advent of the IL-1 inhibitors anakinra, rilonacept and canakinumab for the first time safe and effective therapeutic options are available for this devastating disease. To prevent severe and possible life-threatening disease sequelae, early and correct diagnosis and immediate initiation of therapy are mandatory.
Kunos L, Varga J, Horváth G.	Semmelweis Egyetem, Általános Orvostudományi Kar Pulmonológiai Klinika, Budapest.	Simultaneous occurrence of chronic obstructive pulmonary disease and obstructive sleep apnea: the overlap syndrome. [Article in Hungarian]	Orv Hetil. 2012 Jun 10;153(23):892-7. doi: 10.1556/OH.2012.29394.	Obstructive sleep apnea syndrome is a common disorder in adults associated with several cardiovascular diseases and impaired quality of life. Chronic obstructive pulmonary disease is also a common clinical condition in middle-aged adults. The combination of these two conditions can eventuate a severe combined sleep-related breathing disorder. It is important to recognize coexisting sleep apnea in patients with chronic obstructive pulmonary disease in time and to treat it appropriately.
Lalremruta V, Prasanna GS.	Department of Pharmacology, KLE University's College of Pharmacy, Rajajinagar, Bangalore, India.	Evaluation of protective effect of Aegle marmelos Corr. in an animal model of chronic fatigue syndrome.	Indian J Pharmacol. 2012 May;44(3):351-6. doi: 10.4103/0253-7613.96316.	OBJECTIVE: To evaluate ethanolic extract of leaves of Aegle marmelos in an experimental animal model of chronic fatigue syndrome for potential therapeutic benefit. MATERIALS AND METHODS: Age/weight-matched female Wistar albino rats were grouped into five groups. (Group I- V) (n = 8). Group I served as naïve control and II served as stress control. Except for group I animals, other group animals were subjected to forced swimming every day for 15 minutes to induce a state of chronic fatigue and simultaneously treated with ethanolic extract of Aegle marmelos (EEAM) 150 and 250 mg/kg b.w. and Imipramine (20 mg.kg b.w.), respectively. Duration of immobility, anxiety level and locomotor activity were assessed on day 1, 7, 14 and 21 followed by biochemical estimation of oxidative biomarkers at the end of the study. RESULTS: Treatment with EEAM (150 and 250 mg/kg b.w.) resulted in a statistically significant and dose dependent reduction ($P < 0.001$) in the duration of immobility, reduction in anxiety and increase in locomotor activity. Dose dependent and significant reduction in LPO level and increase in CAT and SOD was observed in extract treated animals. CONCLUSION: The results are suggestive of potential protective effect of A. marmelos against experimentally induced CFS.
Lattie EG, Antoni MH, Fletcher MA, Penedo F, Czaja S, Lopez C, Perdomo D, Sala A, Nair S, Fu SH, Klimas N.	Department of Psychology, University of Miami, Coral Gables, FL 33124, USA.	Stress management skills, neuroimmune processes and fatigue levels in persons with chronic fatigue syndrome.	Brain Behav Immun. 2012 Aug;26(6):849-58. doi: 10.1016/j.bbi.2012.02.008.	OBJECTIVES: Stressors and emotional distress responses impact chronic fatigue syndrome (CFS) symptoms, including fatigue. Having better stress management skills might mitigate fatigue by decreasing emotional distress. Because CFS patients comprise a heterogeneous population, we hypothesized that the role of stress management skills in decreasing fatigue may be most pronounced in the subgroup manifesting the greatest neuroimmune dysfunction. METHODS: In total, 117 individuals with CFS provided blood and saliva samples, and self-report measures of

				emotional distress, perceived stress management skills (PSMS), and fatigue. Plasma interleukin-1-beta (IL-1β, IL-2, IL-6, IL-10, and tumor necrosis factor-alpha (TNF-α), and diurnal salivary cortisol were analyzed. We examined relations among PSMS, emotional distress, and fatigue in CFS patients who did and did not evidence neuroimmune abnormalities. RESULTS: Having greater PSMS related to less fatigue (p=.019) and emotional distress (p<.001), greater diurnal cortisol slope (p=.023) and lower IL-2 levels (p=.043). PSMS and emotional distress related to fatigue levels most strongly in CFS patients in the top tercile of IL-6, and emotional distress mediated the relationship between PSMS and fatigue most strongly in patients with the greatest circulating levels of IL-6 and a greater inflammatory (IL-6):anti-inflammatory (IL-10) cytokine ratio. DISCUSSION: CFS patients having greater PSMS show less emotional distress and fatigue, and the influence of stress management skills on distress and fatigue appear greatest among patients who have elevated IL-6 levels. These findings support the need for research examining the impact of stress management interventions in subgroups of CFS patients showing neuroimmune dysfunction.
Law ST, Ma KM, Li KK.	Department of Medicine and Geriatrics, Tuen Mun Hospital, Tuen Mun, Hong Kong.	Protein-losing enteropathy associated with or without systemic autoimmune disease: what are the differences?	Eur J Gastroenterol Hepatol. 2012 Mar;24(3):294-302. doi: 10.1097/MEG.0b013e32834f3ea0.	OBJECTIVE: The aim of our study was to compare protein-losing enteropathy (PLE) associated with or without systemic autoimmune (SA) diseases. METHODS: Patients diagnosed with PLE were selected, and their clinical characteristics, laboratory, endoscopic and imaging characteristics, treatment, and outcome were analyzed. RESULTS: From 2001 to 2010, 74 patients (60 patients with SA disease) with a female predominance were diagnosed with PLE. The SA group tended to be younger, presented early (4.3 vs. 7 weeks, P=0.08), and had significantly more mucocutaneous-articular involvement (16.7 vs. 0%, P<0.05; 50 vs. 0%, P<0.02; 43.3 vs. 0%, P<0.01), compared with the other group, which showed more weight loss (64.3 vs. 25%, P<0.01), malaise and fatigue (57.1 vs. 28.3%, P<0.02), and tended to have more gastrointestinal (GI) symptoms. The SA group was associated with lymphopenia (0.8 vs. 2.7 × 10^9/l, P<0.01), hyperglobulinemia (43 vs. 31.2 IU/l, P<0.04), lactate dehydrogenase (511.1 vs. 393.5 IU/l, P<0.05), hematuria (48.3 vs. 7.1%, P<0.01), and pyuria (23.3 vs. 0%, P<0.03), whereas the non-SA group had a higher platelet count (402 vs. 262.5 × 10^9/l, P<0.01) and alkaline phosphatase (111 vs. 78.2 IU/l, P<0.03) on admission. A subgroup analysis of patients with SA disease showed that more lupus patients had pericardial effusion (14.6 vs. 0%, P=0.08), polyarthritis (50 vs. 16.7%, P=0.02), lower C3 level (0.5 vs. 0.85 mg/l, P<0.01), antinuclear factors (89.6 vs. 58.3%, P<0.01), and antiextractable nuclear antigen antibody (73.3 vs. 37.5%, P<0.03), whereas nonlupus patients had higher C-reactive protein (87.9 vs. 40 mg/l, P<0.01) and more antineutrophil cytoplasmic antibody (ANCA) (60 vs. 3%, P=0.00). Thirty-seven (71%) patients with SA disease had diffuse nonerosive erythematous GI mucosa with chronic inflammatory cells in the lamina propria layer, and 12 (85.7%) patients without SA disease had focal lesions. The treatment response was comparable between the two groups. However, the time required to normalize the serum albumin

				level (6.3 vs. 12.3 months, P=0.02) of patients with SA disease was much shorter than that of the non-SA group and those of inflammatory markers, specifically, C-reactive protein and complement C3, of its own group (6.3 vs. 11.6 vs. 12.1 months, P<0.04). More patients without SA disease had infective episodes during the management period (14.3 vs. 1.7%, P<0.01). CONCLUSION: Patients with PLE associated with SA disease tend to have a distinct clinical syndrome with regard to the extent of clinical manifestations and laboratory, endoscopic, and histological features compared with those without. Patients without SA disease are more prone to develop complications and mortality. However, both can be effectively treated with comparable treatment response.
Le Bon O, Neu D, Berquin Y, Lanquart JP, Hoffmann R, Mairesse O, Armitage R.	Brugmann University Hospital, Sleep Laboratory and Unit for Chronobiology U78, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium; Hôpital Erasme, Sleep Research Unit, Université Libre de Bruxelles (U.L.B.), Brussels, Belgium. Electronic address: olebon@chu-tivoli.be.	Ultra-Slow delta power in chronic fatigue syndrome.	Psychiatry Res. 2012 Dec 30;200(2-3):742-7. doi: 10.1016/j.psychres.2012.06.027.	The role of sleep in patients diagnosed with chronic fatigue syndrome is not fully understood. Studies of polysomnographic and quantitative sleep electroencephalographic (EEG) measures have provided contradictory results, with few consistent findings in patients with Chronic Fatigue Syndrome (CFS). For the most part, it appears that delta EEG activity may provide the best discrimination between patients and healthy controls. A closer examination of delta activity in the very slow end of the frequency band is still to be considered in assessing sleep in CFS. The present preliminary study compared absolute and relative spectral power in conventional EEG bands and ultra-slow delta (0.5-0.8Hz) between 10 young female patients with the CFS and healthy controls without psychopathology. In absolute measures, the ultra-slow delta power was lower in CFS, about one-fifth that of the control group. Other frequency bands did not differ between groups. Relative ultra-slow delta power was lower in patients than in controls. CFS is associated with lower ultra-slow (0.5-0.8Hz) delta power, underscoring the importance of looking beyond conventional EEG frequency bands. From a neurophysiological standpoint, lower ultra-slow wave power may indicate abnormalities in the oscillations in membrane potential or a failure in neural recruitment in those with CFS.
Lee D, Das Gupta J, Gaughan C, Steffen I, Tang N, Luk KC, Qiu X, Urisman A, Fischer N, Molinaro R, Broz M, Schochetman G, Klein EA, Ganem D, Derisi JL, Simmons G, Hackett J Jr, Silverman RH, Chiu CY.	Department of Laboratory Medicine, University of San Francisco, San Francisco, California, United States of America.	In-depth investigation of archival and prospectively collected samples reveals no evidence for XMRV infection in prostate cancer.	PLoS One. 2012;7(9):e44954. doi: 10.1371/journal.pone.0044954.	XMRV, or xenotropic murine leukemia virus (MLV)-related virus, is a novel gammaretrovirus originally identified in studies that analyzed tissue from prostate cancer patients in 2006 and blood from patients with chronic fatigue syndrome (CFS) in 2009. However, a large number of subsequent studies failed to confirm a link between XMRV infection and CFS or prostate cancer. On the contrary, recent evidence indicates that XMRV is a contaminant originating from the recombination of two mouse endogenous retroviruses during passaging of a prostate tumor xenograft (CWR22) in mice, generating laboratory-derived cell lines that are XMRV-infected. To confirm or refute an association between XMRV and prostate cancer, we analyzed prostate cancer tissues and plasma from a prospectively collected cohort of 39 patients as well as archival RNA and prostate tissue from the original 2006 study. Despite comprehensive microarray, PCR, FISH, and serological testing, XMRV was not detected in any of the newly collected samples or in archival tissue, although archival

				RNA remained XMRV-positive. Notably, archival VP62 prostate tissue, from which the prototype XMRV strain was derived, tested negative for XMRV on re-analysis. Analysis of viral genomic and human mitochondrial sequences revealed that all previously characterized XMRV strains are identical and that the archival RNA had been contaminated by an XMRV-infected laboratory cell line. These findings reveal no association between XMRV and prostate cancer, and underscore the conclusion that XMRV is not a naturally acquired human infection.
Lerner AM, Ariza ME, Williams M, Jason L, Beqaj S, Fitzgerald JT, Lemeshow S, Glaser R.	Department of Medicine, Oakland University William Beaumont School of Medicine, Rochester, Michigan, United States of America.	Antibody to epstein-barr virus deoxyuridine triphosphate nucleotidohydrolase and deoxyribonucleotide polymerase in a chronic fatigue syndrome subset.	PLoS One. 2012;7(11):e47891. doi:10.1371/journal.pone.0047891.	BACKGROUND: A defined diagnostic panel differentiated patients who had been diagnosed with chronic fatigue syndrome (CFS), based upon Fukuda/Carruthers criteria. This diagnostic panel identified an Epstein-Barr virus (EBV) subset of patients (6), excluding for the first time other similar "clinical" conditions such as cytomegalovirus (CMV), human herpesvirus 6 (HHV6), babesiosis, ehrlichiosis, borreliosis, Mycoplasma pneumoniae, Chlamydia pneumoniae, and adult rheumatic fever, which may be mistakenly called CFS. CFS patients were treated with valacyclovir (14.3 mg/kg q6h) for ≥12 months. Each patient improved, based upon the Functional Activity Appraisal: Energy Index Score Healthcare Worker Assessment (EIPS), which is a validated (FSS-9), item scale with high degree of internal consistency measured by Cronbach's alpha. METHODS: Antibody to EBV viral capsid antigen (VCA) IgM, EBV Diffuse Early Antigen EA(D), and neutralizing antibodies against EBV-encoded DNA polymerase and EBV-encoded dUTPase were assayed serially approximately every three months for 13-16 months from sera obtained from patients with CFS (6) and from sera obtained from twenty patients who had no history of CFS. RESULTS: Antibodies to EBV EA(D) and neutralizing antibodies against the encoded-proteins EBV DNA polymerase and deoxyuridine triphosphate nucleotidohydrolase (dUTPase) were present in the EBV subset CFS patients. Of the sera samples obtained from patients with CFS 93.9% were positive for EA(D), while 31.6% of the control patients were positive for EBV EA(D). Serum samples were positive for neutralizing antibodies against the EBV-encoded dUTPase (23/52; 44.2%) and DNA polymerase (41/52; 78.8%) in EBV subset CFS patients, but negative in sera of controls. CONCLUSIONS: There is prolonged elevated antibody level against the encoded proteins EBV dUTPase and EBV DNA polymerase in a subset of CFS patients, suggesting that this antibody panel could be used to identify these patients, if these preliminary findings are corroborated by studies with a larger number of EBV subset CFS patients.
Lewis I, Pairman J, Spickett G, Newton JL.	Institute for Ageing & Health, Newcastle University, Newcastle, UK.	Clinical characteristics of a novel subgroup of chronic fatigue syndrome patients with postural	J Intern Med. 2012 Dec 4. doi: 10.1111/joim.12022.	OBJECTIVES: A significant proportion of patients with chronic fatigue syndrome (CFS) also have postural orthostatic tachycardia syndrome (POTS). We aimed to characterise these patients and differentiate them from CFS patients without POTS in terms of clinical and autonomic features. METHODS: A total of 179 patients with CFS (1994 Centers for Disease Control and Prevention criteria) attending one of the largest Department of Health-funded CFS clinical services were included in the study.

		orthostatic tachycardia syndrome.		Outcome measures were: (i) symptom assessment tools including the fatigue impact scale, Chalder fatigue scale, Epworth sleepiness scale (ESS), orthostatic grading scale (OGS) and hospital anxiety and depression scale (HADS-A and -D, respectively), (ii) autonomic function analysis including heart rate variability and (iii) haemodynamic responses including left ventricular ejection time and systolic blood pressure drop upon standing. RESULTS: CFS patients with POTS (13%, n=24) were younger (29±12 vs. 42±13 years, P<0.0001), less fatigued (Chalder fatigue scale, 8±4 vs. 10±2, P=0.002), less depressed (HADS-D, 6±4 vs. 9±4, P=0.01) and had reduced daytime hypersomnolence (ESS, 7±6 vs. 10±5, P=0.02), compared with patients without POTS. In addition, they exhibited greater orthostatic intolerance (OGS, 11±5; P<0.0001) and autonomic dysfunction. A combined clinical assessment tool of ESS ≤9 and OGS ≥9 identifies accurately CFS patients with POTS with 100% positive and negative predictive values. CONCLUSIONS: The presence of POTS marks a distinct clinical group of CFS patents, with phenotypic features differentiating them from those without POTS. A combination of validated clinical assessment tools can determine which CFS patients have POTS with a high degree of accuracy, and thus potentially identify those who require further investigation and consideration for therapy to control heart rate.
Lewis JD, Wassermann EM, Chao W, Ramage AE, Robin DA, Clauw DJ.	National Institute of Neurological Disorders and Stroke, Behavioral Neurology Unit, Bethesda, MD, USA Uniformed Services University of the Health Sciences, Bethesda, MD, USA.	Central sensitization as a component of post-deployment syndrome	NeuroRehabilitation. 2012 Jan 1;31(4):367-72. doi: 10.3233/NRE-2012-00805.	Many service members and veterans report chronic unexplained symptoms such as pain, fatigue and memory complaints, which have most recently been characterized as post-deployment syndrome (PDS). Chronic widespread pain is a component of this syndrome, producing significant disability and considerable health care costs. The similarity between the nature of these complaints and other medically unexplained illnesses such as fibromyalgia, irritable bowel syndrome, and chronic fatigue syndrome suggest that they may share a common mechanism. Here, we provide support for PDS as a consequence of pain and sensory amplification secondary to neuroplastic changes within the central nervous system, a phenomenon often termed central sensitization. We also discuss how factors such as stress and genetics may promote chronic widespread pain in veterans and service members who develop PDS.
Light AR, Bateman L, Jo D, Hughen RW, Vanhaitsma TA, White AT, Light KC.	Department of Anesthesiology The Brain Institute Department of Neurobiology and Anatomy Department of Exercise and Sport Science, University of Utah, Salt Lake City, UT 84132, USA. alan.light@hsc.utah.ed	Gene expression alterations at baseline and following moderate exercise in patients with Chronic Fatigue Syndrome and Fibromyalgia Syndrome.	J Intern Med. 2012 Jan;271(1):64-81. doi: 10.1111/j.1365-2796.2011.02405.x.	OBJECTIVES: To determine mRNA expression differences in genes involved in signalling and modulating sensory fatigue, and muscle pain in patients with chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FM) at baseline, and following moderate exercise. DESIGN: Forty-eight patients with CFS only, or CFS with comorbid FM, 18 patients with FM that did not meet criteria for CFS, and 49 healthy controls underwent moderate exercise (25 min at 70% maximum age-predicted heart rate). Visual-analogue measures of fatigue and pain were taken before, during and after exercise. Blood samples were taken before and 0.5, 8, 24 and 48 h after exercise. Leucocytes were immediately isolated from blood, number coded for blind processing and analyses and flash frozen. Using real-time, quantitative PCR, the amount of mRNA for 13 genes (relative to control genes) involved in sensory, adrenergic and

	u			immune functions was compared between groups at baseline and following exercise. Changes in amounts of mRNA were correlated with behavioural measures and functional clinical assessments. RESULTS: No gene expression changes occurred following exercise in controls. In 71% of patients with CFS, moderate exercise increased most sensory and adrenergic receptor's and one cytokine gene's transcription for 48 h. These postexercise increases correlated with behavioural measures of fatigue and pain. In contrast, for the other 29% of patients with CFS, adrenergic α-2A receptor's transcription was decreased at all time-points after exercise; other genes were not altered. History of orthostatic intolerance was significantly more common in the α-2A decrease subgroup. FM-only patients showed no postexercise alterations in gene expression, but their pre-exercise baseline mRNA for two sensory ion channels and one cytokine were significantly higher than controls. CONCLUSIONS: At least two subgroups of patients with CFS can be identified by gene expression changes following exercise. The larger subgroup showed increases in mRNA for sensory and adrenergic receptors and a cytokine. The smaller subgroup contained most of the patients with CFS with orthostatic intolerance, showed no postexercise increases in any gene and was defined by decreases in mRNA for α-2A. FM-only patients can be identified by baseline increases in three genes. Postexercise increases for four genes meet published criteria as an objective biomarker for CFS and could be useful in guiding treatment selection for different subgroups.
Light KC, White AT, Tadler S, Iacob E, Light AR.	Departments of Anesthesiology, Neurobiology and Anatomy, and Exercise and Sport Science, The University of Utah, Salt Lake City, UT 84132, USA.	Genetics and Gene Expression Involving Stress and Distress Pathways in Fibromyalgia with and without Comorbid Chronic Fatigue Syndrome.	Pain Res Treat. 2012;2012:427869. doi: 10.1155/2012/427869.	In complex multisymptom disorders like fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS) that are defined primarily by subjective symptoms, genetic and gene expression profiles can provide very useful objective information. This paper summarizes research on genes that may be linked to increased susceptibility in developing and maintaining these disorders, and research on resting and stressor-evoked changes in leukocyte gene expression, highlighting physiological pathways linked to stress and distress. These include the adrenergic nervous system, the hypothalamic-pituitary-adrenal axis and serotonergic pathways, and exercise responsive metabolite-detecting ion channels. The findings to date provide some support for both inherited susceptibility and/or physiological dysregulation in all three systems, particularly for catechol-O-methyl transferase (COMT) genes, the glucocorticoid and the related mineralocorticoid receptors (NR3C1, NR3C2), and the purinergic 2X4 (P2X4) ion channel involved as a sensory receptor for muscle pain and fatigue and also in upregulation of spinal microglia in chronic pain models. Methodological concerns for future research, including potential influences of comorbid clinical depression and antidepressants and other medications, on gene expression are also addressed.
Liu CZ, Lei B.	School of Aesthetic Medicine, Yichun College, Yichun	Effect of acupuncture on serum malonaldehyde	Zhen Ci Yan Jiu. 2012 Feb;37(1):38-40, 58.	OBJECTIVE: To study the effect of acupuncture on blood oxygen free radical metabolism in rats with chronic fatigue syndrome (CFS). METHODS: Thirty male SD rats were randomly divided into control group (n = 10), model group (n = 10) and

	336000, China. liuchangzheng1980@yahoo.com.cn	content, superoxide dismutase and glutathione peroxidase activity in chronic fatigue syndrome rats. [Article in Chinese]		acupuncture group (n = 10). CFS model was established by repeated suspension (1.0-2.5 h) and forced cold water swimming (7 min), once daily continuously for 12 days. For rats in the acupuncture group, bilateral "Zusanli" (ST 36) and "Sanyinjiao" (SP 6) were stimulated by manipulating the acupuncture needles intermittently for 20 min, once daily, and with 7 days being a treatment course. The treatment was conducted for three courses with an interval of 3 days between two courses. Serum malonaldehyde (MDA) content, superoxide dismutase (SOD) activity, and glutathione peroxidase (GSH-PX) activity were detected by thiobarbituric acid chromatometry (TBA), xanthine oxidase (XOD) and dithio-bis-nitrobenzoic acid (DTNB), respectively. RESULTS: In comparison with the control group, serum MDA content was up-regulated significantly, while serum SOD activity and GSH-PX activity were decreased considerably in the model group (P < 0.01). Compared with the model group, serum MDA level was down-regulated apparently, and serum SOD activity and GSH-PX activity were up-regulated remarkably in the acupuncture group (P < 0.01). CONCLUSION: Acupuncture can adjust metabolism of serum oxygen free radicals in CFS rats, which probably contributes to its effect in relieving CFS in clinic.
Liu KP, Fang M, Jiang SY.	Department of Tuina, Yueyang Hospital of Integrated Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 200437.	Effects of tuina on the mechanical properties of skeletal muscles of four limbs in patients with chronic fatigue syndrome. [Article in Chinese]	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2012 May;32(5):599-602.	OBJECTIVE: To study the effects of tuina on the mechanical properties of skeletal muscles of four limbs in patients with chronic fatigue syndrome (CFS). METHODS: Thirty CFS patients were recruited as the test group, while another 30 healthy volunteers were recruited as the healthy control group. Patients in the test group received tuina therapy, 30 min each time, once every other day, for totally 10 times. Isokinetic testing technology was used to compare peak torque (PT), total watt (TW), average power (AP), and flexor/extensor (F/E) ratio in the elbow and knee muscles of CFS patients before and after treatment. The Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale was used to evaluate the fatigue degree before and after treatment, and compared with the healthy control group. RESULTS: After treatment the FACIT fatigue scale score decreased significantly in the test group when compared with before treatment (27.5 +/- 9.1 vs 42.5 +/- 11.2), showing statistical difference (P < 0.05). The pre-treatment PT, TW, AP, and F/E ratio in the skeletal muscle were all lower in the test group than in the healthy control group. Compared with before treatment in the test group, patients' elbow 60 degrees/s angular velocity values during exercise extensor PT and TW, knee 60 degrees/s and 180 degrees/s angular velocity values during exercise flexor PT and TW increased significantly; elbow extensor and knee extensor, flexor AP was significantly elevated; knee in 180 degrees/s angular velocity of movement F/E ratio significantly increased, and all the differences were statistically significant (P < 0.05). The improvement of the fatigue degree in CFS patients and elbow in 60 degrees/s angular velocity values under the flexor and extensor TW, and flexor AP value of the degree of improvement were negatively correlated (r = -0.282, -0.482, -0.285, P < 0.05, P < 0.01). Meanwhile, the muscles with the knee in 180 degrees/s angular velocity was negatively correlated

				with the F/E ratio of the degree of improvement (r = -0. 330, P < 0.05). CONCLUSIONS: CFS patients have lowered mechanical properties of four limbs. Tuina therapy can improve the biomechanical properties of limb skeletal muscle and reduce the overall degree of fatigue in patients. The changes of limb skeletal muscle and mechanical properties can provide objective reference for the clinical diagnosis and assessment of CFS.
Liu Y, Zhang HG, Li XH.	Institute of Materia Medica and Department of Pharmaceutics, College of Pharmacy, Third Military Medical University, Chongqing, 400038, PR China.	A Chinese herbal decoction, Danggui Buxue Tang, improves chronic fatigue syndrome induced by food restriction and forced swimming in rats.	Phytother Res. 2011 Dec;25(12):1825-32. doi: 10.1002/ptr.3499.	Danggui Buxue Tang (DBT), a Chinese medicinal decoction that contains Radix Angelicae sinensis (Danggui) and Radix Astragali (Huangqi) at a ratio of 1:5, is used commonly for treating women's ailments. The present study explored the effects of this preparation on chronic fatigue syndrome (CFS). Rats were subjected to a combination of food restriction and forced swimming to induce CFS, and rats were gavaged once daily with either 12 or 24 g/kg DBT for 28 days. Body weights, T-cell subset counts, (3) H-TdR incorporation measurements and mRNA levels of IL-1β, TNF-α, NF-κB, p38MAPK and JNK were determined on days 14 and 28. The swimming endurance capacity was measured on day 28. Rats that received DBT exhibited increased body weight and endurance capacity, corrected T cell subsets counts, increased (3) H-TdR incorporation and decreased mRNA levels of IL-1β, TNF-α, NF-κB, p38MAPK and JNK compared with rats that did not receive DBT. The results indicate that DBT can ameliorate CFS through immune modulation and may act to normalize cytokines and their related signaling pathways.
Ljøstad U, Mygland Å.	Department of Neurology, Sørlandet Hospital, Kristiansand, Norway. unn.ljostad@sshf.no	The phenomenon of 'chronic Lyme'; an observational study.	Eur J Neurol. 2012 Aug;19(8):1128-35. doi: 10.1111/j.1468-1331.2012.03691.x.	PURPOSES: To chart clinical, laboratory, and psychometric profiles in patients who attribute their complaints to chronic Lyme disease. METHODS: We assessed the patients by clinical examination, laboratory tests, and questionnaires measuring fatigue, depression, anxiety, health-related quality of life, hypochondriasis, and illness perceptions. RESULTS: We found no evidence of ongoing Borrelia burgdorferi (Bb) infection in any of the 29 included patients using current diagnostic guidelines and an extended array of tests. Eight (28%) had other well-defined illnesses. Twenty-one (72%) had symptoms of unknown cause, of those six met the suggested criteria for post-Lyme disease syndrome. Fourteen (48%) had presence of anti-Bb antibodies. The patients had more fatigue and poorer health-related quality of life as compared to normative data, but were not more depressed, anxious, or hypochondriacal. Their beliefs about the illness were characterized by negative expectations. CONCLUSION: Our patients, who all attributed their symptoms to chronic Lyme disease, were heterogeneous. None had evidences of persistent Bb infection, but whether current diagnostic criteria are functional in patients with longstanding complaints is controversial. Other well-defined illnesses or sequelae from earlier Lyme disease were probable as main explanatory factor in some cases. The patients were not more depressed, anxious, or hypochondriacal than the normal population, but they had poorer health-related quality of life, more fatigue, and negative expectations about their illness.

Lloyd S, Chalder T, Rimes KA.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, Weston Education Centre, Cutcombe Road, London SE5 9RJ, UK. Samantha.lloyd@kcl.ac.uk	Family-focused cognitive behaviour therapy versus psycho-education for adolescents with chronic fatigue syndrome: long-term follow-up of an RCT.	Behav Res Ther. 2012 Nov;50(11):719-25. doi: 10.1016/j.brat.2012.08.005.	The aim of this study was to investigate the long term efficacy of family-focused cognitive behaviour therapy (CBT) compared with psycho-education in improving school attendance and other secondary outcomes in adolescents with chronic fatigue syndrome (CFS). A 24 month follow-up of a randomised controlled trial was carried out. Participants received either 13 one-hour sessions of family-focused CBT or four one-hour sessions of psycho-education. Forty-four participants took part in the follow-up study. The proportion of participants reporting at least 70% school attendance (the primary outcome) at 24 months was 90% in CBT group and 84% in psycho-education group; the difference between the groups was not statistically significant (OR = 1.29, p = 0.80). The proportion of adolescents who had recovered in the family-focused CBT group was 79% compared with 64% in the psycho-education, according to a definition including fatigue and school attendance. This difference was not statistically significant (Fisher's exact test, p = 0.34). Family-focused CBT was associated with significantly better emotional and behavioural adjustment at 24 month follow-up compared to psycho-education, as reported by both adolescents (F = 6.49, p = 0.02) and parents (F = 4.52, P = 0.04). Impairment significantly decreased in both groups between six and 24 month follow-ups, with no significant group difference in improvement over this period. Gains previously observed for other secondary outcomes at six month follow-up were maintained at 24 month follow-up with no further significant improvement or group differences in improvement. In conclusion, gains achieved by adolescents with CFS who had undertaken family-focused CBT and psycho-education generally continued or were maintained at two-year follow-up. The exception was that family-focused CBT was associated with maintained improvements in emotional and behavioural difficulties whereas psycho-education was associated with deterioration in these outcomes between six and 24-month follow-up.
Lloyd S, Chalder T, Sallis HM, Rimes KA.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, Weston Education Centre, Cutcombe Road, London, UK. Samantha.lloyd@kcl.ac.uk	Telephone-based guided self-help for adolescents with chronic fatigue syndrome: A non-randomised cohort study	Behav Res Ther. 2012 May;50(5):304-12. doi: 10.1016/j.brat.2012.02.014.	The aim of this study was to gain preliminary evidence about the efficacy of a new telephone-based guided self-help intervention, based on cognitive-behavioural principles, which aimed to reduce fatigue and improve school attendance in adolescents with chronic fatigue syndrome (CFS). A non-randomised cohort design was used, with a two-month baseline period. Sixty-three 11-18 year-old participants recruited from a specialist CFS unit received the intervention. Participants received six half-hour fortnightly telephone sessions and two follow-up sessions. Fatigue and school attendance were the main outcomes and the main time point for assessing outcome was 6 months post-treatment. Using multi-level modelling, a significant decrease in fatigue was found between pre-treatment and 6 month follow-up, treatment effect estimate = - 5.68 (-7.63, -3.72), a large effect size (Cohen's d = 0.79). The decrease in fatigue between pre and post-treatment was significantly larger than between baseline and pre-treatment. A significant increase in school attendance was found between pre-treatment and 6 month follow-up, effect estimate = 1.38 (0.76,

				2.00), a medium effect size (d = -0.48). Univariate logistic regression found baseline perfectionism to be associated with poorer school attendance at six-month follow-up. In conclusion, telephone-based guided self-help is an acceptable minimal intervention which is efficacious in reducing fatigue in adolescents with CFS.
Lo SC, Pripuzova N, Li B, Komaroff AL, Hung GC, Wang R, Alter HJ.	[No address quoted]	Retraction for Lo et al., Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood donors.	Proc Natl Acad Sci U S A. 2012 Jan 3;109(1):346. doi: 10.1073/pnas.1119641109.	Retraction of Lo SC, Pripuzova N, Li B, Komaroff AL, Hung GC, Wang R, Alter HJ. Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15874-9.
Loew SJ, Watson K.	Centre for Bioactive Discovery in Health and Ageing, School of Science & Technology, University of New England, Armidale, Australia.	A prospective genetic marker of the visual-perception disorder Meares-Irlen syndrome.	Percept Mot Skills. 2012 Jun;114(3):870-82.	Prior investigations of scotopic sensitivity or Meares-Irlen syndrome have identified several features also found in attention deficit/hyperactivity disorder, chronic fatigue syndrome, and a subtype of dyslexia in which visual recognition is the primary deficit. In particular, anomalies in lipid metabolism, including low essential fatty acid status and decreased serum cholesterol, have been identified in all three disorders. Genetic expression of the transportermolecule apolipoprotein B-100 (APOB) has been correlated with abnormal lipid metabolism, particularly in relation to levels of cholesterol. Cholesterol esters are important carriers of essential fatty acids entering the retina. The APOB gene coding for apolipoprotein B-100 is located on the short arm of Chromosome 2, and closely neighbours a gene (DYX3) known to confer susceptibility to dyslexia. The APOB locus is also recognised as being one of the most highly polymorphic regions of the human genome, and thus provides a promising tool for genetic researchers. In this pilot study, certain allelic variants of the APOB gene were more common in participants diagnosed with Meares-Irlen syndrome than in individuals without the condition. This study appears to be a first in which a condition known to cause reading difficulties has been associated with the APOB gene.
Lucini D, Pagani M.	Centro di Ricerca Terapia Neurovegetativa e Medicina dell'Esercizio, Dipartimento Scienze Cliniche, Università degli Studi di Milano, Italy. daniela.lucini@unimi.it	From stress to functional syndromes: an internist's point of view.	Eur J Intern Med. 2012 Jun;23(4):295-301. doi: 10.1016/j.ejim.2011.11.016.	In this brief review we address schematically the relationship between two emerging issues in clinical medicine: stress and functional syndromes. It is becoming increasingly clear that they demand a multidimensional approach, considering simultaneously elements of behavioral therapy with traditional pharmacological treatment, guided by a better physiopathological understanding including autonomic assessment. New techniques, based on innovative analysis of continuous segments of electrocardiogram and non invasive arterial pressure recordings capable to extract hidden oscillations, provide quantitative indices of sympathetic and vagal modulation of the cardiovascular system. This more complete diagnostic process facilitates explanation of symptoms and reassurance of patients, based on functional evidence. The described clinical approach implies in addition an active collaboration of patients

				requiring the implementation of a creative alliance. Physical exercise, eating habits and muscular-mental relaxation are combined with pharmacological tools as needed.
Luczkowiak J, Martínez-Prats L, Sierra O, Fiorante S, Rubio R, Pulido F, Otero JR, Delgado R.	Laboratory of Molecular Microbiology, Instituto de Investigación i+12, Hospital Universitario 12 de Octubre, Madrid, Spain.	Lack of the detection of XMRV or polytropic MLV-related sequences in blood cells from HIV-1-infected patients in Spain.	J Acquir Immune Defic Syndr. 2012 Feb 1;59(2):101-4. doi: 10.1097/QAI.0b013e318238b596.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) and polytropic murine leukemia virus (MLV)-related virus are recently described human gammaretroviruses that have been associated with prostate cancer and chronic fatigue syndrome. These studies have been controversial because a number of laboratories have been unable to find evidence of XMRV in similar groups of patients or controls. Because the existence of XMRV raises many questions, we decided to study its presence in a group of patients infected with HIV-1 with a high proportion of intravenous drug use and coinfection by hepatitis C virus. METHODS: Forty HIV-1-infected patients under follow-up in our institution were screened for XMRV/MLV by nested polymerase chain reaction using primers targeting the gag and env region. Specific primers for mouse mitochondrial DNA were used to rule out contamination. RESULTS: No evidence of XMRV or polytropic MLV-related sequences was found in any sample from patients or controls. Four samples yielded polymerase chain reaction bands whose sequence corresponded to murine endogenous retroviral sequences, however, contamination with mouse cell DNA was subsequently confirmed. CONCLUSIONS: XMRV/MLV viruses do not seem to be associated with HIV-1 infection or intravenous drug use. Contamination of samples or reagents by genomic murine DNA or XMRV vectors could account for the sporadic detection of positive samples for XMRV and related agents.
Ma X, Zhou S, Wei M, Chen Y, Li J, Xiong W, Jiang S, Pan C.	The Institute of Human Virology and Department of Biochemistry, Key Laboratory of Tropical Disease Control of Ministry of Education, Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou 510080, China.	Phylogenetic and biological analysis of a laboratory-generated gammaretrovirus xenotropic murine leukemia virus-related virus (XMRV).	Virus Genes. 2012 Oct;45(2):218-24.	A xenotropic murine leukemia virus-related virus (XMRV) has been reported to be an emerging pathogen associated with prostate cancer (PC) and chronic fatigue syndrome (CFS). However, recent studies have demonstrated that XMRV is a laboratory-derived virus resulting from genetic recombination between two mouse viral genomes during serial xenograft tissue transplantation. This study describes a phylogenetic analysis that compared XMRV with the ecotropic murine leukemia viruses (E-MLV), xenotropic MLV (X-MLV), and other retroviruses, including HTLV-1 and HIV-1. We found that sequences corresponding to three XMRV structural proteins (Env, Gag, and Pol) exhibited high degrees of homology with X-MLV (>91 %) and E-MLV (67-96 %), but not HTLV-1 (13-16 %) or HIV-1 (10-15 %), indicating that XMRV was derived from X-MLV and/or E-MLV. We then compared the infectivity of XMRV and E-MLV for human and murine lymphocytes, respectively. Results showed that human PBMCs were not susceptible to XMRV infection, suggesting that XMRV exhibits host cell tropism similar to E-MLV that only infects murine PBMCs. These data suggest that it is unlikely that this laboratory-generated retrovirus could cause disease in humans.
Macciò A, Madeddu C, Mantovani G.	Sirai Hospital, Department of Obstetrics and	Current pharmacotherapy options for cancer	Expert Opin Pharmacother. 2012 Dec;13(17):2453-72. doi: 10.1517/14656566.2012.7342	INTRODUCTION: Anorexia and cachexia syndrome represents a complex clinical picture that occurs in the late stage of several chronic inflammatory diseases, including cancer. Unless counteracted cancer-related anorexia and cachexia

	Gynecology, Carbonia, Italy. a.maccio@tin.it	anorexia and cachexia.	97.	syndrome affects quality of life (QL) and survival. However, to date a standard effective treatment is lacking. AREAS COVERED: The aim of this review is to describe the current pharmacological approaches for anorexia and cachexia syndrome, focusing on cancer-related syndrome. The several pharmacological agents tested so far are discussed, distinguishing them in unproven drugs, effective drugs, and drugs under investigation. Moreover, a section is devoted to the promising use of nutritional supplements and nutraceuticals. The emerging role of a multitargeted combined treatment approach is exhaustively reviewed. EXPERT OPINION: Considering the complex clinical picture and the multifactorial pathogenesis of anorexia and cachexia syndrome, we believe that its clinical management requires a multidisciplinary and multipharmacological approach. In our opinion the anorexia and cachexia syndrome treatment should include drugs that target the following conditions: inflammatory status, oxidative stress, nutritional disorders, muscle catabolism, anemia, immunosuppression, and fatigue. The multidimensional therapies for anorexia and cachexia syndrome should ideally be introduced within a context of the "best supportive care," which includes optimal symptom management and careful psychosocial counseling.
Maddali Bongi S, Di Felice C, Del Rosso A, Landi G, Maresca M, Giambalvo Dal Ben G, Matucci-Cerinic M.	Department of BioMedicine, Division of Rheumatology, University of Florence, and AMuRR, Rehabilitative Medicine and Assistive Devices Centre, Careggi Hospital, Florence, Italy.	Efficacy of the "body movement and perception" method in the treatment of fibromyalgia syndrome: an open pilot study.	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S12-8.	OBJECTIVES: Group exercises may be useful in fibromyalgia syndrome (FMS). The 'Body movement and perception' (BMP) method is based on low impact exercises, awareness of body perception and relaxation, aimed at treating small groups of patients following the Resseguier method (RM) and integrating RM with exercises derived from soft gymnastics. We assessed the effects of BMP method on FMS. METHODS: 40 women with FMS (age and disease duration: 51.7±7.2 and 4.9±3.8 years) participated in an open pilot study. BMP sessions were performer twice a week (50 minutes each) for 8 weeks. Patients were assessed at enrolment (T0) and at the end of the study (T1) by a self-administered questionnaire (temporal characteristics of pain, pain interference in working and recreational activities and in night-time rest, awareness of pain, fatigue, irritability, well-being, quality of movement, ability to focus on perception and to perceive whole body, postural selfcontrol, ability to relax) and a clinical evaluation (tender points, assumption of analgesics/NSAIDs, distribution of pain, pain in sitting and standing position, pain during postural passages and gait, postural body alignment, muscular contractures). RESULTS: At T1, FMS patients significantly improved with respect to T0 in pain, fatigue, irritability, well-being, quality of movement, postural self-control, ability to relax mind and body, movement perception, tender point scores, assumption of analgesic/NSAIDs, body alignment and muscle contractures ($p<0.05$ for all the comparisons T1 versus T0). CONCLUSIONS: In FMS patients, rehabilitation with BMP improves pain and well being, reduces the number of tender points and muscle contractures, thus it is useful in FMS management.
Maes M, Kubera	Maes Clinics, Tria,	Increased IgA and	J Affect Disord. 2012 Dec	BACKGROUND: Recently, we discovered that depression is accompanied by increased

M, Leunis JC, Berk M.	Bangkok, Thailand. dr.michaelmaes@hotmail.com	IgM responses against gut commensals in chronic depression: further evidence for increased bacterial translocation or leaky gut.	1;141(1):55-62. doi: 10.1016/j.jad.2012.02.023.	IgM and IgA responses directed against gram negative gut commensals. The aim of this study was to replicate these findings in a larger study group of depressed patients and to examine the associations between the IgA and IgM responses to gut commensals and staging of depression as well as the fatigue and somatic (F&S) symptoms of depression. METHODS: We measured serum concentrations of IgM and IgA against the LPS of gram-negative enterobacteria, i.e. Hafnia alvei, Pseudomonas aeruginosa, Morganella morganii, Pseudomonas putida, Citrobacter koseri, and Klebsiella pneumoniae in 112 depressed patients and 28 normal controls. The severity of F&S symptoms was measured using the Fibromyalgia and Chronic Fatigue Syndrome Rating Scale. RESULTS: The prevalences and median values of serum IgM and IgA against LPS of these commensals were significantly higher in depressed patients than in controls. The IgM levels directed against the LPS of these commensal bacteria were significantly higher in patients with chronic depression than in those without. The immune responses directed against LPS were not associated with melancholia or recurrent depression. There was a significant correlation between the IgA response directed against LPS and gastro-intestinal symptoms. DISCUSSION: The results indicate that increased bacterial translocation with immune responses to the LPS of commensal bacteria may play a role in the pathophysiology of depression, particularly chronic depression. Bacterial translocation may a) occur secondary to systemic inflammation in depression and intensify and perpetuate the primary inflammatory response once the commensals are translocated; or b) be a primary trigger factor associated with the onset of depression in some vulnerable individuals. The findings suggest that "translocated" gut commensal bacteria activate immune cells to elicit IgA and IgM responses and that this phenomenon may play a role in the pathophysiology of (chronic) depression by causing progressive amplifications of immune pathways.
Maes M, Mihaylova I, Kubera M, Leunis JC, Geffard M.	Maes Clinics, TRIA, Bangkok, Thailand. dr.michaelmaes@hotmail.com	IgM-mediated autoimmune responses directed against multiple neoepitopes in depression: new pathways that underpin the inflammatory and neuroprogressive pathophysiology.	J Affect Disord. 2011 Dec;135(1-3):414-8. doi: 10.1016/j.jad.2011.08.023.	BACKGROUND: There is evidence that depression is accompanied by oxidative and nitrosative stress (O&NS), as indicated by increased free radical levels, lipid peroxidation, and lowered antioxidant levels. The aims of the present study are to examine whether depression is accompanied by autoimmune responses directed against a) neoepitopes that are formed following O&NS damage; and b) the major anchorage molecules, i.e. palmitic and myristic acids and S-farnesyl-L-cysteine. METHODS: We examined serum IgM antibodies to the conjugated fatty acids, palmitic and myristic acids; acetylcholine; S-farnesyl-L-cysteine; and NO-modified adducts in 26 depressed patients and 17 normal controls. Severity of depression was measured with the Hamilton Depression Rating Scale and severity of fatigue and somatic (F&S) symptoms with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: The prevalences and mean values for the serum IgM levels directed against conjugated palmitic and myristic acids, acetylcholine, S-farnesyl-L-cysteine; and the conjugated NO adducts, NO-tyrosine, NO-phenylalanine, NO-aspartate, NO-histidine,

				and NO-creatine were significantly higher in depressed patients than in normal controls. The autoimmune responses were significantly related to FF symptoms, such as fatigue and a flu-like malaise, whereas the indicants of nitrosative stress were related to gastro-intestinal and autonomic symptoms. DISCUSSION: Depression is characterized by IgM-related autoimmune responses directed against a) neoepitopes that are normally not detected by the immune system but that due to damage by O&NS have become immunogenic; and b) anchorage epitopes, i.e. palmitic and myristic acids, and S-farnesyl-L-cysteine. These autoimmune responses play a role in the inflammatory and O&NS pathophysiology of depression and may mediate the cellular dysfunctions that contribute to neuroprogression, e.g. aberrations in signal transduction, cellular differentiation and apoptosis.
Maes M, Mihaylova I, Kubera M, Leunis JC, Twisk FN, Geffard M.	Maes Clinics, TRIA, Piyavate Hospital, 998 Rimklongsamsen Road, Bangkok, 10310, Thailand. dr.michaelmaes@hotmail.com	IgM-mediated autoimmune responses directed against anchorage epitopes are greater in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) than in major depression.	Metab Brain Dis. 2012 Dec;27(4):415-23. doi: 10.1007/s11011-012-9316-8.	Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) and depression are considered to be neuro-immune disorders (Maes and Twisk, BMC Medicine 8:35, 2010). There is also evidence that depression and ME/CFS are accompanied by oxidative and nitrosative stress (O&NS) and by increased autoantibodies to a number of self-epitopes some of which have become immunogenic due to damage by O&NS. The aim of this study is to examine IgM-mediated autoimmune responses to different self-epitopes in ME/CFS versus depression. We examined serum IgM antibodies to three anchorage molecules (palmitic and myristic acid and S-farnesyl-L-cysteine); acetylcholine; and conjugated NO-modified adducts in 26 patients with major depression; 16 patients with ME/CFS, 15 with chronic fatigue; and 17 normal controls. Severity of fatigue and physio-somatic (F&S) symptoms was measured with the Fibromyalgia and Chronic Fatigue Syndrome Rating Scale. Serum IgM antibodies to the three anchorage molecules and NO-phenylalanine were significantly higher in ME/CFS than in depression. The autoimmune responses to oxidatively, but not nitrosatively, modified self-epitopes were significantly higher in ME/CFS than in depression and were associated with F&S symptoms. The autoimmune activity directed against conjugated acetylcholine did not differ significantly between ME/CFS and depression, but was greater in the patients than controls. Partially overlapping pathways, i.e. increased IgM antibodies to a multitude of neo-epitopes, underpin both ME/CFS and depression, while greater autoimmune responses directed against anchorage molecules and oxidatively modified neo-epitopes discriminate patients with ME/CFS from those with depression. These autoimmune responses directed against neoantigenic determinants may play a role in the dysregulation of key cellular functions in both disorders, e.g. intracellular signal transduction, cellular differentiation and apoptosis, but their impact may be more important in ME/CFS than in depression.
Maes M, Mihaylova I, Kubera M, Ringel	Maes Clinics, TRIA, Bangkok, Thailand. dr.michaelmaes@hotm	Activation of cell-mediated immunity in depression:	Prog Neuropsychopharmacol Biol Psychiatry. 2012 Jan 10;36(1):169-75. doi:	BACKGROUND: Depression is characterized by activation of cell-mediated immunity (CMI), including increased neopterin levels, and increased pro-inflammatory cytokines (PICs), such as interleukin-1 (IL-1) and tumor necrosis factor-α (TNFα). These PICs may

K.	ail.com	association with inflammation, melancholia, clinical staging and the fatigue and somatic symptom cluster of depression.	10.1016/j.pnpbp.2011.09.006.	induce depressive, melancholic and chronic fatigue (CF) symptoms. METHODS: We examined serum neopterin and plasma PIC levels in depressive subgroups in relation to the depressive subtypes and the melancholic and CF symptoms of depression. Participants were 85 patients with depression and in 26 normal controls. Severity of depression was assessed with the Hamilton Depression Rating Scale (HDRS) and severity of CF with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Serum neopterin was significantly higher in depressed patients and in particular in those with melancholia. There were positive correlations between serum neopterin, the plasma PICs and the number of previous depressive episodes. Neopterin and TNFα were associated with melancholia, while both PICs were associated with CF. Melancholia-group membership was predicted by the HDRS and neopterin, and CF group membership by age, the FF score and serum TNFα. DISCUSSION: Depression and melancholia are accompanied by CMI activation, suggesting that neopterin plays a role in their pathophysiology, e.g. through activation of oxidative and nitrosative stress and apoptosis pathways. The intertwined CMI and inflammatory responses are potentially associated with the onset of depression and with the melancholic and CF symptoms of depression. Exposure to previous depressive episodes may magnify the size of CMI and PIC responses, possibly increasing the likelihood of new depressive episodes. CMI activation and inflammation may contribute to the staging or recurrence of depression.
Maes M, Ringel K, Kubera M, Berk M, Rybakowski J.	Maes Clinics, TRIA, Piyavate Hospital, Bangkok, Thailand. dr.michaelmaes@hotmail.com	Increased autoimmune activity against 5-HT: a key component of depression that is associated with inflammation and activation of cell-mediated immunity, and with severity and staging of depression.	J Affect Disord. 2012 Feb;136(3):386-92. doi: 10.1016/j.jad.2011.11.016.	BACKGROUND: Depression is characterized by inflammation and cell-mediated immune (CMI) activation and autoimmune reactions directed against a multitude of self-epitopes. There is evidence that the inflammatory response in depression causes dysfunctions in the metabolism of 5-HT, e.g. lowering the 5-HT precursor tryptophan, and upregulating 5-HT receptor mRNA. This study has been undertaken to examine autoimmune activity directed against 5-HT in relation to CMI activation and inflammation. METHODS: 5-HT antibodies were examined in major depressed patients (n=109) versus normal controls (n=35) in relation to serum neopterin and lysozyme, and plasma pro-inflammatory cytokines (PIC), i.e. interleukin-1 (IL-1) and tumor necrosis factor-α (TNFα). Severity of depression was assessed with the Hamilton Depression Rating Scale (HDRS) and severity of fatigue and somatic symptoms with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: The incidence of anti-5-HT antibody activity was significantly higher in depressed patients (54.1%), and in particular in those with melancholia (82.9%), than in controls (5.7%). Patients with positive 5-HT antibodies showed increased serum neopterin and lysozyme, and plasma TNFα and IL-1; higher scores on the HDRS and FF scales, and more somatic symptoms, including malaise and neurocognitive dysfunctions. There was a significant association between autoimmune activity to 5-HT and the number of previous depressive episodes. DISCUSSION: The autoimmune reactions directed against 5-HT might play a role in the pathophysiology of depression

				and the onset of severe depression. The strong association between autoimmune activity against 5-HT and inflammation/CMI activation is explained by multiple, reciprocal pathways between these factors. Exposure to previous depressive episodes increases the incidence of autoimmune activity directed against 5-HT, which in turn may increase the likelihood to develop new depressive episodes. These findings suggest that sensitization (kindling) and staging of depression are in part based on progressive autoimmune responses.
Maes M, Twisk FN, Johnson C.	Maes Clinics, TRIA, Piyavate Hospital, 998 Rimklongsamsen Road, Bangkok 10310, Thailand. Electronic address: http://www.michaelmaes.com.	Myalgic Encephalomyelitis (ME), Chronic Fatigue Syndrome (CFS), and Chronic Fatigue (CF) are distinguished accurately: Results of supervised learning techniques applied on clinical and inflammatory data.	Psychiatry Res. 2012 Dec 30;200(2-3):754-60. doi: 10.1016/j.psychres.2012.03.031.	There is much debate on the diagnostic classification of Myalgic Encephalomyelitis (ME), Chronic Fatigue Syndrome (CFS) and chronic fatigue (CF). Post-exertional malaise (PEM) is stressed as a key feature. This study examines whether CF and CFS, with and without PEM, are distinct diagnostic categories. Fukuda's criteria were used to diagnose 144 patients with chronic fatigue and identify patients with CFS and CF, i.e. those not fulfilling the Fukuda's criteria. PEM was rated by means of a scale with defined scale steps between 0 and 6. CFS patients were divided into those with PEM lasting more than 24h (labeled: ME) and without PEM (labeled: CFS). The 12-item Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale was used to measure severity of illness. Plasma interleukin-1 (IL-1), tumor necrosis factor (TNF)α, and lysozyme, and serum neopterin were employed as external validating criteria. Using fatigue, a subjective feeling of infection and PEM we found that ME, CFS, and CF were distinct categories. Patients with ME had significantly higher scores on concentration difficulties and a subjective experience of infection, and higher levels of IL-1, TNFα, and neopterin than patients with CFS. These biomarkers were significantly higher in ME and CFS than in CF patients. PEM loaded highly on the first two factors subtracted from the data set, i.e. "malaise-sickness" and "malaise-hyperalgesia". Fukuda's criteria are adequate to make a distinction between ME/CFS and CF, but ME/CFS patients should be subdivided into ME (with PEM) and CFS (without PEM).
Maes M, Twisk FN, Kubera M, Ringel K, Leunis JC, Geffard M.	Maes Clinics, TRIA, Bangkok, Thailand. dr.michaelmaes@hotmail.com	Increased IgA responses to the LPS of commensal bacteria is associated with inflammation and activation of cell-mediated immunity in chronic fatigue syndrome.	J Affect Disord. 2012 Feb;136(3):909-17. doi: 10.1016/j.jad.2011.09.010.	BACKGROUND: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is accompanied by a) systemic IgA/IgM responses against the lipopolysaccharides (LPS) of commensal bacteria; b) inflammation, e.g. increased plasma interleukin-(IL)1 and tumor necrosis factor (TNF)α; and c) activation of cell-mediated immunity (CMI), as demonstrated by increased neopterin. METHODS: To study the relationships between the IgA/IgM responses to the LPS of microbiota, inflammation, CMI and the symptoms of ME/CFS we measured the IgA/IgM responses to the LPS of 6 different enterobacteria, serum IL-1, TNFα, neopterin, and elastase in 128 patients with ME/CFS and chronic fatigue (CF). Severity of symptoms was assessed by the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Serum IL-1, TNFα, neopterin and elastase are significantly higher in patients with ME/CFS than in CF patients. There are significant and positive associations between the IgA responses to LPS and serum IL-1, TNFα, neopterin and elastase. Patients with an abnormally high IgA response show increased serum IL-1, TNFα and neopterin levels, and higher

				ratings on irritable bowel syndrome (IBS) than subjects with a normal IgA response. Serum IL-1, TNFα and neopterin are significantly related to fatigue, a flu-like malaise, autonomic symptoms, neurocognitive disorders, sadness and irritability. CONCLUSIONS: The findings show that increased IgA responses to commensal bacteria in ME/CFS are associated with inflammation and CMI activation, which are associated with symptom severity. It is concluded that increased translocation of commensal bacteria may be responsible for the disease activity in some ME/CFS patients.
Maes M, Twisk FN, Kubera M, Ringel K.	Maes Clinics, TRIA, Bangkok, Thailand. dr.michaelmaes@hotmail.com	Evidence for inflammation and activation of cell-mediated immunity in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): increased interleukin-1, tumor necrosis factor-α, PMN-elastase, lysozyme and neopterin.	J Affect Disord. 2012 Feb;136(3):933-9. doi: 10.1016/j.jad.2011.09.004.	BACKGROUND: There is evidence that inflammatory pathways and cell-mediated immunity (CMI) play an important role in the pathophysiology of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Activation of inflammatory and CMI pathways, including increased levels of cytokines, is known to induce fatigue and somatic symptoms. Given the broad spectrum inflammatory state in ME/CFS, the aim of this study was to examine whether inflammatory and CMI biomarkers are increased in individuals with ME/CFS. METHODS: In this study we therefore measured plasma interleukin-(IL)1, tumor necrosis factor (TNF)α, and PMN-elastase, and serum neopterin and lysozyme in 107 patients with ME/CFS, 37 patients with chronic fatigue (CF), and 20 normal controls. The severity of ME/CFS was measured with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Serum IL-1, TNFα, neopterin and lysozyme are significantly higher in patients with ME/CFS than in controls and CF patients. Plasma PMN-elastase is significantly higher in patients with ME/CFS than in controls and CF patients and higher in the latter than in controls. Increased IL-1 and TNFα are significantly correlated with fatigue, sadness, autonomic symptoms, and a flu-like malaise; neopterin is correlated with fatigue, autonomic symptoms, and a flu-like malaise; and increased PMN-elastase is correlated with concentration difficulties, failing memory and a subjective experience of infection. CONCLUSIONS: The findings show that ME/CFS is characterized by low-grade inflammation and activation of CMI. The results suggest that characteristic symptoms of ME/CFS, such as fatigue, autonomic symptoms and a flu-like malaise, may be caused by inflammatory mediators, e.g. IL-1 and TNFα.
Maes M, Twisk FN, Ringel K.	Maes Clinics, TRIA, Bangkok, Thailand. dr.michaelmaes @ hotmail.com	Inflammatory and cell-mediated immune biomarkers in myalgic encephalomyelitis/chronic fatigue syndrome and depression: inflammatory markers are higher in	Psychother Psychosom. 2012;81(5):286-95. doi: 10.1159/000336803.	BACKGROUND: Depression is an inflammatory disorder while many authors declare myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) to be a functional disorder. The aim of the present study is to compare inflammatory and cell-mediated immune (CMI) responses between depression and ME/CFS. METHODS: We measured two proinflammatory cytokines (PICs) in plasma, interleukin-1 (IL-1) and tumor necrosis factor-α (TNF-α), with enzyme-linked immunosorbent assays, and serum neopterin with a radioimmunoassay in controls, ME/CFS and depressive patients. RESULTS: Plasma PICs were significantly higher in ME/CFS than in depression and higher in both patient groups than in controls. Increased PIC levels in depression were attributable to the presence of fatigue and physio-somatic symptoms. Serum

		myalgic encephalomyelitis/chronic fatigue syndrome than in depression.		neopterin did not differ significantly between depression and ME/CFS but was higher in both patient groups than in controls. The significant positive correlations between neopterin and either IL-1 or TNF-α were significantly greater in depression than in ME/CFS. CONCLUSIONS: Since PICs cause depression-like behaviors and fatigue/malaise, we suggest that inflammation may play a role in the pathophysiology of ME/CFS and depression. Increased neopterin also seems to contribute to the pathophysiology of both disorders. This study has detected a shared 'pathway phenotype', i.e. disorders in inflammatory and CMI pathways, which underpins both ME/CFS and depression and, therefore, may explain the co-occurrence of both disorders. ME/CFS and depression are discriminated from each other by increased PICs in ME/CFS and differences in the immune cell communication networks.
Maggi F, Bazzichi L, Sernissi F, Mazzetti P, Lanini L, Scarpellini P, Consensi A, Giacomelli C, Macera L, Vatteroni ML, Bombardieri S, Pistello M.	[No address quoted]	Absence of xenotropic murine leukemia virus-related virus in Italian patients affected by chronic fatigue syndrome, fibromyalgia, or rheumatoid arthritis.	Int J Immunopathol Pharmacol. 2012 Apr-Jun;25(2):523-9.	The xenotropic murine leukemia virus-related virus (XMRV) has been recently linked to chronic fatigue syndrome in a US cohort in whom the virus was demonstrated in 67% patients vs 3.7% healthy controls. Albeit this finding was not substantiated by subsequent reports and eventually considered a laboratory contamination, the matter is still the object of intense debate and scrutiny in various cohorts of patients. In this work we examined well-clinically characterized Italian patients affected by chronic fatigue syndrome, and also fibromyalgia and rheumatoid arthritis, two chronic illnesses of basically unknown etiology which show quite a few symptoms in common with chronic fatigue syndrome. Although we used recently updated procedures and controls, the XMRV was not found in 65 patients with chronic fatigue syndrome diagnosis, 55 with fibromyalgia, 25 with rheumatoid arthritis, nor in 25 healthy controls. These results add to the ever-growing number of surveys reporting the absence of XMRV in chronic fatigue syndrome patients and suggest that the virus is also absent in fibromyalgia and rheumatoid arthritis.
Maggi F, Focosi D, Lanini L, Sbranti S, Mazzetti P, Macera L, Davini S, De Donno M, Mariotti ML, Antonelli G, Scatena F, Pistello M.	Virology Unit, Pisa University Hospital, Pisa, Italy. fabrizio.maggi63@gmail.com	Xenotropic murine leukaemia virus-related virus is not found in peripheral blood cells from treatment-naive human immunodeficiency virus-positive patients.	Clin Microbiol Infect. 2012 Feb;18(2):184-8. doi: 10.1111/j.1469-0691.2011.03580.x.	The human pathogen xenotropic murine leukaemia virus-related virus (XMRV) has been tentatively associated with prostate cancer and chronic fatigue syndrome. Unfortunately, subsequent studies failed to identify the virus in various clinical settings. To determine whether XMRV circulates in humans and the relationship with its host, we searched for the virus in 124 human immunodeficiency virus-infected patients who might have been exposed to XMRV, might be prone to infection as a result of progressive immunodeficiency, and had not yet been treated with antiretroviral drugs. Using nested PCR and single-step TaqMan real-time PCR, both designed on the XMRV gag gene, we could not find any positive samples. These findings add to the growing amount of scepticism regarding XMRV.
Maher-Edwards L, Fernie BA, Murphy G, Nikcevic AV, Spada MM.	Fatigue Service, Royal Free Hospital, London, UK.	Metacognitive factors in chronic fatigue syndrome.	Clin Psychol Psychother. 2012 Nov;19(6):552-7. doi: 10.1002/cpp.757.	Chronic fatigue syndrome (CFS), which is characterized by fatigue and flu-like symptoms that are not alleviated by rest, is a poorly understood condition and an often controversial diagnosis. Earlier research has indicated that general metacognitions are associated with the severity of symptoms in patients with CFS. In the current study, we aimed to determine whether specific metacognitive factors are

				implicated in CFS. Using the metacognitive profiling interview template we investigated the following: (1) whether patients held positive or negative metacognitions about conceptual processes; (2) what their goals with respect to engaging in these processes were; and (3) what indicated that it was appropriate to stop. We also examined attention focus when experiencing CFS symptoms, and its advantages and disadvantages. Results showed that patients endorsed positive and negative metacognitions pertaining to conceptual processes. The goals of engaging in these processes were to identify the cause of, and devise strategies to cope with, symptoms. Patients were either unable to identify a stop signal for conceptual processing or identified an improvement in fatigue-related symptoms as representing the stop signal. Finally, patients reported that their attention focus when experiencing symptoms included distraction and monitoring of symptoms. Advantages to these strategies included symptom management, whereas disadvantages included an escalation of negative affect. The present findings provide preliminary evidence that specific metacognitive factors may be involved in CFS. profiling that may aid assessment and conceptualisation of psychological distress in CFS.
Malaguarnera M.	Research Centre The Great Senescence, University of Catania, Catania, Italy. malaguar@unict.it	Carnitine derivatives: clinical usefulness.	Curr Opin Gastroenterol. 2012 Mar;28(2):166-76. doi: 10.1097/MOG.0b013e3283505a3b.	PURPOSE OF REVIEW: Carnitine and its derivatives are natural substances involved in both carbohydrate and lipid metabolism. This review summarizes the recent progress in the field in relation to the molecular mechanisms. RECENT FINDINGS: The pool of different carnitine derivatives is formed by acetyl-L-carnitine (ALC), propionyl-L-carnitine (PLC), and isovaleryl-carnitine. ALC may have a preferential effect on the brain tissue. ALC represents a compound of great interest for its wide clinical application in various neurological disorders: it may be of benefit in treating Alzheimer's dementia, depression in the elderly, HIV infection, chronic fatigue syndrome, peripheral neuropathies, ischemia and reperfusion of the brain, and cognitive impairment associated with various conditions. PLC has been demonstrated to replenish the intermediates of the tricarboxylic acid cycle by the propionyl-CoA moiety, a greater affinity for the sarcolemmal carrier, peripheral vasodilator activity, a greater positive inotropism, and more rapid entry into myocytes. Most studies of the therapeutic use of PLC are focused on the prevention and treatment of ischemic heart disease, congestive heart failure, hypertrophic heart disease, and peripheral arterial disease. ALC and PLC are considered well tolerated without significant side-effects. SUMMARY: A number of therapeutic effects possibly come from the interaction of carnitine and its derivatives with the elements of cellular membranes.
Mariman A, Vogelaers D, Hanoulle I, Delesie L, Pevernagie D.	Subjective sleep quality and daytime sleepiness in a large sample of patients with chronic fatigue syndrome (CFS).	Department of General Internal Medicine, Infectious Diseases and Psychosomatic Medicine, University	Acta Clin Belg. 2012 Jan-Feb;67(1):19-24.	Chronic fatigue syndrome (CFS) is characterised by incapacitating fatigue in combination with a number of minor criteria, including unrefreshing sleep without further specifications, in the absence of psychiatric and internal disease. As little data exist on subjective sleep quality and daytime sleepiness, these parameters were assessed in a large sample of CFS patients. Consecutive patients with a diagnosis of CFS in a tertiary referral centre filled out the Fatigue Questionnaire (FQ), Medical

		Hospital Ghent, Belgium. an.mariman@ugent.be		Outcomes Study 36-Item Short Form Health Survey (MOS SF-36), Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI). Inclusion comprised 415 individuals (mean age 40.5 yr, SD 7.9, range 18-64; 86% female). Mean FQ (26.90; SD 4.04), mean Global Physical Health from the MOS SF-36 (29.30; SD 12.25) and Global Mental Health from the MOS SF-36 (49.62; SD 18.31) scores corresponded with literature data for similar CFS samples. High mean ESS (10.51; SD 5.52) and global PSQI (10.17; SD 4.02) were observed. No significant relationship was found between ESS and global PSQI. In contrast, regression analysis demonstrated a significant cubic relation between ESS and 'PSQI without daytime dysfunction'. A subgroup (n=69) with an insomnia-like phenotype low ESS (<5), high PSQI (mean 11.51; SD 3.86) was observed. The assessment of subjective sleep quality and daytime sleepiness in a large sample of CFS patients indicated high mean PSQI and ESS values. ESS and 'PSQI without daytime dysfunction' were inversely related at the spectral ends of ESS. A distinct subgroup with clinical features of insomnia was identified.
Mariman A, Vogelaers D, Hanoulle I, Delesie L, Tobback E, Pevernagie D.	Department of General Internal Medicine, Infectious Diseases and Psychosomatic Medicine, University Hospital Ghent, Belgium. an.mariman@ugent.be	Validation of the three-factor model of the PSQI in a large sample of chronic fatigue syndrome (CFS) patients.	J Psychosom Res. 2012 Feb;72(2):111-3. doi: 10.1016/j.jpsychores.2011.11.004.	OBJECTIVE: To evaluate whether a 3-factor model of the Pittsburgh Sleep Quality Index (PSQI) scale would fit the constellation of sleep disturbances in patients with a diagnosis of chronic fatigue syndrome (CFS). METHODS: Consecutive CFS patients filled out the PSQI. Scores from this self-report questionnaire were examined with exploratory and confirmatory factor analysis (CFA). RESULTS: 413 CFS patients were included for analysis in this study. CFA showed that the 7 PSQI component scores clustered into the 3 factors reported by Cole et al. (2006), i.e. Sleep Efficiency, Perceived Sleep Quality and Daily Disturbances. In contrast with the single-factor and all 2-factor models, all factor loadings were significant, and all goodness-of-fit values were acceptable. CONCLUSION: In CFS, the PSQI operates as a 3-factor scoring model as initially seen in healthy and depressed older adults. The separation into 3 discrete factors suggests the limited usefulness of the global PSQI as a single factor for the assessment of subjective sleep quality, as also evidenced by a low Cronbach's alpha (0.64) in this patient sample.
Mariman AN, Vogelaers DP, Tobback E, Delesie LM, Hanoulle IP, Pevernagie DA.	Ghent University Hospital, Department of Internal Diseases, Infectious Diseases and Psychosomatic Medicine, 185 De Pintelaan, 9000 Ghent, Belgium. Electronic address: An.mariman@ugent.be.	Sleep in the chronic fatigue syndrome.	Sleep Med Rev. 2012 Oct 6. pii: S1087-0792(12)00073-1. doi: 10.1016/j.smrv.2012.06.003.	Chronic fatigue syndrome (CFS) is a disabling condition characterized by severe fatigue lasting for more than six months and the presence of at least four out of eight minor criteria. Sleep disturbance presenting as unrefreshing or nonrestorative sleep is one of these criteria and is very common in CFS patients. Biologically disturbed sleep is a known cause of fatigue and could play a role in the pathogenesis of CFS. However, the nature of presumed sleep impairment in CFS remains unclear. Whilst complaints of NRS persist over time, there is no demonstrable neurophysiological correlate to substantiate a basic deficit in sleep function in CFS. Polysomnographic findings have not shown to be significantly different between subjects with CFS and normal controls. Discrepancies between subjectively poor and objectively normal sleep suggest a role for psychosocial factors negatively affecting perception of sleep quality. Primary sleep disorders are often detected in patients who otherwise qualify for a

				CFS diagnosis. These disorders could contribute to the presence of daytime dysfunctioning. There is currently insufficient evidence to indicate that treatment of primary sleep disorders sufficiently improves the fatigue associated with CFS. Therefore, primary sleep disorders may be a comorbid rather than an exclusionary condition with respect to CFS.
Marques M, De Gucht V, Leal I, Maes S.	Health Psychology, Leiden University, Wassenaarseweg 52, P.O. BOX 955, 2300 RB, Leiden, The Netherlands, mmarques@ispa.pt.	A Cross-Cultural Perspective on Psychological Determinants of Chronic Fatigue Syndrome: a Comparison Between a Portuguese and a Dutch Patient Sample.	Int J Behav Med. 2012 Sep 13.	BACKGROUND: Few studies focus on cross-cultural differences in Chronic fatigue syndrome (CFS). PURPOSE: This study aimed to (1) compare fatigue severity and impairment, somatic complaints, psychological distress, and quality of life (QoL) in a population of Portuguese and Dutch patients; (2) explore the differential contribution of behavioral and cognitive determinants of fatigue severity; and (3) investigate the relation between fatigue severity and somatic complaints on one hand and QoL on the other in both populations. METHOD: Eighty-five female patients from Portugal (Mean age = 47.54) and 167 female CFS patients from The Netherlands (Mean age = 44.93) participated in the study. All participants were surveyed for demographic and clinical characteristics, fatigue severity, somatic symptoms, psychological distress, (physical and psychological) QoL, physical activity, behavior regulation patterns, and illness representations. RESULTS: Cross-cultural differences were found in relation to working status, duration of fatigue symptoms, psychological distress, somatic complaints, and psychological QoL. Although behavioral characteristics and illness representations were significantly associated with fatigue severity in both Portuguese and Dutch patients, there were important differences in the determinants of CFS. Moreover, higher levels of fatigue and severity of other somatic complaints were related to poor QoL. CONCLUSIONS: These findings show cross-cultural similarities and differences in clinical characteristics and psychological determinants of CFS that are important in view of diagnosis and treatment.
Marques M, De Gucht V, Maes S, Leal I.	Health Psychology Department, Leiden university, Wassenaarseweg 52, P,O, BOX 955, 2300 RB Leiden, The Netherlands. mmarques@ispa.pt	Protocol for the "four steps to control your fatigue (4-STEPS)" randomised controlled trial: a self-regulation based physical activity intervention for patients with unexplained chronic fatigue.	BMC Public Health. 2012 Mar 19;12:202. doi: 10.1186/1471-2458-12-202.	BACKGROUND: Unexplained Chronic Fatigue is a medical condition characterized by the presence of persistent, severe and debilitating medically unexplained fatigue, leading to impaired functioning and lower quality of life. Research suggests that physical activity can contribute to the reduction of fatigue and other somatic symptoms and can thus significantly improve physical functioning and quality of life in these patients. Based on the self-regulation (SR) theory of behaviour change, we developed a brief physical activity program for patients suffering from unexplained chronic fatigue which focuses on the training of self-regulation skills, the "4-STEPS to control your fatigue" program. METHODS/DESIGN: This is a multi-centre, randomised controlled trial (RCT) that will be carried out in local primary care centres and at the Portuguese Fibromyalgia and Chronic Fatigue Syndrome Patients Association. Patients aged between 18 and 65 and fulfilling operationalized criteria for Idiopathic Chronic Fatigue (ICF) and Chronic Fatigue Syndrome (CFS) will be recruited and randomly allocated to standard care (SC) or standard care plus a self-regulation based physical activity program (4-STEPS). Patients will be assessed at baseline, after the

				intervention (3 months) and at 12 months follow-up. The primary outcome is fatigue severity. DISCUSSION: The results of the RCT will provide information about the effectiveness of a brief self-regulation intervention for promoting physical activity in patients with unexplained chronic fatigue. If the program proves to be effective, it may be considered as an adjunctive treatment for these patients. TRIAL REGISTRATION: ISRCTN: ISRCTN70763996.
Martorell L, Tondo M, Garcia-Fructuoso F, Naudo M, Alegre C, Gamez J, Genovés J, Poo P.	Molecular Genetics Section, Hospital Sant Joan de Deu, Edifici docent C/ Santa Rosa 39, 08950 Barcelona, Spain. lmartorell@hsjdbcn.org	Screening for the presence of FMR1 premutation alleles in a Spanish population with fibromyalgia.	Clin Rheumatol. 2012 Nov;31(11):1611-5. doi: 10.1007/s10067-012-2052-y.	Fragile X mental retardation 1 (FMR1) premutation carriers, who are at risk of having children with fragile X Syndrome, were initially considered as clinically unaffected. However, recent clinical and molecular studies have shifted this point of view. The incidence of premutation in the general population is substantial. Apart from the well-documented fragile X-associated tremor-ataxia and fragile X premature ovarian insufficiency, there is a broad constellation of symptoms including depression, anxiety, muscle pain, autoimmune and thyroid disease, chronic fatigue, and fibromyalgia that has been described, particularly in females with the premutation (55-200 repeats). Fibromyalgia (FM) is the most common cause of widespread pain and comprises a heterogeneous group of patients, affecting 2-3 % of the general population. We analyzed the FMR1 gene in a cohort of females diagnosed with fibromyalgia in order to assess the incidence of premutated alleles. CGG repeat size was determined in 353 females suffering from FM and results were compared with a control group. Four premutated carriers in the FM group were detected. The observed incidence is higher than that described for a normal female population (1/88 vs 1/250). The early detection of premutation carriers for the FMR1 gene among individuals diagnosed with fibromyalgia is important and would be helpful in correct genetic counseling of patients and their families, who may be at risk of having children with fragile X syndrome, the most common known cause of inherited intellectual disability and autism. Our data should be cautiously interpreted based on just this study; nevertheless, screening for the FMR1 gene in FM patients at least with presentations suggestive of FMR1 gene-related disease seems recommendable.
Mastaglia FL.	Australian Neuro-Muscular Research Institute and Centre for Neuromuscular and Neurological Disorders, University of Western Australia, Queen Elizabeth II Medical Centre, Perth, WA, Australia. Electronic address: francis.mastaglia@anri.	The relationship between muscle pain and fatigue	Neuromuscul Disord. 2012 Dec;22 Suppl 3:S178-80. doi: 10.1016/j.nmd.2012.10.003.	Pain and fatigue may occur together during sustained exhausting muscle contractions, particularly as the limit of endurance is approached, and both can restrict muscle performance. Patients with neuromuscular disorders may have chronic myofascial pain (e.g. fibromyalgia) or contraction-induced pain (e.g. in metabolic myopathies). In some patients these two types of pain may coexist and both may inhibit central motor drive during exercise. Little is known about the central motor adaptations that occur in patients with neuromuscular disorders and how the effects of pain are mediated. Transcranial magnetic brain stimulation has made it possible to investigate the changes in excitability of the central motor pathway during fatiguing muscle activity and have thrown light on the mechanisms of fatigue in normal subjects and individuals with chronic fatigue syndrome and multiple sclerosis, but there have been few studies in patients with neuromuscular disorders. Repetitive magnetic brain

	uwa.edu.au.			stimulation protocols can now be used to modulate the excitability of the motor system during exercise to delay the onset of peripheral fatigue, and to reduce chronic pain. The possible application of these techniques in patients with neuromuscular disorders warrants further investigation.
Matsui T, Ii K, Hojo S, Sano K.	Japan Neurological Institute and Matsui Hospital, Kannonji, Kagawa, Japan. t.matsui@matsui-hp.com	Cervical neuro-muscular syndrome: discovery of a new disease group caused by abnormalities in the cervical muscles.	Neurol Med Chir (Tokyo). 2012;52(2):75-80.	Our previous study of whiplash injury found that abnormalities in the cervical muscles cause autonomic dystonia. Further research has found that abnormalities in the cervical muscles cause headache, chronic fatigue syndrome, vertigo, and dizziness. We named this group of diseases cervical neuro-muscular syndrome. Patients treated within a 2-year period from April 1, 2002 to March 31, 2004 reported good outcomes in 83.8% for headache, 88.4% for vertigo and dizziness, 84.5% for chronic fatigue syndrome, 88.0% for autonomic dystonia, and 83.7% for whiplash-associated disorder. A large number of outpatients present with general malaise, including many general physical complaints without identifiable cause. We propose that treatment of the cervical muscle is effective for general malaise.
McCall B.	[No address quoted]	Psychiatrist and journalist win prize for defending science.	Lancet. 2012 Nov 17;380(9855):1725	[No abstract given]
McCarberg BH.	Family Medicine, Kaiser Permanente, Escondido, California 92025, USA. bill.h.mccarberg@kp.org	Clinical overview of fibromyalgia.	Am J Ther. 2012 Sep;19(5):357-68. doi: 10.1097/MJT.0b013e3181ff7bee.	Fibromyalgia (FM) is a complex disorder that affects up to 5% of the general population worldwide, more frequently in women than in men. In addition to chronic widespread pain, patients with FM usually experience other characteristic symptoms, including fatigue, disturbed sleep, stiffness, reduced functioning, dyscognition, and depressed mood. Many patients also have comorbid conditions such as depression, irritable bowel syndrome, temporomandibular disorder, or migraine. Although the etiology of FM remains unclear, evidence suggests that biologic, genetic, and environmental factors are involved. The variability of symptoms and the frequency of comorbidities among patients with FM make this a difficult disorder to diagnose. Diagnosis may be further complicated by the stigmatization of this disorder among treatment providers, the health insurance industry, and the general population. Treating chronic pain disorders such as FM can be time consuming and costly, and other issues such as polypharmacy, treatment adherence, and access to treatment often need to be addressed. The aim of this article is to provide physicians with a general overview of FM, including a brief review of the pathophysiology that explains the biologic and genetic bases of this disorder. Also included is a synopsis of new diagnostic criteria and other useful diagnostic tools and a discussion of various treatment challenges and strategies.
McClellan L. Bodei L, Cremonesi M, Grana CM, Chinol M, Baio SM,	lauriemcclellan@hotmail.com Division of Nuclear Medicine, European Institute of	Chronic Lyme disease: it's time to solve the medical mystery inside an	Health Aff (Millwood). 2012 Mar;31(3):647-9. doi: 10.1377/hlthaff.2011.0792. Eur J Nucl Med Mol Imaging.	Comment in Health Aff (Millwood). 2012 Jun;31(6):1368. Peptide receptor radionuclide therapy (PRRT) consists in the systemic administration of a synthetic peptide, labelled with a suitable beta-emitting radionuclide, able to irradiate tumours and their metastases via the internalization through a specific receptor,

Severi S, Paganelli G.	Oncology, Via Ripamonti 435, 20141 Milan, Italy.	enigma. Yttrium-labelled peptides for therapy of NET.	2012 Feb;39 Suppl 1:S93-102. doi: 10.1007/s00259-011-2002-y.	overexpressed on the cell membrane. After 15 years of experience, we can state that PRRT with (90)Y-labelled peptides is generally well tolerated. Acute side effects are usually mild, some of which are related to the co-administration of amino acids, such as nausea. Others are related to the radiopeptide, such as fatigue or the exacerbation of an endocrine syndrome, which rarely occurs in functioning tumours. Chronic and permanent effects on target organs, particularly the kidneys and the bone marrow, are generally mild if the necessary precautions are taken. Currently, the potential risk to kidney and red marrow limits the amount of radioactivity that may be administered. However, when tumour masses are irradiated with adequate doses, volume reduction may be observed. (90)Y-octreotide has been the most widely used radiopeptide in the first 8-10 years of experience. Unfortunately, all of the published results derive from different and inhomogeneous phase I/II studies. Hence, a direct comparison is virtually impossible to date. Nevertheless, even with these limitations, objective responses are registered in 10-34% of patients. The optimal timing of (90)Y-DOTATOC in the management of somatostatin receptor (SSTR)-positive tumours and the way in which it should be integrated with other treatments have yet to be defined, and prospective phase II/III trials comparing the efficacy and toxicity of different schemes of (90)Y-DOTATOC administration are still warranted.
McCrone P, Sharpe M, Chalder T, Knapp M, Johnson AL, Goldsmith KA, White PD.	Centre for the Economics of Mental and Physical Health, Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, United Kingdom. paul.mccrone@kcl.ac.uk	Adaptive pacing, cognitive behaviour therapy, graded exercise, and specialist medical care for chronic fatigue syndrome: a cost-effectiveness analysis.	PLoS One. 2012;7(8):e40808. doi: 10.1371/journal.pone.0040808.	BACKGROUND: The PACE trial compared the effectiveness of adding adaptive pacing therapy (APT), cognitive behaviour therapy (CBT), or graded exercise therapy (GET), to specialist medical care (SMC) for patients with chronic fatigue syndrome. This paper reports the relative cost-effectiveness of these treatments in terms of quality adjusted life years (QALYs) and improvements in fatigue and physical function. METHODS: Resource use was measured and costs calculated. Healthcare and societal costs (healthcare plus lost production and unpaid informal care) were combined with QALYs gained, and changes in fatigue and disability; incremental cost-effectiveness ratios (ICERs) were computed. RESULTS: SMC patients had significantly lower healthcare costs than those receiving APT, CBT and GET. If society is willing to value a QALY at £30,000 there is a 62.7% likelihood that CBT is the most cost-effective therapy, a 26.8% likelihood that GET is most cost effective, 2.6% that APT is most cost-effective and 7.9% that SMC alone is most cost-effective. Compared to SMC alone, the incremental healthcare cost per QALY was £18,374 for CBT, £23,615 for GET and £55,235 for APT. From a societal perspective CBT has a 59.5% likelihood of being the most cost-effective, GET 34.8%, APT 0.2% and SMC alone 5.5%. CBT and GET dominated SMC, while APT had a cost per QALY of £127,047. ICERs using reductions in fatigue and disability as outcomes largely mirrored these findings. CONCLUSIONS: Comparing the four treatments using a health care perspective, CBT had the greatest probability of being the most cost-effective followed by GET. APT had a lower probability of being the most cost-effective option than SMC alone. The relative cost-effectiveness was even greater from a societal perspective as additional

				cost savings due to reduced need for informal care were likely.
McMahon L, Murray C, Sanderson J, Daiches A.	Tees, Esk & Wear Valleys NHS Foundation Trust, Middlesbrough, UK.	"Governed by the pain": narratives of fibromyalgia.	Disabil Rehabil. 2012;34(16):1358-66. doi: 10.3109/09638288.2011.645114.	PURPOSE: Fibromyalgia (FM) is a chronic syndrome characterized by pain and fatigue. The aim of this study was to explore how individuals with FM make sense of the illness experience and integrate it into their personal biographies. METHOD: Ten women from a pain management service in the north west of England were interviewed for the study. A chronological summary of each life story was produced and narrative features such as plot, tone, imagery and metaphors were identified and compared. RESULTS: Findings are presented in the form of a meta-narrative incorporating all 10 narratives over five phases: (1) making sense of FM: when I was younger, I didn't have any problems at all; (2) onset and diagnosis: you just feel like you're constantly complaining; (3) invasion of FM: you're just trapped; trapped in this body; (4) coping with FM: you try to do things in a pattern it will obey and (5) ongoing struggle: I refuse to give in to it. CONCLUSIONS: The narrative is characterized by a lack of movement and resolution, with participants engaged in an enduring struggle against the challenges of FM. Psychological approaches that facilitate this ongoing adjustment process may prove beneficial in FM treatment and rehabilitation.
McMahon L, Murray C, Simpson J.	Tees Time to Talk IAPT Service, Middlesbrough, UK.	The potential benefits of applying a narrative analytic approach for understanding the experience of fibromyalgia: a review.	Disabil Rehabil. 2012;34(13):1121-30. doi: 10.3109/09638288.2011.628742.	PURPOSE: People with fibromyalgia (FM), a medically unexplained illness, habitually experience widespread pain and fatigue. While some qualitative research has aimed to understand the experiences of people with FM, studies from a specific narrative perspective are particularly lacking. This review argues that future research could be significantly enhanced by studies which analyse the narratives of people with FM. METHOD: This argument is made through reference to an examination of the extant qualitative literature on the experience of FM and theories and narrative studies on chronic illnesses and identity. RESULTS: The empirical literature is reviewed from a narrative perspective; this assumes that the stories people tell reveal much about their identities and social worlds. As such, it is proposed that narrative analysis is particularly well suited for exploring issues of self and culture and for appreciating how meanings evolve over time. Further, it is also argued that consideration of these issues is particularly relevant for understanding the experience of FM given the enigmatic nature of the syndrome and its chronic course. CONCLUSIONS: The review concludes by emphasizing that narrative analysis is a valuable method which offers the potential for uncovering novel insights about the illness experience for these individuals.
Medow MS, Aggarwal A, Baugham I, Messer Z, Stewart JM.	Department of Pediatrics, New York Medical College and The Center for Pediatric Hypotension, Hawthorne, New York.	Modulation of the axon-reflex response to local heat by reactive oxygen species in subjects with chronic fatigue syndrome.	J Appl Physiol. 2013 Jan;114(1):45-51. doi: 10.1152/japplphysiol.00821.2012.	Local cutaneous heating causes vasodilation as an initial first peak, a nadir, and increase to plateau. Reactive oxygen species (ROS) modulate the heat plateau in healthy controls. The initial peak, due to C-fiber nociceptor-mediated axon reflexes, is blunted with local anesthetics and may serve as a surrogate for the cutaneous response to peripheral heat. Chronic fatigue syndrome (CFS) subjects report increased perception of pain. To determine the role of ROS in this neurally mediated response, we evaluated changes in cutaneous blood flow from local heat in nine CFS subjects

				(16-22 yr) compared with eight healthy controls (18-26 yr). We heated skin to 42°C and measured local blood flow as a percentage of maximum cutaneous vascular conductance (%CVC(max)). Although CFS subjects had significantly lower baseline flow [8.75 ± 0.56 vs. 12.27 ± 1.07 (%CVC(max), CFS vs. control)], there were no differences between groups to local heat. We then remeasured this with apocynin to inhibit NADPH oxidase, allopurinol to inhibit xanthine oxidase, tempol to inhibit superoxide, and ebselen to reduce H(2)O(2). Apocynin significantly increased baseline blood flow (before heat, 14.91 ± 2.21 vs. 8.75 ± 1.66) and the first heat peak (69.33 ± 3.36 vs. 59.75 ± 2.75). Allopurinol and ebselen only enhanced the first heat peaks (71.55 ± 2.48 vs. 61.72 ± 2.01 and 76.55 ± 5.21 vs. 58.56 ± 3.66, respectively). Tempol had no effect on local heating. None of these agents changed the response to local heat in control subjects. Thus the response to heat may be altered by local levels of ROS, particularly H(2)O(2) in CFS subjects, and may be related to their hyperesthesia/hyperalgesia.
Meeus M, Ickmans K, De Clerck LS, Moorkens G, Hans G, Grosemans S, Nijs J.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Building L-Mfys, Pleinlaan 2, 1050 Brussels, Belgium. Mira.Meeus@vub.ac.be	Serotonergic descending inhibition in chronic pain: design, preliminary results and early cessation of a randomized controlled trial.	In Vivo. 2011 Nov-Dec;25(6):1019-25.	AIM: We examined whether activation of serotonergic descending pathways improves pain inhibition during exercise in patients with chronic fatigue syndrome (CFS) and comorbid fibromyalgia (FM) in comparison with rheumatoid arthritis (RA) and sedentary, healthy controls in a double-blind randomized controlled trial with cross-over design. PATIENTS AND METHODS: Three female CFS/FM patients, one female RA patient and two healthy women were randomly allocated to the experimental group (2 ml of citalopram intravenously) or the placebo group (2 ml of 0.9% NaCl intravenously). Participants performed a submaximal exercise protocol, preceded and followed by an assessment of endogenous pain inhibition. Seven days later, groups were crossed over. RESULTS: Significant side-effects were observed in all, but one participant immediately after intravenous administration of citalopram. One CFS/FM patient withdrew because of severe post-exertional malaise. CONCLUSION: It was decided that proceeding with the study would be unethical. No conclusion could be made regarding pain inhibition during exercise in CFS/FM compared to RA and controls.
Meeus M, Nijs J, Van Mol E, Truijen S, De Meirleir K.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, Artesis University College Antwerp, Van Aertselaerstraat 31, Merksem, Antwerp, Belgium.	Role of psychological aspects in both chronic pain and in daily functioning in chronic fatigue syndrome: a prospective longitudinal study.	Clin Rheumatol. 2012 Jun;31(6):921-9. doi: 10.1007/s10067-012-1946-z. Epub 2012 Feb 16.	In addition to fatigue, many patients with chronic fatigue syndrome (CFS) experience chronic musculoskeletal pain. We aimed at examining the role of catastrophizing, coping, kinesiophobia, and depression in the chronic pain complaints and in the daily functioning of CFS patients. A consecutive sample of 103 CFS patients experiencing chronic widespread musculoskeletal pain completed a battery of questionnaires evaluating pain, daily functioning, and psychological characteristics (depression, kinesiophobia, pain coping, and catastrophizing). Thirty-nine patients participated in the 6-12-month follow-up, consisting of questionnaires evaluating pain and pressure pain algometry. Correlation and linear regression analyses were performed to identify predictors. The strongest correlations with pain intensity were found for catastrophizing ($r = -.462$, $p < .001$) and depression ($r = -.439$, $p < .001$). The stepwise

				multiple regression analysis revealed that catastrophizing was both the immediate main predictor for pain (20.2%) and the main predictor on the longer term (20.1%). The degree of depression was responsible for 10% in the observed variance of the VAS pain after 6-12 months. No significant correlation with pain thresholds could be revealed. The strongest correlations with daily functioning at baseline were found for catastrophizing ($r = .435$, $p < .001$) and depression ($r = .481$, $p < .001$). Depression was the main predictor for restrictions in daily functioning (23.1%) at baseline. Pain catastrophizing and depression were immediate and long-term main predictors for pain in patients with CFS having chronic widespread musculoskeletal pain. They were also correlated to daily functioning, with depression as the main predictor for restrictions in daily functioning at baseline.
Meeus M, van Eupen I, van Baarle E, De Boeck V, Luyckx A, Kos D, Nijs J.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, Artesis University College Antwerp, Belgium.	Symptom fluctuations and daily physical activity in patients with chronic fatigue syndrome: a case-control study.	Arch Phys Med Rehabil. 2011 Nov;92(11):1820-6. doi: 10.1016/j.apmr.2011.06.023.	OBJECTIVES: To compare the activity pattern of patients with chronic fatigue syndrome (CFS) with healthy sedentary subjects and examine the relationship between the different parameters of performed activity (registered by an accelerometer device) and symptom severity and fluctuation (registered by questionnaires) in patients with CFS. DESIGN: Case-control study. Participants were asked to wear an accelerometer device on the nondominant hand for 6 consecutive days. Every morning, afternoon, and evening patients scored the intensity of their pain, fatigue, and concentration difficulties on a visual analog scale. SETTING: Patients were recruited from a specialized chronic fatigue clinic in the university hospital, where all subjects were invited for 2 appointments (for questionnaire and accelerometer adjustments). In between, activity data were collected in the subject's normal home environment. PARTICIPANTS: Female patients (n=67) with CFS and female age-matched healthy sedentary controls. INTERVENTIONS: Not applicable. MAIN OUTCOME MEASURES: Accelerometry (average activity counts, peak activity counts, ratio peak/average, minutes spent per activity category) and symptom severity (intensity of pain, fatigue, and concentration difficulties). RESULTS: Patients with CFS were less active, spent more time sedentary, and less time lightly active ($P<.05$). The course of the activity level during the registration period (P interaction$>.05$), peak activity, and the staggering of activities (ratio peak/average) on 1 day were not different between groups ($P>.05$). Negative correlations (-.242 varying to -.307) were observed for sedentary activity and the ratio with symptom severity and variation on the same and the next day. Light, moderate, and vigorous, as well as the average activity and the peak activity, were positively correlated (.242 varying to .421) with symptom severity and variation. CONCLUSIONS: The more patients with CFS are sedentary and the better activity is dispersed, the fewer symptoms and variations they experience on the same and next day. Inversely, more symptoms and variability is experienced when patients were more active that day or the previous day. The direction of these relations cannot be determined in a cross-sectional study and requires further study.

Méndez-Vidal MJ, Martínez Ortega E, Montesa Pino A, Pérez Valderrama B, Viciana R.	Hospital Provincial de Córdoba, Córdoba, Spain. mariajose.mendezvidal@gmail.com	Management of adverse events of targeted therapies in normal and special patients with metastatic renal cell carcinoma.	Cancer Metastasis Rev. 2012 Sep;31 Suppl 1:S19-27. doi: 10.1007/s10555-012-9355-y.	Treatment options for metastatic renal cell carcinoma (mRCC) have evolved very rapidly, as reflected by the approval of the many drugs that have shown efficacy in phase III studies. Approved drugs include tyrosine kinase inhibitors (TKI) such as sunitinib, sorafenib and pazopanib, vascular endothelial growth factor inhibitors such as bevacizumab, and mammalian target of rapamycin (mTOR) inhibitors such as temsirolimus and everolimus. These biological agents have toxicity profiles that differ from those accompanying current chemotherapeutic agents, but their novelty leads to a lack of exhaustive clinical data regarding related adverse events (AEs), whose symptoms may overlap with those of the chronic illnesses of patients with mRCC such as hypertension, hyperglycemia, and pneumonitis. Hypertension, hypothyroidism, hand-foot syndrome, and fatigue are AEs frequently associated with TKIs; whereas immunosuppression, stomatitis, metabolic alterations, and non-infectious pneumonitis are AEs of mTOR inhibitors. Recommendations for treating these adverse events in patients with mRCC are usually the same as those for the general population. Mild to moderate toxicities may be managed with supportive and pharmacologic interventions, but higher-grade toxicities usually require external specialist consultation, dose reductions, and treatment interruption or discontinuation. Some groups of patients with mRCC, such as frail, elderly patients, and patients with renal or liver dysfunction, require special management of AEs.
Mendoza R, Silverman RH, Klein EA, Miller AD.	Human Biology Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, United States of America.	No biological evidence of XMRV in blood or prostatic fluid from prostate cancer patients.	PLoS One. 2012;7(5):e36073. doi: 10.1371/journal.pone.0036073.	BACKGROUND: XMRV (xenotropic murine leukemia virus-related virus) was initially discovered in association with prostate cancer and later with chronic fatigue syndrome (CFS). Its association with CFS is now largely discredited, and current results support a laboratory origin for XMRV with no reproducible evidence for infection of humans. However, some results indicating the presence of XMRV in prostate cancer are difficult to attribute to sample contamination. Here we have sought biological evidence that might confirm the presence of XMRV in prostate cancer samples previously having tested positive. METHODS AND RESULTS: We have tested for infectious XMRV and neutralizing antibodies against XMRV in blood plasma from 29 subjects with prostate cancer, and for infectious XMRV in prostate secretions from another five prostate cancer subjects. Nine of these subjects had previously tested positive for XMRV by PCR or by virus assay. We did not detect XMRV or related retroviruses in any sample, and the neutralizing activities of the plasma samples were all very low, a result inconsistent with XMRV infection of the plasma donors. CONCLUSIONS: We find no evidence for XMRV infection of any human subject tested, either by assay for infectious virus or for neutralizing antibodies. Our results are consistent with the majority of published studies on XMRV, which find that XMRV is not present in humans. The observed low to undetectable XMRV neutralization by human plasma indicates a lack of innate restriction of XMRV replication by soluble factors in human blood.
Menzies V, Jallo N.	Virginia	Guided imagery as a	J Holist Nurs. 2011	PURPOSE: Fatigue is one of the most common complaints experienced among the

	Commonwealth University, Richmond, USA. vsmenzies@vcu.edu	treatment option for fatigue: a literature review	Dec;29(4):279-86. doi: 10.1177/0898010111412187.	general population. Because fatigue is recognized as a biobehavioral occurrence, a biobehavioral intervention such as guided imagery may be effective in reducing self-reported fatigue. Therefore, the purpose of this study was to explore the research literature related to the use of guided imagery as a nonpharmacological mind-body intervention for the symptom of fatigue. METHOD: The electronic databases MEDLINE, CINAHL, PsychInfo, Psychology and Behavioral Sciences Collection and the Cochrane Library were searched from January 1980 to June 2010. Findings: Of 24 articles retrieved, eight met the inclusion criteria and were included in this systematic literature review. Findings were inconsistent regarding the effectiveness of guided imagery on fatigue. Studies varied in study length, duration of the applied guided imagery intervention, dosage, and whether the images were targeted to the purpose of the intervention. IMPLICATIONS: Guided imagery is a simple, economic intervention with the potential to effectively treat fatigue, thus further research is warranted using systematic, well-designed methodologies Standardizing guided imagery interventions according to total duration of exposure and targeted imagery in a variety of different populations adequately powered to detect changes will contribute to and strengthen nursing's symptom-management armamentarium.
Merkies IS, Faber CG.	Department of Neurology, Spaarne Hospital, Hoofddorp, The Netherlands; Department of Neurology, Maastricht University Medical Centre, Maastricht, The Netherlands. Electronic address: isjmerkies@planet.nl.	Fatigue in immune-mediated neuropathies	Neuromuscul Disord. 2012 Dec;22 Suppl 3:S203-7. doi: 10.1016/j.nmd.2012.10.014.	Fatigue, a highly debilitating symptom, is reported in most patients with immune-mediated neuropathies, particularly in Guillain-Barré syndrome, chronic immune-mediated demyelinating polyradiculoneuropathy, monoclonal gammopathy of undetermined significance related polyneuropathy, and multifocal motor neuropathy. Aspects like the degree of known fatigue in these disorders, its impact on daily functioning and quality of life, the suggested underlying mechanisms, and possible therapeutic interventions for fatigue will be addressed in this review.
Mi Z, Lu Y, Zhang S, An X, Wang X, Chen B, Wang Q, Tong Y.	Beijing Institute of Microbiology and Epidemiology and Affiliated Hospital, Academy of Military Medical Sciences, Beijing, China. zhiqiangmi@yahoo.com.cn	Absence of xenotropic murine leukemia virus-related virus in blood donors in China.	Transfusion. 2012 Feb;52(2):326-31. doi: 10.1111/j.1537-2995.2011.03267.x.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) is a novel human gammaretrovirus that was first identified in patients with prostate cancer in 2006. Subsequent studies have shown that XMRV is also detected in patients with chronic fatigue syndrome (CFS) and even in some healthy controls and blood donors. However, some conflicting findings have been reported by different laboratories or in different regions. The association of XMRV with human diseases and the prevalence of XMRV in different populations needs to be further determined. STUDY DESIGN AND METHODS: XMRV was screened in 391 blood samples from healthy blood donors in China. Nested reverse transcription-polymerase chain reaction (PCR) was used to amplify gag and env genes of XMRV from total RNA of peripheral blood mononuclear cells (PBMNCs) and plasma, respectively. Quantitative PCR was performed to detect XMRV env gene in genomic DNA of PBMNCs. To enhance the detection sensitivity,

				plasma was added into LNCaP cells to amplify XMRV in the plasma samples. RESULTS: No XMRV was found in the 391 blood donors in China or in the LNCaP cells inoculated with plasma from the blood donors. CONCLUSION: Both PCR and virus isolation in highly permissive LNCaP cells failed to detect XMRV in 391 Chinese blood donors, indicating that XMRV infection might not be present in blood donors in China.
Mikirova N, Casciari J, Hunninghake R.	Riordan Clinic, Wichita, Kansas, USA. nmikirova@riordanclinic.org	The assessment of the energy metabolism in patients with chronic fatigue syndrome by serum fluorescence emission.	Altern Ther Health Med. 2012 Jan-Feb;18(1):36-40.	CONTEXT: Chronic fatigue syndrome (CFS) is a debilitating fatigue illness that has unknown etiology and lacks an objective diagnostic marker. OBJECTIVE: To examine the metabolic component of CFS to determine if practitioners can use serum NAD(P)H concentration measurements to monitor metabolism and fatigue status in patients with CFS. DESIGN: The research team conducted a case-control study, comparing a group of patients who were diagnosed with CFS with a control group of healthy subjects. The team obtained venous blood samples from fasting patients to examine the serum NAD(P)H concentrations. SETTING: The study occurred at the Riordan Clinic in Witchita, Kansas. PARTICIPANTS: The study included 44 CFS patients at the Riordan Clinic and 30 healthy control participants. The CFS patients presented a spectrum of symptoms that had existed for at least 6 months: new, unexplained, persistent, or relapsing chronic fatigue that bed rest did not resolve and that was severe enough to reduce daily activity significantly by 50% in conjunction with headache, muscle pain, pain in multiple joints, and unrefreshing sleep. In the control group, the research team enrolled subjects without diagnosis of disease or injury. OUTCOME MEASURES: The research team determined levels of serum reduced nicotinamide adenine dinucleotides (NADH and NAD[P]H) by measuring serum fluorescence emission at 450 nm. The team then conducted sensitivity and specificity analyses. Results NAD(P)H concentrations in serum of CFS participants averaged 8.0 ± 1.4 (standard deviation [SD]) nmol/mL, while those in the healthy controls averaged 10.8 ± 0.8 (SD) nmol/mL, a statistically significant difference. Using a cut-off concentration of 9.5 nmol/mL, the research team attained a sensitivity of 0.73 and a specificity of 1.0. An analysis of receiver-operator characteristics yielded an area under the curve of 0.9. The research team compared serum NAD(P)H to several endocrine and metabolic lab parameters. Serum NAD(P)H was directly correlated with serum CoQ10 levels and inversely correlated with urine hydroxyhemopyrrolin-2-one levels. CONCLUSIONS: Based on these findings, the research team proposed using serum NAD(P)H, measured as an intrinsic serum-fluorescence emission, to monitor metabolism and fatigue status in patients with CFS. Following patients NAD(P)H levels over time may aid in selecting therapeutic strategies and monitoring treatment outcomes.
Miletić V, Relja M.	University of Zagreb, School of Medicine and Zagreb University Hospital Centre, Department of	Restless legs syndrome.	Coll Antropol. 2011 Dec;35(4):1339-47.	Being of the most frequent causes of insomnia, which in the end leads to chronic fatigue, inadequate performance of daily activities, and serious disruption of quality of living, restless legs syndrome (RLS) is nowadays not only a serious medical problem but a socio-economical one as well. Prevalence of the disorder in general population is estimated at 5 to 15%. Family history is positive in over 50% of idiopathic RLS

	Neurology, Zagreb, Croatia.			patients which points to genetic basis of the disorder. The characteristics of the secondary or acquired form of RLS are symptoms that start later in life as well as a rapid progression of the disease. On the other hand, idiopathic RLS more often starts at a younger age and the prognoses are better. Over twenty disorders and conditions are brought in connection with secondary RLS. Although the cause of primary RLS is still unknown, there is a strong connection between central metabolism of iron as well as dopamine levels and RLS manifestation. A differential diagnosis of RLS includes a wide specter of motor and sensory disorders. Diagnosis is based on clinical features and the history of disease. To correctly diagnose idiopathic RLS one must first eliminate secondary causes of RLS and then also exclude any disorders with clinical features that mimic those of RLS. It has been estimated that some 20 to 25% of patients need pharmacological therapy. Best initial therapy is the application of nonergot dopamine agonists. Anticonvulsants, benzodiazepines and opioides can be given to patients who are refractory to dopaminergic therapy, those suffering from RLS with emphasized painful sensory component and those with RLS connected with insomnia.
Miller P, Iyer M, Gold AR.	[No address quoted]	Treatment resistant adolescent depression with upper airway resistance syndrome treated with rapid palatal expansion: a case report.	J Med Case Rep. 2012 Dec 4;6(1):415	ABSTRACT: INTRODUCTION: To the best of our knowledge this is the first report of a case of treatment-resistant depression in which the patient was evaluated for sleep disordered breathing as the cause and in which rapid palatal expansion to permanently treat the sleep disordered breathing produced a prolonged symptom-free period off medication. CASE PRESENTATION: An 18-year-old Caucasian man presented to our sleep disorders center with chronic severe depression that was no longer responsive to medication but that had recently responded to electroconvulsive therapy. Ancillary, persistent symptoms included mild insomnia, moderate to severe fatigue, mild sleepiness and severe anxiety treated with medication. Our patient had no history of snoring or witnessed apnea, but polysomnography was consistent with upper airway resistance syndrome. Although our patient did not have an orthodontic indication for rapid palatal expansion, rapid palatal expansion was performed as a treatment of his upper airway resistance syndrome. Following rapid palatal expansion, our patient experienced a marked improvement of his sleep quality, anxiety, fatigue and sleepiness. His improvement has been maintained off all psychotropic medication and his depression has remained in remission for approximately two years following his electroconvulsive therapy. CONCLUSIONS: This case report introduces the possibility that unrecognized sleep disordered breathing may play a role in adolescent treatment-resistant depression. The symptoms of upper airway resistance syndrome are non-specific enough that every adolescent with depression, even those responding to medication, may have underlying sleep disordered breathing. In such patients, rapid palatal expansion, by widening the upper airway and improving airflow during sleep, may produce a prolonged improvement of symptoms and a tapering of medication. Psychiatrists treating

				adolescents may benefit from having another treatment option for treatment-resistant depression.
Minelli A, Vaona A.	alessandra.minelli@med.unibs.it.	[Article in Italian]	Reumatismo. 2012 Jul 19;64(3):151-7. doi: 10.4081/reumatismo.2012.151.	Fibromyalgia (FM) is a chronic disorder caused by a dysfunction of central nervous system sensitization. This syndrome is characterized by widespread pain and diffuse tenderness, but often also presents fatigue, sleep disturbances, and a whole range of symptoms such as morning stiffness, decreased physical function and dyscognition. FM is usually treated with pharmacological and non-pharmacological treatments. The non-pharmacological interventions include cognitive behavioral therapy (CBT), physiotherapy, acupuncture and patient education programs. In order to evaluate the efficacy of CBT and compare it with other non-pharmacological treatments, we performed a review of the meta-analytic literature. We evaluated the methodological quality of publications found by following the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. Data showed that CBT does not provide better results than other non-pharmacological treatments on outcomes of pain, fatigue, sleep disturbance and quality of life, at either a short or long-term evaluation. On the contrary, CBT seems to be more effective on symptoms of depression for a short period, whereas it considerably improves the pain self-management and reduces the number of visits to the doctor. The data currently available indicate that cost-effectiveness studies could help us to understand whether the reduction in the number of visits to the doctor could balance the cost of CBT to the health public system.
Missen A, Hollingworth W, Eaton N, Crawley E.	School of Social and Community Medicine, University of Bristol, Bristol, UK.	The financial and psychological impacts on mothers of children with chronic fatigue syndrome (CFS/ME).	Child Care Health Dev. 2012 Jul;38(4):505-12. doi: 10.1111/j.1365-2214.2011.01298.x.	BACKGROUND: Paediatric chronic fatigue syndrome or myalgic encephalopathy (CFS/ME) is relatively common and children can be severely affected attending little or no school for extended periods. There are no studies quantifying the financial impact of having a child with CFS/ME and there is little information of the impact on parental mood. METHODS: Forty mothers of children with CFS/ME from a regional specialist CFS/ME service completed inventories to assess their psychological well-being (Hospital Anxiety and Depression Scale, General Health Questionnaire-12) loss of earnings and increased expenditure. In addition, eight mothers took part in a semi-structured qualitative interview. RESULTS: Most parents of children with CFS/ME experience loss of monthly income (mean = £247) and increase in monthly expenditure (mean = £206). Twenty-eight (72%) mothers were above the cut-off for the General Health Questionnaire-12 compared with 20% in the healthy population (95% CI 55, 85, P < 0.001) suggesting they probably have a mental health problem. This may be explained by the qualitative interviews where mothers described five areas contributing to poor parental health: lack of understanding from others; marital tension; concern about their child's distress; concern about the impact on siblings and emotional distress causing physical symptoms. CONCLUSIONS: The majority of families of children with CFS/ME experience decreased income and increased expenditure with a marked impact on maternal psychological health. Clinicians need

				to be aware of this to provide appropriate support to families who care for children with CFS/ME.
Miwa K, Fujita M.	Department of Internal Medicine, Miwa Naika Clinic, Toyama, Japan. info@miwa-naika.com	Small heart with low cardiac output for orthostatic intolerance in patients with chronic fatigue syndrome.	Clin Cardiol. 2011 Dec;34(12):782-6. doi: 10.1002/clc.20962.	BACKGROUND: The etiology of chronic fatigue syndrome (CFS) is unknown. Orthostatic intolerance (OI) is common in CFS patients. Recently, small heart with low cardiac output has been postulated to be related to the genesis of both CFS and OI. HYPOTHESIS: Small heart is associated with OI in patients with CFS. METHODS: Study CFS patients were divided into groups of 26 (57%) CFSOI(+) and 20 (43%) CFSOI(-) according to the presence or absence of OI. In addition, 11 OI patients and 27 age- and sex-matched control subjects were studied. Left ventricular (LV) dimensions and function were determined echocardiographically. RESULTS: The mean values of cardiothoracic ratio, systemic systolic and diastolic pressures, LV end-diastolic dimension, LV end-systolic dimension, stroke volume index, cardiac index, and LV mass index were all significantly smaller in CFSOI(+) patients than in CFSOI(-) patients and healthy controls, and also in OI patients than in controls. A smaller LV end-diastolic dimension (<40 mm) was significantly (P<0.05) more prevalently noted in CFSOI(+) (54%) and OI (45%) than in CFSOI(-) (5%) and controls (4%). A lower cardiac index (<2 L/min/mm(2)) was more prevalent in CFSOI(+) (65%) than in CFSOI(-) (5%, P<0.01), OI (27%), and controls (11%, P<0.01). CONCLUSIONS: A small size of LV with low cardiac output was noted in OI, and its degree was more pronounced in CFSOI(+). A small heart appears to be related to the genesis of OI and CFS via both cerebral and systemic hypoperfusion. CFSOI(+) seems to constitute a well-defined and predominant subgroup of CFS.
Mohammad A, Carey JJ, Storan E, Scarry M, Coughlan RJ, Lee JM.	Department of Rheumatology, Merlin Park University Hospital, Galway, Ireland. ausafmohammad@gmail.com	Prevalence of fibromyalgia among patients with chronic hepatitis C infection: relationship to viral characteristics and quality of life.	J Clin Gastroenterol. 2012 May-Jun;46(5):407-12. doi: 10.1097/MCG.0b013e3182485528.	OBJECTIVES: We determined the prevalence of fibromyalgia syndrome (FMS) in a cohort of subjects with chronic hepatitis C virus (HCV), and the relationship to subject demographics, viral characteristics, and quality of life. METHODS: In a cross-sectional study of a cohort of HCV-infected individuals, all subjects underwent a standard assessment including history, clinical examination, and functional assessments for pain and disability. RESULTS: A total of 185 subjects met the inclusion criteria. Median age was 48.7 years, and 110 (59%) were women. A total of 106 (57%) of the subjects met criteria for the presence of FMS. Widespread pain and ≥11 tender points were present in all of the subjects with FMS, fatigue in 98 (92%), and depression in 60 (57%). Among those with FMS, mean pain score was 70±11.78 and 36% reported some functional impairment on (HAQ-DI>0), with 17% reporting moderate-to-severe functional impairment (HAQ-DI≥1.5). CONCLUSIONS: This study reveals a high prevalence of FMS (57%) among subjects with chronic HCV infection, one third of whom reported some degree of functional impairment. Recognition and management of this condition in such patients will help improve their quality of life.
Mohan KV, Devadas K, Sainath Rao S, Hewlett I,	Section of Cell Biology, Laboratory of Cellular Hematology, Center for	Identification of XMRV infection-associated	PLoS One. 2012;7(3):e32853. doi: 10.1371/journal.pone.003285	INTRODUCTION: XMRV is a gammaretrovirus that was thought to be associated with prostate cancer (PC) and chronic fatigue syndrome (CFS) in humans until recently. The virus is culturable in various cells of human origin like the lymphocytes, NK cells,

Atreya C.	Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland, United States of America.	microRNAs in four cell types in culture.	3	neuronal cells, and prostate cell lines. MicroRNAs (miRNA), which regulate gene expression, were so far not identified in cells infected with XMRV in culture. METHODS: Two prostate cell lines (LNCaP and DU145) and two primary cells, Peripheral Blood Lymphocytes [PBL] and Monocyte-derived Macrophages [MDM] were infected with XMRV. Total mRNA was extracted from mock- and virus-infected cells at 6, 24 and 48 hours post infection and evaluated for microRNA profile in a microarray. RESULTS: MicroRNA expression profiles of XMRV-infected continuous prostate cancer cell lines differ from that of virus-infected primary cells (PBL and MDMs). miR-193a-3p and miRPlus-E1245 observed to be specific to XMRV infection in all 4 cell types. While miR-193a-3p levels were down regulated miRPlus-E1245 on the other hand exhibited varied expression profile between the 4 cell types. DISCUSSION: The present study clearly demonstrates that cellular microRNAs are expressed during XMRV infection of human cells and this is the first report demonstrating the regulation of miR193a-3p and miRPlus-E1245 during XMRV infection in four different human cell types.
Morelli V.	Department of Family and Community Medicine, Meharry Medical College, 1005 Dr. D.B. Todd Jr. Boulevard, Nashville, TN 37208, USA. vmorelli@mmc.edu	Fatigue and chronic fatigue in the elderly: definitions, diagnoses, and treatments.	Clin Geriatr Med. 2011 Nov;27(4):673-86. doi: 10.1016/j.cger.2011.07.011.	Because fatigue is so prevalent in the elderly population, it is important that physicians be well versed in the evaluation and management of this complaint. This article discusses the clinical manifestations and predisposing factors for the three major categories of fatigue: recent, prolonged, and chronic. The CDC classification of chronic fatigue syndrome is included. Patient dissatisfaction with the care for their fatigue is a common problem. Several pharmaceutical treatment methods are presented. Non-pharmacologic options, such as use of vitamins, exercise, behavior modification,and diet are also discussed.
Morris G, Maes M.	Tir Na Nog, Pembrey, Llanelli, UK.	Increased nuclear factor-κB and loss of p53 are key mechanisms in Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS).	Med Hypotheses. 2012 Nov;79(5):607-13. doi: 10.1016/j.mehy.2012.07.034.	Fukuda's criteria are adequate to make a distinction between Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) and chronic fatigue (CF), but ME/CFS patients should be subdivided into those with (termed ME) and without (termed CFS) post exertional malaise [Maes et al. 2012]. ME/CFS is considered to be a neuro-immune disease. ME/CFS is characterized by activated immuno-inflammatory pathways, including increased levels of pro-inflammatory cytokines, nuclear factor κB (NF-κB) and aberrations in mitochondrial functions, including lowered ATP. These processes may explain typical symptoms of ME/CFS, e.g. fatigue, malaise, hyperalgesia, and neurologic and autonomic symptoms. Here we hypothesize that increased NF-κB together with a loss of p53 are key phenomena in ME/CFS that further explain ME/CFS symptoms, such as fatigue and neurocognitive dysfunction, and explain ME symptoms, such as post-exertional malaise following mental and physical activities. Inactivation of p53 impairs aerobic mitochondrial functions and causes greater dependence on anaerobic glycolysis, elevates lactate levels, reduces mitochondrial density in skeletal muscle and reduces endurance during physical exercise. Lowered p53 and increased NF-κB are associated with elevated reactive oxygen species. Increased NF-κB induces the production of pro-inflammatory

				cytokines, which increase glycolysis and further compromise mitochondrial functions. All these factors together may contribute to mitochondrial exhaustion and indicate that the demand for extra ATP upon the commencement of increased activity cannot be met. In conditions of chronic inflammation and oxidative stress, high NF-κB and low p53 may conspire to promote neuron and glial cell survival at a price of severely compromised metabolic brain function. Future research should examine p53 signaling in ME/CFS.
Morris G, Maes M.	Tir Na Nog, Pembrey, Llanelli, UK.	A neuro-immune model of Myalgic Encephalomyelitis/Chronic fatigue syndrome.	Metab Brain Dis. 2012 Jun 21	This paper proposes a neuro-immune model for Myalgic Encephalomyelitis/Chronic fatigue syndrome (ME/CFS). A wide range of immunological and neurological abnormalities have been reported in people suffering from ME/CFS. They include abnormalities in proinflammatory cytokines, raised production of nuclear factor-κB, mitochondrial dysfunctions, autoimmune responses, autonomic disturbances and brain pathology. Raised levels of oxidative and nitrosative stress (O&NS), together with reduced levels of antioxidants are indicative of an immuno-inflammatory pathology. A number of different pathogens have been reported either as triggering or maintaining factors. Our model proposes that initial infection and immune activation caused by a number of possible pathogens leads to a state of chronic peripheral immune activation driven by activated O&NS pathways that lead to progressive damage of self epitopes even when the initial infection has been cleared. Subsequent activation of autoreactive T cells conspiring with O&NS pathways cause further damage and provoke chronic activation of immuno-inflammatory pathways. The subsequent upregulation of proinflammatory compounds may activate microglia via the vagus nerve. Elevated proinflammatory cytokines together with raised O&NS conspire to produce mitochondrial damage. The subsequent ATP deficit together with inflammation and O&NS are responsible for the landmark symptoms of ME/CFS, including post-exertional malaise. Raised levels of O&NS subsequently cause progressive elevation of autoimmune activity facilitated by molecular mimicry, bystander activation or epitope spreading. These processes provoke central nervous system (CNS) activation in an attempt to restore immune homeostatsis. This model proposes that the antagonistic activities of the CNS response to peripheral inflammation, O&NS and chronic immune activation are responsible for the remitting-relapsing nature of ME/CFS. Leads for future research are suggested based on this neuro-immune model.
Moss JI.	[No address quoted]	Gulf War illnesses are autoimmune illnesses caused by reactive oxygen species which were caused by nerve agent prophylaxis.	Med Hypotheses. 2012 Aug;79(2):283-4. doi: 10.1016/j.mehy.2012.04.043.	Gulf War illnesses (GWI share many of the features of chronic fatigue syndrome (CFS) and both CFS and GWI may be the result of chronic immune system processes. The main suspected cause for GWI, the drug pyridostigmine bromide (PB), has been shown to cause neuronal damage from reactive oxygen species (ROS). ROS have been associated with IgM mediated autoimmune responses against ROS induced neoepitopes in depressed patients and this may also apply to CFS. It therefore follows that the drug used in the Gulf War caused ROS, the ROS modified native molecules,

				and that this trigged the autoimmune condition we refer to as Gulf War illnesses. Similar mechanisms may apply to other autoimmune illnesses.
Mount DL, Johnson DM, Rego MI, Schofield K, Amponsah A, Graham LF.	Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA. Dmount@wfubmc.edu	Preliminary findings exploring the social determinants of Black males' lay health perspectives.	Am J Mens Health. 2012 Jan;6(1):71-9. doi: 10.1177/1557988311420993.	The unequal discussion of Black males' health is a pressing social problem. This study addressed Black males' lay perspectives regarding their health, illness, and mortality, with attention to the determinants of men's health, prevention, lifestyle, and opportunities for health promotion using an exploratory/qualitative research methodology. Participants were 68 Black males aged 15 to 68 years, with an average age of 44 years (SD = 14.5). The narratives represented a complex interplay of biopsychosocial factors, ranging from intrapersonal attitudes, interpersonal experiences to discussions about community and public policy injustices. Five prominent themes emerged: (a) lack of chronic disease awareness, (b) fatalism, (c) fear and anxiety of academic-medical settings, (d) hyperactive masculinity fatigue, and (e) the gay-straight divide. The term Tired Black Male Health syndrome was coined in the forum. Implications of these findings are discussed in the context of culturally relevant strategies for improving Black male community health engagement.
Myhill S, Booth NE, McLaren-Howard J.	Sarah Myhill Ltd Llangunllo, Powys UK.	Targeting mitochondrial dysfunction in the treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) - a clinical audit.	Int J Clin Exp Med. 2013;6(1):1-15.	Report on an audit of 138 ME/CFS patients who attended a private practice and took the ATP Profile biomedical test. The results revealed that all of these patients had measureable mitochondrial dysfunction. A basic treatment regime, based on 1) eating the evolutionary correct stone-age diet, 2) ensuring optimum hours of good quality sleep, 3) taking a standard package of nutritional supplements, and 4) getting the right balance between work and rest, was recommended for all patients. Additions to the basic regime were tailored for each patient according to the results of the ATP Profile and additional nutritional tests and clues from the clinical history. Mitochondrial function is typically impaired in two ways: substrate or co-factor deficiency, and inhibition by chemicals, exogenous or endogenous. For the former, additional nutrients are recommended where there is a deficiency, and for the latter, improvement of anti-oxidant status and selective chelation therapy or far-infrared saunas are appropriate. We show case histories of nine patients who have taken the ATP Profile on three or four occasions, and a before-and-after treatment summary of the 34 patients who have had at least two ATP Profile tests separated by some months. Finally, we summarize the results for the 30 patients who followed all aspects of the treatment regime and compare them with the 4 patients who were lax on two or more aspects of the treatment regime. All patients who followed the treatment regime improved in mitochondrial function by on average a factor of 4.
Mysterud I.	[No address quoted]	Chronic fatigue syndrome and evolution. [Article in Norwegian]	Handb Clin Neurol. 2012;106:573-87. doi: 10.1016/B978-0-444-52002-9.00034-6.	Comment in Tidsskr Nor Laegeforen. 2012 Jun 12;132(11):1317. Comment on Tidsskr Nor Laegeforen. 2012 Feb 21;132(4):400-1.
Naess H, Nyland	Institute of Clinical	Chronic fatigue	BMC Gastroenterol. 2012 Feb	BACKGROUND: A waterborne outbreak of Giardia lamblia gastroenteritis led to a high

M, Hausken T, Follestad I, Nyland HI.	Medicine, Department of Neurology, and Unit for Gastroenterology, Department for Medicine, Haukeland University Hospital, Bergen, Norway. halvor.naess@haukeland.no	syndrome after Giardia enteritis: clinical characteristics, disability and long-term sickness absence.	8;12:13. doi: 10.1186/1471-230X-12-13.	prevalance of long-lasting fatigue and abdominal symptoms. The aim was to describe the clinical characteristics, disability and employmentloss in a case series of patients with Chronic Fatigue Syndrome (CFS) after the infection. METHODS: Patients who reported persistent fatigue, lowered functional capacity and sickness leave or delayed education after a large community outbreak of giardiasis enteritis in the city of Bergen, Norway were evaluated with the established Centers for Disease Control and Prevention criteria for CFS. Fatigue was self-rated by the Fatigue Severity Scale (FSS). Physical and mental health status and functional impairment was measured by the Medical Outcome Severity Scale-short Form-36 (SF-36). The Hospital Anxiety and Depression Scale (HADS) was used to measure co-morbid anxiety and depression. Inability to work or study because of fatigue was determined by sickness absence certified by a doctor. RESULTS: A total of 58 (60%) out of 96 patients with long-lasting post-infectious fatigue after laboratory confirmed giardiasis were diagnosed with CFS. In all, 1262 patients had laboratory confirmed giardiasis. At the time of referral (mean illness duration 2.7 years) 16% reported improvement, 28% reported no change, and 57% reported progressive course with gradual worsening. Mean FSS score was 6.6. A distinctive pattern of impairment was documented with the SF-36. The physical functioning, vitality (energy/fatigue) and social functioning were especially reduced. Long-term sickness absence from studies and work was noted in all patients. CONCLUSION: After giardiasis enteritis at least 5% developed clinical characteristics and functional impairment comparable to previously described post-infectious fatigue syndrome.
Nater UM, Heim CM, Raison C.	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA. nater@uni-marburg.de	Chronic fatigue syndrome.	Handb Clin Neurol. 2012;106:573-87. doi: 10.1016/B978-0-444-52002-9.00034-6.	[No abstract given]
Nater UM, Maloney E, Lin JM, Heim C, Reeves WC.	[No address quoted]	Coping styles in chronic fatigue syndrome: findings from a population-based study.	Psychother Psychosom. 2012;81(2):127-9. doi: 10.1159/000329996.	[No abstract given]
Newton DJ, Kennedy G, Chan KK, Lang CC, Belch JJ, Khan F.	[No address quoted]	Large and small artery endothelial dysfunction in chronic fatigue syndrome.	Int J Cardiol. 2012 Feb 9;154(3):335-6. doi: 10.1016/j.ijcard.2011.10.030.	[No abstract given]
Nguyen RH,	Division of	Co-morbid pain	Psychol Health Med.	Many women with vulvodynia also suffer from other chronic co-morbid pain

Ecklund AM, Maclehose RF, Veasley C, Harlow BL.	Epidemiology & Community Health, University of Minnesota, Minneapolis, MA, USA. nguyen@umn.edu	conditions and feelings of invalidation and isolation among women with vulvodynia.	2012;17(5):589-98. doi: 10.1080/13548506.2011.647703.	conditions. Alone, these pain conditions are associated with feeling invalidated by others and feeling socially isolated. It is unclear, however, how the presence of additional pain co-morbidities are associated with the psychosocial wellbeing of women with vulvodynia. We used data from a survey administered by the National Vulvodynia Association. Women reported clinician-diagnosed vulvodynia, presence of co-morbid pain, and how often they felt that they felt no one believed their pain existed (invalidated) and isolated. Analyses determined prevalence of feeling invalidated or isolated, and the difference in prevalence when co-morbidities existed. Forty-five percent of these 1847 women with vulvodynia reported having at least one of the following five chronic pain conditions, chronic fatigue syndrome, endometriosis, fibromyalgia, interstitial cystitis, or irritable bowel syndrome. Adjusted baseline prevalence among all women of feeling invalidated was 9% and of feeling isolated was 14%. Having a co-morbid condition with vulvodynia, as well as having an increasing number of co-morbid conditions with vulvodynia, was significantly associated with the presence of feeling both invalidated and isolated. Chronic fatigue syndrome was the co-morbidity most strongly associated with feelings invalidation and isolation. One or more co-morbid pain conditions in addition to vulvodynia were significantly associated with psychosocial wellbeing. However, the temporality of the association could not be elucidated and therefore we cannot conclude that these pain conditions cause poor psychosocial wellbeing. Despite this, future studies should explore the utility of promoting validation of women's pain conditions and reducing social isolation for women with chronic pain.
Nijhof SL, Bleijenberg G, Uiterwaal CS, Kimpen JL, van de Putte EM.	Department of Paediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Netherlands. s.l.nijhof@umcutrecht.nl	Effectiveness of internet-based cognitive behavioural treatment for adolescents with chronic fatigue syndrome (FITNET): a randomised controlled trial.	Lancet. 2012 Apr 14;379(9824):1412-8. doi: 10.1016/S0140-6736(12)60025-7. Comment in Lancet. 2012 Apr 14;379(9824):1372-3. Lancet. 2012 Aug 11;380(9841):561; author reply 562. Lancet. 2012 Aug 11;380(9841):561-2; author reply 562. Evid Based Ment Health. 2012 Aug;15(3):81.	BACKGROUND: Chronic fatigue syndrome is characterised by persistent fatigue and severe disability. Cognitive behavioural therapy seems to be a promising treatment, but its availability is restricted. We developed Fatigue In Teenagers on the interNET (FITNET), the first dedicated internet-based therapeutic program for adolescents with this disorder, and compared its effectiveness with that of usual care. METHODS: Adolescents aged 12-18 years with chronic fatigue syndrome were assigned to FITNET or usual care in a 1:1 ratio at one tertiary treatment centre in the Netherlands by use of a computer-generated blocked randomisation allocation schedule. The study was open label. Primary outcomes were school attendance, fatigue severity, and physical functioning, and were assessed at 6 months with computerised questionnaires. Analysis was by intention to treat. Thereafter, all patients were offered FITNET if needed. This trial is registered, number ISRCTN59878666. FINDINGS: 68 of 135 adolescents were assigned to FITNET and 67 to usual care, and 67 and 64, respectively, were analysed. FITNET was significantly more effective than was usual care for all dichotomised primary outcomes at 6 months-full school attendance (50 [75%] vs 10 [16%], relative risk 4·8, 95% CI 2·7-8·9; p<0·0001), absence of severe fatigue (57 [85%] vs 17 [27%], 3·2, 2·1-4·9; p<0·0001), and normal physical functioning (52 [78%] vs 13 [20%], 3·8, 2·3-6·3; p<0·0001). No serious adverse events were

				reported. INTERPRETATION: FITNET offers a readily accessible and highly effective treatment for adolescents with chronic fatigue syndrome. The results of this study justify implementation on a broader scale. FUNDING: Netherlands Organisation for Health Research and Development.
Nijs J, Crombez G, Meeus M, Knoop H, Damme SV, Cauwenbergh V, Bleijenberg G.	Chronic Pain and Chronic Fatigue Research Group, Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussels, Belgium. drlm@thepainmd.com	Pain in patients with chronic fatigue syndrome: time for specific pain treatment?	Pain Physician. 2012 Sep-Oct;15(5):E677-86.	BACKGROUND: Besides chronic fatigue, patients with chronic fatigue syndrome (CFS) have debilitating widespread pain. Yet pain from CFS is often ignored by clinicians and researchers. OBJECTIVES: To examine whether pain is a unique feature of CFS, or does it share the same underlying mechanisms as other CFS symptoms? Second, it is examined whether effective treatments for pain from CFS are currently available. STUDY DESIGN: Narrative review covering the scientific literature up through December 2011. SETTING: Several universities. RESULTS: From the available literature, it is concluded that musculoskeletal factors are unlikely to account for pain from CFS. Pain seems to be one out of many symptoms related to central sensitization from CFS. This idea is supported by the findings of generalized hyperalgesia (including widespread increased responsiveness to painful stimuli) and dysfunctional endogenous analgesia in response to noxious thermal stimuli. Pain catastrophizing and depression partly account for pain from CFS. Pain increases during exercise is probably due to the lack of endogenous analgesia and activation of several genes in response to exercise in CFS. There is currently no evidence in support for the efficacy of complementary medicine in the treatment of pain from CFS. Intensive education about the biology of pain from CFS (within the framework of central sensitization) has positive short-term effects for patients with CFS, and fatigue-targeting cognitive behavioral therapy appears to be effective for pain from CFS as well. LIMITATIONS: The role of the deficient hypothalamus-pituitary-adrenal axis in relation to pain from CFS, as well as the interactions with immune (dys)functioning require further study. CONCLUSION: Recent research has increased our understanding of pain from CFS, including its treatment. It is advocated to optimize current CFS treatment protocols by targeting the underlying mechanism for those patients having severe pain.
Nijs J, Meeus M, Heins M, Knoop H, Moorkens G, Bleijenberg G.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium. Jo.Nijs@vub.ac.be	Kinesiophobia, catastrophizing and anticipated symptoms before stair climbing in chronic fatigue syndrome: an experimental study.	Disabil Rehabil. 2012;34(15):1299-305. doi: 10.3109/09638288.2011.641661.	PURPOSE: Kinesiophobia and catastrophizing are frequent among people with chronic fatigue syndrome (CFS). This study was aimed at examining (1) whether kinesiophobia, anticipated symptoms and fatigue catastrophizing are related to stair climbing performance in people with CFS; and (2) whether kinesiophobia and fatigue catastrophizing are related to daily physical activity in CFS. METHOD: Patients with CFS filled in a set of questionnaires, performed a physical demanding task (two floors stair of climbing and descending) with pre-test and post-test heart rate monitoring and immediate post-stair climbing symptom assessment. Real-time activity monitoring was used between the baseline and second assessment day (7 days later). RESULTS: Kinesiophobia and fatigue catastrophizing were strongly related ($\rho = 0.62$ and 0.67, respectively) to poorer stair climbing performance (i.e. more time required to complete the threatening activity). Kinesiophobia and fatigue catastrophizing were

				unrelated to the amount of physical activity on the first day following stair climbing or during the seven subsequent days. CONCLUSION: These findings underscore the importance of kinesiophobia and fatigue catastrophizing for performing physical demanding tasks in everyday life of people with CFS, but refute a cardinal role for kinesiophobia and fatigue catastrophizing in determining daily physical activity level in these patients.
Nijs J, Meeus M, Van Oosterwijck J, Ickmans K, Moorkens G, Hans G, De Clerck LS.	Department of Human Physiology, Vrije Universiteit Brussel (VUB), Brussels, Belgium. Jo.Nijs@vub.ac.be	In the mind or in the brain? Scientific evidence for central sensitisation in chronic fatigue syndrome.	Eur J Clin Invest. 2012 Feb;42(2):203-12. doi: 10.1111/j.1365-2362.2011.02575.x.	BACKGROUND: Central sensitisation entails several top-down and bottom-up mechanisms, all contributing to the hyperresponsiveness of the central nervous system to a variety of inputs. In the late nineties, it was first hypothesised that chronic fatigue syndrome (CFS) is characterised by hypersensitivity of the central nervous system (i.e. central sensitisation). Since then, several studies have examined central sensitisation in patients with CFS. This study provides an overview of such studies. MATERIALS AND METHODS: Narrative review. RESULTS: Various studies showed generalised hyperalgesia in CFS for a variety of sensory stimuli, including electrical stimulation, mechanical pressure, heat and histamine. Various tissues are affected by generalised hyperalgesia: the skin, muscle tissue and the lungs. Generalised hyperalgesia in CFS is augmented, rather than decreased, following various types of stressors like exercise and noxious heat pain. Endogenous inhibition is not activated in response to exercise and activation of diffuse noxious inhibitory controls following noxious heat application to the skin is delayed. CONCLUSIONS: The observation of central sensitisation in CFS is in line with our current understanding of CFS. The presence of central sensitisation in CFS corroborates with the presence of several psychological influences on the illness, the presence of infectious agents and immune dysfunctions and the dysfunctional hypothalamus-pituitary-adrenal axis as seen in these severely debilitated patients.
Nijs J, Van Cauwenbergh D, De Kooning M, Ickmans K.	Chronic Pain and Chronic Fatigue Research Group (CHROPIVER), Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium Chronic Pain and Chronic Fatigue Research Group (CHROPIVER), Division of Musculoskeletal	Time-contingent pacing and exercise therapy accounting for postexertional malaise and central sensitization in chronic fatigue (central sensitivity) syndrome.	Eur J Clin Invest. 2012 Dec;42(12):1363-5. doi: 10.1111/j.1365-2362.2012.02722.x.	[No abstract given]

	Physiotherapy, Department of Health Care Sciences, Artesis University College, Antwerp, Belgium Department of Physical Medicine and Physiotherapy, University Hospital Brussels, Brussels, Belgium.			
Nugraha B, Karst M, Engeli S, Gutenbrunner C.	Department of Rehabilitation Medicine, Hannover Medical School, Carl-Neuberg-Str. 1, Hannover, Germany. Nugraha.Boya@mh-hannover.de	Brain-derived neurotrophic factor and exercise in fibromyalgia syndrome patients: a mini review.	Rheumatol Int. 2012 Sep;32(9):2593-9. doi: 10.1007/s00296-011-2348-2.	Fibromyalgia syndrome (FMS) is a common chronic pain condition characterized by chronic widespread pain and decreased pain threshold, with hyperalgesia and allodynia. Associated signs include fatigue, morning stiffness, non-restorative sleep, mood disturbance, depression, irritable bowel syndrome, and headache. In addition to the administration of drugs, psychological therapies treatment of FMS mainly consists of physical therapies. Although the precise pathogenesis of FMS remains elucidated, modern understanding conceptualizes FMS as central sensitization as a consequence of altered endogenous pain- and stress-response system and continuous nociceptive input. Altered brain-derived neurotrophic factor (BDNF) levels in FMS suggest that BDNF--well known for its effects on neuronal plasticity--is involved in this sensitization process. Exercise leads to changes in serum BDNF levels, too. This association highlights the importance of exercise in FMS and other chronic pain conditions.
Ocon AJ, Messer ZR, Medow MS, Stewart JM.	Department of Physiology, New York Medical College, Valhalla, NY, USA. anthony_ocon@nymc.edu	Increasing orthostatic stress impairs neurocognitive functioning in chronic fatigue syndrome with postural tachycardia syndrome.	Clin Sci (Lond). 2012 Mar;122(5):227-38. doi: 10.1042/CS20110241.	CFS (chronic fatigue syndrome) is commonly co-morbid with POTS (postural tachycardia syndrome). Individuals with CFS/POTS experience unrelenting fatigue, tachycardia during orthostatic stress and ill-defined neurocognitive impairment, often described as 'mental fog'. We hypothesized that orthostatic stress causes neurocognitive impairment in CFS/POTS related to decreased CBFV (cerebral blood flow velocity). A total of 16 CFS/POTS and 20 control subjects underwent graded tilt table testing (at 0, 15, 30, 45, 60 and 75°) with continuous cardiovascular, cerebrovascular, and respiratory monitoring and neurocognitive testing using an n-back task at each angle. The n-back task tests working memory, concentration, attention and information processing. The n-back task imposes increasing cognitive challenge with escalating (0-, 1-, 2-, 3- and 4-back) difficulty levels. Subject dropout due to orthostatic presyncope at each angle was similar between groups. There were no n-back accuracy or RT (reaction time) differences between groups while supine. CFS/POTS subjects responded less correctly during the n-back task test and had greater nRT (normalized RT) at 45, 60 and 75°. Furthermore, at 75° CFS/POTS subjects responded less correctly and had greater nRT than controls during the 2-, 3- and 4-

				back tests. Changes in CBFV were not different between the groups and were not associated with n-back task test scores. Thus we conclude that increasing orthostatic stress combined with a cognitive challenge impairs the neurocognitive abilities of working memory, accuracy and information processing in CFS/POTS, but that this is not related to changes in CBFV. Individuals with CFS/POTS should be aware that orthostatic stress may impair their neurocognitive abilities.
Oh SJ, Kim YH, Kim SK, Kim MW.	Department of Rehabilitation Medicine, Incheon St. Mary's Hospital, The Catholic University of Korea, Incheon 403-720, Korea.	Painful os peroneum syndrome presenting as lateral plantar foot pain.	Ann Rehabil Med. 2012 Feb;36(1):163-6. doi: 10.5535/arm.2012.36.1.163.	Lateral plantar foot pain can be caused by various entities, and the painful os peroneum syndrome should be considered in the differential diagnosis. Recent developments in musculoskeletal ultrasonography are very useful for initial diagnosis. We discuss a 69-year-old female who experienced lateral plantar foot pain for over one month. Through physical examination, radiography, ultrasound and magnetic resonance imaging, she was diagnosed with the painful os peroneum syndrome with a chronic fatigue fracture of multipartite os peroneum and peroneus longus tenosynovitis, for which she underwent surgery. We herein report this rare condition and reviewed the relevant literature.
Okamoto LE, Raj SR, Peltier A, Gamboa A, Shibao C, Diedrich A, Black BK, Robertson D, Biaggioni I.	Vanderbilt Autonomic Dysfunction Center, Vanderbilt University School of Medicine, Nashville, TN, U.S.A.	Neurohumoral and haemodynamic profile in postural tachycardia and chronic fatigue syndromes.	Clin Sci (Lond). 2012 Feb;122(4):183-92. doi: 10.1042/CS20110200.	Several studies recognized an overlap between CFS (chronic fatigue syndrome) and POTS (postural tachycardia syndrome). We compared the autonomic and neurohormonal phenotype of POTS patients with CFS (CFS-POTS) to those without CFS (non-CFS-POTS), to determine whether CFS-POTS represents a unique clinical entity with a distinct pathophysiology. We recruited 58 patients with POTS, of which 47 were eligible to participate. A total of 93% of them reported severe fatigue [CIS (Checklist of Individual Strength), fatigue subscale >36], and 64% (n=30) fulfilled criteria for CFS (CFS-POTS). The prevalence of CFS symptoms (Centers for Disease Control and Prevention criteria) was greater in the CFS-POTS group, but the pattern of symptoms was similar in both groups. Physical functioning was low in both groups (RAND-36 Health Survey, 40±4 compared with 33±3; P=0.153), despite more severe fatigue in CFS-POTS patients (CIS fatigue subscale 51±1 compared with 43±3; P=0.016). CFS-POTS patients had greater orthostatic tachycardia than the non-CFS-POTS group (51±3 compared with 40±4 beats/min; P=0.030), greater low-frequency variability of BP (blood pressure; 6.3±0.7 compared with 4.8±1.0 mmHg2; P=0.019), greater BP recovery from early to late phase II of the Valsalva manoeuvre (18±3 compared with 11±2 mmHg; P=0.041) and a higher supine (1.5±0.2 compared with 1.0±0.3 ng/ml per·h; P=0.033) and upright (5.4±0.6 compared with 3.5±0.8 ng/ml per h; P=0.032) PRA (plasma renin activity). In conclusion, fatigue and CFS-defining symptoms are common in POTS patients. The majority of them met criteria for CFS. CFS-POTS patients have higher markers of sympathetic activation, but are part of the spectrum of POTS. Targeting this sympathetic activation should be considered in the treatment of these patients.
Oosterheert JJ, Kampschreur L,	Universitair Medisch Centrum Utrecht, afd.	Fatigue after Q fever: nothing new. [Article	Ned Tijdschr Geneeskd. 2012;156(48):A5474.	New guidelines for the diagnosis and treatment of Q-fever related fatigue syndrome have been proposed. However, we argue that Q-fever related fatigue syndrome is

Hoepelman AI.	Interne Geneeskunde en Infectieziekten, Utrecht.	in Dutch]		only just another description of a chronic fatigue syndrome in which a specific micro-organism is implicated. We feel that development of this guideline comes too soon and may be redundant, as relevant diagnosis and treatment protocols for patients with chronic fatigue, without somatic or psychiatric cause, are already available and current evidence does not support a distinct guideline for fatigue after Q fever. Rather, chronic infection with Coxiella Burnetii should be ruled out. Introducing the term 'Q-fever related fatigue syndrome' may only cause confusion, may lead to increased health-care costs, rather than improve patient management.
Op De Beéck K, Maes L, Van den Bergh K, Derua R, Waelkens E, Van Steen K, Vermeersch P, Westhovens R, De Vlam K, Verschueren P, Hooijkaas H, Blockmans D, Bossuyt X.	Catholic University of Leuven, and Experimental Laboratory of Medicine, Immunology, University Hospitals Leuven, Leuven, Belgium.	Heterogeneous nuclear RNPs as targets of autoantibodies in systemic rheumatic diseases.	Arthritis Rheum. 2012 Jan;64(1):213-21. doi: 10.1002/art.33327.	OBJECTIVE: To investigate the abundance of autoantibodies to heterogeneous nuclear RNPs (hnRNPs) in systemic rheumatic diseases. METHODS: Recombinant human hnRNPs A1, B1, C1, E1, F, Gi, H1, I, K, and P2 were prepared. Antibodies to these antigens were determined by Western blotting and by enzyme-linked immunosorbent assay (ELISA) (for hnRNPs B1, E1, F, and H1) in serum samples obtained from patients with chronic fatigue syndrome (control subjects) and from patients with various connective tissue diseases. RESULTS: Western blotting analysis in 106 control subjects and 298 patients with a connective tissue disease revealed that antibodies to all tested hnRNP antigens, except hnRNP Gi, were significantly more prevalent in patients with Sjögren's syndrome (SS) than in control subjects. The highest reactivity was observed for hnRNPs B1, E1, F, and H1 (reactivity in >45% of patients with SS and in 2.8% of control subjects). Reactivity with hnRNPs B1, E1, F, and H1 was also evaluated by ELISA in 89 control subjects and 228 patients with a connective tissue disease. Reactivity with at least 2 of the 4 tested antigens was observed in 1.1% of control subjects, 16% of patients with systemic lupus erythematosus (SLE), and 18% of patients with SS. Reactivity with at least 3 of the 4 antigens was observed in 0% of the control subjects, 3.2% of patients with SLE, and 15% of patients with SS. CONCLUSION: Several hnRNPs are target antigens in SS. The combined presence of antibodies to several hnRNPs was strongly associated with connective tissue disease in general and with SS in particular.
Op De Beéck K, Vermeersch P, Verschueren P, Westhovens R, Mariën G, Blockmans D, Bossuyt X.	Experimental Laboratory Immunology, Catholic University Leuven, Leuven, Belgium.	Antinuclear antibody detection by automated multiplex immunoassay in untreated patients at the time of diagnosis.	Autoimmun Rev. 2012 Dec;12(2):137-43. doi: 10.1016/j.autrev.2012.02.013.	Fully automated multiplex immunoassays are increasingly used as first line screening for antinuclear antibodies. The diagnostic performance of such multiplex assays in untreated patients at the time of diagnosis has not been reported. Antinuclear antibodies were measured by indirect immunofluorescence (IIF) (dilution 1:160) and by BioPlex 2200 ANA screen (antibodies to dsDNA, chromatin, ribosomal protein, SSA-52, SSA-60, SSB, Sm, SmRNP, RNP-A, RNP-68, Scl-70, Jo-1, and centromere B) in 236 patients with a systemic rheumatic disease at the time of diagnosis, 149 blood donors, 139 patients with chronic fatigue syndrome (CFS), and 134 diseased controls. BioPlex ANA screen and IIF were positive in, respectively, 79% and 90% of patients with systemic lupus erythematosus (SLE), 60% and 60% with cutaneous lupus, 72% and 93% with systemic sclerosis (SSc), 100% and 100% with mixed connective tissue disease (MCTD), 89% and 56% with primary Sjögren's (SS) syndrome, 36% and 36%

				with polymyositis/dermatomyositis, 5.4% and 6% of blood donors, 7.2% and 3.6% of patients with CFS, and 11% and 18% of diseased controls. BioPlex test result interval specific likelihood ratios increased with increasing antibody concentration. The simultaneous presence of at least three antibodies by BioPlex was found in 35% of patients with SLE, 4% with SSc, 100% with MCTD, 64% with SS, 7% with inflammatory myopathy, 0.7% of CFS and diseased controls, and none of the blood donors. In conclusion, test result specific likelihood ratios and the presence of multiple autoantibodies help with the interpretation of data generated by multiplex immunoassays.
Ormen B, Türker N, Vardar I, Kaptan F, El S, Ural S, Kaya F, Coşkun NA.	İzmir Atatürk Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İzmir, Turkey. bormen2002@yahoo.com	Attitudes and side effects related to pandemic influenza A (H1N1) vaccination in healthcare personnel. [Article in Turkish]	Mikrobiyol Bul. 2012 Jan;46(1):57-64.	The aims of this study were to evaluate the attitudes towards H1N1 vaccination and to determine the safety and side effects following 2009 pandemic influenza A (H1N1) vaccination. Pandemic influenza vaccine had been administered to the healthcare personnel in our research and training hospital in December 2009. The rate being vaccinated was established as 40% (800/2000). Four months following vaccination, the opinions about vaccination were asked to the healthcare workers, and also side effects were questioned to the vaccinated group. Two different questionnaires (for vaccinated and unvaccinated subjects) were delivered to the volunteers who agreed to participate in the study. Demographic features, reasons related to being vaccinated or not, were questioned. The vaccinated group was also questioned for the presence of chronic diseases, previous vaccinations (pandemic/seasonal influenza), local or systemic reactions that develop after vaccination. A total of 332 volunteers participated in the questionnaire. Of them 247 (74.4%) were vaccinated and 85 (25.6%) were unvaccinated. Male/female ratio of the participants was 1.2, and 55.7% of them were older than 30-year-old. Most of the participants (82.8%) were highly educated (high school and faculty-graduated). Vaccination rates were found statistically significant in advanced age group compared to young adults (p= 0.042); in male gender compared to females (p= 0.001) and in parents compared to subjects who didn't have children (p= 0.021). Vaccination rates were observed to be higher (57.5%) in non-medical staff (cleaning employers, administrative personnel, etc.) than the physicians (29.1%) and nurses (13.4%), and the rate was also high (54.7%) in personnel who worked in intensive care units, emergency department and administrative units than the personnel who worked in the clinics of internal medicine (22.3%) and surgery (23.1%) (p= 0.001). The most important causes of rejecting vaccination were being afraid of the side effects (69.4%) and not believing the effectiveness of the vaccine (56.4%). The leading causes of accepting vaccination were worries about infecting their family (60.3%) and being in a risk group (54.3%). After vaccination, local reactions (pain, swelling and redness at the vaccination site) were described in 43.3% and systemic reactions (weakness, fatigue, muscle aches, influenza-like symptoms, etc.) were described in 43.7% of the subjects. Severe side effects such as vasculitis, neuritis, encephalomyelitis, Guillian-Barre syndrome and

				anaphylactic reaction were not observed in any of the vaccinated cases. It was detected that worries about the safety of vaccine had negative impact for vaccination. Since no serious side effects were detected related to vaccination, it was concluded that the vaccine was safe. In spite of the scientific proofs, negative concerns about the safety of the vaccines can unfavorably affect the vaccination campaigns and can jeopardize efforts of influenza control. As a result, data collection systems about the safety and side effects of the vaccine all over the country and regular reports about these data may more efficiently guide vaccination programs in the future.
Pacini S, Fiore MG, Magherini S, Morucci G, Branca JJ, Gulisano M, Ruggiero M.	Department of Anatomy, Histology and Forensic Medicine, University of Firenze, Viale Morgagni 85, 50134 Firenze, Italy. stefania.pacini@unifi.it	Could cadmium be responsible for some of the neurological signs and symptoms of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Med Hypotheses. 2012 Sep;79(3):403-7. doi: 10.1016/j.mehy.2012.06.007.	According to the World Health Organization, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a neurological disease characterized by widespread inflammation and multi-systemic neuropathology. Aetiology and pathogenesis are unknown, and several agents have been proposed as causative agents or as factors perpetuating the syndrome. Exposure to heavy metals, with particular reference to mercury and gold in dental amalgams, has been considered among the triggers of ME/CFS. Here we hypothesize that cadmium, a widespread occupational and environmental heavy metal pollutant, might be associated with some of the neurological findings described in ME/CFS. In fact, ME/CFS patients show a decrease of the volume of the gray matter in turn associated with objective reduction of physical activity. Cadmium induces neuronal death in cortical neurons through a combined mechanism of apoptosis and necrosis and it could then be hypothesized that cadmium-induced neuronal cell death is responsible for some of the effects of cadmium on the central nervous system, i.e. a decrease in attention level and memory in exposed humans as well as to a diminished ability for training and learning in rats, that are symptoms typical of ME/CFS. This hypothesis can be tested by measuring cadmium exposure in a cohort of ME/CFS patients compared with matched healthy controls, and by measuring gray matter volume in un-exposed healthy controls, exposed non-ME/CFS subjects, un-exposed ME/CFS patients and exposed ME/CFS patients. In addition, we hypothesize that cadmium exposure could be associated with reduced cerebral blood flow in ME/CFS patients because of the disruptive effects of cadmium on angiogenesis. In fact, cadmium inhibits angiogenesis and low global cerebral flow is associated with abnormal brain neuroimaging results and brain dysfunction in the form of reduced cognitive testing scores in ME/CFS patients. This hypothesis can be tested by measuring cerebral cortex blood flow in un-exposed healthy controls, exposed non-ME/CFS subjects, un-exposed ME/CFS patients and exposed ME/CFS patients. If our hypothesis is demonstrated correct, the consequences could affect prevention, early diagnosis, and treatment of ME/CFS. Implications in early diagnosis could entail the evaluation of symptoms typical of ME/CFS in cadmium-exposed subjects as well as the search for signs of exposure to cadmium in subjects diagnosed with ME/CFS. Nutritional supplementation of magnesium and zinc could then be considered, since these elements have been

				proposed in the prophylaxis and therapy of cadmium exposure, and magnesium was demonstrated effective on ME/CFS patients' symptom profiles.
Paolucci S, Piralla A, Zanello C, Minoli L, Baldanti F.	Fondazione IRCCS Policlinico San Matteo, Pavia, Italy.	Xenotropic and polytropic murine leukemia virus-related sequences are not detected in the majority of patients with chronic fatigue syndrome.	New Microbiol. 2012 Jul;35(3):341-4.	XMRV and polytropic MLV-related virus have been controversially associated with chronic fatigue syndrome (CFS). Subsequent reports failed to detect XMRV and MLV-related virus in CFS patients, and the previous results have been interpreted as a massive laboratory contamination by mouse DNA sequences. Among 12 sequential CFS patients, two were positive for XMRV/MLV sequences. In contrast, 40 selected control subjects were negative. CSF patients and controls were negative for mitochondrial mouse-specific DNA sequences. These findings do not confirm the high frequency of MLV-related viruses infection in CFS patients, but also contrast the widespread laboratory contamination previously suggested.
Passeri E, Villa C, Couette M, Itti E, Brugieres P, Cesaro P, Gherardi RK, Bachoud-Levi AC, Authier FJ.	Paris Est-Creteil University & Henri-Mondor University Hospital (APHP): Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye, Creteil, F-94010, France.	Long-term follow-up of cognitive dysfunction in patients with aluminum hydroxide-induced macrophagic myofasciitis (MMF).	J Inorg Biochem. 2011 Nov;105(11):1457-63. doi: 10.1016/j.jinorgbio.2011.08.006. Epub 2011 Aug 22.	Macrophagic myofasciitis (MMF) is characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and cognitive dysfunction. Representative features of MMF-associated cognitive dysfunction (MACD) include (i) dysexecutive syndrome; (i) visual memory; (iii) left ear extinction at dichotic listening test. In present study we retrospectively evaluated the progression of MACD in 30 MMF patients. Most patients fulfilled criteria for non-amnestic/dysexecutive mild cognitive impairment, even if some cognitive deficits seemed unusually severe. MACD remained stable over time, although dysexecutive syndrome tended to worsen. Long-term follow-up of a subset of patients with 3 or 4 consecutive neuropsychological evaluations confirmed the stability of MACD with time, despite marked fluctuations.
Payne B, Hateley C, Ong E, Premchand N, Schmid M, Schwab U, Newton J, Price D.	Department of Infection and Tropical Medicine, Royal Victoria Infirmary, Newcastle-upon-Tyne, UK; Institute of Genetic Medicine, Newcastle University, Newcastle-upon-Tyne, UK.	HIV-associated fatigue in the era of highly active antiretroviral therapy: novel biological mechanisms?	HIV Med. 2012 Sep 23. doi: 10.1111/j.1468-1293.2012.01050.x.	OBJECTIVE: The aim of the study was to determine the prevalence and risk factors for HIV-associated fatigue in the era of highly active antiretroviral therapy (HAART). METHODS: A cross-sectional survey of 100 stable HIV-infected out-patients was carried out. Severity of fatigue was measured using the Fatigue Impact Scale (FIS). Symptoms of orthostatic intolerance (dysautonomia) were evaluated using the Orthostatic Grading Scale (OGS). Data for HIV-infected patients were compared with those for 166 uninfected controls and 74 patients with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (encephalopathy) (ME). RESULTS: Ninety-one per cent of HIV-infected patients were on HAART and 78% had suppressed plasma HIV viral load (≤ 40 HIV-1 RNA copies/mL). Fifty-one per cent of HIV-infected patients reported excessive symptomatic fatigue (FIS ≥ 40), and 28% reported severe fatigue symptoms (FIS ≥ 80). The mean FIS score among HIV-infected patients was 50.8 [standard deviation (SD) 41.9] compared with 13.0 (SD 17.6) in uninfected control subjects, and 92.9 (SD 29.0) in CFS patients ($P < 0.001$ for comparison of HIV-infected patients and uninfected controls). Among HIV-infected patients, fatigue severity was not significantly associated with current or nadir CD4 lymphocyte count, HIV plasma viral load, or whether on HAART. Prior dideoxynucleoside analogue (d-drug) exposure

				(P = 0.016) and the presence of clinical lipodystrophy syndrome (P = 0.011) were associated with fatigue. Additionally, fatigue severity correlated strongly with symptomatic orthostatic intolerance (r = 0.65; P < 0.001). CONCLUSIONS: Fatigue is very common and often severe in HIV-infected out-patients, despite viral suppression and good immune function. In a subgroup of patients, prior d-drug exposure may contribute to fatigue, suggesting a metabolic basis. Dysautonomia may also drive fatigue associated with HIV infection, as in other chronic diseases, and CFS/ME, and should be further evaluated with the potential for a shared therapeutic approach.
Payne C, Wiffen PJ, Martin S.	Faculty of Life and Health Sciences, University of Ulster at Jordanstown, Belfast, UK. c.payne@ulster.ac.uk	Interventions for fatigue and weight loss in adults with advanced progressive illness.	Cochrane Database Syst Rev. 2012 Jan 18;1:CD008427. doi: 10.1002/14651858.CD008427.pub2.	BACKGROUND: Fatigue and unintentional weight loss are two of the commonest symptoms experienced by people with advanced progressive illness. Appropriate interventions may bring considerable improvements in function and quality of life to seriously ill people and their families, reducing physical, psychological and spiritual distress. OBJECTIVES: To conduct an overview of the evidence available on the efficacy of interventions used in the management of fatigue and/or unintentional weight loss in adults with advanced progressive illness by reviewing the evidence contained within Cochrane reviews. METHODS: We searched the Cochrane Database of Systematic Reviews (CDSR) for all systematic reviews evaluating any interventions for the management of fatigue and/or unintentional weight loss in adults with advanced progressive illness (The Cochrane Library 2010, Issue 8). We reviewed titles of interest by abstract. Where the relevance of a review remained unclear we reached a consensus regarding the relevance of the participant group and the outcome measures to the overview. Two overview authors extracted the data independently using a data extraction form. We used the measurement tool AMSTAR (Assessment of Multiple SysTemAtic Reviews) to assess the methodological quality of each systematic review. MAIN RESULTS: We included 27 systematic reviews (302 studies with 31,833 participants) in the overview. None of the included systematic reviews reported quantitative data on the efficacy of interventions to manage fatigue or weight loss specific to people with advanced progressive illness. All of the included reviews apart from one were deemed of high methodological quality. For the remaining review we were unable to ascertain the methodological quality of the research strategy as it was described. None of the systematic reviews adequately described whether conflict of interests were present within the included studies.Management of fatigue Amyotrophic lateral sclerosis/motor neuron disease (ALS/MND) - we identified one systematic review (two studies and 52 participants); the intervention was exercise.Cancer - we identified five systematic reviews (116 studies with 17,342 participants); the pharmacological interventions were eicosapentaenoic acid (EPA) and any drug therapy for the management of cancer-related fatigue and the non pharmacological interventions were exercise, interventions by breast care nurses and psychosocial interventions.Chronic obstructive pulmonary disease (COPD) - we identified three systematic reviews (59 studies and 4048 participants); the

				interventions were self management education programmes, nutritional support and pulmonary rehabilitation.Cystic fibrosis - we identified one systematic review (nine studies and 833 participants); the intervention was physical training.Human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) - we identified two systematic reviews (21 studies and 748 participants); the interventions were progressive resistive exercise and aerobic exercise.Multiple sclerosis (MS) - we identified five systematic reviews (23 studies and 1502 participants); the pharmacological interventions were amantadine and carnitine. The non pharmacological interventions were diet, exercise and occupational therapy.Mixed conditions in advanced stages of illness - we identified one systematic review (five studies and 453 participants); the intervention was medically assisted hydration.Management of weight loss ALS/MND - we identified one systematic review but no studies met the inclusion criteria for the systematic review; the intervention was enteral tube feeding.Cancer - we identified three systematic reviews with a fourth systematic review also containing extractable data on cancer (66 studies and 5601 participants); the pharmacological interventions were megestrol acetate and eicosapentaenoic acid (EPA) (this systematic review is also included in the cancer fatigue section above). The non pharmacological interventions were enteral tube feeding and non invasive interventions for patients with lung cancer.COPD - we identified one systematic review (59 studies and 4048 participants); the intervention was nutritional support. This systematic review is also included in the COPD fatigue section.Cystic fibrosis - we identified two systematic reviews (three studies and 131 participants); the interventions were enteral tube feeding and oral calorie supplements.HIV/AIDS - we identified four systematic reviews (42 studies and 2071 participants); the pharmacological intervention was anabolic steroids. The non pharmacological interventions were nutritional interventions, progressive resistive exercise and aerobic exercise. Both of the systematic reviews on exercise interventions were also included in the HIV/AIDS fatigue section.MS - we found no systematic reviews which considered interventions to manage unintentional weight loss for people with a clinical diagnosis of multiple sclerosis at any stage of illness.Mixed conditions in advanced stages of illness - we identified two systematic reviews (32 studies and 4826 participants); the interventions were megestrol acetate and medically assisted nutrition. AUTHORS' CONCLUSIONS: There is a lack of robust evidence for interventions to manage fatigue and/or unintentional weight loss in the advanced stage of progressive illnesses such as advanced cancer, heart failure, lung failure, cystic fibrosis, multiple sclerosis, motor neuron disease, Parkinson's disease, dementia and AIDS. The evidence contained within this overview provides some insight into interventions which may prove of benefit within this population such as exercise, some pharmacological treatments and support for self management.Researchers could improve the methodological quality of future studies

				by blinding of outcome assessors. Adopting uniform reporting mechanisms for fatigue and weight loss outcome measures would also allow the opportunity for meta-analysis of small studies.Researchers could also improve the applicability of recommendations for interventions to manage fatigue and unintentional weight loss in advanced progressive illness by including subgroup analysis of this population within systematic reviews of applicable interventions.More research is required to ascertain the best interventions to manage fatigue and/or weight loss in advanced illness. There is a need for standardised reporting of these symptoms and agreement amongst researchers of the minimum duration of studies and minimum percentage change in symptom experience that proves the benefits of an intervention. There are, however, challenges in providing meaningful outcome measurements against a background of deteriorating health through disease progression. Interventions to manage these symptoms must also be mindful of the impact on quality of life and should be focused on patient-orientated rather than purely disease-orientated experiences for patients. Systematic reviews and primary intervention studies should include the impact of the interventions on standardised validated quality of life measures.
Peters S, Wearden A, Morriss R, Dowrick CF, Lovell K, Brooks J, Cahill G, Chew-Graham C; FINE Trial Group. Collaborators: Bennett C, Bentall R, Booth L, Brooks J, Cahill G, Chapman A, Chew-Graham C, Connell S, Dowrick C, Dunn G, Fleetwood D, Ibbotson L, Jerman D, Lovell K, Mann J, Morriss R, Peters S, Powell P, Quarmby D, Richardson G, Riste L, Wearden A, Williams J.	School of Psychological Sciences, University of Manchester, Manchester, UK. Sarah.peters@manchester.ac.uk	Challenges of nurse delivery of psychological interventions for long-term conditions in primary care: a qualitative exploration of the case of chronic fatigue syndrome/myalgic encephalitis.	Implement Sci. 2011 Dec 22;6:132. doi: 10.1186/1748-5908-6-132.	BACKGROUND: The evidence base for a range of psychosocial and behavioural interventions in managing and supporting patients with long-term conditions (LTCs) is now well-established. With increasing numbers of such patients being managed in primary care, and a shortage of specialists in psychology and behavioural management to deliver interventions, therapeutic interventions are increasingly being delivered by general nurses with limited training in psychological interventions. It is unknown what issues this raises for the nurses or their patients. The purpose of the study was to examine the challenges faced by non-specialist nurses when delivering psychological interventions for an LTC (chronic fatigue syndrome/myalgic encephalomyelitis [CFS/ME]) within a primary care setting. METHODS: A qualitative study nested within a randomised controlled trial [ISRCTN 74156610] explored the experiences and acceptability of two different psychological interventions (pragmatic rehabilitation and supportive listening) from the perspectives of nurses, their supervisors, and patients. Semi structured in-depth interviews were conducted with three nurse therapists, three supervisors, and 46 patients. An iterative approach was used to develop conceptual categories from the dataset. RESULTS: Analyses identified four sets of challenges that were common to both interventions: (i) being a novice therapist, (ii) engaging patients in the therapeutic model, (iii) dealing with emotions, and (iv) the complexity of primary care. Each challenge had the potential to cause tension between therapist and patient. A number of strategies were developed by participants to manage the tensions. CONCLUSIONS: Tensions existed for nurses when attempting to deliver psychological interventions for patients with CFS/ME in this primary care trial. Such tensions should be addressed before implementing

				psychological interventions within routine clinical practice. Similar tensions may be found for other LTCs. Our findings have implications for developing therapeutic alliances and highlight the need for regular supervision.
Petrov D, Marchalik D, Sosin M, Bal A.	UMDNJ/Robert Wood Johnson Medical School, New Brunswick, NJ, USA.	Factors affecting duration of chronic fatigue syndrome in pediatric patients.	Indian J Pediatr. 2012 Jan;79(1):52-5. doi: 10.1007/s12098-011-0463-4.	OBJECTIVE: To determine factors affecting duration of chronic fatigue syndrome (CFS) in pediatric patients. METHODS: This Retrospective cohort consisted of patients with CFS at the regional referral infectious disease clinic for evaluation of fatigue in children and adolescents. Demographic, clinical, and laboratory data were analyzed to identify the impact on duration and severity of pediatric CFS. RESULTS: A total number of 53 predominantly white (98.1%) patients with CFS, aged 9-18 years, were included in the study. Other than fatigue, headaches and sleep disturbance were the most common symptoms of pediatric CFS. Seropositive status for Borrelia burgdorferi (B. burgdorferi) and Epstein-Barr virus (EBV) was identified in 66% of the patients with the diagnosis of CFS by CDC criteria. No association was found between the CFS symptoms, gender, or age at diagnosis and duration of fatigue symptoms. Duration of CFS was associated with high Body-Mass Index (BMI) in a regression model after adjustment for patient's age, gender, and seropositive status for B. burgdorferi and/or EBV (0.34 ± 0.15, $P < 0.04$). CONCLUSIONS: BMI is significantly associated with prolonged duration of CFS.
Pinquart M.	Department of Psychology, Philipps University, Marburg, Germany	Self-esteem of children and adolescents with chronic illness: a meta-analysis.	Child Care Health Dev. 2012 Jun 19. doi: 10.1111/j.1365-2214.2012.01397.x.	Chronic illness may be a risk factor for low self-esteem; however, previous meta-analyses are inconclusive whether children with a chronic illness have lower self-esteem than their healthy peers. The goal of the present study was to summarize available research in order to compare the self-esteem of children and adolescents with a chronic illness with that of healthy children. Random-effects meta-analysis was used to integrate the results of 621 empirical studies that compare levels of self-esteem of children with a chronic physical illness with healthy peers or general test norms. Studies were identified via the electronic databases Adolesc, Embase, Google Scholar, MEDLINE, PSNYDEX, PSYCINFO, and cross-referencing. Children with chronic illnesses have lower self-esteem than healthy peers or test norms ($g=-0.18$ standard deviation units). The lowest levels of self-esteem were observed in children with chronic fatigue syndrome and chronic headaches. Lower levels of self-esteem in children with a chronic illness were found in girls than in boys, in adolescents than in children, in children from developing or threshold countries, when results were collected from observer ratings rather than child reports, in studies published in the 1990s, and when children with chronic illnesses were directly compared with healthy children instead of test norms. Paediatricians, parents, and teachers should promote experiences of success and positive peer-relations, which are important sources of self-esteem. In addition, psychosocial interventions for children with chronic illnesses should be offered for children with reduced self-esteem.
Poppe C, Crombez G, Hanoulle I,	Department of General Internal Medicine,	Mental quality of life in chronic fatigue is	Qual Life Res. 2012 Oct;21(8):1337-45. doi:	PURPOSE: An accommodative coping style (e.g. acceptance) is related to a better mental health-related quality of life (MHQL) in patients with chronic fatigue syndrome

Vogelaers D, Petrovic M.	Ghent University Hospital, De Pintelaan 185, 9000, Ghent, Belgium. Carine.Poppe@ugent.be	associated with an accommodative coping style and neuroticism: a path analysis.	10.1007/s11136-011-0048-8.	(CFS). We want to explore whether neuroticism is predictive for this coping style and MHQL. Secondly we want to explore the relation between acceptance and physical health-related quality of life (PHQL) and expect that illness-related variables such as fatigue severity and duration are related to PHQL. METHOD: In this cross-sectional study, 117 patients with chronic fatigue syndrome from an outpatient internal medicine clinic completed self-report questionnaires on quality of life (SF-36), acceptance (ICQ), personality traits (NEO-FFI) and fatigue severity (CIS). RESULTS: Regression analyses showed that neuroticism and acceptance are predictors of MHQL (38% of the variance was explained). The path analysis showed that acceptance mediates between neuroticism and MHQL and that PHQL is related to MHQL. PHQL is related to fatigue severity and duration, but not to neuroticism and acceptance. CONCLUSION: Stimulating an 'accepting accommodative coping style' within the treatment for CFS is important in improving mental quality of life. Our results suggest that neuroticism may be negatively related to acceptance and MHQL. This findings support the idea that a psychological diagnostic workout with special attention to personality traits in relation to their coping style is recommended in order to choose the most appropriate therapeutic approach in this population.
Pranjić N, Nuhbegović S, Brekalo-Lazarević S, Kurtić A.	Service of Occupational Health Tuzla in Tuzla Canton, Department of Occupational Pathology and Toxicology, Tuzla, Bosnia and Herzegovina. pranicnurka@hotmail.com	Is adrenal exhaustion synonym of syndrome burnout at workplace?	Coll Antropol. 2012 Sep;36(3):911-9.	The objective of this study is the assessment of the association of burnout syndrome with adrenal exhaustion specific symptoms and signs among 116 patients who were exposed to violence or mobbing at workplace and who were treated during 2005 to 2008 in Department of Occupational Pathology and Toxicology Tuzla; to detect symptoms and signs of adrenal exhaustion differences between patients who were exposed to act of violence as acute catastrophic event and patients who were long-term exposed to mobbing or chronic distress at workplace.MATERIAL AND METHODS: Data of 86 employees who were exposed to mobbing > 1 years (chronic distress syndrome) and data of 30 employees who were exposed to act of violence as acute traumatic crisis situation (evaluation in first week after acute stress situation and post control observation 6 months later). TOOLS FOR ASSESSMENT WERE CLINICAL EXAMINATION AND QUESTIONNAIRES: Occupational stress questionnaire (OSQ short version), self-constructed Questionnaire about symptoms and signs of Adrenal exhaustion; self-constructed mobbing questionnaire; and Maslach--Burnout Inventory.
Prinsen H, Bleijenberg G, Zwarts MJ, Hopman MT, Heerschap A, van Laarhoven HW.	Department of Medical Oncology, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands. h.prinsen@onco.umcn.nl	Physiological and neurophysiological determinants of postcancer fatigue: design of a randomized controlled trial.	BMC Cancer. 2012 Jun 18;12:256. doi: 10.1186/1471-2407-12-256.	BACKGROUND: Postcancer fatigue is a frequently occurring, severe, and invalidating problem, impairing quality of life. Although it is possible to effectively treat postcancer fatigue with cognitive behaviour therapy, the nature of the underlying (neuro)physiology of postcancer fatigue remains unclear. Physiological aspects of fatigue include peripheral fatigue, originating in muscle or the neuromuscular junction; central fatigue, originating in nerves, spinal cord, and brain; and physical deconditioning, resulting from a decreased cardiopulmonary function. Studies on physiological aspects of postcancer fatigue mainly concentrate on deconditioning.

				Peripheral and central fatigue and brain morphology and function have been studied for patients with fatigue in the context of chronic fatigue syndrome and neuromuscular diseases and show several characteristic differences with healthy controls. METHODS/DESIGN: Fifty seven severely fatigued and 21 non-fatigued cancer survivors will be recruited from the Radboud University Nijmegen Medical Centre. Participants should have completed treatment of a malignant, solid tumour minimal one year earlier and should have no evidence of disease recurrence. Severely fatigued patients are randomly assigned to either the intervention condition (cognitive behaviour therapy) or the waiting list condition (start cognitive behaviour therapy after 6 months). All participants are assessed at baseline and the severely fatigued patients also after 6 months follow-up (at the end of cognitive behaviour therapy or waiting list). Primary outcome measures are fatigue severity, central and peripheral fatigue, brain morphology and function, and physical condition and activity. DISCUSSION: This study will be the first randomized controlled trial that characterizes (neuro)physiological factors of fatigue in disease-free cancer survivors and evaluates to which extent these factors can be influenced by cognitive behaviour therapy. The results of this study are not only essential for a theoretical understanding of this invalidating condition, but also for providing an objective biological marker for fatigue that could support the diagnosis and follow-up of treatment. TRIAL REGISTRATION: The study is registered at http://ClinicalTrials.gov (NCT01096641).
Prinsen H, de Vries IJ, Torensma R, Pots JM, Mulder SF, van Herpen CM, Elving LD, Bleijenberg G, Stelma FF, van Laarhoven HW.	Department of Medical Oncology, Radboud University Nijmegen Medical Centre, Geert Grooteplein Zuid 8, 6525, GA, Nijmegen, the Netherlands. h.prinsen@onco.umcn.nl.	Humoral and cellular immune responses after influenza vaccination in patients with chronic fatigue syndrome.	BMC Immunol. 2012 Dec 17;13:71. doi: 10.1186/1471-2172-13-71.	ABSTRACT:BACKGROUND: Chronic fatigue syndrome (CFS) is a clinical condition characterized by severe and disabling fatigue that is medically unexplained and lasts longer than 6 months. Although it is possible to effectively treat CFS, the nature of the underlying physiology remains unclear. Various studies have sought evidence for an underlying disturbance in immunity. The aim of this study was to compare the humoral and cellular immune responses upon influenza vaccination in CFS patients and healthy controls. RESULTS: Identical antibody titers were observed in CFS patients and healthy controls. Patients and controls demonstrated similar seroprotection rates against all three virus-strains of the influenza vaccine, both pre- and post-vaccination. Functional T cell reactivity was observed in both CFS patients and healthy controls. CFS patients showed a non-significant, numerically lower cellular proliferation at baseline compared to controls. Vaccination induced a significant increase in cellular proliferation in CFS patients, but not in healthy controls. Cytokine production and the number of regulatory T cells were comparable in patients and controls. CONCLUSIONS: The humoral and cellular immune responses upon influenza vaccination were comparable in CFS patients and healthy controls. Putative aberrations in immune responses in CFS patients were not evident for immunity towards influenza. Standard seasonal influenza vaccination is thus justified and, when indicated, should be recommended for patients suffering from CFS.
Puri BK, Jakeman	Department of	Regional grey and	Br J Radiol. 2012	OBJECTIVE: It is not established whether myalgic encephalomyelitis/chronic fatigue

PM, Agour M, Gunatilake KD, Fernando KA, Gurusinghe AI, Treasaden IH, Waldman AD, Gishen P.	Imaging, Hammersmith Hospital, London, UK. basant.puri@imperial.ac.uk	white matter volumetric changes in myalgic encephalomyelitis (chronic fatigue syndrome): a voxel-based morphometry 3 T MRI study.	Jul;85(1015):e270-3. doi: 10.1259/bjr/93889091	syndrome (CFS) is associated with structural brain changes. The aim of this study was to investigate this by conducting the largest voxel-based morphometry study to date in CFS. METHODS: High-resolution structural 3 T cerebral MRI scanning was carried out in 26 patients with CFS and 26 age- and gender-matched healthy volunteers. Voxel-wise generalised linear modelling was applied to the processed MR data using permutation-based non-parametric testing, forming clusters at t>2.3 and testing clusters for significance at p<0.05, corrected for multiple comparisons across space. RESULTS: Significant voxels (p<0.05, corrected for multiple comparisons) depicting reduced grey matter volume in the CFS group were noted in the occipital lobes (right and left occipital poles; left lateral occipital cortex, superior division; and left supracalcrine cortex), the right angular gyrus and the posterior division of the left parahippocampal gyrus. Significant voxels (p<0.05, corrected for multiple comparisons) depicting reduced white matter volume in the CFS group were also noted in the left occipital lobe. CONCLUSION: These data support the hypothesis that significant neuroanatomical changes occur in CFS, and are consistent with the complaint of impaired memory that is common in this illness; they also suggest that subtle abnormalities in visual processing, and discrepancies between intended actions and consequent movements, may occur in CFS.
Qiu X, Swanson P, Tang N, Leckie GW, Devare SG, Schochetman G, Hackett J Jr.	Infectious Diseases R&D, Abbott Diagnostics, Abbott Park, Illinois 60064, USA. xiaoxing.qiu@abbott.com	Seroprevalence of xenotropic murine leukemia virus-related virus in normal and retrovirus-infected blood donors.	Transfusion. 2012 Feb;52(2):307-16. doi: 10.1111/j.1537-2995.2011.03395.x.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) has been reported in patients with prostate cancer and chronic fatigue syndrome. Although results have been conflicting, the potential of XMRV as an infectious human retrovirus has raised concerns about transfusion safety. To address this issue, normal and retrovirus-infected blood donors were screened for evidence of XMRV infection. STUDY DESIGN AND METHODS: Plasma from 1000 US, 100 human immunodeficiency virus Type 1-infected Cameroonian, and 642 human T-lymphotropic virus Type I (HTLV-I)-infected or uninfected Japanese blood donors as well as 311 sexually transmitted disease diagnostic specimens were screened for antibodies to XMRV gp70 and p15E using chemiluminescent immunoassays (CMIAs). CMIA-reactive samples were evaluated by p30 CMIA, Western blot, and real-time reverse transcriptase polymerase chain reaction. RESULTS: XMRV seroreactivity was low (0%-0.6%) with the exception of the HTLV-I-infected donors (4.9%). Antibody was detected against only a single XMRV protein (p15E or gp70); none of the seroreactive samples had detectable XMRV pol or env sequences. The elevated seroreactivity in HTLV-I-infected donors was due to an increased p15E seroreactive rate (4.1%). Inspection of XMRV and HTLV sequences revealed a high level of conservation within the immunodominant region (IDR) of the transmembrane protein. In some cases, HTLV IDR peptide competitively reduced the XMRV p15E signal. CONCLUSIONS: Based on the low prevalence of seroreactivity, detection of antibody to only a single XMRV protein and the absence of XMRV sequences, this study finds no compelling evidence of XMRV in normal or retrovirus-infected blood donors. The increased p15E seroreactivity observed in HTLV

				infection is likely due to cross-reactive antibodies.
Ragnarsson O, Berglund P, Eder DN, Johannsson G.	Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, SE-413 45 Göteborg, Sweden. oskar.ragnarsson@medic.gu.se	Long-term cognitive impairments and attentional deficits in patients with Cushing's disease and cortisol-producing adrenal adenoma in remission.	J Clin Endocrinol Metab. 2012 Sep;97(9):E1640-8. doi: 10.1210/jc.2012-1945	CONTEXT: Cognitive function is impaired in patients with active Cushing's syndrome (CS). OBJECTIVE: The aim was to study cognitive function in patients with CS in long-term remission. DESIGN: We conducted a cross-sectional, case-controlled, single center study. PATIENTS: Fifty-five patients previously treated for Cushing's disease (n = 43) and cortisol-producing adrenal adenoma (n = 12) and 55 controls matched for age, gender, and educational level participated in the study. METHODS: Working memory, attention, information-processing speed, verbal fluency, and reading speed were studied using standardized neuropsychological testing and alerting, orienting, and executive control using the Attentional Network Test. Fatigue impact scale and the comprehensive psychopathological rating scale were used to evaluate fatigue and affective disorder. RESULTS: Median (interquartile range) duration of remission was 13 (5-19) yr and the mean ± SD age at follow-up was 54 ± 14 yr. Compared to controls, patients had a higher score on the fatigue impact scale, indicating greater burdens of fatigue, and a higher score on the comprehensive psychopathological rating scale subscales for depression and anxiety. In a multivariate analysis, attention, spatial orienting, alerting, working memory, verbal fluency, and reading speed were all diminished in comparison to controls, independent of scores for affective disorder and fatigue. No overall difference in outcome was seen between patients in long-term remission for Cushing's disease and cortisol-producing adrenal adenoma. CONCLUSION: Patients with CS in remission have impaired cognitive function that cannot be explained by the coexistence of affective disorder or chronic fatigue. The pattern of cognitive and attentional deficits suggests a more global involvement of the brain function than has previously been suggested.
Reme SE, Archer N, Chalder T.	Harvard School of Public Health, Harvard University, Boston, Massachusetts, USA.	Experiences of young people who have undergone the Lightning Process to treat chronic fatigue syndrome/myalgic encephalomyelitis - a qualitative study.	Br J Health Psychol. 2012 Sep 19. doi: 10.1111/j.2044-8287.2012.02093.x	OBJECTIVES: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a serious condition characterized by debilitating but unexplained fatigue. Treatment alternatives are few, and especially so for young people. The aetiology of CFS/ME is still unclear and controversial, but rehabilitative interventions seem so far most promising. The Lightning Process is a 3-day training programme that has recently become available, but no outcome studies have yet been published. It is a non-medical training programme that combines concepts from Neuro-Linguistic Programming, Life Coaching and Osteopathy. The aim of this study was to explore the experiences of young people with CFS/ME after they had undergone the Lightning Process. DESIGN: Qualitative research study. METHODS: Semi-structured interviews were conducted with an opportunistic sample recruited through open advertisements of nine young people, aged 14-26, who had undergone the treatment, and three of their parents. Inductive thematic analysis was used to evaluate the content of the interviews. RESULTS: Mostly positive experiences were reported of the Lightning Process. Two reported dissatisfaction and no improvement, while seven were satisfied and were much improved. Particular helpful aspects were the

				theoretical rationale, practical exercises, and the technique they learned. Less helpful aspects were the intensity and short duration of the treatment with little follow-up, the secrecy surrounding it, and feelings of being blamed if the treatment did not work. CONCLUSIONS: As this is the first report of young people's experiences with the Lightning Process, it will be important to consider the helpful and unhelpful treatment components for future refinement of interventions for CFS/ME. STATEMENT OF CONTRIBUTION: What is already known on this subject? Treatment alternatives for people with CFS/ME are few, especially for young people. The Lightning Process is a popular treatment programme that has recently become available, but no studies involving the treatment have yet been published. Feelings of blame or dismissal in CFS/ME patients lead to withdrawal or disengagement from professionals. What does this study add? The Lightning Process for young people with CFS/ME encompasses many positive aspects, particularly the practical aspects of the treatment programme. The more extreme position taken by the Lightning Process in denying the limitations of the illness seem to produce divergent results in various young people; some found it liberating and therapeutic, whilst others did not respond well to it and were left feeling guilty and blamed.
Reyes Del Paso GA, Pulgar A, Duschek S, Garrido S.	Department of Psychology, University of Jaén, Jaen, Spain. greyes@ujaen.es	Cognitive impairment in fibromyalgia syndrome: the impact of cardiovascular regulation, pain, emotional disorders and medication.	Eur J Pain. 2012 Mar;16(3):421-9. doi: 10.1002/j.1532-2149.2011.00032.x	This study investigated cognitive performance in fibromyalgia syndrome (FMS) and its association with cardiovascular and clinical parameters. Thirty-five patients with FMS and 29 matched healthy controls completed a neuropsychological test measuring attention and arithmetic processing. As possible factors underlying the expected cognitive impairment, clinical pain intensity, co-morbid depression and anxiety disorders, sleep complaints, medication use, as well as blood pressure parameters were investigated. The patients' test performance was substantially reduced, particularly in terms of lower speed of cognitive processing and restricted improvement of performance in the course of the task. While the extent of depression, anxiety, fatigue and sleep complaints was unrelated to test performance, better performance was observed in patients showing lower pain ratings and those using opiate medication. The data corroborate the presence of substantial cognitive impairment in FMS. While the experience of chronic pain is crucial in mediating the deficits, co-morbid depression, anxiety, fatigue and sleep complaints play only a subordinate role. In the control group, but not in the patients, blood pressure was inversely associated with mental performance. This finding is in line with the well known cognitive impairment in hypertension. The lack of this association in FMS confirms previous research showing aberrances in the interaction between blood pressure and central nervous function in the affected patients.
Rico-Villademoros F, Rodriguez-Lopez CM, Morillas-Arques P, Vilchez	Instituto de Neurociencias, Universidad de Granada, Avda de	Amisulpride in the treatment of fibromyalgia: an uncontrolled study.	Clin Rheumatol. 2012 Sep;31(9):1371-5. doi: 10.1007/s10067-012-2012-6.	Some antipsychotics, including amisulpride, have shown to be effective in the treatment of various painful conditions, lessening pain as well as symptoms of anxiety and/or depression. In this open-label, 12-week study, we explored the efficacy and tolerability of amisulpride in patients with fibromyalgia. We recruited 40 patients, 1

JS, Hidalgo J, Calandre EP.	Madrid 11, 18012 Granada, Spain. fernando.ricovillademoros@gmail.com			male and 39 females, aged 46.2 ± 6.8 years, who met the ACR criteria for fibromyalgia and had a score equal to or greater than 4 in the pain severity item of the Fibromyalgia Impact Questionnaire (FIQ). Amisulpride was added to their current treatment regimen at an initial dose of 25 mg/day and titrated according to the clinical response and tolerability (mean final dose, 87.5 ± 41.3 mg/day). In the intent-to-treat analysis (i.e., all recruited patients), using a baseline-observation-carried-forward approach, the mean score in the FIQ decreased from 75.7 ± 10.6 to 73.2 ± 15.4, but this change was not statistically significant. Pain severity, as measured with the visual analogue scale from the FIQ, remained unchanged. Nonsignificant improvements were observed in depressive or anxiety symptoms using the Beck Depression Inventory and the State-Trait Anxiety Inventory, respectively. Twenty-six patients either withdrew from the study, mainly due to adverse reactions, or were lost to follow-up (n = 11, 27.5 %, for each category). Despite its promising results in some chronic painful conditions and in a related illness, such as chronic fatigue syndrome, amisulpride does not seem to provide any benefit to patients with fibromyalgia. Amisulpride was poorly tolerated by our participants.
Robinson MJ, Erlwein O, McClure MO.	Section of Infectious Diseases, Jefferiss Research Trust Laboratories, Imperial College London, St Mary's Campus, London, W2 1PG, UK.	Xenotropic murine leukaemia virus-related virus (XMRV) does not cause chronic fatigue.	Trends Microbiol. 2011 Nov;19(11):525-9. doi: 10.1016/j.tim.2011.08.005.	The xenotropic murine leukaemia virus-related virus (XMRV), a gammaretrovirus, was discovered in prostate cancer tumours by Virochip technology in 2006. It was subsequently detected in chronic fatigue patients in 2009. The association between XMRV and chronic fatigue has proved to be controversial. No study has confirmed these findings and many have refuted them. Here, we present the evidence for our contention that XMRV is not a human pathogen.
Roehr B	[No address quoted]	Researchers find no link between XMRV and chronic fatigue syndrome.	BMJ. 2012 Sep 26;345:e6331. doi: 10.1136/bmj.e6337.	[No abstract given]
Roehr B.	[No address quoted]	Researchers find no link between XMRV and chronic fatigue syndrome.	BMJ. 2012 Sep 19;345:e6331. doi: 10.1136/bmj.e6331.	[No abstract given]
Rosenblum H, Shoenfeld Y, Amital H.	Department of Medicine B, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Tel-Hashomer 52621, Israel.	The common immunogenic etiology of chronic fatigue syndrome: from infections to vaccines via adjuvants to the ASIA syndrome.	Infect Dis Clin North Am. 2011 Dec;25(4):851-63. doi: 10.1016/j.idc.2011.07.012.	Chronic fatigue syndrome (CFS) is characterized by unexplained fatigue that lasts for at least 6 months with a constellation of other symptoms. Most cases start suddenly, and are usually accompanied by a flu-like illness. It is a symptom-based diagnosis of exclusion, the pathogenesis of which is unknown. Studies have examined and hypothesized about the possible biomedical and epidemiologic characteristics of the disease, including genetic predisposition, infections, endocrine abnormalities, and immune dysfunction and psychological and psychosocial factors. Recently, the AISA (autoimmune/inflammatory syndrome induced by adjuvants) syndrome was recognized, indicating the possible contribution of adjuvants and vaccines to the

				development of autoimmunity.
Roth T.	[No address quoted]	Investigating nonrestorative sleep.	Sleep Med. 2012 Jun;13(6):557-8. doi: 10.1016/j.sleep.2012.03.004.	Comment on Sleep Med. 2012 Jun;13(6):561-9.
Rovigatti U.	Department of Oncology, Transplantation and New Biomedical Technologies, University of Pisa Medical School, Pisa, Italy. Electronic address: profrovigatti@gmail.com.	Chronic Fatigue Syndrome (CFS) and Cancer Related Fatigue (CRF): two "fatigue" syndromes with overlapping symptoms and possibly related aetiologies.	Neuromuscul Disord. 2012 Dec;22 Suppl 3:S235-41. doi: 10.1016/j.nmd.2012.10.018.	In July 2010, at the Muscle Fatigue Meeting, I presented an overview of Chronic Fatigue Syndrome and Cancer Related Fatigue, emphasizing a critical interpretation of the potential association between Chronic Fatigue Syndrome and Cancer Related Fatigue and a newly discovered retrovirus: Xenotropic Murine Related Virus. Since this association was hotly debated at that time, I suggested at the Meeting that it was wrong and most likely due to the identification of the wrong virus culprit. Today, 20months after the Meeting, the first part of our prediction has turned out to be correct, as Xenotropic Murine Related Virus was shown to be a laboratory-created artefact. Still, the potential association of fatigue-syndromes with an infection (most likely viral) is sustained by a plethora of evidence and this overview will initially summarize data suggesting prior viral infection(s). The principal hypothesized mechanisms for both peripheral and central Chronic Fatigue Syndrome/Cancer Related Fatigue will be then summarized, also indicating plausible associations and triggering factors. All evidence accrued so far suggests that further research work should be performed in this interesting area and in order to identify an infectious agent for Chronic Fatigue Syndrome/Cancer Related Fatigue. One candidate RNA virus, Micro-Foci inducing Virus, will be described in this overview.
Sáez-Francàs N, Alegre J, Calvo N, Antonio Ramos-Quiroga J, Ruiz E, Hernández-Vara J, Casas M.	Psychiatry and Legal Medicine Department, Hospital Universitari Vall d'Hebron, Institut de Recerca (VHIR), Universitat Autònoma de Barcelona, CIBERSAM, Barcelona, Spain. Electronic address: nasaez2@gmail.com.	Attention-deficit hyperactivity disorder in chronic fatigue syndrome patients.	Psychiatry Res. 2012 Dec 30;200(2-3):748-53. doi: 10.1016/j.psychres.2012.04.041.	Psychopathological disorders are frequent in chronic fatigue syndrome patients. The present study examines the presence of attention-deficit hyperactivity disorder (ADHD) in a sample of adult chronic fatigue syndrome (CFS) patients, and evaluates its clinical consequences in this population. CFS patients were assessed for childhood and adult ADHD by clinical interview and ADHD-specific scales. Psychopathological comorbidities were evaluated by clinical examination and questionnaires. Forty-seven of 158 CSF patients (29.7%) were diagnosed of childhood ADHD and in 33 (20.9%), the condition persisted into adulthood. CFS patients with adult ADHD had an earlier CSF onset, more severe anxiety and depression symptoms, and a higher risk of suicide than CFS patients without ADHD. Using lineal regression analysis, we found that depressive symptoms and ADHD
Sakudo A, Kuratsune H, Kato YH, Ikuta K.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University, Yamadaoka, Suita, Osaka 565-0871,	Visible and near-infrared spectra collected from the thumbs of patients with chronic fatigue syndrome for diagnosis.	Clin Chim Acta. 2012 Oct 9;413(19-20):1629-32. doi: 10.1016/j.cca.2012.05.004.	BACKGROUND: Currently, diagnosis of chronic fatigue syndrome (CFS) is based on clinical symptoms and therefore relies on the experience and skill of the doctors. Here, we have examined the possible diagnosis of CFS based on spectral information and chemometrics analysis, such as principal component analysis (PCA) and soft modeling of class analogy (SIMCA). METHODS: Visible and near-infrared (Vis-NIR) spectroscopy was used to examine possible changes in the region of 600-1100 nm in thumbs and assessed. RESULTS: The Vis-NIR spectra of thumbs from 57 CFS patients and 74 healthy volunteers were subjected to PCA and SIMCA to develop multivariate

	Japan. sakudo@biken.osaka-u.ac.jp			models to discriminate between CFS patients and healthy individuals. The model was further assessed by the prediction of 120 determinations (60 in the healthy group and 60 in the CFS patient group). The PCA model predicted a discrimination of the masked samples; specifically the SIMCA model correctly predicted 51 of 60 (83.3%) healthy volunteers and 42 of 60 (70%) CFS patients. CONCLUSIONS: Despite the relatively small number of subjects involved in this trial, who were exclusively Japanese, our results imply that Vis-NIR spectroscopy of the thumb combined with chemometrics analysis may provide a valuable tool for diagnosing CFS.
Sakuma T, Tonne JM, Malcolm JA, Thatava T, Ohmine S, Peng KW, Ikeda Y	Department of Molecular Medicine, Mayo Clinic, Rochester, Minnesota, United States of America.	Long-term infection and vertical transmission of a gammaretrovirus in a foreign host species.	PLoS One. 2012;7(1):e29682. doi: 10.1371/journal.pone.0029682.	Increasing evidence has indicated natural transspecies transmission of gammaretroviruses; however, viral-host interactions after initial xeno-exposure remain poorly understood. Potential association of xenotropic murine leukemia virus-related virus (XMRV) in patients with prostate cancer and chronic fatigue syndrome has attracted broad interests in this topic. Although recent studies have indicated that XMRV is unlikely a human pathogen, further understanding of XMRV xenoinfection would allow in vivo modeling of the initial steps of gammaretroviral interspecies transmission, evolution and dissemination in a new host population. In this study, we monitored the long-term consequences of XMRV infection and its possible vertical transmission in a permissive foreign host, wild-derived Mus pahari mice. One year post-infection, XMRV-infected mice showed no notable pathological changes, while proviral DNA was detected in three out of eight mice. XMRV-infected mice remained seropositive throughout the study although the levels of gp70 Env- and p30 capsid-specific antibodies gradually decreased. When vertical XMRV transmission was assessed, no viremia, humoral immune responses nor endogenization were observed in nine offspring from infected mothers, yet one offspring was found PCR-positive for XMRV-specific sequences. Amplified viral sequences from the offspring showed several mutations, including one amino acid deletion in the receptor binding domain of Env SU. Our results therefore demonstrate long-term asymptomatic infection, low incidence of vertical transmission and limited evolution of XMRV upon transspecies infection of a permissive new host, Mus pahari.
Sato E, Yoshikawa R, Miyazawa T.	Laboratory of Signal Transduction, Department of Cell Biology, Institute for Virus Research, Kyoto University, 53 Shogoin-Kawaharacho, Sakyo-ku, Kyoto 606–8507, Japan.	Comparison of two quantitative assays for xenotropic murine leukemia virus-related virus.	J Vet Med Sci. 2012 Feb;74(2):255-8.	Xenotropic murine leukemia virus-related virus (XMRV), a novel gammaretrovirus in humans, was found in patients with prostate cancer (PC) and chronic fatigue syndrome (CFS). However, there has been controversy whether XMRV is directly associated with human diseases. In this study, we developed a LacZ marker rescue assay using human embryonic kidney 293T cells and a focus assay using a feline fibroblastic sarcoma-positive leukemia-negative QN10S cells. XMRV induced prominent foci in QN10S cells and the viral titer determined by the focus assay was as high as that by the LacZ marker rescue assay. Because the focus assay is simple and sensitive, it will be useful for monitoring infectious XMRVs in CFS and PC patients and virological studies for XMRV.
Schreurs KM,	University of Twente,	Cognitive	Behav Res Ther. 2011	Cognitive behavioural therapy (CBT) was combined with graded exercise therapy

Veehof MM, Passade L, Vollenbroek-Hutten MM.	Enschede, The Netherlands. k.m.g.schreurs@utwente.nl	behavioural treatment for chronic fatigue syndrome in a rehabilitation setting: effectiveness and predictors of outcome.	Dec;49(12):908-13. doi: 10.1016/j.brat.2011.09.004.	(GET) for patients with chronic fatigue syndrome (CFS) in an uncontrolled implementation study of an inpatient multidisciplinary group therapy. During the intake procedure, 160 CFS patients completed a questionnaire on fatigue related measurements, physical impairment, depression, somatic and psychological attributions, somatic focus, and sense of control over symptoms. Pre-treatment physical activity level was measured with an actometer. At baseline, post-treatment and 6-month follow-up individual strength, subjective fatigue and physical impairment, were reassessed. Large effect sizes were found on subjective fatigue (1.2 post-treatment; 1.2 follow-up) and physical impairment (-.9 post-treatment; -.9 follow-up), Clinically significant improvement was found in 33.8% of the participants at post-treatment and 30.6% at follow-up. Individual strength at post-treatment was predicted by level of physical activity before treatment, and by sense of control over symptoms and physical activity at follow-up. Clinically significant improvement in subjective fatigue was predicted by not receiving a disablement insurance benefit, shorter duration of fatigue, higher sense of control over symptoms and, at follow-up by more pre-treatment physical activity. In conclusion, the intervention was effective for CFS patients. Cognitive behavioural factors that perpetuate fatigue symptoms are also predictors of treatment outcome.
Schrier M, Amital D, Arnson Y, Rubinow A, Altaman A, Nissenabaum B, Amital H.	Department of Medicine 'B', Sheba Medical Center, 52621 Tel-Hashomer, Ramat-Gan, Israel.	Association of fibromyalgia characteristics in patients with non-metastatic breast cancer and the protective role of resilience.	Rheumatol Int. 2012 Oct;32(10):3017-23.	Cancer patients often complain about weakness, fatigue, and pain. The aim of this study was to assess the features of the fibromyalgia syndrome (FMS) characteristics in patients with non-metastatic breast cancer. The study group included 40 women whose age ranged from 40 to 70 years with Stages 0-3 breast cancer. The control group included 40 healthy women matched by age. A diagnosis of FMS was established based on medical history, physical examination, and the Fibromyalgia Impact Questionnaire (FIQ). Pain measures and functional factors were evaluated by the Brief Pain Inventory and the Sheehan Questionnaire. Resilience was assessed by Antanovsky's Sense of Coherence Questionnaire. Psychiatric disturbances were tested by the MINI Questionnaire and Hamilton questionnaires for depression and anxiety. The prevalence of chronic pain was higher in the study group. Statistically significant differences were also found between the group regarding pain, fatigue, and functional measures. The prevalence of depressive or anxious mood, measured by the Hamilton questionnaires, was strongly related to FMS characteristics reflected by FIQ scores (r = 0.79 between FIQ and the Hamilton Depression Index and r = 0.75 between FIQ and the Hamilton Anxiety Scale). The sense of coherence measure for these patients demonstrated an inverse correlation with pain, fatigue, and functional capability. Women with breast cancer tend to develop chronic widespread pain syndromes more often than do healthy women.
Selmi C, Mix E, Zettl UK.	Division of Rheumatology, Allergy, and Clinical	A clear look at the neuroimmunology of multiple sclerosis	Autoimmun Rev. 2012 Jan;11(3):159-62. doi: 10.1016/j.autrev.2011.05.006.	The term neuroimmunology was first coined to refer to a generic involvement of the immune system in the pathogenesis of neurological diseases, particularly of the central nervous system. Since then, the neuroimmunology spectrum has steadily

	Immunology, University of California, Davis, United States.	and beyond.		grown and currently spans from classical autoimmune diseases of the central and peripheral nervous systems to previously unsuspected conditions such as autism spectrum disorders or chronic fatigue syndrome. Multiple sclerosis remains the predominant entity in terms of research efforts and social pressure as well as a good model of organ-specific autoimmune disease with limited therapeutic options. While the fast-pace genome-wide association studies reported a number of genes to be significantly associated with multiple sclerosis, these currently explain only a minor part of disease susceptibility. Further, clinicians are continuously challenged with the clinical classifications of immune-mediated or autoimmune central and peripheral conditions and with other pragmatic questions such as the roles of vaccination and physical therapy. For these reasons the present collection of Autoimmunity Reviews is timely as it will address these major issues related to neuroimmunology.
Senel K, Baygutalp F, Baykal T, Erdal A, Ugur M.	Department of Physical Medicine and Rehabilitation, Atatürk University Medical Faculty, Erzurum, Turkey, kazimsenel@gmail.com .	Melatonin levels in premenopausal women with fibromyalgia syndrome.	Rheumatol Int. 2011 Dec 23.	The fibromyalgia syndrome (FMS) is a chronic, widespread pain disorder of unknown etiology. It has been suggest that familial component, environmental factors, endocrine and neurotransmitter alterations, and psychological factors may contribute to the development of FMS. The role of melatonin in FMS is unclear. Some studies describe a lower nocturnal peak and a decreased secretion of melatonin in women with FMS when compared with healthy matched controls. The aim of the present study was to determine the possible role of melatonin in FMS patients. We examined the characteristics and levels of melatonin in 25 consecutive premenopausal women with FMS. Serum blood samples were collected from 25 patients and 20 the age and gender matched healthy controls. Melatonin levels were measured by enzyme-linked immunosorbent assay. Then, the results were compared with those from healthy subjects. Serum melatonin levels of FMS patients were not statistically different from those of controls ($P > 0.05$). No association was observed between melatonin levels of patients with FMS and disease duration, sleep disturbances, fatigue, and pain scores. Our results demonstrate that melatonin levels were similar in patients with FMS and healthy controls. Further studies are needed to determine the possible role of melatonin.
Seshadri N, Sonoda LI, Lever AM, Balan K.	Department of Nuclear Medicine, Addenbrookes Hospital, Cambridge CB2 0QQ, United Kingdom. s_n_bhushan@yahoo.com	Superiority of 18F-FDG PET compared to 111In-labelled leucocyte scintigraphy in the evaluation of fever of unknown origin.	J Infect. 2012 Jul;65(1):71-9. doi: 10.1016/j.jinf.2012.02.008.	AIM: To compare the accuracy of positron emission tomography (PET) using (18)F-FDG (Fluorodeoxyglucose) PET with (111)In-labelled leucocytes scintigraphy (LS) in patients with fever of unknown origin (FUO). METHODS: Twenty-three consecutive patients with FUO were prospectively studied using whole-body LS and PET. Performance of the two modalities for identifying a cause of FUO was evaluated. Final diagnosis was based on biopsy, microbiological tests, clinical and imaging follow-up. RESULTS: Abnormal tracer uptake was seen in 3/23(13%) and 14/23(61%) patients on LS and PET respectively, suggesting a higher sensitivity ($p < 0.01$) for the latter. All LS positive cases were identified on PET and confirmed as infection. The causes of FUO in the other PET positive patients were: infection (n = 3), vasculitis (n = 3), non-infectious inflammatory conditions (n = 2) and cancer (n = 1). No specific

				diagnosis was reached in 2 patients. Of 13 patients without a definite diagnosis following PET and LS, 10 made a spontaneous recovery during the follow-up period and no definite cause for FUO was found on investigation. Still's disease, Polymyalgia rheumatica and Chronic fatigue syndrome/Myalgic encephalomyelitis were diagnosed in the remaining three patients during follow-up. The results thus showed an overall sensitivity of 86% for PET and 20% for LS ($p < 0.01$). The overall specificity for FDG PET was 78% as against 100% for LS. PET had a PPV of 86% and a NPV of 78% whereas LS had a PPV of 100% and a NPV of 40%. CONCLUSION: PET has a higher sensitivity than LS in identifying the aetiology of FUO. PET/PET-CT, where available, should be used as the non-invasive investigation of choice in the assessment of patients with FUO.
Shin SR, Han AL.	Department of Family Medicine, Wonkwang University College of Medicine, Iksan, Korea.	Improved chronic fatigue symptoms after removal of mercury in patient with increased mercury concentration in hair toxic mineral assay: a case.	Korean J Fam Med. 2012 Sep;33(5):320-5. doi: 10.4082/kjfm.2012.33.5.320	Clinical manifestations of chronic exposure to organic mercury usually have a gradual onset. As the primary target is the nervous system, chronic mercury exposure can cause symptoms such as fatigue, weakness, headache, and poor recall and concentration. In severe cases chronic exposure leads to intellectual deterioration and neurologic abnormality. Recent outbreaks of bovine spongiform encephalopathy and pathogenic avian influenza have increased fish consumption in Korea. Methyl-mercury, a type of organic mercury, is present in higher than normal ranges in the general Korean population. When we examine a patient with chronic fatigue, we assess his/her methyl-mercury concentrations in the body if environmental exposure such as excessive fish consumption is suspected. In the current case, we learned the patient had consumed many slices of raw tuna and was initially diagnosed with chronic fatigue syndrome. Therefore, we suspected that he was exposured to methyl-mercury and that the mercury concentration in his hair would be below the poisoning level identified by World Health Organization but above the normal range according to hair toxic mineral assay. Our patient's toxic chronic fatigue symptoms improved after he was given mercury removal therapy, indicating that he was correctly diagnosed with chronic exposure to organic mercury.
Shungu DC, Weiduschat N, Murrough JW, Mao X, Pillemer S, Dyke JP, Medow MS, Natelson BH, Stewart JM, Mathew SJ.	Department of Radiology, Weill Medical College of Cornell University, New York, NY 10021, USA. dcs7001@med.cornell.edu	Increased ventricular lactate in chronic fatigue syndrome. III. Relationships to cortical glutathione and clinical symptoms implicate oxidative stress in disorder pathophysiology.	NMR Biomed. 2012 Sep;25(9):1073-87. doi: 10.1002/nbm.2772.	Chronic fatigue syndrome (CFS) is a complex illness, which is often misdiagnosed as a psychiatric illness. In two previous reports, using (1)H MRSI, we found significantly higher levels of ventricular cerebrospinal fluid (CSF) lactate in patients with CFS relative to those with generalized anxiety disorder and healthy volunteers (HV), but not relative to those with major depressive disorder (MDD). In this third independent cross-sectional neuroimaging study, we investigated a pathophysiological model which postulated that elevations of CSF lactate in patients with CFS might be caused by increased oxidative stress, cerebral hypoperfusion and/or secondary mitochondrial dysfunction. Fifteen patients with CFS, 15 with MDD and 13 HVs were studied using the following modalities: (i) (1)H MRSI to measure CSF lactate; (ii) single-voxel (1)H MRS to measure levels of cortical glutathione (GSH) as a marker of antioxidant capacity; (iii) arterial spin labeling (ASL) MRI to measure regional cerebral blood flow (rCBF); and (iv) (31)P MRSI to measure brain high-energy phosphates as objective

				indices of mitochondrial dysfunction. We found elevated ventricular lactate and decreased GSH in patients with CFS and MDD relative to HVs. GSH did not differ significantly between the two patient groups. In addition, we found lower rCBF in the left anterior cingulate cortex and the right lingual gyrus in patients with CFS relative to HVs, but rCBF did not differ between those with CFS and MDD. We found no differences between the three groups in terms of any high-energy phosphate metabolites. In exploratory correlation analyses, we found that levels of ventricular lactate and cortical GSH were inversely correlated, and significantly associated with several key indices of physical health and disability. Collectively, the results of this third independent study support a pathophysiological model of CFS in which increased oxidative stress may play a key role in CFS etiopathophysiology.
Simmons G, Glynn SA, Komaroff AL, Mikovits JA, Tobler LH, Hackett J Jr, Tang N, Switzer WM, Heneine W, Hewlett IK, Zhao J, Lo SC, Alter HJ, Linnen JM, Gao K, Coffin JM, Kearney MF, Ruscetti FW, Pfost MA, Bethel J, Kleinman S, Holmberg JA, Busch MP; Blood XMRV Scientific Research Working Group (SRWG). Collaborators: Glynn S, Holmberg JA, Bianco C, Busch MP, Dodd RY, Katz LM, Kleinman SH, Komaroff AL, Mikovits JA, Simmons G, Stramer SL, Tobler LH, Vernon SD, Alter H, Coffin J,	Blood Systems Research Institute and University of California, San Francisco, San Francisco, CA 94118, USA.	Failure to confirm XMRV/MLVs in the blood of patients with chronic fatigue syndrome: a multi-laboratory study.	Science. 2011 Nov 11;334(6057):814-7. doi: 10.1126/science.1213841.	Murine leukemia viruses (MLVs), including xenotropic-MLV-related virus (XMRV), have been controversially linked to chronic fatigue syndrome (CFS). To explore this issue in greater depth, we compiled coded replicate samples of blood from 15 subjects previously reported to be XMRV/MLV-positive (14 with CFS) and from 15 healthy donors previously determined to be negative for the viruses. These samples were distributed in a blinded fashion to nine laboratories, which performed assays designed to detect XMRV/MLV nucleic acid, virus replication, and antibody. Only two laboratories reported evidence of XMRV/MLVs; however, replicate sample results showed disagreement, and reactivity was similar among CFS subjects and negative controls. These results indicate that current assays do not reproducibly detect XMRV/MLV in blood samples and that blood donor screening is not warranted.

Mangan DF, Ruscetti F, Kuehnert MJ, Hendry RM, Heneine W, Monroe SS, Switzer WM, Epstein J, Hewlett IK, Lo SC.				
Singh PK, Chopra K, Kuhad A, Kaur IP.	University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Study, Panjab University, Chandigarh 160014, India.	Role of Lactobacillus acidophilus loaded floating beads in chronic fatigue syndrome: behavioral and biochemical evidences.	Neurogastroenterol Motil. 2012 Apr;24(4):366-e170. doi: 10.1111/j.1365-2982.2011.01861.x. Epub 2012 Feb 1.	BACKGROUND: In recent years the interface between neuropsychiatry and gastroenterology has converged in to a new discipline referred to as enteric neuroscience. Implications of brain-gut communication in the pathogenesis of psychiatric disorders indicate a possible role of suitably packaged/delivered probiotics as newer therapeutic options. In the present study probable role of per-oral administration of free Lactobacillus acidophilus (LAB) and LAB loaded alginate beads in attenuation of the symptoms associated with chronic fatigue syndrome (CFS) were evaluated. METHODS: Chronic fatigue syndrome following physical fatigue was induced in rats by forcing them to swim (forced swim test; FST) in water till exhaustion, after weighing them down with 10% their body weight, daily for 28 days. Immobility (I) and postswim fatigue time (PSF) were taken as suitable markers. Free LAB and LAB loaded floating beads (FBs) were administered, from 21 to 28 days. KEY RESULTS: Immobility and PSF were found to increase considerably in FST rats (665 ± 22 s and 196 ± 6 s) as compared with the naïve (32 ± 7 s and 22 ± 2 s) at 20 days, establishing severe fatigue like behavior. FST control group exhibited significant ($P < 0.05$) hypertrophy of spleen, hypotrophy of thymus, and increased oxido-nitrosative stress in brain and tumor necrosis factor-α (TNF-α) levels in serum. Treatment with LAB and LAB FBs significantly decreased I and PSF and attenuated ($P < 0.05$) oxido-nitrosative stress and TNF-α levels. Spleen and thymus were also restored to their original size in this group. CONCLUSIONS & INFERENCES: The findings suggest a valuable therapeutic role of LAB especially when incorporated into alginate beads for the treatment of CFS.
Skelly JR, Edge D, Shortt CM, Jones JF, Bradford A, O'Halloran KD.	UCD School of Medicine and Medical Science, University College Dublin, Belfield, Dublin 4, Ireland. richskelly@yahoo.com	Respiratory control and sternohyoid muscle structure and function in aged male rats: decreased susceptibility to chronic intermittent hypoxia.	Respir Physiol Neurobiol. 2012 Mar 15;180(2-3):175-82. doi: 10.1016/j.resp.2011.11.004.	Obstructive sleep apnoea syndrome (OSAS) is a common respiratory disorder characterized by chronic intermittent hypoxia (CIH). We have shown that CIH causes upper airway muscle dysfunction in the rat due to oxidative stress. Ageing is an independent risk factor for the development of OSAS perhaps due to respiratory muscle remodelling and increased susceptibility to hypoxia. We sought to examine the effects of CIH on breathing and pharyngeal dilator muscle structure and function in aged rats. Aged (18-20 months), male Wistar rats were exposed to alternating cycles of normoxia and hypoxia (90 s each; F(I)O(2)=5% O(2) at nadir) or sham treatment for 8h/day for 9 days. Following CIH exposure, breathing was assessed by

				whole-body plethysmography. In addition, sternohyoid muscle contractile and endurance properties were examined in vitro. Muscle fibre type and cross-sectional area, and the activity of key oxidative and glycolytic enzymes were determined. CIH had no effect on basal breathing or ventilatory responses to hypoxia or hypercapnia. CIH did not alter succinate dehydrogenase or glycerol phosphate dehydrogenase enzyme activities, myosin heavy chain fibre areal density or cross-sectional area. Sternohyoid muscle force and endurance were unaffected by CIH exposure. Since we have established that this CIH paradigm causes sternohyoid muscle weakness in adult male rats, we conclude that aged rats have decreased susceptibility to CIH-induced stress. We suggest that structural remodelling with improved hypoxic tolerance in upper airway muscles may partly compensate for impaired neural regulation of the upper airway and increased propensity for airway collapse in aged mammals.
Smith C, Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, Weston Education Centre, , London, UK.	Unity of opposites? Chronic fatigue syndrome and the challenge of divergent perspectives in guideline development.	J Neurol Neurosurg Psychiatry. 2012 Nov 17.	Guideline development by its nature is a process and method of integration and synthesis of information, be it originating from research, evidence-based medicine, clinical findings, patient experience and/or individual narratives of an illness or disease. In the majority of cases, it can be assumed that this information and these ideas are travelling in the same direction; however, it is possible that the objective and subjective cannot be synthesised, and appear mutually contradictory. In this commentary, an example of where this might be the case has been analysed: a report published by the Scottish Public Health Network, a Health Care Needs Assessment of Services for people living with myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS). It appears from reflection and analysis of this document that this process may indeed have gone awry. We propose that, if followed, this document would lead to the adoption of dangerous diagnostic criteria for ME/CFS, as well as preventing patients from making informed decisions about treatment options, and discouraging clinicians from following evidence-based medicine and recommending proven treatments for ME/CFS, because of potential implications for future commissioning. This commentary seeks to highlight some of the problems, contradictions and unintended consequences of a divergence between patient perspectives and evidence-based medicine despite probably sharing the same aim, that of improving patient care and striving for better understanding and better treatments for disease.
Smith HS, Elliott JA.	Albany Medical College, Albany, NY, USA.	Opioid-induced androgen deficiency (OPIAD).	Pain Physician. 2012 Jul;15(3 Suppl):ES145-56.	Opioid therapy is one of the most effective forms of analgesia currently in use. In the past few decades, the use of opioids as a long-term treatment for chronic pain has increased dramatically. Accompanying this upsurge in the use of long-term opioid therapy has been an increase in the occurrence of opioid associated endocrinopathy, most commonly manifested as an androgen deficiency and therefore referred to as opioid associated androgen deficiency (OPIAD). This syndrome is characterized by the presence of inappropriately low levels of gonadotropins (follicle stimulating hormone and luteinizing hormone) leading to inadequate production of sex hormones,

				particularly testosterone. Symptoms that may manifest in patients with OPIAD include reduced libido, erectile dysfunction, fatigue, hot flashes, and depression. Physical findings may include reduced facial and body hair, anemia, decreased muscle mass, weight gain, and osteopenia or osteoporosis. Additionally, both men and women with OPIAD may suffer from infertility. While the literature regarding OPIAD remains limited, it is apparent that OPIAD is becoming increasingly prevalent among chronic opioid consumers but often goes unrecognized. OPIAD can have a significant negative impact on the the quality of life of opioid users, and clinicians should anticipate the potential for its occurrence whenever long-term opioid prescribing is undertaken. Once diagnosed, treatment for OPIAD may be offered utilizing a number of androgen replacement therapy options including a variety of testosterone preparations and, for female patients with OPIAD, dehydroepiandrosterone (DHEA) supplementation. Follow-up evaluation of patients receiving androgen replacement therapy should include a review of any unresolved symptoms of hypogonadism, laboratory evaluation, and surveillance for potential adverse effects of androgen replacement therapy including prostate disease in males.:
Son CG.	Liver and Research Center, Daejon Oriental Hospital of Daejon University, Republic of Korea. ckson@dju.ac.kr	Safety of 4-week indirect-moxibustion therapy at CV4 and CV8.	J Acupunct Meridian Stud. 2011 Dec;4(4):262-5. doi: 10.1016/j.jams.2011.09.018.	PURPOSE: Moxibustion therapy is a commonly used treatment in Oriental medicine. Here, we provide evidence for the safety of long-term moxibustion therapy. SUBJECTS: and design: Forty-five subjects (10 men and 35 women) who complained of chronic fatigue were divided into control (5 men and 15 women) and experimental groups (5 men and 20 women) in a randomized double-blind setting. The experimental group was treated with moxibustion to CV4 and CV8 for 4 weeks (administered three times per week); the control group was exposed to simulated burning of moxibustion. Complete blood counts, blood chemistry, and urinalysis results were analyzed before and after each trial. RESULTS: The absolute and relative number of peripheral blood cells did not differ between the pre- and posttreatment measurements of either group. No significant changes in blood chemistry or urinalysis data were observed in either group. CONCLUSIONS: These results suggest that indirect moxibustion has no effect on blood chemistry or urine and is safe for clinical use. These data could be used as reference data for further moxibustion studies.
Spindler J, Hackett J Jr, Qiu X, Wiegand A, Boltz VF, Swanson P, Bream JH, Jacobson LP, Li X, Rinaldo CR, Wolinsky SM, Coffin JM, Kearney MF, Mellors JW.	HIV Drug Resistance Program, National Cancer Institute, Frederick, MD 21702-1201, USA.	Prevalence of XMRV nucleic acid and antibody in HIV-1-Infected men and in men at risk for HIV-1 Infection.	Adv Virol. 2011;2011:268214. doi: 10.1155/2011/268214.	Xenotropic MLV-Related Virus (XMRV) was recently reported to be associated with prostate cancer and chronic fatigue syndrome (CFS). Infection was also reported in 3.7% of healthy individuals. These highly reported frequencies of infection prompted concerns about the possibility of a new, widespread retroviral epidemic. The Multicenter AIDS Cohort Study (MACS) provides an opportunity to assess the prevalence of XMRV infection and its association with HIV-1 infection among men who have sex with men. Reliable detection of XMRV infection requires the application of multiple diagnostic methods, including detection of human antibodies to XMRV and detection of XMRV nucleic acid. We, therefore, tested 332 patient plasma and PBMC samples obtained from recent visits in a subset of patients in the MACS cohort

				for XMRV antibodies using Abbott prototype ARCHITECT chemiluminescent immunoassays (CMIAs) and for XMRV RNA and proviral DNA using a XMRV single-copy qPCR assay (X-SCA). Although 9 of 332 (2.7%) samples showed low positive reactivity against a single antigen in the CMIA, none of these samples or matched controls were positive for plasma XMRV RNA or PBMC XMRV DNA by X-SCA. Thus, we found no evidence of XMRV infection among men in the MACS regardless of HIV-1 serostatus.
St Clair K, Maguire JD.	Center Portsmouth, Portsmouth, VA, USA.	Role of fluconazole in a case of rapid onset ritonavir and inhaled fluticasone-associated secondary adrenal insufficiency.	Int J STD AIDS. 2012 May;23(5):371-2. doi: 10.1258/ijsa.2009.009339.	A 52-year-old man with well-controlled HIV infection taking ritonavir and increasing doses of inhaled fluticasone for chronic bronchitis developed thrush. Within days of discontinuing fluticasone and initiating fluconazole, he presented with fatigue, malaise, lower-extremity oedema and orthostasis. Testing confirmed exogenous Cushing's syndrome and secondary adrenal insufficiency. Although ritonavir-fluticasone interactions have been previously reported as a cause for adrenal insufficiency, we propose that fluconazole increased the rapidity of onset and severity of symptoms through synergistic inhibition of the adrenal axis.
Staud R.	Division of Rheumatology and Clinical Immunology, University of Florida, PO Box 100221, Gainesville, FL 32610-0221, USA. staudr@ufl.edu	Peripheral and central mechanisms of fatigue in inflammatory and noninflammatory rheumatic diseases.	Curr Rheumatol Rep. 2012 Dec;14(6):539-48. doi: 10.1007/s11926-012-0277-z.	Fatigue is a common symptom in a large number of medical and psychological disorders, including many rheumatologic illnesses. A frequent question for health care providers is related to whether reported fatigue is "in the mind" or "in the body"-that is, central or peripheral. If fatigue occurs at rest without any exertion, this suggests psychological or central origins. If patients relate their fatigue mostly to physical activities, including exercise, their symptoms can be considered peripheral. However, most syndromes of fatigue seem to depend on both peripheral and central mechanisms. Sometimes, muscle biopsy with histochemistry may be necessary for the appropriate tissue diagnosis, whereas serological tests generally provide little reliable information about the origin of muscle fatigue. Muscle function and peripheral fatigue can be quantified by contractile force and action potential measurements, whereas validated questionnaires are frequently used for assessment of mental fatigue. Fatigue is a hallmark of many rheumatologic conditions, including fibromyalgia, myalgic encephalitis/chronic fatigue syndrome, rheumatoid arthritis, systemic lupus, Sjogren's syndrome, and ankylosing spondylitis. Whereas many studies have focused on disease activity as a correlate to these patients' fatigue, it has become apparent that other factors, including negative affect and pain, are some of the most powerful predictors for fatigue. Conversely, sleep problems, including insomnia, seem to be less important for fatigue. There are several effective treatment strategies available for fatigued patients with rheumatologic disorders, including pharmacological and nonpharmacological therapies.
Staud R.	Division of Rheumatology and Clinical Immunology, University of Florida,	Abnormal endogenous pain modulation is a shared characteristic	Expert Rev Neurother. 2012 May;12(5):577-85. doi: 10.1586/ern.12.41.	The intensity of acute and chronic pain depends on interactions between peripheral impulse input and CNS pain mechanisms, including facilitation and inhibition. Whereas tonic pain inhibition is a characteristic of most pain-free individuals, pain facilitation can be detected in many chronic pain patients. The capability to inhibit

	PO Box 100221, Gainesville, FL 32610-0221, USA. staudr@ufl.edu.	of many chronic pain conditions.		pain is normally distributed along a wide continuum in the general population and can be used to predict chronic pain. Accumulating evidence suggests that endogenous pain inhibition depends on activation of the prefrontal cortex, periaqueductal gray and rostral ventral medulla. Quantitative sensory test paradigms have been designed to acquire detailed information regarding each individual's endogenous pain inhibition and facilitation. Such tests include: temporal summation of pain, which is mostly used to assess facilitatory pain modulation by measuring the change in pain perception during a series of identical nociceptive stimuli; and conditioned pain modulation, which tests pain inhibition by utilizing two simultaneously applied painful stimuli (the 'pain inhibits pain' paradigm). Considerable indirect evidence seems to indicate that not only increased pain facilitation but also ineffective pain inhibition represents a predisposition for chronic pain. This view is supported by the fact that many chronic pain syndromes (e.g., fibromyalgia, temporomandibular joint disorder, irritable bowel syndrome, headache and chronic fatigue syndrome) are associated with hypersensitivity to painful stimuli and reduced endogenous pain inhibition. However, future prospective studies will be necessary to provide definitive evidence for this relationship. Such research would not only provide important information about mechanisms relevant to chronic pain but would also permit identification of individuals at high risk for future chronic pain.
Steffen I, Tyrrell DL, Stein E, Montalvo L, Lee TH, Zhou Y, Lu K, Switzer WM, Tang S, Jia H, Hockman D, Santer DM, Logan M, Landi A, Law J, Houghton M, Simmons G.	Blood Systems Research Institute, San Francisco, California, United States of America.	No evidence for XMRV nucleic acids, infectious virus or anti-XMRV antibodies in Canadian patients with chronic fatigue syndrome.	PLoS One. 2011;6(11):e27870. doi: 10.1371/journal.pone.0027870.	The gammaretroviruses xenotropic murine leukemia virus (MLV)-related virus (XMRV) and MLV have been reported to be more prevalent in plasma and peripheral blood mononuclear cells of chronic fatigue syndrome (CFS) patients than in healthy controls. Here, we report the complex analysis of whole blood and plasma samples from 58 CFS patients and 57 controls from Canada for the presence of XMRV/MLV nucleic acids, infectious virus, and XMRV/MLV-specific antibodies. Multiple techniques were employed, including nested and qRT-PCR, cell culture, and immunoblotting. We found no evidence of XMRV or MLV in humans and conclude that CFS is not associated with these gammaretroviruses.
Stewart JM, Medow MS, Messer ZR, Baugham IL, Terilli C, Ocon AJ.	Departments of Physiology, New York Medical College, Valhalla, New York. USA. julian_stewart@nymc.edu	Postural neurocognitive and neuronal activated cerebral blood flow deficits in young chronic fatigue syndrome patients with postural tachycardia syndrome.	Am J Physiol Heart Circ Physiol. 2012 Mar 1;302(5):H1185-94. doi: 10.1152/ajpheart.00994.2011.	Neurocognition is impaired in chronic fatigue syndrome (CFS). We propose that the impairment relates to postural cerebral hemodynamics. Twenty-five CFS subjects and twenty control subjects underwent incremental upright tilt at 0, 15, 30, 45, 60, and 75° with continuous measurement of arterial blood pressure and cerebral blood flow velocity (CBFV). We used an n-back task with n ranging from 0 to 4 (increased n = increased task difficulty) to test working memory and information processing. We measured n-back outcomes by the number of correct answers and by reaction time. We measured CBFV, critical closing pressure (CCP), and CBFV altered by neuronal activity (activated CBFV) during each n value and every tilt angle using transcranial Doppler ultrasound. N-back outcome in control subjects decreased with n valve but was independent of tilt angle. N-back outcome in CFS subjects decreased with n value

				but deteriorated as orthostasis progressed. Absolute mean CBFV was slightly less than in control subjects in CFS subject at each angle. Activated CBFV in control subjects was independent of tilt angle and increased with n value. In contrast, activated CBFV averaged 0 in CFS subjects, decreased with angle, and was less than in control subjects. CCP was increased in CFS subjects, suggesting increased vasomotor tone and decreased metabolic control of CBFV. CCP did not change with orthostasis in CFS subjects but decreased monotonically in control subjects, consistent with vasodilation as compensation for the orthostatic reduction of cerebral perfusion pressure. Increasing orthostatic stress impairs neurocognition in CFS subjects. CBFV activation, normally tightly linked to cognitive neuronal activity, is unrelated to cognitive performance in CFS subjects; the increased CCP and vasomotor tone may indicate an uncoupling of the neurovascular unit during orthostasis.
Strauss B, Löschau M, Seidel T, Stallmach A, Thomas A.	Jena University Hospital, Friedrich-Schiller University, Institute of Psychosocial Medicine and Psychotherapy, Germany. Bernhard.strauss@med.uni-jena.de	Are fatigue symptoms and chronic fatigue syndrome following Q fever infection related to psychosocial variables?	J Psychosom Res. 2012 Apr;72(4):300-4. doi: 10.1016/j.jpsychores.2012.01.010.	OBJECTIVE: Fatigue is known as one of the most common long-term sequelae of Q fever infections. The study aimed to determine the prevalence of fatigue symptoms, chronic fatigue, and chronic fatigue syndrome (CFS) in a sample of patients who were exposed to Q fever (Coxiella burnetii) infection compared to controls, and to contrast Q fever patients with and without fatigue symptoms related to somatoform symptoms, hypochondriacal worries and beliefs, psychosocial complaints, and social support. METHODS: Cross-sectional study of 84 Q fever exposed patients from a specific region in Jena (Germany) and 85 matched controls using standardized questionnaires (MFI, SF-12, CDC-SI, SOMS, Whiteley Index, OQ-45 and F-Sozu). Diagnostic interviews were performed to validate questionnaire results in a smaller subsample. RESULTS: Patients who were exposed to a Q fever infection in the past indicated more fatigue symptoms and chronic fatigue than controls (54.8 vs. 20%, 32.1 vs. 4.7%) but did not show more criteria for a CFS (1 patient in each group). Q fever patients showing fatigue symptoms revealed significantly higher scores in the SOMS, the Whiteley-Index, and higher psychosocial complaints measured with the OQ-45. Their health related Quality of Life was reduced, no differences were found related to perceived social support. CONCLUSION: Although in our sample fatigue symptoms were common among Q fever patients, we found no increased prevalence of CFS in contrast to several other studies. The combination of fatigue symptoms with other psychosocial symptoms/problems support the view of a biopsychosocial etiology of fatigue symptoms.
Strayer DR, Carter WA, Stouch BC, Stevens SR, Bateman L, Cimoch PJ, Lapp CW, Peterson DL; Chronic Fatigue	Hemispherx Biopharma, Inc., Philadelphia, Pennsylvania, United States of America. david.strayer@hemispherx.net	A double-blind, placebo-controlled, randomized, clinical trial of the TLR-3 agonist rintatolimod in severe cases of chronic fatigue	PLoS One. 2012;7(3):e31334. doi: 10.1371/journal.pone.0031334.	BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a severely debilitating disease of unknown pathogenesis consisting of a variety of symptoms including severe fatigue. The objective of the study was to examine the efficacy and safety of a TLR-3 agonist, rintatolimod (Poly I: C(12)U), in patients with debilitating CFS/ME. METHODS AND FINDINGS: A Phase III prospective, double-blind, randomized, placebo-controlled trial comparing twice weekly IV rintatolimod versus placebo was conducted in 234 subjects with long-standing, debilitating CFS/ME at 12

Syndrome AMP-516 Study Group, Mitchell WM.		syndrome.		sites. The primary endpoint was the intra-patient change from baseline at Week 40 in exercise tolerance (ET). Secondary endpoints included concomitant drug usage, the Karnofsky Performance Score (KPS), Activities of Daily Living (ADL), and Vitality Score (SF 36). Subjects receiving rintatolimod for 40 weeks improved intra-patient placebo-adjusted ET 21.3% (p = 0.047) from baseline in an intention-to-treat analysis. Correction for subjects with reduced dosing compliance increased placebo-adjusted ET improvement to 28% (p = 0.022). The improvement observed represents approximately twice the minimum considered medically significant by regulatory agencies. The rintatolimod cohort vs. placebo also reduced dependence on drugs commonly used by patients in an attempt to alleviate the symptoms of CFS/ME (p = 0.048). Placebo subjects crossed-over to receive rintatolimod demonstrated an intra-patient improvement in ET performance at 24 weeks of 39% (p = 0.04). Rintatolimod at 400 mg twice weekly was generally well-tolerated. CONCLUSIONS/SIGNIFICANCE: Rintatolimod produced objective improvement in ET and a reduction in CFS/ME related concomitant medication usage as well as other secondary outcomes. TRIAL REGISTRATION: ClinicalTrials.gov NCT00215800.
Sulheim D, Hurum H, Helland IB, Thaulow E, Wyller VB.	Department of Paediatric Medicine, Oslo University Hospital, Rikshospitalet, Oslo, Norway. dag.sulheim@medisin.uio.no.	Adolescent chronic fatigue syndrome; a follow-up study displays concurrent improvement of circulatory abnormalities and clinical symptoms.	Biopsychosoc Med. 2012 Mar 21;6:10. doi: 10.1186/1751-0759-6-10.	BACKGROUND: The pathophysiology of chronic fatigue syndrome (CFS) in adolescents is unknown, and the clinical course and prognosis is still questioned. Recent research indicates that abnormalities of autonomic cardiovascular control may play an important role. The aim of this research project was to perform a follow-up study of adolescents with chronic fatigue syndrome, focusing on clinical symptoms and autonomic cardiovascular control. METHODS: 47 adolescents (12-18 years old) with CFS were recruited from the outpatient clinic at the Department of Pediatrics, Oslo University Hospital. In a primary visit and a follow-up visit (3-17 months later), we evaluated: a) a wide range of complaints and symptoms and b) cardiovascular variables at baseline and during a 20° head-up tilt-test (HUT). RESULTS: At the second visit, patients reported significant improvement regarding functional impairments, fatigue severity, muscular pain, concentration problems, post-exertional malaise and the problem of non-relieving rest. Also, at the second visit, baseline heart rate (HR), blood pressure, total peripheral resistance index (TPRI) and LF/HF (low-frequency:high-frequency heart rate variability ratio, an index of sinus node sympathovagal balance derived from spectral analyses of heart rate) were significant lower, and the increases in HR, mean blood pressure (MBP), diastolic blood pressure (DBP) and TPRI during tilt were significantly less pronounced as compared to the first visit. There was a significant correlation between changes in autonomic symptom score, fatigue severity score and functional impairment score from the first to the second visit. CONCLUSIONS: The majority of adolescents with CFS experienced an improvement over time in functional impairment, self-reported fatigue and additional symptoms, and a concurrent improvement of autonomic cardiovascular control. A possible connection between clinical symptoms and abnormal autonomic control in

				CFS might represent a focus for further research.
Suma S, Veerendra Kumar B.	Department of Oral and Maxillofacial Pathology, DA Pandu Memorial RV Dental College and Hospital, No. CA 37, 24th Main, JP Nagar I Phase, Bangalore, Karnataka, India.	Temporomandibular disorders and functional somatic syndromes: Deliberations for the dentist.	Indian J Dent Res. 2012 Jul;23(4):529-36. doi: 10.4103/0970-9290.104965	Temporomandibular disorder (TMD) is an umbrella term for a collection of disorders affecting the temporomandibular joint (TMJ) and associated tissues. TMD is not a rare pathology for the dentist. The most common presenting symptom is pain, which causes the patient seek immediate treatment. Management is dictated by the cause. The most 'famed' causes include trauma, inflammation, aging, parafunctional habits, infections, neoplasms, and stress; and these are always considered in the differential diagnosis of TMJ pain. There are some less 'famed' causes of TMD, which are characterized by increased pain sensitivity due to psychosocial factors; these include myofascial pain syndrome and functional somatic syndromes (FSS) such as fibromyalgia and chronic fatigue syndrome. They present with chronic pain, fatigue, disability, and impairment in ability to perform daily activities. A non-systematic search in the English literature revealed numerous studies describing the occurrence of TMD in these conditions, along with few other oral manifestations. TMD has been even considered to be a part of the FSS by some. In these patients, TMD remains a recurring problem, and adequate management cannot be achieved by traditional treatment protocols. Awareness of these conditions, with correct diagnosis and modification of management protocols accordingly, may resolve this problem.
Surapaneni DK, Adapa SR, Preeti K, Teja GR, Veeraragavan M, Krishnamurthy S.	Neurotherapeutics Lab, Department of Pharmaceutics, Indian Institute of Technology (Banaras Hindu University), Varanasi 221005 U.P., India.	Shilajit attenuates behavioral symptoms of chronic fatigue syndrome by modulating the hypothalamic-pituitary-adrenal axis and mitochondrial bioenergetics in rats.	J Ethnopharmacol. 2012 Aug 30;143(1):91-9. doi: 10.1016/j.jep.2012.06.002.	ETHNOPHARMACOLOGICAL RELEVANCE: Shilajit has been used as a rejuvenator for ages in Indian ancient traditional medicine and has been validated for a number of pharmacological activities. AIM OF THE STUDY: The effect of processed shilajit which was standardized to dibenzo-α-pyrones (DBPs;0.43% w/w), DBP-chromoproteins (DCPs; 20.45% w/w) and fulvic acids (56.75% w/w) was evaluated in a rat model of chronic fatigue syndrome (CFS). The mitochondrial bioenergetics and the activity of hypothalamus-pituitary-adrenal (HPA) axis were evaluated for the plausible mechanism of action of shilajit. MATERIALS AND METHODS: CFS was induced by forcing the rats to swim for 15mins for 21 consecutive days. The rats were treated with shilajit (25, 50 and 100mg/kg) for 21 days before exposure to stress procedure. The behavioral consequence of CFS was measured in terms of immobility and the climbing period. The post-CFS anxiety level was assessed by elevated plus maze (EPM) test. Plasma corticosterone and adrenal gland weight were estimated as indices of HPA axis activity. Analysis of mitochondrial complex chain enzymes (Complex I, II, IV and V) and mitochondrial membrane potential (MMP) in prefrontal cortex (PFC) were performed to evaluate the mitochondrial bioenergetics and integrity respectively. RESULTS: Shilajit reversed the CFS-induced increase in immobility period and decrease in climbing behavior as well as attenuated anxiety in the EPM test. Shilajit reversed CFS-induced decrease in plasma corticosterone level and loss of adrenal gland weight indicating modulation of HPA axis. Shilajit prevented CFS-induced mitochondrial dysfunction by stabilizing the complex enzyme activities and the loss of MMP. Shilajit reversed CFS-induced mitochondrial oxidative stress in terms of NO concentration

				and, LPO, SOD and catalase activities. CONCLUSION: The results indicate that shilajit mitigates the effects of CFS in this model possibly through the modulation of HPA axis and preservation of mitochondrial function and integrity. The reversal of CFS-induced behavioral symptoms and mitochondrial bioenergetics by shilajit indicates mitochondria as a potential target for treatment of CFS.
Suskind AM, Berry SH, Suttorp MJ, Elliott MN, Hays RD, Ewing BA, Clemens JQ	Department of Urology, University of Michigan Health System, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI, 48109, USA.	Health-related quality of life in patients with interstitial cystitis/bladder pain syndrome and frequently associated comorbidities.	Qual Life Res. 2012 Oct 7.	PURPOSE: To estimate the association of chronic non-urologic conditions [i.e., fibromyalgia (FM), chronic fatigue syndrome (CFS), and irritable bowel syndrome (IBS)] with health-related quality of life (HRQOL) in patients with interstitial cystitis/bladder pain syndrome (IC/BPS). METHODS: A total of 276 women with established diagnoses of IC/BPS completed a telephone interview which included demographics, self-reported medical conditions, the SF-36 health survey, and the interstitial cystitis symptom index (ICSI). Multivariate linear regression analysis was used to identify correlates of SF-36 physical and mental component summary scores. RESULTS: Mean patient age was 45.1 (SD 15.9) years, and 83 % of the subjects were white. Mean values for the SF-36 Physical Component Score (PCS) and Mental Component Score (MCS) means were 39 (SD 14) and 45 (SD 12), respectively, indicating significant HRQOL reductions. Mean ICSI score was 11.27 (SD = 4.86). FM and IBS were significantly associated with worse SF-36 scores: -8 points on the PCS ($p < 0.001$) and -6 points on the MCS ($p < 0.001$). CFS and the presence of other pelvic conditions (overactive bladder, vulvodynia, endometriosis) were not significantly associated with SF-36 PCS and MCS scores. CONCLUSIONS: In patients with IC/BPS, the presence of FM, CFS, and IBS has a significant association with HRQOL, equivalent in impact to the bladder symptoms themselves. These results emphasize the importance of a multidisciplinary approach to treating patients with IC/BPS and other conditions.
Switzer WM, Zheng H, Simmons G, Zhou Y, Tang S, Shankar A, Kapusinszky B, Delwart EL, Heneine W.	Laboratory Branch, Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. bswitzer@cdc.gov	No evidence of murine leukemia virus-related viruses in live attenuated human vaccines.	PLoS One. 2011;6(12):e29223. doi: 10.1371/journal.pone.0029223.	BACKGROUND: The association of xenotropic murine leukemia virus (MLV)-related virus (XMRV) in prostate cancer and chronic fatigue syndrome reported in previous studies remains controversial as these results have been questioned by recent data. Nonetheless, concerns have been raised regarding contamination of human vaccines as a possible source of introduction of XMRV and MLV into human populations. To address this possibility, we tested eight live attenuated human vaccines using generic PCR for XMRV and MLV sequences. Viral metagenomics using deep sequencing was also done to identify the possibility of other adventitious agents. RESULTS: All eight live attenuated vaccines, including Japanese encephalitis virus (JEV) (SA-14-14-2), varicella (Varivax), measles, mumps, and rubella (MMR-II), measles (Attenuvax), rubella (Meruvax-II), rotavirus (Rotateq and Rotarix), and yellow fever virus were negative for XMRV and highly related MLV sequences. However, residual hamster DNA, but not RNA, containing novel endogenous gammaretrovirus sequences was detected in the JEV vaccine using PCR. Metagenomics analysis did not detect any adventitious viral sequences of public health concern. Intracisternal A particle

				sequences closest to those present in Syrian hamsters and not mice were also detected in the JEV SA-14-14-2 vaccine. Combined, these results are consistent with the production of the JEV vaccine in Syrian hamster cells. CONCLUSIONS: We found no evidence of XMRV and MLV in eight live attenuated human vaccines further supporting the safety of these vaccines. Our findings suggest that vaccines are an unlikely source of XMRV and MLV exposure in humans and are consistent with the mounting evidence on the absence of these viruses in humans.
Szu-Ting Fu T, Koutstaal W, Poon L, Cleare AJ.	Institute of Biomedical Sciences, Academia Sinica, 6F, No. 16, Alley 10, Lane 437, Pa-The Rd Sec 2, Taipei 10552, Taiwan. tiffanyfu0821@gmail.com	Confidence judgment in depression and dysphoria: the depressive realism vs. negativity hypotheses.	J Behav Ther Exp Psychiatry. 2012 Jun;43(2):699-704. doi: 10.1016/j.jbtep.2011.09.014.	BACKGROUND AND OBJECTIVES: According to the negativity hypothesis, depressed individuals are over-pessimistic due to negative self-concepts. In contrast, depressive realism suggests that depressed persons are realistic compared to their nondepressed controls. However, evidence supporting depressive realism predominantly comes from judgment comparisons between controls and nonclinical dysphoric samples when the controls showed overconfident bias. This study aimed to test the validity of the two accounts in clinical depression and dysphoria. METHODS: Sixty-eight participants, including healthy controls (n = 32), patients with DSM-IV major depression (n = 20), and dysphoric participants with CDC-defined chronic fatigue syndrome (n = 16) performed an adjective recognition task and reported their item-by-item confidence judgments and post-test performance estimate (PTPE). RESULTS: Compared to realistic PTPE made by the controls, patients with major depression showed significant underconfidence. The PTPE of the dysphoric participants was relatively accurate. Both the depressed and dysphoric participants displayed less item-by-item overconfidence as opposed to significant item-by-item overconfidence shown by the controls. LIMITATIONS: The judgment-accuracy patterns of the three groups need to be replicated with larger samples using non-memory task domains. CONCLUSION: The present study confirms depressive realism in dysphoric individuals. However, toward a more severe depressive emotional state, the findings did not support depressive realism but are in line with the prediction of the negativity hypothesis. It is not possible to determine the validity of the two hypotheses when the controls are overconfident. Dissociation between item-by-item and retrospective confidence judgments is discussed.
Takada S, Shimizu T, Hadano Y, Matsumoto K, Kataoka Y, Arima Y, Inoue T, Sorano S.	Department of General Medicine, Osaka City General Hospital, Miyakojima-ku, Osaka, Japan.	Cryoglobulinemia (review).	Mol Med Report. 2012 Jul;6(1):3-8. doi: 10.3892/mmr.2012.861.	Cryoglobulins are immunoglobulins that precipitate at low temperatures and redissolve upon rewarming. Cryoglobulinemia refers to the presence of circulating cryoglobulins in serum, and generally leads to a systemic inflammatory syndrome characterized by fatigue, arthralgia, purpura, neuropathy and glomerulonephritis. The disease mainly involves small to medium-sized blood vessels and causes vasculitis due to cryoglobulin-containing immune complexes. Cryoglobulinemia is classified into three types (I, II and III) on the basis of immunoglobulin composition. Predisposing conditions include lymphoproliferative disease, collagen disease and hepatitis C virus (HCV) infection. The diagnosis of cryoglobulinemic syndrome is predominantly based on the laboratory demonstration of serum cryoglobulins. Treatment is often directed

				towards the underlying disease state. For patients with chronic HCV infection, anti-viral therapy is indicated. Intense immunosuppressive or immunomodulatory therapy, including steroids, plasmapheresis and cytotoxic agents, is reserved for organ-threatening or recalcitrant disease. In this review, we discuss the clinical characteristics of the three types of cryoglobulinemia.
Tanaka Y.	Health Research Institute, National Institute of Advanced Industrial Science and Technology (AIST).	Biomarkers of stress and fatigue. [Article in Japanese]	Nihon Rinsho. 2012 May;70(5):880-6.	A questionnaire based survey has been commonly used for the assessment of psychological stress and stress-related diseases. Development of a quantitative approach using a non-invasive sample (i.e., saliva, hair or nails) is highly desirable to measure chronic stress. This paper gives a brief explanation of subjective and objective (i.e., physiological signals, and biological markers) methods for stress assessment. Furthermore, it focuses particularly on the current knowledge about the biomarker candidates of chronic psychological stress and chronic fatigue syndrome (CFS). Psychological stress is known to stimulate the autonomic nervous, endocrine, and immune systems. Since chronic stress is associated with suppression of a variety of immune parameters, some immune markers are potentially useful.
Tang N, Frank A, Leckie G, Hackett J Jr, Simmons G, Busch M, Abravaya K.	Abbott Molecular Inc., Des Plaines, IL 60018, USA. ning.tang@abbott.com	Development of sensitive single-round pol or env RT-PCR assays to screen for XMRV in multiple sample types.	J Virol Methods. 2012 Jan;179(1):127-34. doi: 10.1016/j.jviromet.2011.10.010.	The potential association between xenotropic murine leukemia virus-related virus (XMRV) and prostate cancer and chronic fatigue syndrome (CFS) has been much debated. To help resolve the potential role of XMRV in human disease, it is critical to develop sensitive and accurate reverse transcriptase (RT)-PCR assays to screen for the virus. Single-round RT-PCR assays were developed on the automated m2000™ system for detection of the pol or env regions of XMRV in whole blood, plasma, urine cell pellets and urogenital swab samples. Assay performance was assessed by testing two blinded panels, one comprised of whole blood and the other of plasma spiked with serial dilutions of XMRV-infected tissue culture cells and supernatant, respectively, prepared by the Blood XMRV Scientific Research Working Group (SRWG). For both whole blood and plasma panel testing, the assays showed excellent specificity and sensitivity as compared to the other tests included in the SRWG phase I study. Analytical specificity of the assays was also evaluated. Neither pol nor env PCR assays detected a panel of potential cross-reactive microorganisms, although some cross-reaction was observed with mouse genomic DNA. Screening of 196 normal human blood donor plasma, 214 HIV-1 seropositive plasma, 20 formalin-fixed paraffin-embedded (FFPE) prostate cancer specimens, 4 FFPE benign prostate specimens, 400 urine pellets from prostate cancer patients, 166 urine pellets from non-prostate cancer patients, and 135 cervical swab specimens, detected no samples as unequivocally XMRV positive.
Tang S, Zhao J, Haleyur Giri Setty MK, Devadas K, Gaddam D, Viswanath R,	Lab of Molecular Virology, Center for Biologics Evaluation and Research, Food and Drug	Absence of detectable XMRV and other MLV-related viruses in healthy blood donors	PLoS One. 2011;6(11):e27391. doi: 10.1371/journal.pone.0027391.	BACKGROUND: Preliminary studies in chronic fatigue syndrome (CFS) patients and XMRV infected animals demonstrated plasma viremia and infection of blood cells with XMRV, indicating the potential risk for transfusion transmission. XMRV and MLV-related virus gene sequences have also been detected in 4-6% of healthy individuals including blood donors in the U.S. These results imply that millions of persons in the

Wood O, Zhang P, Hewlett IK.	Administration, Bethesda, Maryland, United States of America. tangshixing@hotmail.com	in the United States.		U.S. may be carrying the nucleic acid sequences of XMRV and/or MLV-related viruses, which is a serious public health and blood safety concern. METHODOLOGY/PRINCIPAL FINDINGS: To gain evidence of XMRV or MLV-related virus infection in the U.S. blood donors, 110 plasma samples and 71 PBMC samples from blood donors at the NIH blood bank were screened for XMRV and MLV-related virus infection. We employed highly sensitive assays, including nested PCR and real-time PCR, as well as co-culture of plasma with highly sensitive indicator DERSE cells. Using these assays, none of the samples were positive for XMRV or MLV-related virus. CONCLUSIONS/SIGNIFICANCE: Our results are consistent with those from several other studies, and demonstrate the absence of XMRV or MLV-related viruses in the U.S. blood donors that we studied.
Tian H, Lin JM, Reeves WC.	Chronic Viral Diseases Branch, Division of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. ejq7@cdc.gov	Utilization of two web-based continuing education courses evaluated by Markov chain model.	J Am Med Inform Assoc. 2012 May-Jun;19(3):489-94. doi: 10.1136/amiajnl-2011-000287.	OBJECTIVES: To evaluate the web structure of two web-based continuing education courses, identify problems and assess the effects of web site modifications. DESIGN: Markov chain models were built from 2008 web usage data to evaluate the courses' web structure and navigation patterns. The web site was then modified to resolve identified design issues and the improvement in user activity over the subsequent 12 months was quantitatively evaluated. MEASUREMENTS: Web navigation paths were collected between 2008 and 2010. The probability of navigating from one web page to another was analyzed. RESULTS: The continuing education courses' sequential structure design was clearly reflected in the resulting actual web usage models, and none of the skip transitions provided was heavily used. The web navigation patterns of the two different continuing education courses were similar. Two possible design flaws were identified and fixed in only one of the two courses. Over the following 12 months, the drop-out rate in the modified course significantly decreased from 41% to 35%, but remained unchanged in the unmodified course. The web improvement effects were further verified via a second-order Markov chain model. CONCLUSIONS: The results imply that differences in web content have less impact than web structure design on how learners navigate through continuing education courses. Evaluation of user navigation can help identify web design flaws and guide modifications. This study showed that Markov chain models provide a valuable tool to evaluate web-based education courses. Both the results and techniques in this study would be very useful for public health education and research specialists.
Tjensvoll AB, Harboe E, Gøransson LG, Beyer MK, Greve OJ, Kvaløy JT, Omdal R.	Department of Neurology, Stavanger University Hospital, Stavanger, Norway.	Headache in primary Sjøgren's syndrome: a population-based retrospective cohort study.	Eur J Neurol. 2012 Nov 28. doi: 10.1111/ene.12033	BACKGROUND: We investigated whether the prevalence of primary headaches was higher in patients with primary Sjøgren's syndrome (PSS) than in healthy individuals. METHODS: This retrospective cohort study included 71 patients with PSS (patients) based on the American European Consensus Classification criteria, and 71 age- and gender-matched healthy subjects (controls). Headaches were classified according to the International Classification of Headache Disorders. We measured depression with the Beck Depression Inventory, and fatigue with the Fatigue Severity Scale. RESULTS: Fifty-one patients and 42 controls had headaches in the previous 12 months (71.8% vs. 59.2%, P = 0.10). Thirty-eight patients and 28 controls had tension type headaches

				(TTHs) (53.5% vs. 39.4%, P = 0.12). Eight patients (11.3%) and one control had chronic TTHs (P = 0.05). Migraines and migraines with aura were equally prevalent in patients (26.8% and 11.3%, respectively) and controls (28.2% and 15.5%, respectively; P = 0.61). CONCLUSIONS: In general, patients did not have more migraines or headaches than controls. However, patients had more chronic TTHs than controls. Chronic TTHs were not associated with PSS-related autoantibodies, fatigue, depression, abnormalities on magnetic resonance imaging or abnormalities in the cerebrospinal fluid. Patients with PSS did, however, have higher depression and fatigue scores than controls.
Tomic S, Brkic S, Maric D, Mikic AN.	Clinic for Infectious Diseases, Clinical Center Vojvodina, Novi Sad, Serbia.	Lipid and protein oxidation in female patients with chronic fatigue syndrome.	Arch Med Sci. 2012 Nov 9;8(5):886-91. doi: 10.5114/aoms.2012.31620.	INTRODUCTION: Chronic fatigue syndrome (CFS) is a widely recognized problem, characterized by prolonged, debilitating fatigue and a characteristic group of accompanying symptoms, that occurs four times more frequently in women than in men. The aim of the study was to determine the existence of oxidative stress and its possible consequences in female patients with CFS. MATERIAL AND METHODS: Twenty-four women aged 15-45 who fulfilled the diagnostic criteria for CFS with no comorbidities were recruited and were age matched to a control group of 19 healthy women. After conducting the routine laboratory tests, levels of the lipid oxidation product malondialdehyde (MDA) and protein oxidation protein carbonyl (CO) were determined. RESULTS: The CFS group had higher levels of triglycerides (p = 0.03), MDA (p = 0.03) and CO (p = 0.002) and lower levels of HDL cholesterol (p = 0.001) than the control group. There were no significant differences in the levels of total protein, total cholesterol or LDL cholesterol. CONCLUSIONS: The CFS group had an unfavorable lipid profile and signs of oxidative stress induced damage to lipids and proteins. These results might be indicative of early proatherogenic processes in this group of patients who are otherwise at low risk for atherosclerosis. Antioxidant treatment and life style changes are indicated for women with CFS, as well as closer observation in order to assess the degree of atherosclerosis.
Tomš J.	Univerzita Karlova v Praze, Lekarska fakulta v Hradci Kralove. toms.jan@seznam.cz	Updated view of fibromyalgia. [Article in Czech]	Cas Lek Cesk. 2012;151(9):415-9.	Fibromyalgia is a chronic syndrome characterized by dysfunction of pain processing and regulation. Although the definite etiology has not been recognized yet, the key role in the pathogenesis of this syndrome probably plays the central sensitization process with the development of chronic (central) pain and other associated symptoms (fatigue, stiffness, sleep disorders, cognitive and vegetative disturbance). The absence of objective diagnostic tests often results in delayed diagnosis and patient fluctuation among a number of specialists with uncertainty and fear of a serious disease. The treatment is based on the individually adjusted and multidisciplinary approach to the patient, combining pharmacological and non-pharmacological therapy. New drugs introduced to the therapy in the recent years can have positive effect on symptom reduction and improvement of patients quality of life.
Tort S, Urrútia G,	Iberoamerican	Monoamine oxidase	Cochrane Database Syst Rev.	BACKGROUND: Fibromyalgia (FM) syndrome is a chronic condition of unknown

Nishishinya MB, Walitt B.	Cochrane Centre, Institute of Biomedical Research (IIB Sant Pau), Barcelona, Spain. sera.tort@cochrane.es	inhibitors (MAOIs) for fibromyalgia syndrome.	2012 Apr 18;4:CD009807. doi: 10.1002/14651858.CD009807.	aetiology characterised by musculoskeletal pain that often co-exists with sleep disturbance, cognitive dysfunction and fatigue. Patients often report high disability levels and poor quality of life. Since there is no specific treatment that alters the pathogenesis of FM, drug therapy focuses on pain reduction and improvement of other bothersome symptoms. OBJECTIVES: The objective of this review was to assess the effectiveness and safety of monoamine oxidase inhibitors (MAOIs) in the treatment of FM syndrome. SEARCH METHODS: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library 2010, Issue 10), MEDLINE (1966 to November 2010), EMBASE (1980 to November 2010) and the reference lists of reviewed articles. SELECTION CRITERIA: We selected all randomised, double-blind trials of MAOIs used for the treatment of FM pain in adult participants. DATA COLLECTION AND ANALYSIS: Two authors assessed risk of bias and extracted data independently onto a specially designed pro forma and a third review author cross-checked them. MAIN RESULTS: We included two studies of inconsistent risk of bias with a total of 230 patients diagnosed with FM. We evaluated two MAOIs: pirlindole and moclobemide. Pirlindole showed statistically significant results compared with placebo for several outcomes (pain, tender points and overall assessment by the patient and the physician), whereas moclobemide did not show statistically significant differences between groups. Pooled results of the two studies displayed a modest effect size in pain (mean difference (MD) -1.45 (121 patients; 95% confidence interval (CI) -2.71 to -0.20; number needed to treat (NNT) 2 (95% CI 1 to 12); I(2) = 59%)), implying a minimal clinically important difference (MCID) and a small effect on tender points (standardised mean difference (SMD) -0.36 (121 patients; 95% CI -0.72 to -0.00; I(2) = 31%)). No effect was seen on global assessment by patient. Physical function and sleep disturbance were not measured. The most frequent adverse events were nausea and vomiting, with statistically significant differences between groups (risk ratio (RR) 7.82 (89 patients; 95% CI 1.02 to 59.97; NNT 7 (95% CI 4 to 33)). AUTHORS' CONCLUSIONS: Data suggest that the effectiveness of MAOIs for the treatment of FM symptoms is limited. Although we observed a moderate effect size on pain and a small one on tender points, these results should be taken with caution as they are only based on two studies with a small number of patients and inconsistent risk of bias among them.
Tosun E, Topaloğlu O, Akkalyoncu B.		As a rare cause of drug-induced cough: topiramate.	J Trace Elem Med Biol. 2012 Oct;26(4):291-3. doi: 10.1016/j.jtemb.2012.02.005.	The most common causes of chronic cough in nonsmokers are postnasal drip syndrome, asthma, and gastroesophageal reflux disease. Drugs are also important in the etiology of resistant cough. Most common drugs inducing cough are the ACE inhibitors. Many drugs other than ACE inhibitors can also cause dry cough and one among them is topiramate. It is a new generation, efficacy-proved antiepileptic drug that is used widely for migraine prophylaxis in many countries. Most common adverse events of topiramate are paresthesia, cognitive symptoms, fatigue, insomnia, nausea, loss of apetite, anxiety, and dizziness. There is only one case report about

				topiramate associated cough in the literature. The present report refers to a patient, presenting with cough who is on topiramate treatment for migraine prophylaxis.
Toussaint LL, Whipple MO, Abboud LL, Vincent A, Wahner-Roedler DL.	Department of Psychology, Luther College, Decorah, IA 52101, USA. touslo01@luther.edu	A mind-body technique for symptoms related to fibromyalgia and chronic fatigue.	Explore (NY). 2012 Mar-Apr;8(2):92-8. doi: 10.1016/j.explore.2011.12.003.	CONTEXT: A novel mind-body approach (amygdala retraining) is hypothesized to improve symptoms related to fibromyalgia and chronic fatigue. OBJECTIVE: To examine the use of a mind-body approach for improving symptoms related to fibromyalgia and chronic fatigue. DESIGN: This was a single-blind, randomized controlled trial. SETTING: The study was conducted in a tertiary-care fibromyalgia and chronic fatigue clinic. PATIENTS: Patients with fibromyalgia, chronic fatigue, or both were included. INTERVENTIONS: Patients were randomly assigned to receive amygdala retraining along with standard care or standard care alone. Standard care involved attending a 1.5-day multidisciplinary program. The amygdala retraining group received an additional 2.5-hour training course in which the key tools and techniques adapted from an existing program were taught to the patient. A home-study video course and associated text were provided to supplement the on-site program. Both groups received telephone calls twice a month to answer questions related to technique and to provide support. MAIN OUTCOME MEASURES: Validated self-report questionnaires related to general health, well-being, and symptoms, including Short Form-36, Measure Yourself Medical Outcome Profile, Multidimensional Fatigue Inventory, Epworth Sleepiness Scale, and Fibromyalgia Impact Questionnaire. RESULTS: Of the 44 patients randomly assigned who completed baseline assessments, 21 patients completed the study (14 in the standard care group and 7 in the study group). Median age was 48 years (range, 27-56 years), and female subjects comprised 91% of the group. Analyses demonstrated statistically significant improvements in scores for physical health, energy, pain, symptom distress, and fatigue in patients who received the amygdala retraining compared with standard care.
Trabal J, Leyes P, Fernández-Solá J, Forga M, Fernández-Huerta J.	Servei d´Endocrinología i Nutrició, Hospital Clínic, Barcelona, Spain. joantrabal@gmail.com	Patterns of food avoidance in chronic fatigue syndrome: is there a case for dietary recommendations?	Nutr Hosp. 2012 Mar-Apr;27(2):659-62. doi: 10.1590/S0212-16112012000200046.	OBJECTIVES: To assess the dietary habits and food avoidance-behavior in patients with Chronic Fatigue Syndrome (CFS). METHODS: Cross-sectional pilot study with 28 patients diagnosed with severe CFS. Eating habits were assessed with a food frequency questionnaire and 3-day food records. We analyzed variables related to dietary restrictions induced by symptoms or external information. RESULTS: The most prevalent restrictions were for dairy products and gluten-containing grains, with 22 and 15 restricting patients, respectively. Patients reported different digestive symptoms, which did not improve with the use of exclusion diets. Thirteen patients had received information against the intake of certain foods through different sources. Six cases of grains restriction and 11 of dairy were compatible with a counseling-induced pattern of exclusion. CONCLUSIONS: There is not a homogeneous pattern of food avoidance. Dietary restrictions should be based on a proven food allergy or intolerance. Dietary counseling should be based on sound nutritional knowledge.

Tracy M.	Pump House Surgery, Earls Colne, Essex.	Chronic fatigue syndrome.	Nurs Stand. 2012 Sep 26-Oct 2;27(4):57.	
Trivedi PJ, Chapman RW.	Centre for Liver Research and NIHR Biomedical Research Unit, University of Birmingham, Wolfson Drive, Edgbaston, Birmingham, B15 2TT United Kingdom. doctortrivedi@doctors.org.uk	PSC, AIH and overlap syndrome in inflammatory bowel disease.	Clin Res Hepatol Gastroenterol. 2012 Oct;36(5):420-36. doi: 10.1016/j.clinre.2011.10.007.	Primary sclerosing cholangitis (PSC) is a progressive, cholestatic disorder characterised by chronic inflammation and stricture formation of the biliary tree. Symptoms include pruritus, fatigue and in advanced cases ascending cholangitis, cirrhosis and end-stage hepatic failure. Patients are at an increased risk of malignancy arising from the bile ducts, gallbladder, liver and colon. The majority (>80%) of Northern European patients with PSC also have inflammatory bowel disease (IBD), usually ulcerative colitis (UC). IBD commonly presents before the onset of PSC, although the opposite can occur and the onset of both conditions can be separated by many years. The colitis associated with PSC is characteristically mild although frequently involves the whole colon. Despite the majority of patients having relatively inactive colonic disease, paradoxically the risk of colorectal malignancy is substantially increased. Patients may also develop dominant, stenotic lesions of the biliary tree which may be difficult to differentiate from cholangiocarcinoma and the coexistence of IBD may influence the development of this complication. Ursodeoxycholic acid may offer a chemoprotective effect against colorectal malignancy and improve liver biochemical indices. Evidence of any beneficial effect on histological progression of hepatobiliary disease is less clear. High doses (~25-30 mg/kg/d) may be harmful and should be avoided. Autoimmune hepatitis (AIH) is less common in patients with IBD than PSC, however, an association has been observed. A small subgroup may have an overlap syndrome between AIH and PSC and management should be individualised dependant on liver histology, serum immunoglobulin levels, autoantibodies, degree of biochemical cholestasis and cholangiography.
Tsang BK, Macdonell R.	Department of Neurology, Austin Hospital, Melbourne, Victoria, Australia. bktsang@optusnet.com.au	Multiple sclerosis-diagnosis, management and prognosis.	Aust Fam Physician. 2011 Dec;40(12):948-55.	BACKGROUND: Multiple sclerosis is the most common chronic disabling disease of the central nervous system in young adults. OBJECTIVE: This article summarises the diagnosis, management and prognosis of multiple sclerosis. DISCUSSION: Multiple sclerosis usually starts with an acute episode of neurological disturbance, termed a 'clinically isolated syndrome', followed by an illness phase punctuated by relapses and remissions which may transition after 10 years to a phase of progressive accumulation of disability without relapses.
Tsibris AM.	[No address quoted]	The end of the association between XMRV, MLV-like viruses and chronic fatigue syndrome.	Virulence. 2011 Nov-Dec;2(6):493-4. doi: 10.4161/viru.2.6.18518.	[No abstract given]
Tummers M, Knoop H, van Dam A, Bleijenberg G	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical	Implementing a minimal intervention for chronic fatigue syndrome in a	Psychol Med. 2012 Oct;42(10):2205-15. doi: 10.1017/S0033291712000232.	BACKGROUND: Cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) is an effective but intensive treatment, requiring trained therapists. A minimal intervention based on CBT for CFS, guided self-instruction, was shown to be an effective treatment when delivered in a tertiary treatment centre. Implementing this

	Centre, The Netherlands.	mental health centre: a randomized controlled trial.		intervention in a community-based mental health centre (MHC) will increase the treatment capacity for CFS patients. This study evaluated the effectiveness of guided self-instruction for CFS implemented in an MHC, delivered by nurses. Method One hundred and twenty-three patients were randomly assigned to either guided self-instruction (n=62) or a waiting list (n=61). Randomization was computer generated, with allocation by numbered sealed envelopes. Group allocation was open to all those involved. Patients fulfilled US Centers for Disease Control and Prevention (CDC) criteria for CFS. Primary outcome variables were fatigue severity and physical and social functioning, measured with the Checklist Individual Strength (CIS) and the Medical Outcomes Survey Short Form-36 (SF-36) respectively. RESULTS: After 6 months, patients who followed guided self-instruction reported a significantly larger decrease in fatigue compared to the waiting list [mean difference -8.1, 95% confidence interval (CI) -3.8 to -12.4, controlled effect size 0.70]. There was no significant difference in physical and social functioning. However, post-hoc analyses showed a significant decrease in fatigue and physical disabilities following the intervention in a subgroup of patients with physical disabilities at baseline (SF-36 physical functioning $\leqslant$70). CONCLUSIONS: Implementation of guided self-instruction in a community-based MHC was partially successful. The minimal intervention can be effectively implemented for CFS patients with physical impairments.
Twisk FN, Arnoldus RJ.	[No address quoted]	Graded exercise therapy GET/cognitive behavioural therapy (CBT) is often counterproductive in myalgic encephalomyelitis (ME) and chronic fatigue syndrome (CFS).	Eur J Clin Invest. 2012 Nov;42(11):1255-6; author reply 1257-8. doi: 10.1111/j.1365-2362.2012.02718.x.	Comment on Eur J Clin Invest. 2012 Oct;42(10):1136-44.
Ulus Y, Akyol Y, Tander B, Durmus D, Bilgici A, Kuru O.	Department of Physical Medicine and Rehabilitation, Medical Faculty, Ondokuz Mayis University, Samsun, Turkey. yaseminulus@gmail.com	Sleep quality in fibromyalgia and rheumatoid arthritis: associations with pain, fatigue, depression, and disease activity.	Clin Exp Rheumatol. 2011 Nov-Dec;29(6 Suppl 69):S92-6.	OBJECTIVES: The aim of this study was to compare the sleep quality in patients with rheumatoid arthritis (RA) and fibromyalgia syndrome (FMS); and to evaluate the relationship between sleep quality and pain, fatigue, depression, and disease activity in patients with RA and FMS. METHODS: Forty RA, 40 FMS and 40 healthy controls were enrolled in the study. Disease activity and disease duration were reported in patients. Pain by visual analogue scale (VAS), fatigue by Multidimensional Assesment of Fatigue (MAF), depression by Beck Depression Index (BDI), and sleep quality by Pittsburgh Sleep Quality Index (PSQI) were gathered in all participants. RESULTS: All participants were aged between 20 and 65 years, with a mean age of 42.97±10.75 years. There was no significant difference with respect to demographic characteristics

				among the three study groups. Patients reported more depression than controls, but BDI scores were similar in FMS and RA patients. VAS pain scores and MAF scores were significantly different in the three groups (p<0.001). FMS and RA patients had poor sleep quality (p<0.001). FMS patients had daytime dysfunction due to sleep disorder and had worse habitual sleep efficiency than RA patients (p<0.05). In patients, positive correlations were found between PSQI and clinic assessment variables except disease duration. CONCLUSIONS: FMS and RA may have poor sleep quality when compared to subjects without rheumatologic disorders. The quality of sleep can be impaired by pain, fatigue, depression, and disease activity in such patients.
Van Cauwenbergh D, De Kooning M, Ickmans K, Nijs J.	Chronic Pain and Chronic Fatigue Research Group (CHROPIVER), Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium. jo.nijs@vub.ac.be	How to exercise people with chronic fatigue syndrome: evidence-based practice guidelines.	Eur J Clin Invest. 2012 Oct;42(10):1136-44. doi: 10.1111/j.1365-2362.2012.02701.x. Comment in Eur J Clin Invest. 2012 Nov;42(11):1255-6; author reply 1257-8.	BACKGROUND: Despite the large number of studies emphasizing the effectiveness of graded exercise therapy (GET) and cognitive behavioural therapy (CBT) for people with chronic fatigue syndrome (CFS), clinicians are left wondering how exactly to apply exercise therapy to their patients with CFS. The aim of this literature review is to identify the appropriate exercise modalities (i.e. exercise duration, mode, number of treatment sessions, session length, duration of treatment, exercise intensity and whether or not to apply home exercise program) for people with CFS. MATERIALS AND METHODS: All studies that were identified through electronic databases (PubMed and PEDro) were assessed for methodological quality by using selection criteria (Delphi score). RESULTS: In this literature review, 12 studies fulfilled all study requirements. One study had a low methodological quality. The parameters used in the GET and CBT interventions were divided into subgroups: (i) time or symptom contingent, (ii) exercise frequency and (iii) exercise modality. CONCLUSION: The lack of uniformity in outcome measures and CFS diagnostic criteria make it difficult to compare the findings across studies. Based on the available evidence, exercise therapy for people with CFS should be aerobic and must comprise of 10-11 sessions spread over a period of 4-5 months. A time-contingent approach is preferred over a symptom-contingent way of exercising. In addition, people with CFS can perform home exercises five times a week with an initial duration of 5-15 min per exercise session. The exercise duration can be gradually increased up to 30 min.
Van Den Eede F, Haccuria T, De Venter M, Moorkens G.	[No address quoted]	Childhood sexual abuse and chronic fatigue syndrome.	Br J Psychiatry. 2012 Feb;200(2):164-5. doi: 10.1192/bjp.200.2.164a.	Comment on Br J Psychiatry. 2011 Oct;199(4):323-9.
van der Meer JW, Lloyd AR.	[No address quoted]	A controversial consensus--comment on article by Broderick et al.	J Intern Med. 2012 Jan;271(1):29-31. doi: 10.1111/j.1365-2796.2011.02468.x.	Comment in J Intern Med. 2012 Feb;271(2):213-7. Comment on J Intern Med. 2011 Oct;270(4):327-38.
van Kuppeveld FJ, van der Meer JW.	Department of Medical Microbiology, Radboud University Nijmegen	XMRV and CFS--the sad end of a story.	Lancet. 2012 Feb 4;379(9814):e27-8. doi: 10.1016/S0140-	[No abstract given]

	Medical Centre, 6500 HB Nijmegen, Netherlands. f.vankuppeveld@ncmls.ru.nl		6736(11)60899-4.	
Vaughan AE, Mendoza R, Aranda R, Battini JL, Miller AD.	Human Biology Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA.	Xpr1 is an atypical G-protein-coupled receptor that mediates xenotropic and polytropic murine retrovirus neurotoxicity.	J Virol. 2012 Feb;86(3):1661-9. doi: 10.1128/JVI.06073-11.	Xenotropic murine leukemia virus-related virus (XMRV) was first identified in human prostate cancer tissue and was later found in a high percentage of humans with chronic fatigue syndrome (CFS). While exploring potential disease mechanisms, we found that XMRV infection induced apoptosis in SY5Y human neuroblastoma cells, suggesting a mechanism for the neuromuscular pathology seen in CFS. Several lines of evidence show that the cell entry receptor for XMRV, Xpr1, mediates this effect, and chemical cross-linking studies show that Xpr1 is associated with the Gβ subunit of the G-protein heterotrimer. The activation of adenylate cyclase rescued the cells from XMRV toxicity, indicating that toxicity resulted from reduced G-protein-mediated cyclic AMP (cAMP) signaling. Some proteins with similarity to Xpr1 are involved in phosphate uptake into cells, but we found no role of Xpr1 in phosphate uptake or its regulation. Our results indicate that Xpr1 is a novel, atypical G-protein-coupled receptor (GPCR) and that xenotropic or polytropic retrovirus binding can disrupt the cAMP-mediated signaling function of Xpr1, leading to the apoptosis of infected cells. We show that this pathway is also responsible for the classic toxicity of the polytropic mink cell focus-forming (MCF) retrovirus in mink cells. Although it now seems clear that the detection of XMRV in humans was the result of sample contamination with a recombinant mouse virus, our findings may have relevance to neurologic disease induced by MCF retroviruses in mice.
Verhaeghe J, Van Den Eede F, Van Den Ameele H, Sabbe BG.	Johanna.Verhaeghe@hotmail.com	Neuro-endocrine correlates of burnout. [Article in Dutch]	Tijdschr Psychiatr. 2012;54(6):517-26.	BACKGROUND: The symptoms of burnout are similar to those of depression on the one hand and chronic fatigue syndrome on the other hand. However, the neuro-endocrine correlates of these two syndromes are the opposite, the former being a hyperfunction of the hypothalamic-hypophysial-cortical axis (HPA) and the latter being a hypofunction of the hpa-axis. AIM: To find out, via a systematic review of the literature, whether burnout is associated with either a hyperfunction or a hypofunction of the HPA-axis. METHOD: We searched PubMed using the following search terms: 'burnout syndrome and burnout', 'adrenocorticotropic hormone', 'corticotropin releasing factor', 'hypothalamic pituitary adrenal axis' and 'cortisol'. We retrieved 16 original articles en one meta-analysis were included in the study. RESULTS: Functional stress testing showed hypersuppression of the HPA-axis after dexamethasone. Basal cortisol values were found to be less conclusive, although a meta-analysis pointed to a negative association between burnout and cortisol. We did not find any studies that were carried out with the help of physiological, physical or psychological stress factors in burnout. CONCLUSION: Burnout is associated primarily with a hypofunction of the HPA-axis, which is a neuro-endocrine

				characteristic of exhaustion, rather than of depression. However, further studies involving functional stress testing are needed in order to map the neuro-endocrine profile fully and to clarify the link with the deregulation of the immune system.
Vierck CJ.	Department of Neuroscience and Comprehensive Center for Pain Research, Colleges of Medicine and Dentistry, University of Florida, P.O. Box 100444, 1600 S.W. Archer Road, Gainesville, FL 32610, USA.	A mechanism-based approach to prevention of and therapy for fibromyalgia.	Pain Res Treat. 2012;2012:951354. doi: 10.1155/2012/951354.	Fibromyalgia syndrome (FMS) is characterized by pain referred to deep tissues. Diagnosis and treatment of FMS are complicated by a variable coexistence with regional pain, fatigue, sleep disruption, difficulty with mentation, and depression. The widespread, deep pain of FMS can be a consequence of chronic psychological stress with autonomic dysregulation. Stress acts centrally to facilitate pain and acts peripherally, via sympathetic vasoconstriction, to establish painful muscular ischemia. FMS pain, with or without a coexistent regional pain condition, is stressful, setting up a vicious circle of reciprocal interaction. Also, stress interacts reciprocally with systems of control over depression, mentation, and sleep, establishing FMS as a multiple-system disorder. Thus, stress and the ischemic pain it generates are fundamental to the multiple disorders of FMS, and a therapeutic procedure that attenuates stress and peripheral vasoconstriction should be highly beneficial for FMS. Physical exercise has been shown to counteract peripheral vasoconstriction and to attenuate stress, depression, and fatigue and improve mentation and sleep quality. Thus, exercise can interrupt the reciprocal interactions between psychological stress and each of the multiple-system disorders of FMS. The large literature supporting these conclusions indicates that exercise should be considered strongly as a first-line approach to FMS therapy.
Vincent A, Brimmer DJ, Whipple MO, Jones JF, Boneva R, Lahr BD, Maloney E, St Sauver JL, Reeves WC.	Fibromyalgia and Chronic Fatigue Clinic, Mayo Clinic, Rochester, MN; Division of General Internal Medicine, Mayo Clinic, Rochester, MN. Electronic address: RSTFCFC@mayo.edu.	Prevalence, incidence, and classification of chronic fatigue syndrome in olmsted county, Minnesota, as estimated using the Rochester epidemiology project.	Mayo Clin Proc. 2012 Dec;87(12):1145-52. doi: 10.1016/j.mayocp.2012.08.015.	OBJECTIVE: To estimate the prevalence and incidence of chronic fatigue syndrome in Olmsted County, Minnesota, using the 1994 case definition and describe exclusionary and comorbid conditions observed in patients who presented for evaluation of long-standing fatigue. PATIENTS AND METHODS: We conducted a retrospective medical record review of potential cases of chronic fatigue syndrome identified from January 1, 1998, through December 31, 2002, using the Rochester Epidemiology Project, a population-based database. Patients were classified as having chronic fatigue syndrome if the medical record review documented fatigue of 6 months' duration, at least 4 of 8 chronic fatigue syndrome-defining symptoms, and symptoms that interfered with daily work or activities. Patients not meeting all of the criteria were classified as having insufficient/idiopathic fatigue. RESULTS: We identified 686 potential patients with chronic fatigue, 2 of whom declined consent for medical record review. Of the remaining 684 patients, 151 (22%) met criteria for chronic fatigue syndrome or insufficient/idiopathic fatigue. The overall prevalence and incidence of chronic fatigue syndrome and insufficient/idiopathic fatigue were 71.34 per 100,000 persons and 13.16 per 100,000 person-years vs 73.70 per 100,000 persons and 13.58 per 100,000 person-years, respectively. The potential cases included 482 patients (70%) who had an exclusionary condition, and almost half the patients who met either criterion had at least one nonexclusionary comorbid

				condition. CONCLUSION: The incidence and prevalence of chronic fatigue syndrome and insufficient/idiopathic fatigue are relatively low in Olmsted County. Careful clinical evaluation to identify whether fatigue could be attributed to exclusionary or comorbid conditions rather than chronic fatigue syndrome itself will ensure appropriate assessment for patients without chronic fatigue syndrome.
Volterrani M, Rosano G, Iellamo F.	Cardiovascular Research Unit, Department of Medical Sciences, Centre for Clinical and Basic Research, Istituto di Ricovero e Cura a Carattere Scientifico San Raffaele Pisana, via della Pisana 235, 00163 Rome, Italy. maurizio.volterrani@sanraffaele.it	Testosterone and heart failure.	Endocrine. 2012 Oct;42(2):272-7.	Testosterone deficiency is a generalized phenomenon seen in the course of chronic heart failure (CHF). Reduction in circulating testosterone level is a predictor of deterioration of functional capacity over time, underscoring the role of testosterone deficiency in CHF. Anabolic hormones are determinants of exercise capacity and circulating levels of anabolic hormones strongly determine muscle mass and strength. Testosterone deficiency is involved in the pathophysiology of CHF, contributing to some features of this syndrome, such as the reduced muscle mass, abnormal energy handling, fatigue, dyspnea and, finally, cachexia. This review summarizes current knowledge on the role of testosterone deficiency in the pathophysiology of CHF, gaining insights from the potential implications of testosterone as supplementation therapy.
Vos-Vromans DC, Smeets RJ, Rijnders LJ, Gorrissen RR, Pont M, Köke AJ, Hitters MW, Evers SM, Knottnerus AJ.	Revant Rehabilitation Centre Breda, Brabantlaan 1, 4817, JW, Breda, The Netherlands. d.vos@revant.nl.	Cognitive behavioural therapy versus multidisciplinary rehabilitation treatment for patients with chronic fatigue syndrome: study protocol for a randomised controlled trial (FatiGo).	Trials. 2012 May 30;13:71. doi: 10.1186/1745-6215-13-71.	ABSTRACT:BACKGROUND: Patients with chronic fatigue syndrome experience extreme fatigue, which often leads to substantial limitations of occupational, educational, social and personal activities. Currently, there is no consensus regarding the treatment. Patients try many different therapies to overcome their fatigue. Although there is no consensus, cognitive behavioural therapy is seen as one of the most effective treatments. Little is known about multidisciplinary rehabilitation treatment, a combination of cognitive behavioural therapy with principles of mindfulness, gradual increase of activities, body awareness therapy and pacing. The difference in effectiveness and cost-effectiveness between multidisciplinary rehabilitation treatment and cognitive behavioural therapy is as yet unknown. The FatiGo (Fatigue-Go) trial aims to compare the effects of both treatment approaches in outpatient rehabilitation on fatigue severity and quality of life in patients with chronic fatigue syndrome. METHODS: One hundred twenty patients who meet the criteria of chronic fatigue syndrome, fulfil the inclusion criteria and sign the informed consent form will be recruited. Both treatments take 6 months to complete. The outcome will be assessed at 6 and 12 months after the start of treatment. Two weeks after the start of treatment, expectancy and credibility will be measured, and patients will be asked to write down their personal goals and score their current performance on these goals on a visual analogue scale. At 6 and 14 weeks after the start of treatment, the primary outcome and three potential mediators-self-efficacy, causal attributions and present-centred attention-awareness-will be measured. Primary outcomes are fatigue severity and quality of life. Secondary outcomes are physical activity,

				psychological symptoms, self-efficacy, causal attributions, impact of disease on emotional and physical functioning, present-centred attention-awareness, life satisfaction, patient personal goals, self-rated improvement and economic costs. The primary analysis will be based on intention to treat, and longitudinal analysis of covariance will be used to compare treatments. DISCUSSION: The results of the trial will provide information on the effects of cognitive behavioural therapy and multidisciplinary rehabilitation treatment at 6 and 12 months follow-up, mediators of the outcome, cost-effectiveness, cost-utility, and the influence of treatment expectancy and credibility on the effectiveness of both treatments in patients with chronic fatigue syndrome. TRIAL REGISTRATION: Current Controlled Trials ISRCTN77567702.
Wang X, Tu F, Zhu Y, Gao G.	Key Laboratory of Infection and Immunity, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China.	Zinc-finger antiviral protein inhibits XMRV infection.	PLoS One. 2012;7(6):e39159. doi: 10.1371/journal.pone.0039159.	BACKGROUND: The zinc-finger antiviral protein (ZAP) is a host factor that specifically inhibits the replication of certain viruses, including Moloney murine leukemia virus (MoMLV), HIV-1, and certain alphaviruses and filoviruses. ZAP binds to specific viral mRNAs and recruits cellular mRNA degradation machinery to degrade the target RNA. The common features of ZAP-responsive RNA sequences remain elusive and thus whether a virus is susceptible to ZAP can only be determined experimentally. Xenotropic murine leukemia virus-related virus (XMRV) is a recently identified γ-retrovirus that was originally thought to be involved in prostate cancer and chronic fatigue syndrome but recently proved to be a laboratory artefact. Nonetheless, XMRV as a new retrovirus has been extensively studied. Since XMRV and MoMLV share only 67.9% sequence identity in the 3'UTRs, which is the target sequence of ZAP in MoMLV, whether XMRV is susceptible to ZAP remains to be determined. FINDINGS: We constructed an XMRV-luc vector, in which the coding sequences of Gag-Pol and part of Env were replaced with luciferase-coding sequence. Overexpression of ZAP potently inhibited the expression of XMRV-luc in a ZAP expression-level-dependent manner, while downregulation of endogenous ZAP rendered cells more sensitive to infection. Furthermore, ZAP inhibited the spreading of replication-competent XMRV. Consistent with the previously reported mechanisms by which ZAP inhibits viral infection, ZAP significantly inhibited the accumulation of XMRV-luc mRNA in the cytoplasm. The ZAP-responsive element in XMRV mRNA was mapped to the 3'UTR. CONCLUSIONS: ZAP inhibits XMRV replication by preventing the accumulation of viral mRNA in the cytoplasm. Documentation of ZAP inhibiting XMRV helps to broaden the spectrum of ZAP's antiviral activity. Comparison of the target sequences of ZAP in XMRV and MoMLV helps to better understand the features of ZAP-responsive elements.
Warren JW, Clauw DJ, Langenberg P.	Department of Medicine Department of Epidemiology and Public Health,	Prognostic factors for recent-onset interstitial cystitis/painful	BJU Int. 2012 Aug 9. doi: 10.1111/j.1464-410X.2012.11422.x.	Study Type - Prognosis (case series) Level of Evidence 4 What's known on the subject? and What does the study add? Interstitial cystitis/painful bladder syndrome (IC/PBS) comprises pain perceived to be from the bladder, urinary urgency and frequency, and nocturia. As diagnosed at present, it is primarily identified in adult

	University of Maryland School of Medicine, Baltimore, MD Departments of Anesthesiology and Medicine, University of Michigan School of Medicine, Ann Arbor, MI, USA.	bladder syndrome.		women. It is a chronic disease yet its natural history has not been well studied. In a prospective study of 304 incident female IC/PBS cases followed for a median of 33 months after onset, women with baseline chronic fatigue syndrome had a worse prognosis for IC/PBS. Mild IC/PBS at baseline was the only variable that was directly associated with a good prognosis. OBJECTIVE: • To identify baseline variables that predict the prognosis of interstitial cystitis/painful bladder syndrome (IC/PBS) in women seeking medical care for recent onset of this syndrome. SUBJECTS AND METHODS: • In a prospective study of women with incident IC/PBS (≤12 months of symptoms), we contacted patients at intervals and asked standardized questions about IC/PBS symptoms in the previous week. • Logistic regression analyses assessed baseline variables as predictors of mild vs more severe IC/PBS at the last follow-up. RESULTS: • Median length of follow-up was 33 months after onset of IC/PBS; 304 (97%) patients had at least one follow-up assessment. • Mild IC/PBS at baseline was the only variable that was directly associated with a mild IC/PBS endpoint. • Conversely, a history of chronic fatigue syndrome (CFS) was inversely associated with a mild endpoint of IC/PBS (i.e. individuals with CFS had a worse prognosis for their IC/PBS symptoms). CONCLUSIONS: • At a median of nearly 3 years after onset, baseline mild IC/PBS was directly associated with a milder disease severity. • Baseline co-morbid CFS was associated with more severe disease. • Whether CFS was uniquely associated or represented several co-morbid non-bladder syndromes (NBSs) could not be determined.
Warren JW, Clauw DJ.	Department of Medicine and of Epidemiology, University of Maryland School of Medicine, Baltimore, MD 21201, USA. jwarren@medicine.umaryland.edu	Functional somatic syndromes: sensitivities and specificities of self-reports of physician diagnosis.	Psychosom Med. 2012 Nov-Dec;74(9):891-5. doi: 10.1097/PSY.0b013e31827264aa. Comment in Psychosom Med. 2012 Nov-Dec;74(9):882.	OBJECTIVE: Functional somatic syndromes have no laboratory or pathologic abnormalities and so are diagnosed by symptom-based case definitions. However, many studies, including recent ones, have used self-reports of physician diagnosis rather than the case definitions. Our objective was to determine the sensitivities and specificities of self-report of physician diagnosis for chronic fatigue syndrome (CFS), fibromyalgia (FM), irritable bowel syndrome (IBS), panic disorder, and migraine. METHODS: Each of 312 female patients with incident interstitial cystitis/bladder pain syndrome and matched population-based controls were queried on self-report of physician diagnosis and separately on established case definitions for each of these syndromes. RESULTS: Using the symptom-based case definitions as standards, we found that self-report of physician diagnosis did not identify 90% of the controls who had CFS, 77% who had FM, 69% who had IBS, 43% who had panic disorder, and 23% who had migraine. In addition, it missed most individuals with multiple syndromes. Findings in one cohort (controls) were confirmed in another (patients with interstitial cystitis/bladder pain syndrome). CONCLUSIONS: Self-report of physician diagnosis did not identify most of the three most venerable functional somatic syndromes, IBS, FM, and, especially, CFS; nor did it identify substantial minorities of individuals with panic disorder and migraine. Self-report of physician diagnosis was particularly poor in recognizing persons with multiple syndromes. The insensitivity of this diagnostic test

				has effects on not only prevalence and incidence estimates but also correlates, comorbidities, and case recruitment. To reveal individuals with these syndromes, singly or together, queries of symptoms, not diagnoses, are necessary.
Warren JW, Langenberg P, Clauw DJ.	Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA; Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA. Electronic address: jwarren@medicine.umaryland.edu.	The number of existing functional somatic syndromes (FSSs) is an important risk factor for new, different FSSs.	J Psychosom Res. 2013 Jan;74(1):12-7. doi: 10.1016/j.jpsychores.2012.09.002. Epub 2012 Sep 26.	OBJECTIVE: The objective of this study is to test the hypothesis that the number of functional somatic syndromes (FSSs) predicts new, additional FSSs. METHODS: In a recent case-control study of interstitial cystitis/painful bladder syndrome (IC/PBS), we used symptom-based consensus definitions to identify these FSSs: fibromyalgia (FM), chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), chronic pelvic pain, migraine, sicca syndrome and panic disorder. Those present before the incidence year were called antecedent FSSs; those with onset during the incidence year were called incident FSSs. In each of two groups, 312 IC/PBS cases and 313 controls, rates of incident FSSs were compared among those with 0, 1, 2, or ≥3 antecedent FSSs. Confounding was assessed using logistic regression analyses that included the individual antecedent FSSs, published correlates of these FSSs, and demographic variables. RESULTS: The incidence of a new FSS increased with the number of antecedent FSSs, as did that of incident FM, CFS and IBS studied separately. These findings were not confounded by other variables. The presence of multiple antecedent FSSs generally had the highest odds ratio for new, different, incident FSSs. CONCLUSIONS: This study revealed that the number of antecedent FSSs was among the strongest risk factors for other FSSs, especially incident FM, CFS and IBS. This suggests that the FSSs are linked through a polysyndromic phenotype. If each FSS is heterogeneous, to seek a pathogenesis common to all FSSs, individuals with multiple FSSs should be sought; to seek a pathogenesis unique to a specific FSS, mature persons who have only that FSS should be studied.
Watt T, Oberfoell S, Balise R, Lunn MR, Kar AK, Merrihew L, Bhangoo MS, Montoya JG.	Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University Medical Center, Palo Alto, CA, USA.	Response to valganciclovir in chronic fatigue syndrome patients with human herpesvirus 6 and Epstein-Barr virus IgG antibody titers.	J Med Virol. 2012 Dec;84(12):1967-74. doi: 10.1002/jmv.23411.	Valganciclovir has been reported to improve physical and cognitive symptoms in patients with chronic fatigue syndrome (CFS) with elevated human herpesvirus 6 (HHV-6) and Epstein-Barr virus (EBV) IgG antibody titers. This study investigated whether antibody titers against HHV-6 and EBV were associated with clinical response to valganciclovir in a subset of CFS patients. An uncontrolled, unblinded retrospective chart review was performed on 61 CFS patients treated with 900 mg valganciclovir daily (55 of whom took an induction dose of 1,800 mg daily for the first 3 weeks). Antibody titers were considered high if HHV-6 IgG ≥ 1:320, EBV viral capsid antigen (VCA) IgG ≥ 1:640, and EBV early antigen (EA) IgG ≥ 1:160. Patients self-rated physical and cognitive functioning as a percentage of their functioning prior to illness. Patients were categorized as responders if they experienced at least 30% improvement in physical and/or cognitive functioning. Thirty-two patients (52%) were categorized as responders. Among these, 19 patients (59%) responded physically and 26 patients (81%) responded cognitively. Baseline antibody titers showed no significant association with response. After treatment, the average change in physical and cognitive functioning levels for all patients was +19% and +23%, respectively (P <

				0.0001). Longer treatment was associated with improved response (P = 0.0002). No significant difference was found between responders and non-responders among other variables analyzed. Valganciclovir treatment, independent of the baseline antibody titers, was associated with self-rated improvement in physical and cognitive functioning for CFS patients who had positive HHV-6 and/or EBV serologies. Longer valganciclovir treatment correlated with an improved response.
Wearden AJ, Dunn G, Dowrick C, Morriss RK.	University of Manchester, School of Psychological Sciences, Coupland 1 Building, Oxford Road, Manchester M13 9PL, UK. Alison.wearden@manchester.ac.uk	Depressive symptoms and pragmatic rehabilitation for chronic fatigue syndrome.	Br J Psychiatry. 2012 Sep;201(3):227-32. doi: 10.1192/bjp.bp.111.107474.	BACKGROUND: Previous research has suggested that depressed mood may predict outcome and moderate response to treatment in chronic fatigue syndrome, although findings have differed between studies. AIMS: To examine potential moderators of response to pragmatic rehabilitation v. general practitioner treatment as usual in a recent randomised trial for patients with chronic fatigue syndrome in primary care (IRCTN74156610). METHOD: Simple regressions, with weighting adjustments to allow for missing data, were calculated. Demographic, medical and psychological variables, and treatment arm, were entered separately and as an interaction term. The outcome variable in each case was change in Chalder Fatigue Scale scores, from baseline to 1-year follow-up, our primary outcome point. RESULTS: Longer illness durations predicted poorer outcome across the two treatment arms. For patients allocated to pragmatic rehabilitation compared with those allocated to treatment as usual, higher levels of depressive symptoms at baseline were associated with smaller improvements in fatigue (P = 0.022). CONCLUSIONS: For patients in primary care with higher levels of depressive symptoms, either more intensive or longer pragmatic rehabilitation, or cognitive-behavioural therapy, may be required in order to show a significant improvement in fatigue.
Webb CM, Collin SM, Deave T, Haig-Ferguson A, Spatz A, Crawley E.	St George's University of London, Cranmer Terrace, London, UK.	What stops children with a chronic illness accessing health care: a mixed methods study in children with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME).	BMC Health Serv Res. 2011 Nov 11;11:308. doi: 10.1186/1472-6963-11-308.	BACKGROUND: Paediatric Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is relatively common and disabling with a mean time out of school of more than one academic year. NICE guidelines recommend referral to specialist services immediately if severely affected, within 3 months if moderately affected and within 6 months if mildly affected. However, the median time-to-assessment by a specialist service in the UK is 18 months. This study used a mixed-methods approach to examine factors associated with time taken to access specialist services. METHODS: Time-to-assessment was analysed as a continuous "survival-time" variable in Cox regression models using data from self-completed assessment forms for children attending a regional specialist CFS/ME service between January 2006 and December 2009. Semi-structured interviews about barriers experienced in accessing healthcare for their child were conducted with nine parents of children aged < 17 years (8 individual and one parent couple). Interviews were digitally recorded and analysed using "thematic analysis". RESULTS: 405 children were assessed between 2006 and 2009 and information on school attendance was available on 388. Only 1/125 with severe CFS/ME and 49/263 (19%) with mild to moderate CFS/ME were seen within NICE recommended timeframe. Increased fatigue was associated with shorter time to

				assessment (HR = 1.15; 95% CI 1.03, 1.29 per unit increase in Chalder fatigue score; P = 0.01). Time-to-assessment was not associated with disability, mood, age or gender. Parents described difficulties accessing specialist services because of their own as well as their GP's and Paediatrician's lack of knowledge. They experienced negative attitudes and beliefs towards the child's condition when they consulted GPs, Paediatricians and Child Psychiatrists. Parents struggled to communicate an invisible illness that their child and not themselves were experiencing. CONCLUSIONS: GPs, Child Psychiatrists and Paediatricians need more knowledge about CFS/ME and the appropriate referral pathways to ensure timeliness in referral to specialist services.
Weis J, Faller H.	Klinik für Tumorbiologie an der Universität Freiburg, Breisacher Str. 117, 79106, Freiburg, Deutschland. weis@tumorbio.uni-freiburg.de	Psychosocial issues of long-term cancer survivors. [Article in German]	Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2012 Apr;55(4):501-8. doi: 10.1007/s00103-012-1458-7.	Although cancer incidence rates are increasing, recent statistical studies suggest that cancer patients are showing higher cure rates as well as improved overall survival rates for most cancer locations. These advances are explained by improved strategies in early diagnoses as well as improved cancer therapies. Therefore, the number of long-term cancer survivors has also increased, but only few studies, especially within the last years, have focused on psychosocial issues of this subgroup. Some studies show that overall quality of life of long-term cancer survivors is quite high and comparable to that of the normal population. Nevertheless, a substantial percentage of former patients shows reduced quality of life and suffers from various sequelae of cancer and its treatment. This review focuses on the most common psychosocial issue of long-term survivors such as reduced psychological wellbeing, neuropsychological deficits and cancer-related fatigue syndrome. Finally, recommendations for problem-oriented interventions as well as improvement of psychosocial care of long-term survivors are given.
Wensaas KA, Langeland N, Hanevik K, Mørch K, Eide GE, Rortveit G.	Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway. knut-arne.wensaas@uni.no	Irritable bowel syndrome and chronic fatigue 3 years after acute giardiasis: historic cohort study.	Gut. 2012 Feb;61(2):214-9. doi: 10.1136/gutjnl-2011-300220. Comment in Nat Rev Gastroenterol Hepatol. 2011 Nov;8(11):597.	BACKGROUND: Giardia lamblia is a common cause of gastroenteritis worldwide, but there is limited knowledge about the long-term complications. OBJECTIVE: To estimate the relative risk of irritable bowel syndrome (IBS) and chronic fatigue 3 years after acute giardiasis. DESIGN: Controlled historic cohort study with 3 years' follow-up. Data collected by mailed questionnaire. SETTING: Waterborne outbreak of giardiasis in the city of Bergen, Norway. PARTICIPANTS: 817 patients exposed to Giardia lamblia infection verified by detection of cysts in stool samples and 1128 matched controls. MAIN OUTCOME MEASURES: IBS and chronic fatigue. RESULTS: The prevalence of IBS in the exposed group was 46.1%, compared with 14.0% in the control group, and the adjusted RR=3.4 (95% CI 2.9 to 3.8). Chronic fatigue was reported by 46.1% of the exposed group and 12.0% of the controls, the adjusted RR was 4.0 (95% CI 3.5 to 4.5). IBS and chronic fatigue were associated and the RR for the exposed group of having a combination of the two outcomes was 6.8 (95% CI 5.3 to 8.5). The RR was also increased for having just one of the two syndromes, 1.8 for IBS (95% CI 1.4 to 2.3) and 2.2 for chronic fatigue (95% CI 1.7 to 2.8). CONCLUSIONS: Infection with Giardia lamblia in a non-endemic area was associated with a high prevalence of IBS and chronic fatigue 3 years after acute illness, and the risk was

				significantly higher than in the control group. This shows that the potential consequences of giardiasis are more serious than previously known. Further studies are needed, especially in areas where giardiasis is endemic.
Wessely SC.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK. simon.wessely@kcl.ac.uk	Impact Commentaries. The nature of fatigue: a comparison of chronic "postviral" fatigue with neuromuscular and affective disorders.	J Neurol Neurosurg Psychiatry. 2012 Jan;83(1):4-5. doi: 10.1136/jnnp-2011-301216.	[No abstract given]
White AT, Light AR, Hughen RW, Vanhaitsma TA, Light KC.	Department of Anesthesiology, University of Utah, 30 N 1900 E, Room 3C444, Salt Lake City, UT 84132-2501, USA.	Differences in metabolite-detecting, adrenergic, and immune gene expression after moderate exercise in patients with chronic fatigue syndrome, patients with multiple sclerosis, and healthy controls.	Psychosom Med. 2012 Jan;74(1):46-54. doi: 10.1097/PSY.0b013e31824152ed.	OBJECTIVE: Chronic fatigue syndrome (CFS) and multiple sclerosis (MS) are characterized by debilitating fatigue, yet evaluation of this symptom is subjective. We examined metabolite-detecting, adrenergic, and immune gene expression (messenger ribonucleic acid [mRNA]) in patients with CFS (n = 22) versus patients with MS (n = 20) versus healthy controls (n = 23) and determined their relationship to fatigue and pain before and after exercise. METHODS: Blood samples and fatigue and pain ratings were obtained at baseline and 0.5, 8, 24, and 48 hours after sustained moderate exercise. Leukocyte mRNA of four metabolite-detecting receptors (acid-sensing ion channel 3, purinergic type 2X4 and 2X5 receptors, and transient receptor potential vanilloid type 1) and four adrenergic (α-2a, β-1, and β-2 receptors and catechol-O-methyltransferase) and five immune markers (CD14, toll-like receptor 4 [TLR4], interleukin [IL] 6, IL-10, and lymphotoxin α) was examined using quantitative polymerase chain reaction. RESULTS: Patients with CFS had greater postexercise increases in fatigue and pain (10-29 points above baseline, $p < .001$) and greater mRNA increases in purinergic type 2X4 receptor, transient receptor potential vanilloid type 1, CD14, and all adrenergic receptors than controls (mean ± standard error = 1.3 ± 0.14- to 3.4 ± 0.90-fold increase above baseline, $p = .04$-$.005$). Patients with CFS with comorbid fibromyalgia (n = 18) also showed greater increases in acid-sensing ion channel 3 and purinergic type 2X5 receptors ($p < .05$). Patients with MS had greater postexercise increases than controls in β-1 and β-2 adrenergic receptor expressions (1.4 ± 0.27- and 1.3 ± 0.06-fold increases, respectively, $p = .02$ and $p < .001$) and greater decreases in TLR4 ($p = .02$). In MS, IL-10 and TLR4 decreases correlated with higher fatigue scores. CONCLUSIONS: Postexercise mRNA increases in metabolite-detecting receptors were unique to patients with CFS, whereas both patients with MS and patients with CFS showed abnormal increases in adrenergic receptors. Among patients with MS, greater fatigue was correlated with blunted immune marker expression.
White PD, Chalder T.	Barts and The London School of Medicine and	Chronic fatigue syndrome: treatment	Lancet. 2012 Apr 14;379(9824):1372-3. doi:	Comment on Lancet. 2012 Apr 14;379(9824):1412-8.

	Dentistry, Queen Mary University of London, St Bartholomew's Hospital, London EC1A 7BE, UK. p.d.white@qmul.ac.uk	without a cause.	10.1016/S0140-6736(12)60197-4.	
Wiborg JF, Knoop H, Frank LE, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands. j.wiborg@nkcv.umcn.nl	Towards an evidence-based treatment model for cognitive behavioral interventions focusing on chronic fatigue syndrome.	J Psychosom Res. 2012 May;72(5):399-404. doi: 10.1016/j.jpsychores.2012.01.018.	OBJECTIVE: The purpose of the present study was to develop a treatment model for cognitive behavioral interventions focusing on chronic fatigue syndrome (CFS) based on the model of perpetuating factors introduced by Vercoulen et al. [Journal of Psychosomatic Research 1998;45:507-17]. METHODS: For this purpose, we reanalyzed the data of a previously conducted randomized controlled trial in which a low intensity cognitive behavioral intervention was compared to a waiting list control group. Structural equation modeling was used to test a treatment model in which changes in focusing on symptoms, perceived problems with activity, and sense of control over fatigue were hypothesized to mediate the effect of our intervention on fatigue severity and disability. RESULTS: In the final model, which had a good fit to the data, the effect of treatment was mediated by a decrease in perceived problems with activity and an increase in sense of control over fatigue. CONCLUSION: Our findings suggest that cognitive behavioral interventions for CFS need to change the illness perception and beliefs of their patients in order to be effective.
Wiborg JF, Knoop H, Wensing M, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands. J.Wiborg@nkcv.umcn.nl	Therapist effects and the dissemination of cognitive behavior therapy for chronic fatigue syndrome in community-based mental health care.	Behav Res Ther. 2012 Jun;50(6):393-6. doi: 10.1016/j.brat.2012.03.002.	OBJECTIVE: The purpose of the present study was to explore the role of the therapist in the dissemination of manualized cognitive behavior therapy (CBT) for chronic fatigue syndrome (CFS) outside specialized treatment settings. METHOD: We used the routinely collected outcome data of three community-based mental health care centers (MHCs) which implemented and sustained CBT for CFS during the course of the study. Ten therapists, who all received the same training in CBT for CFS, and 103 patients with CFS were included. RESULTS: Random effects modeling revealed a significant difference in mean post-treatment fatigue between therapists. The effect of the therapist accounted for 21% of the total variance in post-treatment fatigue in our sample. This effect could be explained by the therapists' attitude toward working with evidence-based treatment manuals as well as by the MHC where CBT for CFS was delivered. CONCLUSION: The context in which CBT for CFS is delivered may play an important role in the accomplishment of established therapy effects outside specialized treatment settings. Due to the small sample size of MHCs and the different implementation scenarios in which they were engaged, our findings should be interpreted as preliminary results which are in need for replication.
Wiborg JF, Wensing M, Tummers M, Knoop H,	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical	Implementing Evidence-Based Practice for Patients with Chronic Fatigue	Clin Psychol Psychother. 2012 Dec 11. doi: 10.1002/cpp.1827	The aim of our study was to explore whether community-based mental health care centres (MHCs) are able to implement and sustain cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) with the help of an implementation manual. We monitored the implementation process and treatment outcome data of three Dutch

Bleijenberg G.	Centre, The Netherlands; Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Hamburg-Eppendorf & Schön Klinik Hamburg-Eilbek, Hamburg, Germany. j.wiborg@nkcv.umcn.nl.	Syndrome.		MHCs that implemented or sustained CBT for CFS, one in the context of a stepped care programme. We compared these data with findings of other treatment studies conducted in the context of CBT for CFS. All three MHCs included at least 40 patients with dropout rates between 15% and 35% from intention-to-treat to second assessment. Effect sizes ranged between 0.88 and 1.76 for changes in fatigue severity and 0.43 and 1.23 for changes in physical functioning. With one exception, these outcomes were within the range of our benchmark. Contrary to original expectations, we provided additional implementation support to the two MHCs new with CBT for CFS. We concluded that our implementation manual does not seem to substitute external support for team leaders and associated professions during initial implementation of CBT for CFS but may have the potential to make this assistance more efficient. Particular attention should be paid to challenges of implementing stepped care for CFS. ation of CBT for CFS in community-based MHCs was monitored. External support was provided in addition to an implementation manual during initial implementation of CBT for CFS. Participating MHCs were generally capable of successfully implementing and delivering CBT for CFS. Implementation of low-intensity interventions for CFS might better be postponed until therapists have sufficient experience with conventional CBT for CFS.
Wilkinson K, Shapiro C.	Department of Cell and Systems Biology, University of Toronto, 25 Harbord Street, Toronto, ON M5S 3G5, Canada. katewilk@gmail.com	Nonrestorative sleep: symptom or unique diagnostic entity?	Sleep Med. 2012 Jun;13(6):561-9. doi: 10.1016/j.sleep.2012.02.002. Comment in Sleep Med. 2012 Jun;13(6):557-8.	Nonrestorative sleep (NRS) refers to the subjective experience of sleep as insufficiently refreshing, often despite the appearance of normal sleep according to traditionally assessed objective parameters. This has led researchers to pursue alternative physiological markers of nonrestorative or unrefreshing sleep, though much of this research remains controversial and inconclusive. This review summarizes the recent findings on NRS in the literature and discusses some of the issues inherent in current efforts to define and measure NRS. We offer a summary of recommended clinical approaches to NRS and discuss a new potential paradigm for the assessment of NRS-an approach modelled on current diagnosis of insomnia.
Williams DK, Galvin TA, Ma H, Khan AS.	Laboratory of Retroviruses, Division of Viral Products, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892, USA.	Investigation of xenotropic murine leukemia virus-related virus (XMRV) in human and other cell lines.	Biologicals. 2011 Nov;39(6):378-83. doi: 10.1016/j.biologicals.2011.08.011.	Xenotropic murine leukemia virus-related virus (XMRV) was discovered in human prostate tumors and later in some chronic fatigue syndrome (CFS) patients. However, subsequent studies have identified various sources of potential contamination with XMRV and other murine leukemia virus (MLV)-related sequences in test samples. Biological and nucleotide sequence analysis indicates that XMRV is distinct from known xenotropic MLVs and has a broad host range and cell tropism including human cells. Therefore, it is prudent to minimize the risk of human exposure to infection by evaluating XMRV contamination in cell lines handled in laboratory research and particularly those used in the manufacture of biological products. Nested DNA PCR assays were optimized for investigating XMRV gag and env sequences in various cell lines, which included MRC-5, Vero, HEK-293, MDCK, HeLa, and A549, that may be used in the development of some vaccines and other cell lines broadly used in research. The sensitivity of the DNA PCR assays was <10 copies in approximately 1.8 x

				10(5) cells equivalent of human DNA. The results indicated the absence of XMRV in the cell lines tested; although in some cases DNA fragments identified as cellular sequences were seen following the first round of PCR amplification with the env primer pair.
Wright B, Beverley D.	Child, Adolescent & Family Unit, York, England, UK. Barry.Wright@nyypct.nhs.uk	Pervasive refusal syndrome.	Clin Child Psychol Psychiatry. 2012 Apr;17(2):221-8. doi: 10.1177/1359104511403680.	We report here on a case of severe pervasive refusal syndrome. This is of interest for three reasons. Firstly, most reported cases are adolescent girls; our case is regarding an adolescent boy. Secondly, he was successfully treated at home and thirdly, the serology showed an apparent infective pre-cursor to the illness with evidence of possible autoimmune serology. A 14-year old boy deteriorated from a picture where diagnosed CFS/ME developed into Pervasive Refusal Syndrome. This included the inability to move or speak, with closed eyes, multiple tics, facial grimacing, heightened sensitivity to noise (hyperacusis) and touch (hyperaesthesia), and inability or unwillingness to eat anything except small amounts of sloppy food. Successful rehabilitation is reported. Finally the issue of nomenclature is discussed, raising the question whether Pervasive Refusal Syndrome would be better renamed in a way that does not imply that the condition is always volitional and oppositional, as this can distract focus away from an alliance between family and clinicians.
Wu HS, Davis JE, Natavio T.	College of Nursing, Wayne State University, Detroit, MI, USA. wuh@wayne.edu	Fatigue and disrupted sleep-wake patterns in patients with cancer: a shared mechanism.	Clin J Oncol Nurs. 2012 Apr;16(2):E56-68. doi: 10.1188/12.CJON.E56-E68.	The strong and potentially reciprocal relationship between cancer-related fatigue (CRF) and disrupted sleep-wake patterns suggests a possible shared physiologic pathway. A growing body of evidence supports this and shows that abnormalities in the 24-hour rhythm of stress-related hormones may be related to chronic fatigue and sleep disturbances. Aberrations in the hypothalamic-pituitary-adrenal (HPA) axis, the primary neuroendocrine interface responding to stress, induce important biologic and behavioral consequences. HPA aberrations have long been associated with chronic fatigue syndrome. Many overlapping symptoms exist between chronic fatigue syndrome and CRF, including sleep disruption. Therefore, in the absence of knowledge about CRF mechanisms, emerging biologic models from chronic fatigue syndrome may assist in understanding the cause of CRF. Cancer-associated stressors also may alter the circadian functions of HPA-associated neuroendocrine activities, which result in the symptoms of fatigue and disrupted sleep-wake patterns in patients with cancer. Exploring promising physiologic models furthers the knowledge about CRF and disrupted sleep and may foster hypothesis-based studies of mechanisms that underlie apparent overlapping symptoms, providing the basis for new management to improve sleep and lessen fatigue.
Xu W, Zhou RH, Li L, Jiang MW.	Acupuncture and Moxibustion Department, The Third People's Hospital of Hangzhou City, Hangzhou 310009,	Observation on therapeutic effect of chronic fatigue syndrome treated with coiling dragon needling and moving	Zhongguo Zhen Jiu. 2012 Mar;32(3):205-8.	OBJECTIVE: To compare the differences of therapeutic effect of chronic fatigue syndrome treated with the combined therapy of coiling dragon needling and cupping on back and the western medicine therapy with Prednisone. METHODS: Seventy-two cases were randomly divided into an acupuncture and cupping group (37 cases) and a Prednisone group (35 cases). In acupuncture and cupping group, Jiaji (EX-B 2) points of T1--L5 were applied with coiling dragon needling (once a day), combined with

	Zhejiang Province, China. xwxw217@163.com	cupping on back. [Article in Chinese]		moving cupping on back (once every two days); in Prednisone group, Prednisone tablets were orally taken for 10 mg at 8:00 am. Seven days made one course, and 2 courses were carried on totally. FS-14 scale and BELL's chronic fatigue syndrome integral table were applied to evaluate the fatigue degree of patients before and after treatment, and the therapeutic effects of both groups were compared. RESULTS: After one course of treatment, the BELL's scores of both groups were obviously improved (both P < 0.01), but there was no significant difference between groups (P > 0.05); after two courses of treatment, the BELL's score in acupuncture and cupping group improved more obviously than that in Prednisone group, and the total effective rate of 91.9% (34/37) in acupuncture and cupping group was superior to that of 71.4% (25/35) in Prednisone group (P < 0.05). CONCLUSION: The therapeutic effect of chronic fatigue syndrome treated with coiling dragon needling and moving cupping on back is positive, superior to that of Prednisone with oral administration.
Yamamoto S, Ouchi Y, Nakatsuka D, Tahara T, Mizuno K, Tajima S, Onoe H, Yoshikawa E, Tsukada H, Iwase M, Yamaguti K, Kuratsune H, Watanabe Y.	Department of Physiology, Osaka City University Graduate School of Medicine, Abeno-ku, Osaka, Japan ; Central Research Laboratory, Hamamatsu Photonics KK, Hamakita, Shizuoka, Japan.	Reduction of [(11)C](+)3-MPB Binding in Brain of Chronic Fatigue Syndrome with Serum Autoantibody against Muscarinic Cholinergic Receptor.	PLoS One. 2012;7(12):e51515. doi: 10.1371/journal.pone.0051515.	BACKGROUND: Numerous associations between brain-reactive antibodies and neurological or psychiatric symptoms have been proposed. Serum autoantibody against the muscarinic cholinergic receptor (mAChR) was increased in some patients with chronic fatigue syndrome (CFS) or psychiatric disease. We examined whether serum autoantibody against mAChR affected the central cholinergic system by measuring brain mAChR binding and acetylcholinesterase activity using positron emission tomography (PET) in CFS patients with positive [CFS(+)] and negative [CFS(-)] autoantibodies. METHODOLOGY: Five CFS(+) and six CFS(-) patients, as well as 11 normal control subjects underwent a series of PET measurements with N-[(11)C]methyl-3-piperidyl benzilate [(11)C](+)3-MPB for the mAChR binding and N-[(11)C]methyl-4-piperidyl acetate [(11)C]MP4A for acetylcholinesterase activity. Cognitive function of all subjects was assessed by neuropsychological tests. Although the brain [(11)C](+)3-MPB binding in CFS(-) patients did not differ from normal controls, CFS(+) patients showed significantly lower [(11)C](+)3-MPB binding than CFS(-) patients and normal controls. In contrast, the [(11)C]MP4A index showed no significant differences among these three groups. Neuropsychological measures were similar among groups. CONCLUSION: The present results demonstrate that serum autoantibody against the mAChR can affect the brain mAChR without altering acetylcholinesterase activity and cognitive functions in CFS patients.
Yancey JR, Thomas SM.	Fort Belvoir Community Hospital, Fort Belvoir, VA 22060, USA. joe.yancey@us.army.mil	Chronic fatigue syndrome: diagnosis and treatment.	Am Fam Physician. 2012 Oct 15;86(8):741-6.	Chronic fatigue syndrome is characterized by debilitating fatigue that is not relieved with rest and is associated with physical symptoms. The Centers for Disease Control and Prevention criteria for chronic fatigue syndrome include severe fatigue lasting longer than six months, as well as presence of at least four of the following physical symptoms: postexertional malaise; unrefreshing sleep; impaired memory or concentration; muscle pain; polyarthralgia; sore throat; tender lymph nodes; or new headaches. It is a clinical diagnosis that can be made only when other disease processes are excluded. The etiology of chronic fatigue syndrome is unclear, is likely

				complex, and may involve dysfunction of the immune or adrenal systems, an association with certain genetic markers, or a history of childhood trauma. Persons with chronic fatigue syndrome should be evaluated for concurrent depression, pain, and sleep disturbances. Treatment options include cognitive behavior therapy and graded exercise therapy, both of which have been shown to moderately improve fatigue levels, work and social adjustment, anxiety, and postexertional malaise. No pharmacologic or alternative medicine therapies have been proven effective.
Yoldi B.	[No address quoted]	Cognitive disorder: a reality in the chronic fatigue syndrome. [Article in Spanish]	Med Clin (Barc). 2011 Nov 12;137(12):572; author reply 572-3. doi: 10.1016/j.medcli.2011.03.035 .	Comment on Med Clin (Barc). 2011 Mar 12;136(6):248-9.Med Clin (Barc). 2011 Mar 12;136(6):239-43.
Young JL.	Wayne State University School of Medicine, Detroit, MI, USA; William Beaumont Hospital, Royal Oak, MI, USA; Rochester Center for Behavioral Medicine, Rochester Hills, MI, USA. Electronic address: jyoung@rcbm.net.	Use of Lisdexamfetamine dimesylate in treatment of executive functioning deficits and chronic fatigue syndrome: A double blind, placebo-controlled study.	Psychiatry Res. 2012 Oct 9. pii: S0165-1781(12)00503-3. doi: 10.1016/j.psychres.2012.09.007.	The purpose of this study was to assess the efficacy of lisdexamfetamine dimesylate (LDX) for the treatment of executive functioning deficits in adults (ages 18-60) with chronic fatigue syndrome (CFS). The study's primary outcome measure was the Behavior Rating Inventory of Executive Function-Adult (BRIEF-A). Secondary outcome measures were standardized assessments of fatigue, pain and global functioning. Twenty-six adults who met criteria for CFS and had clinically significant executive functioning deficits were randomly assigned to a flexible morning dose (30, 50, 70mg/day) of either placebo or LDX for a six-week trial. The data were analyzed with standard analysis of variance (ANOVA) procedures. Participants in the LDX group showed significantly more positive change in BRIEF-A scores (M(change)=21.38, SD=15.85) than those in the placebo group (M(change)=3.36, SD=7.26), p=0.005, d=1.46. Participants in the active group also reported significantly less fatigue and generalized pain relative to the placebo group. Although future studies with LDX should examine whether these benefits generalize to larger, more diverse samples of patients, these results suggest that LDX could be a safe and efficacious treatment for the executive functioning deficits often associated with CFS. The possibility that dopaminergic medications could play an important role addressing the symptoms of CFS is also discussed.
Yunus MB.	Section of Rheumatology, Department of Medicine, University of Illinois College of Medicine at Peoria, One Illini Drive, Peoria, IL 61605, USA.	The prevalence of fibromyalgia in other chronic pain conditions.	Pain Res Treat. 2012;2012:584573. doi: 10.1155/2012/584573.	Central sensitivity syndromes (CSS) include fibromyalgia syndrome (FMS), irritable bowel syndrome, temporomandibular disorder, restless legs syndrome, chronic fatigue syndrome, and other similar chronic painful conditions that are based on central sensitization (CS). CSS are mutually associated. In this paper, prevalence of FMS among other members of CSS has been described. An important recent recognition is an increased prevalence of FMS in other chronic pain conditions with structural pathology, for example, rheumatoid arthritis, systemic lupus, ankylosing spondylitis, osteoarthritis, diabetes mellitus, and inflammatory bowel disease. Diagnosis and proper management of FMS among these diseases are of crucial importance so that unwarranted use of such medications as corticosteroids can be

				avoided, since FMS often occurs when RA or SLE is relatively mild.
Zhang HY, Liu ZD, Hu CJ, Wang DX, Zhang YB, Li YZ.	Department of Rheumatology and Clinical Immunology, Peking Union Medical College Hospital, Chinese Academy of Medical Science, No. 1 Shuaifuyuan, Beijing, China.	Up-regulation of TGF-β1 mRNA expression in peripheral blood mononuclear cells of patients with chronic fatigue syndrome.	J Formos Med Assoc. 2011 Nov;110(11):701-4. doi: 10.1016/j.jfma.2011.09.006.	BACKGROUND/PURPOSE: It has been shown that the abnormality in immune cells in chronic fatigue syndrome (CFS) patients is closely associated with the participation of TGF-β. In order to study the relationship between TGF-β1 and CFS, we investigated the mRNA levels of TGF-β1 in peripheral blood mononuclear cells (PBMCs) in patients with CFS. METHODS: Fluorescent quantitative real time reverse-transcription polymerase chain reaction (FQ-RT-PCR) was performed to test TGF-β1 mRNA expression in PBMCs in 63 cases of CFS, 50 cases of disease controls, and 50 cases of healthy controls. RESULTS: The mean value of TGF-β1 mRNA expression in CFS patients was ΔΔCt=1.17±0.58, which was significantly higher than the disease controls (ΔΔCt=0.07±1.08, df=111, $p < 0.01$) and the healthy controls (ΔΔCt=0.00±1.63, df=111, $p < 0.01$). No significant difference was detected between disease and healthy controls ($p > 0.05$). CONCLUSION: The expression of TGF-β1 in PBMCs is significantly elevated in patients with CFS. It might be correlated to the pathogenesis of the disease.
Zhang W, Liu ZS, Xu HR, Liu YS.	Guang'anmen Hospital, China Academy of Chinese Medical Sciences, Beijing 100053, China. zhangwei_7108@sohu.com	Observation on therapeutic effect of acupuncture of Back-shu acupoints for chronic fatigue syndrome patients. [Article in Chinese]	Zhen Ci Yan Jiu. 2011 Dec;36(6):437-41, 448.	OBJECTIVE: To observe the therapeutic effect and safety of acupuncture of Back-shu points [Xinshu (BL 15), Pishu (BL 20), etc.] in the treatment of chronic fatigue syndrome (CFS). METHODS: A total of 120 CFS patients were equally randomized Into acupuncture and control groups. Acupuncture needles were inserted into bilateral Xinshu (BL 15), Pishu (BL 20), and Gaohuang (BL 43) points, once daily for 4 weeks except weekends. For patients of the control group, acupuncture needles were inserted into the shallow layer of the non-acupoints (two mid-points of the horizon lines passing through the crossing-points of the 1st and 2nd branches of the Gallbladder Meridian and the crests of 4th, 5th and 11th thoracic vertebrae). General health scale (SF-20) and Chalder fatigue scale were used to measure the CFS patients' degree of general health. A follow-up survey was carried out 3 months after the last treatment. RESULTS: In comparison with pre-treatment, the scores of Chalder fatigue scale were decreased significantly in both treatment and control groups ($P < 0.01$), while the scores of physiological function (PF) and general health (GH) of SF-20 in both acupuncture groups and those of the role function (RF), social function (SF), mental health (MH) and pain sensation (PS) in the treatment group were increased apparently after the treatment ($P < 0.05$, $P < 0.01$). The scores of Chalder Scale and PF, RF, SF, GH, MH, PS and the CFS patients' satisfication degrees 4 weeks (64.4% and 36.7%) and 3 months (62.3% and 32%) after the treatment in the treatment group were significantly superior to those of the control group ($P < 0.05$). CONCLUSION: Acupuncture at Back-shu point has a good therapeutic effect (including immediate and midterm effect) in the treatment of chronic fatigue syndrome patients.
Zheng H, Jia H, Shankar A, Heneine W,	Laboratory Branch, Division of HIV/AIDS Prevention, National	Detection of murine leukemia virus or mouse DNA in	PLoS One. 2011;6(12):e29050. doi: 10.1371/journal.pone.002905	The xenotropic murine leukemia virus (MLV)-related viruses (XMRV) have been reported in persons with prostate cancer, chronic fatigue syndrome, and less frequently in blood donors. Polytropic MLVs have also been described in persons with

Switzer WM.	Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America.	commercial RT-PCR reagents and human DNAs.	0.	CFS and blood donors. However, many studies have failed to confirm these findings, raising the possibility of contamination as a source of the positive results. One PCR reagent, Platinum Taq polymerase (pol) has been reported to contain mouse DNA that produces false-positive MLV PCR results. We report here the finding of a large number of PCR reagents that have low levels of MLV sequences. We found that recombinant reverse-transcriptase (RT) enzymes from six companies derived from either MLV or avian myeloblastosis virus contained MLV pol DNA sequences but not gag or mouse DNA sequences. Sequence and phylogenetic analysis showed high relatedness to Moloney MLV, suggesting residual contamination with an RT-containing plasmid. In addition, we identified contamination with mouse DNA and a variety of MLV sequences in commercially available human DNAs from leukocytes, brain tissues, and cell lines. These results identify new sources of MLV contamination and highlight the importance of careful pre-screening of commercial specimens and diagnostic reagents to avoid false-positive MLV PCR results.
Zhou Y, Steffen I, Montalvo L, Lee TH, Zemel R, Switzer WM, Tang S, Jia H, Heneine W, Winkelman V, Tailor CS, Ikeda Y, Simmons G.	Blood Systems Research Institute, Department of Laboratory Medicine, University of California at San Francisco, San Francisco, California 94118, USA.	Development and application of a high-throughput microneutralization assay: lack of xenotropic murine leukemia virus-related virus and/or murine leukemia virus detection in blood donors.	Transfusion. 2012 Feb;52(2):332-42. doi: 10.1111/j.1537-2995.2011.03519.x.	BACKGROUND: Xenotropic murine leukemia virus (MLV)-related virus (XMRV) and other related MLVs have been described with chronic fatigue syndrome and certain types of prostate cancer. In addition, prevalence rates as high as 7% have been reported in blood donors, raising the risk of transfusion-related transmission. Several laboratories have utilized microneutralization assays as a surrogate marker for detection of anti-MLV serologic responses--with up to 25% of prostate cancer patients reported to harbor neutralizing antibody responses. STUDY DESIGN AND METHODS: We developed a high-throughput microneutralization assay for research studies on blood donors using retroviral vectors pseudotyped with XMRV-specific envelopes. Infection with these pseudotypes was neutralized by sera from both macaques and mice challenged with XMRV, but not preimmune serum. A total of 354 plasma samples from blood donors in the Reno/Tahoe area were screened for neutralization. RESULTS: A total of 6.5% of donor samples gave moderate neutralization of XMRV, but not control pseudotypes. However, further testing by Western blot revealed no evidence of antibodies against MLVs in any of these samples. Furthermore, no evidence of infectious virus or viral nucleic acid was observed. CONCLUSION: A microneutralization assay was developed for detection of XMRV and can be applied in a high-throughput format for large-scale studies. Although a proportion of blood donors demonstrated the ability to block XMRV envelope-mediated infection, we found no evidence that this inhibition was mediated by specific antibodies elicited by exposure to XMRV or MLV. It is likely that this moderate neutralization is mediated through another, nonspecific mechanism.

From the Bulletin of the IACSF/ME 2005–2012				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Stormorken E	[no address given]	[Media attention]. Article in Norwegian.	Tidsskr Nor Laegeforen. 2012 Mar 6;132(5):509-10	[no abstract available]
[No authors listed]	[no address given]	[No title given]	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P152	Objective: We present case studies/ case series of Fibromyalgia (FMS) patients treated with an interdisciplinary approach. Method: The 4 component model (Klinghardt) for treating chronic pain and disease helps to conceptualize an approach for FMS. This involves identifying and treating underlying root causes for pain and dysfunction in 4 areas: Structural – Biochemical – Psychoemotional – Neurological. This approach as a model for multi-modal/ multi-disciplinary treatment will be illustrated. Results Structural: A case series of 25 FMS patients treated effectively with Botulinum Toxin-A injections will be presented. Such injections into myofascial trigger points and tender points often do not work and may exacerbate FMS pain. Injections do work when done on a biomechanical basis (correcting postural misalignments and upper/ lower crossed syndromes) and when combined with specialized manual therapy and exercise. (Ko G, Whitmore S et.al. J Musculoskel Pain 2007;15(4):55-66.). Preliminary results from a double-blind randomized controlled pilot study may also be presented. Platelet-rich Plasma Prolotherapy for sacroiliac ligament laxity were also helpful in posttraumatic (motor-vehicle accident) cases. (Ko G. Pract Pain Manage 2010;10(7):55-68) Biochemical: Case studies of FMS-CFS patients improved with Functional Medicine and Bioidentical Hormone replacement therapy will be presented. This includes the use of omega 3 fatty acids (at a high dose) to improve pain and mood. (Ko G, Arseneau L et.al. Clin J Pain 2010; 26(2):168-72. Psychoemotional: A FMS case study using EEG biofeedback / neurotherapy will be presented. This patient was followed over 5 years and had significant amelioration of pain, improvement in “fibrofog” and in sleep. (Ko G, Gottfried B et.al Crit Rev Phys Rehabil Med 2005;17:1-30) Neurological: Case series of recalcitrant FMS patients with allodynia who responded to unique multimodal combinations of neuropathic pain medications will be presented. This included combinations of Pregabalin, SNRIs, tramadol and cannabinoids. (Hum A et.al. Pain Res Manage 2008;13:137). Topical medication use from essential oils (J Musculoskel Pain 2007;15(1):11-20) to compounded pain gels will be described as well. Conclusion: These cases demonstrate the diversity in assessment for underlying causes and the need for individualized treatment in FMS. Randomized clinical trials may need to focus on specific subgroups of FMS patients to demonstrate clinical effectiveness.
Alegre, J; DeMeirleir, K; Frémont, M;	Chronic Fatigue Syndrome Unit, Hospital Universitari	Effects of Alpha1-Proteinase Inhibitor in Peripheral Blood	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International	Introduction: Immune dysregulation of 2-5A oligoadenylate synthetase/ribonuclease (RNase) L antiviral pathway has been widely reported in chronic fatigue syndrome (CFS). Proteolytic cleavage of RNase L (83 kDa) by elastase generate hyperactivated

Campuri, S	Vall d'Hebron, Barcelona Spain.	Mononuclear Cells of Chronic Fatigue Syndrome Patients	Conference. Poster Presentations. P167-168.	low molecular weight forms of RNase L (37 kDa) and ankyrin-like fragments in peripheral blood mononuclear cells (PBMC) of CFS patients. Ankyrin-like RNase L domain might disrupt ABC transporter function, accounting for physiological symptoms of CFS [1]. We hypothesized that alpha1-proteinase inhibitor (A1PI) could inhibit intracellular elastase activity to prevent RNase L proteolytic cleavage in PBMC of CFS. Objectives: To demonstrate that A1PI is capable of inhibiting intracellular elastase activity of cultured PBMC from CFS patients. Methods: Peripheral blood was drawn from 7 CFS patients fulfilling Fukuda criteria [2] and 5 healthy subjects. Extracts of freshly isolated PBMC were prepared and PBMC cultures were grown in RPMI medium without serum or antibiotics for 12 hours. One third of cultured cells were left untreated and the rest was treated with human plasma-derived A1PI at two different doses (3 g/l and 6 g/l) for 12 hours. After that, cells were harvested to obtain cytoplasmatic extracts. Elastase activity [3] was measured in all samples (mean ± SD). Results: PBMC extracts showed mean baseline elastase activity levels of 86±33 U/mg in healthy subjects and 323±106 U/mg in CFS patients. After PBMC culture, a marked increase of intracellular elastase activity was observed in both healthy subjects and CFS patients (up to 757 U/mg and 1503 U/mg, respectively). PBMC cultures in presence of A1PI 3 g/l showed significantly lower intracellular elastase activity, with mean values of 70±14 U/mg in healthy subjects and 132±90 U/mg in CFS patients. Similar results were obtained in presence of A1PI 6 g/l, with mean values of 62±10 U/mg in healthy subjects and 73±18 U/mg in CFS patients. Conclusion: In this study it was observed that A1PI strongly inhibited intracellular elastase activity in PBMC of CFS patients. Further research should examine the A1PI effect on proteolytic cleavage of RNase L. Nevertheless, the results indicate that the use human A1PI can be a promising therapeutic agent in the management of CFS.
Alegre, J; Garcia Quintana, AM; Karaki, M; Aliste, E; Montaner, L; Saez, N; Fernandez de Sevilla, T	Unidades del CFS. Hospital Vall d´Hebrón y Centro Médico Delfos. Barcelona. Spain.	Profile of the Patient with Chronic Fatigue Syndrome, Experience with a Population-Based Registry	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P185-186.	Objectives: In Spain, there are no epidemiologic studies analyzing the characteristics of patients diagnosed with chronic fatigue syndrome (CFS) according to the criteria of Fukuda. Thus, the prevalence and incidence of this nosologic condition, which causes considerable disability in personal, social, and work-related activity, is currently unknown. This study determines the sociodemographic, clinical, and therapeutic characteristics of a large series of CFS patients in our setting. Patients and Method: All patients who consulted for disabling chronic fatigue and met the diagnostic criteria of Fukuda were included. Patients underwent a diagnostic protocol that included complete laboratory analyses, chest x-ray, abdominal ultrasound, and psychiatric assessment. Sociodemographic data, symptoms, work situation, and treatments prescribed at the time of the diagnosis were recorded. Results: The study included 981 patients with CFS (91 men and 890 women), with a mean age of 47.9 years, 66% were married, 60% carried out specialized work, and 7% were housewives. Among the total, 60% had a secondary school or university education. There was a family background of CFS in 12%, fibromyalgia in 10%, and other immunological diseases in

				26.4%. The mean age at the onset of symptoms was 37.5 years and the mean interval from the onset of fatigue to the diagnosis was 116,5 months. The onset was sudden in 20% and gradual in 61%. An evident trigger was documented in 60% (infection, delivery, and a stressful life event). At the time of the diagnosis, 62.5% of patients were not working (sick leave 34% and work disability 37%). The treatment received at diagnosis included medication for the symptoms (analgesic, anxiolytic, and antidepressive agents) in 78.3%, alternative treatments in 3%, and programmed physical exercise and/or cognitive behavioural therapy in 5%. Conclusions: When evaluating a patient with incapacitating chronic fatigue, it is essential to identify cases that meet the criteria for CFS. In our setting, this condition predominantly affects middle-aged women who have a secondary or university education and work at specialized jobs. The onset of symptoms often occurs following an identifiable trigger. The condition leads to severe dysfunction in the personal, social, and work-related activities of daily life.
Alegre, J; Garcia-Quintana, AM; Ruiz, E; Aliste, L; Javierre, C; De Meirleir, K; Saez, N; Suarez, A; Fernández de Sevilla, T	Unidades del CFS Vall d´Hebron y Centro Médico Delfos de Barcelona (Spain)	Impact of Neurovegetative Symptoms on Patients Who Are Diagnosed With CFS And Have No History of Syncope	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P196.	Objective: Neurovegetative symptoms, such as dizziness, syncope, abnormal intestinal and bladder rhythms, sweating, and accommodation, were not initially contemplated in the diagnostic criteria of Fukuda for CFS. They acquired more importance later, when the Canadian criteria were established. In this study, the impact of neurovegetative symptoms is investigated in a group of patients with no prior history of syncope and a diagnosis of CFS. Patients and Method: The study included patients with no history of syncope, diagnosed with CFS according to the Fukuda criteria. Sociodemographic and work-related variables, symptoms, and comorbid phenomena were recorded. The impact of fatigue was assessed with the fatigue impact scale (FIS), SF-36 quality of life questionnaire, hospital anxiety and depression scale (HADS), and the maximum oxygen consumption, maximum cardiac output, maximum heart rate, and energy expenditure on stress testing. Biological markers were determined in peripheral blood monocytes (RNase L ratio, RNase L activity and elastase activity), and serum nitric oxide concentration was measured. Symptoms from the neurovegetative, neurocognitive, muscular, and immunological groups were categorized using the Cronbach alpha value. Associations between neurovegetative symptoms and the remaining variables were studied. Results: Thirty-seven CFS patients (4 men, 33 women), with a mean age of 48 years were studied. Among the total, 60% had a middle school educational level and specialized jobs, 65% reported a gradual symptoms onset, and the interval from symptoms onset to the diagnosis was 136 months. Neurocognitive, muscular, and immunologic symptoms were present in 95%, 87%, and 78% of patients, respectively. Neurovegetative symptoms were documented in 90%. Myofascial syndrome was found in 84%, dry syndrome 86%, and tendinopathy 62%. The total FIS score was 131.8, physical subscale 35.6, psychosocial 62.3, and cognitive 40. The SF-36 physical health score was 25.7 and mental health 36.1. The anxiety-depression component was 11.3. In

				addition, maximum oxygen consumption 57.1%, maximum cardiac output 67.1, maximum heart rate, 115.6 bpm and energy expenditure 4.6. RNase L ratio 0.54, RNase L activity 16.9, elastase activity 198.3, and nitric oxide 7.35. There was a significant association between neurovegetative dysfunction and the presence of painful lymph nodes (p=0.012), food intolerance (p=0.013), and monocyte elastase levels (p=0.02). Discussion: In CFS patients with no prior history of syncope, a considerable deterioration in quality of life and physical functional capacity was found, as well as high scores on the fatigue and anxiety-depression scales. Neurovegetative symptoms were common and showed a significant association with immunological symptoms and intracellular parameters of inflammatory activity.
Alegre, J; Moya, A; Garcia-Quintana, AM; Javierre, C; De Meirleir, K; Aliste, L; Fernández de Sevilla, T	Unidades del CFS Vall d´Hebron y Centro Médico Delfos de Barcelona (Spain)	Heart Rate Variability Evaluated with the LF/HF Ratioi of Sympatetic-Parasympathetic Activity in the Assessment of Neurovegetative Dysfunction in Patients with Chronic Fatigue Syndrome and No History of Syncope	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P195-196.	Objective: In chronic fatigue syndrome (CFS) neurovegetative symptoms have acquired relevance through the Canadian diagnostic criteria. As is the case of other highly disabling symptoms of this condition, resources are needed to quantify these neurovegetative manifestations. We propose assessment of heart rate variability by means of the LF/HF ratio determined on orthostatic positioning with tilt table testing in CSF patients with no prior history of syncope. Patients and Method: The study included patients with no history of syncope, diagnosed with CFS according to the Fukuda criteria. Neurovegetative, muscular, neurocognitive, and immunologic symptoms were recorded. Patients were evaluated with the fatigue impact scale (FIS), SF-36 quality of life questionnaire, hospital anxiety and depression scale (HADS), and stress testing (maximum oxygen consumption, maximum cardiac output, maximum heart rate, and energy expenditure). Biological markers were determined (RNase L ratio, RNase L activity, elastase activity, and serum nitric oxide concentration). The LF, HF and LF/HF ratio were evaluated on tilt table testing, with 3 determinations 5 minutes apart in supine position and 8 in orthostatic position. The *t*-test for paired samples was used to analyze trends. Associations between variables were examined with the chi-square test, *t* test, or Mann- Whitney test. Results: Thirty-seven CFS patients were studied (4 men, 33 women), with a mean age of 48 years; 65% had a gradual fatigue onset, and the interval from onset to diagnosis was 136 months. Neurocognitive, muscular, and immunologic symptoms were present in 95%, 87%, and 78% of patients, and neurovegetative symptoms in 90%. The total FIS score was 131.8, physical subscale 35.6, psychosocial 62.3, and cognitive 40. The SF-36 physical health score was 25.7 and mental health 36.1. The anxiety-depression component was 11.3. In addition, maximum oxygen consumption 57.1%, maximum cardiac output 67,1, maximum heart rate, 115.6 bpm and energy expenditure 4,6. RNase L ratio was 0.54, RNase L activity 16,9 elastase activity 198,3, and nitric oxide 7.35. Differences in the heart rate variability parameters (LF, HF and LF/HF ratio) were found between supine position and at 5 minutes of orthostatism, with an increase in the LF or sympathetic component. During the next 30 minutes in orthostasis, no changes were observed in the LF/HF ratio, with persistence of the excess sympathetic response. The

				mean LF/HF ratio was 4.88 and a significant association was found with the presence of Raynaud phenomenon, altered libido, SF-36 role-emotional and total mental health, and the depressive component on the HADS, as well as considerable (but non-significant) associations with the FIS psychosocial subscale (p=0.08) and RNase L (p=0.09) ratio. Discussion: In patients with CFS and neurovegetative symptoms without prior syncope, a maintained, predominantly sympathetic neurovegetative response, as assessed with the LF/HF ratio of heart rate variability, was seen on tilt table testing.
Alegre, J; Moya, A; Garcia-Quintana, AM; Javierre, C; De Meirleir, K; Aliste, L; Ruiz, E; Fernández de Sevilla, T	Unidades del CFS Vall d´Hebron y Centro Médico Delfos de Barcelona (Spain)	TILT Testing to Assess Neurovegetative Dysfunction in Patients with Chronic Fataigue Syndrome (CFS) and No History of Syncope	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P197.	Objective: Neurovegetative symptoms are very debilitating in CFS patients and there are few available resources to measure, quantify, or treat them. In this study we investigate the neurovegetative response to orthostatic positioning with the use of a tilt table in CFS patients with no prior history of syncope. Patients and Method: The study included patients diagnosed with CFS according to the Fukuda criteria, with no history of syncope. Data were compiled on patients' neurovegetative symptoms, scores on the fatigue impact scale (FIS), hospital anxiety and depression scale (HADS), and SF-36 quality of life questionnaire, physical capacity results (maximum oxygen consumption, maximum cardiac output, maximum heart rate, and energy expenditure) during stress testing, biological markers including monocyte RNase L ratio, RNase L activity, and elastase activity, and serum nitric oxide concentration. The following variables were evaluated on tilt table testing: heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, systolic volume, and peripheral vascular resistance (PVR), with 3 determinations 5 minutes apart in the supine position and 8 in orthostatic position. Results: Thirty-seven CFS patients were studied (4 men, 33 women), with a mean age of 48 years at diagnosis, 65% with a gradual onset, and an interval from onset to the diagnosis of 136 months. Neurovegetative symptoms were documented in 90%. The total FIS score was 131.8, physical subscale 35.6, psychosocial 62.3, and cognitive 40. The SF-36 physical health score was 25.7 and mental health 36.1. The anxiety-depression component was 11.3. In addition, maximum oxygen consumption was 57.1%, maximum cardiac output 67,1, maximum heart rate, 115.6 bpm and energy expenditure 4.6. RNase L ratio was 0.54, RNase L activity 16.9, elastase activity 198,3 and nitric oxide 7,35. Tilt table testing was positive in one patient with a mixed cardiovascular response. There were no asymptomatic cardiovascular responses, such as orthostatic intolerance, postural tachycardia or hypertensive tachycardia. Significant differences in the cardiovascular parameters were found between supine position and at 5 minutes of orthostasis, with a pattern characterized by a considerable increase in the PVR, and a smaller increase in systolic blood pressure, with a decrease in the systolic volume and cardiac output. Once the orthostatic position was stabilized, there were no changes in the cardiovascular parameters over the next 30 minutes, with persistence of this predominantly sympathetic response. Discussion: In patients with CFS,

				neurovegetative symptoms, and no prior history of syncope, a predominantly sympathetic noradrenergic response is elicited with tilt table testing.
Alegre, J; Sáez Francàs, N; Calvo, N; Ruiz E; Valero, S; López, MV; Olivreas B; Fernández de Sevilla, T; Casas, M	Unidad del CFS. Hospital Vall d´Hebron, Barcelona. Spain. Servicio de Psiquiatria. Hospital Vall d´Hebrón. Barcelona. Spain.	Adverse Childhood Experiences as a Risk Factor for Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P174.	Introduction: Chronic Fatigue Syndrome (CFS) is characterized by severe, disabling fatigue and other symptoms, including musculoskeletal pain, sleep disturbance, attentional impairment, and anxiety. Although its etiology is not completely understood, it is considered that it is determined by biological, psychological and social factors. Adverse childhood experiences have been described as one of the major environmental risk factors for CFS. Aim: To evaluate the prevalence of different childhood traumas in a sample of adult CFS patients and the contribution of them in CFS symptoms profile. Methods: The initial sample consisted of 142 patients, of whom 9 were excluded because of severe psychopathology or incomplete evaluation. All the patients (age 48±8,9; 92,9% women) received CFS diagnoses according to Fukuda criteria. Childhood traumatic events were assessed by clinical interview in a dichotomous pattern. The scales FIS- 40 and HAD were administrated. Results: 74 (40,4%) patients reported some adverse childhood experience (ACE) [19 (10,4%) physical abuse, 19 (10,4%) sexual abuse, 25 (13,7%) emotional neglect, 27 (14,8%) bulling]. When comparing those with some ACE with those without it, there were no differences in Fukuda criteria profile, FIS-40 (124,47±24,56 vs 124,08±26,26; p=0,94), HAD-Anxiety (10,38±4,95 vs 10,65±5,08; p=0,81) and HAD-Depression (10,54±5,50)
Alegre, Jose; Ruiz, E; Quintana, AM; Karaki, M; Aliste, E; Montaner, L; Saez, N; de Sevilla, T;	Unidades del CFS Hospital Vall d´Hebrón y Centro Médico Delfos, Barcelona. Spain	Profile of the Patient with Chronic Fatigue Syndrome; Experience with a Population Based Registry	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference.p131.	Objectives: In Spain, there are no epidemiologic studies analyzing the characteristics of patients diagnosed with chronic fatigue syndrome (CFS) according to the criteria of Fukuda. Thus, the prevalence and incidence of this nosologic condition, which causes considerable disability in personal, social, and work-related activity, is currently unknown. This study determines the sociodemographic, clinical, and therapeutic characteristics of a large series of CFS patients in our setting. Patients and Method: All patients who consulted for disabling chronic fatigue and met the diagnostic criteria of Fukuda were included. Patients underwent a diagnostic protocol that included complete laboratory analyses, chest x-ray, abdominal ultrasound, and psychiatric assessment. Sociodemographic data, symptoms, work situation, and treatments prescribed at the time of the diagnosis were recorded. Results: The study included 981 patients with CFS (91 men and 890 women), with a mean age of 47.9 years, 66% were married, 60% carried out specialized work, and 7% were housewives. Among the total, 60% had a secondary school or university education. There was a family background of CFS in 12%, fibromyalgia in 10%, and other immunological diseases in 26.4%. The mean age at the onset of symptoms was 37.5 years and the mean interval from the onset of fatigue to the diagnosis was 116,5 months. The onset was sudden in 20% and gradual in 61%. An evident trigger was documented in 60% (infection, delivery, and a stressful life event). At the time of the diagnosis, 62.5% of patients were not working (sick leave 34% and work disability 37%). The treatment received at diagnosis included medication for the symptoms (analgesic, anxiolytic, and

				antidepressive agents) in 78,3%, alternative treatments in 3%, and programmed physical exercise and/or cognitive behavioral therapy in 5%. Conclusions: When evaluating a patient with incapacitating chronic fatigue, it is essential to identify cases that meet the criteria for CFS. In our setting, this condition predominantly affects middle-aged women who have a secondary or university education and work at specialized jobs. The onset of symptoms often occurs following an identifiable trigger. The condition leads to severe dysfunction in the personal, social, and work related activities of daily life.
Alegre, Jose; Santamarina-Perez, P, Eiroa-Orosa, FJ; Jacas, C; Ruiz, E; Casas, M; Fernández de SEvilla, T	Psychiatry Department and Unidad del CFS. Hospital Universitari Vall d´Hebron, Barcelona. Spain	Validation of a Neuropsychological Battery in a Sample of Patients with Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P174-175.	Objectives: Some cognitive deficits have been identified, although the findings are inconsistent and hindered by methodological heterogeneities. One of these limitations is the used neuropsychological battery. Some studies show that cognitive measures that share variance in healthy people can dissociate and contribute to unique variance in people with some cognitive impairment. They suggest that the validity in neuropsychological measures should be tested in homogeneous samples. The aim of this study was to test the validity of a neuropsychological battery in a sample of patients with CFS. Methods: Sixty-eight women, aged between 29 and 67 years-old and diagnosed with CFS according to the criteria of Fukuda were enrolled. We excluded patients with mental disorders (except depression reactive to illness) and organic diseases that can course with cognitive impairment. Patients were assessed with the following neuropsychological test: Mental Control, Paced Auditory Serial Addition Test, Digit Span, Symbol Digit Modalities Test, Stroop Test, Trail-Making Test, verbal fluency test, Tower of London test, Rey Auditory Verbal Learning test, Rey-Osterreith Complex Figure and Grooved pegboard. Twenty-five cognitive measures were obtained. Because the multidimensionality of the cognitive functions studied, principal components analyses including all the measures were carried in order to assure that each one was comprised of only one cognitive dimension. Results: The neuropsychological measures were categorized into 7 specific cognitive domains: Attention/concentration, divided attention, verbal memory, visual memory, executive functioning, problem solving and motor functioning. The Cronbach´s alpha for all analyses was upper than .05. Conclusion: This study proposes a validation of a neuropsychological battery in a homogeneous sample of CFS. This proposition could reduce one of the main limitations in the studies about CFS and cognitive functioning, such as the inconsistent findings associated to the different neuropsychological test used.
Anbu, AT	Dr Anbarasu Theodore Anbu, Consultant General Paediatrician and Clinical lead for Paediatric CFS/ME service, Alder Hey	Audit of Paediatric Chronic Fatigue Syndrome (CFS/ME) specialist service in Alder Hey Children's NHS Foundation	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P184.	Background: Alder Hey Children's NHS Foundation Trust is a teaching hospital in the North West of England. The Paediatric Multidisciplinary (MDT) CFS/ME specialist service was established in 2003 as part of the Department of Health initiative on developing services specifically for children of all ages with CFS/ME. The MDT team included Consultant Paediatrician as the lead, CFS/ME specialist nurse, senior physiotherapist, psychologist, consultant psychiatrist and a medical secretary. There

	Children's NHS Foundation Trust, Eaton Road, Liverpool, L12 2AP. UK. theo.anbu@alderhey.nhs.uk	Trust		were 91 children managed by this service in weekly dedicated CFS/ME MDT clinics by early 2008. This service was delivered based on the already existing guidance from the Chief Medical Officers report, National Service Framework for children, General Medical Council's good medical practice and the RCPCH publication. However in 2007 the National Institute of Clinical Excellence (NICE) published specific evidence based guidelines on the management of adults and children with CFS/ME (CG53) which is being actively followed now. Objectives: The objective of this audit was to review the standard of our care towards children and young people with CFS/ME based on the NICE guidelines CG53. Methods: This was a retrospective case notes audit of 50 children seen by our CFS/ME service between December 2003 and July 2008. The lead clinician completed the audit with the help from the Hospital audit committee. Results: There were 40 female and 10 male children with CFS/ME. The mean age of our study population was 12.3 years (range 7-16 years). 60% of the children were referred by other paediatricians. In 96% of the study population the symptoms persisted for more than 3 months. 62% had missed school at some time during their illness. The diagnosis was established by the MDT team in 42/50 and by other paediatrician in 6/50. Appropriate investigations were undertaken, other underlying diagnosis excluded, child and family focussed treatment plans initiated and additional information on the illness and support was provided to all patients as suggested by the CG53. However only in 93% of patients early symptom advice was provided. The mean duration from referral to the time seen in clinic was 7.4 weeks. Only 49% were seen within 6 weeks of referral as suggested by the CG53. All but one patient were managed as outpatients by the specialist team. Conclusion: Review of clinical care based on established evidence based standards has helped us in identifying areas for improvement and deliver high quality service to our children with CFS/ME. This could be used as a regular exercise on a regular basis.
Anbu, AT	Dr Anbarasu Theodore Anbu, Consultant General Paediatrician and Clinical lead for Paediatric CFS/ME service, Alder Hey Children's NHS Foundation Trust, Eaton Road, Liverpool, L12 2AP. UK. theo.anbu@alderhey.nhs.uk	Patient and Parent Survey in a Specialist Paediatric Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) Service in Alder Hey Children's NHS Foundation Trust	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P184-185.	Background: In the last 2 decades there is an increasing awareness and recognition of CFS/ME in children. The National Health Service in UK has established several specialist CFS/ME centres across the country to treat children with this severe debilitating illness. Unfortunately not all are able to access these services. Even if they access the quality of service delivery is variable. This is primarily due to inequality in service provision, lack of understanding of the aetiology of this condition and varied clinical knowledge and expertise of the clinical teams. In Alder Hey following the Department of Health initiative a local Multi Disciplinary Team (MDT) specialist service was set up in 2003. The team consisted of a consultant paediatrician, specialist nurse, physiotherapist, psychologist and a consultant psychiatrist. As it was relatively new area of practice it was believed that there were lot more to listen and learn from the children and their families how a high quality service could be delivered. Hence in 2008 patient and parent experiences survey was undertaken. Aim: To obtain qualitative information on patients and parents experiences of the CFS/ME service.

				Methods: The Commission for Healthcare Improvement (currently the Care Quality Commission) questionnaire was given to all families who attended the weekly clinics between February and April 2008. They were completed both by the child and the parent. The completed questionnaires were posted in a box to ensure confidentiality. The results were analysed by the audit department. Results: There were 52 children actively being managed at that time. The questionnaires were given to 25 families. 25 (48%) of patient population and 24 (46%) of their parents completed questionnaires. 13 (54%) children were between 16-18yrs of age. 18 (75%) of them were girls. 96% to 100% of the children and parent rated either certainly true or partly true with regards to the attitude and clinical knowledge of the health professionals. Only 83% to 87% of children and parent agreed that their appointments were at a suitable time. When specifically asked about *'what was good about the service'* 16/24 children and 18/24 parent felt that the team listened to them, was very patient, had good knowledge and understanding of the condition, sympathetic, very helpful, concerns taken seriously and believed them. When asked about *'things needed to be improved'* 9/24 children and 9/24 parents felt that they preferred information on alternative therapies and improved communication amongst ward staff and the CFS/ME team if admitted to hospital. Conclusion: It is encouraging to see the families' having positive healthcare experience. This survey focussed on the quality of the service delivery. It is vital that in future survey on the effectiveness of the different modalities of treatment they receive would overall improve how we manage children with CFS/ME.
Arroll, Megan A; Senior, Victoria	Department of Psychology, University of Surrey, Guildford, Surrey GU2 7XH Email: m.arroll@surrey.ac.uk	Symptom Typology and Sub-grouping in Chronic Fatigue Syndrome	Bulletin of the IACSF/ME. 17 (2). Summer 2009.	Background: Chronic Fatigue Syndrome (CFS) is a condition of unknown aetiology with a heterogeneous population. The variability in symptomatology produces difficulties in studying CFS, therefore this study aimed to establish symptom typology and sub-groups within a sample of participants by use of data reduction techniques. Methods: Two-hundred and forty-six participants completed two symptom measures (one of which evaluated CFS-specific symptoms and the other a general symptom checklist) which were subsequently combined and analysed. Symptom types were established with factor analysis, whereas sub-groups within the sample were determined by cluster analysis. Results: Five symptom types resulted from the factor analysis which were labelled *FMS-like, depression/anxiety, fatigue/post-exertional malaise, cognitive/neurological* and *IBS-like symptoms,* with the *FMS-like* accounting for the majority of the variance in the data. Cluster analysis illustrated that the sample could be divided into three sub-groups based upon the symptom reports. The clusters that emerged were formed of a low symptomatology sub-group (LSS-G), a medium symptomatology sub-group (MSS-G) and a high symptomatology sub-group (HSS-G), which, as the names suggests, signified symptom severity. Notably, these sub-groups did not differ in respect to age, sex, illness duration or time taken to gain a diagnosis which infers that the groupings were not influenced by demographic concerns. Conclusion: This study illustrated that symptomatology in CFS can be divided into

				distinct categories that concur with the most recent guidelines for the condition. Additionally, the illness can be separated into discrete sub-groups, although these groupings are linked to overall severity, rather than symptom types.
Baken, Don	Massey University, Palmerston North, NZ	The Third IiME International ME/CFS Conference 2008	Bulletin of the IACSF/ME. 16 (3). Fall 2008. P11-14.	I was lucky enough to attend this conference by adding it on to a previously planned work trip to Europe. I was invited to attend a dinner the night before with most of the speakers. I was struck by their enthusiasm about the issues associated with ME/CFS and their willingness to talk to others about these. This summary is an attempt to provide some of the information presented at the conference to people who were not able to be present.
Baraniuk, J; Raksit, M; Merck, S; RAvindran, M; Zheng, Y; Esteitie, R; Timbol, C; Van Meter, J	Megna Raksit, B.S. Center for Functional and Molecular Imaging, Georgetown UniversityMedical Center, LM 14 3900 Reservoir Road, Washington DC 20007 USA megna.raksit@gmail.com	Gulf War Illness: Effects of Exercise on Working Memory	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P194-195.	Objectives: Over 25% of the active duty military personnel from the First Persian Gulf War developed chronic multisymptom complexes that included Chronic Fatigue Syndrome, Multiple Chemical Sensitivity, and Post Traumatic Stress Disorder. These overlapping disorders form Gulf War Illness (GWI). This heterogeneous disorder presents challenges to delineating underlying causes as well as targeted treatment. We used fMRI to examine the effects of an exercise stressor on working memory to help phenotype subtypes of GWI. Methods: Veterans were eligible if they were active military duty for at least 30 days from 1990-1991. 18 veterans (average age 50; 12 male) were included. Subjects had identical fMRI protocols before and after VO2max bicycle ergometer stress tests that were done on consecutive days. Participants were trained outside of the scanner until proficient in the N-Back paradigm, which requires continual encoding and retrieval of information. Stimuli consisted of single letters (A, B, C, or D) presented randomly. The task was presented using a block design alternating between 0-Back and 2-Back. For 0-Back, participants pressed the correct button corresponding to the letter presented. 2-Back required pressing the button corresponding to the letter presented 2 letters earlier. Accuracy scores were used to separate participants into two groups: those who performed better after exercise and those who performed worse. Functional MRI data was acquired on a 3.0 T Siemens TIM Trio MRI scanner. Data were analyzed using SPM5 using a mixed-effects statistical analysis examining the brain activity for 2-Back>0-Back during the pre- and post-stressor sessions for each group. Results: Ten participants had increased accuracy: 0-Back by +3.12% (ceiling effect) and 2-Back by +19.8%. 8 subjects had decreased performance: 0-Back by -9.74% and 2-Back by -11.1%. The increased accuracy group showed greater activation after exercise in the caudate ($p<0.001$) and precuneus($p<0.001$). These are task related areas, indicating that this group of subjects recruited more cognitive resources to perform better after exercise. In contrast, those with decreased accuracy after exercise had less activation ($p<0.001$) in the dorso-lateral prefrontal cortex (DLPFC). While this area is also reliably activated by the N-Back, decreased DLPFC activation reflects cognitive inefficiency and failure to recruit additional resources. Conclusion: The group that demonstrated improved

				accuracy also showed increased activation in task-related areas, indicating that this group received cognitive benefits from exercise. However, the group of GW patients that suffered exercise related working memory deficits showed decreased DLPFC activation after exercise. This significant change points to their inability to recruit cognitive recourses during exercise-induced fatigue. These two distinct responses to exercise are one indication that the heterogeneous GWI can be subdivided for more targeted treatment.
Baraniuk, James N	James N. Baraniuk, M.D. Room 3004F 3-PHC Building, 3800 Reservoir Road, N.W.,Washington DC 20007-2197 USA cfsresearch@georgetown.edu	A Chronic Fatigue Syndrome (CFS) Severity Score Questionnaire	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P172-173.	Objective: Validate a CFS Severity Score based on the 1994 Fukuda criteria in order to have an instrument to compare subject complaints between groups and over time. Method: Two Cohorts of CFS, and healthy control (HC) subjects had history and physical examinations to see if they met clinical CFS case designation criteria. Subjects with previous psychiatric, chemotherapy, or chronic illness where fatigue was an element were excluded. After Cohort 1 was examined (n=329), different protocols but the same questionnaire were used with, Cohort 2 (n=212). Subjects scored the severities of the 9 Fukuda criteria for the previous 6 months on a 5 point anchored ordinal scale of: *No Complaints* (score=0); *Trivial* (1, symptom present but negligible impact); *Mild* (2); *Moderate* (3); and *Severe* (4). Fatigue scores of 3 or 4 defined CFS and chronic idiopathic fatigue (CIF). HC had Fatigue Scores of 0, 1 or 2. The sum of the 8 minor criteria (Sum8) was tested as a surrogate marker of the overall severity of adjunctive complaints. The distributions of Sum8 were explored to see if the 95th percentile (mean+2σ) for non-CFS groups could be used as a threshold to identify CFS subjects. Results: Fatigue Scores of 0, 1 or 2 defined 236 HC (bars on the left). 305 subjects had Fatigue Scores of 3 or 4. Putative CIF (n=36) had ≤ 3 positive minor criteria. CFS with Fatigue Scores of 3 had a mode for Sum8 at 15 to 19; the mode was 24 when 4 was the Fatigue Score. ROC tests found that Sum8=12 had 98.5% for specificity and sensitivity of 97.8% for CFS in this population. Hierarchical clustering found 4 clades each for CFS and HC. The largest CFS clade (CFS II; n=184) had high severity scores for fatigue, muscle pain, sleep & exertional malaise. The 2nd largest clade (CFS IV, n=51) had lower fatigue, memory, sleep myalgia and exertional malaise scores. CFS clade III (n=30) had fatigue, memory, muscle or joint pain. CFS clade I was an outlier group with fatigue and headache. The largest HC clade (I; n=168, 67% of HC) had low scores for all symptoms. HC II (n=49) had modestly elevated sleep scores (2.4). Myalgia and arthralgia in the mild to moderate range were present in HC III (n=25). HC IV (n=13) had moderate to severe headaches plus sleep and memory problems. These clades of co-existing complaints were highly dissimilar between the CFS and HC groups. Conclusion: The CFS Severity Score was robust for discriminating CFS from HC subjects in this population. Mechanisms underlying the clades are under investigation.
Baraniuk, JN; Timbol, CR; Zheng,	James N. Baraniuk, M.D. Room 3004F 3-	An Hybrid 70% Plus 85% Predicted Heart	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME	Objective: Determine the merits of submaximal and maximal bicycle stress tests for Gulf War Illness (GWI), CFS and healthy veterans and controls (HC) for tandem, 2 day

Y; Surian, A; Esteitie, R; RAvindran, M; Merck, SJ; Rayan, R; Adewuyi, O; O'Brien, S	PHC Building, 3800 Reservoir Road, N.W.,Washington DC 20007-2197 USA gwiresearch@georgetown.edu	Rate Bicycle Stress Test Performed on Two Consecutive Days	Biennial International Conference. Poster Presentations. P199-200.	testing. Methods: Subjects exercised on a Schwinn bicycle ergometer. Cardiopulmonary function was measured using mouthpieces and Vmax software. 27 GWI and 8 HC participated in 3 bicycle exercise stress test protocols: #1. 13 GWI and 2 HC had standardized ramped VO2max tests with exercise until physical limitations caused the test to end (*85%HR*). #2. 6 GWI and 4 HC cycled at 70% of maximum predicted heart rate for 25 min then accelerated to 85% without cardiopulmonary testing (*70%+85%*). #3. 11 GWI and 5 HC had VO2max tests that began with 25 min at 70% maximum heart rate that was followed by acceleration to 85% (*70%+85%* plus VO2max). Symptomatic Responses: Borg Dyspnea Scores were significantly higher for GWI subjects on DAY 1 (3.9; 2.8 to 4.9 [mean; 95% C.I.]; n=25) and DAY 2 (4.1; 3.1 to 5.0) than HC (1.4; 0.1 to 2.6; n=9; p=0.016 by t-test; and 1.3; -0.1 to 2.6; p=0.0053; n=8; respectively). On DAY 1, whole body pain and fatigue scores at rest and after exercise were in the 3 to 15 range on the 20 point anchored ordinal Gracely Scale for GWI (n=15) compared to 0 to 3 for HC (0.032≥p≥0.00005; n=8). DAY 2 results were marginally higher at 6 to 16 for GWI and 0 to 5 for HC (0.043≥p≥0.0000004). None of the HC subjects complained of pain or fatigue on either day. Adverse Events: Protocol #1. Three GWI had to stop because of fatigue and dyspnea with VO2max at 25%, 32% and 50% of predicted. A fourth had dyspnea and oxygen desaturation (88% by pulse oximetry). A fifth GWI subject stopped because their systolic blood pressure dropped by 22% as they neared 70% HR. Protocol #2. Two GWI had to stop after 25 min at 70% of maximum HR because of fatigue or muscle pain. A third GWI subject increased their HR by only 29% before stopping. Protocol #3. One GWI became so exhausted after 70% HR that within 15 minutes he had fallen asleep for 1 hour. One veteran who was otherwise healthy on examination could only exercise to VO2max of 48% of predicted before stopping because of dyspnea on both DAYs. This subject and another otherwise healthy appearing veteran both demonstrated orthostatic tachycardia (ΔHR>30 bpm). Energy Expenditures: In the two *70%+85%* protocols, HC expended more METs to reach 85%HR (7.95; 7.08 to 8.82) than GWI (4.94; 4.16 to 5.72; p=0.0015). On DAY 2, this significant difference was found for 70% HR in HC (5.00; 4.26 to 5.74; n=4 vs. 3.17; 2.54 to 3.80; n=6; p=0.0064). At 85% HR the variance of the GWI data was too large for a significant difference to be detected. Expenditures by GWI subjects were different on DAY 2 from DAY 1. Watts needed to reach 85% HR in ramped exercise for GWI were higher on DAY 1 (202; 160 to 245; n=13) than DAY 2 (170; 138 to 202; n=12; p=0.015 by paired t-test). In contrast, the 70%+85% protocol required more calories on DAY 2 (179; 155 to 203; n=12) than DAY 1 (162; 132 to 191; p=0.033) in a different group of GWI subjects. HC had no differences in energy requirements between DAY 1 and DAY 2. Conclusion: The 70%+85% VO2max test was the optimal provocation.
Baranuik, J; Zheng, Y; Ravindran, M;	Yin Zheng, M.S., Research Assistant	Effects of Exercise on Systemic	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME	Objectives: Thumb pressure tenderness (TPT) is an indicator of systemic hyperalgesia. Post exercise malaise is a chief complaint of Chronic Fatigue Syndrome (CFS). We

Timbol, C; Esteitie, R; Adewuyi, O	3800 Reservoir Rd NW, 3PHC 3004F, Washington DC 20007, USA yz46@georgetown.edu	Hyperalgesia in Gulf War Illness Patients with Chronic Fatigue Syndrome	Biennial International Conference. Poster Presentations. P197-198.	expect two days of bicycle exercise stress test to increase systemic hyperalgesia in Gulf War Illness (GWI) patients with Chronic Fatigue Syndrome. Method: We tested changes in systemic hyperalgesia in 14 GWI patients with CFS. Systemic hyperalgesia was measured by applying precisely controlled pressures to the thumb nail bed. Pressures were applied in ascending and descending fashion for 3 complete cycles, then 1 randomized cycle to eliminate patient expectation of pain levels. After each pressure, subjects reported their level of pain on a 0 to 20 point anchored ordinal scale. TPT test started at 5 pounds per square inch (psi) and ascended by 5 psi increments until subjects rated pain levels of at least 12 out of 20. Then, starting from the last highest psi, decreasing pressures by 5 psi increments were applied until a final pressure of 5 psi. Subjects completed two days of 25minute 70% maximum heart rate submaximal bicycle exercise stress test. TPT testing was performed on the first day (d1), before first exercise stress test on the second day (d2), and after second bicycle exercise stress test on the third day (d3). The plots of ascending/descending painpressure curves and random pain pressures were plotted and analyzed using Microsoft Excel. Results: A hysteresis pattern was observed in the ascending and descending cycle of the pain as function of pressure plots (PfPP). Patients consistently reported higher pain levels on the descending limb of the cycle compared to the ascending limb at the same pressures. The decreasing pressure limb generally had consistent, high pain ratings, even though the pressures were decreasing. Pain reports subsequently dropped rapidly to near 0 at 5 psi. The area between the ascending and descending limb of the PfPP generally decreased from d1 to d3 ($P<0.01$). This may indicate a learning effect by the subject being able to assess and report pain levels more reproducibly on d3 compared to d1. PfPP of randomized TPT testing on each day showed lower slope values postexercise compared to d1 preexercise ($P<0.0002$). A lower slope indicates lower pain levels at same pressure. This demonstrates a decrease in systemic hyperalgesia after two days of exercise stress testing. Conclusion: Thumb pressure tenderness testing effectively measures systemic hyperalgesia. Subjects perceived their nociceptive input on d3 more accurately than d1. This may indicate a spinal or supraspinal adaptation. *Decrease* in systemic hyperalgesia post exercise may indicate mechanism for benefit of exercise to GWI with CFS.
Baranuik, JM; Le, U; Petrie, K; Ali, M; Merck, SJ; Ravindran, M; Zheng, Y; Timbol, CR; Estieitie, R; Rayhan, R; Adewuyi, O	Uyenphuong Le, M.D. Room 3004F 3-PHC Building, 3800 Reservoir Road, N.W., Washington DC 20007-2197 USA cfsresearch@georgetown.edu	Blunted Nasal and Systemic Sympathetic Reflexes in Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P198-199.	Objective: Almost 73% of chronic fatigue syndrome (CFS) subjects have a form of nonallergic rhinitis that may be due to autonomic dysfunction. Isometric handgrip was used as a stimulus for sympathetic cardiovascular effects including tachycardia and the vasoconstriction of peripheral and nasal mucosal blood vessels that leads to hypertension. Methods: Isometric handgrip tests were performed in 41 CFS and 42 healthy control (HC) subjects. Nasal acoustic rhinometry to measure the volume of the nasal airspace and minimum cross-sectional area at the anterior nasal valve, and vital signs were

				measured during a sham period of no contraction, and during forearm and hand contraction to 30% of maximum strength. Results: Although HC were stronger then CFS, there were no differences in duration, pain intensity or tolerance of the handgrip. Incremental changes in vital signs were significant ($p<0.0005$) at exhaustion for both groups. However, only HC had significant increases in nasal Volume and Amin from sham. The % change was significantly greater for HC than CFS for Volume, Amin, SBP, DBP and HR. Some CFS subjects had paradoxical decreases in Volume and Amin, and no changes in vital signs. The study was repeated in 104 CFS and 60 HC (87 CFS and 55 HC had acoustic rhinometry). Significant differences were found for Amin%Δ, SBP%Δ, DBP%Δ and HR%Δ. Gender differences were present. DBP%Δ was significantly greater for HC females (29%; 20% to 38%) than CFS females (13%; 10% to 16%; $p=0.00005$). HR%Δ was significantly greater for HC males (20%; 11% to 29%) than CFS males (9%; 6% to 12%; $p=0.018$). Conclusions: CFS had significantly lower sympathetic effects on heart rate, blood pressure, and nasal vascular vasoconstriction than HC subjects in response to isometric exercise. Averaged acoustic rhinometry results were variable for CFS suggesting subsets with normal and hyporesponsive effects. One pattern of interest was found in CFS subjects who had immediate increases in all measurements when isometric contractions began, but decayed to smaller or negative %Δ with time. Frequency distributions of these responses may identify CFS subsets with dysfunctional "on demand" sympathetic discharge. These data support neurological dysfunction of mucosal and systemic sympathetic reflexes in the pathogenesis of CFS and the nonallergic rhinitis of CFS.
Baranuik, JN	James N. Baraniuk, M.D. Room 3004F 3-PHC Building, 3800 Reservoir Road, N.W.,Washington DC 20007-2197 USA cfsresearch@georgetown.edu	Distinct Cerebrospinal Fluid Proteomic Patterns in Clusters of CFS and Healthy Subjects	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P191-192.	Objective: The protein constituents of cerebrospinal fluid are its proteome. If central nervous system dysfunction contributes to CFS pathophysiology, then proteomes from CFS subjects should differ from healthy controls (HC). If CFS is a homogenous illness, then the patterns of proteins should be similar for all CFS subjects. However, if CFS is a heterogenous disorder, then different patterns of proteins may be found for subsets of CFS subjects. Method: Informed consent was obtained from CFS (n=59) and HC (n=18) subjects to have lumbar punctures. Cerebrospinal fluid was digested with trypsin for mass spectrometry. Of the 4,543 ion peaks detected, 880 were peptide ions that matched to 79 proteins (MASCOT software). Unsequenced ion peaks may be complex metabolites, have posttranslational modifications, or be technical artifacts. Subjects used our CFS Severity Score to estimate the severity of fatigue and the 8 minor (1994 Fukuda) criteria for the previous 6 months. The anchored ordinal scale of scored 0 for no symptoms, 1 for trivial, 2 mild, 3 moderate and 4 severe. Unsupervised hierarchical clustering of Severity Score created a phylogenetic tree with 4 predominant subsets of CFS subjects. Results: CFS clades were clade 1 (*C1*; n=31; 41% female; 47 yr), *C2* (n=9; 78% female, 52 yr), *C3* (n=11; 91% female; 46 yr), and *C4* (n=8; 62% female; 48 yr). The healthy control group (*H1*; n=18) had 44% females and average age of 41 yr. The average signal intensity for all peptide ions in a

				protein were compared between *H1* and the 4 CFS clades by 2-tailed Student's t-tests ($p<0.005$ for significance in this pilot analysis) after ANOVA ($p<0.05$). Proteins with the highest ion counts were NRAP (2 peptides), PTGDS, CAMKK2, ALB (81 peptides), TTR, CST3, TF and CLU. CFS clade 1 (*C1*) had higher levels of CST3, APOE, HP/HPR, APLP1, KLK6, APP, CP and FGA than *H1*. *C2* had 36 proteins with significantly higher average signal intensities than H1. These included the brain proteins AGT, B3GNT1, GSN, XIRP2, FBLN1, EFEMP1, SPARCL1, CLSTN1, NRCAM, NCAM1, and FN1. Complement proteins included CLU, C3, C4A,B, CFB, and CFH/CFHR1. Serine protease inhibitors were common (SERPINs F1, A3, and D1). The pattern suggested that *C2* had higher levels of brain-derived proteins than *H1*. TTR, SERPINA1 and the neural growth inhibitor DKK3 were significantly higher in *C3* than *H1*. These may also have had predominantly brain origins. ALB counts were highest in *H1*, and significantly higher than *C3*. *H1* also had significantly higher immunoglobulin peptides, HPX, APOA1, SERPINC1, and SERPINF2 than *C4*. Half of the proteins that were higher in *C1* or *C2* than *H1* were also higher in *H1* than *C4*. Conclusion: CFS phenotypes were defined by hierarchical clustering of CFS Severity Score results. These clades were associated with significantly different panels of proteins. The 4 CFS clades suggest at least 4 pathophysiologically distinct states. Factors that may enrich the brain protein fraction include brain injury with protein release into cerebrospinal fluid (e.g. *C1* and *C2*), and decreased plasma flux across the blood brain barrier (e.g. *C3*).
Baranuik, JN; Varghese, R; Adewuyi, O; DiPoto, C; Pannell, L; Ravindran, M; Merck, S; Zheng, Y; Timbol, C; Esteitie, R; Rayan, R	Rency Varghese, M.S., Biostatistics, Room 3004F 3-PHC Building, 3800 Reservoir Road, N.W., Washington DC 20007-2197 USA, cfsresearch@georgetown.edu	Distinct Clustering of Cerebrospinal Fluid Peptides and Other Ion Peaks in Clusters of CFS and Healthy Subjects	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P189-190.	Objective: Determine if proteomic differences were present between subsets of CFS. Method: Informed consent was obtained from CFS (n=59) and HC (n=18) subjects to have lumbar punctures. Subjects used our CFS Severity Score to estimate the severity of fatigue and the 8 minor (1994 Fukuda) criteria for the previous 6 months. The anchored ordinal scale of scored 0 for no symptoms, 1 for trivial, 2 mild, 3 moderate and 4 severe. Cerebrospinal fluid proteins were digested into peptides with trypsin before Orbitrap mass spectrometry. Ion peaks from mass spectrometry and CFS subjects' Severity Scores were grouped using "two-dimensional" unsupervised hierarchical clustering (MatLab). Results: The heatmap defined four clades of CFS subjects (*C1* to *C4*, columns) and five clades of ion peaks (*P1* to *P5*, rows) (Figure 1). Clade *P1* ion peaks were equivalent for all CFS clades and *H1* (Table 1). The exception was a subset of C4 (upper right). *P2* ion peaks were ranked *C3≈C4>H1>C1≈C2*. *P3* ions ranked CFS in the opposite way: *C1≈C2>H1>C3≈C4*. *C4* was significantly different from *H1* for peaks in *P4*. Ions in *P5* were ranked *C3≈C2>H1>C2*. Each ion clade had unique results Conclusions: These distinctive cerebrospinal fluid proteomic patterns for CFS subgroups suggest that distinctive pathophysiological mechanisms that lead to unique protein biosignatures may be associated with clinically defined subsets of CFS subjects.

Baranuik. JN; Esteitie, R; Adewuyi, O; Ravindran, M; Merck, S; Zheng, Y; Timbol, C; DiPoto, C; Rayhan, R	James N. Baraniuk, M.D., Room 3004F 3-PHC Building, 3800 Reservoir Road, N.W., Washington DC 20007-2197 USA cfsresearch@georgetown.edu	Medication Responses in Chronic Fatigue Syndrome (CFS) And Non-CFS Subjects	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P187-188.	Objective: There is a clinical perception that Chronic Fatigue Syndrome (CFS) subjects have greater drug sensitivity and "allergy" than the rest of the population. This perception was tested by assessing the symptoms associated with medication use in a group stratified by CFS status and gender. Method: 194 subjects answered a binary (yes-no) questionnaire (Simon GE, Daniell W, Stockbridge H, Claypoole K, Rosenstock L. *Immunologic, psychological, and neuropsychological factors in multiple chemical sensitivity.* Ann Intern Med 1993;119:97–100) to determine if "medications" (not further subdivided by drug class) caused any of 25 symptoms from the neurological (6 symptoms); musculoskeletal (5); airways (7); gastrointestinal (5); and skin (2) systems. Gastrointestinal- nausea, vomiting, diarrhea, abdominal pain, and heartburn; Neurologic- headache, dizziness, confusion, memory loss, nervousness, and visual change; Musculoskeletal- joint pain, joint swelling, muscle pain, weakness, and fatigue; Pulmonary- cough, runny nose, shortness of breath, sneezing, wheezing, sinusitis & chest pain; Dermatologic- skin rash and itching. Subjects used our CFS Severity score to estimate the severity of fatigue and the 8 minor criteria for the previous 6 months. The anchored ordinal scale scored 0 for no symptoms, 1 for trivial, 2 mild, 3 moderate and 4 severe. Fisher's Exact Test and T-tests were used to assess significant effects of gender and CFS status. Result: The subgroup of ALL CFS females had more frequent nausea (32% vs. 13%; p=0.013) and visual changes (19% vs. 4%; p=0.018) than ALL non-CFS females. ALL CFS males had nausea (26%; p=0.003) and dizziness (23%; p=0.006) compared to zero in ALL non-CFS males. However, these differences were misleading because many individuals had no symptoms, and so would not have adverse complaints or contact their physicians. Therefore, the 47% of CFS and 72% of non-CFS subjects with zero symptoms were removed. The remaining 65 CFS subjects had 5.6 symptoms (4.2 to 7.0, 95% CI). The 20 non-CFS subjects had 3.5 symptoms (1.8 to 5.2; not significant by t-test). Females in these subsets had no significant differences in symptoms frequencies. However, CFS males (n = 22) had more nausea (54.5% vs. 0%; p=0.067) and dizziness (50% vs. 0%; p=0.091) for non-CFS males (n = 4). Conclusion: The apparent higher prevalence of medication-related symptoms in CFS than non-CFS was biased by the large number of subjects with zero symptoms. When subjects with no complaints were excluded, there was no difference between CFS and non-CFS females, but a trend for CFS males to have had more gastrointestinal and neurologic symptoms than the non-CFS males. Overall, the equivalence of symptoms in CFS and non-CFS suggests that Multiple Chemical Sensitivity (MCS) may be an independent syndrome. These methods will direct our analysis of other irritants in this multiple chemical sensitivity questionnaire.
Bateman, Lucinda	[No address quoted]	CFS and the Exercise Conundrum	Bulletin of the IACSF/ME. Fall, 2006	Summary: Find a range of well tolerated physical conditioning activities and doggedly stick with it, even if it seems ridiculously insignificant. Learn to pace, assess, and re-adjust the type, intensity and duration of activity day by day to stay under the relapse threshold and avoid post-exertional malaise. Observe any pattern of activity at least a

				week before increasing the duration or intensity. Be careful about advancing any aspect of physical conditioning unless gradual increases are well tolerated. Recognize and respect the reality that CFS patients may have a point at which, physiologically, they will become more ill from physical activity and experience a substantial set back, even if the mechanisms are not entirely clear.
Bateman, Lucinda; Light, AR; White, AT; Hughen, RW; VanHaitsma, TA; Light, KC	Lucinda Bateman, M.D,Adj. Assist. Professor, Depts. of Anesthesiology, Fam and Prev. Medicine, Internal Medicine University of Utah; and Director, Fatigue Consultation Clinic, 1002 East South Temple, Suite 408, Salt Lake City UT 84102 USA. fcclinic@xmission.com	Gene Expression of Sensory Ion Channels, Adrenegic Receptors and Cytokines: Potential Biomarkers for CFS and Fibromyalgia	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P133-134.	Objectives: To determine whether baseline and/or post-exercise expression of genes involved in signaling and modulating sensory fatigue and muscle pain are potential biomarkers for distinguishing patients with Chronic Fatigue Syndrome (CFS) and Fibromyalgia Syndrome (FM) from healthy controls. Methods: Forty eight Patients with CFS-only or CFS with comorbid FM, 18 Patients with FM that did not meet criteria for CFS, and 49 healthy Controls underwent moderate exercise (25 min at 70% of age-predicted maximum heart rate on Air-Dyne). Blood samples were taken before and 0.5, 8, 24, and 48 hours after exercise. Leukocytes were immediately isolated in buffer, number coded for blind processing, and flash frozen. Using real-time, quantitative PCR, the amount of mRNA for 13 genes (relative to control gene) involved in sensory ion channel, adrenergic, and immune functions was compared between groups at baseline and following exercise. Visual-analogue measures of fatigue and pain were taken before, during, and after exercise, including concurrently with all blood samples. Changes in amounts of mRNA were correlated with these measures, with history of orthostatic intolerance and with blinded ratings of disorder severity by the treating physician derived from multiple clinics. Results: No gene expression changes occurred following exercise in Controls except for inconsistent increases in β-1 adrenergic receptor. In 71% of CFS patients, moderate exercise increased most sensory ion channels and adrenergic receptors and one cytokine gene for 48 hours. These post-exercise increases correlated with numerical ratings of fatigue and pain, and greater increases were shown by patients with higher physician ratings of disorder severity. In contrast, for the other 29% of CFS patients, adrenergic α-2A receptor expression was decreased at all time points after exercise; other genes were not altered. History of orthostatic intolerance was significantly more common in the α-2A decrease subgroup. FM only patients showed no post-exercise alterations in gene expression, but their pre-exercise baseline mRNA for two sensory ion channels and one cytokine were significantly higher than Controls. Conclusions: At least two subgroups of CFS patients can be identified by gene expression changes following exercise. The larger subgroup showed increases in mRNA for sensory ion channels and adrenergic receptors and a cytokine. Both self rated and physician-rated symptom severity was associated with greater post-exercise increases in these genes. The smaller subgroup contained most of the CFS patients with orthostatic intolerance, showed no post-exercise increases in any gene, and was defined by decreases in mRNA for α-2A adrenergic receptor. FM only patients can be identified by baseline

				increases in 3 genes. Post-exercise increases for 4 genes meet published criteria as an objective biomarker for CFS, and could be useful in guiding treatment selection for different subgroups.
Bazzichi, L; SErnissi, F; Scarpellini, P; Conseni, A; Giacomelli, C; DeFeo. F; Rossi, A; Bombardieri, S	Laura Bazzichi, Reumatologia - Ospedale Santa Chiara, Via Roma, 67, 56126 Pisa – Italy l.bazzichi@gmail.com	Neurocognitive Impairment in Chronic Fatigue Syndrome: Complained Symptom or Real Deficit? - An Objective Method of Evaluation	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P193.	Objective: Several symptoms reported by chronic fatigue syndrome (CFS) patients - including fatigue, headache, impaired concentration, attention and memory - suggest that the central nervous system may be involved in the pathophysiology of the syndrome. Coexisting psychological distress or a psychiatric disorder also may contribute to neurocognitive (NC) deficits. Since CFS shows a significant overlap with Fibromyalgia syndrome (FM), a comparison of the two groups of patients could be important to understand the relationship between fatigue and NC disorders. The aim of the present study is to investigate the prevalence of NC deficits in CFS patients compared to FM patients, using a standardized set of validated tests, and to understand how psychiatric disorders and intake of psychoactive drugs may interfere. Methods: 49 patients with a diagnosis of CFS (based on Fukuda criteria, 1994) and 26 patients with a diagnosis of FM (ACR criteria, 1990) were consecutively recruited. Patients with axis I current psychiatric diagnosis was excluded. Each CFS or FM patient was asked to fill a set of questionnaires on paper and perform a battery of NC computerized tests after blood analysis (9:00 am). CNS Vital Signs© (CNSVS)1 is a NC test battery developed as a routine clinical screening instrument. It is composed of 7 tests for the evaluation of Composite Memory, Verbal and Visual Memory, Processing Speed (PrS), Executive Function (EF), Psychomotor Speed (PsS), Reaction Time, Complex Attention (CA) and Cognitive Flexibility (CF). It returns a score for each item and a composite NC global score named Neurocognition Index (NCI), normalized for patient's age, school attendance and computer usage frequency. Results: Patients with CFS (♀ 26/49) had a mean age (SD) of 37.8 (11.5) years, while patients with FM (♀ 24/26) had a mean age (SD) of 43.0 (10.3) years (p=0.017). On a total of 75 patients, only 20 (26,6%) did not complain about NC problems. NCI was higher in CFS subjects (p= 0.02) and 16 CFS patients (32.7%) showed a real NC impairment, vs 12 (46.2%) with FM, considering a real deficit with a low or very low NCI. The items that differed the most were the PsS, the EF and the CG. PsS of all the patients correlated with disease duration (p=0.0004). Of the 55 patients with CFS and FM who complained about NC disorders, less than half showed low or very low NCI. Thirty-five patients out of 75 had not a psychiatric lifetime comorbidity, 20 patients (26.7%) had a mood disorder and 20 (26.7%) an anxiety disorder. Patients with such a comorbidity had a lower NCI (p=0.0044), in particular lower CA, PrS, CG, PsS and EF, independently on the diagnosis. Moreover, 23 out of 75 patients were taking antidepressant drugs (AD) and 18 benzodiazepines (BDZ). Between patients treated with BDZ and those treated with AD there were not significant differences. Conclusion: The 32.7% of CFS patients showed a real NC deficit, although the 68.6% complained about it. FM showed more severe NC impairments respect to CFS patients, independently on drug

				assumption and age. A deficit of neurocognitive functions seemed to be predominant in patients with psychiatric lifetime comorbidity, independently on the assumption of antidepressant or anxiolytic drugs and the diagnosis. Thus, CNSVS has proven to be a useful and easy tool for the assessment of NC impairments in clinical trials as well as in routine practice.
Bell, David S	Board Member, AACFS	Sleep Abnormalities in Chronic Fatigue Syndrome	Bulletin of the IACSF/ME. **Winter 2005 - 6**	Conclusion: Sleep symptoms should be pursued aggressively, and only if there is a good clinical response should the diagnosis be changed. Too often the patient with CFS hears the medical provider say, Aha, we have finally found the cause of your symptoms, only to be disappointed when treatment has little or no effect. This treatment failure then encourages alienation of the patient from the medical provider and increases both the frustration and confusion of the patient which, by itself, leads to greater distress.
Bell, David S	Board Member IACFS	Medical Literature Review	Bulletin of the IACSF/ME. Spring 2006	Pilot study of gene expression carrelates of post-infectious fatigue following infection with EBV in 5 subjects compared to 5 HLA-matched controls. Peripheral blood mononuclear cells harvested at diagnosis, every 2 weeks for 3 months then every 3 months for a year. Extracted RNA hybridized to microarrays spotted with 3,800 oligonucleotides. Gene transcription patterns following acute EBV infection in patients who developed prolonged fatigue differed from the matched controls, and some of these genes expressed differently related to immune function. Overall, gene expression during the acute illness was different for twenty three genes, and eight of these remained different after 6 months in cases. Four genes were more highly expressed in controls than post-viral cases. Of the genes expressed differently from controls, and 12 related to mitochondrial functions "including fatty acid oxidation, apoptosis, DNA repair and mitochondrial membrane." The authors concluded that despite a small number of genes evaluated, and small number of cases, "our preliminary results implicate mitochondrial dysfunction as a plausible physiologic perturbation in post-infective fatigue."
Bell, David S	dsbellmd@yahoo.com	Review of the Two-day Exercise Test with a Pediatric Case Report	Bulletin of the IACSF/ME. 16 (1). Spring 2008.	In the most recent *Journal of Chronic Fatigue Syndrome* there are two articles which may be the first to offer an objective proof of disability in ME/CFS. More importantly, if shown to be correct, they may give us an avenue to test and measure the biochemical abnormality which causes the symptom pattern.
Boneva, Roumiana; Jones, James F; Unger, Elizabeth R	Roumiana S. Boneva MD, PhD, Chronic Viral Diseases BranchDivision of High-Consequence Pathogens and	Evidence for Reduced Aldosterone in Persons with Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. p136	Objectives: Aldosterone, a mineralocorticoid hormone of the adrenal gland, controls the absorption of salt and water in the kidneys and the intestine and thus the overall blood volume. Mineralocorticoid receptors in the brain are involved in regulation of blood volume and sympathetic outflow regulation. A few studies have suggested lower blood volume and lower heart stroke volume in persons with chronic fatigue syndrome (CFS) and some persons with CFS experience postural hypotension.

	Pathology, NCEZID, Centers for Disease Control and Prevention, 1600 Clifton Road, MS A15, Atlanta,GA 30333, USA rboneva@cdc.gov			Because altered cortisol secretion has been found in a number of CFS studies, adrenal dysfunction has been suggested. Surprisingly, only one prior study examined aldosterone in CFS, finding lower aldosterone in CFS compared to controls. The current study was performed to explore the hypothesis that aldosterone levels in persons with CFS may differ from those in controls of similar age, sex, and race. Methods: Participants were identified from a population-based study including 70 CFS cases who met the international 1994 CFS case definition and 212 controls of similar age and race. A morning blood sample, collected after participants rested 30 minutes in supine position, was used to test for serum aldosterone. Testing was performed at Quest Diagnostics using liquid chromatography tandem mass spectrometry (analytical sensitivity 1 ng/dL). The Wilcoxon nonparametric test was used for comparison of non-normally distributed numeric variables (aldosterone). Chi square test and logistic regression were used to assess magnitude of associations; for these tests aldosterone was dichotomized at its median value 4 ng/dL in controls, which also equaled the lowest normal lab reference value. Results: Cases and controls did not differ significantly in mean age (47.8 and 47.7, respectively) or race distribution (78.3% and 80.7% Whites, respectively). The CFS group had a higher proportion of women (91.3% vs 67.5%) and a higher mean body mass index than the control group (BMI, 28.9 vs 26.9), p<0.005 for both. The CFS group had lower aldosterone levels compared to controls (mean 4.46, median 3, range 1 to 19 ng/dL vs mean 6.05, median 4, range 1to 76 ng/dL, respectively), p<0.0001 (Wilcoxon non-parametric test). Persons with CFS were 65% more likely to have aldosterone level of <4 ng/dL, OR=1.65 (95% CI, 0.95-2.85), p=0.07. The OR changed slightly after adjusting for BMI, OR=1.58 (0.93-2.74), p=0.11, but minimally after adjusting for sex, OR= 1.69 (95% CI, 0.96- 2.97), p=0.07. A limitation of the study is that aldosterone was measured only in supine position (less sensitive for identifying alterations in aldosterone secretion) and information on dietary salt intake was not available. Conclusions: These results support a previous study's finding of relatively lower aldosterone levels in CFS subjects compared to controls. Further studies of aldosterone in CFS should measure its response to challenge such as salt restriction and changes in aldosterone levels from recumbent to upright position.
Boneva, RS; Jin-Mann, SL; Unger, E	Roumiana S. Boneva MD, PhD, Chronic Viral Diseases Branch, Division of High-Consequence Pathogens and Pathology, NCEZID, Centers for Disease	Risk Factors for CFS in Women: A Case-Control Study of Gynecologic History	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P187.	Objective: Chronic fatigue syndrome (CFS) is more common in females and is predominantly diagnosed in middle-age. We have previously found, in a Mid-Western population, that CFS in women was associated with endometriosis and hysterectomy and a tendency for earlier menopause. In this study, we used a different female population to examine sex-specific risk factors for CFS in women. Methods: A population-based survey in several counties in Georgia, USA, followed up by a nested case-control study. The reproductive histories of 84 women identified as having CFS either at a baseline (2007) and/or follow-up clinical study (2008) were

	Control and Prevention, 1600 Clifton Road, MS A15, Atlanta,GA 30333, USA rboneva@cdc.gov			compared to those of 73 women who were well and non-fatigued (controls) both at baseline and follow up. We used Chi square test for comparison of proportions and calculated odds ratios (OR) with 95% confidence intervals (95% CI) to measure the magnitude of associations between CFS and reproductive history variables. Results: CFS cases and controls were similar in demographic characteristics and had similar mean age at menarche (12 years). However, women from the CFS group reported significantly more gynecologic problems and surgeries than controls. These included: excessive menstrual bleeding [73.8% vs. 26.2%, OR 3.82 (1.95-7.48), p<0.001], bleeding between periods [48.8% vs 23.3%, OR 3.14, p=0.001], endometriosis [30.6% vs. 12.3%, OR= 3.01 (95% CI, 1.30-6.98), p<0.05], being menopausal [62% vs 37% of controls, OR=2.77, 95% CI, 1.38-5.59, p=0.002] and earlier age at menopause [mean±SEM, 37.6±1.3 vs 48.6±0.9 years, p=0.001. Compared to controls, women with CFS were significantly more likely to report: any gynecologic surgery [OR=4.12 (95% CI, 2.11-8.04), p<0.05], especially hysterectomy [OR=5.10 (2.47-10.52), p<0.05], removal of both tubes [OR =2.67 (95% CI,1.14-6.34), p<0.01], removal of ovaries [OR=2.07 (0.97-4.41), p=0.06]. Gynecologic surgeries in the CFS group occurred at a younger mean age than in controls: mean (±sd) 35. 9 (6.8) vs 41.5 (6.3) years for hysterectomy, 38.7 (sd 8.4) vs 45.1 (3.5) years for removal of both ovaries. Onset of fatigue occurred after surgery in 55% of cases (of those with data available) suggesting that not only removal of the uterus and/or ovaries but also pre-existing gynecologic conditions and hormonal abnormalities that lead to these surgeries may predispose to CFS. Conclusions: The high prevalence of excessive menstrual bleeding and bleeding between periods among women with CFS as well as the association between CFS and early menopause suggest that hormonal abnormalities with involvement of the hypothalamo-pituitary-gonadal axis may be contributing to the pathogenesis of CFS in women. The possible mechanism of these associations and their implications for diagnosing and treatment of CFS in women remain to be clarified.
Booth, NE; Myhill, S; McLaren-Howard	Applegate Orchard Lane, East Hendred, Wantage OX12 8JW, UK norman.booth@mansfield.ox.ac.uk	Mitochondrial Medicine for the Treatment of CFS/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P150-151.	In 2009 we showed that 70 out of 71 patients with CFS/ME (Fukuda 1994 criteria) attending a private clinic had measureable mitochondrial dysfunction and were clearly separated from a control group of 53 normal, healthy people 1. The dysfunction was determined by the ATP Profile, a set of 5 different biochemical measurements of white blood cells (neutrophils) and their mitochondria. The degree of dysfunction, the Mitochondrial Energy Score, correlated strongly with the functional ability of the patients as measured on the Bell CFS Ability Scale. The Objectives of the present audit are to see if the mitochondrial dysfunctions can be corrected by a therapeutic protocol consisting of 1) pacing, 2) changes in diet, 3) nutritional supplements known to be essential to the biochemical processes of energy transformation by mitochondria, and 4) detoxification to remove toxic heavy metals and biochemical toxins causing or associated with the dysfunctions. Methods After

				the initial ATP Profile and recording of the CFS Ability patients participated in the basic treatment protocol. Depending upon the progress of each patient and other factors, patients whose results are reported here had the ATP Profile tests carried out a second time and for 4 patients a third time. We can therefore measure changes in mitochondrial function and functional Ability during the treatment protocol. Results All patients improved by at least 1 unit on the Bell Ability Scale (0-10) and some by as much as 6 units. About 25% moved into the normal region in both Mitochondrial Energy Score and CFS Ability, and the strong correlation between these quantities is maintained by the treatment protocol. The results of a patient who had the ATP Profile 3 times clearly demonstrate the importance of the detoxification part of the protocol. Conclusions Whatever the cause of CFS/ME, mitochondrial dysfunction which can affect every cell of the body is a major factor. Improved mitochondrial function produces improved functional ability and these can be achieved by a protocol of targeting mitochondria to give them their essential nutrients and to remove toxins that attack them.
Brenu, E; Marshall-Gradisnik, S; Staines, DR; Van Driel, M; Ashton, KA; Petersen, D	Ekua Weba Brenu, Faculty of Health Science and Medicine, Bond University, Gold Coast,Queensland 4229. Australia Email: ebrenu@student.bond.edu.au	The Effects of Vaccination on Immune Function in Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P171.	Objective: Flu like symptoms are a hallmark of Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). Additionally, most CFS/ME patients experience severe symptoms of toxin intolerance and hypersensitivity. As CFS/ME is associated with periodic immune dysfunction, patients may be more susceptible to influenza episodes compared to the normal population. Conversely, their inability to tolerate certain toxins and hypersensitivity responses may affect their immune response to routine vaccines. The purpose of this study is to examine the effects of routine vaccination on immune function in patients with CFS/ME. Method: CFS patients were selected based on the Centre for Disease Prevention and Control (CDC) case definition of CFS/ME. A total of 20 CFS/ME patients and 20 health controls were recruited for this study. Blood samples were collected from all participants prior to vaccinations, and 7 and 28 days post vaccinations. Immune parameters that were assessed on the samples included Natural Killer (NK) cytotoxic activity, NK phenotypes, cytokine secretion and the expression of lytic proteins. ANOVA and repeated measures were the statistical methods employed to analyse the data with p-value set to 0.05 as the criterion for significance. Result: Preliminary findings suggest a potential role of vaccines in the pathophysiology of CFS/ME. Conclusion: These results may be important for developing effective therapies for the management of CFS/ME and establishment of guidelines for immunization of this population.
Brenu, E; Tajouri, L; Marshall-Gradisnik, S; Staines, DR; Petersen, D	Ekua Weba Brenu HBSc, Grad Dip BMed, Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland	The Relationship between Steroid Hormones and Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P170-171.	Objective: Autoimmune diseases are known to affect more females than males. During pregnancy women with autoimmune diseases such as Multiple Sclerosis and Rheumatoid Arthritis tend to experience an improvement in their symptoms. In Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) which may resemble an autoimmune disorder, a similar observation has been made. Currently, there are limited data on the relationship between pregnancy and CFS/ME symptomatology;

	4229. Australia Email: ebrenu@student.bond.edu.au			however, this may be an important clue to understanding the mechanism of CFS/ME. The purpose of this study is to ascertain the role of gestational period in patients diagnosed with CFS/ME. Method: The study involves 55 patients diagnosed with CFS/ME based on the Centre for Disease Prevention and Control (CDC). Gene expression analyses using quantitative real time reverse transcriptase polymerase chain reaction (qRT-PCR) and genotyping protocols were used in assessing all PBMC collected from these patients. Result: Our preliminary results elucidated differential expression of genes involved in the gestational process in CFS/ME participants. These genes have also been implicated in some aspects of immune function. Conclusion: These results suggest a role of the gestational process in the mechanism of CFS/ME. These findings may be important for diagnostic and therapeutic purposes.
Brenu, Eku; Van Driel, M; Ashton, KJ; Ramos, SB; Keane, J; Staines, DR; Marshall-Gradnisnik S	Ekua Weba Brenu HBSc Grad Dip BMed, Faculty of Health Science and Medicine, Bond University Gold Coast, Queensland 4229, Australia ebrenu@student.bond.edu.au	Disparities In Innate and Adaptive Immune Cell Activities in Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. p125.	Objective: Cell specific immune investigations have demonstrated a possible link between Chronic Fatigue Syndrome (CFS) and failure to maintain immunological homeostasis. The most common immune cells with known dysfunction in CFS are cytotoxic cells, Natural killer cells and CD8+T cells. This study examined cytotoxic function and markers in CFS patients at 6 months intervals to determine the stability of these observations over time. Methods: 90 CFS patients (mean age 46.5yrs ±11.7) and 50 healthy controls (mean age 41.9yrs ± 9.6) participated in the study. Flow cytometeric protocols were used in the assessment of cytotoxic activity and cell phenotypes and RTqPCR analysis in screening for levels of cytoxic molecules that depict the various cytotoxic pathways. These molecules include, granzymes, perforin, interferon (IFN)-γ and tumour necreosis (TNF-α). Results: Preliminary results indicate that compared to the healthy controls, CFS patients demonstrate significant decreases in cytotoxic activity at baseline, at 6 and at 12 months. Additionally, NK CD56 bright cells remained decreased in the CFS participants. Cytotoxic, molecules were also differentially expressed in these cells in comparison to the healthy group. Conclusion: This study demonstrates and confirms reduced immune function in patients with CFS. These findings substantiate the use of NK cell cytotoxic function as a potential biomarker for CFS.
Brenu, Ekua W; Ashton, KJ; Atkinson, G; Van Driel, M; Staines, DR; Marshall-Gradisnik, S	Ekua Weba Brenu,Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4229, Australia ekbrenu@bond.edu.au	Expression Patterns of miRNAs in Lymphocytes in Patients with Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference.p132.	Objective: MicroRNAs (miRNAs) and transcription factors regulate gene expression and thus are important in modulating the immune responses. Changes in these molecules may be implicated in diseases such as Chronic Fatigue Syndrome (CFS). A number of transcription factors have been shown to be upregulated in CFS patients. However, the role of miRNAs remains to be determined. As cytotoxic activity is decreased in Natural Killer (NK) cells and CD8+T cells, this study assesses the role of miRNAs molecules in CD8+T cells and NK cells in CFS patients. Methods: 30 CFS patients meeting the CDC case definition (45.3±11.7 yrs) and 30 healthy controls (41.8±9.6 yrs) were recruited into the study. Blood samples were collected from all participants following which lymphocytes were preferentially isolated via a negative isolation system to yield a pure sample of NK and CD8+T cells. RNA was extracted and

				converted into cDNA and miRNAs of interest were assessed using RT-qPCR. Statistical analysis was performed using the t-test. Results: Of the fifteen miRNAs investigated six were found to be down regulated in both the NK and CD8+T cells in CFS patients compared with healthy controls. Most of these miRNAs target genes that are involved in cell cycle regulation, apoptosis and toll like receptor expression. Conclusion: This study confirms changes in miRNA expression in cytotoxic cells that may be related to the poor function of these cells in CFS patients.
Brenu, Ekua; Ashton, KJ; Van Driel, M; Hardcastle, S; Staines, DR; Marshall-Gradisnik, S	Ekua Weba Brenu, Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4229, Australia ebrenu@student.bond.edu.au	Longitudinal Assessment of Adaptive Immune Regulation in Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference.p125-126.	Objective: Chronic Fatigue Syndrome (CFS) is known to persist for more than 6 months with a very slow recovery rate. It is not known whether immunological abnormalities in CFS remain stable over time or change during the course of the disease. Additionally cytokine measurements have not been consistent across studies which may be associated with the fluctuating pattern of the disease. This longitudinal study assesses proteins and receptors secreted and expressed by CD4+T lymphocytes in CFS patients over time, at baseline, 6 and 12 months. Method: 50 CFS meeting the CDC case definition and 30 non-CFS control participants were recruited from two states in Australia. Peripheral blood mononuclear cells were preferentially isolated from whole blood samples collected from participants. The samples were then assessed for the expression of Th1, Th2, Th17 cytokines, IL-1α, IL-1β and TGF-β using cytometric bead array and flex set kits. Result: At baseline there was an increase in IL-10, TNF-α and IFN-γ in the CFS group compared to the healthy control group. However, after 6 months IL-2 was significantly increased and IL-10 and IL-17A were significantly decreased in the CFS group while after 12 months only IL-2 was observed to be significantly increased in the CFS group. Conclusion: These results suggest that the cytokine profile in CFS changes during disease progression. This may be associated with disease severity and/or concurrent environmental stressors. Hence there is a need to match experimental findings with data on clinical disease progression.
Brenu, EW; Marshall-Gradisnik, S; Staines, DR; Petersen, D	Ekua Weba Brenu, Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4229. Australia Email: ebrenu@student.bond.edu.au	Assessment of Natural Killer Cell Function in Chronic Fatigue Syndrome/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P171-172.	Objective: Immunological abnormalities are recognized as an important component of Chronic Fatigue Syndrome (CFS). Natural Killer (NK) cell dysfunction is the most common immunological finding across studies. It has been suggested that these reductions in NK cell function is caused by decreases in the expression pattern of perforin and granzyme molecules. However, other factors may be involved in NK cell dysfunction. Hence the purpose of this study is to investigate other potential mechanisms of NK cell dysfunction in Methods: This study examined samples collected from 20 CFS/ME subjects and 5 normal controls. CFS participants were preselected by demonstration of low NK cell function and diminished VO2 max on stress testing. Using flow cytometry and real time quantitative PCR, samples were assessed for levels of cytokines, lytic molecules and expression of miRNAs. Results: Preliminary data demonstrated differential expression of cytokines, miRNAs and cytotoxic molecules in the CFS/ME participants compared to healthy controls. Additionally, cytokines, perforin and granzymes were differentially expressed

				between groups for both the serum and CSF. Conclusion: These results confirm the observation of impaired NK cell function in, CFS/ME patients which may be related to alterations in cytokines and lytic proteins.
Brenu, EW; Marshall-Gradisnik, S; Staines, DR; Petersen, D	Ekua Weba Brenu, Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4229Australia Email: ebrenu@student.bond.edu.au	Purinergic Signaling in Chronic Fatigue Syndrome/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P191.	Objective: Chronic Fatigue Syndrome (CFS) is a multi-factorial disease that involves abnormalties of neuro-endocrine immune function. Presently, a number of neuropeptides have been associated with CFS. This may be attributed to their role in regulating immune function. These neuropeptides are involved in purinergic signaling and their compromise may be associated with receptor differences or other derangements of the adenosine pathway. This study examines the expression pattern of purinergic receptors and the molecules in involved in the signaling pathways. Method: Cerebrospinal fluid (CSF) and peripheral blood mononuclear cells (PBMCs) collected from 20 CFS/ME and 5 normal control participants were examined for the expression pattern of the various purinergic receptors and second messenger systems using ELISA and gene expression protocols. Statistical analysis used in this study is ANOVA with p-value set at 0.05. Result: Preliminary data demonstrated differential distribution of purinergic receptors in CFS participants compared to the healthy controls. Similarly, ATP, cAMP and adenosine were also differentially expressed in the CFS/ME participants compared to the controls. Conclusion: These results suggest potential involvement of the CNS in the mechanism of CFS/ME. Further studies are required to assess the potential significance of these findings in CFS/ME.
Broderick, G; Ben Hamo, R; Efroni, Ma; Fletcher, Ma; Nathanson, L; Vernon, SD; Klimas, NG	Gordon Broderick, Ph.D., Associate Professor, Department of Medicine, University of Alberta, Suite 225B CollegePlaza, 8215 112 Street NW, Edmonton, AB, T6G 2C8, Canada; gordon.broderick@ualberta.ca	Prefential Pathway Activation in Gulf War Veterans with Unexplained Neuroendocrine-Immune Imbalances	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P178.	Objectives: Though potentially linked to the basic physiology of stress response we still have no clear understanding of GulfWar Illness (GWI). Indeed clinical presentation of GWI overlaps strongly with that of another stress-mediated illness: Chronic Fatigue Syndrome (CFS). Recent efforts by our group have cast individual molecular messages in the greater context of immune signaling and cellular demographics. Here, we extend this approach by incorporating *a priori* knowledge of biological pathways to support molecular discrimination of these sister illnesses. Methods: *Cohort*. Male CFS (n=7), GWI (n=20) and healthy veterans (n=11), comparable in age, body mass index (BMI) and ethnicity, were assessed using Fukuda criteria. Stress response was stimulated by way of a standard Graded Exercise Test (GXT) and blood drawn 30 minutes prior to exercise, at peak effort (VO2 max) and 4-hours post exercise while controlling for diurnal variation. Gene expression in circulating immune cells was measured using the Affymetrix HG U133 plus 2.0 microarray. *Computation*. Using a novel method we first assessed compatibility in the expression of genes supporting a pathway segment with the expected molecular association dictated by known biochemistry. For pathway segments supported consistently in the data we then estimated the likelihood that these step reactions were active in a specific sample. Pathway segment activity levels were computed in every sample in the response time course and then compared across patient groups using standard non-parametric tests. Results: Even at rest CFS and GWI patients were distinguished from each other

				and from controls with an accuracy of >85% with fewer than 3 pathways. Using progression across all 3 time points, single pathways were sufficient to separate groups. CFS and control subjects were distinguished with 85% accuracy by suppression of *alanine and aspartate metabolism* (KEGG) alone (pWilcoxon<0.0001). Similarly a classification accuracy of close to 80% was obtained for GWI subjects on the basis of activity in the *1- and 2-methylnaphthalene degradation* pathway (KEGG) (pWilcoxon=0.05), which appeared chronically suppressed in this group. Finally, CFS and GWI subjects were best distinguished with activity in *chondroitin sulfate biosynthesis* (KEGG) (accuracy >85%; pWilcoxon<0.0001). Complete separation of these illness groups was achieved with the addition of *aurora A signaling* (NCI/Nature) (pWilcoxon<0.0001) and signaling mediated by transmembrane protein *syndecan-1* (NCI/Nature) (pWilcoxon=0.024). Aurora A activity is a key component in mitosis and meiosis. It has been associated with a range of malignancies and is significantly increased in GWI vs. CFS. Conversely syndecan-1 has been used as a marker of effector B cell activity and is significantly depressed in GWI compared to CFS patients. Conclusion: Together these pathway segments supporting immune signaling, cytotoxic function and metabolism offer not only a framework for molecular diagnosis but also a glimpse into fundamental imbalances in immune cell signaling and metabolism in each illness.
Broderick, Gordon; Ben Hamo, R; Efroni, S; Katz, BZ; O'Gorman, MRG; Nathanson, L; Fletcher, MA; Vernon, SD; Taylor, R	Gordon Broderick, Ph.D, Associate Professor, Department of Medicine, University of Alberta, Suite 225B College Plaza, 8215 112 Street NW, Edmonton, AB, T6G 2C8, Canada gordon.broderick@ualberta.ca	Linking Lymphocyte Metabolites with Clinical Course in Post-Infectious Fatigue	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P127-128.	Objectives: Chronic Fatigue Syndrome (CFS) affects between 1 and 4 million individuals and costs an estimated $35 billion per year in lost productivity and health care. As CFS can follow Epstein-Bar virus (EBV) and other systemic infections, our objective was to describe differences in immune activation in post-infective CFS (PI-CFS) patients compared to recovered controls. Methods: We studied 301 Chicago-area adolescents prospectively over 24 months following diagnosis of monospot-positive infectious mononucleosis (IM). Cluster analysis of subjects chronically fatigued at 24 months (4.3% of cohort) revealed 3 clinical courses: i) a sustained increase in fatigue after an early partial remission (C1), ii) a monotonic decrease in fatigue (C2), or iii) a slow decrease in fatigue after a peak at 12 months (C3). Cryopreserved samples of peripheral blood mononuclear cells (PBMC) were also recovered from 7 PI-CFS subjects and matched recovered controls. Duplicate gene expression profiles were obtained in these samples using the GeneChip Human Gene 1.0 ST microarray (Affymetrix, Santa Clara, CA). A novel computational method was used to assign probabilities of discrete up and down-expressed states for each gene in every individual sample. These probabilities were then combined to identify consistent representation of known molecular interactions and quantify the activity level of close to 600 cellular pathways catalogued in the National Cancer Institute (NCI)/Nature Pathway Interaction Database (PID) and the KEGG database. Patients and patient groups were then compared statistically on the basis of the estimated activity levels of these pathways. Results: Previous analysis of plasma cytokines in this

				cohort indicated immune signaling anomalies specific to PI-CFS subjects and present to different extents in each fatigue sub-group. Consistent with this, 20% of expressed genes (of 92 with fold change>2, p<0.05) supported cell signaling and/or immune function. Close to half however (47%) supported cell metabolic function. Derivation of pathway activity levels in individual subjects greatly reduced the false discovery rates (FDRs) isolating 5 pathways with significantly altered activity in PI-CFS (FDR<0.10, p< 0.005). Phenylalanine metabolism and Trk neuronal receptor signaling were significantly suppressed in PI-CFS (p=0.002, 0.004; FDR=0.08, 0.09) while starch metabolism, glycolysis and pentose phosphate metabolism were up-regulated (p=0.000, 0.001, 0.003; FDR=0.04, 0.07, 0.09). Of these, phenylalanine metabolic activity also supported the separation of fatigue sub-groups, with higher activity being linked to a more favorable prognosis. Conclusion: These preliminary results suggest that observed differences in cytokine expression are consistent with altered metabolic activity in circulating lymphocytes in PI-CFS patients. These differences may also inform on the course and underlying causes of this illness.
Campbell-Smith, Dianna	[no address given]	Whole Body Vibration Used with Positive Psychology Strategies - New and Vital Component of Multi-Modal Treatment for Decreasing the Pain of Fibromyalgia/Chronic Fatigue While Improving Happiness Levels	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P148.	From a psychological perspective, working with clients who have been diagnosed with Fibromyalgia or Chronic Fatigue can be a challenging task in that there are both difficult physiological implications as well as a tendency towards concurrent depression. Using Cognitive Behavioural Therapy (CBT) with these clients has been researched and found to be somewhat effective. There is evidence that using a CBT approach is most effective when combined with exercise therapy and at times, pharmacotherapy as well. From an anecdotal point of view, using CBT alone does not always allow the individual with Fibromyalgia or Chronic Fatigue to move out of their pain enough to learn and integrate new ways of thinking or behaving. The pain is often described by clients as sapping all their energy such that there is little ability to undertake anything but the basics of their day to day requirements. When given homework which may well be able to help clients often say they just do not have the energy to do anything new. The research on multimodal approaches has been encouraging. To move out of depression requires that a client focus on new techniques and strategies but in order to utilize this focus some reduction in the pain and fatigue would more easily allow integration of new materials. There are a handful of research articles looking at the value of WBV to ease pain for Fibromyalgia and Chronic Fatigue clients. One such study used exercise alone as compared to exercise supplemented with whole body vibration. The conclusion of the study showed that exercise supplemented with whole body vibration was beneficial whereas exercise alone was not. Another study concluded that WBV helped with the balance aspects often a problem with Fibromyalgia. Further research into use of whole body vibration machines as part of a multi-modal approach is warranted. In this multi-modal approach it is suggested that clients would be taught how to use of techniques to

				increase their level of happiness while decreasing their experience of pain and fatigue. Given the research into pain reduction through use of wbv, as scant as it is, it suggests a number of sessions on a whole body vibration machine throughout the week. Each session would be increased from a few minutes up to ten minutes three times each week. Pain assessed on a weekly basis to ensure continued reduction would be required. Clients would learn how to integrate new ways of thinking that discover and take advantage of their own strengths such as creativity, love of learning, bravery and valour as determined from the Character Strengths (Peterson and Seligman, 2007). The research into pain reduction through use of WBV, as scant as it is, suggests a number of sessions on a whole body vibration machine throughout the week. In addition, counseling sessions could be used to displace habitual negative thinking by helping clients to integrate positive psychology thinking and activities. As is the case in counseling, a single style of therapy does not work for every client. Some are helped by Cognitive Behavioural Therapy, some by Narrative therapy and others may be helped by Art therapy. It is likely that in order to help a broader range of clients with Fibromyalgia or Chronic Fatigue that a number of different multi-modal strategies should be considered. Given some of the positive studies of whole body vibration, use of this equipment in conjunction with positive psychology techniques to increase happiness levels should be considered. Further research in this area is certainly warranted as anecdotal reports suggest that they may be some benefit.
Carruthers, Bruce M	[no address given]	The New International Consensus Criteria for ME: Content and Context	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P121.	Contents- the general thrust of the 2003 Canadian Consensus Criteria was retained and developed further. Several changes were made- e.g. the 6 month waiting period was no longer required, but left to clinical judgment. The symptom pattern of Post-Exertional- Neuroimmune-Exhaustion (PENE) was kept criterial and further articulated. Symptoms and symptom interactive patterns arising from the following subsystems- neurocognitive, pain processing, sleep disturbances, neurosensory and motor, immune, gastrointestinal, genitourinary and endocrine subsystems as well as energy transport impairments (cardiovascular, microvascular, respiratory, thermostatic homeostasis, intolerance of temperature extremes and stress intolerance) are noted if present. Interactive dynamical pattern matches between PENE symptom patterns and those from pathophysiologial subsystems for individuals and groups of patients are noted for causal projectability over time will be mutually confirmative as real kinds. Modifications for paediatric cases were added. The past historical context is described as well as future implications of this case definition plus any descendents are discussed regarding future research directions, case segregation, and treatments. In conclusion, it is hoped that this case definition and its descendents will continue to emphasize both the clinical/epidemiological/research realms of observation and challenge all participants to integrate them into a mutual confirmation/disconfirmation process that characterizes both clinical medicine, epidemiology and science in general.

Cheney, Paul R	[no address given]	Compassionate Use Treatment of CFS with GcMAF	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P151-152.	Introduction: GcMAF is a partially deglycosylated vitamin D binding protein (VDBP) also known as Gc protein. The functional change in the Gc protein caused by deglycosylation is known as GcMAF. GcMAF is extremely potent and will at very low concentrations activate, regulate and expand macrophages which are the central processing unit of the immune system and capable of modulating and controlling both the innate and cognate immune systems. Methods: Twenty-five CFS patients meeting the 1994 CDC criteria were selected from a national referral practice and under informed consent were self-treated with a semi-synthetic GcMAF administered by sub-lingual route. Previous reports from clinicians in The Netherlands using this commercial-grade version of human GcMAF suggested significant bioactivity and promising clinical responses in CFS cases in The Netherlands. Patients were monitored for blood chemistry, CBC, active and non-active forms of vitamin D as well as Nagalase activity. VDR polymorphisms determined from restriction enzyme products of BsmI and FokI were determined and a clinical instrument for symptom assessment of the seven key CFS symptoms was used to evaluate patient response. The protocol called for administering initially low doses of GcMAF at 20 ng SL every five days for the first 30 days followed by a q 5 day ramp to 100 ng SL using 20 ng increments. The study length was scheduled for 5 months but is being extended on a case-by-case basis. Results: Results are reported here for those eighteen CFS patients who have received a minimum of two months of sub-lingual GcMAF. 6/18 or 33.3% had a significant to clinically resolved response in at least two of seven critical CFS symptoms and two of those were functional cures at 80 KPS units or better. 5/18 or 27.8% failed to respond at all or even got worse over those same seven key symptoms. The remainder or 38.9% (7/18) had a mild to moderate improvement in two or more significant symptoms. A total of 72.2% (13/18) responded to GcMAF. VDR polymorphism data in 11 of 18 patients are known and the balance pending. Of these 11 with known VDR results, 3 of 4 who were non-responders were either BB or ff genotypes suggesting that if you had a BB or ff, you had a 75% chance of being a non-responder. On the other hand, there were no BB's in the best responding group of four suggesting that if you had a BB, there was no chance at all of being a significant responder or cure though there was a 33% chance of being a mild to moderate responder but only a 14% chance of being a member of the combined response group (1 chance in 7). Analysis of calcitriol levels demonstrated that there were three response patterns to GcMAF that were predictive of clinical response. All those with low to normal calcitriol to start with who then had a modest rise in calcitriol in response to GcMAF responded clinically (6/6). All those whose calcitriol was initially low to normal that did not respond at all to initial doses of GcMAF failed to respond clinically (4/4). In those with elevated initial calcitriol (>68) had a mixed response with 5 of 7 responding and 2 of 7 not responding. Initial D3 levels were variable and did not predict response nor did their response to GcMAF predict response. Nagalase activity was elevated in all study

				participants (average 3.4, range 1.3-6.5). 87.5% of the patients tested for XMRV were positive (14/16). In 6 of 8 with known response data, Nagalase activity declined with therapy and one patient declined to zero and is one of the recovered patients (KPS > 80). Conclusions: GcMAF appears to be a relatively benign and generally effective treatment for CFS. Most patients, however, had early though short bouts of what appeared to be exacerbations of CFS symptoms regardless of the eventual outcome. Two patients who were deemed responders developed clinical vitamin D toxicity later in their treatment heralded by a rapid rise in calcitriol above 90 as Nagalase dropped but responded very well to GcMAF dose reduction or elimination with no lasting effect on their previously good responses. Nagalase activity generally fell especially in the best responders and initial calcitriol response was predictive of outcome in most patients.VDR genomic data appears to also be a predictor of the relative chance of response vs. non-response to GcMAF.
Cheney, Paul R	[no address given]	Nagalase Activity is Inversely Correlated with CFS Clinical Status (KPS)	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P181-182.	Introduction: The sera of patients with HIV and cancer possess alpha-N-acetylgalatosidase enzyme activity known as Nagalase activity. This glycosidase activity appears to reside in the proteolytically cleaved gp160 envelope protein of HIV and also found in the similarly cleaved envelope protein of influenza virus and possibly possessed by other classes of virus that probably induces viral virulence as this glycosidase activity appears to be important in both cellular entry by virus-to-membrane fusion and immunosuppression. Nagalase activity specifically destroys the Gc protein (VDBP) precursor capacity for GcMAF activity leading to direct immunosuppression. Cancer cells also secret Nagalase activity that may come from genomic activation of HERV's within these cells or other viruses active within such cancer cells. In metastatic breast cancer, Nagalase activity correlates with tumor burden and Nagalase values dropping to control ranges near zero correlate with eradication of tumor cells resulting in a prolonged cancer free state lasting years. Nagalase has also correlated even better than CD4 counts for clinical status of HIV patients. Methods: We measured Nagalase activity in 50 consecutive CFS cases with an average age of 47.7 years. There were 20 males and 30 females from a national CFS referral center meeting the 1994 CDC CFS case definition. Serum Nagalase activity was measured in nmoles/min/mg protein by a commercial laboratory (ELN Labs, NJ). The idea to measure Nagalase was suggested by the detection of XMRV in the great majority of patients in this national practice (> 75% positive for XMRV with one measurement and > 95% if measured more than once at a CLIA certified laboratory, VIP Dx, NV). All patients during their office visits at this clinic are routinely given a physician assigned functional capacity score known as the Karnofsky Performance Score or KPS which has been well validated in both CFS and other chronic diseases. This clinic has had two decades of experience using this physician applied functional score including FDA sponsored clinical trials. Patients were sent kits for Nagalase testing and then assigned a KPS score in their charts. Inter-assay measures of KPS

				typically can vary plus or minus 5 KPS units over time by chance alone in CFS unless there is a significant shift in clinical status which usually occurs slowly over time. KPS is not a symptom score and expresses what the patient can and cannot do with respect to activities of daily living. Results: The Nagalase activity of 50 consecutive CFS cases reported here averaged 3.0 nmoles/min/mg protein, range 0.8 – 6.7. The Nagalase mean of CFS cases is comparable to HIV and comparable to breast cancer in respect to both mean and range. Average KPS was 59, range 40-90. Correlation statistics were developed for Nagalase vs. KPS. KPS was found to be negatively correlated with an r-square of 0.3, $p < 0.00005$, $N = 50$. The only two CFS cases with a KPS > 80 were at control values for Nagalase and one was our best responder to GcMAF (see GcMAF Abstract). XMRV detection rate in this 50 patient cohort was 77%, mostly single measures by culture and/or serology. Conclusion: Nagalase activity has been previously demonstrated to be an excellent clinical status marker in HIV and cancer. This data supports the hypothesis that Nagalase activity is also a good clinical status marker for CFS. The origin of Nagalase activity in CFS remains unknown but its finding in all disabled cases to date and that it correlates with clinical status along with the finding that almost all of the same cases are XMRV positive supports the hypothesis that XMRV may be the cause or contributes to Nagalase activity in CFS.
Chester. AC;	Alexander C. Chester, MD, Clinical Professor of Medicine, Georgetown University Medical Center, Washington, DC, 3301 New Mexico Ave, NW, Washington DC 20016, achester@foxhallinternists.com	Chronic Rhinosinusitis as an Overlooked Chronic Fatigue Syndrome Exclusionary Condition	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P177-178.	Objectives: To search for symptom similarities between chronic rhinosinusitis (CRS), a chronic fatiguing illness, and unexplained chronic fatigue (UCF). Methods: A MEDLINE literature search of the symptoms and natural history of CRS was performed. Results: Fatigue is one of eight symptom criteria formulated by the American Academy of Otolaryngology–Head and Neck Surgery Rhinosinusitis Task Force to establish the diagnosis of CRS. Chronic rhinosinusitis–related fatigue is associated with symptom severity scores approximating those of other CRS-related symptoms, including facial pressure, headache, and nasal discharge. In one series of patients with CRS, 86% of those surveyed noted fatigue, which was described as severe or very severe in 32% of patients surveyed and as the most disabling CRS symptom in 14% of patients surveyed. In the only meta-analysis comparing CRS vitality scores on the 36-Item Short Form Health Survey (SF-36) before and after sinus surgery, all preoperative vitality scores were below local norms. In the only series comparing CRS vitality scores with other disease norms, vitality scores were significantly lower (worse) than those of patients with congestive heart failure, chronic obstructive pulmonary disease, or chronic back pain. Fatigue associated with CRS improves after sinus surgery. Patients with CRS and severe fatigue demonstrate greater improvement in fatigue than the improvement noted in patients with less severe fatigue after surgery. Similarly, patients with CRS and concurrent fibromyalgia demonstrate greater improvement in fatigue than the fatigue improvement noted in patients without fibromyalgia. In a study of patients with UCF, CRS symptoms were significantly more common than in patients without UCF. Odds ratios (95% confidence intervals) for CRS symptoms in

				that study were 9.7 (5.2-18.2) for facial pressure, 21.9 (10.9- 44.0) for heavy-headedness, 3.1 (1.5-6.6) for sore throat, and 9.2 (4.3-19.7) for tender cervical lymph nodes. In a meta-analysis comparing CRS bodily pain scores on the SF-36 before and after sinus surgery, all preoperative bodily pain scores were below (worse than) local norms. Bodily pain associated with CRS improves after sinus surgery. Chronic rhinosinusitis usually begins with a significant upper respiratory tract infection, as is often observed with UCF. All UCF symptom criteria have been documented in CRS. Like UCF, CRS is not associated with objective findings. In patients with CRS, no abnormalities are noted on routine or specialized blood tests. Although sinus computed tomographic (CT) images can document sinusitis, symptoms usually do not correlate with CT findings, and the extent of abnormalities noted is often similar in patients with and without CRS symptoms. Conclusions: Chronic rhinosinusitis is a fatiguing illness usually unassociated with objective findings and defined by symptoms similar to those of UCF. Therefore, CRS should be considered a possible cause of otherwise unexplained fatigue and should be studied for atypical mechanisms that cause fatigue. In addition, CRS, a treatable illness, may easily be misdiagnosed as UCF.
Chia, John K; Chia, Andrew; El-Habbal, Rabiha;	John K. Chia, M.D., 23560 Crenshaw Blvd., #101, Torrance, Ca 90505, evmed@sbcglobal.net	Pathogenesis of Chronic Enterovirus Infection in Myalgic Encephalomyelitis(ME/CFS) –in vitro and in vivo Studies of Infected Stomach Tissues	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P142.	Objectives: Chronic enterovirus infection has been implicated in the pathogenesis of ME/CFS. Previously, we demonstrated enteroviral protein (VP1), RNA and non-cytopathic viruses from the stomach biopsies of ME/CFS patients. The basis of viral persistence has not been clearly defined. Enterovirus can form double-stranded RNA (dsRNA) in tissue cultures and in muscles of infected mice and human. We evaluated the presence of dsRNA in the stomach biopsies and possible infectivity of stomach tissues in SCID mice. Method: Archived, paraffin-embedded stomach biopsies from CFS patients and controls were stained for dsRNA using antidsRNA monoclonal antibody and immunoperoxidase technique. 9 cryopreserved ,VP1+ and dsRNA+ stomach biopsy samples were injected ip into SCID mice; and 2 boiled RNA+ samples, 4 VP1-neg and dsRNA-neg samples and one sample of culture medium were injected ip into other 7 SCID mice as controls. Mice were sacrificed 3-4 weeks after infection, and organs processed for viral cultures, EV RNA and viral protein staining. Results: 108/132 (82%) and 84/132 (64%) of the stomach biopsies from ME/CFS patients stained positive for VP1 and dsRNA respectively, whereas 4/40 (10%) of the control specimens were positive for dsRNA ($p<0.01$, $\chi 2$ test). Pretreatment with RNase III of selective samples diminished or abolished the dsRNA staining; higher concentrations of enzyme and incubation period were required for specimens from sicker patients. 21/23 (91%) of stomach biopsies previously tested positive for EV RNA by RT-PCR or had grown non-cytopathic virus were positive for dsRNA. Of organs taken from SCID mice injected with stomach biopsies, 7/9 (78%) spleen specimens were positive whereas 0/7 controls were positive for VP1 protein by immunoperoxidase staining ($p<0.01$, $\chi 2$ test). 4/9 lung specimens 0/8 of heart, liver and kidney sections demonstrated VP1 staining. All tissue homogenates were negative for EV RNA or

				growth of virus in BGMK-DAF and WI-38 cells. Conclusion: DsRNA was frequently demonstrated in the VP 1+ stomach biopsies taken from ME/CFS patients, and most EV RNA+ samples had detectable dsRNA. In pilot experiments, dsRNA+ samples were infectious in SCID mice, as compared to control samples. Enteroviral dsRNA may play a central role in the pathogenesis of chronic EV infection and ME/CFS, and the mechanism should be further investigated.
Chia,John K; Chia,Andrew	[no address given]	Rifampin Augments the Effects of Oxymatrine/Equilibrant (oxm/equi) In Patients with Myalgic Encephalomyelitis/CFS	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P117-118.	Objectives: Chronic enterovirus infection has been implicated in the immunopathogenesis of ME/CFS. Previously, we demonstrated the benefit of oxm/equi, an herbal immune booster, in 50% of ME/CFS patients. Concomitant administration of rifampin in one patient resulted in flu-like symptoms and ulceration of infected pharyngeal tissues, which was followed by symptomatic improvement and decrease of chronically elevated Coxsackievirus B3, 4 antibodies. We evaluated the adjunctive effect of rifampin in patients who were taking oxm/equi. Method: 46 patients who fulfilled the CDC criteria for ME/CFS were treated with rifampin 300 mg po bid for 7 days while taking oxm/equi (32 responders and 14 non-responders, duration 1.32±0.86 years). 45 patients treated with oxm/equi without rifampin, and 45 outpatients treated with doxycycline and rifampin for MRSA (methicillinresistant Staphylococcus aureus) infections served as controls. Laboratory studies including CBC, chemistry panel, CPK were obtained before and during treatment if patient had flu-like symptoms. Cytokine gene expression of peripheral blood was performed before and during rifampin treatment for 10 ME/CFS treatments. Results: 31/46 (67%) patients developed significant flu-like symptoms lasting few days during or after the one-week rifampin treatment. 23/33 (70%) of responders and 0/13 non-responders had additional improvement of fatigue and other symptoms ($p < 0.01$, X2 test). 21/33 (64%) responders who had taken oxm/equi ≥ 1-2 years were able to discontinue the herbs within weeks or months of flu-like symptoms and remained in remission. 0/45 ME/CFS patients on oxm/equi alone and 0/45 MRSA-infected patients on doxycycline and rifampin developed flu-like symptoms. Laboratory studies showed no significant changes, and gene expression study of 12 cytokines demonstrated increase of TNF-α and IL-1α,β mRNA while on rifampin and oxm/equi. Conclusion: Flu-like symptoms were commonly observed in patients who took oxm/equi concomitantly with rifampin, as compared to controls. Subsequent symptomatic improvement was observed in > 60% of oxm/equi responders. Short course of rifampin may be beneficial in ME/CFS patients who are responding to oxm/equi. The possible mechanism of enhanced immune response will be discussed and further investigated.
Claw, Daniel J	[no address given]	Session: FIBROMYALGIA: Are tender points necessary? A debate	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P119.	[no abstract available]

		Tender points are Unneccessary		
Coffin, J	Department of Molecular Biology and Microbiology, Tufts University, Boston, MA 02111,USA	The Case AGAINST Human Gamma Retroviruses (HGRV) in CFS/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P116.	Xenotropic MLV-related retrovirus (XMRV) was first reported about 5 in a few cases of prostate cancer, but did not attract much attention until its reported association with a large fraction of chronic fatigue syndrome cases about 2 years ago. The publication of the XMRV-CFS connection created a ripple of excitement and interest in the scientific, medical, and patient communities reminiscent of the reports of the association of another retrovirus— HIV--with AIDS some 25 years previously. However, most of the results of the XMRV paper – isolation of infectious virus from patients, frequent detection of virus in plasma and PBMCs by PCR, detection of antiviral antibodies - remain to be replicated outside of the laboratories that authored the original report despite considerable effort worldwide. Indeed, XMRV is now considered by most virologists to be the consequence of a collection of artifacts originating from endogenous murine leukemia viruses prevalent in laboratory and wild mice. There are several related, but distinct, issues that need to be considered. First, various mouse (*Mus musculus*) subspecies carry over a hundred different endogenous proviruses closely (>90%) related to XMRV in their DNA. Second, mice are extremely widespread, as is their DNA, which can be found sporadically on laboratory surfaces, as well as contaminants of common reagents and materials. Sensitive PCR assays can detect "XMRV" related sequences in DNA from tiny fractions of one cell. To detect such contamination, we developed a more sensitive assay based on mouse IAP sequences present in thousands of copies per cell. Third, although only a few of the endogenous MLV proviruses encode infectious virus, it has been known since the 1970s that some of them can give rise to virus that can infect human tumor lines when passaged through nude mice. Indeed, A virus identical to XMRV is produced by the 22RV1 prostate cancer line that was derived in just this way. In initial reports, however, XMRV did not appear to be sufficiently similar to known proviruses to have been derived this way. However, we have recently shown that this is exactly how it did arise, but not from infection of the precursor CWR22 xenograft with a single virus, but rather with a recombinant between the progeny of two previously undescribed proviruses found in the nude mice used for passage. Since the predicted recombinant is ancestral to all XMRV isolates, and cannot have arisen more than once, it must have found its way into many laboratories as the 22Rv1 cell line was distributed worldwide and, by means that remain to be worked out, into clinical samples from CFS patients.
De Meileir, K; Rowe, C; Frémont, M	Himmunitas Foundation, Brussels, Belgium	*Naglase Activity is A Good Marker For ME/CFS*	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P192.	Objectives: The GcProtein or Vit. D binding protein is naturally transformed in the body by intervention of sialidase of T cells and beta-galactosidase of B cells thus removing 2 sugars from the Gc's protein's trisaccharide group, leaving a single sugar at the threonine location. The protein is now GcMAf and can activate macrophages. Previous research has shown that the enzyme alpha-N-acetylgalactosaminidase, called Nagalase, removes the entire trisaccharide group. Deglycosylated GcProtein

				cannot activate macrophages. Because ME/CFS patients often have reduced macrophage / NK cell function we hypothesized that Nagalase activity would be elevated in these patients. Methods Serum Nagalase activity was determined in 395 ME/CFS patients who met both the Canadian clinical criteria for ME (2003) and the Fukuda criteria for CFS (1994). The Nagalase assay was performed on serum. The blood was centrifuged within one hour of venous blood drawl and serum was frozen immediately till assayed. The assay method used is described in J. Med. Virol. 81:p.9 (2009) by Yamamoto et al. Healthy control sera exhibit very low enzyme activities. Statistical Analysis: A one-sided t test was used to test the hypothesis that the mean value of the ME group is significantly different from the middle of the normal range (representing the normal population). Results: Average serum Nagalase activity was 1.72 nmol/min/mg (range 0.28-4.0). This is significantly higher compared to levels in normal controls (0.35-0.68 nmol/min/mg) (Yamamoto, 2009). Only 12 of 395 patients had a Nagalase activity below 0.69 nmol/min/mg, or 3 % of the study population. Conclusion: When tested in a large cohort of ME/CFS patients, serum Nagalase is increased in 97 % of the study population. Irrespectively of the cause of these findings, serum Nagalase activity is a good marker to distinguish healthy people from ME/CFS patients. These data provide indirect evidence for low macrophage activity in ME patients.
De Meirleir, K	Vrije Universiteit Brussel & Himmunitas Foundation, Brussels, Belgium	Compassionate Use of GcMAF IN ME/CFS Patients	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P142-143	Objectives: Immune dysregulation is an established feature of ME/CFS, reflected in the altered balance of immune activity, allowing reduced protection from certain infections, viral re-activation, excess Th2/Th17 activity causing increased inflammatory symptoms and autoimmunity. This is the foundation for symptom expression as well as additional consequences of reduced immune protection (intracellular infection, fungal overgrowth, parasitic infestation, mould sensitivity). Recently the detection of gamma Retroviral (GRV) Infection involving Murine Leukaemic Virus (MLV) and Xenotropic Murine Retrovirus (XMRV) is shown in a majority ME/CFS and in 3-5% controls (Lombardi et al.). The resultant multisystem illness opens the door to a variety of treatment protocols, but despite this approach, the treatment response is slow, may plateau or not occur. GcMAF has been shown to enhance immune activity and has been used in the role of cancer therapy and in HIV. Its use in addressing the immune dysregulation in ME/CFS and complications has recently started (on compassionate grounds) in those in whom there is no significant response to other therapies, and who suffer marked limitation due to this illness. Methods: Patients (age 18-65) were selected in whom a diagnosis of ME/CFS was made, based upon history, physical examination, routine and specific investigations, and the fulfilment of the Canadian Clinical Criteria and who were diagnosed with XMRV and/or MLV. These included immune and viral studies. They were all XMRV and/or MLV positive. In those patients in whom there was serious illness, were refractory to other treatment protocols and marked limitation due to symptoms

				severity were administered GcMAF. It was used in a concentration of 100 nanograms/ml of physiological serum and administered by weekly injections of 0.25 ml to 1.0 ml by intravenous route or subcutaneously. There was regular follow-up throughout the treatment with review of symptom expression and investigations were performed to monitor treatment response. Duration of Treatment was for 5-40 weeks. *Table 1*- The effectiveness of treatment was assessed by symptom change and expression; monitoring of the condition by routine investigations; measurement of immune response (nagalase, CD57, Perforin, C4A, and comparison with other individual immune parameters shown to be abnormal at the initiation of therapy). Results: - *Table 2: Preliminary data on the outcome: 68/108 (63%) report noticeable improvement.* Side effects were present in 18 %; these mainly, were but not restricted to headaches and sleep disturbances. This was managed by lowering the dose, which usually solved the problem. Therapy was ceased in 7 % because of severe headaches and/or sleep disturbances. Delay in response may be attributed to VDR genotype and so effect of therapy may yet to be expressed amongst those regarded at this stage as non-responders. Conclusion: The use of GCMAF in XMRV+ and/or MLV+ patients ME/CFS patients for whom other treatments were refractory, has been shown to safely produce symptomatic relief when administered weekly for specific periods of time. These "positive" preliminary data need to be confirmed in a double-blind placebo controlled GcMAF study.
De Meirleir, K; Frémont, M	Vrije Universiteit Brussel & Himmunitas Foundation, Brussels, Belgium	GVDR-Fok1 and GVDR-Bsm1 Polymorphisms in ME/CFS Patients	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P190.	Objectives: Several researchers have demonstrated abnormalities in Vitamin D metabolism in ME/CFS patients. The individual degree of responsiveness of Vit. D binding protein – macrophage activating factor (GcMAF) is according to Ruggiero et al. dependent on Vit. D receptor (VDR) gene polymorphism, which can be identified by Bsm1 and Fok1, two SNPs (single nucleotide polymorphisms). VDR is also involved in skeletal metabolism, modulation of immune response and regulation of cell proliferation and differentiation. Fok1 is a T-C polymorphism; the T allele leads to a protein which is less effective in transduction of the Vit. D signal, the C allele with a higher response. Bsm1 is a C-T polymorphism. The C allele is associated with Th1 suppression and breast cancer, the T allele with SLE and RA. Given the published scientific studies on the immune system in ME/CFS, we hypothesized that both for Fok1 and Bsm1, the incidence of low responders to GcMAF is higher than in the general population, thus predisposing to a lower natural defense to viruses, intracellular bacteria, mycoses and parasites (low Th1/Th2 ratio). Methods: 185 ME/CFS patients were included in this study. GVDR-Fok1 & Bsm1 were determined. Based on Ruggiero's work we know that related to GcMAF: Fok1: C/C genotype: high responder (FF genotype) T/C genotype: moderate responder (Ff genotype) T/T genotype: low responder (ff genotype) Bsm1: C/C genotype: high responder (bb genotype) T/C genotype: moderate responder (Bb genotype) T/T genotype: low responder (BB genotype) Results: A one sided t-test was used to test the hypothesis

				that the mean % of the Bsm1 BB/Bb/bb and Fok1 FF/Ff/ff groups is statistically different from the average in the normal population according to reference percentages. For Fok1/Bsm1 ff/BB fenotypes (low responder) were significantly higher than in controls and FF/bb (high responder) were significantly higher in controls ($p < 0.001$). Discussion: When compared to the general population, more ME/CFS patients seem to be genetically low GcMAF responders, possibly explaining higher susceptibility for persistent infection. This finding can be added to the list of genetic predisposition factors which may predispose to the development of ME/CFS.
De Meirleir,K; Frémont, M; Metzger,K; Roelant, C	Vrije Universiteit Brussel, Belgium	Systemic Immune Actication in XMRV Positive CFS/ME Patients	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P140.	Objectives: Chronic activation of the immune system is present in progressive HIV infection and is a better predictor of disease outcome than plasma viral load. Several studies suggest that XMRV is involved in the pathophysiology of CFS/ME. We wanted to test the hypothesis that the systemic immune activation in XMRV positive CFS patients is similar to the one observed in HIV. Methods: Sixteen CFS patients fulfilling the Canadian criteria for CFS and were found positive for XMRV by co-culture technique were included in the study. Reference data were used from a large cohort of healthy individuals. Complete immunophenotyping was performed on venous blood and also elastase activity, C4a, IgG3, cytokines, sCD14, perforin were measured. Stool IgA was also determined. Statistical analysis was performed independently from our group by Professor D. Coomans (Vrije Universiteit Brussel / James Cook University). Results: The number of CD3+ and CD57+ lymphocytes was significantly lower compared to the reference values. C4a and elastase were significantly higher in the XMRV positive CFS population. Soluble CD14 (which codes for LPS in plasma) was significantly higher at $p < 0.001$ as compared to the reference population. The cytokine panel showed increased IL-10, MCP-1, MIP-1 beta and IL-8 serum levels. Other lymphocyte subsets showed no difference from the reference in the XMRV positive patients. Stool IgA and IgG3 were statistically lower in the MRV positive patients. Discussion: The results of this study show that XMRV positive patients have lymphocyte numbers and CD57+ lymphocytes below normal as is observed in HIV. XMRV positive CFS patients have an activated innate immune system (elastase activity and C4a are increased) which could be related to microbial translocation as their sCD14 is significantly higher than expected; sCD14 strongly correlates with plasma LPS. Low stool IgA also indicates dysfunctional mucosa-associated lymphomal tissue (MALT) in XMRV positive CFS patients. Furthermore their IgG3 serum levels are lower than in the controls. Serum levels of the cytokines IL-8, IL-10, MCP-1 and MIP-1beta are increased in the patients and might constitute a biological signature for the viral infection. These observations and other unpublished data on serum LPS in CFS patients, provide evidence for microbial translocation being part of the pathophysiology of XMRV positive CFS patients.
Donalek, Julie G	DePaul University Department of Nursing	Living with a Parent with Chronic Fatigue	Bulletin of the IACSF/ME. 16 (2). Summer 2008. P5-11.	Individuals experiencing ME-CFS are often parents. Yet the responses of family members to the parent's illness have not previously been explored. In this study, eight

		syndrome		children living or having lived in a family with a parent with ME-CFS talked about their lives. They described attempting to make some sense of their parent's illness, at times with limited information and support, attempting to deal with decisions around telling others outside the family, all while carrying increased responsibility within the family. Suggestions are made for assistance to these children and support for the family as a whole.
Dyke, JP; Weiduschat, N; Mao, X; Pillemer, S; Murrough, JW; Natelson, B; Mathew, SJ; Shungu, DC	Jonathan P. Dyke, Ph.D., Assistant Professor of Physics in Radiology, Weill Cornell Medical College, 516 E 72nd St., New York, NY 10065 jpd2001@med.cornell.edu	Assessment of Regional Cerebral Blood Flow in CFS Using Arterial Spin Labeling MRI	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P138-139	Objectives: Chronic Fatigue Syndrome (CFS) is an unexplained illness characterized by debilitating fatigue that is not ameliorated by sleep [1,2]. In two previous independent samples of CFS, we found increased ventricular lactate, which we had postulated to be due to oxidative stress, a secondary mitochondrial dysfunction and/or decreased regional cerebral blood flow (rCBF). To investigate the latter possibility, we used arterial spin labeling MRI[3] to compare rCBF in patients with CFS, and in age-and sex-matched patients with major depressive disorder (MDD) and healthy volunteers (HV). Methods: Fourteen CFS [31.9±8.6 yrs, 3M/11F], 13 MDD [31.4±9.9 yrs, 5M/8F] and 13 HV [27.6±7.4 yrs, 6M/7F] subjects were recruited for this study. The two patient groups were psychotropic medication-free for at least 1 week prior to scanning. rCBF was measured in each participant using ASL on a 3.0T GE MRI system. The resulting rCBF images were reconstructed on-line and normalized to the Montreal Neurological Institute (MNI) PET template. Groupwise voxel-based analysis of the ASL data was performed using SPM version 5, followed by between-group ANCOVA comparisons in which age and gender were covariates. Results: Significantly decreased rCBF values were found in the left anterior cingulate cortex (ACC) [p=0.039] and the right lingual region [p=0.016] in CFS compared to HV, while a trend toward significantly lower rCBF was found in the left ACC region in MDD subjects compared to HV [p = 0.08]. rCBF values for CFS and MDD did not differ significantly [p>0.05]. Conclusion: The present finding of decreased rCBF in CFS is consistent with prior measurements using 111Xe-CT[4] or ASL[5], although less pervasive and more spatially focused, which might be due to methodological differences. Our observation of a trend toward hypoperfusion in the ACC in MDD, a region where we had previously reported finding amino acid neurotransmitter abnormalities[6], provides further evidence for the involvement of this brain structure in the disorder. Due to the relatively limited spatial extent of the rCBF decrease in CFS, it is unclear whether the resulting hypoperfusion would account for our previous observation of elevated ventricular lactate in the disorder. However, it should be noted that the rCBF values in individual voxels throughout the brain were largest in HV and lowest in CFS, which could cumulatively lead to global hypoperfusion and to lactate increases. Larger studies in well-characterized subjects are warranted to confirm this possibility, as well as the overall results of this pilot study. [1] Mathew et al, NMR Biomed 2009; 22:251. [2] Murrough JW et al, NMR Biomed 2010; 23:463. [3] Detre JA, Alsop DC, Eur J Radiol

				1999; 30:115. [4] Yoshiuchi K et al, Clin Physiol Funct Imag 2006; 26:83. [5] Biswal B et al, J Neurol Sci. 2011; 301:9-11. [6] Price RB et al. Biol Psychiatry 2009;65:792..
Enlander, Derek; Riedman, Thomas	[no address given]	Enhanced External Counterpulsation in the Treatment of Chronic Fatigue Syndrome by Improving Cardiac Output	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P148-150	Introduction: The etiology of Chronic Fatigue Syndrome (CFS) is unknown and has been related to many different pathophysiological disorders including virological, immunological, neuroendocrine, genetic and psychiatric sources.[1-9] . In 2003, Peckerman and coworkers [10-12] suggested CFS may be related to impaired circulation, specially reduced stroke volume (SV) and cardiac output (CO) [10]. The more severe patients suffered from postexertional fatigue, the more serious was their CFS, and proportionally the lower their CO. We hypothesized that a treatment that can increase CO may then improve the CFS symptoms. It has been known for many years that abnormal venous return will lead to reduced cardiac output, orthostatic tachycardia and in turn failure.[10-12]. It has been suggested that this disturbance is at a cellular or subcellular mitochondrial level. [13-21] or a carnitine metabolic problem [22-28] Enhanced external counterpulsation (EECP) is a circulatory assist device.[15] . EECP operates by wrapping three sets of cuffs around the lower extremities, compressed during diastole to squeeze both arterial and venous blood back to the heart, increasing coronary perfusion and right ventricular filling pressure. The compression is released during systole, effectively increases peripheral arterial capacitance and lowers the impedance to cardiac ejection as well as systolic workload. The counterpulsing action to the heart by the EECP system has been shown to increase SV, CO, systemic blood flow velocity, and shear stress acting on the endothelial cells, stimulate endothelial function, including release of angiogenesis factors that promote collateral and improve microcirculation. Currently in the United States EECP Therapy has been FDA approved for use in unstable and stable angina pectoris, acute myocardial infarction, congestive heart failure and cardiogenic shock. Objective: The primary objectives of this study were to examine the changes in stroke volume, heart rate, and cardiac output measured by thoracic electrical impedance cardiography (ICG) after a course of EECP therapy in patients suffering from CFS without evidence of coronary artery disease , and to evaluate whether EECP therapy reduced the severity of CFS. EECP treatment has been shown to increase CO in patients with refractory angina, and in patients with heart failure, it has not been used in CFS patients with reasonable normal SV and CO. CFS patients with coronary artery disease were excluded from this study in order to eliminate an important variable. If there were improvements in the functional capabilities of the patients, it is due to reduction in the severity of CFS and not their cardiac functions. Another objective for this study was to identify whether there are any relationships between SV and CO and CFS severity, particularly any relations in the changes in SV and CO to changes in CSF severity after EECP treatment. Methods Patient Selection: This study enrolled twenty patients seeking treatment between 2009 to 2010 in a New York city clinics satisfying the Fukuda case definition of CFS by the Centers for Disease Control

				and Prevention National Center for Infectious Diseases and Canadian Consensus definition [16,17,18] with unexplained persistent or relapsing chronic fatigue that is not the result of ongoing exertion, is not substantially alleviated by rest, and results in substantial reduction in previous levels of occupational, educational, social, or personal activities, and concurrently suffering from four or more of the following symptoms: substantial impairment in short-term memory or concentration; sore throat; tender lymph nodes; muscle pain; multi-joint pain without swelling or redness; headaches of a new type, pattern, or severity; unrefreshing sleep; and post-exertional malaise lasting more than 24 hours. These symptoms must have persisted or recurred during 6 or more consecutive months of illness and must not have predated the fatigue. Conditions that exclude a diagnosis of CFS include any active medical condition that may explain the presence of chronic fatigue, such as untreated hypothyroidism, sleep apnea and narcolepsy, and iatrogenic conditions such as side effects of medications, any past or current diagnosis of a major depressive disorder with psychotic or melancholic features; bipolar affective disorders; schizophrenia of any subtype; delusional disorders of any subtype; dementias of any subtype; anorexia nervosa; or bulemia nervosa, and alcohol or other substance abuse that occurred within 2 years of the onset of chronic fatigue and any time afterwards. Study Design: CFS severity measure: After signing an informed consent form, patients without evidence of coronary artery disease and satisfying the enrollment criteria of suffering from CFS were asked to complete a battery of questionnaires concerning their demographics, medical history, family risk factors, medications and were assigned by a physician Karnofsky Performance Status scores (KPS) to assess their CFS severity levels. KPS is a general activity and medical care requirements measure to evaluate patient's ability to carry on normal daily activity and work or require custodial care using a 0-100 point scale, ranging from 0-30 as severely disable, unable to care for self, 50-70 as unable to work but able to live at home with varying amount of assistance needed, and 80-100 as patients who were able to carry on normal activity and to work. CFS severity levels were reassessed by the physician at the end of the last EECP treatment hour. Cardiac stroke volume and output: The SV and CO of each patient were measured using an impedance cardiography device (Casmed, Lifegard® ICG Non-Invasive Hemodynamic Monitor, Branford, CT, USA). The device sends out a constant electrical current via electrodes in the neck and abdominal to quantify the heart’s mechanical activity by measuring the changes in impedance to the current which is proportional to the resulting change in blood volume (stroke volume) and velocity in the aorta (cardiac output) with each cardiac cycle. Patients were asked not to consume anything with caffeine for 4 hours before measurement performed in a quiet temperature controlled room in the supine position. The means of two recordings of 30 seconds data were used for analysis. Heart rates were measured using an electrocardiograph unit. The SV and CO measurements were done at

				baseline before the first hour of EECP and repeated post-EECP after the last hour of treatment. Enhanced External Counterpulsation: The treatment is administered to patients on an outpatient basis. EECP therapy systems are Food and Drug Administration (FDA) cleared for marketing in the treatment of stable and unstable angina, congestive heart failure, acute myocardial infarction, and cardiogenic shock. Patients The EECP treatment system (Vasomedical, AngioNew VI, Westbury, NY) consists of three sets of inflatable pressure cuffs wrapped around the calves, the lower and upper thighs, including the buttocks. The cuffs are rapidly and sequentially inflated, starting from the calves and proceeding upward to the buttocks at the beginning of diastole of each cardiac cycle, creating an arterial retrograde flow along the aorta towards the heart and significantly increasing blood flow to the coronary arteries at a time when resistance to coronary blood flow is at its lowest level. The inflation of the cuffs also simultaneously increases the volume of venous blood returned to the right side of the heart providing greater filling of the right and left ventricles. Just prior to the next heartbeat, when the heart begins to contract, all three cuffs simultaneously deflate, leaving an empty vascular space in the lower extremities to receive blood ejecting from the heart, thereby significantly reducing the workload of the heart. The inflation/deflation activity is monitored constantly and coordinated by a microprocessor that interprets electrocardiogram signals, monitors heart rhythm and rate information, and actuates the inflation and deflation in synchronization with the cardiac cycle. The inflation/deflation cycle is repeated for every heartbeat, increasing energy supply to the heart, improving SV and CO, while at the same time reducing the workload of the heart. Patients in this study received 35 hours of EECP treatment, one hour daily, five days per week over seven weeks for a total of 35 sessions. Statistical Analysis: The severity of CFS as evaluated by KPS scores as well as SV and CO measured by ICG before and after EECP treatment were compared using 2-tailed paired Student t-test. Changes in CFS severity versus changes in SV and CO were analyzed using a paired-difference t-test. Correlation between CFS severity levels versus SV and CO were analyzed using Pearson R values as well as linear regression analysis. All data are reported as mean ± SD with p values < 0.05 being accepted as statistically significant in all analyses. Results: This study enrolled 20 patients, 5 males and 15 females, average age 46.4 ± 14.0 (range 29 to 75) years old. All patients had no evidence of coronary artery disease (CAD), but 35% had immediate family history of CAD. All patients reported suffering from massive fatigue during the past 9 months to 30 years, 85% with difficulty sleeping and serious depression. All patients completed the 7 weeks EECP treatment without any adverse events or complications due to the application of pressure to their lower extremities. Effects of EECP treatment in CFS and hemodynamic functions. The severity levels of CFS as measured by KPS before and after 35 hours of EECP therapy improved significantly from 56.2 ± 8.3 to 62.1 ± 9.6 ($p<0.05$) while the SV also increased

				significantly from 50.2 ± 10.6 to 58.5 ± 11.9 ml (p=0.02), as shown in Figure 1. The heart rate did not change from 79.2 ± 10.2 before EECP to 77.7 ± 8.5 beats/min after EECP treatment. CO also increased significantly from 3.9 ± 0.7 to 4.5 ± 0.8 L/min (p=0.017), also shown in Figure1.
Evangård, Birgitta	Professor of Infectious Diseases, Umeå University, Sweden	When the American Association of Chronic Fatigue Syndrome turned international	Bulletin of the IACSF/ME. 16 (4). Winter 2008/2009. P3-6.	We have known for many years that Chronic Fatigue Syndrome, CFS, can be found in all countries. It was already described in 1869 as a syndrome by the American neurologist George Beard and has since been described as occurring in epidemic form in the US (1934) , Iceland (1948) and in the UK during the 1950ths. In the 1980's an outbreak was described in the Lake Tahoe area in the US and at the end of last century researchers recognised the size of the problem in Japan. After the outbreak in Nevada, the US government funded American researchers through the Centers for Disease Control (CDC) and the National Institutes of Health (NIH) to research the syndrome. Except for the outbreaks described, cases have been reported as sporadically occurring. Epidemiological research has shown similar prevalence rates in the US, Japan, and Europe with CFS occurring in around 0.5% of the population.
Falkenberg, Virginia R; Whistler, Toni; Murray, Janna; Unger, Elizabeth R; Mangalathu, S	Virginia R. Falkenberg PhD, Chronic Viral Diseases Branch, Division of High-Consequence Pathogens and Pathology, NCEZID, Centers for Disease Control and Prevention, 1600 Clifton Road, MS G-41, Atlanta, GA 30333, USA fse9@cdc.gov	Promoter DNA Methylation and Expression of Perforin in CFS and Controls	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P126-127.	Objectives: Perforin plays a key role in immune surveillance and several studies report decreased perforin protein and mRNA in peripheral blood of patients with chronic fatigue syndrome (CFS). Factors that modulate gene-environmental interaction and thus the pathophysiology of disease include gene silencing by DNA methylation. The objectives of this study were to determine the pattern of perforin gene methylation in conjunction with perforin gene expression and whether these features were altered in CFS. Methods: Subjects (34 CFS and 47 non-fatigued, NF) selected from a population based study underwent the Trier Social Stress Test (TSST), a standardized psychosocial test that induces stress, and is known to influence cortisol secretion. Blood samples were collected prior to (10:30am, T1), and after the TSST (3:05 pm, T2). DNA extracted from peripheral blood mononuclear cells (PBMC) was used to examine site-specific CpG methylation levels in the methylation sensitive region (MSR) of the promoter (sites -876, -776, -744, -720, -691, -670 and -650). This was quantified by bisulfite treatment of DNA followed by pyrosequencing. RNA from PBMCs collected at the same time points was used to quantify perforin mRNA expression by LightCycler real-time RT-PCR. Total RNA from peripheral blood collected at the same time points was used in the Affymetrix Human Exon Array 1.0 platform. Results: Methylation of the MSR ranged from 38%-79% and no differences in CpG site-specific methylation of perforin was detected between CFS and NF at T1 or T2. In PBMC, there was no difference in the perforin expression between CFS and NF at T1 but expression was significantly higher in CFS than NF (1.4 fold, p=0.02) at T2. NF subjects had reduced perforin expression (0.8 fold, p=0.008) and methylation levels were increased by 4% (range 2.6-4.3, p= 0.01-0.05) at four CpG sites (-876, -744, -691, and -670) at T2 compared to T1. However in CFS subjects, methylation levels were increased by 6%

				(range 4.7-6.8, p=0.02-0.03) at T2 compared to T1 at two positions (-776 and -744) without a corresponding change in expression. Expression results by real-time RT-PCR and exon arrays were concordant. Conclusion: While increased promoter DNA methylation correlated with reduced perforin expression in NF, this relationship was not seen in CFS. The small but statistically significant differences in methylation were detected over the course of the day were different for the NF and CFS groups. Further studies are needed to confirm these results and to evaluate explanations (changes in cell population, circadian rhythm or stress) for the observed dynamics in perforin DNA methylation and expression.
Fennell, P	Patricia Fennell, MSW, LCSW-R, President, Albany Health Management Associates, Inc., 582 New Loudon Rd., Latham NY 11210, USA; communications@albanyhealthmanagement.com	Working the Third Phase: 5 Capacities For Coping With Trauma and Loss In CFS/ME and Fibromyalgia	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations.	Objectives: To live a full life with CFS/ME, fibromyalgia, or other chronic illnesses, individuals and families must learn to accept their circumstances and find meaning in the experience. The arts -- music, humor, movement, writing, painting, or other methods -- helps individuals with chronic conditions develop this acceptance and meaning for enhanced coping. Methods: An online program was launched in mid-2010 that uses the arts to help people develop a healthy response to chronic illness. This program helps people with chronic illnesses use five capacities of improvisation that are explored through the arts and that people coping with chronic illnesses need to acquire to establish acceptance and meaning. These capacities are 1) Tolerate ambiguity, 2) Take risks, 3) Become curious, 4) Improvise, and 5) Innovate. The program, initiated in May 2010 in collaboration with the DePaul Chronic Illness Initiative, is derivative of the evidence-based Fennell Four-Phase Model, which has established that people experience Four Phases – 1) Crisis, 2) Stabilization, 3) Resolution, and 4) Integration -- on their way to defining a new self and a new life with chronic illness. It is in the Resolution Phase where individuals begin to find meaning in their experience and develop a supportive, meaningful philosophy. Creativity and the arts are a mechanism for using improvisation to progress toward and through the Third Phase. Results: The tools of improvisation offer a pathway toward establishing meaning in the chronic illness experience for enhanced coping. Conclusion: Improvisation, the skill of top artists, can offer new ways to respond better to change. In improvisation, we use our existing knowledge and skills to create something new in an unplanned, innovative way. The web-based community offers an effective method for developing these capacities with people with disabling chronic illnesses, such as CFS/ME and fibromyalgia, who may find it difficult to travel to group meetings on a regular basis. Relationship to Conference Theme: A pre- and post-intervention instrument, under development, combined with the validated Fennell Four Phase Inventory, can assess how participants use the five capacities and how they influence their current Phase placement and the development of meaning. By learning the principles of the five capacities of improvisation, patients can emerge with tools to cull prior experiences for better assessment of present circumstances

				and create innovative ways to respond to change.
Fennell, P;	Patricia Fennell, MSW, LCSW-R, President, Albany Health Management Associates, Inc., 582 New Loudon Rd., Latham NY 11210, USA; E-mail: communications@albanyhealthmanagement.com	Six Functional Capacities That Impact People with CFS/ME and/or Fibromyalgia	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P173-174.	Objectives: CFS/ME, fibromyalgia and related chronic illnesses have a significant impact on educational, work, and social success, as well as on activities of daily living, including self care, school, work and socialization. Workplaces, schools, social communities and other systems are challenged to provide appropriate accommodations to help people with chronic illnesses succeed to their highest capacity. A unique challenge is that, because these chronic illnesses relapse and remit, the accommodations must be flexible enough to change along with the person's health status. Methods: This presentation will outline the six functions that that are impacted by chronic illness and that affect the patient's participation in work or school. These are: 1. Pain; 2. Fatigue ("tired and wired," sleepy); 3. Sleep Quality; 4. Mood/Presentation; 5. Cognition/Mental Focus; and 6. Ambulation/Movement. It will also explain the Fennell Four Phase Model of chronic illness, an empirically validated model that describes four phases of adaptation that occur in chronic illnesses and trauma. These phases -- 1. Crisis; 2. Stabilization; 3. Resolution; 4. Integration -- describe a predictable passage that patients navigate on their way to defining a new self and a new life after the onset of chronic illness. Results: Research shows that people with CFS/ME and fibromyalgia pass through Four Phases as they learn to manage and cope with their decreased or impaired function, and the individual's health, functional status and Phase placement impact one another over time. Conclusion: By assessing a person's functional status and Phase placement, professionals can implement accommodations that give the patient the highest likelihood of success in the workplace, classroom and other environments. Relationship to Conference Theme: By conceptualizing the experiences of people with chronic illnesses with the functional capacity and phase placement concepts, professionals across disciplines can step outside of a medical/clinical framework and describe commonly shared human experiences in a substantive and meaningful manner that supports the individual's success. In addition, patients and families can utilize these functional area and phase placement concepts as a personal insight tool that helps them understand their current abilities and limitations, work within the parameters they are experiencing, and allow them to make better decisions about how to utilize their time, schedule and energy, on any given day.
Fennell, Patricia A	[No address quoted]	CFS/ME in the Chronic Illness Era	Bulletin of the IACSF/ME. Spring 2007.	There is a paradigm shift occurring in medicine, from models focused on treating acute illnesses to those concerned with managing chronic conditions. This shift coincides with the higher prevalence of chronic illnesses resulting from factors such as lower mortality from formerly fatal illnesses and an aging population. The chronically ill do not fare well in an acute care model and, as a result, it has become imperative to develop new models of care and comprehensive, coordinated case management models that will be effective for these chronic conditions. This shift in medicine toward chronic conditions will force CFS/ME to compete to an even higher degree for

				already limited research dollars and attention, but may provide benefits in the clinical arena, as health care adapts to serve the expanding universe of the chronically ill.
Fernandez Solà, A; Colilles, R; Gilibets, S	Centre Sanitari del Solsonès (CSS) Solsonés Central Catalonia	Usefulness of a Joint and Multidisciplinary Unit for the Diagnosis, and Management of Chronic Fatigue Syndrome (CFS), Multiple Chemical Sensitivity (MCS) and Fibromyalgia	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P173.	We present the structure and functioning of our unit as an example of multidisciplinary and co-management of the central sensitization syndromes. The Centre Sanitari del Solsonès (CSS) is a public medical center serving the region of Solsonés, an area of Central Catalonia around 15000 inhabitants. In 2010 we created a unit for the diagnosis and management of the diseases that has an internal medicine physician expert on the three diseases, a nurse, a psychologist and a physiotherapist. The patient arrives at the unit referred by primary care physicians. The nurse manages and cites the patients for the first medical visit where the doctor takes the patient's medical history. Subsequently, the patient is sent to the nurse who performs the nursing history, assessment tests of fatigue (FT. SF-36), pain (FIQ) and chemical sensitivity (QEESI). The patient is then referred to the psychologist who performed psychological and neurocognitive assessment. Subsequently, clinical meetings are held together for determining the diagnosis, the degree of impairment and the proper course of action. The unit has also a group of cognitive-behavioural treatment involving all the professionals of the same. Diagnosed patients enter the patient registry that records the incidence and prevalence of the three diseases as well as clinical and epidemiological parameters. Currently, and after a year of operation the registry has more than 50 patients. Conclusion: We believe that the joint multidisciplinary units that treat the three diseases are the best tool for correct diagnosis, grading, handling and study of these pathologies.
Frémont, Marc; Coomans, Danny; DeMeirleir	Marc Frémont, Ph.D., R.E.D Laboratories, Z.1 Researchpark 100, 1731 Zellik Belgium email: mfremont@redlabs.com	High-Throughput 16s rDNA Sequencing Reveals Alterations of Intestinal Microflora in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Patients	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P158-159.	Objectives: Human intestinal microflora plays an important role in the maintenance of host health by providing energy, nutrients, and immunological protection. Intestinal dysfunction is a frequent complaint in ME-CFS patients, and previous reports suggest that dysbiosis, i.e. the overgrowth of abnormal populations of bacteria in the gut, is linked to the pathogenesis of the disease. Recently developed technologies are able to provide a comprehensive overview of the gut bacterial populations (metagenomics approach). We used high-throughput 16s rDNA sequencing to investigate the presence of specific alterations in the gut flora of ME-CFS patients from Belgium and Norway. Methods: 39 ME-CFS patients and 35 healthy controls were included in the study. Bacterial DNA was extracted from stabilized stool samples and PCR amplification was performed on conserved 16S rDNA regions. PCR amplicons were then sequenced using Roche FLX 454 genome sequencer (6000-10000 sequences per sample). Bacteria were classified by phylum, family and genus; diversity indexes (Chao and Shannon) were also calculated. Data were analyzed using Mann-Whitney test and step-wise linear discriminant analysis. Results: ME-CFS patients presented altered levels of specific bacterial populations: Prevotella, Asaccharobacter, Lactonifactor, Eubacterium. Linear discriminant analysis showed that a significant (p<0,001) discrimination between control and patient populations could be achieved by using a

				combination of Asaccharobacter, Turicibacter, Ruminococcus and Enterococcus as variables. Differences could be seen between males and females, as well as between people from different geographical origins (Belgium vs. Norway). Conclusions: ME-CFS patients present significant alterations of their gut flora composition. More research has to be done to fully understand how intestinal bacteria can contribute to the pathogenesis of the disease (production of toxic metabolites, interaction with host immune cells…), but also how host factors (especially genetic factors) and external factors like diet or viral infections can influence the response of the body to gut bacteria. Metagenomics is a useful tool to diagnose dysbiosis in ME-CFS patients and to help designing treatments based on gut flora modulation (antibiotics, pre- and probiotics supplementation).
Friedberg, Fred	[No address quoted]	Ultra-Brief Self-Management of CFS in Medical Care	Bulletin of the IACSF/ME. Spring 2007.	This article will highlight background studies demonstrating the efficacy of behavioural self-management for many illness conditions, including CFS. I will also suggest how physicians and other professionals can advise their CFS patients about healthy lifestyle change and stress reduction in order to lessen illness severity and, for some patients, promote significant improvement.
Friedberg, Fred	Stony Brook University, New York	Cognitive-Behavioural Intervention in Chronic Fatigue Syndrome: Benefits, Limitations, and Open Questions	Bulletin of the IACSF/ME. 16 (4). Winter 2008/2009. P22-27.	The cognitive-behavioral model of chronic fatigue syndrome (CFS) postulates fear-based avoidance behavior and physical deconditioning to explain symptoms and impairments. This article examines these assumptions and provides a brief critical perspective of CBT trials in patients with CFS. Although CBT is effective to varying degrees in reducing symptoms and improving functioning, published reports often do not address (a) the influence of baseline functioning on intervention rationale; (b) clinical vs. statistical significance of outcomes; (c) patient non-response to CBT; and (d) the potential role of biological variables in predicting response to intervention. A balanced assessment of the effectiveness of CBT in CFS is important in providing accurate information to both professionals and patients
Friedberg, Fred; Coronel, Janna	Department of Psychiatry, Putnam Hall/South Campus, Stony Brook University, Stony Brook NY 11794-8790. fred.friedberg@stonybrook.edu	Brief Self-Management of UCF/CFS in Primary Care: A Randomized Trial	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P118.	Objective: The objective of this study was to test a brief self-management protocol in a primary care setting, in people with medically unexplained chronic fatigue (UCF) and chronic fatigue syndrome (CFS). An effective self-management plan has the potential (1) to improve the generally poor outcomes for UCF and CFS patients in primary care, (2) to greatly expand the availability of behavioral health care for UCF and CFS, and (3) to reduce medical and behavioral utilization for UCF and CFS. The proposed study is an extension of an efficacious two-session self-management clinical trial for CFS in secondary care (Powell et al., 2001). The hypothesis was tested that a brief self-management- focused cognitive-behavioral intervention will yield improvements in fatigue, physical and role functioning, and psychological distress in comparison to the two control conditions: standard medical care alone or standard medical care plus an attention control symptom monitoring condition. Methods: We

				tested the efficacy of a two - session self-management-focused cognitive-behavioral intervention in a target sample of 108 persons with UCF or CFS. Participants were randomly assigned to one of three study conditions: (1) standard medical care alone; (2) standard medical care plus a nurse-delivered attention control condition of symptom monitoring; or (3) standard medical care plus a nurse-delivered self-management cognitive behavioural treatment delivered by a nurse. Results: At the three month follow-up, sample sizes were as follows: fatigue self-management (FSM) = 21; Symptom Monitoring (SM) = 26; and Usual care (UC) = 21. Forty percent met Fukuda criteria for CFS. Controlling for age, sex and illness duration at the three-month follow-up assessment, a significant reduction was found on the fatigue severity scale ($p<.05$). No significant changes were found on diary fatigue ratings, the SF-36PF, Beck Anxiety Inventory or the Beck Depression Inventory. Actigraphy significantly declined across all conditions ($p<.05$). Patient global impression of change (PGIC) ratings were as follows for the three conditions (FSM/SM/UC): Improved (13/ 6/4); Unchanged (5/9/11); Worse (2/5/2). Despite little change on our standard measures, brief interviews with study participants revealed that both worsened and unchanged patients across conditions attributed their PGIC ratings to external negative events or lack of healthy activities, whereas improved patients reported increased awareness of their behaviors and affirmative steps to pursue healthy activities. Conclusion: A brief, standardized illness management service for UCF/CFS showed modest improvement in fatigue severity and PGIC ratings. PGIC ratings of improved, unchanged, and worsened overall appeared to reflect different attitude toward the illness and/or differential exposures to negative major life events. These findings indicate a role for self-management activities in generating improved outcomes.
Garcia, Lina; Kerr, Jonathon; Fletcher, Mary Ann; Sol, Connie; Klimas, Nancy;	University of Miami Miller School of Medicine and Miami VA Medical Center. klimas@miami.edu	Comparing Gene Expression Patterns in CFS and GWI Using the Kerr ME/CFS Platform	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P134-135.	There have been a number of studies utilizing genomics to better understand and define CFS/ME. Jonathan Kerr's group published a series of studies that defined 79 genes associated with this illness, then used the same method to develop biologically defined subgroups (1). The Miami group has been studying both GWI and CFS/ME using gene activation patterns and proteomics, before during and after an exercise challenge to better understand the mediators of persistence and relapse. In this study we collaborated with Dr Kerr, comparing CFS/ME (n=25), control (n=53) and GWI samples (n=25), the GWI samples studied were drawn prior to the exercise challenge. The data from the CFS/ME cohort confirmed the findings from Dr. Kerr's earlier studies. There were significant differences when compared to controls in expression of genes that regulate intracellular pathways mitochondrial function, cell wall and signaling pathways. Genes which regulate cytokine regulation were also significantly different than controls, particularly the pro-inflammatory cytokines TNFa and IL6; antiviral pathways Interferon alpha, beta and omega, and the anti-inflammatory cytokine IL10. When compared to Gulf War Illness there are some important overlaps:

				EB12, an EBV induction gene is 6 fold higher than controls in CFS/ME, 2 fold higher in GWI, both significant differences (p<.005) ETS1, a viral oncogene was also upregulated in both groups. (p<.-0005) Transcription factor 3, which regulates immunoglobulin production, was markedly elevated in GWI, less so though significantly elevated in CFS/ME. (p<.005) Apoptosis genes were markedly upregulated in both groups though GWI saw elevations were 400 fold higher than CFS/ME. (p<.0005). However, the overall trend was that most of the gene regulation abnormalities that are associated with CFS in the Kerr platform were not significantly different in GWI than in controls , and often moved in the opposite direction down regulating intracellular processes in GWI that were upregulated in CFS (73 of 87 genes studied). Using a comprehensive platform, additional genes specific for GWI have been identified by the Miami group (presented separately). 1. Kerr JR, et al. 2008. Gene expression subtypes in patients with chronic fatigue syndrome/myalgic encephalomyelitis. J Infect Dis 197(8):1171-84.
Gottfries, Carl-Gottfries, Carl-Gerhard[1]; Hāger, Ove[1]; Gottfries, Johan[2]; Zachrisson, Olof[1]	[1] Institute of Neuroscience and Physiology at The Sahlgrenska Academy, University of Gothenburg, Sweden. Gottfries Clinic, Krokslätts Torg 5, SE-431 37 Mölndal, Sweden. E-Mail cgg@gottfries.se oz@gottfries.se [2] Umeå University, SE 90187 Umeå Sweden. E-Mail johan.gottfries@chem.umu.se Address for correspondence: Carl-Gerhard Gottfries, Professor emeritus Gottfries Clinic, Krokslätts Torg 5, SE-	Immunotherapy of Fibromyalgia and Chronic Fatigue Syndrome by a Staphylococcus Toxoid Vaccine	Bulletin of the IACSF/ME. 17 (4). Winter 2009/2010.	Background In previous clinical double blind investigations a significant effect is recorded in patients with fibromyalgia and/or chronic fatigue syndrome when treated with a staphylococcus vaccine. The aim of this study is to report long-term efficacy and safety of this immunotherapy. Methods One hundred and sixty patients with fibromyalgia and chronic fatigue syndrome who had previously participated in vaccine treatment studies were continuously observed during one year in a follow up study. At inclusion mean age was 53±11 years and mean treatment time 22±10 months. In a subgroup of 97 younger patients (48±10 years) with a mean treatment time of 50.4±17.8 months a Principal Components Analysis (PCA) was performed. The patients were on immunotherapy by a staphylococcus vaccine administered subcutaneously in a dose of 1 mL every 3rd to 4th week. Medically educated and trained staff using the rating scale CPRS-15 evaluated efficacy. Safety was evaluated continuously. Results Ratings showed improvement from start of treatment and further improvement was recorded during the follow-up period. The total mean rating CPRS-15 score was reduced by more than 50 %. Five items (Concentration difficulties, Failing memory, Irritability, Sadness and Autonomic disturbances) had mean levels below one at the time of the last rating, indicating that these symptoms on a group level were within the range of normality. The PCA also indicated improvement in the subgroup of 97 middle- aged patients. Adverse events were few and the adherence to the treatment was surprisingly fine. During the observation period of one year 14% withdrew from treatment. Conclusions The result was considered impressive and in view of the lack of effective treatment in fibromyalgia and chronic fatigue syndrome the results are of interest but need to be confirmed.

	431 37 Mölndal, Sweden.			
Goudsmit, Ellen M[1]; Stouten, Bart[2]; Howes, Sandra[2]	*[1]Health Psychologist, 23 Melbourne Road, Teddington, Middlesex, TW11 9QX, UK[2],Co-editor, ME and CFS References, ellengoudsmit@hotmail.com*	Fatigue in Myalgic Encephalomyelitis	Bulletin of the IACSF/ME. 16 (3). Fall 2008. P4-10.	**Background:** The objectives of this study were to measure fatigue in patients with well-defined Myalgic Encephalomyelitis (ME) and to assess if there are any problems associated with the Chalder Fatigue Scale, which has been widely used to assess fatigue in patients with chronic fatigue syndrome (CFS). **Methods:** Twenty-six patients were recruited from a local support group. All had been diagnosed by physicians and met research criteria for ME. They completed the 11-item Chalder Fatigue Scale and were also asked to rate the severity of their illness. The fatigue scores were calculated using both the Likert method (0, 1, 2,3) and the bimodal method (0,0,1,1,). **Results:** The mean Likert score was 26.65 (SD 5.36) and the mean bimodal score was 9.81 (SD 2.04). Fifty per cent of the patients recorded the maximum score using the bimodal method and 77% recorded the two highest scores. Moreover, there was a marked overlap between those who rated themselves as moderately or severely ill. These findings are indications of a low ceiling. **Conclusions:** The findings from this study using the Chalder Fatigue Scale show that the low ceiling associated with the bimodal method means that this scoring system is not suitable for use in clinical trials. Researchers may wish to consider alternative instruments to obtain a more accurate measure of fatigue in patients with moderate to severe ME and similar conditions.
Hallman, G	Geoffrey Hallmann, PhD Candidate, Southern Cross University, School of Exercise Science & Sport Management, PO Box 157 East Lismore, NSW 2480, geoffhallmann@yahoo.com	ME/CFS and Bullying in Context of Social Interactions	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P179.	Objectives: To examine the nature and impact of bullying of persons with ME/CFS when engaged in an institutional encounter. Method: The initial phase of the research involved a thorough review of the available literature to establish the interaction of those with ME/CFS with social institutions. A focus for this paper was made on the incidence of bullying behaviour that participants reported as having experienced during such interactions and attention was paid to the consequences of such experiences. In the data collection phase, a pilot study involving an investigation of the Australian perspective of the experience of ME/CFS was obtained. This was expanded in the main study and participants were provided the opportunity to reveal their stories. Participants were required to have a diagnosis of CFS, ME or ME/CFS from a medical practitioner and self-select themselves as compliant to the Fukuda CFS Criteria, Canadian ME/CFS Criteria and Ramsay ME Criteria. A background questionnaire was provided to give an insight into the history of the participant, particularly interactions with social institutions and pathways to diagnosis. The interview drew upon the questionnaire for guidance, with the primary questions derived from information gained from the literature review. The interviews were transcribed, coded and the relationships and issues identified in order to guide the second phase of the research which was conducted further into the study. The pilot study involved 3 participants, followed by a second, more comprehensive phase

				comprising 16 participants. Stories emerged from within those interviews with respect to interactions with society and these were broken down to reveal particular themes relevant to those experiences. Results: A total of 19 interviews were conducted. The average age of participants was 91.95 with all 14 females and 5 male participants. The mean duration of the condition was 17.66 years, with 8.35 years from onset until diagnosis. A number of issues arose, revealing an insight into the nature of the relationships that exist between persons with ME/CFS and various social institutions. Relationships of power, politics, policies, practices and social relations were revealed to play an important role in the experience of ME/CFS. Bullying appeared to occur across every facet of the participant's lives, particularly in dealings with the medical profession, insurance companies, educators, employment, family, friends and the media. Whilst apparently present such behaviour was not named as such nor addressed. Conclusion: Persons with ME/CFS are subject to bullying directly or indirectly because of their diagnosis and the contested nature of the condition. This experience has an adverse impact upon the person – both physically and emotionally. Patients reveal that such encounters can influence their dealings with people within social institutions and impact adversely upon their condition and manner in which they address future interactions. Rarely is bullying identified, nor is action taken against the perpetrators. Knowledge of steps to be taken and inability to pursue action against perpetrators due to illness prevented protection of rights and self. Providing a more settled understanding of the condition and education within society is indicated as a counter measure to identify and prevent the incidence of bullying.
Hallman, G	Geoffrey Hallmann, PhD Candidate, Southern Cross University, School of Exercise Science & Sport Management, PO Box 157, East Lismore NSW 2480 geoffhallmann@yahoo.com	ME/CFS: First Do No Harm	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P179-180.	Objectives: To examine the nature and impact of the medical encounter by persons with ME/CFS. Method: The initial phase of the research involved a thorough review of the available literature to establish the interaction of those with ME/CFS with social institutions. A focus for this paper was made on the interactions between doctors and medical staff with persons with ME/CFS to establish the current evidence. In the data collection phase, a pilot study involving an investigation of the Australian perspective of the experience of ME/CFS was obtained. This was expanded in the main study and participants were provided the opportunity to reveal their stories. Participants were required to have a diagnosis of CFS, ME or ME/CFS from a medical practitioner and selfselect themselves as compliant to the Fukuda CFS Criteria, Canadian ME/CFS Criteria and Ramsay ME Criteria. A background questionnaire was provided to give an insight into the history of the participant, particularly interactions with social institutions and pathways to diagnosis. The interview drew upon the questionnaire for guidance, with the primary questions derived from information gained from the literature review. The interviews were transcribed, coded and the relationships and issues identified in order to guide the second phase of the research which was conducted further into the study. The pilot study involved 3 participants, followed by a second, more comprehensive phase comprising 16 participants. Stories emerged

				from within those interviews with respect to interactions with the medical community and these were broken down to reveal particular themes relevant to those experiences. Results: A total of 19 interviews were conducted. The average age of participants was 91.95 with all 14 females and 5 male participants. The mean duration of the condition was 17.66 years, with 8.35 years from onset until diagnosis. A number of issues arose, revealing an insight into the nature of the relationships that exist between persons with ME/CFS and medical staff. Relationships of power, politics, policies, practices and social relations were revealed to play an important role in the experience of ME/CFS. Positive and negative experiences revealed issues relating to belief, awareness, education, research, school of thought, attitude, investigation, historical analysis, guidelines, personal experience, finances, and politics. Thematically the participants identified empathy, knowledge, and management as attributes that pointed towards what patients consider to be best practice when dealing with medical practitioners. The stories provide a significant insight into the various medical personnel and medical settings that participants have encountered and how that interaction impacted upon their perceptions and the status of their condition. Conclusion: The relationship between persons with ME/CFS and medical staff, particularly doctors is very important to the progress of the patient. The experiences reveal the importance of knowledge, empathy and management to the patient-doctor relationship. Poor experiences have led patients to adverse reactions within their condition and led them look to alternative therapies due to a lack of faith in the medical profession. Beliefs, knowledge and understanding of their condition also had bearing upon the experience.
Hallmann, G	Geoffrey Hallmann, PhD Candidate, Southern Cross University, School of Exercise Science & Sport Management, PO Box 157, East Lismore NSW 2480, geoffhallmann@yahoo.com	ME/CFS: Harsh Realities of the Real World	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P183-184.	Objectives: To conduct a preliminary examination of the experiences of persons with ME/CFS when dealing with society and the social institutions that form the fabric of day to day interactions. Method: The initial phase of the research involved a thorough review of the available literature to establish the interaction of those with ME/CFS with social institutions. A focus for this paper was made on the experiences of dealing with social institutions on a daily basis when the diagnosis was known. In the data collection phase, a pilot study involving an investigation of the Australian perspective of the experience of ME/CFS was obtained. This was expanded in the main study and participants were provided the opportunity to reveal their stories. Participants were required to have a diagnosis of CFS, ME or ME/CFS from a medical practitioner and self-select themselves as compliant to the Fukuda CFS Criteria, Canadian ME/CFS Criteria and Ramsay ME Criteria. A background questionnaire was provided to give an insight into the history of the participant, particularly interactions with social institutions and pathways to diagnosis. The interview drew upon the questionnaire for guidance, with the primary questions derived from information gained from the literature review. The interviews were transcribed, coded and the relationships and issues identified in order to guide the second phase of the research which was

				conducted further into the study. The pilot study involved 3 participants, followed by a second, more comprehensive phase comprising 16 participants. Stories emerged from within those interviews with respect to interactions with society and these were broken down to reveal particular themes relevant to those experiences. Results: A total of 19 interviews were conducted. The average age of participants was 91.95 with all 14 females and 5 male participants. The mean duration of the condition was 17.66 years, with 8.35 years from onset until diagnosis. A number of issues arose, revealing an insight into the nature of the relationships that exist between persons with ME/CFS and various social institutions. Relationships of power, politics, policies, practices and social relations were revealed to play an important role in the experience of ME/CFS. Positive and negative experiences arose. The contested nature of the condition, its invisibility, lack of community awareness, lack of education, misrepresentation in the media, name, vulnerability of those affected, lack of evidence, barriers to justice and limited support systems all play a role in the way those with the condition experience the social world. Conclusion: Persons with ME/CFS are faced with major difficulties when they deal with social institutions. The various factors that play a role in the absence of knowledge and understanding the condition have perpetuated misconceptions within the community. This experience has an adverse impact upon the person – physically, emotionally and financially. Patients reveal that such encounters can influence their dealings with society and can impact adversely upon their condition. Whilst there are mechanisms that can address issues that arise during their life, there exist barriers that prevent protection of rights, access to appropriate investigation, management and care, and little assistance for day to day issues.
Hanson, M; Lee,LL; Lin,L; Bell,DE; Ruppert,D; Levine,S; Bell, DS	Maureen R. Hanson, Ph.D., Liberty Hyde Bailey Professor ,Dept. of Molecular Biology and Genetics, Cornell University, Biotech. Bldg., Ithaca, NY 14853 USA E-mail - mrh5@cornell.edu	*Detection of MLV-like gag Sequences in Blood and Cell Lines Incubated With Plasma From CFS Patients and Controls*	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P114.	Objectives: To determine whether viruses related to XMRV could be detected in peripheral blood from adult subjects who are either ill with CFS, are recovered from CFS, or have no history of a CFS diagnosis. Methods: Subjects were divided into five groups. Ten subjects were severely ill with CFS, ten met Fukuda criteria at one time but now considered themselves recovered, and ten subjects from the same geographic area in Western New York were healthy and had never been diagnosed with CFS. Standard instruments were administered to assess the health status of the subjects in these three groups. An additional ten ill subjects and ten control subjects lacking any CFS history were recruited from a physician's practice in New York City and a different region of upstate New York, respectively. Blood was collected in EDTA tubes and nucleic acids made from PBMCs or whole blood. Plasma was incubated with human cells in culture. Nested PCR with USB Hot-Start IT FideliTaq was performed with *gag* primers. Any PCR products of expected sizes were sequenced. Samples were tested for mouse contamination with primers to IAP and/or mouse mitochondrial DNA. Control experiments in which human nucleic acid samples were spiked with mouse DNA were performed to determine the sensitivity of the assays for

				mouse contamination. Results: The SF-36 scores of the ten individuals who considered themselves recovered were significantly lower than ten members of the healthy control group from the same Western New York area, according to Hotelling's T2 test. Tukey's multiple comparison of means indicates that there are highly significant differences between the scores of the Western New York "severe" and controls on all 7 instruments. *gag* sequences were detected in CFS subjects' blood as well as in some healthy controls. *gag* sequences were detected that were more similar to the MLV-like sequences reported by Lo et al. (2010) than to the XMRV sequences reported by Lombardi et al. (2009). MLV-like *gag* sequences could be detected in nucleic acids prepared from whole and fractionated blood that were negative for the presence of mouse DNA when sensitive assays were performed. Possible reasons for false positive and false negative results when performing highly sensitive PCR assays will be presented. Conclusion: *gag* sequences were detected by PCR in whole blood genomic DNAs that were negative for mouse IAP and mitochondrial DNA. *gag* sequences similar to polytropic MLVs were obtained. The sensitivity of the PCR assays used requires extreme caution in interpreting results.
Hardcastle, SL; Brenu, EW; Staines, DR; Van Driel, M; Petersen, D; Marshall-Gradisnik, S	Sharni Lee Hardcastle , Faculty of Health Science and Medicine, Bond University, Gold Coast, Queensland 4229 Australia Email: Sharni.Hardcastle@student.bond.edu.au	Assessment of Natural Killer Cell Receptors in Severe and Moderate Chronic Fatigue Syndrome / Myalgic Encephalomyelitis	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P170.	Objective: A common finding within sufferers of Chronic Fatigue Syndrome (CFS/ME) is abnormalities in the immune system. One of the most consistent findings from a variety of studies to date is that CFS/ME subjects have compromised Natural Killer (NK) cell function. The exact cause of reduced NK function is unknown although there are indications for an involvement in cytolytic proteins. Additionally it is unknown whether decreases NK function is related to NK receptors especially within severely affected CFS/ME patients. Therefore, the purpose of this study is to examine NK phenotypes and lysis as well as receptors within moderate and severely affected CFS/ME subjects in comparison to normal controls. Method: Blood samples from 20 normal control participants, 20 moderately affected CFS/ME subjects and 20 severely affected CFS/ME patients. The CFS/ME participants were firstly pre-screened for decreased NK function. Using flow cytometry isolated NK cells were assessed for NK receptor expression and NK phenotypes. Result: Preliminary data from CFS/ME patients showed differences within NK cell receptor function when compared to the healthy control group. Conclusion: Results suggest that NK cell receptor function may be dysfunctional in CFS/ME patients which could potentially explain why these patients have a decrease in NK lysis function.
Harvey, Jeanna M; Barnes, ZM; Sol, C; Zend, MA; Klimas, N	Jeanna M. Harvey, M.D. Candidate, UM Miller School of Medicine. 1600 NW 10th Ave, Miami, FL 33135, USA. jharvey3@med.miami.	Exercise Effects on Biomarkers in GWI, CFS and Healthy Controls	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P164-165.	Objective: To determine the effects of an aerobic exercise challenge on potential biomarkers in Gulf War Illness (GWI), Chronic Fatigue Syndrome (CFS0 and healthy controls (HC).

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Hyde, Byron M; Chor, Allie	Byron M. Hyde, BA(Chem), MD, Chairman, Nightingale Research Foundation, 121 Iona Street Ottawa, Ontario, Canada, K1Y 3M1 bhyde@nightingale.ca	Canadian Techniques of Investigation of M.E. / CFS & FS Patients and Resulting Anatomical, Patho-Physiological and Genetic Findings	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P157.	The Canadian health care system, provides free physicians, investigation and non-pharmaceutical treatment to all patients. Tests include all blood, urine, tissue and technological testing such as cardiovascular, ultrasound, MRI, PET, SPECT, Nerve Conduction, Radiological or Nuclear Medicine examinations. Any corrective surgery, procedural care or hospitalization are also provided free of charge. Unlike in the UK, Australia and many other European countries any physician in Canada can order any test available in Canada. Unlike US physicians, we do not have to ask whether the patient has insurance coverage since all are covered. M.E. and CFS Patients: This system allows an understanding of the patho-physiological basis of why a patient is chronically ill with either a fatigue, cognitive or pain syndrome or a combination of these symptoms. This free assessment has resulted in a significant difference in the understanding of the cause of M.E. and CFS illness. Chronic Fibromyalgia & Fibromyalgia Syndromes (FS): Due to long term follow up and the ability to do significant testing over years at no cost to the patient, we have shown that a majority of chronically ill fibromyalgia patients actually suffer from developing rheumatoid, arthritic, structural, medication induced or genetic illnesses. How to examine & test M.E. and CFS patients: This paper will demonstrate the techniques and difficulties of total body (system and organ) assessment over the past 26 years. The paper will demonstrate the reasons why patients with M.E. and CFS, irrespective of the initiating cause(s), remain chronically ill with brain and fatigue dysfunctions. The Multiple Pathologies of M.E., CFS and FS Patients: This paper will also demonstrate the findings which suggest many patients diagnosed with M.E. or CFS are treatable and many require more specific treatment research.
Hyde, Byron M; Chor, Allie	Byron M. Hyde, BA(Chem), MD, Chairman, Nightingale Research Foundation, 121 Iona Street Ottawa, Ontario, Canada, K1Y 3M1 bhyde@nightingale.ca	Ten Important Facts Derived from M.E./CFS History That Can Improve M.E./CFS Research	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P157.	An increasing number of world experts are contributing to M.E./CFS research, but many do not have a good understanding of the historical lessons already learned in these epidemic illnesses. A better understanding of M.E./CFS history will contribute to more efficient research in understanding, virology, cognitive and brain dysfunction. For instance, a recent published discovery of an abnormal protein in spinal fluid of CFS patients was already demonstrated by Harvard's Dr Charles Poser in 1990. For 26 years, since 1984 to 2011 my medical practice has been limited to the full time investigation of M.E., CFS & FS patients. During the earlier period I visited multiple epidemic sites, interviewed & examined patients & discussed & at times resided with many of the chief investigators of these epidemics. The patients & epidemic sites personally investigated include: (a) Los Angeles County General Hospital epidemic 1934, (b) Akureyri Epidemic Iceland 1947-48, (c) Royal Free Hospital Epidemics 1955-1956, (d) Cumberland Epidemic 1955, (e) Newton-le-Willow Epidemic 1956. The earlier researchers include Drs. Melvin Ramsay, Betty Dowsett, John Richardson, Eleanor Bell, James Mowbray, Andrew Wallis family, J. Gordon Parish. W.H. Lyle, Charles Poser, Alberto Marinacci, Ismael Mena, Sheila Bastien, Alexis Shelokov, Peter

				Snow & Clem Boughton to name a few. Dr Byron Hyde will review ten important largely forgotten facts learned from 26 years of investigating various world epidemics and questioning the experts who investigated these epidemics that will assist M.E., CFS &Fibromyalgia researchers..
Hyde, Byron; Green, Tracy	Byron M. Hyde, BA(Chem), MD, Chairman, Nightingale Research Foundation, 121 Iona Street Ottawa, Ontario, Canada, K1Y 3M1 bhyde@nightingale.ca	Thyroid Malignancy Associated with Severe Cognitive Dysfunction, Cortical & Subcortical NeuroSPECT changes in Patients Presenting with a Myalgic Encephalomyelitis / Chronic Fatigue Syndrome (ME/CFS)	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P156.	In our investigations, thyroid malignancy in ME/CFS patients greatly exceeds the normal incidence in any known subgroup. Various published studies over recent years have suggested an increasing incidence in the general public from 15 up to 30 per 100,000. However in 100 consecutive patients with M.E./CFS evaluated in our clinic by total body investigation, the malignancy incidence exceeds 6,000 per 100,000. Each patient's evaluation includes ultrasound and needle biopsy of suspicious nodules. Malignant nodules are usually noted as solitary, hypervascular nodules 1 cc in diameter or larger, although all hypervascular nodules have been biopsied. We suggest that as part of their investigation, all ME/CFS patients should be examined by thyroid ultrasound for evidence of thyroid pathology and malignancy. Thyroid pathology may be missed in this group of patients if investigation relies only upon serum testing for TSH, FT3, FT4, microsomal and thyroglobulin antibodies, which are usually normal in the case of malignancy. Unfortunately, corrective treatment by surgical and / or nuclear techniques plus appropriate hormonal replacement medication has not improved the symptoms of fatigue, cognitive and pain syndromes nor the SPECT brain changes. A newly recognized syndrome may exist in ME/CFS patients characterized by: (a) thyroid malignancy, (b) persistent pathological cortical and subcortical SPECT brain scans (NeuroSPECT), (c) failure of thyroidectomy surgery and hormone replacement to correct the fatigue syndrome, (d) an unusual high incidence of cervical v ertebrae pathophysiology. The question remains unresolved as to whether the NeuroSPECT changes consistent with a chronic low grade encephalopathy that we associate with cognitive dysfunction, precedes the thyroid malignancy and may provoke increased malignancy. A long term follow up of these M.E./CFS patients with NeuroSPECT evidence of encephalopathy but without thyroid malignancy is in progress to evaluate whether this group of patients is more prone to developing thyroid and other malignancies. We have also found a significant higher rate of development of all thyroid disease in this same group of M.E./CFS patients. This and other anomalies will be discussed with SPECT brain images of these patients.
Jason, Leonard A; Porter, Nicole; Brown, Molly; Anderson, Valerie; Brown, Abigail; Hunnell, Jessica; Lerch, Athena	Leonard A. Jason, Ph.D., Director, Center for Community Research, 990 W. Fullerton Ave., Suite 3100, Chicago, IL, 60614 email:	CFS: A Review of Epidemiology and Natural History Studies	Bulletin of the IACSF/ME. 17 (3). Fall 2009.	Almost all studies with samples of patients who have chronic fatigue syndrome (CFS) have relied on referrals from physicians or health facilities. Under-served minorities, who not only tend to manifest higher levels of chronic illness, but are also less likely to seek and receive adequate medical care, have not been represented in these studies (1). This may have contributed to an under-estimation of CFS among minority groups (2). Few studies have derived their samples from socioeconomically and ethnically diverse community-based populations. A technical report issued by the

	Ljason@depaul.edu			Agency for Healthcare Research and Quality (3) concluded that estimating rates of recovery/improvement or relapse from CFS are not possible because there are so few natural history studies and those that are available have involved selected referral populations. This paper provides a review of epidemiologic studies of CFS followed by a discussion of diagnostic issues and risk factors for the illness. Findings from Jason et al.'s (4) epidemiologic study in a multi-ethnic, economically diverse urban area are highlighted as this research group is now examining the natural course of CFS over the past 10 years with this community-based sample. The current study will add to current epidemiologic and risk factors research by assessing the course, progression, and risk factors of CFS among a demographically diverse sample of participants who are unbiased by illness, help-seeking behaviors, or differential access to the health care system
Jason, Leonard A; Porter, Nicole; Okasinski, Jennifer; and Benton, Mary	DePaul University	Issues Involved in Name Change Recommendations	Bulletin of the IACSF/ME. Spring 2007	Summary: Many feel that there is considerable benefit of maintaining the name Myalgic Encephalomyelitis, which is the most consistently used and most widely recognized name worldwide, with an established neurological WHO ICD code and a well-documented history of outbreaks along with extensive epidemiological investigations. Researchers and clinicians need to be aware of the strong sentiments that patients have for Myalgic Encephalomyelitis, which is a historically correct (Ramsay, 1981) and has been used internationally (Hyde, Goldstein, & Levine, 1992).
Jason, Leonard; Brown, Abigail; Clyne, Erin; Bartgis, Lindsey; Meredyth, Evans; Brown, Molly	Leonard A. Jason, Ph.D., Director, Center for Community Research, DePaul University, 990, W. Fullerton Ave, Suite3100, Chicago Il. 60614. E-mail - Ljason@depaul.edu	Contrasting Case Definitions	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P122.	Objectives: There has been considerable debate about what case definition to use with the illness commonly known as CFS. For example, some have speculated that the initial definitions of ME ((Dowsett et al., 1994; Goudsmit et al., 2009; Ramsay, 1988)) and later on the Canadian criteria of ME/CFS (Carruthers et al., 2003) select a group of patients that have more severe functional impairments than the Fukuda et al. (1994) criteria. This presentation contrasts individuals diagnosed with the Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) Canadian case definition (Carruthers et al., 2003) with those that did not meet these criteria (Non-ME/CFS) but met the Fukuda et al. (1994) chronic fatigue syndrome (CFS) criteria. The study also compared individuals diagnosed with another case definition involving Myalgic Encephalomyelitis (ME) (based on criteria from Dowset et al., 1994; Goudsmit et al., 2009; Hyde, 2007; Ramsay, 1988) with those that did not meet these criteria (Non-ME), but met the Fukuda et al. criteria. Methods: The sample of patients had been diagnosed with CFS by the Fukuda et al. criteria and were later categorized as meeting ME/CFS and/or ME criteria. Results: In general, the ME/CFS criteria identified a group of patients with more functional impairments and physical, mental and cognitive problems than the Non-ME/CFS criteria. The ME criteria identified patients with more functional impairments, and more severe physical and cognitive symptoms than the Non-ME condition. Katon and Russo (1992) have argued that a requirement of more symptoms to meet criteria could inadvertently select for individuals with psychiatric

				problems. Similarly, Kroenke (2003) found similar results examining 15 variables within a fatigued sample. It is certainly possible that the differences on so many measures between the ME/CFS and the Non-ME/CFS groups was due to the larger number of symptoms of higher frequency and severity who met the ME/CFS criteria. Conclusion: The current CFS case definition of Fukuda et al. (1994) has been used internationally by researchers for over 15 years. It is possible that some patients meeting these criteria do not have core symptoms such as post-exertional malaise or memory/concentration problems. By specifying 7 symptoms as with the ME/CFS criteria or by specifying 4 symptoms with the ME criteria, it may be possible to identify a more homogenous and impaired group of patients. The current study suggests that these other ME and ME/CFS criteria might be used to identify patients with possibly more homogenous and severe symptomatology and functional impairment. Both ME/CFS and ME criteria appear to select a more severe group of patients than those that only meet the Fukuda et al. criteria.
Jason, Leonard; Porter, Nicole; Hunnell, Jessica; Rademaker, Alfred; Richman, Judith A;	Leonard A. Jason, Ph.D, Director, Center for Community Research, DePaul University, 990 W. Fullerton Ave, Suite 3100, Chicago, Il. 60614. Ljason@depaul.edu	Natural History	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P129-130.	Objectives: Despite growing knowledge about long-term predictors of chronic fatigue syndrome (CFS) outcomes, many followup studies are not prospective in that they either rely on retrospective self-report at a single point in time or they consist of longitudinal data that are analyzed in a cross-sectional manner without taking into account the influence of baseline findings. Clearly, there is a need for more research on the incidence and course of CFS in ethnically and socioeconomically diverse, community populations. Methods: The present project was carried out in two stages. In Stage 1, we attempted to re-contact the 213 adults who were medically and psychiatrically evaluated from 1995-1997. These adults were previously evaluated in our original Wave 1 CFS epidemiology project (Jason, Jordan et al., 1999). Stage 2 of the study encompasses a structured psychiatric assessment and a complete physical examination and a structured medical history. The original Wave 1 sample is a stratified random sample of several neighborhoods in Chicago specifically selected to contain individuals from different ethnic and socioeconomic profiles. Although the CFS group had a high rate of follow-up, those in the other groups were much more difficult to track over time. Fortunately, we did not find significant sociodemographic differences at Wave 1 between those we retained in the sample versus those that we were not able to re-contact, and this provides support for the generalizability of the outcomes to the larger sample. Results: The study's major finding was that rates of CFS appear to have been relatively stable over the period of time from Wave 1 to 2. As rates of CFS were .42% in Wave 1 (Jason, Richman et al., 1999), estimates from our current natural history study suggest that these rates have stayed relatively constant over the past decade. Sixty-seven percent of participants with CFS at Wave 1 continued to have CFS in our sample at Wave 2. Of the new cases of CFS over time, 75% came from the ICF group, suggesting that this group is at higher risk of developing CFS. In addition, 50% of the remitters went from a CFS diagnosis to the ICF

				group, indicating that while remitters no longer met CFS case definition, half were still suffering from chronic severe fatigue. Among all the variables in this study, only for post-exertional malaise did the CFS group significantly differ from the other conditions. This reaffirms the importance of this being a cardinal and critical symptom for CFS, and all of the individuals in the CFS group had this symptom either at Waves 1 or 2. Finally, a high level of mortality was found (18% of those with medical or psychiatric exclusions group, 12.5% for the CFS group). Conclusion: There are few studies that have been able to provide estimates of long term CFS outcomes, particularly in culturally diverse, community-based samples. In the present 10 year natural history study, the CFS group for the most part remained rather ill over time.
Jason, Leonard; Skendrovia, Beth; Furst, Jacob; Brown, Molly; Evans, Meredyth; Brown, Abbey	Leonard A. Jason, Ph.D., Director, Center for Community Research, DePaul University 990 W. Fullerton Ave, Suite 3100, Chicago, Il. 60614 E-mail - Ljason@depaul.edu	Data Mining	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P122-123	Objectives: Data mining may be a useful tool in aiding in the diagnosis of ME/CFS. There are many challenges in diagnosing ME/CFS. Some symptoms associated with it are common of other illnesses, and there are competing definitions that investigators may use. More work with data mining in ME/CFS research could aid in further identification of cardinal symptoms, leading to better diagnostic ability. This would also combine an objective, computer driven decision with a physician's medically influenced decision to come up with a better and more reliable way to diagnose and treat ME/CFS. This article contrasts two case definitions for Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS). We compared the empiric CFS case definition (Reeves et al., 2005) and the Canadian ME/CFS Clinical case definition (Carruthers et al., 2003) with a sample of individuals with CFS as defined by the Fukuda et al. (1994) criteria versus those without CFS from a community-based sample. Methods: Data mining with decision trees was used to identify the best items to identify patients with CFS. Data mining is a statistical technique that was used to help determine which of the survey questions were most effective for accurately classifying cases as defined by the two case definitions versus others contained by the study. Results: The empiric criteria identified 79% of patients with CFS and the Canadian criteria identified 87% of patients with CFS. Items identified by the Canadian criteria had more construct validity. ME/CFS is often thought to include post-exertional malaise and neurocognitive disorders, and both did emerge as predictive factors for the Canadian criteria, but not when using the Reeves et al. (2005) empiric case criteria. In addition, sleeping disorders and pain symptoms, other key symptoms of ME/CFS, did emerge for the Canadian criteria as well as in the immune areas (i.e., sore throat and multiple chemical sensitivities), and this supports evidence for the Canadian criteria. In contrast, the empiric criteria tended to identify more general areas, including less activity, social and role functioning problems, and some pain issues. However, critical symptoms such as post-exertional malaise, neurocognitive symptoms and sleep disorders were not identified as discriminating symptoms with the Reeves et al. (2005) criteria. Conclusion: The study's overall findings were that the Reeves et al. (2005) criteria were not as capable of identifying cases from non-cases

				as the Canadian criteria (Carruthers et al., 2003). The Reeves criteria have been criticized as being more general and broader than the Fukuda et al. (1994) criteria, and the results of this study suggest that these criteria are only able to discriminate 79% of cases from others, whereas the Canadian criteria were able to 87% of cases. In addition, when examining the items selected in both analyses, it is apparent that the Canadian criteria appear to select cardinal and central features of the illness.
Johdoi, Takako[1]; Kawatani, Junko[1]; Shiraish, Seisi[1]; Tomota, Akemi[1]; Miike, Teruhisa[2]	1. Department of Child Development, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University Graduate School, 1-1-1 Honjo, Kumamoto 860-8556, Kumamoto, Japan. 2. Hyogo Children's Sleep and Development Medical Research Center 1070 Akebono-cho, Nishi-ku, kobe 651-2181, Hyogo, Japan	Childhood Chronic Fatigue Syndrome and School Phobia in Junior High Students in Japan	Bulletin of the IACSF/ME. 17 (3). Fall 2009.	The Japanese Ministry of Education, Culture, Sports, Science and Technology reported in 2007 that 105,000 junior high school students (2.91% of all students) had "school phobia". Over the last 15 years, a considerable number of students diagnosed with school phobia have been found to fulfill diagnostic criteria for childhood chronic fatigue syndrome (CCFS). Symptoms of CCFS are similar to those seen in adult chronic fatigue syndrome. In this study, 128 junior high school students with the chief complaint of school non-attendance were presented to the Department of Child Development Outpatient Clinic at Kumamoto University (Jan.-Dec. 2008). They were medically examined using the 2007 international CCFS case definition, and given a Performance Status Score, a measure of functional status. Results showed that 72 (56.3%) students fulfilled CCFS criteria for severe or moderate illness, and 35 students (27.3%) were diagnosed with atypical CCFS or CCFS- like disorder. Twenty one patients (16.4%) either met criteria for other conditions including hyperthyroidism, major depression and narcolepsy or were without clear diagnosis. The results suggest that a diagnosis of CCFS is often associated with school non-attendance or school phobia in Japan.
Jolly, Ken	kjols@xtra.co.nz	Information Sheet: Trying Out Alternative Treatments	Bulletin of the IACSF/ME. 16 (1). Spring 2008.	Most people with ME/CFS at some time or other will try alternative treatments in order to get better. This would seem a reasonable and understandable approach, considering how difficult this illness can be at times... However this doesn't mean that patients should necessarily blindly accept such treatments. A reasoned and careful approach is in order.
Kaseeska, Kristen; Brown, Molly; Jason, Leonard	Leonard Jason, Center for Community Research, 990 W. Fullerton Ave., Suite 3100, Chicago, IL 60614 email: ljason@depaul.edu	Comparing Two Fibromyalgia Diagnostic Criteria in a Cohort of Chronic Fatigue Syndrome Patients	IACSF/ME. 19 (1). Summer 2011.	Two different diagnostic criteria for Fibromyalgia, 1, 2 produced by The American College of Rheumatology were compared with a chronic fatigue syndrome (CFS) sample. While the original Wolfe et al[1] criteria included a patient's tender points, the newer Wolfe et al[2] criteria introduced a total of 44 somatic symptoms in addition to areas of pain throughout the body. The original criteria identified fewer patients with CFS as having co-occurring Fibromyalgia than the newer criteria. In addition, the 1990 criteria better differentiated physical functioning limitations among those with and without Fibromyalgia. The implications of these findings are discussed.
Katz, Benjamin; O'Gorman, Maurice; Wang,	Ben Z. Katz, MD, Professor of Pediatrics, Northwestern	Natural Killer Cell Number and Function in a	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International	Introduction: Chronic fatigue syndrome (CFS) is a complex condition involving severe fatigue and disabling musculoskeletal and cognitive symptoms. Whether immunologic dysfunction accompanies CFS is controversial. Arguably the most consistent

Deli; Mears, Cynthia; Shiraishi, Yukiko; Taylor, Renee	University Feinberg, School of Medicine, Attending Physician, Division of Infectious Diseases, Children's Memorial Hospital 2300 Children's Plaza, Chicago,IL60614 bkatz@northwestern.edu	Prospective Cohort of Adolescents with Chronic Fatigue Syndrome and Controls Following Mononucleosis	Conference. P124-125	immunologic disturbance associated with CFS is reduced function of natural killer (NK) cells. Objectives: We examined NK function in our cohort of adolescents following infectious mononucleosis (IM) and recovered controls matched for age, sex and Tanner stage. Methods: Nine adolescents with CFS and 9 matched, recovered controls had blood drawn for NK cell quantitation and functional analysis that was performed blinded at 6, 12 and 24 months following IM. At each time point, NK cell quantification was ascertained by flow cytometry as %CD56+ cells, and NK cell function was determined using K562 cells and 3 different dilutions of patient lymphocytes. NK cell numbers were scored as high, normal or low. NK cell function was scored as normal, low or borderline by pre-determined parameters by an investigator blinded as to the patient's diagnosis. Statistical analysis was conducted using generalized linear mixed model with repeated measurements and linear mixed model with SAS 9.2. Results: There were 27 evaluable time points for the CFS patients and 25 for the controls. There was no difference in NK numbers between cases and recovered controls. NK function was significantly higher in case patients with CFS 6 months following IM than in recovered controls (p=0.02). Conclusion: We could not confirm decreased NK cell function in adolescents with CFS following IM.
Kaur, Manraj; Mehta, Saurabh	Manraj Kaur, MSc Rehabilitation Science Student, McMaster University, IAHS, Room 308, 1400 Main St. W. Hamilton ON, L8S 1C7 kaurmn@mcmaster.ca	Are Walls Better Than ill-Defined Bridges? Revisiting Descartes' Biomedical Model From a Biopsychosocial Perspective in Chronic Pain Due to Osteoarthritis	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P158.	Introduction: Biopsychosocial and biomedical model are two remarkably different and most argued perspectives on chronic pain. In contrast to biomedical model, biopsychosocial model facilitated greater understanding of the contribution of mental and social health to chronic pain experience. This led to a theoretical and practical shift from traditional unidimensional towards integrated models of chronic pain. However, these multidimensional models have failed to offer a uniform definition, classification system, diagnostic criteria or treatment strategies to manage chronic pain especially in that observed in osteoarthritis (OA) population. Instead, it has faced criticism for ill-defined integrating links which foster no standardization of research or clinical practice and therefore no future directions. Objectives: The purposes of the paper were i) to re-visit the philosophical underpinnings of the Descartes' biomedical model, ii) to discuss and critique the contributions of the biopsychosocial model over the biomedical model in chronic pain related to OA. Methods: A topical review of the studies concerning biopsychosocial and/or biomedical model and chronic musculoskeletal pain published in peer reviewed journals since 1960 was conducted. Patient population was restricted to osteoarthritis in the elderly age group. Results: Re-examining Descartes' philosophy reveals that much of the interpretation of his work does not reflect or elucidate the aspects of chronic pain as experienced by those with OA. Using the example of chronic pain in OA, this paper proposes that biopsychosocial model is essentially biomedical model with some additions and does

				not offer any significant advancement over the biomedical model. Conclusion: Efforts are to be directed towards a more absolute conceptualisation of chronic pain with collaboration of researchers and trans-disciplinary healthcare teams leading to explicit models that could possibly unravel the mind body dilemma in healthcare field.
Keller, Betsy A; Micale, FG	Betsy A. Keller, PhD, Professor Exercise & Sport Sciences Ithaca College, 318 Center for Health Sciences, Ithaca, NY 14850	Exercise Testing to Quantify Effects of Fatigue on Functional Capacity in Patients With CFS	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P123-124.	Objective: The purpose of this study was to assess the effects of post-exertional malaise (PEM) on functional capacity and anaerobic threshold in subjects diagnosed with chronic fatigue syndrome (CFS). Methods: Subjects were 10 females and 2 males (41.3+1.11 yrs) diagnosed with CFS by a physician experienced in the diagnosis of CFS. To induce PEM, each subject completed a maximum exercise test on a cycle ergometer. A second maximum exercise test was performed 24 hrs later to assess the effects of exercise-induced PEM on functional capacity. Maximum oxygen consumption (VO2max), maximum heart rate (HRmax), anaerobic threshold (AT), maximum workload (Wmax), workload at AT (ATwork), and respiratory exchange ratio (RER) were measured. RER is an objective indicator of substrate utilization and subject effort during exercise. Results: Significant decreases from test 1 to test 2 were 13.5% for VO2max (21.5 to 18.6 ml.kg-1.min-1; p<0.01), 8 bpm for HRmax (p<0.01), 18.8% for AT (12.0 to 9.7 ml.kg-1.min-1; p<0.05), 9.4% for Wmax (121 to 109 W, p<0.05), and 17.3% for ATwork (58.3 to 48.2 W; p<0.05). However, there was no change in maximum RER indicating that subject effort was maximum and also comparable during both tests. Conclusion: Results indicate that PEM decreased maximum functional capacity by more than 13% to below 5 METS; a level at or below that which is required by many job-related activities and IADLs. To compare, VO2max in healthy individuals is highly reproducible over days and even months (r>.95)1, with a SEM of < 6%1,2. Thus, for subjects in this study, an expected variation between tests would be ±1.29 ml.kg-1.min-1 in contrast to the observed decrease of 2.9 ml.kg-1.min-1. Furthermore, PEM decreased AT to below 3 METS (e.g., light-moderate speed walking), which is a level of many activities considered to be sedentary in nature. Thus, completion of sedentary ADLs and IADLs for those with CFS requires production of energy via anaerobic processes that will further contribute to PEM and exacerbate symptoms of CFS. Since many daily activities fall into the 3-5 MET range, individuals with CFS will exacerbate symptoms associated with PEM simply by completing normal daily activities.
Kindlon, T	Information Officer (voluntary position), **Irish ME/CFS Association,** PO Box 3075, Dublin 2, Rep. of Ireland, Email: tkindlon@maths.tcd.ie	Reporting of Harms Associated with Graded Exercise Therapy and Cognitive Behavioural Therapy in Myalgic	IACSF/ME. 19 (2). Fall 2011.	Across different medical fields, authors have placed a greater emphasis on the reporting of efficacy measures than harms in randomised controlled trials (RCTs), particularly of nonpharmacologic interventions. To rectify this situation, the Consolidated Standards of Reporting Trials (CONSORT) group and other researchers have issued guidance to improve the reporting of harms. Graded Exercise Therapy (GET) and Cognitive Behavioural Therapy (CBT) based on increasing activity levels are often recommended for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome

	or info@irishmecfs.org	Encephalomyelitis/Chronic Fatigue Syndrome		(ME/CFS). However, exercise-related physiological abnormalities have been documented in recent studies and high rates of adverse reactions to exercise have been recorded in a number of patient surveys. Fifty-one percent of survey respondents (range 28-82%, n=4338, 8 surveys) reported that GET worsened their health while 20% of respondents (range 7-38%, n=1808, 5 surveys) reported similar results for CBT. Using the CONSORT guidelines as a starting point, this paper identifies problems with the reporting of harms in previous RCTs and suggests potential strategies for improvement in the future. Issues involving the heterogeneity of subjects and interventions, tracking of adverse events, trial participants' compliance to therapies, and measurement of harms using patient-oriented and objective outcome measures are discussed. The recently published PACE (Pacing, graded activity, and cognitive behaviour therapy: a randomised evaluation) trial which explicitly aimed to assess "safety", as well as effectiveness, is also analysed in detail. Healthcare professionals, researchers and patients need high quality data on harms to appropriately assess the risks versus benefits of CBT and GET.
Kindlon, Tom	Information Officer (voluntary position) Irish ME/CFS Association, PO Box 3075, Dublin 2, Rep. of Ireland	Letter to the Editor Re: A pilot study of the process of change in a group Chronic Fatigue Syndrome management programme. Bulletin of the IACFS/ME. 2009;17(2):53-68	Bulletin of the IACSF/ME. 17 (3). Fall 2009.	Group interventions based around encouraging CFS patients to increase activity levels have shown modest results. Royle and Pimm (1) state "cognitive-behavioural therapy [CBT] and graded exercise therapy [GET] are efficacious therapies in patients with Chronic Fatigue Syndrome (CFS)". But is this true for group programmes? See also: Royle, G, and Pimm,J. Response to letter from Tom Kindlon. Bulletin of the IACSF/ME. 17 (3). Fall 2009.
Klapow, LA; Nathan, N	Klapow Bioscience and Gordon Medical Associates, Santa Rosa, California	Live, Moving Varestrongylus klapowi: an Atypical, Chronic Nematode Parasite in the Nasal Washings of CFS Patients	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P176-177.	Objectives: • Obtain "proof of life" evidence for the atypical *V. klapowi* (Vk) parasite by documenting the vital movements of living worms. • Develop a rapid accurate method for diagnosing the infection by analyzing washings from nasal membranes.• Determine the ethanol concentration for effective nasal spray disinfectants. Methods: A nasal irrigation bottle was used to force warm physiological saline (0.9% NaCl, ~90°F) up one nostril to collect fluid (~60 ml) through the other nostril of CFS patients who were previously shown to be positive for the Vk parasite by sputum analysis. Vk specimens were allowed to settle to the bottom of a 50 ml test-tube suspended in warm water (~90°F), gently pipetted to a warm dish and video-graphed under a stereo-microscope. Moving worms were also video-graphed using intense halogen lighting on a compound microscope equipped with two polarizers (one in the illumination, the other in the image path) to reduce glare. Four Vk positive patients previously diagnosed by sputum analysis (inhalation of 1% ethanol for 30 minutes, then self induce coughing) were re-tested by the nasal washing method. Two patients

				inhaled the fumes of 40% ethanol through the nose for 10 breaths just prior to the nasal washing which my have helped release live worms. Results: Video-graphs showed gross body locomotion as well as rhythmic movements of internal organs. Repeated thrusting movements of the head were seen in the tissue boring fourth stage larva. Whole body contractions were seen in males. Rapid repeated rhythmic contractions of the digestive track (esophagus and intestine) and associated glands were seen in these and other stages. All four patients who were positive by sputum analysis were also positive by the nasal washing method. Previous experiments had shown that inhalation of one percent nebulized ethanol for 30 minutes sterilized sputum from the lungs. Higher concentrations, currently being studied, will likely achieve more rapid sterilization of nasal membranes. Conclusions: *Varestrongylus klapowi* is an anatomically specialized nematode, not an artifact, as evidenced by the vital movements of live specimens showing both gross locomotion and rhythmic movements of internal organs. It has recently been isolated from nasal washings of CFS patients who were previously positive by sputum analysis. The infections are chronic and widely disseminated as they occur in the same individuals over many years, in sputum, intestinal, and now, nasal washings. A study using the nasal washing method is being planned which will attempt to confirm previously reported, statistically significant, blinded sputum analysis linking the infection to CFS. Dilute ethanol sprays can kill the Vk parasite on mucus membranes.
Klimas, Nancy (Chair), Case Presentations by: Lapp, Charles Bateman, Lucinda Vallings, Rosamund Enlander, Derek	[no address given]	Session: DIAGNOSING CFS/ME; DIFFICULT CLINICAL CASES	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P119-121	In this workshop, experts will present difficult cases, and discuss the diagnostic and management implications. Cases may include “look alike cases” that presented with the signs and symptoms of ME, but in fact were found to be caused by another disorder; complex management issues; medication use and medication intolerance and other issues of interest to the practicing clinician. Related conditions such as Gulf War Illness will be included in the case discussion. The workshop will welcome interchange with the clinicians attending the session. Basic scientists may also hear in this discussion some of the issues that trigger further research ideas. Charles Lapp, M.D., Lucinda Bateman, MD, Rosamund Vallings, MNZM, MB BS, and Derek Enlander, M.D. will present cases that will serve as a platform for discussion.
Knight, K	Kim Knight, Certified Mickel Therapist and Mickel Therapy trainer for Australasia, BA (Hons), Director of the Art of Health and Mickel Therapy Clinic (New Zealand), PO Box 84318, Westgate, Massey 0657,	To Show How the Propensity for Chronic Fatigue Is Set Up During Infancy and Childhood	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P182.	Objectives: To show how the seeds and propensity for chronic fatigue and related syndromes are sown during infancy and childhood via the mental patterning and emotional conditioning set in place in the environment. So-said patterns and conditions result in the formation of limiting self-beliefs and ensuing disempowering behaviours which put the body into an abnormal and perpetual state of stress. This eventually rewires the cells into illness. Methods: By taking a detailed case history from birth to the present with more than 500 clients and noting in particular the mental and emotional perceptions or responses to upsetting and traumatic events. Results: In every case, without fail, unconscious negative and self-limiting beliefs were set up in childhood which in turn led to disempowering behaviours towards self. This

	Auckland, New Zealand info@artofhealth.co.nz			put the body into a perpetual state of stress (sympathetic response) from a very early age which over time resulted in physical depletion such as adrenal exhaustion and a weakened immune system which opened itself up to viruses. This in turn eventually led to chronic fatigue. Conclusion: The propensity for chronic fatigue is set up in childhood via environmental factors, in particular mental belief systems and emotional patterns which lead the client to perpetuate life-depleting behaviours which result in illness. Therefore it is essential when looking for solutions to take into account the person's current and past history in its totality. The ongoing evidence can then be used again in practice.
Kozak,C	Laboratory of Molecular Microbiology, National Institute of Allergy and Infectious Diseases, Bethesda, MD, 20892-0460, USA	Gammaretroviruses of Mice and Their Links to Prostate Cancer and CFS/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P112.	Gammaretroviruses of three distinct host range tropisms have been isolated from the laboratory mouse. These viruses differ in receptor usage, distribution among wild mouse species and strains of laboratory mice, pathogenicity and sensitivity to host restriction factors. Two of these three host range groups, the xenotropic and polytropic mouse leukemia viruses (together termed XP-MLVs) are widely distributed in house mouse species, mice that live in closest contact with humans. XP-MLVs rely on the XPR1 receptor for entry into cells as does the xenotropic murine leukemia virus-related virus (XMRV) initially identified in human patient samples. Despite their initial description as viruses incapable of infecting mouse cells, the xenotropic viruses have the broadest host range of the MLVs. Nearly all nonrodent mammals are susceptible to X-MLVs, as are all wild mouse species and some inbred strains of laboratory mice. Their XPR1 receptor is highly polymorphic, and there are 5 functional variants of *Xpr1* in *Mus* species and laboratory mouse strains that differ in their ability to support entry of XMRV and various isolates of XP-MLVs. The distribution of XP-MLVs and *Xpr1* variants in wild mouse populations provides a good example of how diversifying selection can be driven by genetic conflicts. Restrictive receptor variants evolved in Eurasian house mouse populations exposed to XP-MLV infection suggesting that positive selection favors antiviral alleles in virus-infected species. The ecotropic and polytropic MLVs have long been linked to disease induction in mice, and the discovery that all wild mice and some laboratory strains are also susceptible to X-MLV has made it possible to examine the disease inducing potential of these viruses in mice as well as in other model systems. X-MLVs are capable of establishing infection in mice carrying permissive XPR1 alleles, but X-MLV does not induce or accelerate disease in mice with permissive receptors inoculated as adults or neonates, and X-MLVs do not readily establish productive infection in monkeys. Host factors that restrict retroviruses effectively limit virus spread and disease induction in mice and other species.
Kuratsune, H; Nojima, Junzo	Kansai University of Welfare Science, Osaka e-mail: kura@fuksi-kagk-u.ac.jp	Objective Biomarkers For The Fatigue State -The Changes Of Oxidation Stress	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster	Background: It is well known that the accurate evaluation of fatigue states in each subject is quite difficult, because the levels of fatigue depend on the subjective feeling. Since 2009, the study group (head: Hirohiko Kuratsune) supported by Japanese Ministry of Health, Labor and Welfare has been working for the

			Presentations. P180-181.	establishment of objective biomarkers to diagnose the fatigue states in Japan. We present here the relationship between the fatigue states and the changes of oxidation stress. Materials and Methods: To investigate the role of oxidative stress in the pathogenesis of fatigue states, we measured both oxidation and anti-oxidation activities simultaneously in sera from 303 patients with chronic fatigue syndrome (CFS), 24 people with severe industrial fatigue, 20 healthy students before and after 3 hour mental workload and 312 healthy volunteers by using the d-ROMs test and the BAP test (Diacron; Grosseto, Italy). The oxidation stress index (OSI) was calculated by the following formula: OSI = (d-ROMs / BMP) × 8・85 (a coefficient for standardization to set the mean of healthy individuals to 1.0). Results: The oxidation activities (d-ROMs) in 312 healthy controls are 286.9 ± 50.1 unit (mean ± SD), and the d-ROMs are related to their age. The d-ROMs are higher in female than in male. On the other hand, the anti-oxidation activities (BAP) in 312 healthy volunteers are 2541 ± 60.8 μmol/L, and the BAP are not related to the age and sex. In the CFS group, the d-ROMs and the BAP are 328.8 ± 81.3 units and 2508 ± 102.6 μmol/L, respectively. The d- ROMs are significantly higher in the CFS group than in the control group ($p<0.001$), and the BAP are significantly lower in the CFS group than in the control group ($p<0.001$). The OSI are related to the Performance Status in the CFS patients ($p<0.005$). In the severe industrial fatigue group, the d-ROMs are 410.0 ± 67.0 units, and they are significantly higher in the severe industrial fatigue group than in the control group ($p<0.001$). The BAP are 2527 ± 115.5 μmol/L, and there is no significant difference in the BAP between the severe industrial fatigue group and the control group. When we studied the d-ROMs and the BAP before and after 3 hour mental workload in 20 healthy students, the d-ROMs and the BAP are 301.3 ± 23.6 unit and 2389.6 ± 81.2 μmol/L before workload, and 321.2 ± 33.0 unit and 2438.8 ± 92.9 μmol/L after workload, respectively. After mental workload, both the d-ROMs and the BAP are significantly increased as compared to those before mental workload, and there is no difference in the OSI between before and after workload. Conclusion: The evaluation of oxidation and anti-oxidation activities by using the d-ROMs test and the BAP test reflects not only the clinical condition with or without fatigue state, but also the etiology of fatigue state. Therefore, these evaluations might make useful objective markers for diagnostic evaluation of fatigue states.
Lange, Gudrun	Pain and Fatigue Study Centre, UMDNJ-New Jersey Medical School	Multi-tasking: A challenge for patients with CFS	Bulletin of the IACSF/ME. 17 (1). Spring 2009. P32-36	As a researcher and a practicing clinical neuropsychologist my task is to assess cognitive function in CFS patients. Once the test measures given are scored and the results interpreted, I provide feedback about my findings. Very often the findings are consistent with decreased information processing speed and poor working memory while overall intellectual function is usually intact. These results are not uncommon in CFS and are supported by increasing research evidence (1, 2). During feedback sessions, I aim to explain the deficits found, but are frequently asked the question: "How do these findings relate to what I am experiencing in my daily life and what, if

				anything, can I do about it?" I will use this brief essay to begin to address these questions.
Larson, B; Davenport, TE; Stevens, SR; Steens, J; Van Ness, JM; Snell, CR	Benjamin M. Larson , 895 El Paseo St. Undergraduate Researcher, Pacific Fatigue Laboratory Turlock, CA 95380 b_larson2@u.pacific.edu	Effort Perception in Chronic Fatigue Syndrome Is Not Impaired	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P182-183.	Background and Objectives: Activity pacing is one cornerstone of rehabilitation management for CFS. Optimal criteria for pacing are currently unclear, because patients with CFS may have an impaired ability to self-assess their level of physical exertion. However, this hypothesis has yet to be directly tested. The purpose of this study was to determine the association between subjective and objective indicators of physical effort in patients with CFS and matched controls. Materials and Methods: Sixteen patients with CFS and 14 age- and sex-matched non-disabled, sedentary individuals were tested. Each subject received 2 maximal cardiopulmonary exercise tests (CPETs) on a braked bicycle ergometer that were administered 24 hours apart. Heart rate (HR) was measured continuously and rating of perceived exertion (RPE) was assessed at each minute from rest and unloaded cycling until peak exercise. Descriptive statistics (mean ± standard deviation) were calculated for all dependent variables (DVs), including peak HR (HRpeak), HR at VT (HRVT), peak RPE (RPEpeak) and RPE at VT (RPVT). 2x2 analysis of variance (ANOVA) was used to assess the main and interaction effects of group and test on DV measurements. Repeated measures ANOVA was used to assess group and time main and interaction effects on DV measurements. Pearson's correlations (r) were calculated to determine the within-groups associations between HR and RPE during each CPET. Criterion for statistical significance of differences was $\alpha \leq .05$. Results: All subjects met standard criteria for maximal effort during each CPET. HRpeak was significantly lower for patients with CFS (CPET1: 158±15 beats per minute [bpm]; CPET2: 156±17bpm) compared to controls (CPET1: 182±13bpm; CPET2: 183±11bpm) on both CPETs ($p<.01$). HRVT also was significantly lower for patients with CFS (CPET1: 113±21bpm; CPET2: 111±14bpm) compared to controls (CPET1: 122±15bpm; CPET2: 131±17bpm) on both CPETs ($p<.01$). RPEpeak was significantly greater in patients with CFS (CPET1: 19.4±1.0; CPET2: 19.6±0.07) compared to controls (CPET1: 19.4±0.8; CPET2: 18.7±2.1) on both CPETs ($p<.01$). RPEVT also was significantly greater patients with CFS (CPET1: 13.2±2.5; CPET2: 12.7±2.6) compared to controls (CPET1: 10.2±2.5; CPET2: 11.2±2.4) on both CPETs ($p<.01$). Time series analysis revealed significant group effects for HR ($p<.01$) and significant group and group x time effects for RPE ($p<.01$). HR and RPE demonstrated moderate to high correlation in subjects with CFS (CPET1: $r=.769$, $r2=.591$; $p<.001$; CPET2: $r=.765$, $r2=.591$; $p<.001$) and control subjects (CPET1: $r=.742$, $r2=.551$; $p<.001$; CPET2: $r=.688$, $r2=.473$; $p<.001$). Conclusion: Subjects with CFS demonstrated significantly greater effort ratings than control subjects during each CPET. HR and RPE were significantly correlated in subjects with CFS and matched control subjects. Clinical Relevance: The significant association between HR and RPE indicates patients with CFS can accurately perceive their level of physical exertion. Thus, patients' perceptions of physical exertion can be used with confidence as a basis

				for pacing self-management programs.
Leonard A. Jason[1]; Judith Richman[2]; Nicole Porter[1]; Mary Benton[3]	DePaul University [1]; University of Illinois, Chicago[2]; Wichita State University[3]	Why the Name of An Illness is of Importance	Bulletin of the IACSF/ME. Fall 2006.	Despite its chronicity and severity, CFS remains highly controversial (Richman, & Jason, 2001). A particularly high percentage of patients with this illness have experienced disrespect and poor treatment by the health care system. Below, we review an issue involving the name given to this illness, which may have contributed to the diagnostic scepticism and stigma that those with this illness encounter.
Letcher, MA; Klimas, NG	Mary Ann Fletcher, Ph.D. Professor, University of Miami Miller School of Medicine.1600 NW 10th Ave, Miami, FL 33135, USA mfletche@med.miami.edu	Biomarkers in CFS/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P169-170.	Objectives: Validated laboratory tests are essential for diagnosis and for monitoring therapy of CFS/ME. Diagnosis using the case definition [Fukuda, et al, 1994] requires the exclusion of any other medical explanation for these symptoms, yielding an inefficient, slow, error prone process. This is also costly because the current clinical diagnosis typically involves tertiary care specialists. The search for biomarkers included lymphocyte functions as well as molecules associated with lymphocyte activation, with stress and with inflammation. Methods: CFS/ME patients were drawn from the University of Miami (UM) Miller School of Medicine CFS/ME and Immunodeficiency Clinic. All were participants in funded studies (NIH, DOD, Chronic Fatigue Immunodeficiency Syndrome Association (CFIDS) or the Veterans Affairs Merit grant). Prospective biomarkers included natural killer cell cytotoxicity (NKCC), T lymphocyte proliferation in vitro in response to mitogen (LPA), lymphocyte activation markers (CD26, CD38), 16 plasma cytokines and neuropeptide Y. All laboratory evaluations of prospective biomarkers were done in the UM/VA clinical immunology laboratories. The diagnostic accuracy of biomarkers was assessed in terms of true positive (sensitivity) versus true negative (specificity) rates using nonparametric receiver operating characteristics (ROC) curve analyses. Results: These studies provided credible biomarker status for NKCC, LPA, and markers of lymphocyte activation in CFS/ME. A significant elevation in the relative amounts of 4 of 5 pro-inflammatory cytokines in peripheral blood plasma of patients with CFS/ME was found when compared with the controls Only tumor necrosis factor (TNF)a was unchanged. In cases, lymphotoxin (LT)a was elevated by 257% and IL-6 by 100% over the controls. Both interleukin (IL)-4 and IL-5 were elevated in CFS/ME, with the median of IL-4 240% and of IL-5 95% higher in cases over controls. The anti-inflammatory cytokine IL-13 was significantly lower (15%) in CFS/ME patients while IL-10 was not different. Plasma levels of IL-2 and IFN. in CFS were similar to those in controls. However, IL-12 was significantly elevated (120%) and IL-15 decreased 15% in cases compared to controls. IL-8 (CXCL8) was 42% lower in the CFS/ME patients. IL-17 and IL-23 were not significantly different in CFS cases compared to controls. ROC analyses calculating area under the curve (AUC) for IL-5 (0. 84), LTa (0.77), IL-4 (0.77), IL-12 (0.76) indicated good biomarker potential. The AUC of IL-6 (0.73), IL-15 (0.73), IL-8 (0.69), IL-13 (0.68) IL-1a (0.62), IL-1ß (0.62) showed fair potential as biomarkers. The stress hormone, NPY, was elevated in plasma of CFS/ME cases and positively

				correlated with perceived stress, anger, depression, negative thoughts and maladaptive coping. ROC analysis indicated that the predictive ability of plasma NPY was significantly better than chance alone in distinguishing patients with CFS/ME from healthy controls. Conclusions: Fifteen useful biomarkers were identified in these studies. The differences of these markers in CFS/ME compared to controls also give important information regarding the pathophysiology of the disorder. The association of low LPA response, elevated proportion of activated CD4 and CD8 T cells, defective NKCC, elevated TH2 cytokines with CFS/ME cases suggests that T cells are metabolically limited in performing their helper function. All but one of the inflammatory cytokines measured were elevated as was the stress hormone, NPY – supporting the hypotheses that inflammation and abnormal stress responses are important components in the pathophysiology of CFS/ME.
Levine, SM; Sterling,M	Susan Levine, MD 115 East 72nd Street, Suite 1A, New York, NY 10021, e-mail cfssuelev@earthlink.net	Results of Head Upright Tilt Table Test as a Predictor of Disability in a Group of Chronic Fatigue Syndrome Patients	IACSF/ME. 18 (1). Spring 2010.	*Background:* Chronic Fatigue Syndrome (CFS) is a complex illness characterized by the presence of debilitating fatigue, myalgias, sore throats, headaches and cognitive disturbances. Autonomic dysfunction or orthostatic intolerance (OI) characterized by the presence of dizziness, palpitations and frank syncope has been implicated as a cause of some of the debility experienced by a subgroup of CFS patients. *Methods:* Using the results of Head Upright Tilt Table Testing (HUT), in addition to the frequency of symptoms of both CFS and OI reported by 15 subjects chosen randomly from S.L.'s private practice, we sought to determine whether the presence of autonomic dysfunction was associated with a likelihood of disability among these patients. *Results:* Of the CFS patients studied 13/15 had a positive HUT. Twelve of the thirteen patients who had a positive outcome on HUT were fully disabled and receiving disability benefits. Three of the thirteen patients who were positive had a history of syncopal episodes and demonstrated syncope on HUT. *Conclusion:* Results of this study suggest that HUT in addition to a strong history of autonomic symptoms, especially syncope, may be useful in determining disability status among CFS patients. It is important to note that methodological differences among testing sites including experience with the method in general, angle of tilt, and monitoring of ambient conditions during HUT, may affect the interpretability of the HUT data. In addition, variability among CFS patients including comorbid medical conditions, such as presence of Mitral Valve Prolapse or Asthma or the use of vasoactive medications prior to testing, may influence the outcome of this procedure.
Martin Lerner, A; Ariza, M; Williams, M; Jason, L; Beqaj, S; Glaser, R	A. Martin Lerner, M.D., 32804 Pierce Street, Beverly Hills, MI 48025, www.treatmentcenterforcfs.com	Epstein-Barr Virus Latent Abortive Reactivation Replication of the Encoded Gene Products	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P141-142	Methods: With a specific ME/CFS diagnostic panel, 6 patients with Epstein-Barr Virus (EBV) subset were treated with valacyclovir (14.3 mg/Kg q 6 h) for greater than or equal to 12 consecutive months. EBV assays were repeated every 6-12 weeks in each patient. ELISA assays included EBV, Early Antigen (Diffuse) EBV EA(D), Viral Capsid Antigen (VCA) IgM. Neutralization assays included EBV dUTPase and EBV/DNA polymerase. Results: a) EBV VCA, IgM: 51 separate sera were tested for EBV VCA IgM.

		Deoxyuridine Triphosphate (dUTPase) and Deoxyribonucleotide polymerase (DNA polymerase) in Myalgia Encephalomyelitis Chronic Fatigue Syndrome (ME/CFS)		All were negative. b) EBV EA(D): 48 separate sera were tested for EBV EA(D). 46 of 48 assays (95.8%) were positive c) EBV dUTPase: three of 9 (33.3%) positive assays; patient one: five of 7 (71.4%) positive assays; patient two: three of 10 (30%) positive assays; patient three: eight of 10 (80%) positive assays; patient four: three of 8 (37.5%) positive assays; patient five: two of 7 (28.6%) positive assays. Therefore, all 6 patients had positive assays for elevated antibody titers to dUTPase, d) EBV/DNA polymerase: Eight of 10 (80%) patient one: four of 7 (57.1%) patient two: seven of 10 (70%) patient three: nine of 10 (90%) patient four: seven of 8 (88%) patient five:six of 7 (71.4%) were positive assays for EBV DNA polymerase. Therefore, all 6 patients had positive assays fpr elevated antibody titers to EBV DNA polymerase. Conclusions: There was no evidence of EBV lytic replication in these ME/CFS patients. There were 47/50 (94%) EBV EA(D) positive assays, 24/51 (47%) dUTPase positive assays, and the 41/52 (78.8%) DNA polymerase positive assays. These data document EBV latent abortive reactive replication in these six ME/CFS patients and suggest a possible etiologic relationship to the ME/CFS.
Meirleir,KD; Frémont, M; Khaliboulina, S; Lombardi,VC; Puccinelli, C; Metzger,K; Mikovits,JA	Department of Human Physiology, Vrije Universiteit Brussel, Pleinlaan 2, B- 1051 Brussels Belgium, Email: de.meirleir@telenet.be	Detection Of Anti-XMRV Antibodies In Serum of CFS Patients and Healthy Blood Donors in Belgium	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P113-114.	Objectives: Xenotropic murine leukemia virus–related virus (XMRV) is a new human gammaretrovirus originally identified in prostate cancer patients with a deficiency in the antiviral enzyme RNase L. An association has been made between XMRV and Chronic Fatigue Syndrome (CFS), with a 2009 study reporting the presence of XMRV DNA in the blood of 67% of CFS patients, whereas only 3,7% of healthy controls tested positive. In 2010 another study detected murine leukemia virus (MLV)-like GAG sequences in 86.5% of CFS patients, versus only 6,8% of healthy blood donors. A number of other studies, however, have failed to detect XMRV DNA in the blood of CFS patients. The objectives of this study were to investigate the association between CFS and XMRV in a Belgian population of patients, and to estimate the prevalence of XMRV infections in the general population in Belgium. Methods: A flow cytometry-based assay was used to detect the presence of circulating anti-XMRV antibodies in the serum of 84 Belgian CFS patients. A subgroup of these patients (21) developed CFS after receiving a blood transfusion. Serum obtained from 44 Red Cross healthy blood donors was also tested. Samples were collected in Belgium and sent, blinded, to the Whittemore Peterson Institute in Reno for analysis. Results: 48 out of 84 patients (57%) presented circulating antibodies against XMRV (10 out of the 21 patients who received a transfusion). In contrast, only 7 out of 44 controls had anti-XMRV antibodies (16%). Conclusions: The higher prevalence of serology positives in the patient population, compared to the controls, supports the idea that XMRV is involved in the pathogenesis of CFS. The finding that 16% of healthy blood donors present evidence of infection with XMRV or a related virus raises questions regarding the need to screen blood donors for asymptomatic XMRV infections.

Miike, Terusha; Ymamashita, Nobuyuki	Teruhisa Miike, M.D. Ph.D, Chief of Hyogo Children's Sleep and Development Medical Research Center, 1070, Akebono-Cho Nishi-Ku Kobe, Hyogo, 651-2181, Japan E-mail: t_miike@hwc.or.jp	A Trial for Prevention of CCFS Onset from The View Point of Sleep Issue	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P128.	Objectives: We have been considering that CCFS has been completed with the following order. 1) In spite of night active modern type daily life, people should keep classical morning active daily life, 2) which causes chronic sleep deprivation, 3) developed failure of neuronal function maintenance, 4) induced the derangement of the biological clock which is important and necessary for a human social life and life itself, 5) resulted neuronal fatigue and loss of neurons,6) these conditions connected with each other, finally complete the failure of the everyday life, 7) resulted in school non-attendance and/or so called CCFS. Therefore we think that we will be able to prevent CCFS by reading sleep deficient sign from everyday life of children. Methods: Then we investigated the habit of the sleep-wake rhythm for 5,100 students (ranged 6-15 years of age) in Yawatacity, Kyoto to get actual information to contribute to our purpose. We asked all students to record the consecutive 14 days sleep-wake log and studied following subjects, 1) total sleep time, 2) sleep onset time, 3) wake-up time and 4) sleep-wake pattern. The sleep log was classified into the 8 kinds of patterns, which was made beforehand. (1: holiday sleep supply, 2:short sleep, 3:long sleep, 4:irregular sleep, 5:sleep after get home, 6:sleep fragmentation, 7:overlapping, 8:normal sleep) Results and Conclusion: Average bed time (First grader: 9:14, Second 9:15, Third 9:16, Fourth 9:33, Fifth 10:03, Sixth 10:21, Seventh 10:49, Eighth 11:15, Ninth 11:51 pm).. Average rise time (First grader: 6:58, Second 7:01, Third 7:01, Fourth 7:00, Fifth 7:06, Sixth 7:10, Seventh 7:03, Eighth 7:14, Ninth 7:31am). Average total sleep time (First grader: 9.8, Second 9.7, Third 9.7, Fourth 9.5, Fifth 9.0, Sixth 8.8, Seventh 8.2, Eighth 8.0, Ninth 7.7 hrs). In addition we found that prolonged short sleep and irregular sleep pattern are the strong risk factors that suggest a difficulty of performing daily school life, in this study. It is considered that sleep deprivation and irregular life style has a direct connection to the CCFS. According to these data we conceived that it may be possible to prevent CCFS by observing a lifestyle, especially a sleep-wake rhythm of children.
Mikovits, Judy	Judy A Mikovits, PhD, Research Director, Whittemore Peterson Institute, University of Nevada, Reno MS 0552, 1664 N Virginia St Reno NV 89557-0552	The Case FOR XMRV/Human Gammaretroviruses (HGRVs) in ME/CFS	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P115-116.	In 2009 using a classical virology approach of viral isolation and transmission, electron microscopy, serology and PCR, Lombardi et al demonstrated the first isolation of XMRV from blood from patients with chronic fatigue syndrome (CFS) predominately from the west coast of the United States. In 2010, Lo et al. extended these studies by detecting nucleic acids of MLV-related variants in the peripheral blood mononuclear cells of CFS from the northeastern United States suggesting additional strains capable of infecting humans exist. In a study of 300 CFS patients, 13 developed lymphoproliferative disorders. Of those tested, 11/11 were positive for XMRV and 9/9 positive for clonal TCR gamma rearrangements. Spontaneous development of four immortalized B cells lines occurred during culture of cells from CFS patients. Three developed from B cells isolated from the peripheral blood (two of whom had B cell lymphoma) and one from a bone marrow biopsy. The B cell lines have a mature CD20+, CD23+ phenotype and produce infectious XMRV. Virus production occurred

				despite extensive hypermutation of the proviruses in these cells by APOBEC3G. Therefore, XMRV infection may accelerate the development of B cell malignancies by either indirect chronic stimulation of the immune system and/or by direct infection of the B-cell lineage. Since viral load in peripheral blood is low, these data suggest that B cells in tissues such as spleen and lymph nodes could be an *in vivo* reservoir for XMRV. We have also identified an inflammatory cytokine and chemokine signature that distinguishes XMRV infected CFS patients from healthy controls with 94% sensitivity and specificity. Monitoring immune dysfunction affords the opportunity to begin to understand the pathogenesis of XMRVs. In addition to these data, recent advances in developing tests for detection and characterization of variants of XMRV will be also be discussed
Miller, Andrew H; Jones, JF; Drake, Df; Tian, H; Unger, ER; Pagnoni, G	Andrew H. Miller, M.D., Department of Psychiatry and BehavioralSciences, Emory University School of Medicine, 1365-B Clifton Rd., 5th Floor, Room B5101, Atlanta, GA, 30322, USA, amill02@emory.edu	Decreased Basal Ganglia Activation in CFS Subjects is Associated With Increased Fatigue	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference.p137-138	Objectives: Altered basal ganglia function has been associated with fatigue in a number of neurologic disorders, as well as in patients exposed to chronic immune stimulation. Patients with chronic fatigue syndrome (CFS) have been shown to exhibit symptoms suggestive of decreased basal ganglia function as reflected by psychomotor slowing on neurocognitive testing, which in turn correlated with fatigue. In addition, CFS patients have been found to have increased markers of immune activation. In order to directly test the hypothesis of decreased basal ganglia function in CFS, we conducted a functional magnetic resonance (fMRI) study on a sample of CFS patients and matched controls, using a reward-processing experimental protocol. Methods: A community-derived sample of 59 male and female subjects, including 18 patients diagnosed with CFS according to 1994 CDC criteria and 41 non-fatigued healthy controls, participated in the study. All subjects were free of psychotropic medications as well as significant depressive symptoms, as determined by a Zung Depression score <60. Groups were similar in age, sex, and race. While undergoing fMRI scanning, subjects performed a monetary gambling task previously shown to strongly activate basal ganglia in the 'win versus lose' condition. To focus our analysis on the specific basal ganglia regions activated by the task, the following procedure was employed: (1) a whole-brain group analysis revealing the general activation pattern for the win-lose contrast across all subjects was performed; (2) the resultant statistical parametric brain map thresholded at $p<0.05$, corrected for multiple comparisons, was intersected with a set of basal ganglia regions of interest (ROIs: caudate nucleus, putamen, and globus pallidus), obtained from a probabilistic cytoarchitectonic brain atlas included in the SPM Anatomy Toolbox; (3) for each subject, the average value of win-lose activation contrast in each ROI was extracted for group comparisons and correlational analyses. Results: Compared to non-fatigued controls, patients with CFS exhibited significantly decreased activation in the right caudate ($p=0.01$) and right globus pallidus ($p=0.02$). Decreased activation in the right globus pallidus was significantly correlated with increased mental fatigue ($r2=0.49$, $p=0.001$), general fatigue ($r2=0.34$, $p=0.01$) and reduced activity ($r2=0.29$, $p=0.02$), as measured by the Multidimensional

				Fatigue Inventory. No such relationships were found in control subjects. Conclusions: These data suggest that reduced basal ganglia activation may contribute to symptoms of fatigue in CFS subjects. Given the central role of dopamine in basal ganglia regulation, these data also indicate that alterations in dopamine metabolism may be involved. Further understanding of potential alterations of dopamine transmission and metabolism in basal ganglia, due to activated immune pathways or other causes, may lead to new pharmacologic strategies targeting dopamine and the basal ganglia for the treatment of CFS symptoms.
Miller, Andrew H; Jones, JF; Rajendra, J; Drake, D; Miller, A; Under, ER; Tian, H; Pagnoni, G	James F. Jones, 1600 Clifton Rd, MS-A15, Atlanta GA, 30333, USA, jaj9@cdc.gov	Interaction of Self-And Illness-Related Cognitive Processing in the Right Anterior Insula of CFS Patients: An MRI study	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P136-137	Objectives: Based on the core clinical complaints of CFS patients several groups have suggested that CFS symptoms may be at least partially linked to altered cognitive or pre-cognitive processing in the central nervous system. Targeting the identification of the neural substrates of alterations of internal body signals and self-related information seems warranted. This study investigates brain responses to self- and illness-related semantic information in a sample of CFS patients compared to matched control subjects, using functional magnetic resonance imaging (fMRI). We focus on the right anterior insula (rAIC), for its purported role in interoceptive processing and awareness (Craig 2002, 2009, Nat Rev Neurosci), and on the interaction of the self-related and illness-related semantic processing. Methods: Twenty-one subjects meeting the 1994 International criteria for CFS, and 42 non-fatigued (NF) subjects performed a semantic processing task while undergoing an fMRI scan. The stimuli consisted of visually presented short sentences requiring the participants to provide a "true" or "false" answer. The semantic content was arranged according to a 2 x 2 x 2 factorial design, where the three factors were (a) Self-related: yes/no, (b) Illness-related: yes/no, and (c) Valence: negative/positive. We assessed the effect of processing Self-related versus Non self-related semantic information, across the two groups of CFS and NF subjects in a single acquisition run of functional images by examining a set of regions of interest. Results: In both CFS and NF subjects: 1) the insular response to self-related sentences tended to decrease compared to response to non- self-related sentences, in both CFS and NF subjects; 2) the insular response to non-self sentences did not differ with respect to illness-related material or not; 3) the insular response to self-related/illness-related sentences was greater than that for self-related/non illness-related only in CFS subjects. A qualitatively similar pattern was observed for the response time data. The statistical significance for the group difference in the interaction effect (3-way ANOVA: Group x Self-related x Illness-related) was p=0.0034 for the rAIC activation data and p=0.0022 for the reaction time data. Conclusions: Self is a multifaceted construct that relies in part on interoception (monitoring of internal physiology and consequences of external stimuli) via the anterior insular cortex through recognition of subjective feelings (Craig). The changes observed here in CFS subjects indicate responses to an increased mental load or to a cognitive conflict within the semantic dimensions of self and illness. This is evidence

				that (1) there is a real alteration of body physiology underlying the CFS symptoms, and the observed altered rAIC response reflects the (normal) cognitive and pre-cognitive acquisition of an abnormal physiological landscape in the body; or (2) the actual interoceptive landscape is acquired cognitively and pre-cognitively in an altered way in CFS subjects, enhancing the prominence of normal bodily signals related to fatigue.
Moldofsky, H; Patchai J	[No address quoted]	Chronic Widespread Musculoskeletal Pain, Fatigue, Depression and Disordered Sleep in Chronic Post- SARS Syndrome; A Case-Controlled Study	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P115.	The long term adverse effects of Severe Acute Respiratory Syndrome (SARS), a viral disease, are poorly understood. Methods: Sleep physiology, somatic and mood symptoms of 22 Toronto subjects, 21 of whom were healthcare workers, (19 females, 3 males, mean age 46.29 yrs.+/- 11.02) who remained unable to return to their former occupation (mean 19.8 months, range: 13 to 36 months following SARS) were compared to 7 healthy female subjects. Because of their clinical similarities to patients with fibromyalgia syndrome (FMS) these post-SARS subjects were similarly compared to 21 drug free female patients, (mean age 42.4 +/- 11.8 yrs.) who fulfilled criteria for fibromyalgia. Results: Chronic post-SARS is characterized by persistent fatigue, diffuse myalgia, weakness, depression, and non-restorative sleep with associated REM-related apneas/hypopneas, an elevated sleep EEG cyclical alternating pattern, and alpha EEG sleep anomaly. Post- SARS patients had symptoms of pre and post-sleep fatigue and post sleep sleepiness that were similar to the symptoms of patients with FMS, and similar to symptoms of patients with chronic fatigue syndrome. Both post-SARS and FMS groups had sleep instability as indicated by the high sleep EEG cyclical alternating pattern rate. The post-SARS group had a lower rating of the alpha EEG sleep anomaly as compared to the FMS patients. The post-SARS group also reported less pre-sleep and post-sleep musculoskeletal pain symptoms. Conclusions: The clinical and sleep features of chronic post-SARS form a syndrome of chronic fatigue, pain, weakness, depression and sleep disturbance, which overlaps with the clinical and sleep features of FMS and chronic fatigue syndrome. Publication: Moldofsky and Patcai: Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. BMC Neurology 2011 11:37. See: http://www.biomedcentral.com/1471-2377/11/37
Moriya,J; Yamakawa, J; Motoo, Y	Junji Moriya (Assistant Professor.), Department of General Medicine, Kanazawa Medical University, 1-1 Daigaku, Uchinada-machi,Kahoku-gun, Ishikawa 920-0293, Japan	Resveratrol Improves Hippocampal Atrophy in Mice with Chronic Fatigue	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P144-145	Abstract: Neuroimaging evidence showed structural and/or functional abnormalities existing in the central nervous system, especially the hippocampus, in chronic fatigue syndrome (CFS) patients. However, its pathophysiologic mechanisms are unclear in part due to the lack of an applicable animal model. We established a chronic fatigue murine model by six repeated injections of *Brucella abortus* antigen to mice, which was manifested as reduced daily running activity and hippocampal atrophy. Thereafter, resveratrol, a polyphenolic activator of sirtuin 1, was used for treatment in this model. Daily running activity was increased by more than 20%, and the hippocampus was enlarged after 4-week resveratrol therapy. Furthermore,

	moriya@kanazawa-med.ac.jp			resveratrol inhibited neuronal apoptosis and expression of hippocampal acetylated p53 in the fatigue mice. Resveratrol also improved neurogenesis and expression of brain-derived neurotrophic factor mRNA in the hippocamous. We concluded that repeated injection of *B. abortus* antigen could induce hypoactivity and hippocampal atrophy in mice. Resveratrol may be effective for improving fatigue symptoms and enlarging the atrophic hippocampus by repressing apoptosis and promoting neurogenesis. Objectives: Neuroimaging indicates that structural and/or functional abnormalities exist in the central nervous system, especially in the hippocampus of patients with chronic fatigue syndrome (CFS). However, the pathophysiological mechanisms of CFS are still unclear, which is partly because of the lack of a suitable animal model. Methods: In the present study, we established a mouse model of chronic fatigue by six repeated injections of *Brucella abortus* antigen into Balb/c mice. Results: Which was manifested as a significant reduction in daily spontaneous running activity, and hippocampal atrophy. Thereafter, resveratrol (RSV), a polyphenolic activator of sirtuin 1 (Sirt1) was used for the treatment of this model. The daily spontaneous running activity was increased by more than 20%, and the hippocampus was enlarged after 4 weeks RSV therapy. Furthermore, RSV inhibited neuronal apoptosis and the expression of hippocampal acetylatedp53 in the chronic fatigue mice model, which may have contributed to the upregulated deacetylation of p53 by Sirt1. In addition, RSV improved neurogenesis and expression of brain-derived neurotrophic factor mRNA in the hippocampus. In conclusion, six repeated injections of *B. abortus* antigen induced hippocampal hypoactivity and atrophy in Balb/c mice. Conclusion: It is speculated that RSV is an effective agent for improving fatigue symptoms and enlarging the atrophic hippocampus, by repressing apoptosis and promoting neurogenesis, which might be one possible mechanism for recovery from fatigue.
Murvska, M; Chapenko, S; Krumina, A; Logina, I; Rasa, S; Chistyakov, M; Sultanova, A; Viksna, L	Modra Murovska, M.D., Ph.D., Director, August Kirchenstein Institute of Microbiology and Virology, Riga, Stradins University, Ratsupites St. 5, Riga, Latvia, LV-1067, e-mail: modra@latnet.lv; Modra.Murovska@rsu.lv	*Presence of Active HHV-6, HHV-7 and Parvovirus B19* Infection/Co-Infection In Patients With Chronic Fatigue Syndrome/Myalgic Encephalomyelitis	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P140-141.	Introduction: CFS/ME is a chronic neuro-immune illness defined by combination of non-specific symptoms of uncertain cause and pathogenesis. Immunomodulating viruses (HHV-6, HHV-7, parvovirus B19) are considered as possible trigger factors for CFS/ME development. The aim of this study was to evaluate frequency of HHV-6, HHV-7 and B19 infection activation/co-activation and association with clinical findings in CFS/ME patients. Methods: 108 patients (71 females and 37 males, mean age 37 years) with clinically diagnosed CFS/ME corresponding to CDC definition criteria were enrolled in the study. Plasma/serum samples were tested for HHV-6 and B19 IgG and IgM antibodies using ELISA. Qualitative and quantitative PCRs were used for viral genomic sequences detection in PBL and cell-free plasma DNA samples. Results: HHV-6 specific IgG and IgM antibodies were detected in 81.5% and 14.8% patients, respectively, B19 specific IgG and IgM antibodies - in 73.1% and 26.9% patients, respectively. Virus specific sequences were detected in 70/108 (64.8%) patients

				plasma DNA samples, from them single virus sequence - in 41 (38.0%) DNA samples (HHV-6 - 2, HHV-7 - 28, B19 - 11) and double or triple virus sequences - in 29 (27.0%) samples (HHV-6+HHV-7 - 10, HHV-7+B19 - 15, HHV-6+HHV-7+B19 - 4). HHV-6-PBL load was higher in patients with active HHV-6 and HHV-7 co-infection then in patients with single HHV-6 infection (1007.8±367.1x103, 133.0±10.3x103, copies/µg DNA, respectively). Severe chronic fatigue for at least six months or longer was recognized in all patients independently from the causation of the active infection. Subfebrility, tender cervical or axillary lymph nodes and post-exertional malaise were not revealed in patients with single B19 infection but were detected in patients with single HHV-7 infection (50.0%, 75.0%, 100%, respectively) and HHV-6+HHV-7 co-infection (68.9%, 83.4%, 88.9%, respectively). Persistent muscle and muscular weakness were detected in all patients with manifestation more severe in patients with HHV-6, HHV- 7 and HHV-6+HHV-7 infection. Multi-joint pain also was determined in all patients with stronger symptoms in HHV- 7+B19 (82.5%) and HHV-6+HHV-7+B19 (100%) co-infection cases. Neuropsychological disturbances were detected in all patients: impaired memory – in 85.0% patients with active HHV-7 and HHV-6+HHV-7 infection, and impaired concentration – in all patients with active B19, HHV-7+B19 and HHV-6+HHV-7+B19 infection. Unrefreshing sleep was revealed in all patients with sleepiness more characteristic in patients with HHV-7, HHV 6+HHV-7 (87.5%) and HHV-6+HHV-7+B19 infection, and sleepless – in all patients with HHV-6, B19 and HHV-7+B19 infection. Headaches of new type were reported from all patients with B19 infection versus 41.7% in patients with HHV-7 and HHV- 6+HHV-7 infection. Conclusion: High rate of active HHV-6, HHV-7, B19 infection or in combination suggest that each from these immunomodulating pathogens could be trigger factor for CFS/ME development. The association between high frequency of active coinfection and distinctive types of clinical symptoms show necessity of simultaneous study of these viral infections to define possible subsets of CFS/ME.
Nacul, Luis Carlos[1]; Lacerda, Eliana Mattos[1]; Sakellariou, Dikaios[2]	[1] Nutrition and Public Health Interventions Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT [2]Department of Occupational Therapy, School of Healthcare Studies, Cardiff University, Cardiff CF14 4XN.	Is there an association between the exposure to chemicals and chronic fatigue syndrome? Review of the evidence.	Bulletin of the IACSF/ME. 17 (1). Spring 2009. P3-15	Background: Chronic fatigue syndrome or myalgic encephalomyelitis (CFS/ME) is characterised by persistent or recurrent incapacitating fatigue which can have a considerable impact on the function of the patients. A number of chemical substances have been reported to be associated with fatigue. However, it remains uncertain whether exposure to chemicals at levels usually considered safe is related to chronic fatigue. This paper provides an overview of the existing evidence of association between chemical exposures, particularly in low levels, and CFS/ME. Methods: The Pubmed and the Scopus databases were searched using combinations of relevant terms, including 'chronic fatigue', 'chronic fatigue syndrome', 'chemicals', 'toxicants' and the names of specific 'toxicants' and classes of toxicants. Standard toxicology textbooks were also reviewed. Results: The existing studies were in small number and had many limitations. Most studies were descriptive and only a handful of analytic studies were located, which seldom compared cases of CFS/ME with healthy controls.

	Correspondence:*Dr Luis C Nacul, Department of Epidemiology and Public Health, Nutrition and Public Health Research Unit (NPHIRU), London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT Email: luis.nacul@lshtm.ac.uk			None of them was prospective and they were commonly prone to selection and information biases. The results are presented under the subheadings: organophosphates and other pesticides/insecticides; carbon monoxide (CO); heavy metals; solvents, ciguatera and other chemicals; and multiple exposures, including in Gulf War troops. Conclusions: The existing evidence remains inconclusive as to the association between exposure to chemicals and chronic fatigue syndrome, and there is therefore a need for further well designed epidemiological studies.
Oldfield, Margaret	MEDes, PhD Candidate, 407-550 Ontario St., Toronto, Ontario,M4X 1X3 Canada. Email: margaret.oldfield@utoronto.ca	You're Too Sick to Work: Messages about Fibromyalgia and Paid Work in Information Materials on the Web	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P153.	Messages about fibromyalgia (FM) infuse clinician-patient relationships. Both parties bring these messages into their understandings of FM: its diagnosis, symptoms, treatments, and prognosis. This poster will describe a study that examined messages about FM in information targeted to people with fibromyalgia on the Web. It is important to understand how these messages shape the clinical relationship: First, if clinicians and their patients develop an awareness of these messages, they can examine their usefulness for each individual patient care plan. Second, understanding these messages can help foster trust in the clinical relationship, thereby promoting clinician-patient collaboration to improve treatment efficacy. This trust and collaboration can reduce the likelihood of conflicts between clinical and lay understandings of FM. Objectives: This study examined messages about doing paid work with fibromyalgia (FM) in information materials targeted to people with FM. Methods: This qualitative study used Critical Discourse Analysis to examine text in self-help, rehabilitation, and medical websites that women with FM in the Canadian province of Ontario might access in seeking information. Results: Many of the messages about FM in information materials offer little hope for feeling better and returning to work. Indeed, few information materials mention work. Materials that do mention work focus on individuals' responsibility for managing their FM in the workplace, rather than accommodation of FM-related disability by employers. Conclusion: Staying in the workforce offers women with FM many benefits, among them decent income, sense of self-worth, social relationships, daily routine, and distraction from pain. Encouragement to remain in the workplace, or to return after short-term disability leave, is needed. Workplace accommodations of FM-related disability may be required.
Pall, Martin	Washington state University	The NO/ONOO- Cycle as the Cause of CFS	Bulletin of the IACSF/ME. 16 (1). Spring 2008.	CFS and such related illnesses as fibromyalgia and multiple chemical sensitivity have been puzzling illnesses. There has not been any accepted mechanism for how cases of

	martin_pall@wsu.edu	and Related Illnesses		these illnesses get initiated, why they are chronic, how the diverse symptoms are generated, why these illnesses tend to be comorbid and, most importantly, how they should be treated. I have published a series of 16 papers in the scientific literature, developing a mechanism for these in CFS and other diseases/illnesses that provides answers to these features and many other previously puzzling features for these illnesses.
Patricia Fennell	Patricia Fennell, MSW, LCSW-R, President, Albany Health Management Associates, Inc., 582 NewLoudon Rd., Latham NY 11210, USA; communications@albanyhealthmanagement.com	Riding the CFS/ME Research Rollercoaster	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P146.	Objectives: Research advances, such as the potential association of CFS with XMRV, bring knowledge, excitement, and scientific validation to patients, families and professionals working in this field. But these developments also have the potential to cause confusion and distress, as conflicting findings emerge and new research is published that may clarify or further muddy understanding of CFS/ME and fibromyalgia. As media attention to CFS increases as a result of this research, patients gain much-needed validation of the severity of their illness, but also find themselves having to explain to family members, friends, healthcare providers, media, and concerned members of the community how this research relates to their lives, including addressing fears associated with potential contagion. At the same time, patients must continue to cope with the CFS rollercoaster itself, which brings relapses and remittances and demands flexibility in coping strategies, depending on their current health status. As the research rollercoaster rolls on, patients need strategies to cope effectively as they continue their daily lives, and healthcare professionals need tools to help their patients interpret the impact of research findings on their own lives. Methods: There are twin rollercoasters at play in CFS/ME patients' lives -- one caused by increased media and research attention and the other related to the ongoing illness and its relapsing remitting patterns. Gaining an understanding of these rollercoasters is essential in helping patients develop coping strategies for both. The Fennell Four-Phase Model of chronic illness (1. Crisis; 2. Stabilization; 3. Resolution; 4. Integration) describes a predictable passage that patients navigate on their way to defining a new self and a new life after the onset of chronic illness. Results: The FFPM helps patients gain new coping skills, enhances quality of life, generates meaning, and improves responses to community, medical, family, media, and other concerns. Conclusion: Understanding FFPM and the twin rollercoasters of CFS/ME research, as well as how they are influenced by the media, the community and health status, improves patients' ability to cope with variable patterns, and also assists clinicians in helping patients navigate complex, confusing circumstances.
Perdomo, D; Antoni, M; Czaja, SJ; Lattie, E; Sala-Guerrero, A	Dolores Perdomo, Ph.D. Department of Psychiatry and Behavioral Sciences, Center on Aging1695 N.W. 9th Avenue, Suite	*The TeleHealth Study: Memory Problems in Patients with Chronic Fatigue and Their Psychosocial Impact*	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P193-194.	Objectives: Present preliminary findings from the TeleHealth Study, a 4-year randomized trial that evaluated a technology based intervention for individuals diagnosed with Chronic Fatigue Syndrome (CFS). This presentation will focus on the prevalence of memory problems in individuals with CFS and their impact on psychosocial outcomes such as social interaction/engagement and depression. Methods: Baseline interview data was evaluated from a sample of 116 CFS

	3204L, Miami, Fl 33136, USA dperdomo@med.miami.edu			participants including 19 males and 97 females who ranged in age from 23 years to 73 years. The sample was primarily Caucasian (78.4%) and most participants had beyond a high school education (89.6%). Two independent variables were analyzed to evaluate possible cognitive deficits reported by study sample, in particular memory problems such as forgetfulness and confusion. Frequency of forgetfulness was obtained from the CDC Symptom Inventory and reported feelings of confusion bewilderment from the Profile of Mood States (POMS) confusion- bewilderment subscale. The psychosocial impact of these cognitive problems was further analyzed by examining the relationship between these cognitive problems and the participant's levels of social interaction/engagement and symptoms of depression. The Sickness Impact Profile (SIP) subscales measuring disruption in social interaction and engagement in recreation/past times, and the Center for Epidemiologic Studies Depression (CES-D) score and the POMS depression-dejection subscale were used as dependent variables in the analyses. Results: The analyses revealed that nearly 88% of the study sample (N = 102) reported having experienced forgetfulness/memory problems that caused them to substantially cut back on activities since the onset of CFS. Of those who reported experiencing forgetfulness/memory problems, 65% indicated experiencing these symptoms everyday at moderate (45.1%) to severe (33.3%) levels. A one-way ANOVA demonstrated that those participants who experienced forgetfulness/memory problems reported greater social isolation scores, $F(1,114)=11.215$, $p=0.001$, and less engagement in leisure activities, $F(1,114)=5.912$, $p=0.017$. Higher scores on the POMS confusion bewilderment subscale were also correlated with greater social isolation, $r(114)=.448$, $p<.001$ and less leisure activities, $r(114)=2.16$, $p=.020$. Greater amounts of confusion-bewilderment was also related to high levels of depression symptomatology as measured by the CES-D, $r(114)=.653$,$p<.001$ and the POMS depression-dejection scale, $r(114)=.674$,$p<.001$. Conclusion: A significant number of CFS patients report having memory problems that interfere with their daily activity and affect their mood and ability to engage in social activities. Those patients with memory problems are particularly at risk of being socially isolated and depressed. Overall these results suggest that future interventions for these patients should also focus on strategies to help remediate memory problems.
Pheby, Derek[1]; Sneddon, Peter[2]; Heinrich, Inge[3]	[1]Derek Pheby, Project Coordinator, National ME Observatory Visiting Professor, Faculty of Society and Health, Buckinghamshire New University, 106, Oxford	Severe ME/CFS in Adults – A report from the CHROME Database	Bulletin of the IACSF/ME. 17 (4). Winter 2009/2010.	Background: Case History Research on ME (CHROME) was established in 1994 to undertake research on severely affected patients. Since 1995 CHROME has collected data on volunteers with severe ME/CFS. All are medically diagnosed, conform to Fukuda criteria, are or were house-bound, and ill for at least two years. Participants complete initial and annual follow-up questionnaires, and report their condition at onset of illness, a year previously, on recruitment, and annually thereafter. Method: We report symptom severity and ability to undertake activities of daily living in 324 participants recruited between 1995 and 1998, their evolution through time, and, for

	Road, Uxbridge, Middlesex, UB8 1NA, UKTel.: e-mail : derekpheby@btinternet.com [2]Dr. Peter Sneddon, M.A., PhD. School of Health and Social Sciences, Middlesex University and CHROME Research Group 7 Wilderton Road, London, N16 5QY, UK e-mail : Peter.Sneddon@btinternet.com [3]Dr. Inge Heinrich, MSc, PhD, Medical Statistician (retired), "Thurne", Gore Road, Eastry, Sandwich, Kent, CT13 0LP, UK. e-mail : inge.heinrich@virgin.net			later onset (age 17+) subjects, changes occurring between recruitment and the latest questionnaire. Significance was assessed using the McNemar test or its binomial equivalent. Results: For most features, subjects deteriorated between onset and recruitment, with subsequent improvement, often slow and uneven, among later onset cases. Complete recovery was unusual. There were marked individual variations, and many subjects remained severely incapacitated or deteriorated. All features examined were more prevalent and severe in patients with a younger age of onset. Age at onset was bimodal, with peaks at 11-20 and 31-40. Most subjects, at recruitment, had been ill for 2-10 years. The proportion of early onset cases rose significantly in the mid-1980s. Conclusions: Caution is necessary in interpreting the results, given problems of self- selection, recall bias, and subjective interpretations of symptom ratings. It is unclear whether the reported trends are inevitable features of ME/CFS, or perhaps due to poor management at the outset.
Pinxsterhuis, Irma	Irma Pinxsterhuis, ME/CFS-Centre, Oslo University Hospital, Postboks 4956 Nydalen, 0424 Oslo, Norway. E-mail: irpi@uus.no	Illness Course in Chronic Fatigue Syndrome – What Can Be Done To Prevent Deterioration and Promote Improvement of Occupational Performance?	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P186.	Objectives: Chronic fatigue syndrome (CFS) often leads to extensive problems with occupational performance. Different disciplines disagree about what treatment strategy is best with regard to improving occupational performance. Few studies are based on the patients' opinion about this issue. This study focuses therefore on CFS patients' understanding of which factors and processes which influence their occupational performance, both before and after they were diagnosed. Methods: Semi-structured interviews were used for data collection. The sample consists of 15 women with mean age 42 years (range 31 to 58) that were diagnosed with CFS between 9 months and 17 years ago. All participants met the CDC criteria for CFS. Eight participants had been severely ill and were totally bedridden between 15 months and 7-8 years. All participants still had a mild to severe degree of CFS at the time they were interviewed, but all had improved. Results: The participants were diagnosed with CFS from 6 months to 20 years after they became ill. Symptoms changed and fluctuated over time, while they experienced an increasing intolerance

				for physical and mental activity. Lack of support and understanding, expectations and demands from themselves and others, as well as financial insecurity caused stress and over-exertion that influenced their occupational performance negatively over time. Two participants got bedridden before they got diagnosed. The CFS-diagnosis made it possible to find information about how to cope with the illness. They experienced that pacing activities, energy conservation, rest/relaxation, stress management, lower expectations to themselves, social support, changes in nutrition, financial security, as well as acceptance improved their occupational performance and reduced symptom-fluctuation over time. Some continued with over-exertion after they got diagnosed with CFS and got bedridden. While bedridden they learnt that it was important to be nursed by a few persons, according to routines they had agreed upon and with respect for their symptoms and needs. They needed above all peace of mind, and a feeling that they and their family were taken care of, so that they could use all their energy on getting better. When they started to feel better, they felt that it was important to mobilize in their own pace and not to be pushed by anyone. They improved very much in the same way as those who weren't bedridden, but had to start at a very low activity level. Their intolerance for physical and mental activity improved over time. Some improved quicker after Lightning Process, while others didn't have any effect or just a temporary effect. Conclusion: Diagnosing CFS at an early stage may prevent deterioration over time. In addition, patients need information and help in order to cope with CFS in an adequate way. Those who are able to avoid over-exertion stabilise, and improve their occupational performance over time. At the ME/CFS-centre, a multidisciplinary team applies the results of this study when they give advice to CFS-patients about how to deal with the illness at all stages of the illness course.
Pinxsterhuis, Irma; Sveen, Unni	Irma Pinxsterhuis, ME/CFS-Centre, Oslo University Hospital, Postboks, 4956 Nydalen, 0424 Oslo, Norway. E-mail: irpi@uus.no.	Chronic Fatigue Syndrome – Three Case Studies Concerning the Very Severely Ill	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P154.	Objectives: Chronic fatigue syndrome (CFS) often leads to extensive problems with occupational performance, and some get bedridden for a period of time. No studies so far have focused on the very severely ill. This study focuses therefore on CFS patients', as well as their relatives' and health care workers' understanding of how CFS patient' can be helped to prevent them from becoming bedridden and to promote improvement over time. Methods: Semi-structured interviews were used for data collection. The sample consists of three women, and from each of these women: One close relative or friend, and one health care worker, a total of 9 participants. All three patients met the CDC criteria for CFS. Anita (age 35), Sarah (age 44) and Helen (age 48) were totally bedridden from 15 months to 2.5 years. Sarah and Helen had a mild degree of CFS at the time they were interviewed, while Anita still had a severe degree of CFS. Results: Anita, Sarah and Helen had vague, fluctuating symptoms, and experienced an increasing intolerance for physical and mental activity. Over-exertion caused deterioration over time. When they got diagnosed with CFS, Helen was already bedridden. Sarah and Anita continued with over-exertion and got bedridden

				after some time. While bedridden they learned that it was important to be nursed by a few persons, according to routines they had agreed upon, and with respect for their symptoms and needs. They needed above all peace of mind and a feeling that they and their family were taken care of, so that they could use all their energy on getting better. When they started to feel better, they mobilised themselves with the support of health care workers and others, but in their own pace. They started at a very low activity level, but their intolerance for physical and mental activity improved over time. Pacing activities, energy conservation, rest/relaxation, lower expectations to themselves, stress management, social support, changes in nutrition, as well as acceptance improved their occupational performance over time. Sarah got much better after Lightning Process, while Anita just had a temporary effect. They all needed psychological help to cope with their illness-experiences. The patients' husbands, children, and close friends were affected by the illness too. Husbands and close friends got an overload of tasks, obligations and concerns, while the children were concerned about their mothers' condition and experienced that both their parents became less available. The situation deteriorated for Anita and Helen, and their families, while waiting for adequate help. Some of their children needed professional help to cope with psychological reactions. Sarah and her family got adequate help as soon as Sarah got bedridden. She stabilised and improved much quicker, and her family members did cope much better. Conclusion: Diagnosing CFS at an early stage may prevent deterioration over time. In addition, patients and their families need information and help to cope with CFS in an adequate way. Those who are able to avoid over-exertion stabilise and improve over time. At the ME/CFS-centre, a multidisciplinary team applies the results of this study to give advice to patients, their families and health care workers about how to deal with CFS at all stages of the illness course.
Porter, Nicole; Paavola, Erin; Jason, Leonard A	DePaul University	Content Analysis of ME/CFS in Medical Training Textbooks	Bulletin of the IACSF/ME. Spring 2007.	Medical textbooks serve as a cornerstone for the training of medical students and residents, as well as providing authoritative references for experienced healthcare providers (Rabow et al., 2000). Given the importance of medical textbooks in codifying best practices, several authors have engaged in textbook analyses on topics such as end of life issues (Lynn, 1997) and nurses' assessment of symptoms (Ferrell, 1999). However, no reviews have analyzed the content of medical textbook references for ME/CFS.
Rajeevan, Mangalathu; Dimulescu, Irina; Murray, Janna; Khin, Maung M; Falkenberg,	Mangalathu S. Rajeevan PhD, Chronic Viral Diseases Branch, Division of High-Consequence, Pathogens and	Pathway-focused Genetic Evolution of Immune and Inflammation Related Genes in CFS	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P132-133.	Objectives: There is evidence that immune and inflammatory alterations are important in CFS. The objective of this study was to determine if genetic variants in inflammation and immune pathways could be linked to CFS as well as to quantitative measures of functional impairment, fatigue and symptom inventory. Methods: Participants were identified from a population-based study. This analysis included 362 Caucasian subjects: 121 non-fatigued (NF); 50 CFS with no medical/psychiatric

Virginia; Unger, Elizabeth R	Pathology, NCEZID, Centers for Disease Control and Prevention, 1600 Clifton Road, MS G-41,Atlanta, GA 30333, USA mor4@cdc.gov			exclusions (CFS); 129 fatigued but insufficient symptoms or fatigue for CFS (ISF) with no medical or psychiatric conditions; and 62 CFS except for medical/psychiatric exclusions (CFS-exclusions). We used a pathway-focused genetic analysis of immune and inflammation related genes with the Affymetrix Immune and Inflammation Chip that covers 11K single nucleotide polymorphisms (SNP) in 1000 genes representing 38 sub-pathways in immune response and inflammation. The manufacturer's protocol was followed for genotyping and accuracy was validated by pyrosequencing. Golden Helix SVS software was used for genetic analysis. SNP functional annotation was done using SPOT and GenomePipe programs. Results: Compared to NF controls, CFS was associated with 34 functionally relevant SNPs (p=2.68 x10-2 – 1.31 x10-5). Twelve of these SNPs are in genes playing a role in pathways related to complement cascade (*SERPINA5*, *CFB*, *CFH*, *MASP1* and *C6*), chemokines (*CXCL16*, *CCR4*, *CCL27*), cytokines/cytokine signaling (*IL18*, *IL17B*, *IL2RB*), and Toll-like receptor signaling (*TIRAP*, *IRAK4*). While 11 out of 34 SNPs remained associated with ISF compared to NF, only 4 of the 34 SNPs remained associated with CFS-exclusions. A polymorphism (rs11214105) in the 5'upstream regulatory region of *IL18* was associated with both CFS and ISF (CFS, p=1.52 x 10-2; ISF, p=2.03 x 10-2). In CFS, this SNP associated with MFI subscale of physical fatigue (p=7.1 x10-3), SF-36 subscale of body pain (p=9.7 x10-3) and summary score for CFS case defining symptoms (2.6 x 10-5). With all these associations, the minor allele increased the risk of the associated phenotype. Similarly, the minor allele of rs7616342 in *KCNH8,* representing the p38/MAPK signaling pathway, increased the risk for CFS (p=1.31 x 10-5), and was also associated with MFI mental fatigue subscale (p=9.0 x 10-3). Conclusion: This study identified a number of novel and functionally relevant genetic variants in complement cascade, chemokine and cytokine signaling pathways associated with CFS. Differences in these associations found for subjects with exclusionary conditions otherwise meeting criteria for CFS (CFS-exclusions) suggests important differences between these groups. Further replication and functional studies are needed to support the results of this study.
Roelant, C; De Meirleir, K	Chris Roelant, Ph.D., CEO Protea Biopharma N.V., De Tyraslaan 111, 1120 Neder-Over-Heembeek, Belgium. croelant@proteabiopharma.com	Easy Monitoring of the Th1/Th2 Balance Status in Health and Disease with Special Emphasis on CFS/ME	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P175.	Objective: It is generally agreed that CFS/ME is a Th2 shifted condition. However, simple self-tests allowing physicians and CFS/ME patients to follow-up on Th1/Th2 balance during therapy are lacking and therefore it still remains very difficult for an individual to evaluate whether the treatment he or she is undergoing is really effective. In addition, the effectiveness of over the counter sold products claiming to balance Th1/Th2 status such as antioxidants, pro-biotics and other should be evaluable on a personal basis. A lot of CFS/ME patients are trying to improve their condition by exploring so-called neutraceuticals by "trial and error" without realizing the potential risk of further deterioration of their health by randomly taking products that may even further disturb their Th1/Th2 balance. Therefore we developed a simple "self-test" principle allowing patients to determine their Th1/Th2 profile over

				short periods of time and to follow-up on the effect of therapy and intake of drugs and neutraceuticals or any other strategy to balance Th1/Th2 status. Methods: By analyzing a massive number of first morning urine samples obtained from patients facing conditions associated with an overactive Th2 arm (ulcerative colitis, autism, blastocystis, mercury poisoning, viral infection) we came across a reaction principle that uses a colorimetric substrate changing color upon reaction with metabolites contained in the urine samples from yellow (neutral) over light green and brown (moderate Th2) to deep purple and black (strongly Th2 shifted). The development of the color is time-dependent and quantitative. Results: More than 80% of urine samples obtained from CFS/ME patients produced a time-dependent quantitative change in color compared to 4% of the controls (perfectly healthy population). Conclusion: The urine test principle we've developed offers an easy way to determine and to follow-up on Th1/Th2 balance in health and disease and more in particular at the same time provides further evidence that CFS/ME is a condition merely associated with an overactive Th2 arm.
Roelant, C; De Meirleir, K	Chris Roelant, Ph.D., CEO Protea Biopharma N.V., De Tyraslaan 111, 1120 Neder-Over-Heembeek, Belgium. croelant@proteabiopharma.com	Role of Cellular Prion Proteins (PrPc) in CFS/ME and other Chronic Diseases	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P176.	Objective: Cellular prion proteins (PrPc) are small glycoproteins attached to the outer leaflet of the plasmamembrane of mammalian cells by a glycosylphosphatidyl anchor. The isoform of the prion protein is expressed in hematopoietic stem cells, neuronal cells, T and B lymphocytes, natural killer cells, muscle, intestinal tract, spleen, adrenal glands, endothelial cells, platelets. PrPc binds copper, plays a role in calcium uptake, protects cells against oxidative stress, prevents cells from apoptosis, interacts with viruses (binds gp-120), is involved in neuroprotection and plays an important role in immune and angiogenic responses. Therefore we estimated that hallmarks of CFS/ME such as oxidative stress, calcium channelopathy, T-cell dysfunction, copper uptake changes, altered red blood cells and oxygen transport, coagulation and hormonal responses (HPA-axis) as well as viral entry could be attributed to aberrant PrPc function which could than ultimately explain the "multi-system" character of the CFS/ME disorder. In order to investigate PrPc function in CFS/ME, we first needed to develop a test allowing to measure "activity" of PrPc in "real time". Methods: We have developed a cell-based chemiluminometric (CL) assay accordingly to the following principle: cells or tissue under study are incubated in an appropriate buffer in the presence of a chemiluminometric probe (CLP). Next a PrPc redox-trigger is added that stimulates PrPc-mediated reactive oxygen species (ROS) production which is proportional to the active state of the PrPc and which ROS react with CLP to produce a basal glow of light (Lb) that can be detected in front of a photomultiplier. Next, to an identical sample and CLP an additional trigger is added that stimulates cells to produce ROS at maximum capacity, producing maximum glow type chemiluminescence (Lmax). Lmax/Lb defines a PrPc functional stimulation index (SI) that can be compared for different tissues and cells obtained from controls and patient populations. Results: Peripheral blood mononuclear cells (PBMC's) obtained

				from CFS/ME patients show aberrant SI's (extremely low SI<3 or extremely high SI>20 compared to controls (SI=10 +/- 3). In addition we could demonstrate the influence of heparin, minocyclin, metals (copper, mercury) and other agents on PrPc function by means of this luminometric technique Conclusion: PrPc functionality of PBMC's is altered in CFS/ME. Chemiluminometric analysis provides a useful tool to further develop and explore PrPc functional tests and PrPc drug interaction platforms (drug discovery) in CFS/ME and other chronic diseases (fibromyalgia, rheumatoid arthritis, autism, cancer).
Roesner, Nicole; Porter, Nicole; Holiday, Patrick; Delucca, Gina; Robinson, Ashley; Walano, Nicolette; Natanek, Ian; Clautier, Catherine; Jason, Leonard A	DePaul University, Center for Community Research, Email-nroesner@depaul.edu	An Alternative Way to Help People with ME/CFS	Bulletin of the IACSF/ME. 16 (4). Winter 2008/2009. P12-21.	In 1996, a Buddy program began at DePaul University. Participants with ME/CFS were provided a Buddy, who was a volunteer DePaul University student. Over the years, we have found that both participants and Buddies have been able to gain from their participation. This report provides information about this Buddy program as well as qualitative data from both participants and the Buddies.
Rowe, Katherine; Moon, Judith	Royal Children's Hospital, Melbourne, Australia	What is the Natural History of Chronic Fatigue Syndrome in Young People?	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P129.	Objectives: To follow up consecutive patients referred to the CFS clinic at the Royal Children's Hospital between 1991 and 2009 regarding their level of functioning, self-reported perception of recovery, duration of illness and the usefulness of management strategies. Methods: Seven hundred and eighty eight young people age 6-18 years (mean 15 years) (M:F 1:3), were referred from family doctors or consultant pediatricians for diagnosis and management or secondary consultation. Diagnosis required a defined onset over hours or days of persistent or relapsing, debilitating fatigue, which was exacerbated with exercise and did not resolve with bed rest, duration of illness greater than 6 months, and fulfilling the criteria of Holmes et al (1988) and Fukuda et al., (1994). Standardised historical, symptom and psychological data were obtained from 398 and standardised history only, from an additional 390. 398 were followed up prospectively with questionnaires approximately each 2 years, while the second group were contacted by phone during 2010 and 2011, and a questionnaire sent if consent was obtained. The follow up questionnaire recorded functional outcomes, demographics, duration of illness, use of alternative health practitioners and reported usefulness of management strategies. Results: Questionnaire follow up data were obtained on at least one occasion for 342 of the 398 (86%). Six occasions between 1996 and 2008 provided 804 returns allowing more accurate timing of reported recovery with multiple data points. 78% of the additional 390 were able to be traced and provided information. The follow up for both groups ranged from 1.7 years to 21 years. The average duration of illness was reported as 5 years with range 1-15 years. By 5 years 60% reported recovery. By 12 years, 88%

				reported recovery (n=256), although in approximately 1/3 there was an indication that they were conscious of monitoring their workload. Less than 5% were not either studying or working part or full time, often due to other factors than CFS. Many had married (n=38) and those with children (n=15) reported being well. 90% completed or intended to complete post-secondary training. The only alternative practitioners that were deemed helpful were those that provided some relief for muscle pain with massage, or who provided good dietary advice. Restrictive diets and supplements did not reach placebo levels of response. Symptom management and the strategy of balancing social contact, physical activity, educational input and a commitment to regularly attend at least one activity each week as the most useful assistance. Every young person devised a different balance of activities and program depending on severity of illness, stage of education, family circumstances and life interests. Engagement in education was best predictor of functional outcome. Conclusion: The outcomes for young people in Australia are generally positive although prolonged. Ongoing support particularly in navigating the education system was highlighted by them as an essential contributor to the quality of their life and their ability to cope.
Royle, Genevieve H; Pimm, John T	*Requests for reprints should be addressed to Dr Genevieve H Royle, Durdans, Elm Green Lane, Danbury, Essex, CM3 4DR, UK., [1]Oxford Doctoral Course in Clinical Psychology, Oxford, UK, Address: 5 Belmont Terrace, Remuera, Auckland 1050, New Zealand Email: genaikman@hotmail.com [2]Community Neurological Rehabilitation Services, Buckinghamshire Primary Care Trust, Aylesbury, UK, Address: Rayners Hedge, Croft Road, Aylesbury, Bucks, HP21 7RD, United Kingdom	A Pilot Study of the Process of Change in a Group Chronic Fatigue Syndrome Management Programme	Bulletin of the IACSF/ME. 17 (2). Summer 2009.	Background: Cognitive-behavioural therapy and graded exercise therapy are efficacious therapies in patients with Chronic Fatigue Syndrome (CFS). There is some evidence for the efficacy of group programmes that employ the same principles of rehabilitation. Little is known about the process of change with these interventions, however it is important to understand why change occurs in order to improve outcomes. Objectives: To investigate the process of change and related outcomes in participants in a CFS group management programme. Method: Task analysis was used to generate a health professionals' model specifying the psychological shifts thought necessary for participants to improve. Following this, data from participant interviews were analysed to see whether they matched the shifts specified in the model. Results: Participants were able to identify 'key moments' which they thought were involved in change. One commonly cited key moment involved participants coming to the realization that they were not unique in their difficulties and there were others in the group who understood, and had experienced similar problems. Four of the six shifts identified by health professionals were also identified as key moments by participants. Conclusions: This study highlights the potential benefits of group work for people with CFS/ME including opportunities for validation from peers, sharing and modelling, all of which are suggested to be important in the process of change. See also: Kindlon, T. Letter to Editor **Re:** A pilot study of the process of change in a group Chronic Fatigue Syndrome management programme**.** Bulletin of the IACSF/ME. 17 (3). Fall 2009.

	John.Pimm@buckspct.nhs.uk			
Royle, Genevieve; Pimm, John	[No address quoted]	Response to letter from Tom Kindlon. Re: A pilot study of the process of change in a group Chronic Fatigue Syndrome management programme. Bulletin of the IACFS/ME. 2009;17(2):53-68	Bulletin of the IACSF/ME. 17 (3). Fall 2009.	One of the aims of our study was to investigate whether a number of interventions (i.e. CBT & GET), shown to be effective when delivered in an individualized format, could also be effectively delivered in a group format. We know from the literature (referenced in our original article) that patients report particular benefits from group-based therapies and it would therefore seem logical to investigate whether any of these benefits could be used to increase the efficacy of interventions for CFS/ME. While Kindlon rightly points out that the current NICE guidelines recommend individual treatment only, this is due to the fact that NICE guidelines are based on the literature as it stands at the time and as yet there is only emerging evidence for group treatments for CFS/ME. The group-based studies referenced in our original article do indicate some benefits for group-based interventions (1, 2), however there is no doubt that there is clearly a need for more research in this area. Our study sought to contribute to this.
Rusu, C; Bancej, C; Roberts, KC	Corneliu Rusu, Analyst, Chronic Disease Surveillance and Monitoring Division, Centre for Chronic Disease Preventionand Control, Public Health Agency of Canada, 785 Carling Avenue, Ottawa, Ontario, K1A 0K9, Canada, corneliu.rusu@phac-aspc.gc.ca	The Epidemiology of Self-Reported Chronic Fatigue Syndrome in Canada	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P188-189.	Objective To determine for the first time the prevalence of Chronic Fatigue Syndrome (CFS) in the household population of Canadians 12 years of age and over, and to explore its relationship with various key determinants of health. Methods Data were obtained from the Canadian Community Health Survey, Cycle 3.1 (2005). Weighted prevalence rates (PRs) for CFS in the Canadian population and specific sub-groups based on various key determinants of health were calculated. The 95% confidence intervals (CIs) around PRs were calculated using exact standard errors generated through bootstrap re-sampling techniques. Results In 2005, 331525 Canadians reported having CFS (PR 1.22%, 95%CI: 1.13-1.31), with a female-to-male PR ratio of roughly two to one. The prevalence of CFS among women peaked in the 45-64 age group and fell thereafter, whereas the increase among men was monotonic across all ages. Women in the 45-64 age group accounted for more than a third of all reported cases of CFS. Sub-group analyses based on various key determinants of health showed that people who reported lower income, altered employment status or living in food-insecure households were more likely to report having CFS. A greater PR of CFS was found among people who reported being inactive, dealing with activity limitations, needing help with daily tasks, having difficulty with social situations as well as among those facing discrimination or unfair treatment due to their health condition. Finally, heavy users of health care services as well as those with unmet health care or home care needs showed increased PRs of self-reported CFS. Conclusions To our knowledge, this is the first study examining the prevalence of CFS in the household Canadian population and among various sub-groups based on key determinants of health. The PR of self-reported CFS was several-fold higher than the national PR among sub-groups with poorer measures on a variety of health determinants, including

				determinants of unmet health needs and access to care. Further investigations are required to decipher the true nature of these associations, in order to develop effective preventive and/or disease management measures.
Ryll,ED	**Erich D. Ryll, M.D. 383l San Juan Avenue, Carmichael, CA 95608, Email:** Eryll@sbcglobal.net	A 30-year Historic Review of a Community Hospital Epidemic Outbreak	IACSF/ME. 19 (1). Summer 2011.	A 1975 outbreak, characterized by severe venous involvement, affected nurses and staff of a California community hospital spreading to other health care workers and unrelated persons. Spread from epidemic to quintary cases was noted. The purpose of this report is to delineate the hallmark symptoms of the outbreak and determine the functional state of affected patients 30 years later. Methods Sixty-one hospital epidemic cases were reviewed, and 30-year follow-up assessed by questionnaire, interview, and physical examination. Results Painful veins; flu-like symptoms; and severe generalized pain, exhaustion, weakness, cognitive disturbances, and nervous system abnormalities marked the outbreak. In 2006, 30 patients were available for follow-up, 14 were deceased, and 17 were lost to follow-up. Of the living, 29 never became well citing generalized pain; energy absence; confusion, memory loss, other neurologic problems; and leg discomfort. Only eight were able to return to work, five of who functioned with difficulty. Of those deceased, 11 never worked after onset. Conclusions A severe viral-like epidemic, apparently communicable and carried latently with pronounced venous inflammation resulted in permanent disability in 75% of those surveyed 30 years later.
Sampson, D	[No address quoted]	Letter to Editor: Response to Professor White's comments	IACSF/ME. 18 (4). Winter 2011.	Firstly I welcome Prof. White's acknowledgement that broad based definitions of ME/CFS that include co-morbid mood disorder/psychiatric illness are predicted by different factors than those that do not, and that subjects with purely psychiatric disorders were included in broad based definitions of ME/CFS such as the Oxford criteria. However he seems not to have grasped the main focus of my paper—the inclusion of patients with psychiatric reasons for their fatigue alongside those with bona fide ME/CFS. It is patently clear from my analysis of his own data and the risk factors that accompany these two groups of patients that they are completely different illnesses/conditions. This is at best tautology and at worst very poor science. Not only in the study he refers to showing Graded Exercise as an effective treatment for CFS/ME (which ostensibly excluded patients with co-morbid mood disorder) were 30% of the participants receiving normal dose antidepressant therapy or low dose tricyclic antidepressant hypnotic medication but furthermore those with appreciable sleep disturbance (one of the hallmarks of CFS/ME) were excluded. As nearly 90% of even CDC defined CFS sufferers report profound sleep disturbance) this was clearly not a study of ME/CFS but of psychogenic fatigue with no physical basis. Finally he refers to the PACE trial, the largest ever trial of Graded Exercise of which he is Principal Investigator—the results of which have not yet been announced. It is of interest that the ME/CFS criteria selected for use in this study are the Oxford Criteria, which preferentially select patients with psychiatric reasons for their fatigue as his own data clearly demonstrate. No other researchers examining ME/CFS in the world

				currently utilize such broad criteria as they clearly fail to exclude patients with primary psychiatric diagnosis in the absence of physical symptoms.
Sampson, D	[No address quoted]	Letter to Editor: Comment on the Results of the PACE trial	IACSF/ME. 18 (4). Winter 2011.	The results of the PACE trial in terms of treatment efficacy for both Cognitive Behavioural Therapy (CBT) and Graded Exercise Therapy (GET) are extremely modest to say the least and certainly not by any stretch of the imagination remotely curative—a decrease in fatigue score (range 0-33) at 52 weeks of 3.4 and 3.2 points respectively, and an increase in physical function score (range 0-100) of 7.1 and 9.4 points for each treatment respectively, compared with standard medical care. (1) This despite the adoption of the Oxford criteria, which are so broad that they clearly fail to exclude patients with primary psychiatric diagnosis in the absence of physical symptoms. (2) Conversely the results of a another large scale evaluation of the efficacy of both CBT and GET conducted in Spain and published earlier this year demonstrated that after 12 months, intervention with CBT and GET not only failed to improve health-related quality of life HRQL scores but led to worse SF-36 physical function and bodily pain scores in the group receiving these treatments compared with standard medical care alone. (3) It is of interest that two such similar studies both utilising comparable timescales, interventions and measures of outcome should produce such discrepant and diametrically opposed results. Even if we take the results of the PACE trial at face value, of the 3158 patients presenting with fatigue at specialist Chronic Fatigue Syndrome clinics for potential inclusion in the PACE trial, only 641 were eventually selected for inclusion in the study. This means that 4 out of every 5 potential participants were excluded. This is remarkable—given the obvious delay between primary outpatient appointment and specialist hospital CFS clinic attendance most if not all would naturally meet Oxford criteria in the absence of major psychosis, organic brain disease and substance abuse. How only 1 in 5 of these were eventually selected for inclusion in the study and the exact criteria for such exclusion leading to such an unusual/unrepresentative ME/CFS sample are questions that must warrant further investigation.
Sampson, DP	9 Cherry Tree Road, London N2 9QL Email: davidsamps@aol.com	Close Analysis of a Large Published Cohort Trial into Fatigue Syndromes and Mood Disorders That Occur After Documented Viral Infection	IACSF/ME. 18 (2). Summer 2010.	This paper presents a close analysis of a large published cohort trial into predictors (risk factors) for developing a fatigue syndrome or mood disorder following either infectious mononucleosis or an upper respiratory tract infection - White et al (16). Critically, in addition to utilising broad based definitions of ME/CFS, such as the Oxford and CDC CFS criteria, White et al also utilise a further definition, Empirical Fatigue Syndrome, which excludes current psychiatric illness. This provides important additional insights into the results, leading to conclusions which are materially different to those that the author draws, in relation to the inherent validity of broad based definitions of CFS and in relation to the significance of deconditioning as a perpetuating factor in this illness. Examination of the data shows that the highest risk factor for developing a non-psychiatrically defined Fatigue Syndrome (i.e. Empirical

				Fatigue Syndrome), even 6 months later, is documented clinical evidence of viral infection (infectious mononucleosis) not previous psychiatric morbidity. Furthermore under the Empirical definition, no significant correlation exists between bed rest at onset and subsequent development of a fatigue syndrome; this suggests that deconditioning is not an important perpetuating factor under this definition. Conversely, wider definitions of ME/CFS that do not exclude individuals with psychological/psychiatric reasons for their fatigue (such as the Oxford and CDC criteria) reduce the importance of clinical factors (infectious mononucleosis) and increase the importance of factors such as G.P. attendance in year before onset, mood disorder at 2 months and past psychiatric illness, which are consistent predictors of subsequent mood disorder quite independently of the existence or otherwise of a fatigue syndrome. This analysis and the original data in the White et al. paper strongly calls into question the validity of broad based definitions of ME/CFS, such as the Oxford (and to lesser extent CDC) criteria. This is in large part due to the clear inclusion within such criteria of significant numbers of patients with primarily mood disorder/psychiatric illness in addition to those with ME/CFS. See also: White,P. Reply to Sampson. IACSF/ME. 18 (3). Fall 2010.
Scott, A; Norton, M; Mabillard, H; Newton, JL	Professor Julia L Newton, Institute for Ageing and Health Medical School, Framlington Place, Newcastle-upon-Tyne, NE2 4HH, Email: julia.newton@ncl.ac.uk	Brief Report: Shortened QTc interval in chronic fatigue syndrome	IACSF/ME. 19 (3/4). Summer 2012.	Abstract Chronic fatigue syndrome (CFS) is a common, debilitating disease that is frequently associated with autonomic dysfunction. One previous study of a selected population using a manual measurement technique suggested CFS is associated with a shortened QTc interval. Here we assessed QTc in a large UK population of CFS patients using automated, clinically applicable, measurement techniques and confirmed that QTc is significantly shortened in CFS patients compared to non-CFS fatigued and control populations. Automated measurement of QTc in clinical practise has potential utility as a diagnostic biomarker in CFS.
Shoemaker, RC	Center for Research on Biotoxin Associated Illnesses Pocomoke, Md	Vasoactive Intestinal Polypeptide (VIP) Lowers C4a and TGF beta-1, Corrects Refractory Symptoms and Normalizes Abnormal Biomarkers in Patients with CFS	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P144.	Background: CFS patients invariably have low levels of vasoactive intestinal polypeptide (VIP). In two case series of patients meeting the case definition for adult CFS (N=1682), deficiency of VIP occurred in 98% of patients. Less than 10% of controls were VIP deficient. VIP raises cAMP; lowers pulmonary artery (PASP) responses to exercise, blocks peripheral innate immune activation; reduces apoptosis of glial cells undergoing oxidative stress; raises VEGF; restores circadian rhythm; regulates response to olfactory stimuli in the suprachiasmatic nucleus; regulates dendritic cells; regulates Th17 function in autoimmunity; enhances IL-10 production; and modulates innate immunity. In a pilot study in 2010, use of VIP was shown to be safe in human volunteers, providing (1) marked reduction in symptoms and (2) blunted accentuated pulmonary artery response to exercise. We studied the clinical responses in 100 consecutive CFS patients with refractory illness to intranasally administered VIP. Methods: After informed consent, patients with symptoms meeting the Fukuda definition of CFS were treated with 50 mcg of VIP given four times a day via nasal aerosol for two months. There were no dropouts in the study. Pre- and post- VIP

				measures included symptoms; visual contrast sensitivity (VCS); levels of VIP, VEGF, MSH, C4a, TGF beta-1, MMP9, testosterone, estradiol, lipase, vitamin D 25-OH, CBC and CMP. Exclusion criteria included three indicators known to be associated with reduced benefit (1) depressed visual contrast sensitivity; (2) ERMI > 2; (3) presence of multiply antibiotic resistant biofilm-forming coagulase negative staphylococci in deep nasal aerobic spaces. Results: Patients tolerated the drug well. Symptom reduction occurred in all patients with normalization of mean VEGF, MMP9, C4a and TGF beta-1. Testosterone rose and estradiol fell in males with no changes in females. No adverse effects on CBC and CMP were noted. Abnormal vitamin D 25-OH normalized. One person developed an elevated level of lipase without abdominal pain. Discussion: Treatment with VIP provided restored clinical functioning in a cohort of patients with severe CFS illness. As a regulatory neuropeptide, VIP has multiple salutary effects on human physiology. Replenishment of deficiency states returns quality of life and stabilizes inflammatory responses. Conclusions: Evaluation of clinical use of VIP will require additional clinical trials but early results show safety and marked benefit in severely affected CFS patients.
Shoemaker, Ritchie C	Center for Research on Biotoxin Associated Illnesses; Pocomoke, Md	T Regulatory Cell Abnormalities in CFS: Another Varying Biomarker is Unveiled That Adds to Understanding of Pathophysiology, Diagnosis and Treatment	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P168-169.	Background: Deficiency of T regulatory (Treg) cells is now recognized in a number of chronic fatiguing illnesses including Post- Lyme, “mold illness” (chronic inflammatory response syndrome from water-damaged buildings, CIRS-WDB), chronic lymphocytic lymphoma and multiple sclerosis (MS) among many others. Correction of Treg deficiency is associated with clinical benefit. Data from this clinic and others internationally have shown that CFS is marked by absence of neuropeptide (MSH and VIP) control of innate immune inflammatory mediators, especially C4a, MMP9 and TGF beta-1. Successful treatment of affected patients requires correction of these abnormalities, but even with that successful treatment, we noted a subset of patients that remained persistently affected. Because of the known effects of high TGF beta-1 on populations of CD4+CD25+ T reg cells, and in an effort to establish the role of abnormal Treg in CFS, levels in CFS patients were stratified by clinical condition. Methods: 150 patients in a single practice were identified as controls, untreated cases, treated cases, VIP-treated cases and relapses. CD4+CD25+ levels were measured by flow cytometry by Quest Diagnostics. Patients with symptoms not responsive to standard interventions of reduction of inflammatory markers (N=43) were treated with 50 mcg VIP administered by nasal aerosol QID. Results: CD4+CD25+ levels in controls were 16.8; untreated cases 6.2; treated cases 17.1; vasoactive intestinal polypeptide (VIP)-treated cases 22.6 and relapses 5.3. Those with the lowest CD4+CD25+ levels were the most symptomatic. Treatment of low CD4+CD25+ with VIP by nasal aerosol led to symptom reduction with rising levels of CD4+CD25+. Use of VIP without correction of underlying innate immune abnormalities did not show significant benefit. In 12 patients, prospective exposure of CFS patients with MSH < 35 pg/ml to WDB with an Environmental Relative Mold Index (ERMI) of > 2 was

				associated with relapse of symptoms and fall in CD4+CD25+. Discussion: Rising levels of TGF beta-1 induces production of CD4+CD25+ regulatory T cells. In inflamed tissue, CD4+CD25+ cells are reported to be altered in situ creating pathogenic T cells which in turn release additional TGF beta-1. Correction of (1) deficiency of CD4+CD25+ cells; and (2) elevated TGF beta-1 result in clinical benefit. Preexisting CFS is a risk factor for relapse of illness and reduction of Tregs after exposure to WDB. Conclusions: Cellular immunity plays an important role in CFS. Reduced levels of Treg cells can be corrected by treatment of inflammatory mediators, with persistent illness responding to use of replacement VIP. CFS patients are at risk for acquisition of additional inflammatory and cellular immune injuries due to exposure to WDB.
Shoemaker, Ritchie C; Maizel, Margaret S	Center for Research on Biotoxin Associated Illnesses, 500 Market St, Suite 102, Pocomoke, D, 21851 Corresponding author: RC Shoemaker MD, ritchieshoemaker@msn.com.	Exposure to Interior Environments of Water-Damaged Buildings Causes a CFS-like Illness in Pediatric Patients: a Case/Control Study	Bulletin of the IACSF/ME. 17 (2). Summer 2009.	The case definition for pediatric chronic fatigue syndrome (CFS) is symptom based, with a defined set of exclusions for confounding illnesses. These exclusions form a differential diagnosis of chronic fatiguing illnesses; the list of exclusions will grow as potential confounders are newly confirmed. Patients sickened by exposure to water-damaged buildings (WDB) have a multi-system, multisymptom illness, but only recently has fatigue become commonly accepted in WDB literature as a common symptom. Published data on symptoms in patients with WDB illness show fatigue is present in over 90% of adult patients. Physiologic disturbances in these patients are densely present and contribute to form a case definition for WDB illness in adults that demonstrates that each patient has a chronic, systemic inflammatory response syndrome (CIRS), with abnormalities in regulatory neuropeptides; markers of pro-inflammatory cytokine response; genetic association shown by HLA DR; TGF beta-1; autoimmunity; and split products of complement activation. We reviewed our pediatric cases of WDB illness comparing cases to a roster of controls, a group of well patients seen in the practice for well-child or well-adolescent care. Each case, but no controls, met the current pediatric case definition of CFS; each case, but no controls, had CIRS. We propose that (1) the pediatric case definition of CFS be modified to specifically exclude patients with exposure to WDB that lasts more than 30 days (2) environmental exposure to WDB be included in a pediatric CFS history (3) laboratory testing in all potential pediatric CFS patients include assessment of CIRS (4) pediatric patients currently diagnosed with CFS be reviewed to exclude WDB illness as shown by exposure and CIRS markers.
Shor, S	Samuel Shor, MD, FACP, Associate Clinical Professor, George Washington University Health Care Sciences, Internal Medicine of Northern Virginia, 1860	Retrospective Analysis of a Cohort of Internationally Case Defined Chronic Fatigue Syndrome Patients in a Lyme Endemic Area	IACSF/ME. 18 (4). Winter 2011.	**Background** Chronic fatigue syndrome is a diagnosis of exclusion for which there are no markers. Lyme disease is the most common vector borne illness in the United States for which chronic fatigue is a frequent clinical manifestation. Intervention of patients with Lyme disease with appropriately directed antimicrobials has been associated with improved outcomes. **Methods** An arbitrary date was chosen such that all patients registered in the database of the practice of the PI, which is located in the Lyme endemic area of Northern Virginia area were reviewed. The diagnosis of

	Town Center Drive #230, Reston, Virginia 20190 E mail - samshormd@gmail.com			clinically significant fatigue > 6 months was chosen. Inclusion criteria required fulfilling the International Case Definition for CFS. **Results** Of the total 210 included in the analysis, 209 or 99% were felt to represent a high likelihood of "seronegative Lyme disease." Initiating various antimicrobial regimen, involved at least a 50% improvement in clinical status in 130 or 62%. Although not achieving the 50% threshold according to the criteria discussed, another 55 patients subjectively identified a beneficial clinical response to antimicrobials, representing a total of 188 or 88% of the total identified as having a high potential for seronegative Lyme disease. **Conclusions** A potentially substantial proportion of patients with what would otherwise be consistent with internationally case defined CFS in a Lyme endemic environment actually have a perpetuation of their symptoms driven by a persistent infection by Borrelia burgdorferi. By treating this cohort with appropriately directed antimicrobials, we have the ability to improve outcomes.
Shor, Samuel	Associate Clinical Professor, George Washington University, Health Care Sciences	Retrospective Analysis of a Cohort of Internationally Case Defined Chronic Fatigue Syndrome Patients in a Lyme Endemic Erea	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P159-164.	Goals: a. To determine the prevalence of seronegative Lyme in a CFS clinic in a Lyme endemic region, that actually represented persistent borrelial infection. b. To determine if antimicrobial intervention as an integral part of treatment was able to assist in the delineation of this potential cohort. Chronic Fatigue Syndrome represents a symptom complex often including in addition to clinically significant fatigue, the co-morbidities of fractured nonrestorative sleep, endocrinopathies [such as decreased cortisol production], autonomic dysfunction [such as neurally mediated hypotension and postural orthostatic tachycardia] [8]. It is the interpretation of the author that this "CFS like complex" represents a valid model for the management of many patients with chronic persistent Lyme infection [9]. The adverse societal impact of CFS was reported by Reynolds et al in 2004. Estimates were of a 37% decline in household productivity and a 54% reduction in labor force productivity among people with CFS. The annual total value of lost productivity in the United States was $9.1 billion which represents about $20,000 per person with CFS or approximately one-half of the household and labor force productivity of the average person with this syndrome [2]. The following data would suggest that we have the capacity to better characterize a substantial number of "CFS" patients as having "seronegative" persistent Lyme infection for which adjustments in intervention are shown to improve outcomes. Thus, we are attempting to provide evidence to the etiology of Chronic Fatigue Syndrome, while also providing input as to the clinical manifestation of persistent Lyme infection. The management of Lyme disease regarding diagnosis and treatment unfortunately is wrought with controversy. There is one evidence based school of thought that Lyme disease is easily diagnosed and easily treated [10-11]. This set of guidelines has had questions raised as to the quality of the evidence with which the recommendations have been generated: "…The IDSA guideline recommendations are primarily based on low-quality evidence derived from nonrandomized studies or expert opinion. These findings highlight the limitations of current clinical infectious

				diseases research that can provide high-quality evidence…"[12-14]. There is an alternative, evidence based position that suggests that the diagnosis of Lyme disease is associated with insensitivities and that the management of those identified with this condition regularly have protracted, and relapsing courses often requiring prolonged antimicrobial therapy [15].
Simmons,G; Coffin,JM[2]; Hewlett,IK[3]; Lo,S-C[4];Mikovits, JA[5]; Switzer,WH[6]; Linnen,JM[7]; Ruscetti, F[8]; Glynn,SA[9]; Busch, MP[1]	1 Blood Systems Research Institute and Department of Laboratory Medicine, University of California, San Francisco, San Francisco, CA 94118, USA 2 National Cancer Institute and Department of Molecular Biology & Microbiology and Program in Genetics, Tufts University, Boston, MA 02111, USA. 3 Office of Blood Research and Review, FDA, Bethesda, MD 20892, USA 4 Division of Cellular and Gene Therapies and Division of Human Tissues, FDA, Bethesda, MD 20892, USA 5 Whittemore Peterson Institute and University of Nevada, Reno, NV 89557, USA Bulletin of the IACFS/ME 113 6 Division of HIV/AIDS Prevention, CDC, Atlanta, GA 30333, USA	Multi-laboratory Evaluations of XMRV Detection Assays	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P112-113.	Background: The Blood XMRV Scientific Research Working Group was established to design and coordinate collaborative studies to investigate the prevalence of XMRV in blood donors using standardized XMRV assays. Materials And Methods: A multi-phase study has been designed to evaluate XMRV nucleic acid and serological detection assays in terms of sensitivity, specificity and reproducibility; assess assay performance on various specimen types represented in existing blood donor/recipient repositories, and determine the prevalence of XMRV in blood donors. Phase I involved production of whole blood (WB) and plasma analytical performance panels spiked with XMRV infected cells or virus, respectively. These panels were tested in a blinded fashion using XMRV nucleic acid amplification testing (NAT) developed by seven participating laboratories. Phase II represented pilot studies to compare XMRV detection using frozen PBMCs, WB and plasma derived from individuals identified as XMRV viremic in a previous study. Additionally, serology was performed on plasma by two laboratories. Phase III involves further evaluation of the clinical sensitivity and specificity of candidate NAT, serology and culture assays by using a blinded panel of 15 pedigreed positive samples, together with pedigreed negative samples and spiked positive controls Results: In phase I, all laboratories detected at least 136 proviral copies/ml and 5/7 assays demonstrated even more sensitive limits of detection. 5/7 plasma RNA assays performed similarly, with limits of detection of 80 RNA copies/ml or less. The initial unblinded pilot study in phase II resulted in two laboratories detecting MLV-like sequences in the plasma, but not PBMCs or WB, from all four subjects. A third laboratory detected no viral sequences. A second, blinded, pilot study using the same four subjects and two validated negative controls was less conclusive, with three laboratories detecting no viral sequences with any of the samples. A FACS-based serological assay detected antibodies in 3/4 XMRV-positive individuals, but also in 1/2 negative controls. A western-based assay found no evidence of serology in any sample. Results from Phase III are expected soon. Conclusions: The Blood XMRV SRWG has established a collaboration between many of the laboratories conducting research into XMRV and its detection in blood and has initiated steps to compare performance of XMRV assays using analytical and clinical panels comprised of blood samples from XMRV-positive and negative pedigreed subjects.

	7 Gen-Probe Incorporated, San Diego, CA, USA 8 Laboratory of Experimental Immunology, National Cancer Institute-Frederick, Frederick, MD 21701, USA 9 Transfusion Medicine and Cellular Therapeutics Branch, NHLBI, Bethesda, MD 20892, USA			
Snell, Christopher	[no address given]	The Importance of Exercise Challenge	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P124.	The absence of reliable diagnostic laboratory tests or biomarkers presents significant problems for persons with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), treating physicians, and the ME/CFS research community alike. Typically ME/CFS diagnoses rely on self-report measures. An alternative to this approach is to employ direct, objective multi-system, measures of physical function that may also provide insights to the underlying pathophysiology of ME/CFS. One such methodology is cardiopulmonary exercise testing (CPET). The principles underlying CPET are simple. Physical exertion requires that the cardiovascular system supply oxygen (O2) to active muscles and the pulmonary system remove carbon dioxide (CO2) from the blood. Taxing these systems has the capacity to reveal abnormalities that may not be apparent at rest and thus elucidate the mechanisms underlying exercise intolerance in ME/CFS. Some key measures available from CPET include: maximal aerobic capacity (Peak VO2 or VO2 max); ventilatory or anaerobic threshold (VT); and peak respiratory exchange ratio (RER). CPET permits accurate comparison of subjects across serial exercise tests and should be of prime consideration for any clinical intervention trial with functional endpoints. CPET data also allow for the more reliable interpretation of results when an exercise challenge is used to elicit ME/CFS symptoms. As a quantifiable measure of both physiological stress and effort, CPET enables direct comparison between patients and controls on these measures. CPET also has the capacity to objectively document PEM in ME/CFS patients. A significant change in exercise capacity over consecutive tests, it could be argued, is clear evidence of PEM.
Staines, DR; Brenu, EW; Marshall-Gradisnik, S	Ekua Weba Brenu, Faculty of Health Science and Medicine Bond University Queensland 4229,	Novel pathomechanisms in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis:	IACSF/ME. 18 (1). Spring 2010.	CFS/ME is, in some cases, a serious fatigue-related condition exhibiting a range of neurological, immunological and metabolic dysfunctions in symptom presentation. The present paper explores the possibility of perturbations of purinergic signalling (PS) as a pathomechanism of CFS/ME involving glial cell dysfunction, disruption of neuronal transmission, neuroinflammation and possible disturbances in the

	Australia Email: ebrenu@student.bond.edu.au Dr Donald R. Staines Associate Professor and Public Health Physician, Gold Coast Population Health Unit, 10-12 Young Street, Southport 4215, Queensland, Australia E-mail: Don_Staines@health.qld.gov.au Dr Sonya Marshall , Associate Professor Biochemistry Faculty of Health Sciences and Medicine ,Bond University, Queensland 4229, Australia Email: smarshal@bond.edu.au	Do purinergic signalling perturbations and gliosis play a role?		functioning of the blood-brain and blood-spinal barriers (BBB/BSB). This paper discusses the possibility that the putative neuroinflammatory processes may occur through perturbations of PS involving vasoactive neuropeptide (VN) dysfunction (e.g. through autoimmune mechanisms). Pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP) function as neurotransmitters, vasodilators and regulators of immunity, nociception and hypoxic injury. They are important in the central nervous system (CNS) by activating adenylate cyclase (AC) to produce cAMP from ATP. Compromise of ATP metabolism may promote neuronal and glial toxicity through impaired cAMP production or impaired ATP metabolism and these may alter BBB/BSB function. Although speculative, diagnostic and therapeutic implications may exist for CFS/ME if VN compromise, along with perturbations of PS, do indeed disrupt neurological and glial cell functioning. Treatment opportunities involving phosphodiesterase inhibitors (PDEIs) and purinergic modulators may plausibly exist.
Staud, Ronald	[no address given]	Session: FIBROMYALGIA: Are tender points necessary? A debate Tender points are Important	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P118-119.	Population studies have demonstrated moderately strong associations (odds ratios range 1.3-3.1) between the presence of pain in a body segment and the presence of tender points within that segment. Further, there is evidence of increasing number of tender points with increasing number of painful segments. The reporting of non-Bulletin of the specific pain, aching, or stiffness, is also associated with high tender point counts. Importantly, there is no unique cut off at which local pains and tender points occur concurrently in a widespread form. This is consistent with the observation that fibromyalgia (FM) represents one end of a spectrum of musculoskeletal pain and tender points, and that both traits are continuous in the general population. Tender points have been successfully used for the definition of study populations like fibromyalgia. For clinical purposes, however, tender points seem to provide little mechanistic information about individuals' pain and associated symptoms.
Steele, Lea	Lea Steele, Ph.D.,	Gene-Exposure	IACSF/ME. 19 (2). Fall 2011.	Objectives: Epidemiologic and clinical studies have implicated wartime exposures to

	Research Professor of Biomedical Studies, Baylor University, Director, Baylor Complex Illness Research Initiative, One Bear Place, Box # 97224, Waco, TX 76798, Email: Lea_Steele@baylor.edu	Interactions in the Etiology of Gulf War Illness: Evidence of Increased Vulnerability to Neurotoxicants in Identifiable Veteran Subgroups	Abstracts from IACFS/ME Biennial International Conference. P134.	neurotoxicants (pyridostigmine anti-nerve gas pills, pesticides, and low-level nerve agents) as risk factors for Gulf War illness (GWI), but it is unclear why some troops developed GWI after the 1991 Gulf War (GW) while others, with similar experiences and exposures, remained healthy. This study investigated whether genotype or activity of paraoxonase (PON1), a circulating enzyme whose isoforms differentially hydrolyze pesticides and nerve agents, is associated with variable risk for GWI in veterans of the 1991 Gulf War. Methods: Case-control study of a population-based sample of 91 veterans who served in the Army as enlisted personnel during the 1991 Gulf War: 49 Gulf War veterans with GWI, 19 GW veteran controls, and 23 nondeployed veteran controls. Veterans provided information on wartime experiences and exposures, and blood samples for determining PON1 genotype at position 192, and PON1 activity in three substrates: paraoxon, phenyl acetate, and diazoxon. In addition to general case-control comparisons, exploratory analyses evaluated interactions between genotype and exposures in the risk for GWI. Results: Overall, a somewhat higher proportion of GW cases (22%) than GW controls (6%) were PON1192 RR homozygotes (p=0.09). PON1 activity in paraoxon was significantly lower in GW controls than in GWI cases (p=0.04) and nondeployed controls (p=0.05), with no significant differences noted in other substrates. In exploratory evaluation of GWI risk in PON1192 genetic subgroups, QQ homozygotes were at significantly increased risk for GWI if they reported wearing pesticide-treated uniforms (OR = 21.0, exact p<0.01) or prolonged use of pyridostigmine bromide (OR=11.2, exact p<0.01), although these exposures were not associated with GWI in veterans with QR and RR genotypes. Among veterans with QR and RR genotypes, the only significant GWI risk factor was hearing chemical alarms in theater (OR=7.6, exact p=0.04), while hearing alarms was not a risk factor for QQ homozygotes (OR= 0.75, exact p=0.34). Conclusions: Findings support earlier indicators that GWI may be associated with PON1 genotype and activity levels, with GW PON1192RR homozygotes at somewhat increased risk for GWI overall. Detailed investigations from our small sample provided significant results in support of the following hypotheses: 1) GW veterans whose PON1 genotype (QQ) is known to provide slower hydrolysis of some organophosphate pesticides were at increased risk for GWI in relation to reported use of pesticides and prolonged use of pyridostigmine bromide during deployment, and 2) GW veterans who carry the R allele at PON1192, which is known to provide inefficient hydrolysis of sarin, were at increased GWI risk if they heard chemical alarms in theater. These preliminary findings identify significant gene exposure interactions in the directions expected for substrates preferentially hydrolyzed by PON1192 Q and R isozymes, and warrant further evaluation in a larger sample.
Stein, Eleanor	Private practice psychiatry; Calgary,	Diagnosing psychiatric disorder	Bulletin of the IACSF/ME. **Winter 2005 - 6**	A frequently voiced concern of physicians in clinical practice is how to accurately diagnose and treat psychiatric disorders in people with chronic fatigue syndrome

	Alberta , Canada	in patients with ME/CFS		(ME/CFS). The objective of this paper is to suggest some simple ways to differentiate between ME/CFS and primary depression and anxiety, as well as how to approach secondary psychiatric issues when they are present. These guidelines are based on close reading of the diagnostic criteria of ME/CFS, a review of the literature and clinical experience with both discrete and mixed populations.
Stein, Eleanor	Myalgic Encepahalomyelitis/Chronic Fatigue Syndrome and related disorders, Psychiatrist in Private Practice, Clinical Assistant Professor Dept of Psychiatry, University of Calgary, 4523 – 16 A Street SW Calgary, Alberta T2T 4L8 e-mail: espc@shaw.ca	Development of Standardised Patient Scenarios as a Teaching Tool for ME/CFS	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P155-156	Objectives: 1. To describe the process of developing two "standardized patient" clinical teaching tools for ME/CFS 2. To evaluate the effectiveness of these tools in a mixed health care professional audience attending an educational workshop on Methods: The process started with two focus groups of physicians who were unfamiliar with ME/CFS. The groups identified their top learning priorities with regards to ME/CFS. Clinical cases were developed to address these identified needs based on the Canadian Consensus Guidelines. The cases were then "workshopped" extensively by expert clinicians and patient focus groups and standardized patient trainers. The final standardized scenarios will be presented in vivo at an accredited CME medical education workshop April 30, 2011. Evaluations of the April 30th, 2011 workshop will provide data on the acceptability of these tools to health care professionals. Results: Patient feedback to the two scenarios: 1. diagnosis and 2. symptom management was extremely positive. Patient input ensured that the scenarios reflect that ME/CFS is a biomedical condition which due to its severity, variability and uncertain prognosis can cause depression, anxiety and stress. They also stressed the importance of clinicians asking about the lived experience of patients with ME/CFS. This is a qualitative evaluation of new teaching tools. The presentation will include verbatim comments from participants, evaluation data and may include video clips. Conclusions: These standardized clinical scenarios are well received by patients with ME/CFS and have promise as teaching tools for health care professionals
Stein, Eleanor; Stormorken, Eva	Eleanor Stein MD FRCP(C), Myalgic Encepahalomyelitis/Chronic Fatigue Syndrome and related disorders, Psychiatrist in Private Practice, Clinical Assistant Professor, Dept of Psychiatry, University of Calgary, 4523 – 16 A Street SW	Working Successfully With Patients Who Have Contested Conditions: The Case of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P153-154	Objectives: 1. To provide an understanding of the impact on the therapeutic relationship of ME/CFS being a contested condition - one in which there is no proven etiology, diagnostic test or treatment. 2. To recommend solutions to the challenges and misunderstanding that arise in the relationships between patients with ME/CFS and their health care practitioners as a result of the contested status. Methods: Non-systematic literature review and clinical experience. Results: Therapeutic relationships between patients with ME/CFS and their medical practitioners are impacted by contextual issues including: debate about causality, lack of recognition, and lack of objective diagnostic markers. These issues lead to common therapeutic challenges including: debate over validity of the condition, the need to differentiate ME/CFS from primary psychiatric disorders, frustration due to lack of symptom improvement, altered power balance between the patient and practitioner, interaction with patients who feel unheard, and the need to close the gap between needed and available services. Strategies which deserve further research include: keeping an open mind,

				clarifying symptom profiles, collaboratively searching for hope, clarifying expertise of patient and practitioner, listening to the whole story and building a coalition to advocate for needed services. Conclusions: Identifying and openly discussing contextual issues which impact the therapeutic relationship allows patient and practitioner to form a working relationship against the illness and societal stigma rather than fighting each other. This collaboration may improve the quality of therapeutic relationships thereby improving patient care and outcomes.
Stevens, SR; Davenport,TE	1 Executive Director, Pacific Fatigue Laboratory, Department of Sport Sciences, University of the Pacific, Stockton, CA, USA 2 Assistant Professor, Department of Physical Therapy, Thomas J. Long School of Pharmacy and Health Sciences, University of the Pacific, Stockton, CA, USA	Functional Outcomes of Anaerobic Rehabilitation in a Patient with Chronic Fatigue Syndrome: Case Report with 1-year follow-up	IACSF/ME. 18 (3). Fall 2010.	This case study aimed to document the effect of pacing self-management and short-duration exercise on physiological functioning and disability in an individual with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). A 28-year-old woman with CFS/ME received a rehabilitation program that involved: (1) pacing self-management using a heart rate monitor to maintain heart rate below ventilatory threshold and (2) a pragmatic approach to restorative strengthening and flexibility exercises conducted at an intensity below anaerobic threshold, which were completed 3 times weekly. Cardiopulmonary exercise testing (CPET) with analysis of expired gases and functional self-report were obtained before and 1 year after initiation of intervention. At 1-year follow-up, the patient reported she was able to complete daily activities without reproducing symptoms and 75% improvement in time to recover from CPET. Prior to intervention, patient demonstrated impaired cardiovascular and pulmonary responses at peak and anaerobic threshold, which improved at 1-year follow-up. Pacing self-management combined with short-duration restorative exercise resulted in a favorable clinical outcome in this patient with CFS/ME. Additional research is necessary to determine the efficacy and mechanism of action for this treatment.
Stouten, B[1]; Goudsmit, EM[2]	1. Einsteindreef 67A, Utrecht, The Netherlands 2. University of East London, UK	How Valid id the Model Behind Cognitive Behaviour Therapy For Chronic Fatigue Syndrome? An Evaluation of the Additional Data from the Trial by Pins et al	IACSF/ME. 18 (2). Summer 2010.	The cognitive behavior therapy (CBT) program studied by Prins et al. is based on a model of chronic fatigue syndrome that posits that fatigue and functional impairment are perpetuated by physical inactivity, somatic attributions, focusing on bodily symptoms and a low sense of control. A recent analysis of the data from three trials based on a model devised by Vercoulen et al. concluded that the effect of CBT on fatigue could not be attributed to a persistent increase in physical activity. We therefore examined the effect of treatment on the remaining three variables in the model using data from one of the trials, available in the public domain. The results from the groups given CBT, Guided Support and treatment as usual revealed that CBT had no significant impact on somatic attributions and focusing on bodily symptoms, and that in line with established guidelines, these two variables were not mediating factors. The only variable in the model showing an effect of CBT was sense of control. We submit that there is now sufficient evidence to warrant a review of CFS guidelines which advocate interventions aimed particularly at increasing physical activity and challenging somatic attributions, and that more flexible programs which address loss

				of control deserve further consideration and evaluation.
Strayar, DR; Mikovits, JA[2]; Vurimindi, V[1]; Carter, WA[1];	[1]Hemispherx Biopharma, Inc., Philadelphia, PA [2]Whittemore Peterson Institute, Reno, NV	Health/Performance and Response Status of XMRV/pMRV Antibody Positive vs. Negative Chronic Fatigue Syndrome (CFS) Subjects in a Phase III Clinical Trial	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P116-117.	Background: CFS is a severe disorder consisting of profound fatigue and a variety of other debilitating symptoms that affects up to 4 million Americans. Recently, one of us (JAM) identified DNA from a human gamma retrovirus (XMRV) in 67% of CFS subjects. Evidence also suggested that approximately 50% of the CFS infected subjects mounted a specific antibody response against XMRV (Science 326, 585-589 (2009)). The objective of this study was to compare demographic parameters, health/performance status and response of XMRV/pMRV antibody positive vs. negative CFS subjects enrolled in a Phase III clinical trial evaluating the safety and efficacy of a toll-like receptor 3 (TLR3) agonist, rintatolimod (PolyI:PolyC12U, Ampligen®). Materials and Methods: Two-hundred-eight (208) evaluable subjects, who met the 1988/1994 Case Definitions for CFS, participated in this randomized, placebo-controlled, double-blinded, multicenter study. Only severely debilitated patients were selected for this study. The primary endpoint was exercise treadmill duration. Subjects received rintatolimod (200-400 mg) or an equivalent volume of placebo twice weekly by IV infusion for 40 weeks. Baseline (or earliest available specimen) serum samples from all 208 subjects were analyzed for antibodies directed against XMRV/pMRV. Results: Seventy (33.7%) of the 208 CFS subjects were positive for antibodies directed against XMRV/pMRV, while 138 (66.3%) were negative. There was no significant difference in the number of CFS subjects positive or negative for antibody with regard to age, gender, duration of CFS, cognitive dimension (SCL90-R), exercise treadmill duration, or SF-36 vitality score (p>0.3). However, the subjects negative for antibody had a lower Activity of Daily Living score (66.9 vs.71.2, p=0.010, ANOVA) and a lower overall activity level based upon a lower activity monitor score (183K vs. 210K, p=0.033, ANOVA). The percent of subjects with a >25% increase in exercise treadmill tolerance (ETT) at Week 40 compared to Baseline was significantly greater for subjects receiving rintatolimod (39%) vs. placebo (23%), p=0.016 (2 tailed Fisher's Exact Test). Although, there was a trend for greater improvement in exercise duration with rintatolimod treatment for both the XMRV/pMRV antibody cohorts receiving rintatolimod, the antibody positive subgroup had a greater relative percent of subjects showing a >25% increase in ETT with rintatolimod compared to placebo than the antibody negative cohort. An analysis of concomitant medications utilized by CFS subjects to help treat symptoms of CFS showed that, when compared to placebo, the rintatolimod treated cohort positive for antibodies had a greater percentage of subjects with a decrease in CFS-related medication use at the end of the study (24%), p=0.039 vs. the antibody negative subjects (13%), p>0.10. Conclusions: These results indicate that approximately 1/3 of the CFS subjects have a detectable immune response directed against XMRV/pMRV and that this antibody positive group may respond more favorably to rintatolimod, an antiviral and immune modulator, than the antibody negative cohort. Additional studies to further evaluate XMRV/pMRV in this

				CFS population are underway.
Sugino, T; Ishigami, K; Kajimoto,O	Tomohiro Sugino, Representative Director, Soiken Inc., Master of Science in Biology, Senri Life Science Center 13F, 1-4-2, Shinsenri-higashimachi, Toyonaka, Osaka, 560-0082, Japan sugino@soiken.com	Supplementation of Imidazole Dipeptides Attenuates Fatigue Induced by Various Causes in Human	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P147-148	Objective: Oxidative stress is known to cause physical and mental fatigue, so antioxidants are potential candidates for antifatigue agents. Imidazole dipeptides (carnosine and anserine) which chicken breast is rich in, are reported to have strong antioxidative effects. This is the reason migratory birds can fly thousands of miles without rest? Here, we investigated the effect of imidazole dipeptides derived from chicken breast on fatigue induced by physical task or by daily activities in human. Methods: (Study I) In a double-blinded, placebo-controlled, crossover study, 17 subjects took dipeptides 400 mg/day or placebo for 29 days. As a fatigue-inducing physical task, subjects performed workload trials on a cycle ergometer at fixed workloads for 4 hours and then rested for 4 hours. We evaluated physical performance by 10-second high power test, subjective sensation of fatigue by visual analogue scale (VAS) and antioxidant and its related effects by biochemical parameters in blood and urine. (Study II) In a double-blinded, placebo-controlled, parallel study, 207 subjects who have fatigue feeling from daily activities were randomly divided into three groups; and provided with imidazole dipeptides 200 mg/day, 400 mg/day, or placebo for 8 weeks. We evaluated the subjective sensation of fatigue primarily by VAS. Results: (Study I) Oral imidazole dipeptides administration inhibited the impaired physical performance and the increased level of fatigue sensation, and suppressed the increased levels of the urinary oxidative stress parameters [8- isoprastane and 8-hydroxy-deoxy-guanosine (8-OHdG)] and plasma transforming growth factor (TGF)-b by physical task. (Study II) The VAS score was significantly lower in the imidazole dipeptides 200 and 400 mg/day groups compared with that in the placebo group. The effect was remarkable especially in the 400/day group. Conclusion: These results suggest that the antioxidant effect of imidazole dipeptides inhibited tissue damage and attenuated fatigue by physical task, moreover the dipeptides decreased in fatigue sensation from daily activities. Imidazole dipeptides have the effects on attenuating fatigue induced by various causes, so supplementation of the dipeptides (drink, capsule, tablet etc.) is one of the promising remedies for fatigue in human.
Tajima, Seiki; Matsuzawa, Shigeyuki; Takai, Kazumi; Miike, Teruhisa	Seiki Tajima, MD., 1070 Akebono-cho, Nishi-ku Kobe, 651-2181, Japan. s_tajima@hwc.or.jp	Therapeutic Outcome by Two-months Intensive Sleep-Wake Circadian Rhythm Treatments in Japanese Children and Adolescents with Chronic Fatigue	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P128-129.	Objectives: In the last two decades, we have reported relationship between biological clock system and childhood chronic fatigue (CCF). Biological clock dysfunction is associated with energy metabolism, immune system and frontal lobe dysfunction. Based on these evidences, we have treated patients with CCF at new medical research center for CCF and developmental disorder since April 2009. Here we show the therapeutic outcome of our first year trial for translating evidence into practice. Methods: 30 patients (15 boys and 15 girls, age 11 to 25) with chronic fatigue caused by sleep deprivation were admitted in the first year of our center. All patients were treated for 8 weeks with bright light therapy, thermal therapy, medication, cognitive behavioral therapy and lifestyle teaching. Self-sleep-logs (S-log) have been recorded

				during hospitalization. 48hr core body temperature (CBT) monitoring was performed at the beginning and the end of therapy. Delay of circadian rhythm (≥60min.), poor daily variation (ΔCBT<1.0°C) and totally high CBT (1.0°C higher than control) were detected in CBT recordings. Long total sleep time (≥10hr), delayed sleep phase (sleep onset later than 24:00), irregularity of sleep onset and offset (larger variation than 90min.) and sleep segmentation (segmented more than 7 days per 2 weeks) were also detected in S-log recordings. With or without these factors were compared between the beginning and the end of therapy using fisher's exact test. Results: Delay of CBT circadian rhythm ($p<0.01$), long total sleep time ($p<0.0001$), delayed sleep phase ($p<0.05$) and irregularity of sleep onset and offset ($p<0.0001$) were significantly improved at the end of therapy. Conclusion: Intensive sleep-wake circadian rhythm treatments were effective to improve circadian rhythm. However, recoveries of other chronic fatigue related symptoms and poor performances were insufficient at the time of discharge. Therefore, just a part of patients has resumed normal activity yet. Recovery from sleep disturbance is not the goal but the first stage of improvement for the patients with chronic fatigue. From this point of view, more clinical trials will be needed.
Torres-Harding, Susan[1]; Sorenson, Matthew[2]; Jason, Leonard A[2]; Maher, Kevin[3]; Fletcher, Mary Ann[4]	[1]Roosevelt University; [2]DePaul University; [3]Labcorp and University of Miami, [4]University of Miami	Evidence for T-helper 2 Shift and Association with Illness Parameters in Chronic Fatigue Syndrome (CFS)	Bulletin of the IACSF/ME. 16 (3). Fall 2008. P19-33.	Few immunological markers have been consistently reported in CFS. However, a shift to a T-helper 2 (Th2) type immune response has been hypothesized for individuals with CFS. The current study investigated whether individuals with CFS who exhibited a stronger shift towards a Th2 type of immune response would also exhibit more severe symptoms, poorer neurocognitive functioning, and poorer physical and psychosocial functioning. The current investigation measured the percentage of Th1-like and Th2-like memory cells using cell surface flow cytometry in 114 individuals with CFS. The associations between the ratio of Th1 and Th2 memory cells and various illness parameters measures were then examined, including symptom severity, psychiatric functioning, neurocognitive functioning, salivary cortisol levels, and chronic pain status. Results indicated that individuals who exhibited a more extreme shift towards a Th2 immune response also exhibited poorer sleep and high levels of basal salivary cortisol. The implications of these findings are discussed.
Treasdaden, IH; Puri, BK	Dr. Ian H. Treasaden, Consultant Psychiatrist and Honorary Clinical Senior Lecturer, West London MHT and Imperial College London; Head of Forensic Neuroscience, Department of	Regional Grey and White Matter volumetric changes in Chronic Fatigue Syndrome (Myalgic Encephalomyelitis): A Voxel-based Morphometry 3T MRI Study	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P135-136	Objectives: It is not established whether or not myalgic encephalomyelitis/chronic fatigue syndrome (CFS) is associated with structural brain changes. The aim of this study was to investigate this by conducting the largest voxel-based morphometry study to date in CFS. Methods: High-resolution structural 3-T cerebral MRI scanning was carried out in 26 CFS patients and 26 age- and gendermatched healthy volunteers. Voxel-wise generalized linear modeling was applied to the processed MR data using permutation-based non-parametric testing, forming clusters at $t > 2.3$ and testing clusters for significance at $p < 0.05$, corrected for multiple comparisons across space. Results: Significant voxels ($p < 0.05$, corrected for multiple comparisons),

	Imaging, Imperial College, UK.Three Bridges Unit, West London Mental Health NHS Trust, Uxbridge Road, Southall, Middlesex UB1 3EU, England,UK. E-mail: ian.treasaden@wlmht.nhs.uk			depicting reduced grey matter volume in the CFS group, were noted in the occipital lobes (right and left occipital poles; left lateral occipital cortex, superior division; and left supracalcrine cortex); the right angular gyrus; and the posterior division of the left parahippocampal gyrus. Significant voxels ($p < 0.05$, corrected for multiple comparisons), depicting reduced white matter volume in the CFS group, were also noted in the left occipital lobe. Conclusion: These data support the hypothesis that significant neuroanatomical changes occur in CFS, and are consistent with the complaint of impaired memory that is common in this illness; they also suggest that subtle abnormalities in visual processing, and discrepancies between intended actions and consequent movements, may occur in CFS.
Unger, Elizabeth	Elizabeth R. Unger PhD, MD, Chronic Viral Diseases Branch, Division of High-Consequence Pathogens and Pathology, NCEZID Centers for Disease Control and Prevention, 1600 Clifton Road, MS G41 Atlanta,GA 20222, USA. eunger@cdc.gov	Pathways to Pathogenesis: Standardized Measures of CFS/ME Illness Domains	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P123.	Case definitions are used in at least two different circumstances. First, a case definition, when simply and easily applied, may be used as a substitute for a specific diagnostic test to measure disease in a population. This would be done when use of the diagnostic test is impractical for delivering information in a timely and cost-effective manner. An example of this situation is use of “flu-like illness” determined by telephone interview as a surrogate to monitor seasonal or pandemic influenza. A second circumstance occurs when there is no diagnostic test, and case identification requires the use of specific descriptive measures. This is the current situation with CFS/ME, a complex and heterogeneous disorder likely to involve multiple pathways to pathogenesis. Case definitions are essential for public health agencies to determine burden of illness, for clinicians to appropriately diagnose and manage patients, and for researchers to identify risk factors and the underlying biologic basis for illnesses. Limitations in the ability of case definitions to identify homogenous patient populations could be addressed by standardizing how the definitions are applied, or by narrowing the definitions through increased criteria needed to meet the definition, or both. An alternative approach is to improve measures of illness domains (questionnaires and biologic) to allow patients identified by any case definition to be phenotypically sub-grouped in a way that allows the underlying biology to be discovered.
Unger, Elizabeth; Brimmer, Dana J; Boneva, Roumiana S; Jones, James F;	Dana J. Brimmer, Ph.D., M.P.H, Behavioral Scientist, McKing and CDC, 1600 Clifton Road, MS-A15, Atlanta, Georgia, 30333 dyv4@cdc.gov	CFS Knowledge and Illness Management Behavior Among US Healthcare Providers and The Public	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. P130-131.	Objectives: Chronic fatigue syndrome (CFS) is a challenge because of unknown etiology and diagnostic biomarkers, and treatment relies on symptom management. Previous research has shown positive CFS knowledge, attitudes and beliefs among physicians and awareness among the public. We compared CFS knowledge and illness management behavior between healthcare providers (HCP) and the public in order to identify gaps and need for educational interventions. Methods: We used DocStyles, a 2009 web-based panel survey of primary care physicians, OB/GYNs, pediatricians, dermatologists, and nurse practitioners, and HealthStyles, a 2010 public consumer mail survey to ask questions about CFS knowledge and illness management behavior.

				The HCP sample is drawn from an opt-in, verified Epocrates Honors panel. HealthStyles used stratified random sampling to match the national population on region, income, age, and household size. Both surveys asked about CFS awareness, CFS symptoms, and if CFS is a medical or psychiatric condition. HCP were also asked if they have ever made a CFS diagnosis and how they treat and manage CFS. HealthStyles respondents were asked if they knew someone diagnosed with CFS, and then also if they or someone they knew thought they had CFS, what they would do to find out more about the illness. Results: The response rate was 46% for DocStyles and 67% for HealthStyles with a sample size of 2,000 and 4,184 participants, respectively. Males comprised 65% of DocStyles physicians and 48% of the HealthStyles sample. Among HCP, 94% heard of CFS compared to 57% of the public. HCP had two to three times higher recognition rates on eight CFS symptom criteria as compared to the general public. When asked if CFS were both medical and psychiatric, 71% of HCP agreed as compared to 30% of the public. Two percent of the public considered CFS a psychiatric condition vs 14% of HCP. A higher proportion of the public considered CFS a medical condition: 27% vs 8% of HCP. Uncertainty whether CFS was either a medical or a psychiatric condition was higher among the public (42%) compared to HCP (8%). Thirty-seven percent of HCP reported ever making a diagnosis of CFS and nearly 10% of the public knew someone diagnosed with CFS. HCP who reported ever diagnosing CFS were more likely to categorize CFS as a medical condition (Chi-square = 98.6, $p<0.01$). Top three ways in which HCP manage CFS were: referring to a medical specialist (35%), prescribing medications (29%), and referring to a psychologist (26%) or prescribing graded exercise therapy (26%). If diagnosed with CFS, the public would seek information by talking to a family doctor (72%), searching the Internet (54%), and talking to medical specialist (25%). Only 7% would join a support group. Conclusion: Our results are consistent with findings that HCP have high awareness and knowledge of CFS, and nearly 80% of HCP classified CFS as a medical or as both medical and psychiatric condition. However, HCP and public view of medical or psychiatric conditions differed. History of CFS diagnosis for HCP may influence this classification. More than 1/3 of HCP had ever diagnosed CFS, which is notable considering the relatively low prevalence of CFS. Study results support development and maintenance of CFS educational materials for the Internet and providing family doctors with tools to engage patients in conversations about CFS.
Vallings, Rosamund	vallings@xtra.co.nz	The Current CFS/ME Situation in NZ	Bulletin of the IACSF/ME. 16 (1). Spring 2008.	Here in New Zealand we are fortunate that our government accepts without question the diagnosis of CFS/ME in assessments for social welfare benefits. But many patients do fell between the cracks and have difficulty accessing home help, suitable housing and other extra health needs.
Vallings, Rosamund	vallings@xtra.co.nz	ME CFS Conference – May 2008 –	Bulletin of the IACSF/ME. 16 (2). Summer 2008. P12-19.	On May 6, 2008 I attended the International Conference on ME/CFS Biomedical Research at Hinxton, Cambridge, UK. 130 people attended and cutting edge research

		Cambridge, UK		was presented from around the globe. The conference was sponsored jointly by ME Research UK and the Irish ME Trust. Sadly, Vance Spence, who had organised the conference and was going to give an introductory overview, was too ill to attend.
Vallings, Rosamund	New Zealand ME/CFS Association vallings@xtra.co.nz	Skepticism in CFS/ME	Bulletin of the IACSF/ME. 16 (2). Summer 2008. P29-33.	One of the hardest things for those with CFS/ME has been the issue of "no-one seems to believe I am ill". Fortunately I am hearing this less and less these days because I think this illness is becoming better understood and validated by current research thinking did change, as we entered the era of mind-body medicine. ... Thankfully with the emergence and development of sciences such as immunology, genetics and biochemistry, illnesses such as CFS/ME are becoming validated and acknowledged by the wider medical and research community. ... It is just like any other illness with physical and mental aspects. So why do patients still have problems with convincing doctors and others in their lives that they have a "real" illness and are seriously afflicted?
Vallings, Rosamund	[No address quoted]	A Little Bit of History	Bulletin of the IACSF/ME. 16 (3). Fall 2008. P15-18.	On a recent visit to the United Kingdom to attend the Cambridge conference, I spent some time in London and decided to experience a little CFS/ME history again. I had done my medical training at the London Hospital, soon after the flu like epidemic that had affected many at the Royal Free Hospital, another of the 12 big London teaching hospitals, situated in Gray's Inn Road. In 1955, nearly 300 of the medical and nursing staff had remained seriously ill following this epidemic, and as we were a nearby teaching hospital, we had many of these people as inpatients for investigation.
Vallings,R	140, North Road, RD2 Papakura, 2582, New Zealand	Letter to Editor: CFS following H1N1 Flu	IACSF/ME. 18 (3). Fall 2010.	In early 2009 I had a case study published in the *Journal of Clinical Pathology* (1). This involved a young teenage boy who was diagnosed as suffering from Chronic Fatigue Syndrome (CFS) following an attack of swine flu (HIN1). His initial illness was severe, and he developed many symptoms in the following weeks. Three months later he was still very ill, and a diagnosis of CFS was deemed appropriate, according to the pediatric version of the Canadian criteria (2, 3). Since that time he has gradually improved although is still unwell and unable to participate fully in everyday activities or attend school regularly. Here in New Zealand we have just emerged from another winter and already I have seen a further 5 patients with CFS following HIN1 swine flu. I feel that primary care physicians need to be alerted to this possibility, and to identify at risk patients, so that suitable intervention can be instated. Early recognition of diagnostic vulnerability should give a better chance of earlier recovery. Any person suffering a very prolonged recovery following acute infection needs careful follow up. Suitable intervention would include: adequate rest, freedom from stress, cautious gentle exercise and a sensible diet. Most of these patients will have problems with sleep, necessitating regular bedtime routine, and medication may be needed. As pain is also a frequent symptom, a low dose tricyclic such as nortriptyline 5mg a few hours before bedtime may be appropriate. These simple measures can enhance an earlier

				recovery. Another associated issue for patients already suffering from CFS, or those who have recovered, is whether to have annual influenza immunisation. The immunisation here does incorporate HIN1 also. In general I recommend avoidance of any immunisation unless deemed absolutely necessary, as there seems to be accompanying risk of relapse for some patients. I have seen several patients each year who have relapsed after various immunisations, and I also have documented a number of CFS patients whose illness actually began following an immunisation. This does indeed produce a dilemma for both patient and physician. It would be interesting to hear from other physicians regarding their experiences, and hopefully this letter could generate some useful research to help guide us in future recommendations.
Van Hoof, Elke LS; De Becker, Pascale J; Lapp, Charles; De Meirleir, Kenny L	Elke Van Hoof, Department of cognitive and biological psychology, Faculty of psychological and educational sciences, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels - Belgium	How do adolescents with chronic fatigue syndrome perceive their social environment? A quantitative study.	Bulletin of the IACSF/ME. 17 (1). Spring 2009. P16-31	Some concern has been raised regarding the inappropriateness of the adult Center for Disease Control criteria for use in children. This resulted in a pediatric case definition being published in 2006. Unfortunately, the case definition does not prevent confusion and doubt with regards to the experienced symptoms in school personnel who deal with young persons with chronic fatigue syndrome (CFS). In order to provide more insight into pediatric chronic fatigue syndrome, twenty-seven chronic fatigue syndrome adolescents were interviewed by means of questionnaires. Results showed that it took about one and a half years before children received a diagnosis of chronic fatigue syndrome. Their symptom pattern seems comparable with that of an adult sample, except for stomach aches. The majority experienced conflicts at school due to their condition. Almost every adolescent with chronic fatigue syndrome abandoned their leisure activities. Adolescents with chronic fatigue syndrome were frequently confronted with negative remarks if they attempted their usual leisure activities.
Van Konynenburg, Richard A	Livermore, CA	The Glutathione Depletion – Methylation Cycle Block Hypothesis for CS/ME, Implications for treatment	Bulletin of the IACSF/ME. 16 (2). Summer 2008. P20-28.	At the January, 2007, IACFS/ME Scientific Conference in Fort Lauderdale, I presented a poster paper describing a new biochemical hypothesis for the etiology, pathogenesis, pathophysiology and symptomatology of CFS/ME, which I call the "Glutathione Depletion—Methylation Cycle Block (GD—MCB)" hypothesis. This hypothesis is able to explain many of the biochemical and symptomatic features of CFS/ME in a straightforward, specific and testable manner. Since the conference, I have continued to develop this hypothesis, and a clinical research study using a treatment protocol based on it is currently underway. The GD--MCB hypothesis has not yet been described in a peer-reviewed publication, and controlled clinical trials of treatment based on it have not yet been performed. Nevertheless, I believe it is in the best interest of the CFS/ME community for IACFS/ME members to receive an update on this hypothesis and the implications for treatment at this time.
Van Konynenburg,R	Richard A. Van Konynenburg, Ph.D.,	A Comprehensive Biochemical Model	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME	Objective: To build a comprehensive model for the pathogenesis and pathophysiology of ME/CFS that will lead to accurate diagnosis and effective treatment in clinical

	444 Ontario Drive, Livermore, CA 94550, USA, richvank@aol.com	for the Pathogenesis and Pathophysiology of ME/CFS, and Effective Treatment Based on It	Biennial International Conference. Poster Presentations. P145-146	practice. Methods: This paper builds on work presented at the previous three conferences of the IACFS/ME and its predecessors. In 2004, the author emphasized the importance of glutathione depletion in the pathogenesis and pathophysiology of ME/CFS (1). In 2007, he linked this to a partial block in the methylation cycle (2). In 2009, he and a physician presented evidence from a clinical study of a treatment based on this mechanism in a private practice, which was found to produce significant benefits for most of the patients, in terms of both symptomatic improvement and normalization of lab measured parameters (3). Results: Since the previous conference, further progress has been made in developing a comprehensive model of the pathogenesis and pathophysiology of ME/CFS at the biochemical level, which is consistent with available research on this disorder, clinical experience, and patient health histories, symptoms, and treatment outcomes. To the author's knowledge, this hypothesis is the only proposed model at the biochemical level that is capable of explaining the wide variety of features of this disorder in a straightforward manner. It draws together the specialized work of other researchers in epidemiology, genomics, nutrition, allopathic load, toxicology, gastroenterology, metabolism, exercise science, sleep science, gene expression, cardiology, neuroendocrinology, immunology and virology. It offers measurable biomarkers and guidance for effective clinical treatment. This model also has the potential to mesh well with retroviral involvement in ME/CFS, owing to the known silencing of gene expression by methylation. A significant number of patients, under the care of several clinicians, are currently receiving treatment based on this work, and most are experiencing improvement. A small number of what appear to be complete recoveries have been reported. Conclusion: Treatment to lift the partial methylation cycle block appears to be an important component of an overall treatment protocol for ME/CFS.
Vera, MA; Garcia, L; Valencia, W; Barnes, Z; Fletcher, M-A; Klimas, NG	Maria A. Vera-Nunez, MD, PG-Y 3 Internal Medicine Resident, University of Miami, Clinical Research Building, University of Miami Miller School of Medicine, 1150 N.W. 14th Street, Miami FL 33136, mveranunez@med.miami.edu	Abnormal Cytokine Levels in Patients with CFS Regardless of Metabolic Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P166.	Background: Metabolic Syndrome (MetSd) is a known risk factor for significant morbidity and mortality, including cardiovascular and cerebrovascular disease. It has been described that inflammation plays an important role in the pathogenesis of MetSd, with up-regulation of both TH1 and TH2 cytokines. Previous studies have shown that patients with CFS were 2-fold as likely to have metabolic syndrome compared with healthy controls. Objective: To compare cytokine levels in patients with Chronic Fatigue Syndrome (CFS) with and without metabolic syndrome. Methods: With a cross-sectional study design, we evaluated the data from participants of the National Institutes of Health funded "Good Day, Bad Day" research study, and collected information on demographics: age, gender, race; anthropometrics: weight, height, waist circumference. Using a multiplex method (Quansys), plasma cytokines:Interleukin (IL) 1α, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12, IL-13, IL-15, IL-17, IL-23, Interferon gamma (IFNγ), Tumor necrosis factor alpha (TNFα) were measured. Metabolic syndrome (MetSd) was defined according to the Adult Treatment Panel III criteria. Normal values for cytokines were obtained from 93

				healthy controls. We used independent sample t test to compare means of continuous variables. Results: 66 charts of patients with CFS contained available information and pertinent data to complete the analysis of this study. Demographics: age 53±11.5, 85% female, 72.8% non-hispanic white, 18.2% Hispanic, 3% black, 1.5% Asian, and more than 1 ethnicity 4.5%. MetSd was present in 17 patients (26%), 71% female, 82% white. MetSd was not present in 49 (74%) Cytokine levels were compared between these two groups and no statistical differences were found. Further cytokine level comparison was made between CFS with MetSd and 93 healthy controls, 75% female. Here we found statistically significant differences in IL1α, IL-4, IL-5, IL-6, IL-8, IL-15, IFNγ and TNFα. Conclusion: The prevalence of metabolic syndrome in a CFS population was 26%. Plasma cytokine levels in CFS patients with and without co-morbid MetSd were not different. Similarly to our previously reported findings in CFS, CFS + MetSd patients had abnormalities in proinflamatory, Th2, Th1 and IL-8 when compared to healthy controls. Affected individuals would be biased towards a T-helper (TH) 2 type, or humoral immunity-oriented cytokine pattern accompanied by autoantibody production, inappropriate fatigue, myalgia and arthralgia, as well as changes in mood and sleep patterns. Large longitudinal studies should be performed to determine the contributing factors to this increased risk, and whether the course of metabolic syndrome is altered in this inflammatory state.
Vera, MA; Rey, I; Garcia, L; Harvey, J; Eugene, G; Barnes, Z; Fletcher, M-A; Klimas, NG	Maria A.Vera, MD, PG-Y 3 Internal Medicine Resident, University of Miami, Clinical Research Building, University of Miami Miller School of Medicine, 1150 N.W. 14th Street, Miami FL 33136, mveranunez@med.miami.edu	Vitamin D and IL 10 in Chronic Fatigue Syndrome	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P165-166.	Chronic Fatigue Syndrome (CFS) is considered a state of chronic inflammation. Vitamin D inhibition of pro-inflammatory processes has been observed and one of the proposed mechanisms is the ability to modulate T regulatory cell (Treg) function. Also a possible effect of vitamin D in IL-10 pathway (which is an anti-inflammatory cytokine) has been shown as IL-10-secreting T regs can be induced following activation in the presence of vitamin D. Objective: To determine vitamin D levels in a group of CFS patients and also evaluate if this level correlates with IL-10 levels. Methods: Data of subjects evaluated at the Center for Multidisciplinary Research on CFS, was obtained in a cross-sectional manner, from January to June 2010, in which vitamin D and IL-10 were measured in their first visit before therapeutic intervention. Collected data include demographics (age, gender), vitamin D and IL-10 levels and natural killer cytotoxic activity. Vitamin D deficiency was considered if its level was less or equal to 30ng/mL (75nmol/L), based on the recommendation of the International Osteoporosis Foundation Statistic analysis included descriptive statistics and correlation calculated with Pearson's r. Results: There were 54 people (13 men and 41 women) with pertinent available information, age 47.78±14.9, vit D 33.68 ±16.6, IL-10 15.7±16.1, nk activity 9%±5.6. The prevalence of vitamin D deficiency in this group was 57.4% (46.2% in men and 58.5% in women). Correlation between vitamin D and IL-10 levels was 0.228 (p=0.048). There was no correlation between vitamin D and NK activity or age in the studied group. Conclusion: The prevalence of Vitamin D deficiency was 57.4% and there was a significant correlation between VitD

				and IL-10 levels in this group of CFS patients. Clinical randomized-controlled studies that evaluate the immunomodulatory effect of vitamin D in patients with CFS are necessary.
Vogelsberger, W; Kamp, M; Blätter, G; Arends, W; Gringinger, F; Colizoli, L	[no address given]	Healing On The Spiritual Path Through The Teachings of Bruno Groening – Medically Verifiable: Three Documented Healings of ME and Two Documented Healings ofFybromyalgie	IACSF/ME. 19 (2). Fall 2011. Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P155.	In a time of world-wide health crisis with steadily growing numbers of chronically sick people, an interest in handed down traditional healing is growing. Natural healing, Homeopathy, Acupuncture, Phytotherapy and others have achieved ever growing significance in the last decade in medical practice. But also the oldest form of healing, the picking up and passing on of life energy or bio-energy, very often referred to as spiritual healing, finds more and more attention among medical specialists. Already in the 50's The British Council of Medical Doctors stated the fact that, "through spiritual healing the regaining of health is possible, which by today´s perception must be looked at as inexplicable."1 Since that time more and more hospitals of the Public Health Service have opened their doors to spiritual healing. The happenings around Bruno Gröning (1906-1959) in Germany, who is regarded as one of the most significant healers, has become the foundation-stone for a unique work of enlightenment by doctors of many countries in our time.1, 2 Thanks to the systematic work of our working group a great number of medically inexplicable progressions of healing from the most varied diseases could be recorded.3,4,5 Documentation is taking place world-wide by means of detailed recordings and analyses of the existing diseases and of the changes that have led to the healing. By means of a certain physical and mental attitude it was possible for the observed persons, mostly after a few minutes to sense a light feeling of energizing in their bodies. Often there occurred characteristic reactions in the body as a forerunner to the healing. It was interesting to observe in many cases an increase in the existing symptoms or pain appeared mostly in the exact topographic region of the affected organ in the body. Frequently it happened that in clear timely connection with these reactions chronic disorders ceased to exist. It is interesting that these phenomena have been described by such important representatives of medical science of the last centuries, such as Paracelsus (Switzerland), and by the well -known European doctor of the beginning of modern times, Hahnemann of Germany, the founder of Homeopathy. Similar knowledge exists in the Asian culture. The perceptions of our working group are presented in publications, in congresses, in different universities with medical students, and passed on in public lectures worldwide. In the last decade over 100.000 people in more than seventy countries have attended these lectures. The Focal point of the lecture will be the personal healing report of Mrs Anneke Hagen-de Waal from Germany. Mrs Hagen-de Waal received the healing after seven and a half years of suffering by putting into practical terms the teachings of Bruno Groening. This particular healing and two additional healings of ME and two healings of Fybromylagie will be presented and commented on by a medical doctor.
Whistler, T;	Toni Whistler, PhD.	Transient	IACSF/ME. 19 (2). Fall 2011.	Objective: Studies have shown that individuals differ appreciably in their

Kryston, C; Panicker, G; Unger, ER	Research Microbiologist, Centers for Disease Control and Prevention, 1600 Clifton Rd, G41,Atlanta, GA, 30333. USA. taw6@cdc.gov.	Responsiveness of Inflammatory Cytokines to an Acute Stressor: Comparisons Between CFS and NF	Abstracts from IACFS/ME Biennial International Conference. Poster Presentations. P167.	inflammatory responses to acute psychosocial stress, and as cytokines have been implicated in the pathogenesis and clinical manifestations of CFS, we wanted to determine if stress-induced immune-modulation was altered between CFS and non-fatigued controls. Methods: Subjects with CFS and matched well controls identified from the general population participated in a 3-day in hospital study. On the final day, participants were exposed to a standardized psychosocial stressor (the Trier Social Stress Test, TSST), which included free speech and mental arithmetic tasks in front of an audience. Blood was collected at nine time points before, during and after the test. Plasma was assayed for 10 cytokines (IL1b, IL4, IL5, IL6, IL8, IL10, IL12p70, IL15, TNFα and IFNγ) in a multiplexed high-sensitivity assay for the Meso Scale Discovery platform. All analyses was performed on log2-transformed data to correct for non-normal distributions, and analysis of covariance for repeated measures were performed co-varying for age, sex, race and BMI. Area under the curve (AUCs) for each cytokine was computed using the trapezoidal rule on the raw data and response AUCs were calculated by subtracting baseline from post-baseline AUCs. The data was then log-transformed and used to look at factors such as length of illness, MFI and SF36 scores using Pearson correlation coefficients. Results: Significant baseline differences between CFS and NF were noted for IFNγ and IL8, with levels of each being higher in the well controls. Data for IL1b was not included in the analyses as many measures were below the 0.35 pg/ml lower limit of detection. For all cytokines, the TSST elicited a significant increase in cytokine secretion as determined by a paired t-test of each subject's peak level after baseline compared to baseline. All analytes showed a significant change after multiple test correction. Repeated measure MANOVA's were computed for overall TSST differences between CFS cases and well controls (group-effect) which showed differences for IFNg, IL15 and IL6. Differences were seen in response profiles (group by time-effects) for IL15 and IL12p70. Conclusions: We show that a psychosocial stressor modulates inflammatory activity. The precise mechanism of this is not known, it could possibly be attributed to the transient mobilization of leukocytes to the periphery caused by sympathetic nervous activation. The mechanism becomes important if we are to understand the differences evident between CFS subjects and well controls in their response to a stressor. The different response profiles between CFS people and NF controls for IL15 and IL12p70 are interesting as IL15 regulates T- and natural killer (NK) cell activation and proliferation, and IL12 plays an important role in the activities of T- and NK-cells. This study attempts to further our understanding of the pathophysiology of CFS using a new paradigm to look at differences between well controls, the application of a stressor and monitoring the response over time.
White,P	Barts and the London School of Medicine,	Letter to Editor: Reply to Sampson	IACSF/ME. 18 (3). Fall 2010.	Dear Editor, In the last edition of the *Bulletin*, Sampson published a criticism (1) of a cohort study

	Queen Mary University of London, St Bartholomew's Hospital, London, EC1A 7BE, UK E-mail - p.d.white@qmul.ac.uk			of patients recovering from infectious mononucleosis (IM), written by myself and colleagues (2). He suggests that our conclusion was wrong, and even suggests that part of our analysis was incorrect and misleading. Sampson concluded essentially that our data suggest that broad based definitions of CFS that include comorbid psychiatric disorders are predicted by different factors than those that do not. That is also what we concluded: "The predictors of a prolonged fatigue syndrome after an infection differ with both definition and time, depending particularly on the presence or absence of comorbid mood disorders."(2) He also implies that we included some subjects with psychiatric disorders without declaring this. We did not: all subjects received a standardised psychiatric interview and full details were published in the paper (2). Finally he suggests that we did not find that lack of physical fitness predicted CFS. We did, no matter how we defined CFS (2). Sampson went on to develop an argument that graded exercise therapy (GET) is not an effective treatment for CFS in the absence of comorbid mood disorders. It is: the first published trial of GET excluded patients with comorbid mood disorders (3). The PACE trial, which is the largest ever trial of graded exercise therapy, compared to other rehabilitative interventions, for people with CFS will report next year (4). This will provide the most definitive test so far of both the efficacy and safety of this treatment. See also: IACSF/ME. 18 (4). Winter 2011. Sampson, Reply to White; and White, Response to Sampson

2011				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No authors listed]		Patients' power and PACE.	Lancet. 2011 May 28;377(9780):1808. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36.	
[No authors listed]		Cause for concern.	Nature. 2011 Mar 17;471(7338):266.	
[No authors listed]		Too soon to translate?	Nat Med. 2011 Jul 7;17(7):751. doi: 10.1038/nm0711-751.	
Acehan D, Vaz F, Houtkooper RH, James J, Moore V, Tokunaga C, Kulik W, Wansapura J, Toth MJ, Strauss A, Khuchua Z.	Department of Pediatrics, Cincinnati Children's Hospital Medical Center and the University of Cincinnati, Cincinnati, Ohio 45229, USA.	Cardiac and skeletal muscle defects in a mouse model of human Barth syndrome.	J Biol Chem. 2011 Jan 14;286(2):899-908. Epub 2010 Nov 9.	Barth syndrome is an X-linked genetic disorder caused by mutations in the tafazzin (taz) gene and characterized by dilated cardiomyopathy, exercise intolerance, chronic fatigue, delayed growth, and neutropenia. Tafazzin is a mitochondrial transacylase required for cardiolipin remodeling. Although tafazzin function has been studied in non-mammalian model organisms, mammalian genetic loss of function approaches have not been used. We examined the consequences of tafazzin knockdown on sarcomeric mitochondria and cardiac function in mice. Tafazzin knockdown resulted in a dramatic decrease of tetralinoleoyl cardiolipin in cardiac and skeletal muscles and accumulation of monolysocardiolipins and cardiolipin molecular species with aberrant acyl groups. Electron microscopy revealed pathological changes in mitochondria, myofibrils, and mitochondrion-associated membranes in skeletal and cardiac muscles. Echocardiography and magnetic resonance imaging revealed severe cardiac abnormalities, including left ventricular dilation, left ventricular mass reduction, and depression of fractional shortening and ejection fraction in tafazzin-deficient mice. Tafazzin knockdown mice provide the first mammalian model system for Barth syndrome in which the pathophysiological relationships between altered content of mitochondrial phospholipids, ultrastructural abnormalities, myocardial and mitochondrial dysfunction, and clinical outcome can be completely investigated.
Alberts B.	Editor-in-Chief, Science, American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005, USA.	Editorial Expression of Concern.	Science. 2011 Jun 2. [Epub ahead of print]	In the issue of 23 October 2009, Science published a study by Lombardi et al. purporting to show that a retrovirus called XMRV (xenotropic murine leukemia virus-related virus) was present in the blood of 67% of patients with chronic fatigue syndrome (CFS) compared with 3.7% of healthy controls. A number of studies published elsewhere have failed to replicate these findings. In conjunction with two new Reports that strongly support the growing view that the association between XMRV and CFS likely reflects contamination of laboratories and research reagents with the virus, Science is publishing an Editorial Expression of Concern about the Lombardi et al. Report.

Alberts B.		Editorial expression of concern.	Science. 2011 Jul 1;333(6038):35. Comment on Science. 2009 Oct 23;326(5952):585-9.	
Alberts B.		Retraction. Retraction of Lombardi VC, Ruscetti FW, Das Gupta J, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA. Science. 2009 Oct 23;326(5952):585-9.	Science. 2011 Dec 23;334(6063):1636.	Science is fully retracting the report "Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome" (V. C. Lombardi et al., Science 326, 585 (2009); 10.1126/science.1179052)
Albright F, Light K, Light A, Bateman L, Cannon-Albright LA.	Pharmacotherapy Outcomes Research Center, Department of Pharmacotherapy, College of Pharmacy, University of Utah, USA. frederick.albright@pharm.utah.edu	Evidence for a heritable predisposition to Chronic Fatigue Syndrome.	BMC Neurol. 2011 May 27;11:62.	BACKGROUND: Chronic Fatigue Syndrome (CFS) came to attention in the 1980s, but initial investigations did not find organic causes. Now decades later, the etiology of CFS has yet to be understood, and the role of genetic predisposition in CFS remains controversial. Recent reports of CFS association with the retrovirus xenotropic murine leukemic virus-related virus (XMRV) or other murine leukemia related retroviruses (MLV) might also suggest underlying genetic implications within the host immune system. METHODS: We present analyses of familial clustering of CFS in a computerized genealogical resource linking multiple generations of genealogy data with medical diagnosis data of a large Utah health care system. We compare pair-wise relatedness among cases to expected relatedness in the Utah population, and we estimate risk for CFS for first, second, and third degree relatives of CFS cases. RESULTS: We observed significant excess relatedness of CFS cases compared to that expected in this population. Significant excess relatedness was observed for both close ($p < 0.001$) and distant relationships ($p = 0.010$). We also observed significant excess CFS relative risk among first (2.70, 95% CI: 1.56-4.66), second (2.34, 95% CI: 1.31-4.19), and third degree relatives (1.93, 95% CI: 1.21-3.07). CONCLUSIONS: These analyses provide strong support for a heritable contribution to predisposition to Chronic Fatigue Syndrome. A population of high-risk CFS pedigrees has been identified, the study of which may provide additional understanding.
Ali MA, Dale JK, Kozak CA, Goldbach-Mansky	Medical Virology Section, Laboratory of	Xenotropic murine leukemia virus-related virus is not	Virol J. 2011 Sep 24;8:450.	BACKGROUND: In 2009, xenotropic murine leukemia virus-related virus (XMRV) was reported in 67% of patients with chronic fatigue syndrome (CFS) compared to 4% of controls. Since then numerous reports failed to detect XMRV in other cohorts of CFS

R, Miller FW, Straus SE, Cohen JI.	Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA.	associated with chronic fatigue syndrome in patients from different areas of the us in the 1990s.		patients, and some studies suggested that XMRV sequences in human samples might be due to contamination of these samples with mouse DNA. RESULTS: We determined the prevalence of XMRV in patients with CFS from similar areas in the United States as the original 2009 study, along with patients with chronic inflammatory disorders and healthy persons. Using quantitative PCR, we initially detected very low level signals for XMRV DNA in 15% of patients with CFS; however, the frequency of PCR positivity was no different between patients with CFS and controls. Repeated attempts to isolate PCR products from these reactions were unsuccessful. These findings were supported by our observations that PHA and IL-2 stimulation of peripheral blood mononuclear cells from patients with apparently low levels of XMRV, which induced virus replication in the 2009 report, resulted in the disappearance of the signal for XMRV DNA in the cells. Immunoprecipitation of XMRV-infected cell lysates using serum from patients from whom we initially detected low levels of XMRV DNA followed by immunoblotting with antibodies to XMRV gp70 protein failed to detect antibody in the patients, although one control had a weak level of reactivity. Diverse murine leukemia virus (MLV) sequences were obtained by nested PCR with a similar frequency in CFS patients and controls. Finally, we did not detect XMRV sequences in patients with several chronic inflammatory disorders including rheumatoid arthritis, Bechet's disease, and systemic lupus erythematosus. CONCLUSIONS: We found no definitive evidence for XMRV DNA sequences or antibody in our cohort of CFS patients, which like the original 2009 study, included patients from diverse regions of the United States. In addition, XMRV was not detected in a cohort of patients with chronic inflammatory disorders.
Alraek T, Lee MS, Choi TY, Cao H, Liu J.	National Research Center for Complementary and Alternative Medicine, University of Tromsø, Norway. terje.alrak@uit.no	Complementary and alternative medicine for patients with chronic fatigue syndrome: a systematic review.	BMC Complement Altern Med. 2011 Oct 7;11:87.	BACKGROUND: Throughout the world, patients with chronic diseases/illnesses use complementary and alternative medicines (CAM). The use of CAM is also substantial among patients with diseases/illnesses of unknown aetiology. Chronic fatigue syndrome (CFS), also termed myalgic encephalomyelitis (ME), is no exception. Hence, a systematic review of randomised controlled trials of CAM treatments in patients with CFS/ME was undertaken to summarise the existing evidence from RCTs of CAM treatments in this patient population. METHODS: Seventeen data sources were searched up to 13th August 2011. All randomised controlled trials (RCTs) of any type of CAM therapy used for treating CFS were included, with the exception of acupuncture and complex herbal medicines; studies were included regardless of blinding. Controlled clinical trials, uncontrolled observational studies, and case studies were excluded. RESULTS: A total of 26 RCTs, which included 3,273 participants, met our inclusion criteria. The CAM therapy from the RCTs included the following: mind-body medicine, distant healing, massage, tuina and tai chi, homeopathy, ginseng, and dietary supplementation. Studies of qigong, massage and tuina were demonstrated to have positive effects, whereas distant healing failed to do so. Compared with placebo, homeopathy also had insufficient evidence of symptom improvement in CFS.

				Seventeen studies tested supplements for CFS. Most of the supplements failed to show beneficial effects for CFS, with the exception of NADH and magnesium. CONCLUSIONS: The results of our systematic review provide limited evidence for the effectiveness of CAM therapy in relieving symptoms of CFS. However, we are not able to draw firm conclusions concerning CAM therapy for CFS due to the limited number of RCTs for each therapy, the small sample size of each study and the high risk of bias in these trials. Further rigorous RCTs that focus on promising CAM therapies are warranted. © 2011 Alraek et al; licensee BioMed Central Ltd.
Anderson VR, Jason LA, Hlavaty LE, Porter N, Cudia J.	Department of Psychology, Michigan State University, East Lansing, USA.	A review and meta-synthesis of qualitative studies on Myalgic Encephalomyelitis/chronic fatigue syndrome.	Patient Educ Couns. 2012 Feb;86(2):147-55. Epub 2011 May 14.	OBJECTIVE: To review and synthesize findings across qualitative studies on Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS). METHODS: Articles were systematically reviewed and analyzed within a meta-analytic framework. Analyses included a multi-perspective examination of ME/CFS, as well as a comparative analysis of ME/CFS versus other chronic conditions. RESULTS: Thirty-four qualitative studies on ME/CFS were included. Findings include three substantive thematic areas that focus on: (1) experiences of people with ME/CFS, (2) experiences of physicians, and (3) themes that intersect both of these groups. For patients, illness development influenced identity, reductions in functioning, and coping. Physician-specific themes described lack of awareness about ME/CFS and recommended improvement in educational resources. Intersecting themes expressed issues with diagnosis creating tensions and fueling the stigmatization of ME/CFS. CONCLUSIONS: Findings indicate multilayered, context-specific experiences and ways in which both people with ME/CFS, as well as those involved in their lives (e.g., family or the medical community), interpret this illness. Future qualitative studies should recognize the various facets of the ME/CFS experience, the network members of people with ME/CFS, and the sociocultural environment through which the illness is understood. PRACTICE IMPLICATIONS: Health care professionals can gain unique insight from patient experiences, allowing for more accurate diagnoses and treatment recommendations. Copyright © 2011 Elsevier Ireland Ltd. All rights reserved.
Antiel RM, Caudill JS, Burkhardt BE, Brands CK, Fischer PR.	Department of Pediatric & Adolescent Medicine, Division of General Pediatric and Adolescent Medicine, Mayo Clinic, Rochester, MN 55905, USA. antiel.ryan@mayo.edu	Iron insufficiency and hypovitaminosis D in adolescents with chronic fatigue and orthostatic intolerance.	South Med J. 2011 Aug;104(8):609-11.	OBJECTIVES: More than 10% of adolescents suffer from severe fatigue and/or orthostatic intolerance. Adult studies show correlations between iron insufficiency and fatigue as well as between hypovitaminosis D and non-specific pain. We sought to determine whether there were correlations between nutritional factors (iron status, and serum vitamin D levels) and chronic ill health. METHODS: We reviewed records of 188 adolescents with symptoms of fatigue and/or orthostatic intolerance and who underwent autonomic reflex screening. RESULTS: Of the 188 patients, 130 patients (69%) had excessive postural tachycardia (PT) with a heart rate (HR) change of ≥30 bpm. 62 patients (47%, n = 131) had iron insufficiency with low iron stores, and 29 patients (22%, n = 131) were iron deficient. HR change did not correlate to ferritin level (P = 0.15). 21 patients (22%, n = 95) had hypovitaminosis D (25-hydroxyvitamin D ≤20 ng/mL). There was a significant association with hypovitaminosis D and

				orthostatic intolerance (P = 0.024). CONCLUSION: In patients presenting with chronic fatigue and/or orthostatic intolerance, low ferritin levels and hypovitaminosis D are common, especially in patients with PT.
Anty R, Marjoux S, Bekri S, DeGalleani L, Dainese R, Gelsi E, Cherikh F, Tran A, Piche T.	INSERM U895, Centre Hospitalier Universitaire of Nice-Digestive Center, Nice Cedex 3, France.	Plasma carnitine is associated with fatigue in chronic hepatitis C but not in the irritable bowel syndrome.	Aliment Pharmacol Ther. 2011 Apr;33(8):961-8. doi: 10.1111/j.1365-2036.2011.04608.x. Epub 2011 Mar 2. Comment in Aliment Pharmacol Ther. 2011 Jun;33(11):1252-3. Nat Rev Gastroenterol Hepatol. 2011 May;8(5):246.	BACKGROUND: Fatigue is an important determinant of altered quality of life in patients affected by chronic hepatitis C or the irritable bowel syndrome (IBS). AIM: In this study, we aimed at determining the contributory role of plasma levels of leptin and carnitine on fatigue in chronic hepatitis C and IBS. METHODS: We enrolled 81 patients with chronic hepatitis C, 42 with IBS and 44 healthy subjects. Fatigue was evaluated using the Fatigue Impact Scale questionnaire. Body composition was assessed through impedance analysis. Plasma carnitine and leptin were measured. RESULTS: Fatigue scores were significantly more elevated in patients with chronic hepatitis C and IBS than in healthy subjects. Patients with chronic hepatitis C but not IBS, had significant lower plasma levels of total and free carnitine adjusted for fat mass compared with healthy subjects. In patients with chronic hepatitis C and not with IBS, fatigue scores were negatively correlated with plasma levels of carnitine. Levels of free carnitine were significantly and independently associated with the severity of fatigue in patients with chronic hepatitis C [OR=2.019, P=0.02, CI 95% (1.01-1.23)]. CONCLUSIONS: In patients with chronic hepatitis C, the severity of fatigue is associated with a low level of carnitine, suggesting that an oral supplementation may be effective to relieve fatigue in chronic hepatitis C. The underlying mechanism of fatigue in IBS does not seem to involve carnitine. © 2011 Blackwell Publishing Ltd.
Arnett SV, Alleva LM, Korossy-Horwood R, Clark IA.	Research School of Biology, Australian National University, Australia. simon.arnett@anu.edu.au	Chronic fatigue syndrome--a neuroimmunological model.	Med Hypotheses. 2011 Jul;77(1):77-83. Epub 2011 Apr 6.	The aetiological and pathophysiological basis of chronic fatigue syndrome (CFS) remains a controversial field of inquiry in the research community. While CFS and similar disease conditions such as fibromyalgia (FM) and post-infectious encephalopathy have been the focus of intense scrutiny for the past 20 years, results of research were often contradictory and a cohesive pathological model has remained elusive. However, recent developments in understanding the unique immunophysiology of the brain may provide important clues for the development of a truly comprehensive explanation of the pathology of CFS. We argue that CFS pathogenesis lies in the influence of peripheral inflammatory events on the brain and the unique immunophysiology of the central nervous system. There is also evidence that CFS patients have a relative immunodeficiency that predisposes to poor early control of infection that leads to chronic inflammatory responses to infectious insults. The neurological and endocrine changes have been described in CFS patients support the view that CFS has an inflammatory pathogenesis when considered as a whole. An inflammatory model of disease also provides an explanation for the marked female sex bias associated with CFS. This review therefore posits the hypothesis that CFS as a disease of long-term inflammatory processes of the brain. We will also provide an investigative framework that could be used to justify the use of anti-TNF biological

				agents as a reliable and effective treatment approach to CFS, a syndrome that to date remains frustratingly difficult for both patients and health care professionals to manage. Copyright © 2011 Elsevier Ltd. All rights reserved.
Arredondo M, Hackett J, de Bethencourt FR, Treviño A, Escudero D, Collado A, Qiu X, Swanson P, Soriano V, de Mendoza C.	Hospital Carlos III, Infectious Diseases, Madrid, Spain; arredondo.miguel@gmail.com.	Prevalence of XMRV infection in different risk populations in Spain.	AIDS Res Hum Retroviruses. 2011 Dec 29. [Epub ahead of print]	Human infection with the xenotropic murine leukemia virus-related virus (XMRV) has been associated controversially with prostate cancer and chronic fatigue syndrome. Information is lacking about the mechanisms of transmission and potential risk groups for XMRV infection. Plasma and peripheral blood mononuclear cells (PBMCs) from individuals with retroviral infections, chronic viral hepatitis, autoimmune diseases, prostate cancer, chronic fatigue syndrome and blood donors were tested for XMRV markers. Antibodies to XMRV proteins p15E and gp70 were examined using research assays. DNA extracted from PBMCs was tested for the presence of XMRV gag and env sequences. A total of 1103 specimens belonging to individuals with chronic fatigue syndrome and/or fibromyalgia (437), prostate cancer (69), HIV-1 (149), HTLV-1/2 (31), chronic hepatitis B (81), chronic hepatitis C (72), autoimmune diseases (18) and blood donors (246) were examined. Overall, 3 samples (0.3%) were p15E seroreactive (2 HTLV-1 and 1 HCV patient). Another 15 (1.4%) were gp70 seroreactive (6 chronic fatigue syndrome-fibromyalgia, 4 blood donors, 2 HIV-1, 1 prostate cancer, 1 HBV and 1 HCV). Four specimens were initially positive for XMRV gag sequences, but none could be confirmed by repeated testing. In summary, no evidence of XMRV infection was found in populations with retroviral and viral hepatitis infections in Spain. Likewise, XMRV was not recognized in patients with autoimmune diseases, chronic fatigue syndrome-fibromyalgia, prostate cancer or healthy blood donors.
Asberg M, Wahlberg K, Wiklander M, Nygren A.	Institutionen för medicinska vetenskaper, Karolinska institutet vid Danderyds sjukhus, Stockholm. marie.asberg@ki.se	[Mental illness caused by stress...diagnostics, physiopathology and rehabilitation]. [Article in Swedish]	Lakartidningen. 2011 Sep 7-13;108(36):1680-3.	
Atzeni F, Cazzola M, Benucci M, Di Franco M, Salaffi F, Sarzi-Puttini P.	Rheumatology Unit, L. Sacco University Hospital, Milan, Italy. atzenifabiola@hotmail.com	Chronic widespread pain in the spectrum of rheumatological diseases.	Best Pract Res Clin Rheumatol. 2011 Apr;25(2):165-71.	Fibromyalgia (FM) is a rheumatic disease characterised by musculoskeletal pain, chronic diffuse tension and/or stiffness in joints and muscles, fatigue, sleep and emotional disturbances and pressure pain sensitivity in at least 11 of 18 tender points. There are currently no instrumental tests or specific diagnostic markers, and the characteristic symptoms of the disease overlap those of many other conditions classified in a different manner. FM is often associated with other diseases that act as confounding and aggravating factors, including primary Sjögren's syndrome (pSS), systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). It has been

				reported to coexist in 25% of patients with RA, 30% of patients with SLE and 50% of patients with pSS. Its clinical diagnosis is not easy because FM-like symptoms are frequent, and its differential diagnosis with other causes of chronic diffuse pain is difficult. This is even more true in the case of patients who are positive for antinuclear antibodies (ANAs) because, although sensitive, ANA positivity is not specific for SLE or connective tissue diseases, and can also be found in 10-15% of FM patients. Furthermore, composite indices such as the disease activity score (DAS)-28, which are widely used in everyday clinical practice and clinical trials, may be insufficient to evaluate real inflammatory activity in patients with RA associated with chronic pain syndromes such as FM, and can lead to an overestimate of disease activity in RA. The presence of diffuse pain in autoimmune rheumatic diseases compromises the quality of life of the patients, although overall mortality is not increased. A misdiagnosis harms the patients and the community. Rheumatologists should be able to recognise and distinguish primary and secondary FM, and need new guidelines and instruments to avoid making mistakes.
Bai N.		Donor fatigue. The Red Cross has banned chronic fatigue syndrome sufferers from giving blood. But does a virus really cause the disease?	Sci Am. 2011 Jul;305(1):26.	
Bakker RJ, van de Putte EM, Kuis W, Sinnema G.	Department of Pediatrics, Antonius Ziekenhuis, Sneek, The Netherlands. robhelbz@telfort.nl	Effects of an educational video film in fatigued children and adolescents: a randomised controlled trial.	Arch Dis Child. 2011 May;96(5):457-60. Epub 2010 Sep 22.	BACKGROUND: In many cases standard management for chronic fatigue syndrome (CFS) in children and adolescents is ineffective. OBJECTIVE: To evaluate the efficacy of a video film intervention in preventing the development of persistent fatigue and significant school absence in fatigued children and adolescents. DESIGN: Randomised controlled trial. PARTICIPANTS: 91 patients with fatigue; 50 were randomly assigned to receive the intervention (video film plus usual care) and 41 to usual care only. INTERVENTION: A video film on CFS and coping behaviour. MAIN OUTCOME MEASURES: Self-reported fatigue severity, physical activity, motivation, concentration and school absence. RESULTS: 79 patients had complete data at 12 months (42 in the video film and 37 in the usual care group). Mean fatigue severity and school absenteeism scores did not differ significantly, but in the intervention group the score for reduced motivation was higher (difference 2.9 (CI 0.1 to 5.7), p=0.038). 18% more patients in the intervention compared to the usual care group also had persistent fatigue with significant school absence. The odds of developing persistent fatigue and of missing >50% of school classes was 3.3 times higher in the intervention than in the usual care group (OR 3.3 (CI 1.0 to 11.3), p=0.046). CONCLUSION: This particular video

				film intervention plus usual care in children and adolescents with unexplained fatigue did not prevent an unfavourable outcome and possibly had an adverse effect in that it reduced motivation and increased the incidence of persistent fatigue with significant school absence. The use of this particular film is not recommended.
Balada E, Castro-Marrero J, Felip L, Vilardell-Tarrés M, Ordi-Ros J.	Research Unit in Systemic Autoimmune Diseases, Vall d'Hebron Research Institute, Vall d'Hebron Hospital, Autonomous University of Barcelona, Barcelona, Spain. ebalada@ir.vhebron.net	Xenotropic murine leukemia virus-related virus (XMRV) in patients with systemic lupus erythematosus.	J Clin Immunol. 2011 Aug;31(4):584-7. Epub 2011 Apr 21.	OBJECTIVES: Xenotropic murine leukemia virus-related virus (XMRV)-specific proviral DNA has been recently detected in peripheral blood mononuclear cells of patients with chronic fatigue syndrome. Since chronic fatigue is commonly reported in patients with systemic lupus erythematosus (SLE) we aimed at testing the presence of this virus in these patients. METHODS: Ninety-five SLE patients, 45 of whom had a Fatigue Severity Scale score higher than 3, were included. Molecular analyses were performed by PCR from DNA obtained from the whole blood of both SLE patients and 50 healthy controls. RESULTS: None of the 145 samples analyzed yielded the specific XMRV PCR product. CONCLUSIONS: We conclude that XMRV is not detected in blood neither from SLE patients nor from healthy controls. It leads to infer that other environmental and biological triggers (different from XMRV) may account for the increased levels of fatigue over the course of SLE.
Ballantyne AJ, Rogers WA.	Department of Primary Health Care and General Practice, School of Medicine and Health Sciences, Otago University Wellington, Wellington, New Zealand. angela.ballantyne@otago.ac.nz	Sex bias in studies selected for clinical guidelines.	J Womens Health (Larchmt). 2011 Sep;20(9):1297-306. Epub 2011 Aug 8.	OBJECTIVE: To determine the proportions of female participants in research studies selected to inform the development of national clinical guidelines and to assess these against the proportions of women affected by the conditions. METHODS: We assessed 392 published articles, involving a total of 5.2 million participants, cited as references in five influential clinical guidelines addressing the use of antiarrhythmics, chronic fatigue, depression, diabetes, and colorectal cancer. For each article, we extracted the number of female participants to determine any discrepancies in the sex of participants and if the proportion of female participants as research subjects reflected the sex distribution of patients affected by the condition. RESULTS: The overall and median percentages (per study) of females per guideline were: use of antiarrhythmics (35%, median 38%), chronic fatigue (70%, median 73%), colorectal cancer (67%, median 46%), depression (66%, median 66%), and diabetes (63%, median 50%). The baseline prevalence rates used for comparison purposes were (percentage female): antiarrhythmics (60% of patients 75(+) years); chronic fatigue (66%), colorectal cancer (46%), depression (66%), and diabetes (46%). CONCLUSIONS: The colorectal cancer, depression, and chronic fatigue guidelines were based on research populations that accurately reflected the sex distribution of the condition in the general population. Women were slightly overrepresented in the research studies supporting the diabetes guidelines and were significantly underrepresented in the research studies supporting the guidelines on the use of antiarrhythmics. Guideline developers should be aware of and comment on the potential impact of sex. Where

				the evidence base is lacking, guideline developers should highlight this and, where necessary, limit their specific conclusions to populations on whom the research was performed.
Bansal AS, Bradley AS, Bishop KN, Kiani-Alikhan S, Ford B.	Dept. of Immunology, Epsom and St. Helier University Hospitals NHS Trust, Carshalton, Surrey, SM5 1AA and Chronic Illness Research Team, Stratford Campus, University of East London, London E15 4LZ, UK. Amolak.Bansal@ESTH.nhs.uk	Chronic fatigue syndrome, the immune system and viral infection.	Brain Behav Immun. 2012 Jan;26(1):24-31. Epub 2011 Jul 2.	The chronic fatigue syndrome (CFS), as defined by recent criteria, is a heterogeneous disorder with a common set of symptoms that often either follows a viral infection or a period of stress. Despite many years of intense investigation there is little consensus on the presence, nature and degree of immune dysfunction in this condition. However, slightly increased parameters of inflammation and pro-inflammatory cytokines such as interleukin (IL) 1, IL6 and tumour necrosis factor (TNF) α are likely present. Additionally, impaired natural killer cell function appears evident. Alterations in T cell numbers have been described by some and not others. While the prevalence of positive serology for the common herpes viruses appears no different from healthy controls, there is some evidence of viral persistence and inadequate containment of viral replication. The ability of certain herpes viruses to impair the development of T cell memory may explain this viral persistence and the continuation of symptoms. New therapies based on this understanding are more likely to produce benefit than current methods.
Barnden LR, Crouch B, Kwiatek R, Burnet R, Mernone A, Chryssidis S, Scroop G, Del Fante P.	Department of Nuclear Medicine, The Queen Elizabeth Hospital, Adelaide, South Australia. Leighton.Barnden@health.sa.gov.au	A brain MRI study of chronic fatigue syndrome: evidence of brainstem dysfunction and altered homeostasis.	NMR Biomed. 2011 Dec;24(10):1302-12. doi: 10.1002/nbm.1692. Epub 2011 May 11.	To explore brain involvement in chronic fatigue syndrome (CFS), the statistical parametric mapping of brain MR images has been extended to voxel-based regressions against clinical scores. Using SPM5 we performed voxel-based morphometry (VBM) and analysed T(1) - and T(2) -weighted spin-echo MR signal levels in 25 CFS subjects and 25 normal controls (NC). Clinical scores included CFS fatigue duration, a score based on the 10 most common CFS symptoms, the Bell score, the hospital anxiety and depression scale (HADS) anxiety and depression, and hemodynamic parameters from 24-h blood pressure monitoring. We also performed group × hemodynamic score interaction regressions to detect locations where MR regressions were opposite for CFS and NC, thereby indicating abnormality in the CFS group. In the midbrain, white matter volume was observed to decrease with increasing fatigue duration. For T(1) -weighted MR and white matter volume, group × hemodynamic score interactions were detected in the brainstem [strongest in midbrain grey matter (GM)], deep prefrontal white matter (WM), the caudal basal pons and hypothalamus. A strong correlation in CFS between brainstem GM volume and pulse pressure suggested impaired cerebrovascular autoregulation. It can be argued that at least some of these changes could arise from astrocyte dysfunction. These results are consistent with an insult to the midbrain at fatigue onset that affects multiple feedback control loops to suppress cerebral motor and cognitive activity and disrupt local CNS homeostasis, including resetting of some elements of the autonomic nervous system (ANS).

Barregard L, Rekić D, Horvat M, Elmberg L, Lundh T, Zachrisson O.	Department of Occupational and Environmental Medicine, Sahlgrenska Academy, University of Gothenburg, SE 405 30 Gothenburg, Sweden. lars.barregard@amm.gu.se	Toxicokinetics of mercury after long-term repeated exposure to thimerosal-containing vaccine.	Toxicol Sci. 2011 Apr;120(2):499-506. Epub 2011 Jan 20.	The preservative thimerosal contains ethyl mercury (EtHg). Concerns over possible toxicity have re-emerged recently due to its presence in (swine and other) flu vaccines. We examined the potential accumulation of mercury in adults given repeated injections of a thimerosal-preserved vaccine for many years. Fifteen female patients were recruited from an outpatient clinic running a clinical trial with repeated injections (1 ml every 3-4 weeks) of a staphylococcus toxoid vaccine containing 0.01% thimerosal to treat chronic fatigue syndrome. Fifteen untreated female patients with the same diagnoses served as controls. Blood samples were taken before injecting the vaccine, 1 day later, about 2 weeks later, and just before the next injection. In the 15 controls, samples were taken twice. Blood was analyzed for total mercury and EtHg. The toxicokinetics were assessed for each patient separately as well as with a population-based pharmacokinetic model. Total mercury in blood increased on Day 1 in all treated patients (median: 0.33, range: 0.17-1.3 µg/l), as did EtHg (median: 0.14 µg/l, range: 0.06-0.43 µg/l). After a few weeks, levels were back to normal and similar to those in controls. Levels of methyl mercury (MeHg; from fish consumption) were much higher than those of EtHg. After exclusion of an outlier, the mean half-life in a population-based model was 5.6 (95% CI: 4.8-6.3) days. The results indicate that mercury from thimerosal is not accumulated in blood in adults. This is in accordance with short half-lives and rapid metabolism of EtHg to inorganic mercury.
Barros SM, Carvalho JF.	Rheumatology Division, Hospital Naval Marcílio Dias, Rio de Janeiro, Brazil.	Shoenfeld's syndrome after pandemic influenza A/H1N1 vaccination.	Acta Reumatol Port. 2011 Jan-Mar;36(1):65-8.	Recently, reports have suggested grouping different autoimmune conditions that are triggered by external stimuli as a single syndrome called autoimmune/inflammatory syndrome induced by adjuvants (ASIA). This syndrome is characterized by the appearance of myalgia, myositis, muscle weakness, arthralgia, arthritis, chronic fatigue, sleep disturbances, cognitive impairment and memory loss, and the possible emergence of a demyelinating autoimmune disease caused by systemic exposure after vaccines and adjuvants. In the current study, the authors reported the first Brazilian case of a woman who developed ASIA, which was characterized by arthralgia, changes in inflammatory markers, and chronic fatigue, after the pandemic anti-influenza A/H1N1 vaccine without causing any other rheumatic disease, and it had a positive outcome.
Bhui KS, Dinos S, Ashby D, Nazroo J, Wessely S, White PD.	Centre for Psychiatry, Wolson Institute of Preventive Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University	Chronic fatigue syndrome in an ethnically diverse population: the influence of psychosocial adversity and physical inactivity.	BMC Med. 2011 Mar 21;9:26.	BACKGROUND: Chronic fatigue syndrome (CFS) is a complex multifactorial disorder. This paper reports the prevalence of chronic fatigue (CF) and CFS in an ethnically diverse population sample and tests whether prevalence varies by social adversity, social support, physical inactivity, anxiety and depression. METHODS: Analysis of survey data linking the Health Survey for England (1998 and 1999) and the Ethnic Minority Psychiatric Illness Rates in the Community (EMPIRIC) study undertaken in 2000. The study population comprised a national population sample of 4,281 people ages 16 to 74 years. CF and CFS were operationally defined on the basis of an interview in the EMPIRIC study, alongside questions about psychosocial risk factors. Previous illnesses were reported in the Health Survey for England during 1998 and

	of London, London, UK. k.s.bhui@qmul.ac.uk			1999, as was physical inactivity. RESULTS: All ethnic minority groups had a higher prevalence of CFS than the White group. The lowest prevalence was 0.8% in the White group, and it was highest at 3.5% in the Pakistani group (odds ratio (OR), 4.1; 95% confidence interval (95% CI), 1.6 to 10.4). Anxiety (OR, 1.8; 95% CI, 1.4 to 2.2), depression (OR, 1.4; 95% CI, 1.1 to 1.8), physical inactivity (OR, 2.0; 95% CI, 1.1 to 3.8), social strain (OR, 1.24; 95% CI, 1.04 to 1.48) and negative aspects of social support (OR, 2.12; 95% CI, 1.4 to 3.3) were independent risk factors for CFS in the overall sample. Together these risk factors explained ethnic differences in the prevalence of CFS, but no single risk factor could explain a higher prevalence in all ethnic groups. CONCLUSIONS: The prevalence of CFS, but not CF, varies by ethnic group. Anxiety, depression, physical inactivity, social strain and negative aspects of social support together accounted for prevalence differences of CFS in the overall sample.
Biswal B, Kunwar P, Natelson BH.	Department of Radiology, UMDNJ-New Jersey Medical School, Newark NJ, USA.	Cerebral blood flow is reduced in chronic fatigue syndrome as assessed by arterial spin labeling.	J Neurol Sci. 2011 Feb 15;301(1-2):9-11. Epub 2010 Dec 16.	BACKGROUND: Chronic fatigue syndrome is diagnosed by a set of clinical criteria and therefore is probably heterogeneous. Earlier reports tested the hypothesis that the syndrome had a neurological substrate by doing studies of cerebral blood flow (CBF) but with discrepant results. One possible reason for the discrepancy was that relative CBF was assessed. We found reduced CBF in an earlier study of absolute CBF using xenon-CT. The purpose of this study was to use a second method of assessing CBF and to look within the study group for heterogeneity of responses. METHOD: Eleven CFS patients and 10 age matched healthy controls underwent neuroimaging using arterial spin labeling to determine their regional and global absolute CBF. A template was constructed based on the control data, and individual patient montages were compared on a case by case basis to determine if differences in regions of interest occurred. RESULTS: The patients as a group had significantly lower global CBF than the controls. The reduction in CBF occurred across nearly every region assessed. Nine of the 11 patients showed these reductions compared to the average control data, while two patients showed actual increases relative to the controls. CONCLUSION: The data extend our earlier observation that CFS patients as a group have broad decreases in CBF compared to healthy controls. However, as expected, the effect was not homogeneous in that 2 of the 11 patients studied showed actual increases in CBF relative to controls. Copyright © 2010 Elsevier B.V. All rights reserved.
Blankfield A.	Adele Blankfield B.Sc. M.B., B.Ch., 29 Wills Street, KEW VIC 3101, AUSTRALIA, Email: gjshnier@bigpond.net.au.	Kynurenine pathway Hypothesis: The nature of the chronic Fatigue syndrome (cFs) Revisited.	Int J Tryptophan Res. 2011;4:47-8. Epub 2011 Jul 31.	
Blazquez A,	a Faculty of	Psycho-physiological	Psychol Health Med.	The quality of dyadic adjustment is likely to play an important role in patients'

Guillamó E, Alegre J, Ruiz E, Javierre C.	Medicine, Department of Physiological Sciences II , Medical School, University of Barcelona , IDIBELL. L'Hospitalet , Barcelona , Spain.	impact on women with chronic fatigue syndrome in the context of their couple relationship.	2011 Jul 11. [Epub ahead of print]	relational problems and may also be associated with the clinical presentation of chronic fatigue syndrome (CFS) symptoms. The objective of this study was (1) to determine whether CFS patients and their partners have similar perceptions of their dyadic adjustment and (2) to evaluate whether the influence of dyadic satisfaction in women with CFS, as well as common psychological parameters such as anxiety, may correlate with physiological responses at rest and/or when performing very low intensity exercise. Forty females with CFS and their partners completed the Dyadic Adjustment Scale, the State-Trait Anxiety Inventory, and the Hospital Anxiety and Depression scale. The cardiovascular adaptation of patients was evaluated during resting conditions and on a precalibrated cycle ergometer while performing very low intensity exercise. Patients and partners had similar perceptions of their marital relationship. Both at rest and during very low workload, various physiological parameters in the patient group showed statistical correlations with certain psychological parameters. Several psychological variables, such as anxiety and dyadic adjustment, were associated with the cardioventilatory response monitored at rest and during very low intensity exercise. Further studies are needed to determine the nature of this association.
Bleijenberg G, Knoop H.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Netherlands. G.Bleijenberg@nkcv.umcn.nl	Chronic fatigue syndrome: where to PACE from here?	Lancet. 2011 Mar 5;377(9768):786-8. Epub 2011 Feb 18. Comment on Lancet. 2011 Mar 5;377(9768):823-36.	
Blomberg J, Sheikholvaezin A, Elfaitouri A, Blomberg F, Sjösten A, Mattson Ulfstedt J, Pipkorn R, Källander C, Ohrmalm C, Sperber G.	Section of Clinical Microbiology, Department of Medical Sciences, Uppsala University, 751 05 Uppsala, Sweden.	Phylogeny-directed search for murine leukemia virus-like retroviruses in vertebrate genomes and in patients suffering from myalgic encephalomyelitis/chronic fatigue syndrome and prostate cancer.	Adv Virol. 2011;2011:341294. Epub 2011 Sep 4.	Gammaretrovirus-like sequences occur in most vertebrate genomes. Murine Leukemia Virus (MLV) like retroviruses (MLLVs) are a subset, which may be pathogenic and spread cross-species. Retroviruses highly similar to MLLVs (xenotropic murine retrovirus related virus (XMRV) and Human Mouse retrovirus-like RetroViruses (HMRVs)) reported from patients suffering from prostate cancer (PC) and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) raise the possibility that also humans have been infected. Structurally intact, potentially infectious MLLVs occur in the genomes of some mammals, especially mouse. Mouse MLLVs contain three major groups. One, MERV G3, contained MLVs and XMRV/HMRV. Its presence in mouse DNA, and the abundance of xenotropic MLVs in biologicals, is a source of false positivity. Theoretically, XMRV/HMRV could be one of several MLLV transspecies infections. MLLV pathobiology and diversity indicate optimal strategies for investigating XMRV/HMRV in humans and raise ethical concerns. The alternatives that XMRV/HMRV may give a hard-to-detect "stealth"

				infection, or that XMRV/HMRV never reached humans, have to be considered.
Boneva RS, Maloney EM, Lin JM, Jones JF, Wieser F, Nater UM, Heim CM, Reeves WC.	Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. rboneva@cdc.gov	Gynecological history in chronic fatigue syndrome: a population-based case-control study.	J Womens Health (Larchmt). 2011 Jan;20(1):21-8. Epub 2010 Nov 20.	BACKGROUND: Chronic fatigue syndrome (CFS) affects disproportionately more women than men, and the condition is more common at perimenopause. We examined gynecological history events as risk factors for CFS. METHODS: In a case-control study from a randomly selected population sample from Wichita, Kansas, 36 women with CFS and 48 nonfatigued controls, of similar age, race, and body mass index (BMI), answered a structured gynecological history questionnaire. RESULTS: CFS cases and controls had the same mean age (51 years) and age at menarche (12 years). Overall, a greater proportion of women with CFS than controls reported pelvic pain unrelated to menstruation (22.2% vs. 1.7%, p = 0.004), endometriosis (36.1% vs. 16.7, %, p = 0.046), and periods of amenorrhea (53.9 % vs. 46.2%, p = 0.06). Compared to controls, women in the CFS group had a higher mean number of pregnancies (2.8 vs 2.0, p = 0.05) and gynecological surgeries (1.8 vs. 1.1, p = 0.05). Similar proportions of the CFS (69.4%) and control (72.9%) groups were menopausal. Although menopausal women in the CFS and control groups had similar mean age (55.5 and 55.8, respectively), menopause occurred about 4.4 years earlier in the CFS group (41.7 years vs. 46.1 years, respectively, p = 0.11). Among menopausal women, 76% of the CFS group reported hysterectomy vs. 54.6% of controls (p = 0.09), and 56% of women with CFS reported oophorectomy vs. 34.3% of controls (p = 0.11). CONCLUSIONS: The higher prevalence of gynecological conditions and gynecological surgeries in women with CFS highlights the importance of evaluating gynecological health in these patients and the need for more research to clarify the chronologic and the pathophysiological relationships between these conditions and CFS.
Bould H, Lewis G, Emond A, Crawley E.	Centre for Child and Adolescent Health, University of Bristol, Cotham Hill, Bristol, UK.	Depression and anxiety in children with CFS/ME: cause or effect?	Arch Dis Child. 2011 Mar;96(3):211-4. Epub 2010 Jul 26.	
Braz Ade S, de Paula AP, Diniz Mde F, de Almeida RN.	Universidade Federal da Paraiba, UFPB, Brazil. alessabraz@gmail.com	Non-pharmacological therapy and complementary and alternative medicine in fibromyalgia. [Article in English, Portuguese]	Rev Bras Reumatol. 2011 Jun;51(3):269-82.	Fibromyalgia is a chronic painful syndrome that affects up to 5% of the world population. It is associated with sleep and mood disorders, fatigue, and functional disability. Its pathogenesis involves a disorder of the central modulation of pain, impairment of the descending inhibitory system, and hyperactivity of substance P. Because of the extensive symptomatology of patients with fibromyalgia and its multifactorial pathogenesis, its ideal treatment requires a multidisciplinary approach including the association of pharmacological and non-pharmacological therapies. The pharmacological therapy currently recommended for the syndrome includes antidepressants, calcium-channel modulators, muscle relaxants, and analgesics. In most cases, the non-pharmacological treatment consists of patient education, supervised aerobic physical activity, and cognitive-behavioral therapy. However, many patients do not respond satisfactorily, or have side effects associated with the long-

				term use of drugs, in addition to reporting difficulties in adhering to a therapy based on exercises and physical medicine. Thus, physicians and patients are increasingly interested in an alternative and complementary therapy for fibromyalgia. This review approaches the different therapeutic modalities used in fibromyalgia, emphasizing the evidence of non-pharmacological therapy and use of alternative and complementary medicine for these patients.
Brenu EW, van Driel ML, Staines DR, Ashton KJ, Ramos SB, Keane J, Klimas NG, Marshall-Gradisnik SM.	Population Health and Neuroimmunology Unit, Faculty of Health Science and Medicine, Bond University, Robina, Queensland, Australia.	Immunological abnormalities as potential biomarkers in Chronic Fatigue Syndrome/Myalgic Encephalomyelitis.	J Transl Med. 2011 May 28;9:81.	BACKGROUND: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is characterised by severe prolonged fatigue, and decreases in cognition and other physiological functions, resulting in severe loss of quality of life, difficult clinical management and high costs to the health care system. To date there is no proven pathomechanism to satisfactorily explain this disorder. Studies have identified abnormalities in immune function but these data are inconsistent. We investigated the profile of markers of immune function (including novel markers) in CFS/ME patients. METHODS: We included 95 CFS/ME patients and 50 healthy controls. All participants were assessed on natural killer (NK) and CD8(+) T cell cytotoxic activities, Th1 and Th2 cytokine profile of CD4(+) T cells, expression of vasoactive intestinal peptide receptor 2 (VPACR2), levels of NK phenotypes (CD56(bright) and CD56(dim)) and regulatory T cells expressing FoxP3 transcription factor. RESULTS: Compared to healthy individuals, CFS/ME patients displayed significant increases in IL-10, IFN-γ, TNF-α, CD4(+)CD25(+) T cells, FoxP3 and VPACR2 expression. Cytotoxic activity of NK and CD8(+) T cells and NK phenotypes, in particular the CD56(bright) NK cells were significantly decreased in CFS/ME patients. Additionally granzyme A and granzyme K expression were reduced while expression levels of perforin were significantly increased in the CFS/ME population relative to the control population. These data suggest significant dysregulation of the immune system in CFS/ME patients. CONCLUSIONS: Our study found immunological abnormalities which may serve as biomarkers in CFS/ME patients with potential for an application as a diagnostic tool.
Brkić S, Tomić S, Ruzić M, Marić D.	Hospital for Infectious Diseases, Clinical Centre of Vojvodina, Hajduk Veljkova 1-9, 21000 Novi Sad, Serbia. tomkis@eunet.rs	Chronic fatigue syndrome.	Srp Arh Celok Lek. 2011 Mar-Apr;139(3-4):256-61.	Chronic fatigue syndrome (CFS) is defined by a profound, debilitating fatigue, lasting for at least 6 months and resulting in a substantial reduction of occupational, personal, social and educational status. CFS is a relatively poorly recognized clinical entity, although everyday experience shows that there are many patients with CFS symptoms. The incidence and prevalence of CFS remain unknown in most countries; however, the working population is most affected with predominantly female patients in generative period. Although, CFS was first mentioned four centuries ago, mysterious aethiopathogensis of CFS still intrigues scientists as hundreds of studies are still published every year on the subject. About 80 different aetiological CFS factors are mentioned, which can be classified into five basic groups: genetics, immunology, infectious diseases, endocrinology and neuropsychiatry-psychology. Even today the condition is passed established based on the diagnosis by exclusion of organic and psychiatric disorders, which demands a multidisciplinary approach. As the

				syndrome is often misdiagnosed and mistreated, self-medication is not uncommon in CFS patients'. In addition, such patients usually suffer for years tolerating severe fatigue. Thus, at the moment there are three priorities regarding CFS; understanding pathogenesis, development of diagnostic tests and creating efficient treatment program.
Brooks J, Lycett-Lambert K, Caminiti K, Merks H, McMillan R, Sandstrom P.	National HIV & Retrovirology Laboratories, National Microbiology Laboratory, Public Health Agency of Canada, Ottawa, Canada. james.brooks@phac-aspc.gc.ca	No evidence of cross-species transmission of mouse retroviruses to animal workers exposed to mice.	Transfusion. 2012 Feb;52(2):317-25. doi: 10.1111/j.1537-2995.2011.03463.x. Epub 2011 Dec 30.	BACKGROUND: Although recent data have brought into question the association between xenotropic murine leukemia virus-related virus (XMRV) and chronic fatigue syndrome, one group has reported evidence of human infection with distinct polytropic murine leukemia viruses (MLVs). Occult retroviral infection among humans poses a significant public health risk should it be introduced into the blood supply. To explore the possibility of cross-species transmission of MLVs to humans, we sought molecular and serologic evidence of XRMV/MLV infection among a cohort of animal workers highly exposed to mice. STUDY DESIGN AND METHODS: Before the commencement of the study, the laboratory and equipment were demonstrated to be free of XMRV/MLV DNA sequences. DNA extracted from 43 animal workers was tested using nested polymerase chain reaction (PCR) with published primer sets, targeting regions of XMRV and MLV gag. Negative controls were assayed in a 1:1 ratio with specimens. Serum specimens were tested using a validated immunoblot assay containing cross-reactive XMRV antigens. RESULTS: Initial molecular assays demonstrated that the physical space and laboratory equipment were free of MLV and XMRV DNA sequences. Nested PCR assays using multiple primer sets successfully amplified XMRV and MLV sequences from positive controls with high sensitivity. A single, nonreproducible, false-positive result from one specimen was shown to be the result of subsequent contamination. Immunoblotting of all subjects' sera failed to demonstrate any evidence of seroreactivity to XMRV proteins. CONCLUSIONS: There was no evidence of human infection with XMRV/MLV among a cohort of individuals highly exposed to mice. These data suggest that the likelihood of cross-species transmission events of MLV from mice to humans is low. © 2012 American Association of Blood Banks.
Brooks SK, Rimes KA, Chalder T.	Department of Psychological Medicine, King's College London, UK.	The role of acceptance in chronic fatigue syndrome.	J Psychosom Res. 2011 Dec;71(6):411-5. Epub 2011 Sep 16.	OBJECTIVE: In this paper we consider the role that acceptance plays in fatigue and physical and social functioning. We predicted that lack of acceptance would be positively correlated with fatigue and impairment in functioning; that there would be a significant relationship between perfectionism and acceptance; and cognitive behavioural therapy (CBT) would increase acceptance. METHODS: Two hundred and fifty nine patients with chronic fatigue syndrome (CFS) completed questionnaires measuring fatigue, physical functioning, work and social adjustment, lack of acceptance, perfectionism and depression. Ninety consecutive attenders received a course of CBT and completed further questionnaires at discharge and 3months post-treatment. Correlations and multiple hierarchical regressions were used to determine relationships between acceptance, perfectionism and clinical outcome variables.

				RESULTS: At baseline, lack of acceptance was the key factor associated with impaired physical functioning and work and social adjustment. Lack of acceptance and doubts about actions were associated with fatigue in a multiple regression analysis. At discharge and follow-up patients showed significantly increased acceptance, as well as reduced Concern over Mistakes, less fatigue and impairment of physical functioning, and improved work and social adjustment. CONCLUSION: This is the first study to our knowledge which shows a change in acceptance after CBT and a relationship between acceptance and perfectionism. Acceptance may be an important factor to consider within treatments for CFS. 2011 Elsevier Inc. All rights reserved.
Brown M, Kaplan C, Jason L.	DePaul University, Chicago, USA.	Factor Analysis of the Beck Depression Inventory-ii With Patients With Chronic Fatigue Syndrome.	J Health Psychol. 2011 Nov 21. [Epub ahead of print]	This study examined the properties of the Beck Depression Inventory-II (BDI-II) in a sample of 111 patients with chronic fatigue syndrome (CFS). Exploratory factor analysis identified two factors. The mean score for the Somatic-Affective factor was significantly higher than the Cognitive factor. Convergent and discriminant validity were assessed for BDI-II total score, the two factor scores, and the BDI for Primary Care (BDI-PC). The BDI-PC and Cognitive factor demonstrated superior validity. Results suggest patients endorse BDI-II somatic items that overlap with CFS symptoms at a high rate. Factor scores should be evaluated separately, or the BDI-PC should be utilized with this population.
Brown M, Khorana N, Jason LA.	DePaul University. mbrown59@depaul.edu	The role of changes in activity as a function of perceived available and expended energy in nonpharmacological treatment outcomes for ME/CFS.	J Clin Psychol. 2011 Mar;67(3):253-60. doi: 10.1002/jclp.20744. Epub 2010 Oct 25.	Nonpharmacological interventions for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) often emphasize gradual increases in activity to promote improvement in physical functioning and fatigue. The energy envelope theory may provide a framework for understanding the relationship between changes in activity level and outcomes for patients with ME/CFS. This study examined the relationship between energy envelope and changes in activity after nonpharmacological interventions in a sample of 44 adults with ME/CFS. Results showed that those who were within their energy envelope before treatment showed more improvement in physical functioning and fatigue compared with those outside of their energy envelope. These findings suggest that an assessment of perceived available and expended energy could help guide the development of individualized nonpharmacological interventions for people with ME/CFS. © 2010 Wiley Periodicals, Inc.
Burgess M, Andiappan M, Chalder T.	South London & Maudsley Trust, London, UK.	Cognitive Behaviour Therapy for Chronic Fatigue Syndrome in Adults: Face to Face versus Telephone Treatment - A Randomized Controlled Trial.	Behav Cogn Psychother. 2012 Mar;40(2):175-91. Epub 2011 Sep 20.	Background: Previous research has shown that face to face cognitive behaviour therapy (CBT) is an effective treatment for chronic fatigue syndrome (CFS)/Myalgic Encephalomyelitis (ME). However, some patients are unable to travel to the hospital for a number of reasons. Aims: The aim of this study was to assess whether face to face CBT was more effective than telephone CBT (with face to face assessment and discharge appointment) for patients with CFS. Method: Patients aged 18-65 were recruited from consecutive referrals to the Chronic Fatigue Syndrome (CFS) Research and Treatment Unit at The South London and Maudsley NHS Trust in London. Participants were randomly allocated to either face to face CBT or telephone CBT by a

				departmental administrator. Blinding of participants and care givers was inappropriate for this trial. A parallel-groups randomised controlled trial was used to compare the two treatments. The primary outcomes were physical functioning and fatigue. Results: Significant improvements in the primary outcomes of physical functioning and fatigue occurred and were maintained to one year follow-up after discharge from treatment. Improvements in social adjustment and global outcome were noted and patient satisfaction was similar in both groups. Conclusions: Results from this study indicate that telephone CBT with two face to face appointments is a mild to moderately effective treatment for CFS and may be offered to patients where face to face treatment is not a viable option. Despite these encouraging conclusions, dropout was relatively high and therapists should be aware of this potential problem.
Burkhardt BE, Fischer PR, Brands CK, Porter CB, Weaver AL, Yim PJ, Pianosi PT.	Department of Pediatric Cardiology and Congenital Heart Disease, University Medical Center Freiburg, Freiburg, Germany.	Exercise performance in adolescents with autonomic dysfunction.	J Pediatr. 2011 Jan;158(1):15-9, 19.e1. Epub 2010 Sep 1. Comment in J Pediatr. 2011 Jan;158(1):4-6.	OBJECTIVE: To test the hypothesis that excessive postural tachycardia is associated with deconditioning rather than merely being an independent sign of autonomic dysfunction in patients with postural orthostatic tachycardia syndrome (POTS). STUDY DESIGN: We retrospectively analyzed records from 202 adolescents who underwent both head up-tilt and maximal exercise testing. Patients were classified as POTS if they had ≥ 30 min(-1) rise in heart rate (HR) after tilt-table test; and deconditioned if peak O(2) uptake was < 80% predicted. Changes in HR during exercise and recovery were compared between groups. RESULTS: Two-thirds of patients were deconditioned, irrespective of whether they fulfilled diagnostic criteria for POTS, but peak O(2) uptake among patients with POTS was similar to patients without POTS. HR was higher at rest and during exercise; whereas stroke volume was lower during exercise, and HR recovery was slower in patients with POTS compared with patients without POTS. CONCLUSIONS: Most patients who presented with chronic symptoms of dizziness, fatigue, or pre-syncope, were deconditioned, but, because the proportion of deconditioned patients was similar in POTS vs non-POTS groups, we conclude that HR changes in POTS are not solely because of inactivity resulting in deconditioning. Copyright © 2011 Mosby, Inc. All rights reserved.
Busch AJ, Webber SC, Brachaniec M, Bidonde J, Bello-Haas VD, Danyliw AD, Overend TJ, Richards RS, Sawant A, Schachter CL.	School of Physical Therapy, University of Saskatchewan, 1121 College Drive, Saskatoon, Saskatchewan S7N 0W3, Canada. angela.busch@usask.ca	Exercise therapy for fibromyalgia.	Curr Pain Headache Rep. 2011 Oct;15(5):358-67.	Fibromyalgia syndrome, a chronic condition typically characterized by widespread pain, nonrestorative sleep, fatigue, cognitive dysfunction, and other somatic symptoms, negatively impacts physical and emotional function and reduces quality of life. Exercise is commonly recommended in the management of people with fibromyalgia, and interest in examining exercise benefits for those with the syndrome has grown substantially over the past 25 years. Research supports aerobic and strength training to improve physical fitness and function, reduce fibromyalgia symptoms, and improve quality of life. However, other forms of exercise (e.g., tai chi, yoga, Nordic walking, vibration techniques) and lifestyle physical activity also have been investigated to determine their effects. This paper highlights findings from recent randomized controlled trials and reviews of exercise for people with fibromyalgia, and includes information regarding factors that influence response and

				adherence to exercise to assist clinicians with exercise and physical activity prescription decision-making to optimize health and well-being.
Bürgel B, Friesland M, Koch A, Manns MP, Wedemeyer H, Weissenborn K, Schulz-Schaeffer WJ, Pietschmann T, Steinmann E, Ciesek S.	Division of Experimental Virology, TWINCORE, Centre for Experimental and Clinical Infection Research, Medical School Hannover (MHH) and Helmholtz Centre for Infection Research (HZI), Hannover, Germany.	Hepatitis C virus enters human peripheral neuroblastoma cells - evidence for extra-hepatic cells sustaining hepatitis C virus penetration.	J Viral Hepat. 2011 Aug;18(8):562-70. doi: 10.1111/j.1365-2893.2010.01339.x. Epub 2010 Jun 23.	Patients with chronic hepatitis C virus (HCV) infection show an increased incidence of nervous system disorders such as chronic fatigue syndrome, depression and cognitive dysfunction. It is unclear whether this is because of HCV replication in the brain and in peripheral neuronal cells or to more indirect effects of HCV infection on the central or peripheral nervous system. The aim of this study was to investigate whether cells originating from these tissues are permissive for HCV cell entry, RNA replication and virus assembly. Among eight cell lines analysed, the human peripheral neuroblastoma cell line SKNMC expressed all HCV entry factors and was efficiently infected with HCV pseudoparticles (HCVpp) independent of the HCV genotype. All remaining cell types including human neuroblastoma and glioblastoma cell lines and microglial cells lacked expression of at least one host factor essential for HCV entry. When transfected with HCV luciferase reporter virus RNA, inoculated with HCV reporter viruses or challenged with high-titre cell culture-derived HCV, none of these cells supported detectable HCV RNA replication. Thus, in conclusion, this comprehensive screening did not reveal evidence directly strengthening the notion that HCV enters and replicates in the central nervous system. However, productive viral entry into the peripheral neuroblastoma cell line SKNMC indicates that HCV may penetrate into certain nonhepatic cell types which may serve as viral reservoirs and could modulate viral pathogenesis. © 2010 Blackwell Publishing Ltd.
Callaway E.		Virology: Fighting for a cause.	Nature. 2011 Mar 17;471(7338):282-5.	
Caminero A, Bartolomé M.	Multiple Sclerosis Unit, Department of Neurology, Complejo Asistencial de Ávila, Spain. acaminero@saludcastillayleon.es	Sleep disturbances in multiple sclerosis.	46. J Neurol Sci. 2011 Oct 15;309(1-2):86-91. Epub 2011 Aug 3.	OBJECTIVES: The frequency of sleep disturbances in multiple sclerosis (MS), and their impact on the quality of life of MS patients, have traditionally been underestimated. Here we review the most common sleep disorders seen in this disease, their prevalence, pathophysiology, clinical manifestations and current treatments. METHOD: We begin with a brief description of epidemiological data on sleep disturbances in MS, explain how these disturbances increase potential associated morbidities, and discuss the bidirectional relationship established between these two comorbid conditions (i.e. MS worsens sleep disturbances and vice versa). We then analyze the main dyssomnias and parasomnias described in MS: insomnia, circadian rhythm disorders, drug-induced sleep disturbances, restless legs syndrome (RLS) and periodic leg movements (PLM), respiratory disorders during sleep, narcolepsy-cataplexy syndrome and REM sleep behavior disorder (RBD). We also review the relationship between sleep disturbances and chronic fatigue syndrome, which is very frequent in MS patients. CONCLUSION: Sleep disturbances are more common in MS patients than in the general population and limit these patients' quality of life. Therefore, we believe that these disturbances should be a focal point in any multidisciplinary treatment for MS. Copyright © 2011 Elsevier B.V. All rights reserved.

Cao Y, Hu Y, Liu P, Zhao HX, Zhou XJ, Wei YM.	Department of Clinical Pharmacology, Chinese PLA General Hospital, Beijing 100853, China.	Effects of a Chinese traditional formula Kai Xin San (KXS) on chronic fatigue syndrome mice induced by forced wheel running.	J Ethnopharmacol. 2012 Jan 6;139(1):19-25. Epub 2011 Aug 22.	ETHNOPHARMACOLOGICAL RELEVANCE: In traditional medicine, Kai Xin San (KXS), composed of ginseng (Panax ginseng), hoelen (Wolfiporia cocos), polygala (Polygala tenuifolia) and Acorus gramineus, is famous for the treatment of emotion-thought disease, such as settling fright, quieting the spirit and nourishing the heart. AIM OF THE STUDY: The present study investigated the effect of KXS on chronic fatigue syndrome (CFS) mice induced by forced wheel running. MATERIALS AND METHODS: Seventy two healthy adult male Kunming mice were randomly divided into six groups: home cage control group, CFS group, CFS group with Modafinil treatment at 13 mg/kg/d doge, KXS treatment at 175 mg/kg/d, 350 mg/kg/d and 700 mg/kg/d doge. CFS mice were induced by forced wheel running with higher speed for 4 weeks and then taken an exhausted exercise. The biochemical parameters including serum lactate dehydrogenase (LDH), serum urea nitrogen (SUN), serum testosterone (T), liver glycogen (LG), muscle glycogen (MG) and muscle lactic acid (MLA) were determined by using commercially available kits. The splenocytes proliferation from mice was examined by MTT method. The levels of interleukin-2 (IL-2) and interleukin-4 (IL-4) secreted by splenocytes were determined by ELISA. RESULTS: CFS mice with KXS administration exhibited less electric shock time when compared with CFS group without drug treatment. The effect of KXS has after demonstrated reduction in SUN, LDH and MLA levels and an increase in T, LG and MG levels. CFS mice with KXS could improve the proliferation of splenocytes compared with CFS group without drug treatment. The cultured splenocytes from CFS mice without KXS supplementation produced more interleukin-2 (IL-2) but less interleukin-4 (IL-4) when compared with home cage control mice. The cultured splenocytes of CFS mice with KXS supplementation produced more interleukin-2 (IL-2) but less interleukin-4 (IL-4) when compared with CFS group without drug treatment. CONCLUSIONS: The results of this preliminary study provide evidence that KXS could ameliorate CFS by affecting the physiological markers for fatigue. This study also supported the use of KXS against CFS by improving the proliferation of splenocytes from CFS mice and modulating the disturbance of cytokines induced by CFS. Copyright © 2011 Elsevier Ireland Ltd. All rights reserved.
Carruthers BM, van de Sande MI, De Meirleir KL, Klimas NG, Broderick G, Mitchell T, Staines D, Powles AC, Speight N, Vallings R, Bateman L, Baumgarten-	Department of Physiology and Medicine, Vrije University of Brussels, Himmunitas Foundation, Brussels, Belgium. bcarruth@telus.net	Myalgic encephalomyelitis: International Consensus Criteria.	J Intern Med. 2011 Oct;270(4):327-38. doi: 10.1111/j.1365-2796.2011.02428.x. Epub 2011 Aug 22. Comment in J Intern Med. 2012 Jan;271(1):29-31.	The label 'chronic fatigue syndrome' (CFS) has persisted for many years because of the lack of knowledge of the aetiological agents and the disease process. In view of more recent research and clinical experience that strongly point to widespread inflammation and multisystemic neuropathology, it is more appropriate and correct to use the term 'myalgic encephalomyelitis' (ME) because it indicates an underlying pathophysiology. It is also consistent with the neurological classification of ME in the World Health Organization's International Classification of Diseases (ICD G93.3). Consequently, an International Consensus Panel consisting of clinicians, researchers, teaching faculty and an independent patient advocate was formed with the purpose of developing criteria based on current knowledge. Thirteen countries and a wide

Austrheim B, Bell DS, Carlo-Stella N, Chia J, Darragh A, Jo D, Lewis D, Light AR, Marshall-Gradisbik S, Mena I, Mikovits JA, Miwa K, Murovska M, Pall ML, Stevens S.				range of specialties were represented. Collectively, members have approximately 400 years of both clinical and teaching experience, authored hundreds of peer-reviewed publications, diagnosed or treated approximately 50 000 patients with ME, and several members coauthored previous criteria. The expertise and experience of the panel members as well as PubMed and other medical sources were utilized in a progression of suggestions/drafts/reviews/revisions. The authors, free of any sponsoring organization, achieved 100% consensus through a Delphi-type process. The scope of this paper is limited to criteria of ME and their application. Accordingly, the criteria reflect the complex symptomatology. Operational notes enhance clarity and specificity by providing guidance in the expression and interpretation of symptoms. Clinical and research application guidelines promote optimal recognition of ME by primary physicians and other healthcare providers, improve the consistency of diagnoses in adult and paediatric patients internationally and facilitate clearer identification of patients for research studies. © 2011 The Association for the Publication of the Journal of Internal Medicine.
Carvalho EE, Costa DC, Crescêncio JC, Santi GL, Papa V, Marques F, Schmidt A, Marin-Neto JA, Simões MV, Gallo Junior L.	Departamento de Clínica Médica Laboratório de Fisiologia do Exercício, Divisão de Cardiologia, Faculdade de Medicina de Ribeirão Preto, USP, Brazil. carvalhoeev@usp.br	Heart failure: comparison between six-minute walk test and cardiopulmonary test. [Article in English, Portuguese, Spanish]	Arq Bras Cardiol. 2011 Jul;97(1):59-64. Epub 2011 May 6. Comment in Arq Bras Cardiol. 2011 Nov;97(5):440; author reply 440-1.	BACKGROUND: Chronic heart failure (HF) is a syndrome characterized by reduced cardiac output in relation to the metabolic needs of the organism, as well as metabolic and neurohormonal axis abnormalities. Symptoms such as fatigue and dyspnoea are notorious and stress tests are widely used to assess functional capacity, prognosis and effectiveness of therapeutic interventions in this syndrome. OBJECTIVE: To evaluate the reproducibility of the six-minute walk test (6MW) in patients with HF and correlate the magnitude of the variables reached at peak exercise of the 6MWT with a cardiopulmonary exercise test (CPET). METHODS: We studied 16 patients (12 men and 4 women) diagnosed with HF FC I-II (NYHA). The volunteers underwent two 6MWT (6MWT'1 and 6MWT'2) with 30-minute interval between them; then, they underwent a maximum CPET. RESULTS: All variables obtained in the two 6MWT' proved to be significant with high correlations: distance walked (DW) ($r = 0.93$, $p < 0.0001$), heart rate (HR) ($r = 0.89$, $p < 0.0001$), oxygen consumption (VO2) ($r = 0.93$, $p < 0.0001$) and scale of perceived exertion ($r = 0.85$, $p < 0.0001$). In turn, all variables analyzed in the 6MWT' showed significant and moderate correlations with the variables obtained from the CPET, namely: peak HR ($r = 0.66$; $p = 0.005$); VO2 ($r = 0.57$; $p = 0.02$) and VO2 in the CPET and DT in the 6MWT'2 ($r = 0.70$; $p = 0.002$). CONCLUSION: The 6MWT was reproducible in this group of patients with HF (NYHA - I-II) and correlated with the CPET. Therefore, it is a tool for reliable evaluation, and a suitable, safe and low-cost alternative for the prescription of aerobic exercise in patients with HF.
Castori M, Sperduti I, Celletti C, Camerota F, Grammatico P.	Medical Genetics, Department of Molecular Medicine,	Symptom and joint mobility progression in the joint hypermobility	Clin Exp Rheumatol. 2011 Nov-Dec;29(6):998-1005.	OBJECTIVES: To evaluate progression of symptoms and joint mobility in the joint hypermobility syndrome (JHS) in order to identify specific disease pictures by age at presentation. METHODS: Fifty JHS patients (44 females, 6 males) were evaluated by Beighton score (BS) calculation, and presence/absence and age at onset of 20 key

	Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy. mcastori@scamilloforlanini.rm.it.	syndrome (Ehlers-Danlos syndrome, hypermobility type).		symptoms. Incidence and prevalence rates by age at onset and sex were calculated and compared by chi-square, Fisher's exact test and Mann-Whitney U-test. Relationship between BS and age at examination was evaluated by the Spearman rho correlation. The existence of an age cut-off separating patients with or without a positive BS was analysed by the receiver operating characteristic analysis. Influence of age on the single components of the BS was also investigated. RESULTS: Except for isolated features, the overall clinical presentation was the same between sexes. In the whole sample, statistically significant differences by age at presentation were registered for fatigue, myalgias, muscle cramps, strains/sprains, dislocations, tendon ruptures, tendonitis, gastroesophageal reflux, chronic gastritis, constipation/diarrhoea and abdominal hernias. A clear inverse correlation between age at examination and BS was demonstrated with an age cut-off fixed at 33 years. Among the components of the BS, spine and elbow joints were not significantly influenced by age. CONCLUSIONS: This study confirmed the existence of a protean clinical history of JHS which may be exemplified in different phases with distinguishable presentations. The knowledge of the peculiarities of each of them will help the practitioner in recognising and, hopefully, treating this condition.
Castori M, Sperduti I, Celletti C, Camerota F, Grammatico P.	Medical Genetics, Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy. mcastori@scamilloforlanini.rm.it.	Symptom and joint mobility progression in the joint hypermobility syndrome (Ehlers-Danlos syndrome, hypermobility type).	Clin Exp Rheumatol. 2011 Nov 30. [Epub ahead of print]	OBJECTIVES: To evaluate progression of symptoms and joint mobility in the joint hypermobility syndrome (JHS) in order to identify specific disease pictures by age at presentation. METHODS: Fifty JHS patients (44 females, 6 males) were evaluated by Beighton score (BS) calculation, and presence/absence and age at onset of 20 key symptoms. Incidence and prevalence rates by age at onset and sex were calculated and compared by chi-square, Fisher's exact test and Mann-Whitney U-test. Relationship between BS and age at examination was evaluated by the Spearman rho correlation. The existence of an age cut-off separating patients with or without a positive BS was analysed by the receiver operating characteristic analysis. Influence of age on the single components of the BS was also investigated. RESULTS: Except for isolated features, the overall clinical presentation was the same between sexes. In the whole sample, statistically significant differences by age at presentation were registered for fatigue, myalgias, muscle cramps, strains/sprains, dislocations, tendon ruptures, tendonitis, gastroesophageal reflux, chronic gastritis, constipation/diarrhoea and abdominal hernias. A clear inverse correlation between age at examination and BS was demonstrated with an age cut-off fixed at 33 years. Among the components of the BS, spine and elbow joints were not significantly influenced by age. CONCLUSIONS: This study confirmed the existence of a protean clinical history of JHS which may be exemplified in different phases with distinguishable presentations. The knowledge of the peculiarities of each of them will help the practitioner in recognising and, hopefully, treating this condition.
Castori M, Celletti C, Camerota F,		Chronic fatigue syndrome is	Clin Exp Rheumatol. 2011 May-	

Grammatico P.		commonly diagnosed in patients with Ehlers-Danlos syndrome hypermobility type/joint hypermobility syndrome.	Jun;29(3):597-8. Epub 2011 Jun 30.	
Castro-Sánchez AM, Matarán-Peñarrocha GA, Granero-Molina J, Aguilera-Manrique G, Quesada-Rubio JM, Moreno-Lorenzo C.	Department of Nursing and Physical Therapy, University of Almería (UAL), 04120 Almería, Spain.	Benefits of massage-myofascial release therapy on pain, anxiety, quality of sleep, depression, and quality of life in patients with fibromyalgia.	Evid Based Complement Alternat Med. 2011;2011:561753. Epub 2010 Dec 28.	Fibromyalgia is a chronic syndrome characterized by generalized pain, joint rigidity, intense fatigue, sleep alterations, headache, spastic colon, craniomandibular dysfunction, anxiety, and depression. The purpose of the present study was to determine whether massage-myofascial release therapy can improve pain, anxiety, quality of sleep, depression, and quality of life in patients with fibromyalgia. A randomized controlled clinical trial was performed. Seventy-four fibromyalgia patients were randomly assigned to experimental (massage-myofascial release therapy) and placebo (sham treatment with disconnected magnotherapy device) groups. The intervention period was 20 weeks. Pain, anxiety, quality of sleep, depression, and quality of life were determined at baseline, after the last treatment session, and at 1 month and 6 months. Immediately after treatment and at 1 month, anxiety levels, quality of sleep, pain, and quality of life were improved in the experimental group over the placebo group. However, at 6 months postintervention, there were only significant differences in the quality of sleep index. Myofascial release techniques improved pain and quality of life in patients with fibromyalgia.
Cella M, Sharpe M, Chalder T.	Institute of Psychiatry, King's College London, UK. matteo.cella@kcl.ac.uk	Measuring disability in patients with chronic fatigue syndrome: reliability and validity of the Work and Social Adjustment Scale.	J Psychosom Res. 2011 Sep;71(3):124-8. Epub 2011 Apr 3.	BACKGROUND: Disability is a defining feature of chronic conditions, and it is an increasingly used measure of therapy effectiveness. The Work and Social Adjustment Scale (WSAS) is a simple and clear measure of disability. Although the scale is widely used, no study has yet investigated its psychometric properties in patients with chronic fatigue syndrome (CFS). METHODS: Data from two samples of patients were used, one from a multicenter randomized controlled clinical trial of treatments for CFS (n =639) and the other from a clinic that specializes in CFS (n=384). All patients completed the WSAS as well as other measures. RESULTS: Internal consistency and the Spearman-Brown split-half coefficient values indicated that the scale is reliable. CFS patients who had comorbid diagnoses of depression, anxiety or fibromyalgia had higher WSAS scores. High levels of disability were associated with high number of physical symptoms, severe fatigue, depression, anxiety, poor sleep quality and poor physical fitness, with correlation coefficients ranging between 0.41 and 0.11. Lower scores on the WSAS were modestly associated with better physical functioning as well as higher levels of physical capacity as assessed by a walking test. Sensitivity to change was evaluated in a subgroup of patients who had undergone a course of cognitive behavioral therapy. Disability significantly decreased after therapy and

				remained stable at follow-ups. CONCLUSION: The WSAS is a reliable and valid assessment tool for disability in patients with CFS. Copyright © 2011 Elsevier Inc. All rights reserved.
Cella M, Stahl D, Reme SE, Chalder T.	King's College, Department of Psychological Medicine, Institute of Psychiatry, London, UK.	Therapist effects in routine psychotherapy practice: an account from chronic fatigue syndrome.	Psychother Res. 2011 Mar;21(2):168-78.	The effect of therapists in psychotherapy is a much debated topic, with a number of studies showing therapist variance being large while other studies show little or no variability in outcomes due to therapists. The aim of this study was to investigate therapist effects in a well-defined sample of patients and therapists from an outpatient service which specializes in providing cognitive behaviour therapy (CBT) for patients with chronic fatigue syndrome (CFS). Therapy was provided in a highly specialized clinical setting for CFS and was delivered by qualified CBT therapists with at least 2 years experience with this client group. Three hundred and seventy-four patients with CFS and 12 cognitive behavioural psychotherapists took part. Therapist effects on the primary outcomes of fatigue and disability were investigated with multilevel random effects models and variance component analysis. Different models were computed and compared. Results showed a reduction in fatigue and disability scores after therapy. Variance explained by therapists, when demographic covariates were accounted for, was 0% for fatigue and under 2% for disability. A number of important factors may have played a significant role in minimizing therapist effects in our study. These are: specialist setting, single centre, patients with the same primary diagnosis, therapists of the same orientation and training, shared environment and supervision. Future studies may stress the importance of these factors in the investigation of the therapist effect in psychotherapy.
Cella M, Chalder T, White PD.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, UK. matteo.cella@kcl.ac.uk	Does the heterogeneity of chronic fatigue syndrome moderate the response to cognitive behaviour therapy? An exploratory study.	Psychother Psychosom. 2011;80(6):353-8. Epub 2011 Aug 6.	BACKGROUND: Chronic fatigue syndrome (CFS) is a heterogeneous condition. A few studies have shown that some independent factors predict outcomes after cognitive behaviour therapy (CBT). Two recent systematic reviews suggest that heterogeneity may moderate treatment outcomes. However, no study has explored whether subgroups of CFS predict response to treatment. METHODS: We used both latent class analysis (LCA) and latent class regression (LCR) to clarify the relationship between subgroups of CFS patients (n = 236), diagnosed using the Oxford diagnostic criteria, and the response to CBT. We measured symptoms, demographics, mood, and cognitive and behavioural responses to illness to define subgroups. RESULTS: We found 5 latent classes by LCA, which did not differ in the direction of their response to CBT, with all classes showing improvement. In contrast, an exploratory LCR identified 4 latent classes, 1 of which predicted a poor response to CBT, whereas the other 3 predicted a good outcome, accounting for more than 70% of the patients. The negative outcome class was defined by weight fluctuations and physical shakiness, anxiety, pain and being focused on symptoms. CONCLUSIONS: CBT should be offered to all classes of patients with CFS, when defined by these measures. It may be possible to predict a minority group with a negative outcome, but this exploratory work needs replication. Copyright © 2011 S. Karger AG, Basel.

Chaipan C, Dilley KA, Paprotka T, Delviks-Frankenberry KA, Venkatachari NJ, Hu WS, Pathak VK.	HIV Drug Resistance Program, National Cancer Institute-Frederick, P. O. Box B, Building 535, Room 334, Frederick, MD 21702-1201, USA.	Severe restriction of xenotropic murine leukemia virus-related virus replication and spread in cultured human peripheral blood mononuclear cells.	J Virol. 2011 May;85(10):4888-97. Epub 2011 Feb 16.	Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus recently isolated from human prostate cancer and peripheral blood mononuclear cells (PBMCs) of patients with chronic fatigue syndrome (CFS). We and others have shown that host restriction factors APOBEC3G (A3G) and APOBEC3F (A3F), which are expressed in human PBMCs, inhibit XMRV in transient-transfection assays involving a single cycle of viral replication. However, the recovery of infectious XMRV from human PBMCs suggested that XMRV can replicate in these cells despite the expression of APOBEC3 proteins. To determine whether XMRV can replicate and spread in cultured PBMCs even though it can be inhibited by A3G/A3F, we infected phytohemagglutinin-activated human PBMCs and A3G/A3F-positive and -negative cell lines (CEM and CEM-SS, respectively) with different amounts of XMRV and monitored virus production by using quantitative real-time PCR. We found that XMRV efficiently replicated in CEM-SS cells and viral production increased by >4,000-fold, but there was only a modest increase in viral production from CEM cells (<14-fold) and a decrease in activated PBMCs, indicating little or no replication and spread of XMRV. However, infectious XMRV could be recovered from the infected PBMCs by cocultivation with a canine indicator cell line, and we observed hypermutation of XMRV genomes in PBMCs. Thus, PBMCs can potentially act as a source of infectious XMRV for spread to cells that express low levels of host restriction factors. Overall, these results suggest that hypermutation of XMRV in human PBMCs constitutes one of the blocks to replication and spread of XMRV. Furthermore, hypermutation of XMRV proviruses at GG dinucleotides may be a useful and reliable indicator of human PBMC infection.
Chandraratne NK, Gunawardena NS.	Public Health Department, Colombo Municipal Council, Sri Lanka. radkamil@yahoo.com	Premenstrual syndrome: the experience from a sample of Sri Lankan adolescents.	J Pediatr Adolesc Gynecol. 2011 Oct;24(5):304-10.	SETTING: Government schools of Colombo. MAIN OUTCOME MEASURES: Premenstrual symptomatology (PMS) was determined by a modified version of Premenstrual Symptom screening tool and American College of Obstetricians and Gynecologists (ACOG) diagnostic criteria were used in categorizing study units as having PMS. Other outcome measures were demographic and reproductive factors thought to be correlates of PMS, health seeking behavior for premenstrual symptoms, and how premenstrual symptoms impact their daily life. RESULTS: Individual premenstrual symptoms were experienced by 65.7% of the population. The most common somatic symptom was fatigue (29.9%) and affective symptom was feeling sad/hopeless (29.6%). Prevalence of PMS was 8.75% (95%CI: 6.43-11.07). Multivariate analysis revealed the presence of: chronic physical illness (P = 0.001); dysmenorrhea (P < 0.0001), and regular menstrual cycles (P = 0.006) as correlates of PMS. Presence of PMS significantly disturbed "in school" activities, relationships and daily routines (P < 0.005) indicating a high negative influence on adolescents' daily life. Only 9.7% sought help from (western) medical practitioners for their premenstrual symptoms and a majority has not perceived it as a condition to report. CONCLUSION: Premenstrual syndrome is a common condition among adolescent schoolgirls with a

				high negative influence on their daily life. The health care seeking behavior is poor, indicating the necessity to address the subject at adolescent reproductive health programs. Copyright © 2011 North American Society for Pediatric and Adolescent Gynecology. Published by Elsevier Inc. All rights reserved.
Check JH, Cohen R.	The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at Camden Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ, USA. laurie@ccivf.com	Sympathetic neural hyperalgesia edema syndrome, a frequent cause of pelvic pain in women, mistaken for Lyme disease with chronic fatigue.	Clin Exp Obstet Gynecol. 2011;38(4):412-3.	PURPOSE: To show that chronic fatigue syndrome can be mistakenly attributed to Lyme disease rather than considering sympathetic neural hyperalgesia edema syndrome. This common disorder of women, frequently, but not always causing pelvic pain, can present simply as chronic fatigue. METHODS: A water load test was performed in a woman reactive for B-Burgdorferi with chronic fatigue whose symptoms did not improve despite three months of treatment with doxycycline. A water load test was performed. RESULTS: She failed the water load test by excreting only 50% ingested load standing for four hours. She showed marked improvement following treatment with dextroamphetamine sulfate. CONCLUSIONS: This very treatable disorder of the sympathetic nervous system should be considered in women with an unknown cause of chronic fatigue or if the symptoms persist despite treatment of another potential cause.
Chew-Graham C, Brooks J, Wearden A, Dowrick C, Peters S.	School of Community-Based Medicine, University of Manchester, Manchester, UK. cchew@manchester.ac.uk	Factors influencing engagement of patients in a novel intervention for CFS/ME: a qualitative study.	Prim Health Care Res Dev. 2011 Apr;12(2):112-22.	AIM: To establish what factors are important for patients to engage in a new intervention for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and make recommendations to general practitioners (GPs) on preparing a patient for referral to such a service. BACKGROUND: NICE guidelines recommend a prominent role for primary care in the management of patients with CFS/ME, with prompt diagnosis and appropriate referral for evidence-based treatments. METHODS: A qualitative study nested within a multi-centre randomised controlled trial of two new nurse therapist delivered interventions. Semi-structured interviews carried out with 19 patients who had received pragmatic rehabilitation (PR) in the trial. Interviews were transcribed verbatim and an iterative approach used to develop themes from the data set. FINDINGS: Factors that influence whether or not a patient engages with PR for CFS/ME are ensuring that the patient feels accepted and believed, that they accept the diagnosis, and that the model implicated by the treatment offered to the patient matches the model of illness held by the patient. If patients hold a clearly incompatible model of their illness, it is unlikely that they will engage with, and successfully complete, therapy. It is vital that the GP elicits and explores such illness beliefs either before making a referral to maximise patient engagement in therapy, or that an initial session with the therapist explores attitudes to the treatment model

				offered and then works with the patient's model.
Chia J, Chia A, El-Habbal R.	EV Med Research, Lomita, California 90717, USA. evmed@sbcglobal.net	Carcinoid tumour associated with enterovirus infection.	J Clin Pathol. 2011 Aug;64(8):722-4. Epub 2011 Jan 28.	Enteroviruses commonly infect the gastrointestinal tract, and replication of enteroviruses has been well documented in the Peyer patches of the small bowel. Chronic enterovirus infection has been found in the stomach and terminal ileum of patients with myalgic encephalomyelitis/chronic fatigue syndrome. The authors report the unexpected finding of enterovirus VP1 protein, by immunoperoxidase staining, in carcinoid tumours found in one patient with myalgic encephalomyelitis/chronic fatigue syndrome and another patient with chronic lower quadrant abdominal pain, and suggest a possible association between enteroviruses and tumorigenesis.
Cingöz O, Paprotka T, Delviks-Frankenberry KA, Wildt S, Hu WS, Pathak VK, Coffin JM.	Department of Molecular Biology and Microbiology, Genetics Program, Sackler School of Graduate Biomedical Sciences, Tufts University, Boston, Massachusetts, USA.	Characterization, mapping, and distribution of the two XMRV parental proviruses.	J Virol. 2012 Jan;86(1):328-38. Epub 2011 Oct 26.	Xenotropic murine leukemia virus-related virus (XMRV) was previously reported to be associated with human prostate cancer and chronic fatigue syndrome. Our groups recently showed that XMRV was created through recombination between two endogenous murine retroviruses, PreXMRV-1 and PreXMRV-2, during the passaging of a prostate tumor xenograft in nude mice. Here, multiple approaches that led to the identification of PreXMRV-2, as well as the distribution of both parental proviruses among different mouse species, are described. The chromosomal loci of both proviruses were determined in the mouse genome, and integration site information was used to analyze the distribution of both proviruses in 48 laboratory mouse strains and 46 wild-derived strains. The strain distributions of PreXMRV-1 and PreXMRV-2 are quite different, the former being found predominantly in Asian mice and the latter in European mice, making it unlikely that the two XMRV ancestors could have recombined independently in the wild to generate an infectious virus. XMRV was not present in any of the mouse strains tested, and among the wild-derived mouse strains analyzed, not a single mouse carried both parental proviruses. Interestingly, PreXMRV-1 and PreXMRV-2 were found together in three laboratory strains, Hsd nude, NU/NU, and C57BR/cd, consistent with previous data that the recombination event that led to the generation of XMRV could have occurred only in the laboratory. The three laboratory strains carried the Xpr1(n) receptor variant nonpermissive to XMRV and xenotropic murine leukemia virus (X-MLV) infection, suggesting that the xenografted human tumor cells were required for the resulting XMRV recombinant to infect and propagate.
Clark C, Goodwin L, Stansfeld SA, Hotopf M, White PD.	Centre for Psychiatry, Barts & the London School of Medicine & Dentistry, Queen Mary University of London,	Premorbid risk markers for chronic fatigue syndrome in the 1958 British birth cohort.	Br J Psychiatry. 2011 Oct;199(4):323-9. doi: 10.1192/bjp.bp.110.083956. Epub 2011 Aug 18.	BACKGROUND: Little is known about the aetiology of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME); prospective studies suggest a role for premorbid mood disorder. AIMS: To examine childhood and early adult adversity, ill health and physical activity as premorbid risk markers for CFS/ME by 42 years, taking psychopathology into account. METHOD: Data were from the 1958 British birth cohort, a prospective study from birth to 42 years (n = 11 419). The outcomes were self-reported CFS/ME (n = 127) and operationally defined CFS-like illness (n = 241) at 42 years. RESULTS: Adjusting for psychopathology, parental physical abuse (odds ratio

	Charterhouse Square, UK. c.clark@qmul.ac.uk			(OR) = 2.10, 95% CI 1.16-3.81), childhood gastrointestinal symptoms (OR = 1.58, 95% CI 1.00-2.50) and parental reports of many colds (OR = 1.65, 95% CI 1.09-2.50) were independently associated with self-reported CFS/ME. Female gender and premorbid psychopathology were the only risk markers for CFS-like illness, independent of comorbid psychopathology. CONCLUSIONS: This confirms the importance of premorbid psychopathology in the aetiological pathways of CFS/ME, and replicates retrospective findings that childhood adversity may play a role in a minority.
Clauw DJ, Arnold LM, McCarberg BH; FibroCollaborative.	Department of Anesthesiology, University of Michigan, Ann Arbor, MI 48106, USA. dclauw@med.umich.edu	The science of fibromyalgia.	Mayo Clin Proc. 2011 Sep;86(9):907-11.	Fibromyalgia (FM) is a common chronic widespread pain disorder. Our understanding of FM has increased substantially in recent years with extensive research suggesting a neurogenic origin for the most prominent symptom of FM, chronic widespread pain. Neurochemical imbalances in the central nervous system are associated with central amplification of pain perception characterized by allodynia (a heightened sensitivity to stimuli that are not normally painful) and hyperalgesia (an increased response to painful stimuli). Despite this increased awareness and understanding, FM remains undiagnosed in an estimated 75% of people with the disorder. Clinicians could more effectively diagnose and manage FM if they better understood its underlying mechanisms. Fibromyalgia is a disorder of pain processing. Evidence suggests that both the ascending and descending pain pathways operate abnormally, resulting in central amplification of pain signals, analogous to the "volume control setting" being turned up too high. Patients with FM also exhibit changes in the levels of neurotransmitters that cause augmented central nervous system pain processing; levels of several neurotransmitters that facilitate pain transmission are elevated in the cerebrospinal fluid and brain, and levels of several neurotransmitters known to inhibit pain transmission are decreased. Pharmacological agents that act centrally in ascending and/or descending pain processing pathways, such as medications with approved indications for FM, are effective in many patients with FM as well as other conditions involving central pain amplification. Research is ongoing to determine the role of analogous central nervous system factors in the other cardinal symptoms of FM, such as fatigue, nonrestorative sleep, and cognitive dysfunction.
Clemons A, Vasiadi M, Kempuraj D, Kourelis T, Vandoros G, Theoharides TC.		Amitriptyline and prochlorperazine inhibit proinflammatory mediator release from human mast cells: possible relevance to chronic fatigue syndrome.	J Clin Psychopharmacol. 2011 Jun;31(3):385-7.	
Cobankara V, Unal UO, Kaya A,	Rheumatology Clinic, Internal	The prevalence of fibromyalgia among	Int J Rheum Dis. 2011 Oct;14(4):390-4. doi:	AIM: Fibromyalgia (FM) is characterized by chronic widespread pain, fatigue, reduced sleep quality and multiple tender points. A recent population study from Turkey

Bozkurt AI, Ozturk MA.	Medicine Department, Pamukkale University Faculty of Medicine, Denizli, Turkey.	textile workers in the city of Denizli in Turkey.	10.1111/j.1756-185X.2011.01620.x. Epub 2011 Jun 29.	found the prevalence of FM as 3.6%. A prevalence study among workers has not yet been performed. We performed a prevalence survey among working population in the city of Denizli in Turkey. METHODS: The field survey was done in two stages. In the first stage 655 (523 female, 132 male) textile workers from four factories were asked to fill a screening questionnaire. In the next stage, participants who had widespread pain were examined by an experienced rheumatologist. Patients who had 11 tender points according to ACR 1990 FM classification criteria were diagnosed as FM syndrome and later a detailed clinical and laboratory evaluation was done. RESULTS: Forty-eight patients (7.3%) (one male [0.76% of males], 47 females [9.0% of females]) among 655 textile workers were diagnosed as FM. The clinical features were as follows: all patients had widespread pain, 12.5% had arthralgia, 14.6% had Raynaud's phenomenon, 41.6% had sleep disturbance, 87.5% had headache, 52% had irritable bowel disease. Age, gender, marital status, income level, education level, smoking status, and body mass index level of workers were evaluated by logistic regression analysis; multiple analysis. Only three variables (age, gender and annual income level) were significantly affected FM prevalence. CONCLUSION: This is the first study investigating FM prevalence among workers from Turkey. The prevalence of FM appears higher among females, older workers, and workers with low annual money income. © 2011 The Authors. International Journal of Rheumatic Diseases © 2011 Asia Pacific League of Associations for Rheumatology and Blackwell Publishing Asia Pty Ltd.
Cohen J.		Virology. The waning conflict over XMRV and chronic fatigue syndrome.	Science. 2011 Sep 30;333(6051):1810.	
Cohen J, Enserink M.		Virology. False positive.	Science. 2011 Sep 23;333(6050):1694-701. Erratum in Science. 2011 Nov 4;334(6056):594.	
Cohen J.		Retrovirology. More negative data for link between mouse virus and human disease.	Science. 2011 Mar 11;331(6022):1253-4. Erratum in Science. 2011 Apr 15;332(6027):306.	
Cohen J.		Intellectual property. Dispute over lab notebooks lands researcher in jail.	Science. 2011 Dec 2;334(6060):1189-90.	
Collin SM, Crawley	School of Social &	The impact of	BMC Health Serv Res.	BACKGROUND: Few studies have investigated factors associated with discontinuation

E, May MT, Sterne JA, Hollingworth W; UK CFS/ME National Outcomes Database. Collaborators: O'Dowd H, Butt K, Dunn D, Pemberton S, White P, Murphy M, Mullick Y, Bansal A.	Community Medicine, Centre for Child & Adolescent Health, University of Bristol, Oakfield House, Oakfield Grove, BS8 2BN, UK.	CFS/ME on employment and productivity in the UK: a cross-sectional study based on the CFS/ME national outcomes database.	2011 Sep 15;11:217.	of employment in patients with CFS/ME or quantified its impact on productivity. METHODS: We used patient-level data from five NHS CFS/ME services during the period 01/04/2006-31/03/2010 collated in the UK CFS/ME National Outcomes Database. We used logistic regression to identify factors associated with discontinuation of employment. We estimated UK-wide productivity costs using patient-level data on duration of illness before assessment by a CFS/ME service, duration of unemployment, age, sex and numbers of patients, in conjunction with Office for National Statistics income and population data. RESULTS: Data were available for 2,170 patients, of whom 1,669 (76.9%) were women. Current employment status was recorded for 1,991 patients (91.8%), of whom 811 patients (40.7%) were currently employed and 998 (50.1%) had discontinued their employment "because of fatigue-related symptoms". Older age, male sex, disability, fatigue, pain, and duration of illness were associated with cessation of employment. In a multivariable model, age, male sex, and disability remained as independent predictors. Total productivity costs among the 2,170 patients due to discontinuation of employment in the years preceding assessment by a specialist CFS/ME service (median duration of illness=36 months) were £49.2 million. Our sample was equivalent to 4,424 UK adults accessing specialist services each year, representing productivity costs to the UK economy of £102.2 million. Sensitivity analyses suggested a range between £75.5-£128.9 million. CONCLUSIONS: CFS/ME incurs huge productivity costs amongst the small fraction of adults with CFS/ME who access specialist services.
Constant EL, Adam S, Gillain B, Lambert M, Masquelier E, Seron X.	Department of Psychiatry, Université Catholique de Louvain, 1200 Brussels, Belgium. Eric.Constant@uclouvain.be	Cognitive deficits in patients with chronic fatigue syndrome compared to those with major depressive disorder and healthy controls.	Clin Neurol Neurosurg. 2011 May;113(4):295-302. Epub 2011 Jan 20.	OBJECT: Chronic fatigue syndrome (CFS) patients report usually cognitive complaints. They also have frequently comorbid depression that can be considered a possible explanation for their cognitive dysfunction. We evaluated the cognitive performance of patients with CFS in comparison with a control group of healthy volunteers and a group of patients with MDD. PATIENTS AND METHODS: Twenty-five patients with CFS, 25 patients with major depressive disorder (MDD), and 25 healthy control subjects were given standardized tests of attention, working memory, and verbal and visual episodic memory, and were also tested for effects related to lack of effort/simulation, suggestibility, and fatigue. RESULTS: Patients with CFS had slower phasic alertness, and also had impaired working, visual and verbal episodic memory compared to controls. They were, however, no more sensitive than the other groups to suggestibility or to fatigue induced during the cognitive session. Cognitive impairments in MDD patients were strongly associated with depression and subjective fatigue; in patients with CFS, there was a weaker correlation between cognition and depression (and no correlation with fatigue). CONCLUSIONS: This study confirms the presence of an objective impairment in attention and memory in patients with CFS but with good mobilization of effort and without exaggerated suggestibility.

Cook DB, Stegner AJ, Nagelkirk PR, Meyer JD, Togo F, Natelson BH.	1Department of Kinesiology, University of Wisconsin - Madison 2Research Service, William S. Middleton Memorial Veterans Hospital 3School of Physical Education, Sport & Exercise Science, Ball State University 4Graduate School of Education, The University of Tokyo 5Pain and Fatigue Study Center, Beth Israel Medical Center.	Responses to Exercise Differ For Chronic Fatigue Syndrome Patients with Fibromyalgia.	Med Sci Sports Exerc. 2011 Dec 12. [Epub ahead of print]	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are chronic multisymptom illnesses with substantial clinical and diagnostic overlap. We have previously shown that when controlling for aerobic fitness and accounting for comorbid FM, CFS patients do not exhibit abnormal cardiorespiratory responses during maximal aerobic exercise compared to healthy controls, despite differences in pain and exertion. PURPOSE: The purpose of the present study was to examine cardiac and perceptual responses to steady-state, submaximal exercise in CFS patients and healthy controls. METHODS: Twenty-one CFS patients [13 CFS with comorbid FM (CFS+FM)] and 14 controls completed 20 minutes of submaximal cycling exercise. Impedance cardiography was used to determine cardiac responses during exercise. Systolic blood pressure (SBP), perceived exertion (RPE) and leg-muscle pain were also measured. Data were analyzed using a doubly-multivariate, repeated-measures MANOVA to model the exercise response. RESULTS: There was a significant multivariate Time by Group interaction ($p < 0.05$). The CFS+FM group exhibited an exercise response characterized by higher stoke index, ventilatory equivalents for oxygen and carbon dioxide and RPE, lower SBP and similar HR responses. CONCLUSIONS: The present results extend upon our previous work with maximal exercise and show that CFS and CFS+FM differ in their responses to steady-state exercise. These resultshighlight the importance of accounting for comorbid conditions when conducting CFS research, particularly when examining psychophysiological responses to exercise.
Cool M, Bouchard N, Massé G, Laganière B, Dumont A, Hanna Z, Phaneuf D, Morisset R, Jolicoeur P.	Laboratory of Molecular Biology, Clinical Research Institute of Montreal, Montreal, Quebec, Canada H2W 1R7.	No detectable XMRV in subjects with chronic fatigue syndrome from Quebec.	Virology. 2011 Nov 10;420(1):66-72. Epub 2011 Sep 16.	We investigated the presence of XMRV in a cohort of Quebec patients with chronic fatigue syndrome (CFS). DNA was purified from activated peripheral blood mononuclear cells (PBMCs) and PCR was used to detect XMRV gag and env in 72 patients. Anti-XMRV antibodies were searched in sera of 62 patients by Western blot analysis. Attempts to detect XMRV antigens was made, using immunofluorescence with Gag anti-p30 antiserum on activated PBMC from 50 patients. Plasma viremia was measured by RT-PCR on 9 subjects. Finally, detection of infectious virus in 113 CFS subjects was made by co-culture of PHA+IL-2 activated PBMC with human LNCaP carcinoma cells, and by infecting the same susceptible cells with plasma, using a reverse transcriptase (RT) assay as a readout in both experiments. No detection of XMRV footprints nor infectious virus was detected with any of the approaches, in any of the tested individuals.
Cornes O.	ollie@cornes.org	Commentary: Living with CFS/ME.	BMJ. 2011 Jun 22;342:d3836. doi: 10.1136/bmj.d3836.	
Coughlin SS, Kang	Environmental	Alcohol use and	Prev Chronic Dis. 2011	INTRODUCTION: A sizable literature has analyzed the frequency of alcohol

HK, Mahan CM.	Epidemiology Service (135), Office of Public Health and Environmental Hazards, Department of Veterans Affairs, 810 Vermont Ave NW, Washington, DC 20420, USA. steven.coughlin@va.gov	selected health conditions of 1991 Gulf War veterans: survey results, 2003-2005.	May;8(3):A52. Epub 2011 Apr 15.	consumption and patterns of drinking among veterans. However, few studies have examined patterns of alcohol use in veterans of the first Gulf War or factors associated with problem drinking in this population. We examined the frequency and patterns of alcohol use in male and female veterans who served in the 1991 Gulf War or during the same era and the relationships between alcohol use and selected health conditions. METHODS: We analyzed data from a follow-up survey of health information among population-based samples of 15,000 Gulf War and 15,000 Gulf Era veterans. Data had been collected from 9,970 respondents during 2003 through 2005 via a structured questionnaire or telephone survey. RESULTS: Posttraumatic stress disorder (PTSD), major depressive disorder (MDD), unexplained multisymptom illness (MSI), and chronic fatigue syndrome (CFS)-like illness were more frequent among veterans with problem drinking than those without problem drinking. Approximately 28% of Gulf War veterans with problem drinking had PTSD compared with 13% of Gulf War veterans without problem drinking. In multivariate analysis, problem drinking was positively associated with PTSD, MDD, unexplained MSI, and CFS-like illness after adjustment for age, sex, race/ethnicity, branch of service, rank, and Gulf status. Veterans who were problem drinkers were 2.7 times as likely to have PTSD as veterans who were not problem drinkers. CONCLUSION: These findings indicate that access to evidence-based treatment programs and systems of care should be provided for veterans who abuse alcohol and who have PTSD and other war-related health conditions and illnesses.
Coughlin SS, Kang HK, Mahan CM.	Environmental Epidemiology Service (135), Office of Public Health and Environmental Hazards, Department of Veterans Affairs, 810 Vermont Avenue, NW, Washington, DC 20420, USA.	Selected Health Conditions Among Overweight, Obese, and Non-Obese Veterans of the 1991 Gulf War: Results from a Survey Conducted in 2003-2005.	Open Epidemiol J. 2011;4:140-146.	BACKGROUND: Several health conditions and concerns have been reported to be increased among Gulf War veterans including post-traumatic stress disorder (PTSD), chronic fatigue syndrome (CFS), CFS-like illness, and unexplained multi-symptom illness (MSI). As the cohort of Gulf War veterans advance in age, they are likely to be at risk of not only certain deployment-related health conditions but also chronic diseases associated with lifestyle factors. METHODS: To clarify relationships between PTSD, CFS-like illness, MSI, and obesity, we analyzed data from a cross-sectional survey of health information among population-based samples of 15,000 Gulf War veterans and 15,000 veterans who served during the same era. Data had been collected from 9,970 respondents in 2003-2005 via a structured questionnaire or telephone survey. RESULTS: Based upon body mass index (BMI) estimated from self-reported information about height and weight, the percentages of Gulf War and Gulf Era veterans who were overweight (BMI 25 to ≤ 29.9), were 46.8% and 48.7%, respectively. The percentages who were obese (BMI ≥ 30) were 29.6% and 28.3%, respectively. Without adjustment for Gulf deployment status (Gulf War vs Gulf Era), age, sex, or other factors, PTSD, MSI, CFS-like illness, and other chronic health conditions were more common among obese veterans than those who were normal weight (BMI 18.5 to ≤ 24.9). In multivariate analyses, PTSD was positively associated with obesity after adjustment for age, sex, Gulf deployment status, rank, income,

				education, and current smoking. In the model for PTSD, the adjusted odds ratio for obesity was 1.5 (95% CI 1.2-1.8). No associations were observed between BMI categories and CFS-like illness or MSI in multivariate analysis. CONCLUSIONS: Gulf War and Gulf Era veterans who were obese were more likely to have certain chronic health conditions including PTSD. Associations between Gulf status and CFS-like illness and MSI identified in the 2003-2005 follow-up survey were not accounted for by group differences in the prevalence of overweight or obesity.
Crawley EM, Emond AM, Sterne JA.	Centre for Child and Adolescent Health, School of Social and Community Medicine, Bristol, UK.	Unidentified Chronic Fatigue Syndrome/myalgic encephalomyelitis (CFS/ME) is a major cause of school absence: surveillance outcomes from school-based clinics.	BMJ Open. 2011 Dec 12;1(2):e000252. Print 2011.	Objective To investigate the feasibility of conducting clinics for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in schools. Design School-based clinical project. Participants Children aged 11-16 years were enrolled in three state secondary schools in England. Main outcome measures Number of children newly diagnosed as having CFS/ME. Methods Attendance officers identified children missing ≥20% of school in a 6-week term without a known cause, excluding those with a single episode off school, a known medical illness explaining the absence or known to be truanting. Children with fatigue were referred to a specialist CFS/ME service for further assessment. The authors compared children with CFS/ME identified through school-based clinics with those referred via health services. Outcomes of CFS/ME were evaluated at 6 weeks and 6 months. Results 461 of the 2855 enrolled children had missed ≥20% school over a 6-week period. In 315, of whom three had CFS/ME, the reason for absence was known. 112 of the 146 children with unexplained absence attended clinical review at school; two had been previously diagnosed as having CFS/ME and 42 were referred on to a specialist clinic, where 23 were newly diagnosed as having CFS/ME. Therefore, 28 of the 2855 (1.0%) children had CFS/ME. Children with CFS/ME identified through surveillance had been ill for an amount of time comparable to those referred via health services but had less fatigue (mean difference 4.4, 95% CI 2.2 to 6.6), less disability (mean difference -5.7, 95% CI -7.9 to -3.5) and fewer symptoms (mean difference 1.86, 95% CI 0.8 to 2.93). Of 19 children followed up, six had fully recovered at 6 weeks and a further six at 6 months. Conclusions Chronic fatigue is an important cause of unexplained absence from school. Children diagnosed through school-based clinics are less severely affected than those referred to specialist services and appear to make rapid progress when they access treatment.
Daniels J, Wearden AJ.	Department of Psychology, University of Bath, Claverton Down, Bath, UK. jo.daniels@live.com	Socialization to the model: the active component in the therapeutic alliance? A preliminary study.	Behav Cogn Psychother. 2011 Mar;39(2):221-7. Epub 2010 Nov 22.	BACKGROUND: Therapeutic alliance has been found to be a significant predictor of outcome in psychotherapy yet what constitutes therapeutic alliance remains unclear. Examining the common constructs of therapeutic alliance, it is possible that there may be a conceptual overlap between active components of therapeutic alliance and socialization to the treatment model. Aim: To investigate the relationship between socialization to the model and therapeutic alliance. METHOD: Participants (N = 43) were taken from the active treatment arm in a RCT for the treatment of chronic fatigue syndrome (CFS/ME). Therapeutic alliance was measured using a 5-item questionnaire (brief CALPAS) and socialization to the model was extracted from

				therapy tapes using a novel coding system. RESULTS: Key findings were that when patients and therapists agreed about goals of treatment, there were higher levels of concordance, less evidence of applying principles incongruent to the model, and less resistance during the treatment sessions. CONCLUSIONS: The outcome of this preliminary study contributes to the potential understanding of active components in the therapeutic alliance, and supports further research to achieve a more detailed picture of "non-specific" factors in therapy, including the active process of socialization in therapeutic alliance.
Dansie EJ, Furberg H, Afari N, Buchwald D, Edwards K, Goldberg J, Schur E, Sullivan PF.	Center for Clinical and Epidemiological Research, University of Washington, Seattle, WA 98101, USA. Edansie@uw.edu	Conditions comorbid with chronic fatigue in a population-based sample.	Psychosomatics. 2012 Jan;53(1):44-50. Epub 2011 Sep 22.	BACKGROUND: Chronic fatigue syndrome (CFS) has been found to be comorbid with various medical conditions in clinical samples, but little research has investigated CFS comorbidity in population-based samples. OBJECTIVE: This study investigated conditions concurrent with a CFS-like illness among twins in the population-based Mid-Atlantic Twin Registry (MATR), including chronic widespread pain (CWP), irritable bowel syndrome (IBS), and major depressive disorder (MDD). METHOD: A survey was mailed to participants in the MATR in 1999. Generalized estimating equations were used to estimate odds ratios to assess associations between CFS-like illness and each comorbid condition. RESULTS: A total of 4590 completed surveys were collected. Most participants were female (86.3%); mean age was 44.7 years. Among participants with a CFS-like illness, lifetime prevalences of CWP, IBS, and MDD were 41%, 16%, and 57% respectively. Participants reporting at least one of the three comorbid conditions were about 14 times more likely to have CFS-like illness than those without CWP, IBS, or MDD (95% confidence interval 8.1%-21.3%). Only MDD showed a temporal pattern of presentation during the same year as diagnosis of CFS-like illness. Age, gender, body mass index, age at illness onset, exercise level, self-reported health status, fatigue symptoms, and personality measures did not differ between those reporting CFS-like illness with and without comorbidity. CONCLUSION: These results support findings in clinically based samples that CFS-like illness is frequently cormorbid with CWP, IBS, and/or MDD. We found no evidence that CFS-like illnesses with comorbidities are clinically distinct from those without comorbidities. Copyright © 2012 The Academy of Psychosomatic Medicine. Published by Elsevier Inc. All rights reserved.
Davenport TE, Stevens SR, Baroni K, Van Ness JM, Snell CR.	Department of Physical Therapy, Thomas J. Long School of Pharmacy and Health Sciences, University of the Pacific, Stockton, California, USA.	Reliability and validity of Short Form 36 Version 2 to measure health perceptions in a sub-group of individuals with fatigue.	Disabil Rehabil. 2011;33(25-26):2596-604. Epub 2011 Jun 20.	PURPOSE: To determine the validity and reliability of Short Form 36 Version 2 (SF36v2) in sub-groups of individuals with fatigue. METHOD: Thirty subjects participated in this study, including n = 16 subjects who met case definition criteria for chronic fatigue syndrome (CFS) and n = 14 non-disabled sedentary matched control subjects. SF36v2 and Multidimensional Fatigue Inventory (MFI-20) were administered before two maximal cardiopulmonary exercise tests (CPETs) administered 24 h apart and an open-ended recovery questionnaire was administered 7 days after CPET challenge. The main outcome measures were self-reported time to recover to pre-challenge functional and symptom status, frequency of post-exertional symptoms and

	tdavenport@pacific.edu			SF36v2 sub-scale scores. RESULTS: Individuals with CFS demonstrated significantly lower SF36v2 and MFI-20 sub-scale scores prior to CPET. Between-group differences remained significant post-CPET, however, there were no significant group by test interaction effects. Subjects with CFS reported significantly more total symptoms ($p < 0.001$), as well as reports of fatigue ($p < 0.001$), neuroendocrine ($p < 0.001$), immune ($p < 0.01$), pain ($p < 0.01$) and sleep disturbance ($p < 0.01$) symptoms than control subjects as a result of CPET. Many symptom counts demonstrated significant relationships with SF36v2 sub-scale scores ($p < 0.05$). SF36v2 and MFI-20 sub-scale scores demonstrated significant correlations ($p < 0.05$). Various SF36v2 sub-scale scores demonstrated significant predictive validity to identify subjects who recovered from CPET challenge within 1 day and 7 days ($p < 0.05$). Potential floor effects were observed for both questionnaires for individuals with CFS. CONCLUSION: Various sub-scales of SF36v2 demonstrated adequate reliability and validity for clinical and research applications. Adequacy of sensitivity to change of SF36v2 as a result of a fatiguing stressor should be the subject of additional study.
Davenport TE, Stevens SR, Baroni K, Van Ness M, Snell CR.	Department of Physical Therapy, Thomas J. Long School of Pharmacy and Health Sciences, University of the Pacific, Stockton, CA 95211, USA. tdavenport@pacific.edu	Diagnostic accuracy of symptoms characterising chronic fatigue syndrome.	Disabil Rehabil. 2011;33(19-20):1768-75. Epub 2011 Jan 6.	PURPOSE: To determine the diagnostic accuracy for single symptoms and clusters of symptoms to distinguish between individuals with and without chronic fatigue syndrome (CFS). METHODS: A cohort study was conducted in an exercise physiology laboratory in an academic setting. Thirty subjects participated in this study ($n = 16$ individuals with CFS; $n = 14$ non-disabled sedentary matched control subjects). An open-ended symptom questionnaire was administered 1 week following the second of two maximal cardiopulmonary exercise tests administered 24 h apart. RESULTS: Receiver operating characteristics (ROC) curve analysis was significant for failure to recover within 1 day (area under the curve = 0.864, 95% confidence interval [CI]: 0.706-1.00, $p = 0.001$) but not within 7 days. Clinimetric properties of failure to recover within 1 day to predict membership in the CFS cohort were sensitivity 0.80, specificity 0.93, positive predictive value 0.92, negative predictive value 0.81, positive likelihood ratio 11.4, and negative likelihood ratio 0.22. Fatigue demonstrated high sensitivity and modest specificity to distinguish between cohorts, while neuroendocrine dysfunction, immune dysfunction, pain, and sleep disturbance demonstrated high specificity and modest sensitivity. ROC analysis suggested cut-point of three associated symptoms (0.871, 95% CI: 0.717-1.00, $p < 0.001$). A significant binary logistic regression model ($p < 0.001$) revealed immune abnormalities, sleep disturbance and pain accurately classified 92% of individuals with CFS and 88% of control subjects. CONCLUSIONS: A cluster of associated symptoms distinguishes between individuals with and without CFS. Fewer associated symptoms may be necessary to establish a diagnosis of CFS than currently described.
Davidson JR, Crawford C, Ives JA, Jonas WB.	Department of Psychiatry and Behavioral	Homeopathic treatments in psychiatry: a	J Clin Psychiatry. 2011 Jun;72(6):795-805.	OBJECTIVE: To systematically review placebo-controlled randomized trials of homeopathy for psychiatric conditions. DATA SOURCES: Eligible studies were identified using the following databases from database inception to April 2010:

	Science, Duke University Medical Center, Durham, North Carolina, USA. jonathan.davidson@duke.edu	systematic review of randomized placebo-controlled studies.		PubMed, CINAHL, PsycINFO, Hom-Inform, Cochrane CENTRAL, National Center for Complementary and Alternative Medicine grantee publications database, and ClinicalTrials.gov. Gray literature was also searched using Google, Google Scholar, the European Committee for Homeopathy, inquiries with homeopathic experts and manufacturers, and the bibliographic lists of included published studies and reviews. Search terms were as follows: (homeopath* or homoeopath*) and (placebo or sham) and (anxiety or panic or phobia or post-traumatic stress or PTSD or obsessive-compulsive disorder or fear or depress* or dysthym* or attention deficit hyperactivity or premenstrual syndrome or premenstrual disorder or premenstrual dysphoric disorder or traumatic brain injury or fibromyalgia or chronic fatigue syndrome or myalgic encephalitis or insomnia or sleep disturbance). Searches included only English-language literature that reported randomized controlled trials in humans. STUDY SELECTION: Trials were included if they met 7 criteria and were assessed for possible bias using the Scottish Intercollegiate Guidelines Network (SIGN) 50 guidelines. Overall assessments were made using the Grading of Recommendations Assessment, Development and Evaluation procedure. Identified studies were grouped into anxiety or stress, sleep or circadian rhythm complaints, premenstrual problems, attention-deficit/hyperactivity disorder, mild traumatic brain injury, and functional somatic syndromes. RESULTS: Twenty-five eligible studies were identified from an initial pool of 1,431. Study quality according to SIGN 50 criteria varied, with 6 assessed as good, 9 as fair, and 10 as poor. Outcome was unrelated to SIGN quality. Effect size could be calculated in 16 studies, and number needed to treat, in 10 studies. Efficacy was found for the functional somatic syndromes group (fibromyalgia and chronic fatigue syndrome), but not for anxiety or stress. For other disorders, homeopathy produced mixed effects. No placebo-controlled studies of depression were identified. Meaningful safety data were lacking in the reports, but the superficial findings suggested good tolerability of homeopathy. A funnel plot in 13 studies did not support publication bias ($\chi(2)(1) = 1.923$, $P = .166$). CONCLUSIONS: The database on studies of homeopathy and placebo in psychiatry is very limited, but results do not preclude the possibility of some benefit. © Copyright 2011 Physicians Postgraduate Press, Inc.
de Carvalho Leite JC, de L Drachler M, Killett A, Kale S, Nacul L, McArthur M, Hong CS, O'Driscoll L, Pheby D, Campion P, Lacerda E, Poland F.	School of Allied Health Professions, University of East Anglia, Norwich, England, United Kingdom, NR4 7TJ, UK. f.poland@uea.ac.	Social support needs for equity in health and social care: a thematic analysis of experiences of people with chronic fatigue syndrome/myalgic encephalomyelitis.	Int J Equity Health. 2011 Nov 2;10(1):46.	ABSTRACT:BACKGROUND: Needs-based resource allocation is fundamental to equitable care provision, which can meet the often-complex, fluctuating needs of people with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME). This has posed challenges both for those providing and those seeking support providers, in building shared understanding of the condition and of actions to address it. This qualitative study reports on needs for equity in health and social care expressed by adults living with CFS/ME. METHODS: The participants were 35 adults with CFS/ME in England, purposively selected to provide variation in clinical presentations, social backgrounds and illness experiences. Accounts of experienced needs and needs-

	uk.			related encounters with health and social services were obtained through a focus group (n = 6) and semi-structured interviews (n = 35). These were transcribed and needs related topics identified through data-led thematic analysis. FINDINGS: Participants emphasised needs for personalised, timely and sustained support to alleviate CFS/ME impacts and regain life control, in three thematic areas: (1) Illness symptoms, functional limitations and illness management; (2) practical support and social care; (3) financial support. Access of people with CFS/ME to support from health and social services was seen to be constrained by barriers stemming from social, cultural, organisational and professional norms and practices, further heightened for disadvantaged groups including some ethnic minorities. These reduced opportunities for their illness to be explained or associated functional limitations and social disadvantages to be addressed through social support. Participants sought more understanding of bio-psycho-social aspects of CFS/ME, of felt needs of people with CFS/ME and of human rights and disability rights, for providing person-centred, equitable care. CONCLUSIONS: Changes in attitudes of health practitioners, policy makers and general public and more flexibly organised health and social care provision are needed to address equity issues in support needs expressed by people with CFS/ME, to be underpinned by research-based knowledge and communication, for public and professional education. Policy development should include shared decision-making and coordinated action across organizations working for people with CFS/ME, human rights and disadvantaged groups. Experiences of people with CFS/ME can usefully inform an understanding of equity in their health and social care.
De Luca C, Raskovic D, Pacifico V, Thai JC, Korkina L.	Tissue Engineering & Skin Pathophysiology Laboratory and 2nd Dermatology Division, Dermatological Research Institute (IDI IRCCS), Via Monti di Creta 104, Rome 00167, Italy. c.deluca@idi.it	The search for reliable biomarkers of disease in multiple chemical sensitivity and other environmental intolerances.	Int J Environ Res Public Health. 2011 Jul;8(7):2770-97. Epub 2011 Jul 1.	Whilst facing a worldwide fast increase of food and environmental allergies, the medical community is also confronted with another inhomogeneous group of environment-associated disabling conditions, including multiple chemical sensitivity (MCS), fibromyalgia, chronic fatigue syndrome, electric hypersensitivity, amalgam disease and others. These share the features of poly-symptomatic multi-organ cutaneous and systemic manifestations, with postulated inherited/acquired impaired metabolism of chemical/physical/nutritional xenobiotics, triggering adverse reactions at exposure levels far below toxicologically-relevant values, often in the absence of clear-cut allergologic and/or immunologic involvement. Due to the lack of proven pathogenic mechanisms generating measurable disease biomarkers, these environmental hypersensitivities are generally ignored by sanitary and social systems, as psychogenic or "medically unexplained symptoms". The uncontrolled application of diagnostic and treatment protocols not corresponding to acceptable levels of validation, safety, and clinical efficacy, to a steadily increasing number of patients demanding assistance, occurs in many countries in the absence of evidence-based guidelines. Here we revise available information supporting the organic nature of these clinical conditions. Following intense research on gene polymorphisms of phase

				I/II detoxification enzyme genes, so far statistically inconclusive, epigenetic and metabolic factors are under investigation, in particular free radical/antioxidant homeostasis disturbances. The finding of relevant alterations of catalase, glutathione-transferase and peroxidase detoxifying activities significantly correlating with clinical manifestations of MCS, has recently registered some progress towards the identification of reliable biomarkers of disease onset, progression, and treatment outcomes.
de Souza PA, Matheus SM, Castan EP, Campos DH, Cicogna AC, Carvalho RF, Dal-Pai-Silva M.	Department of Morphology, Institute of Biosciences, UNESP, Botucatu, São Paulo, Brazil. pats_souza@yahoo.com.br	Morphological aspects of neuromuscular junctions and gene expression of nicotinic acetylcholine receptors (nAChRs) in skeletal muscle of rats with heart failure.	J Mol Histol. 2011 Dec;42(6):557-65. Epub 2011 Sep 18.	HF is syndrome initiated by a reduction in cardiac function and it is characterized by the activation of compensatory mechanisms. Muscular fatigue and dyspnoea are the more common symptoms in HF; these may be due in part to specific skeletal muscle myopathy characterized by reduced oxidative capacity, a shift from slow fatigue resistant type I to fast less fatigue resistant type II fibers and downregulation of myogenic regulatory factors (MRFs) gene expression that can regulate gene expression of nicotinic acetylcholine receptors (nAChRs). In chronic heart failure, skeletal muscle phenotypic changes could influence the maintenance of the neuromuscular junction morphology and nAChRs gene expression during this syndrome. Two groups of rats were studied: control (CT) and Heart Failure (HF), induced by a single intraperitoneal injection of monocrotaline (MCT). At the end of the experiment, HF was evaluated by clinical signs and animals were sacrificed. Soleus (SOL) muscles were removed and processed for morphological, morphometric and molecular NMJ analyses. Our major finding was an up-regulation in the gene expression of the alpha1 and epsilon subunits of nAChR and a spot pattern of nAChR in SOL skeletal muscle in this acute monocrotaline induced HF. Our results suggest a remodeling of nAChR alpha1 and epsilon subunit during heart failure and may provide valuable information for understanding the skeletal muscle myopathy that occurs during this syndrome.
de Tommaso M, Federici A, Serpino C, Vecchio E, Franco G, Sardaro M, Delussi M, Livrea P.	Neurophysiopathology of Pain Unit, Neurological and Psychiatric Sciences Department, Medical Faculty, Policlinico General Hospital, Aldo Moro University, Neurological Building, Piazza Giulio Cesare 11,	Clinical features of headache patients with fibromyalgia comorbidity.	J Headache Pain. 2011 Dec;12(6):629-38. Epub 2011 Aug 17.	Our previous study assessed the prevalence of fibromyalgia (FM) syndrome in migraine and tension-type headache. We aimed to update our previous results, considering a larger cohort of primary headache patients who came for the first time at our tertiary headache ambulatory. A consecutive sample of 1,123 patients was screened. Frequency of FM in the main groups and types of primary headaches; discriminating factor for FM comorbidity derived from headache frequency and duration, age, anxiety, depression, headache disability, allodynia, pericranial tenderness, fatigue, quality of life and sleep, and probability of FM membership in groups; and types of primary headaches were assessed. FM was present in 174 among a total of 889 included patients. It prevailed in the tension-type headache main group (35%, $p < 0.0001$) and chronic tension-type headache subtype (44.3%, $p < 0.0001$). Headache frequency, anxiety, pericranial tenderness, poor sleep quality, and physical disability were the best discriminating variables for FM comorbidity, with 81.2% sensitivity. Patients presenting with chronic migraine and chronic tension-type

	70124, Bari, Italy. m.detommaso@neurol.uniba.it			headache had a higher probability of sharing the FM profile (Bonferroni test, $p < 0.01$). A phenotypic profile where headache frequency concurs with anxiety, sleep disturbance, and pericranial tenderness should be individuated to detect the development of diffuse pain in headache patients.
Delviks-Frankenberry KA, Chaipan C, Bagni R, Wyvill K, Yarchoan R, Pathak VK.	Viral Mutation Section, HIV Drug Resistance Program, National Cancer Institute at Frederick, National Institutes of Health, Frederick, MD 21702, USA.	Lack of Detection of Xenotropic Murine Leukemia Virus-Related Virus in HIV-1 Lymphoma Patients.	Adv Virol. 2011;2011:797820. Epub 2011 Sep 8.	Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus reported to be associated with human prostate cancer and chronic fatigue syndrome. Since retroviruses cause various cancers, and XMRV replication might be facilitated by HIV-1 co-infection, we asked whether certain patients with HIV-associated lymphomas are infected with XMRV. Analysis of PMBCs and plasma from 26 patients failed to detect XMRV by PCR, ELISA, or Western blot, suggesting a lack of association between XMRV and AIDS-associated lymphomas.
Desai R, Neuberger J.		Safety of solid-organ transplantation from donors with chronic fatigue syndrome.	Transplantation. 2011 Apr 15;91(7):e51-2.	
Dittner AJ, Rimes K, Thorpe S.	South London & Maudsley NHS Trust, Chronic Fatigue Syndrome Unit, London, SE5 8AZ UK.	Negative perfectionism increases the risk of fatigue following a period of stress.	Psychol Health. 2011 Mar;26(3):253-68. Epub 2010 Feb 18.	Cognitive-behavioural models of excessive fatigue suggest that people who believe that failure to meet high standards indicates unacceptability to others (a form of 'negative perfectionism') are at risk of fatigue after a period of illness or stress. The present study investigates this using a prospective design and possible mediating factors between such beliefs and fatigue were also investigated. Undergraduate students completed questionnaires at the beginning of the academic year (time 1; n = 436) and again following a time of academic pressure, 16 weeks later (time 2; n = 206). Participants were significantly more fatigued at time 2 than at time 1. Negative perfectionism was positively associated with all measures of fatigue and predicted subsequent levels of physical fatigue after controlling for time 1 fatigue. Time 1 negative perfectionism was not associated with time 2 perfectionist studying behaviours, distress about academic work or specific health behaviours, but was associated with time 2 depression. Results also indicated that time 2 depression may account for the relationship between baseline negative perfectionism and subsequent fatigue. This is the first prospective study to demonstrate a significant relationship between perfectionism and subsequent fatigue.
Diószeghy P.	Jósa András Oktatókórház Egészségügyi Szolgáltató Nonprofit Kft., Neurológiai	[Diagnosis of immune-mediated neuropathies]. [Article in Hungarian]	Orv Hetil. 2011 Sep 25;152(39):1560-8.	Separate discussion of immune-mediated neuropathies from other neuropathies is justified by the serious consequences of the natural course of these diseases, like disability and sometimes even life threatening conditions. On the other hand nowadays effective treatments already exist, and with timely and correct diagnosis an appropriately chosen treatment may result in significant improvement of quality of life, occasionally even complete recovery. These are rare diseases, and the increasing

	Osztály, Nyíregyháza. dioszeghy@josa.hu			number of different variants makes it more difficult to recognize them. Their diagnosis is based on the precise knowledge of clinical signs and symptoms, and it is verified by the help of neurophysiologic and laboratory, first of all CSF examinations. Description of clinical features of the classic acute immune-mediated neuropathy, characterized by ascending paresis and demyelination is followed by a summary of characteristics of newly recognized axonal, regional and functional variants. Chronic immune-mediated demyelinating polyneuropathies are not diagnosed in due number even today. This paper does not only present the classic form but it also introduces the ever increasing special variants, like distal acquired demyelinating sensory neuropathy, Lewis-Sumner syndrome, multifocal motor neuropathy and paraproteinemic neuropathies. Vasculitic neuropathies can be divided into two groups: systemic and non-systemic ones. The first sign of a vasculitic neuropathy is a progressive, painful mononeuropathy; the classic clinical presentation is the mononeuritis multiplex. It is characterized by general signs like fever, loss of weight, fatigue. In systemic vasculitis organ specific symptoms are also present. From the paraneoplastic diseases the subacute sensory neuropathy and the sensory neuronopathy are members of the immune-mediated neuropathies, being most frequently associated with small cell lung cancer.
Djukic M, Schmidt-Samoa C, Nau R, von Steinbüchel N, Eiffert H, Schmidt H.	Department of Neurology, University of Goettingen, Goettingen, Germany.	The diagnostic spectrum in patients with suspected chronic Lyme neuroborreliosis--the experience from one year of a university hospital's Lyme neuroborreliosis outpatients clinic.	Eur J Neurol. 2011 Apr;18(4):547-55. doi: 10.1111/j.1468-1331.2010.03229.x. Epub 2010 Oct 27.	BACKGROUND AND PURPOSE: Studies addressing the diagnostic relevance of anti-Borrelia burgdorferi (BB) serum antibodies in patients with non-specific symptoms and suspected chronic Lyme neuroborreliosis (LNB) are scarce. METHODS: In this study, we enrolled within 1 year 122 patients with suspected chronic LNB. One hundred and fourteen patients had previously tested positive for BB. All patients had previously received antibiotic treatment. Each patient received a clinical examination and measurement of BB-specific antibodies. The diagnosis of neuroborreliosis was made according to the national guidelines of the German Society of Neurology. Nine patients had acute borreliosis. One of the nine met the criteria of acute LNB. Of the remaining 113 patients, 85 patients underwent a lumbar puncture. Ten seronegative subjects without lumbar puncture were also considered. In 61.8% of these 95 patients the quality of life, of sleep, mood, and anxiety were assessed. RESULTS: Of 95 patients, 25.3% had symptoms without a somatic cause or evidence of borreliosis, 38.9% had a well-defined illness unrelated to BB infection, and 29.5% suffered from symptoms without a detectable somatic cause, displaying antibodies against BB. Six patients were grouped as post-LNB syndrome. Most common symptoms in all categories were arthralgia, myalgia, dysaesthesia, depressive mood and chronic fatigue. CONCLUSION: Patients with persistent symptoms with elevated serum antibodies against BB but without signs of cerebrospinal fluid inflammation require further diagnostic examinations to exclude ongoing infection and to avoid co-infections and other treatable conditions (e.g. autoimmune diseases). One patient with acute LNB, who was treated with ceftriaxone for 3 weeks suffered from LNB with

				new headaches and persistent symptoms 6 months later. These data should encourage further studies with new experimental parameters. © 2010 The Author(s). European Journal of Neurology © 2010 EFNS.
Dodd RY, Hackett J Jr, Linnen JM, Dorsey K, Wu Y, Zou S, Qiu X, Swanson P, Schochetman G, Gao K, Carrick JM, Krysztof DE, Stramer SL.	American Red Cross Holland Laboratory, Rockville, Maryland 20855, USA. dodd@usa.redcross.org	Xenotropic murine leukemia virus-related virus does not pose a risk to blood recipient safety.	Transfusion. 2012 Feb;52(2):298-306. doi: 10.1111/j.1537-2995.2011.03450.x. Epub 2011 Nov 21.	BACKGROUND: When xenotropic murine leukemia virus-related virus (XMRV) was first reported in association with chronic fatigue syndrome, it was suggested that it might offer a risk to blood safety. Thus, the prevalence of the virus among blood donors and, if present, its transmissibility by transfusion need to be defined. STUDY DESIGN AND METHODS: Two populations of routine blood donor samples (1435 and 13,399) were obtained for prevalence evaluations; samples from a linked donor-recipient repository were also evaluated. Samples were tested for the presence of antibodies to XMRV-related recombinant antigens and/or for XMRV RNA, using validated, high-throughput systems. RESULTS: The presence of antibodies to XMRV could not be confirmed among a total of 17,249 blood donors or recipients (0%; 95% confidence interval [CI], 0%-0.017%); 1763 tested samples were nonreactive for XMRV RNA (0%; 95% CI, 0%-0.17%). Evidence of infection was absent from 109 recipients and 830 evaluable blood samples tested after transfusion of a total of 3741 blood components. CONCLUSIONS: XMRV and related murine leukemia virus (MLV) markers are not present among a large population of blood donors and evidence of transfusion transmission could not be detected. Thus, these viruses do not currently pose a threat to blood recipient safety and further actions relating to XMRV and MLV are not justified. © 2012 American Association of Blood Banks.
Dodd RY.	Research & Development, American Red Cross, Holland Laboratory, Rockville, MD 20855, USA. dodd@usa.redcross.org	Chronic fatigue syndrome, XMRV and blood safety.	Future Microbiol. 2011 Apr;6(4):385-9.	In the past few months, there has been public discussion relating to a new perspective on blood safety and specifically upon measures to prevent or discourage donation by individuals with a diagnosis of myalgic encephalopathy-chronic fatigue syndrome. This reflects an intriguing interplay between science, public health and public concern and illustrates some of the difficulties of making decisions in the face of uncertainty and inadequate information.
Duffy FH, McAnulty GB, McCreary MC, Cuchural GJ, Komaroff AL.	Department of Neurology, Children's Hospital Boston and Harvard Medical School, 300 Longwood Ave, Boston, Massachusetts 02115, USA.	EEG spectral coherence data distinguish chronic fatigue syndrome patients from healthy controls and depressed patients--a case control study.	BMC Neurol. 2011 Jul 1;11:82.	BACKGROUND: Previous studies suggest central nervous system involvement in chronic fatigue syndrome (CFS), yet there are no established diagnostic criteria. CFS may be difficult to differentiate from clinical depression. The study's objective was to determine if spectral coherence, a computational derivative of spectral analysis of the electroencephalogram (EEG), could distinguish patients with CFS from healthy control subjects and not erroneously classify depressed patients as having CFS. METHODS: This is a study, conducted in an academic medical center electroencephalography laboratory, of 632 subjects: 390 healthy normal controls, 70 patients with carefully defined CFS, 24 with major depression, and 148 with general fatigue. Aside from fatigue, all patients were medically healthy by history and examination. EEGs were

	fhd@sover.net			obtained and spectral coherences calculated after extensive artifact removal. Principal Components Analysis identified coherence factors and corresponding factor loading patterns. Discriminant analysis determined whether spectral coherence factors could reliably discriminate CFS patients from healthy control subjects without misclassifying depression as CFS. RESULTS: Analysis of EEG coherence data from a large sample (n = 632) of patients and healthy controls identified 40 factors explaining 55.6% total variance. Factors showed highly significant group differentiation ($p < .0004$) identifying 89.5% of unmedicated female CFS patients and 92.4% of healthy female controls. Recursive jackknifing showed predictions were stable. A conservative 10-factor discriminant function model was subsequently applied, and also showed highly significant group discrimination ($p < .001$), accurately classifying 88.9% unmedicated males with CFS, and 82.4% unmedicated male healthy controls. No patient with depression was classified as having CFS. The model was less accurate (73.9%) in identifying CFS patients taking psychoactive medications. Factors involving the temporal lobes were of primary importance. CONCLUSIONS: EEG spectral coherence analysis identified unmedicated patients with CFS and healthy control subjects without misclassifying depressed patients as CFS, providing evidence that CFS patients demonstrate brain physiology that is not observed in healthy normals or patients with major depression. Studies of new CFS patients and comparison groups are required to determine the possible clinical utility of this test. The results concur with other studies finding neurological abnormalities in CFS, and implicate temporal lobe involvement in CFS pathophysiology.
Dyer C.		Scientist who linked chronic fatigue syndrome to XMRV is sacked.	BMJ. 2011 Oct 11;343:d6541. doi: 10.1136/bmj.d6541.	
Dyer C.		GMC rules against doctor who used unconventional tests and treatments for chronic fatigue syndrome.	BMJ. 2011 Nov 7;343:d7220. doi: 10.1136/bmj.d7220.	
Dyer C.		Researcher into chronic fatigue syndrome is released on bail.	BMJ. 2011 Nov 25;343:d7683. doi: 10.1136/bmj.d7683.	
Eglinton R, Chung MC.	Independent Medical and Psychological Services, Taunton,	The relationship between posttraumatic stress disorder, illness	Psychiatry Res. 2011 Jul 30;188(2):245-52. Epub 2011 May 19.	This study investigated, firstly, the rate of posttraumatic stress disorder (PTSD) and the level of psychological well-being amongst people with chronic fatigue syndrome (CFS); and secondly, the extent to which illness cognitions, defence styles and PTSD symptom severity related to fatigue severity and psychological well-being. Seventy-

	United Kingdom.	cognitions, defence styles, fatigue severity and psychological well-being in chronic fatigue syndrome.		eight participants with a diagnosis of CFS completed the Chalder Fatigue Scale, the General Health Questionnaire-28, the Posttraumatic Stress Diagnostic Scale, the Illness Cognition Questionnaire and the Defence Style Questionnaire. Fifty-nine participants were recruited from the general public to form the non-fatigued control group. CFS participants had significantly higher levels of PTSD symptoms, lower levels of psychological well-being and more traumatic life events compared to the non-fatigued controls. Trauma exposure and PTSD severity both predicted CFS status. However, regression analyses demonstrated no significant relationship between PTSD symptoms and fatigue severity or the degree of psychological well-being. 'Helplessness' predicted both physical and mental fatigue and psychological well-being, whilst the 'mature' defence styles predicted fatigue severity only. The results offer support to previous research showing that the rate of traumatic life events and PTSD are significantly higher amongst the CFS population. The lack of relationship between PTSD symptoms and fatigue severity or psychological well-being indicates that these processes may operate independently of one another, via different appraisal processes. This study focused on fatigue severity, but it may be that the role of pain in CFS is a key element in the previously reported association between PTSD and CFS. Copyright © 2011 Elsevier Ireland Ltd. All rights reserved.
Eichenauer DA, Engert A.	First Department of Internal Medicine, University Hospital of Cologne, Cologne, Germany.	Therapy-related myeloid neoplasms in patients treated for hodgkin lymphoma.	Mediterr J Hematol Infect Dis. 2011;3(1):e2011046. Epub 2011 Oct 24.	Hodgkin lymphoma (HL) is a malignancy of the lymphatic system with an incidence of 2-3/100.000/year in developed countries. With modern multi-agent chemotherapy protocols optionally combined with radiotherapy (RT), 80% to 90% of HL patients achieve long-term remission and can be considered cured. However, current standard approaches bear a considerable risk for the development of treatment-related late effects. Thus, one major focus of current clinical research in HL is reducing the incidence of these late effects that include heart failure, infertility, chronic fatigue and therapy-related myelodysplastic syndrome/acute myeloid leukemia (t-MDS/t-AML). In previous analyses, t-MDS/t-AML after treatment for HL was associated with a poor prognosis. Nearly all patients died rapidly after diagnosis. However, more recent analyses indicated an improved outcome among patients with t-MDS/t-AML who are eligible for modern anti-leukemic treatment and allogeneic stem cell transplantation (aSCT). This article gives an overview of recent reports on the incidence and the treatment of t-MDS/t-AML after HL therapy and describes the efforts currently made to reduce the risk to develop this severe late effect.
Elfaitouri A, Shao X, Mattsson Ulfstedt J, Muradrasoli S, Bölin Wiener A, Golbob S, Ohrmalm C,	Section of Clinical Virology, Department of Medical Sciences, University of Uppsala, Uppsala, Sweden.	Murine gammaretrovirus group G3 was not found in Swedish patients with myalgic encephalomyelitis/chronic fatigue	PLoS One. 2011;6(10):e24602. Epub 2011 Oct 12.	BACKGROUND: The recent report of gammaretroviruses of probable murine origin in humans, called xenotropic murine retrovirus related virus (XMRV) and human murine leukemia virus related virus (HMRV), necessitated a bioinformatic search for this virus in genomes of the mouse and other vertebrates, and by PCR in humans. RESULTS: Three major groups of murine endogenous gammaretroviruses were identified. The third group encompassed both exogenous and endogenous Murine Leukemia Viruses (MLVs), and most XMRV/HMRV sequences reported from patients suffering from

Matousek M, Zachrisson O, Gottfries CG, Blomberg J.		syndrome and fibromyalgia.		myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Two sensitive real-time PCRs for this group were developed. The predicted and observed amplification range for these and three published XMRV/HMRV PCRs demonstrated conspicuous differences between some of them, partly explainable by a recombinatorial origin of XMRV. Three reverse transcription real-time PCRs (RTQPCRs), directed against conserved and not overlapping stretches of env, gag and integrase (INT) sequences of XMRV/HMRV were used on human samples. White blood cells from 78 patients suffering from ME/CFS, of which 30 patients also fulfilled the diagnostic criteria for fibromyalgia (ME/CFS/FM) and in 7 patients with fibromyalgia (FM) only, all from the Gothenburg area of Sweden. As controls we analyzed 168 sera from Uppsala blood donors. We controlled for presence and amplifiability of nucleic acid and for mouse DNA contamination. To score as positive, a sample had to react with several of the XMRV/HMRV PCRs. None of the samples gave PCR reactions which fulfilled the positivity criteria. CONCLUSIONS: XMRV/HMRV like proviruses occur in the third murine gammaretrovirus group, characterized here. PCRs developed by us, and others, approximately cover this group, except for the INT RTQPCR, which is rather strictly XMRV specific. Using such PCRs, XMRV/HMRV could not be detected in PBMC and plasma samples from Swedish patients suffering from ME/CFS/FM, and in sera from Swedish blood donors.
Erlwein O, Robinson MJ, Kaye S, Wills G, Izui S, Wessely S, Weber J, Cleare A, Collier D, McClure MO.	Jefferiss Research Trust Laboratories, Section of Infectious Diseases, Wright-Fleming Institute, Faculty of Medicine, Imperial College London, London, United Kingdom.	Investigation into the presence of and serological response to XMRV in CFS patients.	PLoS One. 2011 Mar 9;6(3):e17592.	The novel human gammaretrovirus xenotropic murine leukemia virus-related virus (XMRV), originally described in prostate cancer, has also been implicated in chronic fatigue syndrome (CFS). When later reports failed to confirm the link to CFS, they were often criticised for not using the conditions described in the original study. Here, we revisit our patient cohort to investigate the XMRV status in those patients by means of the original PCR protocol which linked the virus to CFS. In addition, sera from our CFS patients were assayed for the presence of xenotropic virus envelope protein, as well as a serological response to it. The results further strengthen our contention that there is no evidence for an association of XMRV with CFS, at least in the UK.
Erlwein O, Robinson MJ, Dustan S, Weber J, Kaye S, McClure MO.	Jefferiss Research Trust Laboratories, Section of Infectious Diseases, Imperial College London, London, United Kingdom.	DNA extraction columns contaminated with murine sequences.	PLoS One. 2011;6(8):e23484. Epub 2011 Aug 18.	Sequences of the novel gammaretrovirus, xenotropic murine leukemia virus-related virus (XMRV) have been described in human prostate cancer tissue, although the amounts of DNA are low. Furthermore, XMRV sequences and polytropic (p) murine leukemia viruses (MLVs) have been reported in patients with chronic fatigue syndrome (CFS). In assessing the prevalence of XMRV in prostate cancer tissue samples we discovered that eluates from naïve DNA purification columns, when subjected to PCR with primers designed to detect genomic mouse DNA contamination, occasionally gave rise to amplification products. Further PCR analysis, using primers to detect XMRV, revealed sequences derived from XMRV and pMLVs

				from mouse and human DNA and DNA of unspecified origin. Thus, DNA purification columns can present problems when used to detect minute amounts of DNA targets by highly sensitive amplification techniques.
Etzioni A.		Chronic fatigue syndrome: still a long way to go.	Isr Med Assoc J. 2011 Dec;13(12):761.	
Evering RM, Tönis TM, Vollenbroek-Hutten MM.	Roessingh Research and Development, Post Box 310, 7500 AH Enschede, The Netherlands. r.evering@rrd.nl	Deviations in daily physical activity patterns in patients with the chronic fatigue syndrome: a case control study.	J Psychosom Res. 2011 Sep;71(3):129-35. Epub 2011 May 18.	OBJECTIVES: Deviations in daily physical activity patterns may play an important role in the development and maintenance of fatigue in the chronic fatigue syndrome (CFS). The aim of this study is to gain insight into the objective daily physical activity pattern of patients with CFS in comparison with healthy controls. The secondary objective is studying the awareness in performing physical activities. METHODS: The objective daily physical activity pattern was measured with a tri-axial accelerometer in 35 patients with CFS and in 35 age- and gender-matched healthy controls. The objective daily physical activity level and distribution of physical activities at low, medium and high intensity levels during the day were measured. Moreover, variability in performing physical activities within and between subjects was computed. Subjective ratings of self-reported daily physical activity levels were assessed at a visual analog scale. RESULTS: CFS patients were significantly less physically active in the afternoon and evening, and spent fewer activities at high intensity levels and more at low intensity levels. Moreover, CFS patients showed more variability in their own physical activity pattern during the afternoon. The heterogeneity in the physical activity pattern between subjects within the CFS and control group did not differ. Finally, CFS patients were more aware about their daily physical activity level than healthy controls. CONCLUSION: CFS patients showed deviations in the objectively measured daily physical activity pattern. Future research should elucidate the relation between impaired balances in daily physical activity patterns and fatigue severity in CFS. Copyright © 2011 Elsevier Inc. All rights reserved.
Evering RM, van Weering MG, Groothuis-Oudshoorn KC, Vollenbroek-Hutten MM.	Roessingh Research and Development, Enschede, The Netherlands. r.evering@rrd.nl	Daily physical activity of patients with the chronic fatigue syndrome: a systematic review.	Clin Rehabil. 2011 Feb;25(2):112-33. Epub 2010 Oct 13.	OBJECTIVE: To give an overview of the physical activity level of patients with chronic fatigue syndrome in comparison with asymptomatic controls. DATA SOURCES: MEDLINE, Web of Science, EMBASE, PsycINFO, Picarta, the Cochrane Controlled Trial Register that is included in the Cochrane Library and reference tracking. REVIEW METHODS: A systematic literature search was conducted focusing on studies concerning physical activity levels of patients with chronic fatigue syndrome compared to controls. A meta-analysis was performed to pool data of the studies. RESULTS: Seventeen studies were included with 22 different comparisons between patients with chronic fatigue syndrome and controls. Fourteen studies, including 18 comparisons, showed lower physical activity levels in patients with chronic fatigue syndrome as compared to controls. Four studies, including four comparisons, showed no differences between both groups. The meta-analysis included seven studies and showed a daily physical activity level in patients with chronic fatigue syndrome of only

				68% of the physical activity level observed in control subjects. The pooled mean coefficient of variation in patients with chronic fatigue syndrome was higher as compared to control subjects (34.3% versus 31.5%), but this difference did not reach significance. CONCLUSION: Patients with chronic fatigue syndrome appear to be less physically active compared with asymptomatic controls. There is no difference in variation of physical activity levels between patients with chronic fatigue syndrome and healthy control subjects, but the validity and reliability of some methods of measuring physical activity is questionable or unknown.
Falkenberg VR, Whistler T, Murray JR, Unger ER, Rajeevan MS.	Division of High-Consequence Pathogens and Pathology, Centers for Disease Control & Prevention, Atlanta, GA, 30333, USA. MRajeevan@cdc.gov.	Identification of Phosphoglycerate Kinase 1 (PGK1) as a reference gene for quantitative gene expression measurements in human blood RNA.	BMC Res Notes. 2011 Sep 6;4:324.	ABSTRACT:BACKGROUND: Blood is a convenient sample and increasingly used for quantitative gene expression measurements with a variety of diseases including chronic fatigue syndrome (CFS). Quantitative gene expression measurements require normalization of target genes to reference genes that are stable and independent from variables being tested in the experiment. Because there are no genes that are useful for all situations, reference gene selection is an essential step to any quantitative reverse transcription-PCR protocol. Many publications have described appropriate genes for a wide variety of tissues and experimental conditions, however, reference genes that may be suitable for the analysis of CFS, or human blood RNA derived from whole blood as well as isolated peripheral blood mononuclear cells (PBMCs), have not been described. FINDINGS: Literature review and analyses of our unpublished microarray data were used to narrow down the pool of candidate reference genes to six. We assayed whole blood RNA from Tempus tubes and cell preparation tube (CPT)-collected PBMC RNA from 46 subjects, and used the geNorm and NormFinder algorithms to select the most stable reference genes. Phosphoglycerate kinase 1 (PGK1) was one of the optimal normalization genes for both whole blood and PBMC RNA, however, additional genes differed for the two sample types; Ribosomal protein large, P0 (RPLP0) for PBMC RNA and Peptidylprolyl isomerase B (PPIB) for whole blood RNA. We also show that the use of a single reference gene is sufficient for normalization when the most stable candidates are used. CONCLUSIONS: We have identified PGK1 as a stable reference gene for use with whole blood RNA and RNA derived from PBMC. When stable genes are selected it is possible to use a single gene for normalization rather than two or three. Optimal normalization will improve the ability of results from PBMC RNA to be compared with those from whole blood RNA and potentially allows comparison of gene expression results from blood RNA collected and processed by different methods with the intention of biomarker discovery. Results of this study should facilitate large-scale molecular epidemiologic studies using blood RNA as the target of quantitative gene expression measurements.
Falkenberg VR, Gurbaxani BM, Unger ER,	Division of Viral and Rickettsial Diseases, Centers	Functional genomics of serotonin receptor 2A (HTR2A):	Neuromolecular Med. 2011 Mar;13(1):66-76. Epub 2010 Oct 13.	Serotonergic neurotransmission plays a key role in the pathophysiology of neuropsychiatric illnesses. The functional significance of a promoter polymorphism, -1438G/A (rs6311), in one of the major genes of this system (serotonin receptor 2A,

Rajeevan MS.	for Disease Control & Prevention, Atlanta, GA 30333, USA.	interaction of polymorphism, methylation, expression and disease association.		HTR2A) remains poorly understood in the context of epigenetic factors, transcription factors and endocrine influences. We used functional and structural equation modeling (SEM) approaches to assess the contributions of the polymorphism (rs6311), DNA methylation and clinical variables to HTR2A expression in chronic fatigue syndrome (CFS) subjects from a population-based study. HTR2A was up-regulated in CFS through allele-specific expression modulated by transcription factors at critical sites in its promoter: an E47 binding site at position -1,438, (created by the A-allele of rs6311 polymorphism), a glucocorticoid receptor (GR) binding site encompassing a CpG at position -1,420, and Sp1 binding at CpG methylation site -1,224. Methylation at -1,420 was strongly correlated with methylation at -1,439, a CpG site that is dependent upon the G-allele of rs6311 at position -1,438. SEM revealed a strong negative interaction between E47 and GR binding (in conjunction with cortisol level) on HTR2A expression. This study suggests that the promoter polymorphism (rs6311) can affect both transcription factor binding and promoter methylation, and this along with an individual's stress response can impact the rate of HTR2A transcription in a genotype and methylation-dependent manner. This study can serve as an example for deciphering the molecular determinants of transcriptional regulation of major genes of medical importance by integrating functional genomics and SEM approaches. Confirmation in an independent study population is required.
Feehan SM	Liverpool ME Support Group.	The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1831-2. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36.	
Felger JC, Cole SW, Pace TW, Hu F, Woolwine BJ, Doho GH, Raison CL, Miller AH.	Department of Psychiatry and Behavioral Sciences, Emory University, Atlanta, GA, USA.	Molecular signatures of peripheral blood mononuclear cells during chronic interferon-α treatment: relationship with depression and fatigue.	Psychol Med. 2011 Dec 9:1-13. [Epub ahead of print]	BACKGROUND: Interferon-alpha (IFN-α) treatment for infectious disease and cancer causes high rates of depression and fatigue, and has been used to investigate the impact of inflammatory cytokines on brain and behavior. However, little is known about the transcriptional impact of chronic IFN-α on immune cells in vivo and its relationship to IFN-α-induced behavioral changes.MethodGenome-wide transcriptional profiling was performed on peripheral blood mononuclear cells (PBMCs) from 21 patients with chronic hepatitis C virus (HCV) either awaiting IFN-α therapy (n=10) or at 12 weeks of IFN-α treatment (n=11). RESULTS: Significance analysis of microarray data identified 252 up-regulated and 116 down-regulated gene transcripts. Of the up-regulated genes, 2'-5'-oligoadenylate synthetase 2 (OAS2), a gene linked to chronic fatigue syndrome (CFS), was the only gene that was differentially expressed in patients with IFN-α-induced depression/fatigue, and correlated with depression and fatigue scores at 12 weeks (r=0.80, p=0.003 and r=0.70, p=0.017 respectively). Promoter-based bioinformatic analyses linked IFN-α-

				related transcriptional alterations to transcription factors involved in myeloid differentiation, IFN-α signaling, activator protein-1 (AP1) and cAMP responsive element binding protein/activation transcription factor (CREB/ATF) pathways, which were derived primarily from monocytes and plasmacytoid dendritic cells. IFN-α-treated patients with high depression/fatigue scores demonstrated up-regulation of genes bearing promoter motifs for transcription factors involved in myeloid differentiation, IFN-α and AP1 signaling, and reduced prevalence of motifs for CREB/ATF, which has been implicated in major depression. CONCLUSIONS: Depression and fatigue during chronic IFN-α administration were associated with alterations in the expression (OAS2) and transcriptional control (CREB/ATF) of genes linked to behavioral disorders including CFS and major depression, further supporting an immune contribution to these diseases.
Fernández AA, Martínez MI.		[Cognitive impairment: a reality in chronic fatigue syndrome]. [Article in Spanish]	Med Clin (Barc). 2011 Mar 12;136(6):248-9. Epub 2010 Dec 18. Comment in Med Clin (Barc). 2011 Nov 12;137(12):572; author reply 572-3.	
Fernández-Solá J.		[Chronic fatigue syndrome: current situation]. [Article in Spanish]	Rev Clin Esp. 2011 Sep;211(8):407-9. Epub 2011 Jul 30. Comment on Rev Clin Esp. 2011 Sep;211(8):385-90.	
Fiest KM, Currie SR, Williams JV, Wang J.	Department of Psychiatry, University of Calgary, Canada.	Chronic conditions and major depression in community-dwelling older adults.	J Affect Disord. 2011 Jun;131(1-3):172-8. Epub 2010 Dec 18.	OBJECTIVES: To estimate (1) the prevalence of long-term medical conditions and of comorbid major depression, and (2) the associations between major depression and various chronic medical conditions in a general population of older adults (over 50 years of age) and in persons who are traditionally classified as seniors (65 years and older). METHODS: Data from the Canadian Community Health Survey- Mental Health and Wellbeing (CCHS-1.2) were analyzed. Non-institutionalized individuals over 15 years of age in the 10 Canadian provinces were sampled in the CCHS-1.2. The entire sample of the CCHS-1.2 consisted of 36,894 individuals, for the main analyses in this study the dataset was restricted to those aged 50 and over (n=15,591). Chronic health conditions were assessed using a self-report method of doctor diagnosis. The World Mental Health-Composite Diagnostic Interview was used to asses major depressive episodes based on DSM-IV criteria. RESULTS: The overall prevalence of having at least one chronic condition in those over 50 years of age was 82.4%, compared to 62.0% in those under 50. The prevalence of a major depressive episode in those over 50 with one chronic condition was 3.7%, compared with 1.0% in those without a long-term

				medical condition. The top 3 chronic health conditions in seniors aged 65 or older were arthritis/rheumatism, high blood pressure and back problems. Chronic Fatigue Syndrome, fibromyalgia and migraine headache had the highest comorbidity with major depression in the senior population. LIMITATIONS: The use of self-report data on chronic health conditions, potential diagnostic overlap between conditions, and the inability to make causal inferences due to the cross-sectional nature of the data are all limitations of the current study. CONCLUSIONS: Differences were found between rates of chronic conditions and major depression between the general population, older adults and seniors in this study. Further research is needed to delineate the direction of these relationships in seniors. Primary and secondary prevention efforts should target seniors who exhibit symptoms of depression or highly prevalent chronic health conditions. Copyright © 2010 Elsevier B.V. All rights reserved.
Fitzgerald K.	Institute for Functional Medicine, USA. kf@drkarafizgerald.com	A case report of a 53-year-old female with rheumatoid arthritis and osteoporosis: focus on lab testing and CAM therapies.	Altern Med Rev. 2011 Sep;16(3):250-62.	A 53-year-old female presented with rheumatoid arthritis and osteoporosis. Additional conditions and symptoms included Raynaud syndrome, fatigue, irritable bowel syndrome associated constipation (IBS-C), gastroesophageal reflux (GERD), menopausal symptoms, chronic urinary tract and upper respiratory infections, and weight gain. She was taking Arthrotec (a combination of diclofenac and misoprostol - for pain and inflammation), Fosamax Plus D (alendronate with vitamin D3 - recently prescribed because of low bone density), and Catapres (clonidine - for menopausal symptoms). Against the advice of her rheumatologist, she had recently discontinued taking Plaquenil (hydroxychloroquine), methotrexate, and prednisone due to significant side effects. Lab tests to identify underlying imbalances and to direct treatment were ordered. Treatment included dietary, nutritional, hormonal, and mind/body support. After one year of therapy, the patient experienced improvement with all of her presenting conditions and symptoms, which enabled her to discontinue several medications. She became versed in identifying and avoiding the environmental triggers of her disease, including foods (dairy, wheat, eggs, and soy), molds, and emotional stress. Antinuclear antibodies were normalized. She experienced a 7.5-percent improvement in left trochanteric bone density - comparable to bisphosphonate therapy. Mild improvements were also noted in the spine and bilateral femoral neck.
Fluge Ø, Bruland O, Risa K, Storstein A, Kristoffersen EK, Sapkota D, Næss H, Dahl O, Nyland H, Mella O.	Department of Oncology and Medical Physics, Haukeland University Hospital, Bergen, Norway. oystein.fluge@gm	Benefit from B-lymphocyte depletion using the anti-CD20 antibody rituximab in chronic fatigue syndrome. A double-blind and placebo-controlled	PLoS One. 2011;6(10):e26358. Epub 2011 Oct 19.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disease of unknown aetiology. Major CFS symptom relief during cancer chemotherapy in a patient with synchronous CFS and lymphoma spurred a pilot study of B-lymphocyte depletion using the anti-CD20 antibody Rituximab, which demonstrated significant clinical response in three CFS patients. METHODS AND FINDINGS: In this double-blind, placebo-controlled phase II study (NCT00848692), 30 CFS patients were randomised to either Rituximab 500 mg/m(2) or saline, given twice two weeks apart, with follow-up for 12 months. Xenotropic murine leukemia virus-related virus (XMRV) was not detected in any of the

	ail.com	study.		patients. The responses generally affected all CFS symptoms. Major or moderate overall response, defined as lasting improvements in self-reported Fatigue score during follow-up, was seen in 10 out of 15 patients (67%) in the Rituximab group and in two out of 15 patients (13%) in the Placebo group (p = 0.003). Mean response duration within the follow-up period for the 10 responders to Rituximab was 25 weeks (range 8-44). Four Rituximab patients had clinical response durations past the study period. General linear models for repeated measures of Fatigue scores during follow-up showed a significant interaction between time and intervention group (p = 0.018 for self-reported, and p = 0.024 for physician-assessed), with differences between the Rituximab and Placebo groups between 6-10 months after intervention. The primary end-point, defined as effect on self-reported Fatigue score 3 months after intervention, was negative. There were no serious adverse events. Two patients in the Rituximab group with pre-existing psoriasis experienced moderate psoriasis worsening. CONCLUSION: The delayed responses starting from 2-7 months after Rituximab treatment, in spite of rapid B-cell depletion, suggests that CFS is an autoimmune disease and may be consistent with the gradual elimination of autoantibodies preceding clinical responses. The present findings will impact future research efforts in CFS. TRIAL REGISTRATION: ClinicalTrials.gov NCT00848692.
Ford AC, Talley NJ.	Leeds Gastroenterology Institute, D Floor, Clarendon Wing, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK. alexf12399@yahoo.com	Mucosal inflammation as a potential etiological factor in irritable bowel syndrome: a systematic review.	J Gastroenterol. 2011 Apr;46(4):421-31. Epub 2011 Feb 18.	BACKGROUND: The causes of irritable bowel syndrome (IBS) remain obscure. Some investigators have proposed chronic low-grade mucosal inflammation as a potential etiological factor. We performed a systematic review to examine this issue in detail. METHODS: MEDLINE, EMBASE, and EMBASE classic were searched up to December 2010 to identify studies of case-control design applying tests for low-grade inflammation to either full-thickness intestinal or endoscopic mucosal biopsies from patients with IBS. Controls were required to be healthy individuals, or asymptomatic patients undergoing investigation for reasons other than the reporting of upper or lower gastrointestinal symptoms. Individual study results were summarized descriptively. RESULTS: The literature search identified 1388 citations, of which 16 studies were eligible for inclusion. Individual study results were diverse, partly as a consequence of the different surrogate markers for inflammatory mechanisms studied. Mast cells, T lymphocytes, B lymphocytes, and mucosal cytokine production all appeared altered among cases with IBS in individual studies, while no study demonstrated a significant difference in numbers of plasma cells, neutrophils, or eosinophils. Some studies suggested a relationship between mast cell abnormalities and symptom severity and frequency, as well as co-existent fatigue and depression. Studies were limited by the lack of comparability of controls, and the fact that most were conducted in highly selected groups of patients with IBS. CONCLUSIONS: Low-grade mucosal inflammation, particularly mast cell activation, may be a contributory factor in the pathogenesis of IBS. Mast cell stabilizers warrant further assessment as a potential therapy in the condition.

Frampton D, Kerr J, Harrison TJ, Kellam P.	Department of Infection, Division of Infection and Immunity, University College London, London, United Kingdom.	Assessment of a 44 gene classifier for the evaluation of chronic fatigue syndrome from peripheral blood mononuclear cell gene expression.	PLoS One. 2011 Mar 30;6(3):e16872.	Chronic fatigue syndrome (CFS) is a clinically defined illness estimated to affect millions of people worldwide causing significant morbidity and an annual cost of billions of dollars. Currently there are no laboratory-based diagnostic methods for CFS. However, differences in gene expression profiles between CFS patients and healthy persons have been reported in the literature. Using mRNA relative quantities for 44 previously identified reporter genes taken from a large dataset comprising both CFS patients and healthy volunteers, we derived a gene profile scoring metric to accurately classify CFS and healthy samples. This metric out-performed any of the reporter genes used individually as a classifier of CFS.To determine whether the reporter genes were robust across populations, we applied this metric to classify a separate blind dataset of mRNA relative quantities from a new population of CFS patients and healthy persons with limited success. Although the metric was able to successfully classify roughly two-thirds of both CFS and healthy samples correctly, the level of misclassification was high. We conclude many of the previously identified reporter genes are study-specific and thus cannot be used as a broad CFS diagnostic.
Frost J, Okun S, Vaughan T, Heywood J, Wicks P.	VU Amsterdam, KankerNL, Amsterdam, Netherlands. jeana.frost@gmail.com	Patient-reported outcomes as a source of evidence in off-label prescribing: analysis of data from PatientsLikeMe.	J Med Internet Res. 2011 Jan 21;13(1):e6.	BACKGROUND: Evaluating a new use for an existing drug can be expensive and time consuming. Providers and patients must all too often rely upon their own individual-level experience to inform clinical practice, which generates only anecdotal and unstructured data. While academic-led clinical trials are occasionally conducted to test off-label uses of drugs with expired patents, this is relatively rare. In this work, we explored how a patient-centered online research platform could supplement traditional trials to create a richer understanding of medical products postmarket by efficiently aggregating structured patient-reported data. PatientsLikeMe is a tool for patients, researchers, and caregivers (currently 82,000 members across 11 condition-based communities) that helps users make treatment decisions, manage symptoms, and improve outcomes. Members enter demographic information, longitudinal treatment, symptoms, outcome data, and treatment evaluations. These are reflected back as longitudinal health profiles and aggregated reports. Over the last 3 years, patients have entered treatment histories and evaluations on thousands of medical products. These data may aid in evaluating the effectiveness and safety of some treatments more efficiently and over a longer period of time course than is feasible through traditional trials. OBJECTIVE: The objective of our study was to examine the illustrative cases of amitriptyline and modafinil - drugs commonly used off-label. METHODS: We analyzed patient-reported treatment histories and drug evaluations for each drug, examining prevalence, treatment purpose, and evaluations of effectiveness, side effects, and burden. RESULTS: There were 1948 treatment histories for modafinil and 1394 treatment reports for amitriptyline reported across five PatientsLikeMe communities (multiple sclerosis, Parkinson's disease, mood conditions, fibromyalgia/chronic fatigue syndrome, and amyotrophic lateral sclerosis). In these reports, the majority of members reported taking the drug for off-label uses.

				Only 34 of the 1755 (1%) reporting purpose used modafinil for an approved purpose (narcolepsy or sleep apnea). Only 104 out of 1197 members (9%) reported taking amitriptyline for its approved indication, depression. Members taking amitriptyline for off-label purposes rated the drug as more effective than those who were taking it for its approved indication. While dry mouth is a commonly reported side effect of amitriptyline for most patients, 88 of 220 (40%) of people with amyotrophic lateral sclerosis on the drug reported taking advantage of this side effect to treat their symptom of excess saliva. CONCLUSIONS: Patient-reported outcomes, like those entered within PatientsLikeMe, offer a unique real-time approach to understand utilization and performance of treatments across many conditions. These patient-reported data can provide a new source of evidence about secondary uses and potentially identify targets for treatments to be studied systematically in traditional efficacy trials.
Furuta RA, Miyazawa T, Sugiyama T, Kuratsune H, Ikeda Y, Sato E, Misawa N, Nakatomi Y, Sakuma R, Yasui K, Yamaguti K, Hirayama F.	Department of Research, Japanese Red Cross Osaka Blood Center, 2-4-43 Morinomiya, Joto-ku, Osaka 536-8505, Japan. furuta@osaka.bc.jrc.or.jp	No association of xenotropic murine leukemia virus-related virus with prostate cancer or chronic fatigue syndrome in Japan.	Retrovirology. 2011 Mar 17;8:20.	BACKGROUND: The involvement of xenotropic murine leukemia virus-related virus (XMRV) in prostate cancer (PC) and chronic fatigue syndrome (CFS) is disputed as its reported prevalence ranges from 0% to 25% in PC cases and from 0% to more than 80% in CFS cases. To evaluate the risk of XMRV infection during blood transfusion in Japan, we screened three populations--healthy donors (n = 500), patients with PC (n = 67), and patients with CFS (n = 100)--for antibodies against XMRV proteins in freshly collected blood samples. We also examined blood samples of viral antibody-positive patients with PC and all (both antibody-positive and antibody-negative) patients with CFS for XMRV DNA. RESULTS: Antibody screening by immunoblot analysis showed that a fraction of the cases (1.6-3.0%) possessed anti-Gag antibodies regardless of their gender or disease condition. Most of these antibodies were highly specific to XMRV Gag capsid protein, but none of the individuals in the three tested populations retained strong antibody responses to multiple XMRV proteins. In the viral antibody-positive PC patients, we occasionally detected XMRV genes in plasma and peripheral blood mononuclear cells but failed to isolate an infectious or full-length XMRV. Further, all CFS patients tested negative for XMRV DNA in peripheral blood mononuclear cells. CONCLUSION: Our data show no solid evidence of XMRV infection in any of the three populations tested, implying that there is no association between the onset of PC or CFS and XMRV infection in Japan. However, the lack of adequate human specimens as a positive control in Ab screening and the limited sample size do not allow us to draw a firm conclusion.
Galbraith S, Cameron B, Li H, Lau D, Vollmer-Conna U, Lloyd AR.	School of Mathematics and Statistics, Faculty of Science, University of New South Wales,	Peripheral blood gene expression in postinfective fatigue syndrome following from three different triggering infections.	J Infect Dis. 2011 Nov 15;204(10):1632-40. Epub 2011 Sep 29.	BACKGROUND: Several infections trigger postinfective fatigue syndromes, which share key illness characteristics with each other and with chronic fatigue syndrome (CFS). Previous cross-sectional case-control studies of CFS have suggested that unique gene expression signatures are evident in peripheral blood samples. METHODS: Peripheral blood transcriptomes in samples collected longitudinally, in 18 subjects with a fatigue syndrome lasting ≥ 6 months after acute infection due to Epstein-Barr

	Sydney, Australia.			virus, Ross River virus, or Coxiella burnetii (Q fever), and 18 matched control subjects who had recovered promptly, were studied by microarray (n = 127) and confirmatory quantitative polymerase chain reaction (PCR). Gene expression patterns associated with CFS were sought by univariate statistics and regression modeling. RESULTS: There were 23 genes with modest differential expression (0.6-2.3-fold change) in within-subject comparisons of early, symptomatic time points with late, recovered time points. There were modest differences found in 63 genes, either in cross-sectional comparison of cases and controls at 6 months after infection onset or in the regression model. There were 223 genes significantly correlated with individual symptom domains. Quantitative PCR confirmed 33 (73%) of 45 genes-none were consistent across cohorts. CONCLUSIONS: Although the illness characteristics of patients with postinfective fatigue syndromes have more similarities than differences, no reliable peripheral blood gene expression correlate is evident.
Gardner A, Boles RG.	Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden. agtorndal@odenhall.se	Beyond the serotonin hypothesis: mitochondria, inflammation and neurodegeneration in major depression and affective spectrum disorders.	Prog Neuropsychopharmacol Biol Psychiatry. 2011 Apr 29;35(3):730-43. Epub 2010 Aug 5.	For many years, a deficiency of monoamines including serotonin has been the prevailing hypothesis on depression, yet research has failed to confirm consistent relations between brain serotonin and depression. High degrees of overlapping comorbidities and common drug efficacies suggest that depression is one of a family of related conditions sometimes referred to as the "affective spectrum disorders", and variably including migraine, irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia and generalized anxiety disorder, among many others. Herein, we present data from many different experimental modalities that strongly suggest components of mitochondrial dysfunction and inflammation in the pathogenesis of depression and other affective spectrum disorders. The three concepts of monoamines, energy metabolism and inflammatory pathways are inter-related in many complex manners. For example, the major categories of drugs used to treat depression have been demonstrated to exert effects on mitochondria and inflammation, as well as on monoamines. Furthermore, commonly-used mitochondrial-targeted treatments exert effects on mitochondria and inflammation, and are increasingly being shown to demonstrate efficacy in the affective spectrum disorders. We propose that interactions among monoamines, mitochondrial dysfunction and inflammation can inspire explanatory, rather than mere descriptive, models of these disorders. Copyright © 2010 Elsevier Inc. All rights reserved.
Garson JA, Kellam P, Towers GJ.	MRC Centre for Medical Molecular Virology, Division of Infection and Immunity, University College London, 46	Analysis of XMRV integration sites from human prostate cancer tissues suggests PCR contamination rather than genuine human infection.	Retrovirology. 2011 Feb 25;8:13.	XMRV is a gammaretrovirus associated in some studies with human prostate cancer and chronic fatigue syndrome. Central to the hypothesis of XMRV as a human pathogen is the description of integration sites in DNA from prostate tumour tissues. Here we demonstrate that 2 of 14 patient-derived sites are identical to sites cloned in the same laboratory from experimentally infected DU145 cells. Identical integration sites have never previously been described in any retrovirus infection. We propose that the patient-derived sites are the result of PCR contamination. This observation further undermines the notion that XMRV is a genuine human pathogen.

	Cleveland St, London W1T 4JF, UK.			
Giakoumakis J.		The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1831; author reply 1834-5. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5.	
Glise K, Anderson AL, Jonsdottir IH.	Institutet för stressmedicin, Göteborg. kristina.glise@vgregion.se	[Physical activity good against stress-related psychological morbidity]. [Article in Swedish]	Lakartidningen. 2011 Sep 7-13;108(36):1692-4.	
Godderis L, Dours G, Laire G, Viaene MK.	Katholieke Universiteit Leuven, Department of Occupational, Environmental and Insurance Medicine, Leuven 3000, Belgium. Lode.Godderis@med.kuleuven.be	Sleep apnoeas and neurobehavioral effects in solvent exposed workers.	Int J Hyg Environ Health. 2011 Jan;214(1):66-70. Epub 2010 Sep 16.	BACKGROUND: Exposure to organic solvents may cause an increase of sleep apnoeas, which may explain the excess of fatigue, concentration and memory problems reported in exposed workers. METHODS: Polysomnography was performed in 21 long-term exposed printers and 27 controls. In addition, a questionnaire regarding sleep related complaints, Q16 questionnaire and computerized neurobehavioral tests were administered. The groups matched well regarding age, weight, neck circumference and schooling level. A semi-quantitative cumulative exposure index was calculated. RESULTS: Excessive sleepiness while watching TV ($p<0.01$) and diminished sexual interest ($p=0.03$) was found in the organic solvent-workers. The sleep complaints score correlated positively with the exposure index and duration (both $p=0.01$). The polysomnography results showed an increase of central apnoeas in the exposed workers (67%) compared to the referents (30%). The presence of central apnoeas was positively correlated with the exposure index ($p<0.05$) in regression models. Of the neurobehavioral test only hand-eye coordination was dose-related impaired in the exposed workers. The co-existence of abnormal values on at least one neurobehavioral test and the presence of central apnoeas was observed in the exposed workers, but did not reach significance. CONCLUSIONS: Workers chronically exposed to low organic solvent levels may experience mild sleeping problems, however, our data do not support the hypothesis that the clinical picture of chronic toxic encephalopathy can be primarily caused by the induction of sleep apnoea syndrome. It seems thus that the risk to experience central apnoeas rather accompanies the risk of impaired neurobehavioral performance with increasing

				exposure in a working population. Copyright © 2010 Elsevier GmbH. All rights reserved.
Goodwin L, White PD, Hotopf M, Stansfeld SA, Clark C.	Centre for Psychiatry, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK. l.goodwin@qmul.ac.uk	Psychopathology and physical activity as predictors of chronic fatigue syndrome in the 1958 british birth cohort: a replication study of the 1946 and 1970 birth cohorts.	Ann Epidemiol. 2011 May;21(5):343-50.	PURPOSE: In this study, we investigate whether prospective associations between psychopathology, physical activity, and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) observed in the 1946 and 1970 birth cohorts were replicable in the 1958 British birth cohort. METHODS: Prospective study using the 1958 British birth cohort, which included 98.7% of births from 1 week in March 1958 in England, Wales, and Scotland. The outcome was self-reported CFS/ME by the age of 42 years, at which point 11,419 participants remained in the study. Psychopathology was assessed by the Rutter scales in childhood and the Malaise Inventory in adulthood. Physical activity was reported by the cohort member, mother and teacher in childhood and adulthood. RESULTS: The prevalence of CFS/ME was 1.0% (95% confidence interval [CI] = 0.9-1.3) and the median age of onset was 34 years. Premorbid psychopathology at 23 years (odds ratio [OR] = 1.85, 95% CI = 1.06-3.22) and 33 years (OR = 2.81, 95% CI = 1.28-6.18) significantly increased the odds of developing CFS/ME, supporting the 1946 cohort findings. Childhood psychopathology, sedentary behavior in childhood, and persistent exercise in adulthood were not associated with CFS/ME. CONCLUSIONS: In cohort studies premorbid psychopathology in adulthood is a replicated risk marker for CFS/ME, whereas premorbid extremes of physical activity are not. Copyright © 2011 Elsevier Inc. All rights reserved.
Goudsmit EM, Nijs J, Jason LA, Wallman KE.	School of Psychology, University of East London , Stratford, London, E15 4LZ , UK.	Pacing as a strategy to improve energy management in myalgic encephalomyelitis/chronic fatigue syndrome: a consensus document.	Disabil Rehabil. 2011 Dec 19. [Epub ahead of print]	Purpose: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a debilitating condition characterized by a number of symptoms which typically worsen following minimal exertion. Various strategies to manage the limited energy levels have been proposed. Of these, pacing has been consistently rated as one of the most helpful in surveys conducted by patient groups. This review is a response to the paucity of the information on pacing in the scientific literature. Method: We describe the principle of pacing and how this can be adapted to meet individual abilities and preferences. A critical evaluation of the research was conducted to ascertain the benefits and limitations of this strategy. Results: Based on various studies, it is proposed that pacing can help to stabilize the condition and avoid post-exertional malaise. Conclusion: Pacing offers practitioners an additional therapeutic option which is acceptable to the majority of patients and can reduce the severity of the exertion-related symptoms of ME/CFS. [Box: see text].
Graham KF.		Dietary salt restriction and chronic fatigue syndrome: a hypothesis.	Med Hypotheses. 2011 Sep;77(3):462-3. Epub 2011 Jun 15.	
Gray ER, Garson	Department of	No evidence of XMRV	PLoS One. 2011 Mar	BACKGROUND: Several studies have implicated a recently discovered

JA, Breuer J, Edwards S, Kellam P, Pillay D, Towers GJ.	Infection and Immunity, University College London, London, United Kingdom. e.gray@ucl.ac.uk	or related retroviruses in a London HIV-1-positive patient cohort.	23;6(3):e18096.	gammaretrovirus, XMRV (Xenotropic murine leukaemia virus-related virus), in chronic fatigue syndrome and prostate cancer, though whether as causative agent or opportunistic infection is unclear. It has also been suggested that the virus can be found circulating amongst the general population. The discovery has been controversial, with conflicting results from attempts to reproduce the original studies. METHODOLOGY/PRINCIPAL FINDINGS: We extracted peripheral blood DNA from a cohort of 540 HIV-1-positive patients (approximately 20% of whom have never been on anti-retroviral treatment) and determined the presence of XMRV and related viruses using TaqMan PCR. While we were able to amplify as few as 5 copies of positive control DNA, we did not find any positive samples in the patient cohort. CONCLUSIONS/SIGNIFICANCE: In view of these negative findings in this highly susceptible group, we conclude that it is unlikely that XMRV or related viruses are circulating at a significant level, if at all, in HIV-1-positive patients in London or in the general population.
Güthlin C, Anton A, Kruse J, Walach H.	1Johann Wolfgang Goethe University, Frankfurt/Main, Germany.	Subjective concepts of chronically ill patients using distant healing.	Qual Health Res. 2012 Mar;22(3):320-31. Epub 2011 Sep 14.	Distant healing procedures consist of benevolent intentions, often taking the form of prayers for a patient. Despite inconclusive evidence regarding distant healing, prayers are a widespread health-related technique. We studied subjective concepts of distant healing in 17 patients suffering from chronic fatigue syndrome and multiple chemical sensitivity who were given distant healing during a randomized controlled trial. We applied reconstructive interview analysis when analyzing the results. The overall theme was the tension between mainstream medicine and the immaterial healing procedure. Several components highlighted this tension: (a) patterns of legitimizing the use of distant healing, (b) distant healing and the social setting, (c) integrating distant healing into their belief system, and (d) reconstruction of effects by means of hindsight. The interviews showed that patients felt the need to legitimize having tried distant healing. They had to bear the full ambiguity of biomedicine being in competition with distant healing, though also experiencing distant healing as giving support.
Haba-Rubio J, de Seigneux S, Heinzer R.	Centre d'investigation et de recherche sur le sommeil, CHU Vaudois (CHUV), BH 06-204, 1011 Lausanne, Suisse.	[Sleep disorders in chronic renal failure.] [Article in French]	Nephrol Ther. 2011 Sep 29. [Epub ahead of print]	Sleep disorders are common in patients with chronic renal failure (CRF), especially in those receiving hemodialysis. Sleep-related complaints in this patient population may include insomnia, daytime sleepiness or fatigue and depression. In addition to causing impairment of daytime function and quality of life, sleep apnea may also increase the cardiovascular morbidity and mortality, especially in dialysis patients. In CRF patients, an increased prevalence of sleep apnea, restless legs syndrome and periodic limb movement during sleep has been reported. Epidemiology, pathophysiology and treatment of sleep disorders in CRF and dialysis patients are still unclear and require further research. Copyright © 2011 Association Société de néphrologie. Published by Elsevier SAS. All rights reserved.
Haldorsen K, Bjelland I, Bolstad	Broegelmann Research	A five-year prospective study of	Arthritis Res Ther. 2011 Oct	ABSTRACT: INTRODUCTION: Fatigue is prevalent in primary Sjögren's syndrome (pSS), and contributes to the considerably reduced health related quality of life in this

Al, Jonsson R, Brun JG.	Laboratory, The Gade Institute, Laboratory Bldg,, Haukeland University Hospital, N-5021 Bergen, Norway. karstein.haldorsen@uib.no.	fatigue in primary Sjögren's syndrome.	13;13(5):R167. [Epub ahead of print]	disease. The symptom is included in proposed disease activity and outcome measures for pSS. Several studies indicate that there is an inflammatory component of fatigue in pSS and other chronic inflammatory rheumatic diseases. The purpose of this study was to investigate fatigue change in pSS in a longitudinal study, and explore whether any clinical or laboratory variables at baseline, including serum cytokines, were associated with a change in fatigue scores over time. METHODS: A clinical and laboratory investigation of 141 patients fulfilling the American-European consensus criteria of pSS was undertaken in the period May 2004 to April 2005. Median time since diagnosis was 5.5 years. Examinations included the fatigue questionnaires: fatigue severity scale (FSS), fatigue visual analogue scale (VAS), functional assessment of chronic illness therapy - fatigue (FACIT-F) and medical outcome study short form-36 (SF-36) vitality, which were repeated in a follow-up investigation in January and February 2010. RESULTS: A total of 122 patients (87%) responded at both time-points. Thirty-five percent of patients experienced a clinically significant FSS increase. On the group level, fatigue measures did not change except that there was a slight deterioration in SF-36 vitality score. High serum anti-Sjögren's syndrome A antigen (anti-SSA) showed weak associations with high baseline fatigue, and patients with increasing fatigue had lower baseline unstimulated whole salivary volume. Weak associations between increasing fatigue and serum immunoglobulin G (IgG), and the pro-inflammatory cytokine interleukin-17 (IL-17), were observed. Baseline sicca symptoms correlated with higher fatigue both at baseline and with increasing fatigue over time. Linear regression analysis did not identify any predictive ability of clinical or laboratory measures on fatigue change over time. CONCLUSIONS: Fatigue remained mainly unchanged over time. Using multivariate models did not reveal any clinical or laboratory predictors of fatigue change over time.
Hamaguchi M, Kawahito Y, Takeda N, Kato T, Kojima T.	Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465, Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan. seele@koto.kpu-m.ac.jp	Characteristics of chronic fatigue syndrome in a Japanese community population : chronic fatigue syndrome in Japan.	Clin Rheumatol. 2011 Jul;30(7):895-906. Epub 2011 Feb 8.	This study seeks to estimate the prevalence of chronic fatigue syndrome (CFS) and assess the characteristics of CFS in a community population in Japan using laboratory tests and questionnaires for lifestyle, fatigue states, and depression states. The design of this study is a cross-sectional observational study. The setting of this study is a medical health checkup program in a general hospital. This study was conducted with 1,430 Japanese (867 men and 563 women), 20 to 78 years of age. We classified participants who complained of fatigue according to the case definition of CFS proposed by the Centers for Disease Control and Prevention in the USA in 1994. Alcohol, caffeine, catechin and total polyphenol consumption, smoking status, sleep duration, and physical activity were evaluated using questionnaires. The prevalence of CFS was 1.0% (95% CI 0.5-1.6%) of a community population in Japan. Although various lifestyle factors of the participants with CFS were similar to those without chronic fatigue, average sleep duration was significantly shorter among the participants with CFS (5.5 ± 0.8 h) compared to those without chronic fatigue (6.3 ± 0.9 h, $P < 0.001$). Proportion at subjects having average sleep duration of less than 6 h was 64.3%

				among the participants with CFS in contrast to only 15.0% in those without chronic fatigue (P < 0.001). Among the eight case-defining symptoms, "Unrefreshing sleep" had high sensitivity and high specificity for screening CFS in Japanese population (92.9% and 87.8%, respectively). The average sleep duration was notably shorter in Japanese suffering from CFS. Further longitudinal study is needed to evaluate the possibility of extreme short sleep duration as a major cause of CFS in Japan.
Hambrook D, Oldershaw A, Rimes K, Schmidt U, Tchanturia K, Treasure J, Richards S, Chalder T.	Division of Psychological Medicine and Psychiatry, Section of Eating Disorders, King's College London, Institute of Psychiatry, UK.	Emotional expression, self-silencing, and distress tolerance in anorexia nervosa and chronic fatigue syndrome.	Br J Clin Psychol. 2011 Sep;50(3):310-25. doi: 10.1348/014466510X519215. Epub 2011 Mar 8.	OBJECTIVES. Difficulties in processing emotional states are implicated in the aetiology and maintenance of diverse health conditions, including anorexia nervosa (AN) and chronic fatigue syndrome (CFS). This study sought to explore distress tolerance, self-silencing, and beliefs regarding the experience and expression of emotions in individuals diagnosed with AN and CFS. These conditions were chosen for this study because their clinical presentation is characterized by physical symptoms, yet cognitive behavioural models suggest that emotional processing difficulties contribute to the aetiology and maintenance of both. DESIGN. A between-subjects cross-sectional design was employed. METHODS. Forty people with AN, 45 with CFS, and 48 healthy controls (HCs) completed the Distress Tolerance Scale (DTS), Silencing the Self Scale (STSS), Beliefs about Emotions Scale (BES), and measures of clinical symptomatology. RESULTS. Initial group comparisons found that both AN and CFS participants scored higher than HCs on a subscale measuring difficulties in distress tolerance. AN and CFS participants were also more likely to judge themselves by external standards, endorse statements reflecting a tendency to put the needs of others before themselves, and present an outwardly socially compliant image of themselves whilst feeling hostile within. Relative to HCs, AN participants reported more maladaptive beliefs regarding the experience of having negative thoughts and feelings and revealing these emotions to others, with CFS participants showing a non-significant trend in the same direction. After controlling for differences in age, anxiety, and depression the only significant difference to remain was that observed for the STSS care as self-sacrifice subscale. More maladaptive beliefs about the experience and expression of emotions were associated with greater degree of eating disorder symptomatology in the AN group. CONCLUSIONS. Differences in emotional processing are present in AN and CFS compared to HCs, with some disorder-specific variation, and may be associated with greater clinical symptomatology. These findings support current explanatory models of both AN and CFS, and suggest that emotional processing should be addressed in the assessment and treatment of individuals with these illnesses. ©2010 The British Psychological Society.
Hareide L, Finset A, Wyller VB.	Akershus Universitetssykehus, Seksjon Klosteret, Alexander	Chronic fatigue syndrome: a qualitative investigation of young patient's	Disabil Rehabil. 2011;33(23-24):2255-63. Epub 2011 Apr 7.	PURPOSE: The aim of this pilot study was to explore illness beliefs and coping strategies among adolescent patients with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME), applying a qualitative methodology. Recent studies have explored the illness beliefs and coping strategies of adult patients with CFS/ME as possible contributing factors to the disease aetiology. These studies have mainly used

	Kiellands Gate 11, 2000 Lillestrøm, Lillestrøm, Norway. livehareide@hotmail.com	beliefs and coping strategies.		quantitative methods, finding that patients often explain their illness as being due to physical causes, deny psychological causes and make use of passive and avoidant coping strategies. METHOD: Semi-structured, in-depth interviews were conducted with nine adolescent patients with CFS/ME, thematic analysis was adapted to the material and the results were interpreted in light of theories of attribution and coping. RESULTS: The qualitative method allowed for more complex and nuanced accounts of illness experience. The findings showed that the adolescents differ from what has previously been reported, applying more varied and flexible illness attributions and coping mechanisms than expected. CONCLUSIONS: The heterogeneity suggested in the results has implications. We suggest three perspectives should be taken into account, both for further research and in clinical practice: (1) individual differences; (2) a developmental perspective and (3) interactive relational focus.
Hauser SL, Johnston SC.		Extraordinary claims require extraordinary evidence.	Ann Neurol. 2011 Apr;69(4):A9-A10. doi: 10.1002/ana.22434. Comment on Ann Neurol. 2011 Apr;69(4):735-8.	
Hawkes N.		Researcher who linked chronic fatigue syndrome to mouse virus is arrested.	BMJ. 2011 Nov 22;343:d7573. doi: 10.1136/bmj.d7573.	
Hawkes N.	nigel.hawkes1@btinternet.com	Dangers of research into chronic fatigue syndrome.	BMJ. 2011 Jun 22;342:d3780. doi: 10.1136/bmj.d3780.	
Haywood KL, Staniszewska S, Chapman S.	Royal College of Nursing Research Institute, School of Health and Social Studies, University of Warwick, Coventry CV4 7AL, UK. k.l.haywood@warwick.ac.uk	Quality and acceptability of patient-reported outcome measures used in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review.	Qual Life Res. 2012 Feb;21(1):35-52. Epub 2011 May 18.	PURPOSE: To review the quality and acceptability of condition-specific, domain-specific and generic multi-item patient-reported outcome measures (PROMs) used in the assessment of adults with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). METHODS: Systematic literature searches were made to identify PROMs. Quality and acceptability was assessed against an appraisal framework, which captured evidence of both the thoroughness and results of evaluations: evidence of measurement (reliability, validity, responsiveness, interpretability, data quality/precision) and practical properties (feasibility, patient acceptability), and the extent of active patient involvement was sought. RESULTS: A total of 11 CFS/ME-specific, 55 domain-specific and 11 generic measures were reviewed. With the exception of the generic SF-36, all measures had mostly limited evidence of measurement and/or practical properties. Patient involvement was poorly reported and often cursory. CONCLUSIONS: The quality and acceptability of reviewed PROMs is limited, and recommendations for patient-reported assessment are difficult.

				Significant methodological and quality issues in PROM development/evaluation were identified by the appraisal framework, which must be addressed in future research. Clear discrepancies exist between what is measured in research and how patients define their experience of CFS/ME. Future PROM development/evaluation must seek to involve patients more collaboratively to measure outcomes of importance using relevant and credible methods of assessment.
Heins MJ, Knoop H, Lobbestael J, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands. m.heins@nkcv.umcn.nl	Childhood maltreatment and the response to cognitive behavior therapy for chronic fatigue syndrome.	J Psychosom Res. 2011 Dec;71(6):404-10. Epub 2011 Jun 30.	OBJECTIVE: To examine the relationship between a history of childhood maltreatment and the treatment response to cognitive behavior therapy for chronic fatigue syndrome (CFS). METHODS: A cohort study in a tertiary care clinic with a referred sample of 216 adult patients meeting the Centers for Disease Control and Prevention criteria for CFS, and starting cognitive behavior therapy. Main outcome measures changes between pre- and post therapy in fatigue (Checklist Individual Strength fatigue subscale), disabilities (Sickness Impact Profile total score), physical functioning (short form 36 health survey subscale) and psychological distress (Symptom checklist 90 total score). RESULTS: At baseline, patients with a history of childhood maltreatment had significantly more limitations and a higher level of psychological distress, but were not more severely fatigued. Change scores on the outcome measures after cognitive behavior therapy did not differ significantly between patients with or without a history of childhood maltreatment, or between the different types of childhood maltreatment. However, patients with a history of childhood maltreatment still experienced more limitations and a higher level of psychological distress after CBT. CONCLUSIONS: A history of childhood maltreatment was not related to the treatment response of cognitive behavior therapy for CFS. In patients with a history of childhood maltreatment CFS symptoms can be treated with CBT just as well as those without. 2011 Elsevier Inc. All rights reserved.
Hlavaty LE, Brown MM, Jason LA.	Center for Community Research, DePaul University, Chicago, IL 60614, USA. leahlavaty@gmail.com	The effect of homework compliance on treatment outcomes for participants with myalgic encephalomyelitis/chronic fatigue syndrome.	Rehabil Psychol. 2011 Aug;56(3):212-8.	PURPOSE: This study examined the relationship between level of treatment engagement through completion of homework on treatment outcomes within nonpharmacological interventions for participants with ME/CFS. METHOD: A sample of 82 participants with ME/CFS was randomly assigned to one of four nonpharmacological interventions. Each intervention involved 13 sessions over the course of 6 months. Change scores were computed for self-report measures taken at baseline and 12-month follow-up. Homework compliance was calculated as the percentage of completed assignments across the total number of sessions and grouped into three categories: minimum (0-25%), moderate (25.1-75%), or maximum (75.1-100%). RESULTS: Findings revealed that after controlling for treatment condition, those who completed a maximum amount of homework had greater improvement on a number of self-report outcome measures involving role, social, and mental health functioning. There were no differential improvements in physical and fatigue functioning based on level of homework compliance. IMPLICATIONS: Findings from this study suggest homework compliance can have a positive influence on some

				aspects of physical, social, and mental health functioning in participants with ME/CFS. It should be emphasized that these interventions do not cure this illness. The lack of significant changes in physical functioning and fatigue levels suggests a need for more multidisciplinary treatment approaches that can elicit improvement in these areas.
Hoeck AD, Pall ML.	ad.hoeck@t-online.de	Will vitamin D supplementation ameliorate diseases characterized by chronic inflammation and fatigue?	Med Hypotheses. 2011 Feb;76(2):208-13. Epub 2010 Oct 25.	Chronic NF-κB activation has been supposed as a key event in chronic fatigue syndrome (CFS) and many other better-defined pro-inflammatory diseases. Knowledge about the impact of deficiency vitamin D on chronic NF-κB activation could open a new disease approach. Whereas NF-κB activation leads at first to a pro-inflammatory immune response, later on a vitamin D-dependent anti-inflammatory response ensues. Binding of the active vitamin D metabolite 1,25(OH)(2)D(3) to vitamin D receptor (VDR) yields a transcription factor which represses NF-κB activation, and additionally modulates and down-regulates adaptive, but enhances innate immune responses, and improves redox balance, thus counterbalancing inflammation on multiple levels. However, this built-in late counterbalance against inflammation works only when stores of calcium and 25(OH)D(3) are abundant. Therefore a connection between lowered vitamin D-metabolism and persistent NF-κB activation, augmented nitrosative-oxidative stress, redox imbalance, chronic inflammation, and concomitant fatigue can be postulated. In order to confirm this hypothesis, randomized controlled clinical studies about the clinical effects of supplementation of calcium and vitamin D(3) would be necessary in diseases characterized by persistent NF-κB activation and chronic inflammation and fatigue. Copyright Â© 2010 Elsevier Ltd. All rights reserved.
Hohn O, Bannert N.	Center for HIV and Retrovirology, Robert Koch Institute, Berlin, Germany. HohnO@rki.de	Origin of XMRV and its demise as a human pathogen associated with chronic fatigue syndrome.	Viruses. 2011 Aug;3(8):1312-9. Epub 2011 Jul 27.	Retroviruses are well known pathogens of mammals, birds and fish. Their potential to induce cancer in chickens was already described almost 100 years ago and murine retroviruses have been a subject of study for 50 years. The first human retroviruses, HTLV and HIV, were discovered more than 30 years ago, surprising researchers and physicians by the profound differences in the diseases they cause. HTLV-1 is able to induce, after decades of infection, lymphomas/leukemia or neuroimmune disorders whereas untreated HIV infection leads almost inevitably to AIDS. The recently described XMRV (xenotropic murine leukemia virus-related virus) appeared to possess many of the features known for HTLV and was regarded by some to be the third human retrovirus. However, recent publications by Knox et al. and Paprotka et al. have shed new light on this gammaretrovirus. Knox and colleagues clearly demonstrate that XMRV is absent in patients belonging to a chronic fatigue syndrome cohort who had previously been reported to be XMRV-positive. This supports the growing suspicion that laboratory contamination was responsible for the postulated link between XMRV and the disease. Furthermore, Paprotka et al's identification of XMRV's origin and the phylogenetic analysis of known XMRV sequences are further nails in the coffin to the notion that XMRV is a clinically relevant infectious human retrovirus.

Holgate ST, Komaroff AL, Mangan D, Wessely S.	University of Southampton, Infection, Inflammation and Immunity Division, School of Medicine, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD, UK. sth@soton.ac.uk	Chronic fatigue syndrome: understanding a complex illness.	Nat Rev Neurosci. 2011 Jul 27;12(9):539-44. doi: 10.1038/nrn3087.	Chronic fatigue syndrome (CFS) is a debilitating illness that affects many people. It has been marred by controversy, from initial scepticism in the medical community about the existence of the condition itself to continuing disagreements--mainly between some patient advocacy groups on one side, and researchers and physicians on the other--about the name for the illness, its aetiology, its pathophysiology and the effectiveness of the few currently available treatments. The role of the CNS in the disease is central in many of these discussions. Nature Reviews Neuroscience asked four scientists involved in CFS research about their views on the condition, its causes and the future of research aimed at improving our understanding of this chronic illness.
Hollingsworth KG, Hodgson T, Macgowan GA, Blamire AM, Newton JL.	From Newcastle Magnetic Resonance Centre, Institute of Cellular Medicine, Newcastle University, NE4 5PL Department of Cardiology, Freeman Hospital, Newcastle upon Tyne, NE7 7DN and Institute of Genetic Medicine, Newcastle University, NE1 3BZ Institute for Ageing and Health, Newcastle University, NE4 5PL; Newcastle upon Tyne, UK.	Impaired cardiac function in chronic fatigue syndrome measured using magnetic resonance cardiac tagging.	J Intern Med. 2011 Jul 27. doi: 10.1111/j.1365-2796.2011.02429.x. [Epub ahead of print]	Abstract. Hollingsworth KG, Hodgson T, MacGowan GA, Blamire AM, Newton JL (Institute of Cellular Medicine, Campus for Ageing and Vitality; Institute of Genetic Medicine; and Institute for Ageing and Health, Campus for Ageing and Vitality; Newcastle University, Newcastle, UK). Impaired cardiac function in chronic fatigue syndrome measured using magnetic resonance cardiac tagging. J Intern Med 2011; 10.1111/j.1365-2796.2011.02429.x. Objectives. Impaired cardiac function has been confirmed in patients with chronic fatigue syndrome (CFS). Magnetic resonance cardiac tagging is a novel technique that assesses myocardial wall function in vivo. We hypothesized that patients with CFS may have impaired development and release of myocardial torsion and strain. Methods. Cardiac morphology and function were assessed using magnetic resonance imaging and cardiac tagging methodology in 12 CFS patients (Fukuda) and 10 matched controls. Results. Compared to controls, the CFS group had substantially reduced left ventricular mass (reduced by 23%), end-diastolic volume (30%), stroke volume (29%) and cardiac output (25%). Residual torsion at 150% of the end-systolic time was found to be significantly higher in the patients with CFS (5.3 ± 1.6°) compared to the control group (1.7 ± 0.7°, P = 0.0001). End-diastolic volume index correlated negatively with both torsion-to-endocardial-strain ratio (TSR) (r = -0.65, P = 0.02) and the residual torsion at 150% end-systolic time (r = -0.76, P = 0.004), so decreased end-diastolic volume is associated with raised TSR and torsion persisting longer into diastole. Reduced end-diastolic volume index also correlated significantly with increased radial thickening (r = -0.65, P = 0.03) and impaired diastolic function represented by the ratio of early to late ventricular filling velocity (E/A ratio, r = 0.71, P = 0.009) and early filling percentage (r = 0.73, P = 0.008). Conclusion. Patients with CFS have markedly reduced cardiac mass and blood pool volumes, particularly end-diastolic volume: this results in significant impairments in stroke volume and cardiac output compared to controls. The CFS group appeared to have a delay in the release of

				torsion. © 2011 The Association for the Publication of the Journal of Internal Medicine.
Houghton CA, Steels EL, Fassett RG, Coombes JS.	School of Human Movement Studies, University of Queensland, St Lucia, Qld 4067, Australia. christine.houghton@uqconnect.edu.au	Effects of a gliadin-combined plant superoxide dismutase extract on self-perceived fatigue in women aged 50-65 years.	Phytomedicine. 2011 Apr 15;18(6):521-6. Epub 2010 Nov 1.	Fatigue syndromes exist on a continuum of severity from mild and transient to the disabling chronic fatigue syndrome, with oxidative stress linked to its pathogenesis. A thermolabile gliadin-combined plant superoxide dismutase (SOD) extract has shown potential in clinical trials as a therapeutic antioxidant. This study investigated the effects of 12 weeks of 500 mg/day of a SOD/gliadin supplement on fatigue. Thirty-eight women aged 50-65 years with self-perceived fatigue entered this randomized, double-blind, placebo-controlled trial. The primary outcome measure was general fatigue determined by the Multidimensional Fatigue Inventory (MFI). Secondary outcome measures included other measures of fatigue from the MFI and blood measures of oxidative stress, antioxidant status and hormones. There were no significant (P>0.05) differences between, or within groups, for decreases in general fatigue (active=1.6%, placebo=4.1%). There were no within or between group differences (P>0.05) in other measures of fatigue (physical fatigue, reduced activity, reduced motivation, mental fatigue and total fatigue score). In regard to the biochemical measures, there were non-significant (P>0.05) differences in increases in plasma SOD activity (active=7.1%, placebo=12.2%), plasma GPx activity (active=2.4%, placebo=0.7%), red blood cell GPx activity (active=9.8%, placebo=4.4%). Markers of oxidative stress were decreased but there were no differences (P>0.05) within or between groups; malondialdehyde (active=4.1%, placebo=1.6%), F-2 isoprostanes (active=14.7%, placebo=22.4%). There was a trend (P=0.08) for a decrease in cortisol in the active group (24.6%), however this was not significantly different from the decrease in the placebo participants (4.1%). DHEA differences were not significant (P<0.05) and declined 1.3% in the active group and 14.4% in the placebo group. In summary, the thermolabile SOD/gliadin supplement had no significant effect on self-perceived fatigue, antioxidants, oxidative stress or hormones in women aged 50-65 years. Copyright © 2010 Elsevier GmbH. All rights reserved.
Hsu ES.	Department of Anesthesiology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. ehsu@mednet.ucla.edu	Acute and chronic pain management in fibromyalgia: updates on pharmacotherapy.	Am J Ther. 2011 Nov;18(6):487-509.	Fibromyalgia (FM) is a mysterious pain syndrome with progressive and widespread pain, explicit areas of tender points, stiffness, sleep disturbance, fatigue, and psychological distress without any obvious disease. FM is commonly perceived as a condition of central pain and sensory augmentation. There are documented functional abnormalities in pain and sensory processing in FM. Central sensitization and lack of descending analgesic activity are the 2 leading mechanisms that have been demonstrated by advance in both basic and clinical research. The pathogenesis of FM may also be attributed to the genetic polymorphisms involving serotoninergic, dopaminergic, and catecholaminergic systems. Any psychiatric disorders and psychosocial influences in FM may also affect the severity of pain. The various external stimuli or trigger such as infection, trauma, and stress may all contribute to proceed to presentation of FM. The recent launches of 3 US Food and Drug

				Administration-approved pharmacotherapy for FM namely pregabalin, duloxetine, and milnacipran have certainly raised the profile of optimal chronic pain management. However, appropriate evaluation and efficacious management of acute pain has not been as well publicized as chronic pain in FM. Acute pain or flare up caused by any trauma or surgery certainly may present a real challenge for patients with FM and their health care providers. Pre-emptive analgesia and pro-active treatment may offer the momentum for acute pain control based on model of central sensitization and pain in FM. This review article on FM appraises the modern practice of multimodal therapy focus on both acute and chronic pain management. Meanwhile, the evolving nonpharmacological approach is summarized and stressed as an essential component of integrated care in FM.
Huang Y, Liu YH.	Department of Orthodontics, School of Stomatology, Tongji University, Shanghai, China.	Effects of phytoestrogens on genioglossus contractile properties in ovariectomized rats exposed to chronic intermittent hypoxia may be independent of their estrogenicity.	Eur J Oral Sci. 2011 Apr;119(2):128-35. doi: 10.1111/j.1600-0722.2011.00815.x.	Chronic intermittent hypoxia (CIH) is a frequent feature of obstructive sleep apnea/hypopnea syndrome (OSAHS), and it may alter upper airway muscle endurance. We have previously reported the positive effects of estrogen on genioglossus fatigue resistance in rats. Our present study was designed to evaluate the effects of two phytoestrogens - genistein and coumestrol - on genioglossus contractile function and estrogen receptor (ER) expression in female rats exposed to CIH. Eight-wk-old female rats were ovariectomized and exposed to CIH for 5 wk. Genistein and coumestrol, respectively, were administered by intraperitoneal injection, at a dose of 2.5 mg kg(-1) d(-1), during the last 4 d of exposure to CIH. The contractile properties of the genioglossus were measured. Real-time RT-PCR and western blotting were performed to determine the expression of ERs in the genioglossus. Phytoestrogens were found to significantly increase genioglossus fatigue resistance, the effect of genistein being more powerful than that of coumestrol. However, higher levels of ER mRNA and protein were detected in the coumestrol group than in the genistein group. We conclude that phytoestrogens, especially genistein, could improve the endurance of the genioglossus muscle in ovariectomized rats exposed to CIH, and this effect is, in part, not related to its estrogenic action. © 2011 Eur J Oral Sci.
Hunter M.		Chronic fatigue syndrome could be costing UK economy pound 100m a year, study says.	BMJ. 2011 Sep 19;343:d5905. doi: 10.1136/bmj.d5905.	
Hurley BF, Hanson ED, Sheaff AK.	Department of Kinesiology, School of Public Health, University of Maryland, College Park,	Strength training as a countermeasure to aging muscle and chronic disease.	Sports Med. 2011 Apr 1;41(4):289-306. doi: 10.2165/11585920-000000000-00000.	Strength training (ST) has long been considered a promising intervention for reversing the loss of muscle function and the deterioration of muscle structure associated with advanced age but, until recently, the evidence was insufficient to support its role in the prevention or treatment of disease. In recent decades, there has been a long list of quality reviews examining the effects of ST on functional abilities and a few on risk factors for specific diseases, but none have provided a comprehensive assessment of

	Maryland 20742, USA. benhur@umd.edu			ST as an intervention for a broad range of diseases. This review provides an overview of research addressing the effectiveness of ST as an intervention for the prevention or treatment of the adverse consequences of (i) aging muscle; (ii) the metabolic syndrome (MetS) and its components, i.e. insulin resistance, abdominal obesity, hyperlipidaemia and hypertension; (iii) fibromyalgia; (iv) rheumatoid arthritis; and (v) Alzheimer's disease. Collectively, these studies indicate that ST may serve as an effective countermeasure to some of the adverse consequences of the MetS, fibromyalgia and rheumatoid arthritis. Evidence in support of the hypothesis that ST reduces insulin resistance or improves insulin action comes both from indirect biomarkers, such as glycosylated haemoglobin (HbA(1c)), and insulin responses to oral glucose tolerance tests, as well as from more direct procedures such as hyperglycaemic and hyperinsulinaemic-euglycaemic clamp techniques. The evidence for the use of ST as a countermeasure of abdominal obesity is less convincing. Although some reports show statistically significant reductions in visceral fat, it is unclear if the magnitude of these changes are physiologically meaningful and if they are independent of dietary influences. The efficacy of ST as an intervention for reducing dyslipidaemia is at best inconsistent, particularly when compared with other pharmacological and non-pharmacological interventions, such as aerobic exercise training. However, there is more consistent evidence for the effectiveness of ST in reducing triglyceride levels. This finding could have clinical significance, given that elevated triglyceride is one of the five criterion measures for the diagnosis of the MetS. Small to moderate reductions in resting and exercise blood pressure have been reported with some indication that this effect may be genotype dependent. ST improves or reverses some of the adverse effects of fibromyalgia and rheumatoid arthritis, particularly pain, inflammation, muscle weakness and fatigue. Investigations are needed to determine how these effects compare with those elicited from aerobic exercise training and/or standard treatments. There is no evidence that ST can reverse any of the major biological or behavioural outcomes of Alzheimer's disease, but there is evidence that the prevalence of this disease is inversely associated with muscle mass and strength. Some indicators of cognitive function may also improve with ST. Thus, ST is an effective countermeasure for some of the adverse effects experienced by patients of many chronic diseases, as discussed in this review.
Hurum H, Sulheim D, Thaulow E, Wyller VB.	Oslo University Hospital, Norway.	Elevated nocturnal blood pressure and heart rate in adolescent chronic fatigue syndrome.	Acta Paediatr. 2011 Feb;100(2):289-92. doi: 10.1111/j.1651-2227.2010.02073.x. Epub 2010 Nov 17.	AIM: To compare ambulatory recordings of heart rate (HR) and blood pressure in adolescents with chronic fatigue syndrome (CFS) and healthy controls. We hypothesized both HR and blood pressure to be elevated among CFS patients. METHODS: Forty-four CFS patients aged 12-18 years were recruited from our paediatric outpatient clinic. The controls were 52 healthy adolescents having similar distribution of age and gender. 24-h ambulatory blood pressure and HR were recorded using a validated, portable oscillometric device. RESULTS: At night (sleep),

				HR, mean arterial blood pressure and diastolic blood pressure were significantly higher in CFS patients as compared with controls ($p < 0.01$). During daytime, HR was significantly higher among CFS patients ($p < 0.05$), whereas blood pressures were equal among the two groups. CONCLUSIONS: The findings support previous experimental evidence of sympathetic predominance of cardiovascular control in adolescent CFS patients. Also, the findings prompt increased focus on cardiovascular risk assessment and suggest a possible target for therapeutic intervention. © 2010 The Author(s)/Acta Paediatrica © 2010 Foundation Acta Paediatrica.
Hussain SA, Al-Khalifa II, Jasim NA, Gorial FI.	Department of Pharmacology and Toxicology, College of Pharmacy, University of Baghdad, Baghdad, Iraq. saad_alzaidi@yahoo.com	Adjuvant use of melatonin for treatment of fibromyalgia.	J Pineal Res. 2011 Apr;50(3):267-71. doi: 10.1111/j.1600-079X.2010.00836.x. Epub 2010 Dec 16.	Fibromyalgia syndrome (FMS) is a chronic musculoskeletal disorder characterized by generalized muscular pain accompanied by fatigue and tenderness at specific anatomic sites called tender points. Although preliminary evidence indicates that melatonin may be effective in treating the pain associated with FMS, no definitive evidence supports this claim. This study was designed to evaluate the significance of using different doses of melatonin, alone or in combination with fluoxetine for the management of FMS. A double-blind, placebo-controlled clinical study was performed on 101 patients (95 women and 6 men) who fulfilled the criteria of the American College of Rheumatology (ACR) of FMS. The patients were randomized into four groups: group A (24 patients) treated with 20 mg/day fluoxetine alone; group B (27 patients) treated with melatonin 5 mg alone; group C (27 patients) treated with 20 mg fluoxetine plus 3 mg melatonin; group D (23 patients) treated with 20 mg fluoxetine plus 5 mg melatonin. Both drugs were given once daily in the morning and night time, respectively, for 8 wk. Each patient was clinically evaluated through direct interview with the patients using the Fibromyalgia Impact Questionnaire (FIQ) at zero time and after 8 wk. Using melatonin (3 mg or 5 mg/day) in combination with 20 mg/day fluoxetine resulted in significant reduction in both total and different components of FIQ score compared to the pretreatment values. In conclusion, administration of melatonin, alone or in a combination with fluoxetine, was effective in the treatment of patients with FMS. © 2010 The Authors. Journal of Pineal Research © 2010 John Wiley & Sons A/S.
Iqbal R, Mughal MS, Arshad N, Arshad M.	Zoology Department, G. C. University, Lahore, 54000, Pakistan.	Pathophysiology and antioxidant status of patients with fibromyalgia.	Rheumatol Int. 2011 Feb;31(2):149-52. Epub 2010 Apr 8.	Fibromyalgia syndrome (FMS) is characterized by systemic pain of unknown etiology and is often accompanied by various psychological symptoms. Research on different parameters in fibromyalgia (FM) indicates that multifactors are involved in its pathophysiology; such as genetic factors, substance P, serotonin, hypothalamic pituitary adrenal axis (HPA), muscles metabolic dysfunction, reactive oxygen species (ROS) and reactive nitrogen species (RNS). Oxidative stress has also been implicated in the pathophysiology of FM; therefore, supplementation with antioxidants may be important in modulation of the effects of ROS in patients with FM.
Israeli E, Pardo A.	The Chaim Zabludowicz Center for	The sick building syndrome as a part of the autoimmune	Mod Rheumatol. 2011 Jun;21(3):235-9. Epub 2010 Dec 29.	Sick building syndrome (SBS) is a term coined for a set of clinically recognizable symptoms and ailments without a clear cause reported by occupants of a building. In the 1990s the term "functional somatic syndromes" was applied to several

	Autoimmune Diseases, Chaim Sheba Medical Center, 52621 Tel-Hashomer, Israel. eitanister@gmail.com	(auto-inflammatory) syndrome induced by adjuvants.		syndromes, including SBS, multiple chemical sensitivity, repetition stress injury, the side effects of silicone breast implants, the Gulf War syndrome (GWS), chronic fatigue syndrome, the irritable bowel syndrome, and fibromyalgia. Recently, Shoenfeld and Agmon-Levin suggested that four conditions--siliconosis, macrophagic myofascitis, the GWS, and post-vaccination phenomena--which share clinical and pathogenic resemblances, may be included under a common syndrome entitled the "autoimmune (auto-inflammatory) syndrome induced by adjuvants". Comparison of the clinical manifestations, symptoms, and signs of the four conditions described by Shoenfeld and Agmon-Levin with those described for SBS shows that nine out of ten main symptoms are present in all 5 conditions. Shoenfeld and Agmon-Levin further propose several major and minor criteria, which, although requiring further validation, may aid in the diagnosis of this newly defined syndrome. We propose here that SBS may also be included as a part of "Shoenfeld's syndrome".
Itoh Y, Shigemori T, Igarashi T, Fukunaga Y.	Department of Pediatrics, Nippon Medical School, Sendagi, Bukyo City, Tokyo, Japan.	Fibromyalgia and chronic fatigue syndrome in children.	Pediatr Int. 2011 Nov 24. doi: 10.1111/j.1442-200X.2011.03514.x. [Epub ahead of print]	Background: Fibromyalgia (FM) is characterized by widespread persistent pain and the presence of multiple discrete tender points. Chronic fatigue syndrome (CFS) is a syndrome characterized by debilitating fatigue associated with a variable number of non-specific complaints. Because neither condition had necessarily been recognized in children until recently, those patients have been treated as having school refusal without being diagnosed as having either syndrome. There is a considerable overlap of clinical symptoms between these two syndromes. It is therefore controversial as to whether these syndromes have the same pathogenesis or not. The aim of the present study was to clarify the relationship between these syndromes in children. Methods: Fifteen patients with FM and 21 patients with CFS were investigated both clinically and immunologically. Immunological assessments included thorough analysis of autoantibodies using several techniques. Results: Anti-nuclear antibody titers were higher and the prevalence of anti-Sa antibody was far more frequent in CFS patients than in FM patients. Conclusion: CFS and FM are different from each other at least in childhood, from an immunological aspect, although some patients could have both conditions. © 2011 The Authors. Pediatrics International © 2011 Japan Pediatric Society.
Jacobson E.	Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA. eric_jacobson@hms.harvard.edu	Structural integration, an alternative method of manual therapy and sensorimotor education.	J Altern Complement Med. 2011 Oct;17(10):891-9. Epub 2011 Oct 12.	OBJECTIVES: The objectives of this report are to review the clinical practice of Structural Integration (SI), an alternative method of soft-tissue manipulation and sensorimotor education, and to summarize the evidence to date for mechanism and clinical efficacy. METHODS: The author's personal knowledge of SI literature, theory, and practice was supplemented by a database search, consultation with other senior SI practitioners, and examination of published bibliographies and websites that archive SI literature. RESULTS: SI purports to improve biomechanical functioning as a whole by progressively approximating specific ideals of posture and movement, rather than to treat particular symptoms. Hypothesized mechanisms at the level of local tissue change include increases in soft-tissue pliability, release of adhesions

				between adjacent soft-tissue structures, and increased interstitial fluid flow with consequently improved clearance of nociceptive potentiators. Hypothesized mechanisms for more global changes include improved biomechanical organization leading to reductions in mechanical stress and nociceptive irritation, a perception of improved biomechanical efficiency and coordination that generalizes to the self, and improvements in sensory processing and vagal tone. Emotional catharsis is also thought to contribute to psychologic changes. Limited preliminary evidence exists for improvements in neuromotor coordination, sensory processing, self-concept and vagal tone, and for reductions in state anxiety. Preliminary, small sample clinical studies with cerebral palsy, chronic musculoskeletal pain, impaired balance, and chronic fatigue syndrome have reported improvements in gait, pain and range-of-motion, impaired balance, functional status, and well-being. Adverse events are thought to be mild and transient, although survey data are not available. Contraindications are thought to be the same as for massage. CONCLUSIONS: Evidence for clinical effectiveness and hypothesized mechanisms is severely limited by small sample sizes and absence of control arms. In view of the rapidly increasing availability of SI and its use for treatment of musculoskeletal pain and dysfunction, more adequate research in warranted.
Jammes Y, Steinberg JG, Delliaux S.	UMR MD2 P2COE, Faculty of Medicine, Aix-Marseille University and Clinical Respiratory Physiology and Exercise Testing Laboratory, Thorax Pole, National Assistance - Hospitals in Marseille, Marseille, France.	Chronic fatigue syndrome: acute infection and history of physical activity affect resting levels and response to exercise of plasma oxidant/antioxidant status and heat shock proteins.	J Intern Med. 2011 Nov 24. doi: 10.1111/j.1365-2796.2011.02488.x. [Epub ahead of print]	Abstract. Jammes Y, Steinberg JG, Delliaux S (Aix-Marseille University, Marseille, France). Chronic fatigue syndrome: acute infection and history of physical activity affect resting levels and response to exercise of plasma oxidant/antioxidant status and heat shock proteins. J Intern Med 2012; doi: 10.1111/j.1365-2796.2011.02488.x. Objectives. A history of high-level physical activity and/or acute infection might constitute stress factors affecting the plasma oxidant-antioxidant status and levels of heat shock proteins (HSPs) in patients with chronic fatigue syndrome (CFS). Design. This case-control study compared data from 43 CFS patients to results from a matched control group of 23 healthy sedentary subjects. Setting and subjects. Five patients had no relevant previous history (group I). Eighteen had practised high-level sport (group II), and severe acute infection had been diagnosed in nine patients (group III). A combination of sport practice and infection was noted in 11 patients (group IV). Interventions. After examination at rest, all subjects performed a maximal cycling exercise test. Plasma levels of two markers of oxidative stress [thiobarbituric acid reactive substances (TBARS) and reduced ascorbic acid (RAA)] and both HSP27 and HSP70 were measured. Results. At rest, compared with the control group, the TBARS level was higher in groups II, III and IV patients, and the RAA level was lower in groups III and IV. In addition, HSP70 levels were significantly lower in all CFS groups, compared with controls, but negative correlations were found between resting HSP27 and HSP70 levels and the history of physical activity. After exercise, the peak level of TBARS significantly increased in groups II, III and IV, and the variations in HSP27 and HSP70 were attenuated or suppressed, with the greatest effects in groups

				III and IV. Conclusion. The presence of stress factors in the history of CFS patients is associated with severe oxidative stress and the suppression of protective HSP27 and HSP70 responses to exercise. © 2011 The Association for the Publication of the Journal of Internal Medicine.
Jason L, Sorenson M, Sebally K, Alkazemi D, Lerch A, Porter N, Kubow S.	Department of Psychology, DePaul University, Chicago, IL 60614, United States.	Increased HDAC in association with decreased plasma cortisol in older adults with chronic fatigue syndrome.	Brain Behav Immun. 2011 Nov;25(8):1544-7. Epub 2011 Apr 28.	Hypocortisolism is a frequent finding in individuals with chronic fatigue syndrome (CFS) with other research findings implying potential dysregulation of glucocorticoid signaling. Glucocorticoid signaling is under the influence of several pathways, several of which are of interest in the study of CFS. Oxidative stress and decreased antioxidant capacity are known to disrupt the hypothalamic-pituitary-adrenal (HPA) axis (Epel et al., 2004) and the presence of histone deacetylases (HDAC) could also impact glucocorticoid signaling. The intent of this pilot study was to investigate the relationship among oxidative stress elements, select HDAC's (2/3) and glucocorticoid receptor signaling in an elderly sample with CFS. Findings suggest increased histone deacetylase activity, lower total antioxidant power, in the context of decreased plasma cortisol and increased plasma dehydroepiandrosterone concomitant with decreased expression of the encoding gene for the glucocorticoid receptor. These findings support the presence of HPA axis dysregulation in elderly individuals with CFS. Copyright © 2011 Elsevier Inc. All rights reserved.
Jason L, Brown M, Evans M, Anderson V, Lerch A, Brown A, Hunnell J, Porter N.	Center for Community Research, DePaul University, Chicago, IL 60614, USA. ljason@depaul.edu	Measuring substantial reductions in functioning in patients with chronic fatigue syndrome.	Disabil Rehabil. 2011;33(7):589-98. Epub 2010 Jul 9.	PURPOSE: All the major current case definitions for chronic fatigue syndrome (CFS) specify substantial reductions in previous levels of occupational, educational, social, or personal activities to meet criteria. Difficulties have been encountered in operationalizing 'substantial reductions.' For example, the Medical Outcomes Study Short Form-36 Health Survey (SF-36) has been used to determine whether individuals met the CFS disability criterion. However, previous methods of using the SF-36 have been prone to including people without substantial reductions in key areas of physical functioning when diagnosing CFS. This study sought to empirically identify the most appropriate SF-36 subscales for measuring substantial reductions in patients with CFS. METHOD: The SF-36 was administered to two samples of patients with CFS: one recruited from tertiary care and the other a community-based sample; as well as a non-fatigued control group. Receiver operating characteristics were used to determine the optimal cutoff scores for identifying patients with CFS. RESULTS: The SF-36 Role-Emotional subscale had the worst sensitivity and specificity, whereas the Vitality, Role-Physical, and Social Functioning subscales had the best sensitivity and specificity. CONCLUSION: Based on the evidence from this study, the potential criteria for defining substantial reductions in functioning and diagnosing CFS is provided. © 2011 Informa UK, Ltd.
Jason LA, Skendrovic B, Furst J, Brown A, Weng A, Bronikowski C.	DePaul University, USA. Ljason@depaul.edu	Data mining: comparing the empiric CFS to the Canadian ME/CFS	J Clin Psychol. 2012 Jan;68(1):41-9. doi: 10.1002/jclp.20827. Epub 2011 Aug 5.	This article contrasts two case definitions for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). We compared the empiric CFS case definition (Reeves et al., 2005) and the Canadian ME/CFS clinical case definition (Carruthers et al., 2003) with a sample of individuals with CFS versus those without. Data mining with decision

		case definition.		trees was used to identify the best items to identify patients with CFS. Data mining is a statistical technique that was used to help determine which of the survey questions were most effective for accurately classifying cases. The empiric criteria identified about 79% of patients with CFS and the Canadian criteria identified 87% of patients. Items identified by the Canadian criteria had more construct validity. The implications of these findings are discussed. © 2011 Wiley Periodicals, Inc.
Jason LA, Evans M, Brown M, Porter N, Brown A, Hunnell J, Anderson V, Lerch A.	DePaul University.	Fatigue Scales and Chronic Fatigue Syndrome: Issues of Sensitivity and Specificity.	Disabil Stud Q. 2011 Winter;31(1). pii: 1375.	Few studies have explored issues of sensitivity and specificity for using the fatigue construct to identify patients meeting chronic fatigue syndrome (CFS) criteria. In this article, we examine the sensitivity and specificity of several fatigue scales that have attempted to define severe fatigue within CFS. Using Receiver Operating Characteristic (ROC) curve analysis, we found most scales and sub-scales had either significant specificity and/or sensitivity problems. However, the post-exertional subscale of the ME/CFS Fatigue Types Questionnaire (Jason, Jessen, et al., 2009) was the most promising in terms of specificity and sensitivity. Among the more traditional fatigue scales, Krupp, LaRocca, Muir-Nash, and Steinberg's (1989) Fatigue Severity Scale had the best ability to differentiate CFS from healthy controls. Selecting questions, scales and cut off points to measure fatigue must be done with extreme care in order to successfully identify CFS cases.
Jason LA, Sorenson M, Porter N, Belkairous N.	DePaul University, Center for Community Research. Fullerton Ave., Chicago, USA.	An Etiological Model for Myalgic Encephalomyelitis/Chronic Fatigue Syndrome.	Neurosci Med. 2011 Mar 1;2(1):14-27.	Kindling might represent a heuristic model for understanding the etiology of Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS). Kindling occurs when an organism is exposed repeatedly to an initially sub-threshold stimulus resulting in hypersensitivity and spontaneous seizure-like activity. Among patients with ME/CFS, chronically repeated low-intensity stimulation due to an infectious illness might cause kindling of the limbic-hypothalamic-pituitary axis. Kindling might also occur by high-intensity stimulation (e.g., brain trauma) of the limbic-hypothalamic-pituitary axis. Once this system is charged or kindled, it can sustain a high level of arousal with little or no external stimulus and eventually this could lead to hypocortisolism. Seizure activity may spread to adjacent structures of the limbic-hypothalamic-pituitary axis in the brain, which might be responsible for the varied symptoms that occur among patients with ME/CFS. In addition, kindling may also be responsible for high levels of oxidative stress, which has been found in patients with ME/CFS.
Jason LA, Porter N, Hunnell J, Brown A, Rademaker A, Richman JA.	DePaul University. Ljason@depaul.edu	A natural history study of chronic fatigue syndrome.	Rehabil Psychol. 2011 Feb;56(1):32-42.	OBJECTIVE: There is a need for natural history chronic fatigue syndrome (CFS) studies from random, community-based, multi-ethnic populations. DESIGN: The present study examined the course of CFS from Wave 1 to Wave 2, which spanned over a ten year period of time, and, assessed whether socio-environmental and symptomatology factors were associated with CFS status over the ten year period. RESULTS: There was relative stability over time on critical measures of disability, fatigue, support, optimism and coping over time. One cardinal symptoms of CFS, post-exertional malaise, best differentiated the CFS group from the others. By Wave 2, of the original group of 32 individuals diagnosed with CFS, 4 had died, and 24 were found and

				agreed to be re-evaluated, and of this group, 16 continued to have CFS, 5 developed exclusionary illnesses, 2 were classified as Idiopathic chronic fatigue, and one had remitted. CONCLUSIONS: The current study found that over time in a community-based sample, unbiased by help seeking behavior the CFS group remained rather ill with a variety of different conditions over time. (c) 2011 APA, all rights reserved
Jason LA, Brown AA, Clyne E, Bartgis L, Evans M, Brown M.		Contrasting Case Definitions for Chronic Fatigue Syndrome, Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Myalgic Encephalomyelitis.	Eval Health Prof. 2011 Dec 7. [Epub ahead of print]	This article uses data from patients recruited using the 1994 case definition of chronic fatigue syndrome (CFS) to contrast those meeting criteria for the Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) Canadian case definition with those that did not meet these criteria. The study also contrasts those meeting criteria for Myalgic Encephalomyelitis (ME) based on criteria from Ramsay and other theorists with those that did not meet the ME criteria. The ME/CFS case definition criteria identified a subset of patients with more functional impairments and physical, mental, and cognitive problems than the subset not meeting these criteria. The ME subset had more functional impairments, and more severe physical and cognitive symptoms than the subset not meeting ME criteria. When applied to a population meeting the 1994 CFS case definition, both ME/CFS and ME criteria appear to select a more severe subset of patients.
Jason LA.	DePaul University, Chicago, IL, USA, ljason@depaul.edu.	Small Wins Matter in Advocacy Movements: Giving Voice to Patients.	Am J Community Psychol. 2011 Aug 20. [Epub ahead of print]	In this article, the various players are delineated in a story of a contested illness and patient advocacy, played out within the corridors of federal power. It is suggested that the mistreatment and negative attitudes that health care providers and others have towards those with chronic fatigue syndrome (CFS) is possibly due to the social construction of this illness as being a "Yuppie flu" disease. Institutional factors are identified that created these norms and attributions, as well as the multiple stakeholders and constituent groups invested in exerting pressure on policy makers to effect systemic change. This article also provides examples of how the field of Community Psychology, which is fundamentally committed to/based on listening to and giving voice to patients, is broadly relevant to patient activism communities. This approach focused, over time, on epidemiological studies, the name, the case definition, and ultimately the change in CFS leadership at the Centers for Disease Control and Prevention. Keys to this "small wins" approach were coalition building, use of "oppositional experts" (professionals in the scientific community who support patient advocacy goals) to challenge federal research, and taking advantage of developing events/shifts in power. Ultimately, this approach can result in significant scientific and policy gains, and changes in medical and public perception of an illness.
Jason LA, Porter N, Hunnell J, Rademaker A, Richman JA.	DePaul University, USA. Ljason@depaul.edu	CFS prevalence and risk factors over time.	J Health Psychol. 2011 Apr;16(3):445-56. Epub 2011 Jan 11.	The present natural history study examined the course of CFS from 1995-97 (Wave 1) to approximately 10 years later (Wave 2) from a random, community-based, multi-ethnic population. The rate of CFS remained approximately the same over the period of time from Wave 1 to Wave 2, although a high level of mortality was found (18% of those with medical or psychiatric exclusions group, 12.5% for the CFS group). Physical measures of disability and fatigue, along with measures of specific somatic symptoms,

				better differentiate individuals who later are diagnosed with CFS than more psychosocial measures such as stress and coping.
Jerome KR, Diem K, Huang ML, Selke S, Corey L, Buchwald D.	Department of Laboratory Medicine, University of Washington, Seattle, WA 98105, USA. kjerome@fhcrc.org	Xenotropic murine leukemia virus-related virus in monozygotic twins discordant for chronic fatigue syndrome.	Diagn Microbiol Infect Dis. 2011 Sep;71(1):66-71. Epub 2011 Jul 26.	A recent report suggested an association between xenotropic murine leukemia virus-related virus (XMRV) and chronic fatigue syndrome (CFS). If confirmed, this would suggest that antiretroviral therapy might benefit patients suffering from CFS. We validated a set of assays for XMRV and evaluated the prevalence of XMRV in a cohort of monozygotic twins discordant for CFS. Stored peripheral blood mononuclear cell (PBMC) samples were tested with 3 separate polymerase chain reaction (PCR) assays (one of which was nested) for XMRV DNA, and serum/plasma was tested for XMRV RNA by reverse transcription (RT)-PCR. None of the PBMC samples from the twins with CFS or their unaffected co-twins was positive for XMRV, by any of the assays. One plasma sample, from an unaffected co-twin, was reproducibly positive by RT-PCR. However, serum from the same day was negative, as was a follow-up plasma sample obtained 2 days after the positive specimen. These data do not support an association of XMRV with CFS. Copyright © 2011 Elsevier Inc. All rights reserved.
Jones DE, Hollingsworth KG, Jakovljevic DG, Fattakhova G, Pairman J, Blamire AM, Trenell MI, Newton JL.	Institute of Cellular Medicine Newcastle, Newcastle University, Newcastle, UK.	Loss of capacity to recover from acidosis on repeat exercise in chronic fatigue syndrome: a case-control study.	Eur J Clin Invest. 2012 Feb;42(2):186-94. doi: 10.1111/j.1365-2362.2011.02567.x. Epub 2011 Jul 12.	BACKGROUND: Chronic fatigue syndrome (CFS) patients frequently describe difficulties with repeat exercise. Here, we explore muscle bioenergetic function in response to three bouts of exercise. METHODS: A total of 18 CFS (CDC 1994) patients and 12 sedentary controls underwent assessment of maximal voluntary contraction (MVC), repeat exercise with magnetic resonance spectroscopy and cardio-respiratory fitness test to determine anaerobic threshold. RESULT: Chronic fatigue syndrome patients undertaking MVC fell into two distinct groups: 8 (45%) showed normal PCr depletion in response to exercise at 35% of MVC (PCr depletion >33%; lower 95% CI for controls); 10 CFS patients had low PCr depletion (generating abnormally low MVC values). The CFS whole group exhibited significantly reduced anaerobic threshold, heart rate, VO(2) , VO(2) peak and peak work compared to controls. Resting muscle pH was similar in controls and both CFS patient groups. However, the CFS group achieving normal PCr depletion values showed increased intramuscular acidosis compared to controls after similar work after each of the three exercise periods with no apparent reduction in acidosis with repeat exercise of the type reported in normal subjects. This CFS group also exhibited significant prolongation (almost 4-fold) of the time taken for pH to recover to baseline. CONCLUSION: When exercising to comparable levels to normal controls, CFS patients exhibit profound abnormality in bioenergetic function and response to it. Although exercise intervention is the logical treatment for patients showing acidosis, any trial must exclude subjects who do not initiate exercise as they will not benefit. This potentially explains previous mixed results in CFS exercise trials. © 2011 The Authors. European Journal of Clinical Investigation © 2011 Stichting European Society for Clinical Investigation Journal Foundation.
Jones DE, Gray J,	UK NIHR	Fatigue severity	J Intern Med. 2011	OBJECTIVES: to examine fatigue variability over time in chronic fatigue syndrome

Frith J, Newton JL.	Biomedical Centre in Ageing, Institute of Cellular Medicine, Institute for Ageing and Health, Newcastle University, Newcastle, UK.	remains stable over time and independently associated with orthostatic symptoms in chronic fatigue syndrome: a longitudinal study.	Feb;269(2):182-8. doi: 10.1111/j.1365-2796.2010.02306.x. Epub 2010 Nov 14.	(CFS) and the effect of other symptoms on its predictability. DESIGN: longitudinal cohort study of patients with CFS (Fukuda criteria). SETTING: specialist CFS clinical service. SUBJECTS: phase 1: 100 patients who participated in a study of CFS symptoms in 2005 were revisited in 2009. Phase 2: 25 patients completed fatigue diaries to address intra- and inter-day variability in perceived fatigue. MAIN OUTCOME MEASURES: phase 1: subjects completed fatigue impact scale (FIS), Epworth sleepiness scale (ESS), orthostatic grading scale (OGS) and hospital anxiety and depression scale (HADS). Changes in variables represented the differences between 2005 and 2009. Phase 2: subjects rated fatigue on a scale of 0 (no fatigue) to 10 (severe fatigue) four times a day for 5 weeks. RESULTS: symptom assessment tools were available in both 2005 and 2009 for 74% of patients. FIS and HADS depression (HAD-D) and anxiety (HAD-A) scores significantly improved during follow-up whereas ESS and OGS remained stable. FIS improved in 29/74 (39%) subjects, and by ≥ 10 points in 19 (26%). FIS worsened by ≥ 10 points in 33/74 (45%) subjects. On multivariate analysis, independent predictors of current fatigue (FIS in 2009) were FIS in 2005, HAD-D in 2009, OGS in 2009 and change in HAD-A. Reported fatigue was stable from week to week and from day to day. Patients reported higher fatigue in the morning (mean ± SD; 6.4 ± 2), becoming significantly lower at lunchtime (6.2 ± 2; $P < 0.05$) and increasing again to 7 ± 2 at bedtime. CONCLUSIONS: current fatigue is independently associated with current autonomic symptom burden, current depression and change in anxiety during follow-up. These findings have implications for targeted symptom management in CFS.
Juel J, Markvardsen LH, Jakobsen J.	Neurologisk Afdeling F, Aarhus Universitetshospital, Aarhus Sygehus, Denmark. jju@studmed.au.dk	[Haemolytic anaemia as a complication to intravenous infusion of human immunoglobulin]. [Article in Danish]	Ugeskr Laeger. 2011 Aug 15;173(33):1963-4.	A 85-year-old female treated for chronic inflammatory demyelinating polyradiculoneuropathy had three episodes of anaemia one week following treatment with large doses (2g/kg body weight) of immunoglobulin (Ig). At the final episode, she presented with haemolytic anaemia with fatigue, jaundice and loss of appetite. During the next two months anaemia was recognized in two additional cases. Subsequently, a series of twelve conseuntively studied IVIg treated patients showed a significant decrease of haemoglobin of 0.80 mmol/l 8-15 days after infusion. Haemolytic anaemia is a severe side effect that seems to be more frequent than previously recognized. It may possibly be prevented by the use of lyophilized Ig-preparations with low isohaemagglutinin titers or by slower Ig infusion rates.
Kaiser J.		Chronic fatigue syndrome. Studies point to possible contamination in XMRV findings.	Science. 2011 Jan 7;331(6013):17.	
Kallet RH.	Department of Anesthesia, University of	Patient-ventilator interaction during acute lung injury, and	Respir Care. 2011 Feb;56(2):181-9.	Since the early 1970s there has been an ongoing debate regarding the wisdom of promoting unassisted spontaneous breathing throughout the course of critical illness in patients with severe respiratory failure. The basis of this debate has focused on the

	California, San Francisco, CA, USA. rkallet@sfghsom.ucsf.edu	the role of spontaneous breathing: part 1: respiratory muscle function during critical illness.		clinical relevance of opposite problems. Historically, the term "disuse atrophy" has described a situation wherein sustained inactivity of the respiratory muscles (ie, passive ventilation) results in deconditioning and weakness. More recently it has been referred to as "ventilator-induced diaphragmatic dysfunction." In contrast, "use atrophy" describes a situation where chronic high-tension inspiratory work causes structural damage to the diaphragm and weakness. Both laboratory and clinical studies demonstrated that relatively brief periods of complete respiratory muscle inactivity, as well as intense muscle loading, result in acute inflammation, loss of muscle mass, and weakness. Yet in critical illness other factors also affect respiratory muscle function, including prolonged use of neuromuscular blocking agents, administration of corticosteroids, and sepsis. This makes the attribution of acquired respiratory muscle weakness and ventilator-dependence to either ventilator-induced diaphragmatic dysfunction or loaded breathing extremely difficult. Regardless, the clinical implications of this research strongly suggest that passive mechanical ventilation should be avoided whenever possible. However, promotion of unassisted spontaneous breathing in the acute phase of critical illness also may carry a substantial risk of respiratory muscle injury and weakness. Use of mechanical ventilation modes in a manner that induces spontaneous breathing effort, while simultaneously reducing the work load on the respiratory muscles, is probably sufficient to minimize both problems.
Kang DE, Lee MC, Das Gupta J, Klein EA, Silverman RH.	Glickman Urological and Kidney Institute, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA.	XMRV Discovery and Prostate Cancer-Related Research.	Adv Virol. 2011;2011:432837. Epub 2011 Jun 21.	Xenotropic murine leukemia virus-related virus (XMRV) was first reported in 2006 in a study of human prostate cancer patients with genetic variants of the antiviral enzyme, RNase L. Subsequent investigations in North America, Europe, Asia, and Africa have either observed or failed to detect XMRV in patients (prostate cancer, chronic fatigue syndrome-myalgic encephalomyelitis (CFS-ME), and immunosuppressed with respiratory tract infections) or normal, healthy, control individuals. The principal confounding factors are the near ubiquitous presence of mouse-derived reagents, antibodies and cells, and often XMRV itself, in laboratories. XMRV infects and replicates well in many human cell lines, but especially in certain prostate cancer cell lines. XMRV also traffics to prostate in a nonhuman primate model of infection. Here, we will review the discovery of XMRV and then focus on prostate cancer-related research involving this intriguing virus.
Katz BZ, Stewart JM, Shiraishi Y, Mears CJ, Taylor R.		Autonomic symptoms at baseline and following infectious mononucleosis in a prospective cohort of adolescents.	Arch Pediatr Adolesc Med. 2011 Aug;165(8):765-6.	
Katzourakis A, Hué	Department of	Phylogenetic analysis	J Virol. 2011	Xenotropic murine leukemia virus (MLV)-related virus (XMRV) has been amplified

S, Kellam P, Towers GJ.	Zoology, University of Oxford, South Parks Road, Oxford OX13PS, United Kingdom.	of murine leukemia virus sequences from longitudinally sampled chronic fatigue syndrome patients suggests PCR contamination rather than viral evolution.	Oct;85(20):10909-13. Epub 2011 Aug 17.	from human prostate cancer and chronic fatigue syndrome (CFS) patient samples. Other studies failed to replicate these findings and suggested PCR contamination with a prostate cancer cell line, 22Rv1, as a likely source. MLV-like sequences have also been detected in CFS patients in longitudinal samples 15 years apart. Here, we tested whether sequence data from these samples are consistent with viral evolution. Our phylogenetic analyses strongly reject a model of within-patient evolution and demonstrate that the sequences from the first and second time points represent distinct endogenous murine retroviruses, suggesting contamination.
Kawatani J, Mizuno K, Shiraishi S, Takao M, Joudoi T, Fukuda S, Watanabe Y, Tomoda A.	Department of Child Development, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan.	Cognitive dysfunction and mental fatigue in childhood chronic fatigue syndrome--a 6-month follow-up study.	Brain Dev. 2011 Nov;33(10):832-41. Epub 2011 May 6.	OBJECTIVES: Cognitive function was investigated in patients with childhood type chronic fatigue syndrome (CCFS) using the modified advanced trail making test (mATMT). METHODS: mATMT was performed on 19 patients with CCFS and 25 healthy controls of comparable age and sex. The effectiveness of combined treatment with cognitive behavioral therapy (CBT) and pharmacotherapy and its relationship to cognitive function was investigated by evaluation of Chalder's fatigue scale and behavior state before and after treatment for 6 consecutive months. RESULTS: All three tasks (motor skill, selective and alternative attention, and spatial working memory) of the mATMT, especially the difference in reaction time of the alternative attention task, could discriminate CCFS patients from control subjects with 70.5% accuracy (P=0.007). CCFS patients showed significantly lower alternative attention and Chalder's fatigue score before treatment (P=0.037 and 0.002, respectively). A significant improvement in performance status scores was found during the 6 months follow-up period with combined treatment with CBT and medication (P<0.001). Improvement of their cognitive symptoms was significantly correlated with improvement of alternative attention (r=0.653, P=0.002). CONCLUSIONS: Higher-order level cognitive dysfunction affects CCFS pathogenesis. Alternative attention performance evaluated by the mATMT may be used to monitor improvement in patients with CCFS. Combined treatment with CBT and medication may be effective to improve poor attention characteristics associated with CCFS.
Kearney MF, Lee K, Bagni RK, Wiegand A, Spindler J, Maldarelli F, Pinto PA, Linehan WM, Vocke CD, Delviks-Frankenberry KA, Devere White RW, Del Prete GQ, Mellors JW, Lifson	HIV Drug Resistance Program, National Cancer Institute at Frederick, Frederick, MD 21702-1201, USA.	Nucleic Acid, Antibody, and Virus Culture Methods to Detect Xenotropic MLV-Related Virus in Human Blood Samples.	Adv Virol. 2011;2011:272193. Epub 2011 Nov 17.	The MLV-related retrovirus, XMRV, was recently identified and reported to be associated with both prostate cancer and chronic fatigue syndrome. At the National Cancer Institute-Frederick, MD (NCI-Frederick), we developed highly sensitive methods to detect XMRV nucleic acids, antibodies, and replication competent virus. Analysis of XMRV-spiked samples and/or specimens from two pigtail macaques experimentally inoculated with 22Rv1 cell-derived XMRV confirmed the ability of the assays used to detect XMRV RNA and DNA, and culture isolatable virus when present, along with XMRV reactive antibody responses. Using these assays, we did not detect evidence of XMRV in blood samples (N = 134) or prostate specimens (N = 19) from two independent cohorts of patients with prostate cancer. Previous studies detected

JD, Kewalramani VN, Pathak VK, Coffin JM, Le Grice SF.				XMRV in prostate tissues. In the present study, we primarily investigated the levels of XMRV in blood plasma samples collected from patients with prostate cancer. These results demonstrate that while XMRV-related assays developed at the NCI-Frederick can readily measure XMRV nucleic acids, antibodies, and replication competent virus, no evidence of XMRV was found in the blood of patients with prostate cancer.
Kempke S, Luyten P, Van Houdenhove B, Goossens L, Bekaert P, Van Wambeke P.	Department of Psychology, University of Leuven, Tiensestraat 102, 3000 Leuven, Belgium. stefan.kempke@psy.kuleuven.be	Self-esteem mediates the relationship between maladaptive perfectionism and depression in chronic fatigue syndrome.	Clin Rheumatol. 2011 Dec;30(12):1543-8. Epub 2011 May 17.	Patients with chronic fatigue syndrome (CFS) often experience depression which may negatively affect prognosis and treatment outcome. Research has shown that depression in CFS is associated with maladaptive or self-critical perfectionism. However, currently, little is known about factors that may explain this relationship, but studies in nonclinical samples suggest that low self-esteem may be an important mediator of this relationship. The present study therefore examined whether self-esteem mediated the cross-sectional association between maladaptive perfectionism and severity of depression in 192 patients meeting Centres for Disease Control and Prevention criteria for CFS. Patients completed self-report measures of maladaptive perfectionism, self-esteem, depression, and fatigue. Regression analyses and more direct tests of indirect effects (i.e., the Sobel test and bootstrapping) were used to test for mediation. Congruent with expectations, we found that self-esteem fully mediated the relationship between maladaptive perfectionism and depression in CFS. Findings from this study suggest that self-esteem may explain the link between maladaptive perfectionism and depression in CFS, which may have important implications for the treatment and prevention of depression in these patients.
Kempke S, Van Houdenhove B, Luyten P, Goossens L, Bekaert P, Van Wambeke P.	Department of Psychology, University of Leuven, Leuven, Belgium. stefan.kempke@psy.kuleuven.be	Unraveling the role of perfectionism in chronic fatigue syndrome: is there a distinction between adaptive and maladaptive perfectionism?	Psychiatry Res. 2011 Apr 30;186(2-3):373-7. Epub 2010 Oct 18.	In the current study, we investigated whether the distinction between adaptive (i.e. high personal standards) and maladaptive (i.e. concern over mistakes and doubt about actions) perfectionism that has been found in the literature, is also valid in patients with chronic fatigue syndrome (CFS). We hypothesized that maladaptive, but not adaptive, perfectionism would be significantly and positively related to severity of fatigue and depression in CFS. We examined this hypothesis in a sample of 192 CFS patients using structural equation modelling (SEM). Although the two perfectionism dimensions were related to each other, results supported a model in which only maladaptive perfectionism was positively related to severity of fatigue and depression. Further, we found that depression fully mediated the effect of maladaptive perfectionism on fatigue. The results suggest that adaptive and maladaptive perfectionism are two distinct, albeit related, dimensions in CFS. Findings of this study have important implications for theory and treatment of CFS, particularly for cognitive-behavioral treatment. Copyright © 2010 Elsevier Ireland Ltd. All rights reserved.
Kenyon JC, Lever AM.	Department of Medicine, University of Cambridge,	XMRV, prostate cancer and chronic fatigue syndrome.	Br Med Bull. 2011;98:61-74. Epub 2011 May 6.	BACKGROUND: A new retrovirus, xenotropic murine leukaemia virus-related virus (XMRV), was identified in 2006 and an association was claimed between it and a genetic polymorphism predisposing to cancer of the prostate. In 2009 the same virus was identified in a cohort of patients with chronic fatigue syndrome (CFS). In 2010 a

	Addenbrooke's hospital, Cambridge, UK.			second related virus was identified in a separate group of CFS patients. A series of studies from disparate geographical areas have failed to substantiate this work. Most recently several papers have suggested that the detection of these viruses was explained by laboratory contamination. SOURCES OF DATA: All papers including the wording XMRV were abstracted from the NIH library of medicine database and included in the analysis. AREAS OF AGREEMENT: XMRV is a newly described retrovirus whose nucleic acid has been identified in samples from patients with both prostate cancer and CFS. AREAS OF CONTROVERSY: Opinions differ as to whether the detected nucleic acid indicates infection with this virus in this disease or whether laboratory contamination of samples accounts for its presence. GROWING POINTS: An increasing number of papers now refute the association of XMRV with human disease in humans although there is some evidence of serological reactivity to the virus. While it is unlikely that XMRV is a major cause of either prostate cancer or CFS, it can infect human cells and might yet have a role in human disease. AREAS TIMELY FOR DEVELOPING RESEARCH: Further studies to either prove or disprove the disease association of the virus are ongoing.
Kewley AJ.		The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1832; author reply 1834-5. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5.	
Kim JW, Lee JO, Han SW, Oh DY, Im SA, Kim TY, Bang YJ.	Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea.	Clinical outcomes of sorafenib treatment in patients with metastatic hepatocellular carcinoma who had been previously treated with fluoropyrimidine plus platinum-based chemotherapy.	Am J Clin Oncol. 2011 Apr;34(2):125-9.	OBJECTIVES: There has been no report on sorafenib therapy in patients with metastatic hepatocellular carcinoma (HCC) who had been treated with systemic chemotherapy. The objectives of this analysis were to investigate efficacy and safety of sorafenib in these patients and to elucidate risk factors associated with clinical outcomes. METHODS: We analyzed patients with metastatic HCC who were treated with sorafenib after failure of fluoropyrimidine plus platinum-based chemotherapy between April 2007 and December 2008. RESULTS: Twenty-four patients (male, 79.2%) were included. Median age was 53 years. Chronic hepatitis B was the predominant cause of HCC (79.2%), followed by chronic hepatitis C (4.2%) and alcohol (4.2%). Twenty patients (83.3%) were Child-Pugh A and 4 patients (16.7%) were Child-Pugh B. Median follow-up duration was 11.1 months. No objective response was observed. Fourteen patients (58.3%) had stable disease. The disease control rate was 58.3%. Median progression-free survival was 2.3 months (95% confidence interval, 0.5-4.1) and overall survival was 7.1 months (95% confidence

				interval, 3.5-10.7). Grade 3 neutropenia was observed in 1.4% and grade 3 anemia in 1.4%. Grade 3 or 4 nonhematologic toxicities were hand-foot syndrome (16.7%), skin rash (8.3%), diarrhea (4.2%), headache (4.2%), and fatigue (4.2%). Four patients (16.7%) discontinued the therapy because of toxicities. CONCLUSIONS: Sorafenib had modest efficacy and tolerable toxicity in patients with metastatic HCC who had received fluoropyrimidine plus platinum-based chemotherapy.
Kindlon T.		The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1833; author reply 1834-5. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5.	
Kindlon T.		Educational programs for chronic fatigue syndrome need to take cognizance of the condition's abnormal response to exercise.	Arch Phys Med Rehabil. 2011 Jun;92(6):1015; author reply 1015-6. Comment on Arch Phys Med Rehabil. 2010 Aug;91(8):1153-9.	
Kindlon T.		Harms of cognitive behaviour therapy designed to increase activity levels in chronic fatigue syndrome: questions remain.	Psychother Psychosom. 2011;80(2):110-1; author reply 112. Epub 2011 Jan 4. Comment on Psychother Psychosom. 2010 Jun;79(4):249-56.	
Kindt S, Van Oudenhove L, Mispelon L, Caenepeel P, Arts J, Tack J.	Center for Gastroenterological Research, Department of Pathophysiology, University Hospital Gasthuisberg,	Longitudinal and cross-sectional factors associated with long-term clinical course in functional dyspepsia: a 5-year follow-up study.	Am J Gastroenterol. 2011 Feb;106(2):340-8. Epub 2010 Oct 26.	OBJECTIVES: Functional dyspepsia (FD) is a heterogeneous disorder with different pathophysiological mechanisms underlying the symptom pattern, but little is known about its clinical course. The aims of this study were to study the long-term evolution of symptoms in a clinical FD population and to identify factors associated with outcome. METHODS: FD patients who previously underwent gastric function testing and filled out a dyspepsia symptom score (DSS) were contacted. At follow-up, patients indicated whether symptoms had worsened, remained unchanged, improved, or disappeared. Anxiety and depression, DSS, chronic fatigue symptoms, irritable bowel

	University of Leuven, Leuven, Belgium.			syndrome (IBS) comorbidity, and FD-specific quality of life (QoL) were assessed using mailed questionnaires. Bivariate associations between different patient characteristics and DSS and QoL at follow-up were tested; multiple linear regression was used to identify factors associated with the outcomes, both longitudinally and cross-sectionally. RESULTS: Data were obtained from 253 patients (84.9% of the eligible and consenting population (n=298) and 53.2% of the original population (n=476)). The mean duration of follow-up was 68±2 months. Disappeared, improved, unchanged, and worsened symptoms were reported by 17.4, 38.3, 30.8, and 13.4% of the patients, respectively. Correlations between dyspepsia symptoms at initial visit and follow-up were small to moderate in magnitude. DSS at initial visit and trait anxiety were longitudinally associated with DSS at follow-up, with a trend found for weight loss; depression, chronic fatigue, and IBS at follow-up were cross-sectionally associated with DSS. Trait anxiety, weight loss, and DSS at initial visit were independently associated with QoL at follow-up; depression as well as DSS and chronic fatigue at follow-up were cross-sectionally associated. CONCLUSIONS: About half of FD patients reported disappeared or improved symptoms after a mean follow-up of 5 years. Although stability of symptom levels is low to moderate, DSS at initial visit, trait anxiety, and initial weight loss are more strongly associated with outcome than gastric sensorimotor function.
Kishi A, Natelson BH, Togo F, Struzik ZR, Rapoport DM, Yamamoto Y.	Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, Tokyo, Japan.	Sleep-stage dynamics in patients with chronic fatigue syndrome with or without fibromyalgia.	Sleep. 2011 Nov 1;34(11):1551-60.	STUDY OBJECTIVES: Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained conditions that often have overlapping symptoms, including sleep-related complaints. However, differences between the 2 conditions have been reported, and we hypothesized that dynamic aspects of sleep would be different in the 2 groups of patients. PARTICIPANTS: Subjects were 26 healthy control subjects, 14 patients with CFS but without FM (CFS alone), and 12 patients with CFS and FM (CFS+FM)-all women. MEASUREMENTS AND RESULTS: We studied transition probabilities and rates between sleep stages (waking, rapid eye movement [REM] sleep, stage 1 [S1], stage 2 [S2], and slow-wave sleep [SWS]) and duration distributions of each sleep stage. We found that the probability of transition from REM sleep to waking was significantly greater in subjects with CFS alone than in control subjects, which may be the specific sleep problem for people with CFS alone. Probabilities of (a) transitions from waking, REM sleep, and S1 to S2 and (b) those from SWS to waking and S1 were significantly greater in subjects with CFS+FM than in control subjects; in addition, rates of these transitions were also significantly increased in subjects with CFS+FM. Result (a) might indicate increased sleep pressure in subjects with CFS+FM whereas result (b) may be the specific sleep problem of subjects with CFS+FM. We also found that shorter durations of S2 sleep are specific to patients with CFS+FM, not to CFS alone. CONCLUSIONS: These results suggest that CFS and FM may be different illnesses associated with different problems of sleep regulation.

Kmietowicz Z.		Researchers get 1.6m pound to look at scientific basis of chronic fatigue syndrome.	BMJ. 2011 Dec 21;343:d8281. doi: 10.1136/bmj.d8281.	
Knox K, Carrigan D, Simmons G, Teque F, Zhou Y, Hackett J Jr, Qiu X, Luk KC, Schochetman G, Knox A, Kogelnik AM, Levy JA.	Wisconsin Viral Research Group, Milwaukee, WI 53226, USA.	No evidence of murine-like gammaretroviruses in CFS patients previously identified as XMRV-infected.	Science. 2011 Jul 1;333(6038):94-7. Epub 2011 May 31. Comment in Nat Rev Urol. 2011 Aug;8(8):409.	Members of the gammaretroviruses--such as murine leukemia viruses (MLVs), most notably XMRV [xenotropic murine leukemia virus (X-MLV)-related virus--have been reported to be present in the blood of patients with chronic fatigue syndrome (CFS). We evaluated blood samples from 61 patients with CFS from a single clinical practice, 43 of whom had previously been identified as XMRV-positive. Our analysis included polymerase chain reaction and reverse transcription polymerase chain reaction procedures for detection of viral nucleic acids and assays for detection of infectious virus and virus-specific antibodies. We found no evidence of XMRV or other MLVs in these blood samples. In addition, we found that these gammaretroviruses were strongly (X-MLV) or partially (XMRV) susceptible to inactivation by sera from CFS patients and healthy controls, which suggested that establishment of a successful MLV infection in humans would be unlikely. Consistent with previous reports, we detected MLV sequences in commercial laboratory reagents. Our results indicate that previous evidence linking XMRV and MLVs to CFS is likely attributable to laboratory contamination.
Knudsen AK, Henderson M, Harvey SB, Chalder T.	Research Section of Mental Health Epidemiology, Department of Health Promotion and Development, Faculty of Psychology, University of Bergen, Christiesgt. 13, N-5020 Bergen, Norway. Ann.Knudsen@psych.uib.no	Long-term sickness absence among patients with chronic fatigue syndrome.	Br J Psychiatry. 2011 Nov;199(5):430-1. Epub 2011 Sep 8.	Chronic fatigue syndrome is associated with high levels of occupational disability. Consecutive out-patients at a chronic fatigue syndrome treatment service were studied for associations between occupational status, symptom severity and cognitive and behavioural responses to symptoms. All patients had high symptom levels; however, those on long-term sickness absence had significantly more physical fatigue ($\beta = 0.098$, $P<0.05$) and worse sleep ($\beta = 0.075$, $P<0.05$). Patients with long-term sickness absence also demonstrated more embarrassment avoidance cognitions ($\beta = 0.086$, $P<0.05$) and avoidance resting behavioural responses ($\beta = 0.078$, $P<0.05$). Identifying and addressing avoidance behaviours and cognitions regarding embarrassment in interventions may enhance the chances of individuals returning to work.
Knudsen AK, Omenås AN, Harvey SB, Løvvik CM, Lervik LV,	Department of Health Promotion and Development,	Chronic fatigue syndrome in the media: a content analysis of	JRSM Short Rep. 2011 May;2(5):42. Epub 2011 May 25.	OBJECTIVES: Although cognitive behavioural therapy and graded exercise treatment are recognized evidence-based treatments for chronic fatigue syndrome/myalgic encephalomyelitis (ME), their use is still considered controversial by some patient groups. This debate has been reflected in the media, where many patients gather

Mykletun A.	Faculty of Psychology, University of Bergen , Bergen , Norway.	newspaper articles.		health information. The aim of this study was to examine how treatment for chronic fatigue syndrome/ME is described in the newspaper media. DESIGN: Content analysis of newspaper articles. SETTING: The digitalized media archive Atekst was used to identify Norwegian newspaper articles where chronic fatigue syndrome/ME was mentioned. PARTICIPANTS: Norwegian newspaper articles published over a 20-month period, from 1 January 2008 to 31 August 2009. MAIN OUTCOME MEASURES: Statements regarding efficiency of various types of treatment for chronic fatigue syndrome/ME and the related source of the treatment advice. Statements were categorized as being either positive or negative towards evidence-based or alternative treatment. RESULTS: One hundred and twenty-two statements regarding treatment of chronic fatigue syndrome/ME were identified among 123 newspaper articles. The most frequent statements were positive statements towards alternative treatment Lightning Process (26.2%), negative statements towards evidence-based treatments (22.1%), and positive statements towards other alternative treatment interventions (22.1%). Only 14.8% of the statements were positive towards evidence-based treatment. Case-subjects were the most frequently cited sources, accounting for 35.2% of the statements, followed by physicians and the Norwegian ME association. CONCLUSIONS: Statements regarding treatment for chronic fatigue syndrome/ME in newspapers are mainly pro-alternative treatment and against evidence-based treatment. The media has great potential to influence individual choices. The unbalanced reporting of treatment options for chronic fatigue syndrome/ME in the media is potentially harmful.
Komaroff AL, Cho TA.	Division of General Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA. Komaroff@hms.harvard.edu	Role of infection and neurologic dysfunction in chronic fatigue syndrome.	Semin Neurol. 2011 Jul;31(3):325-37. doi: http://dx.doi.org/10.1055/s-0031-1287654. Epub 2011 Sep 30.	Chronic fatiguing illnesses following well-documented infections and acute "infectious-like" illnesses of uncertain cause have been reported for many decades. Chronic fatigue syndrome (CFS) was first formally defined in 1988. There is considerable evidence that CFS is associated with abnormalities of the central and autonomic nervous systems. There also is evidence linking several infectious agents with CFS, although no agent has been proven to be a cause of the illness. Most of the infectious agents that have been linked to CFS are able to produce a persistent, often life-long, infection and thus are a constant incitement to the immune system. Most also have been shown to be neuropathogens. The evidence is consistent with the hypothesis that CFS, in some cases, can be triggered and perpetuated by several chronic infections that directly or indirectly affect the nervous system, and that symptoms are a reflection of the immune response to the infection. © Thieme Medical Publishers.
Korenromp IH, Heijnen CJ, Vogels OJ, van den Bosch JM, Grutters JC.	Department of Pulmonology, St. Antonius Hospital Nieuwegein; , University	Characterization of chronic fatigue in patients with sarcoidosis in clinical remission.	Chest. 2011 Aug;140(2):441-7. Epub 2011 Feb 17.	BACKGROUND: Patients with sarcoidosis frequently complain of fatigue, even when sarcoidosis has come into clinical remission. The primary aim of this study was to assess the severity of fatigue in patients with sarcoidosis in clinical remission and to characterize it according to the international criteria for chronic fatigue syndrome (CFS). Furthermore, we evaluated whether fatigue is associated with depression and

	Medical Center Utrecht, Utrecht, The Netherlands.			anxiety, health status, and patient-reported sleep quality, and we recorded physical activity levels and muscle strength as objective assessments of fatigue. METHODS: Data on 75 patients with sarcoidosis in clinical remission were obtained by questionnaires (Checklist Individual Strength [CIS], Symptom Checklist-90, Beck Depression Inventory for primary care, Medical Outcomes Study 36-Item Short-Form Health Survey), standardized interview (CFS criteria), sleep diary, accelerometer, and muscle strength tests. RESULTS: Fatigue severity mean score in patients with sarcoidosis in clinical remission was high (CIS fatigue severity 30.5 ± 15.5), and criteria for CFS were met in 47% of fatigued participants. Median time since diagnosis was 9 years. Fatigue was associated with depression (P = .01), anxiety (P = .013), and reduced health status (P < .001). Scores on sleep quality were normal. Physical activity levels were reduced in fatigued participants. Muscle strength, particularly handgrip (P = .006) and quadriceps strength (P < .001), was significantly associated with fatigue. CONCLUSIONS: Fatigue in patients with sarcoidosis in clinical remission is a frequent symptom and can be characterized as a severe and long-lasting problem, symptomatically similar to CFS. Psychologic distress and reduced health status are associated with fatigue. Interestingly, we observed significantly reduced physical activity and muscle weakness in fatigued patients.
Kreijkamp-Kaspers S, Brenu EW, Marshall S, Staines D, Van Driel ML.	Academic General Practice, Faculty of Health Sciences & Medicine, Bond University, Gold Coast, Queensland. skreijka@bond.edu.au	Treating chronic fatigue syndrome - a study into the scientific evidence for pharmacological treatments.	Aust Fam Physician. 2011 Nov;40(11):907-12.	BACKGROUND: Chronic fatigue syndrome, or myalgic encephalomyelitis (CFS), is a severe disabling condition. Patients with CFS usually trial many different medicines, both conventional and complementary. An overview of the pharmacological treatments used by CFS patients and the available evidence underpinning the use of these treatments would be of great value to both patients and their healthcare providers. METHODS: Ninety-four CFS patients recruited into an Australian study investigating immunological biomarkers filled out a questionnaire assessing the medicines they were taking. Evidence from randomised clinical trials was sought in biomedical databases. RESULTS: The 94 CFS patients used 474 different medicines and supplements. The most commonly used medicines were antidepressants, analgesics, sedatives, and B vitamins. We identified 20 randomised controlled trials studying these medicines in CFS patients. DISCUSSION: While conventional and complementary medicines are widely used by CFS patients, the evidence for effectiveness in CFS is very limited.
Kumar A, Garg R, Gaur V, Kumar P.	Department of Pharmacology, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh-160	Nitric oxide modulation in protective role of antidepressants against chronic fatigue syndrome in mice.	Indian J Pharmacol. 2011 May;43(3):324-9.	BACKGROUND AND OBJECTIVE: The present study was designed to elucidate the possible nitric oxide (NO) mechanism in the protective effect of antidepressants using mice model of chronic fatigue syndrome (CFS). MATERIALS AND METHODS: Male albino laca mice were forced to swim for each 6 min session for 7 days and immobility period was measured on every alternate day (1(st), 3(rd), 5(th), 7(th)). After 7 days various behavioral tests (locomotor, mirror chamber, and plus maze tests for anxiety) were performed and biochemical estimations (lipid peroxidation, nitrite levels, GSH (reduced glutathione), and catalase activity) in mice brain were performed. Animals

	014, India.			were pretreated with citalopram (5 and 10 mg/kg) and imipramine (10 and 20 mg/kg) daily for 7 days. RESULTS: The present study showed that continued forced swimming for 7 days caused chronic fatigue-induced anxiety-like behavior as assessed in mirror chamber, plus maze tests, and impairment in locomotor activity followed by oxidative damage (as evidenced by increased lipid peroxidation, nitrite levels, depleted reduced glutathione, and catalase activity) in animals. Seven days pretreatment with citalopram (5 and 10 mg/kg) and imipramine (10 and 20 mg/kg) significantly improved behavioral and biochemical alterations. Further, L-nitro-arginine methyl ester (L-NAME,5 mg/kg) and methylene blue (MB, 10 mg/kg) pretreatment with citalopram (5 mg/kg) or imipramine (10 mg/kg) potentiated their protective effect. However, l-arginine (100 mg/kg) pretreatment with citalopram (5 mg/kg) or imipramine (10 mg/kg) reversed their protective effect as compared with their effect per se ($P < 0.05$). CONCLUSION: The present study suggests that protective effect of citalopram and imipramine might be due to its NO modulation against chronic fatigue induced behavioral and biochemical alterations.
Kutlubaev MA, Mead GE.		Letter by Kutlubaev and Mead regarding article, "Exertion fatigue and chronic fatigue are two distinct constructs in people post-stroke".	Stroke. 2011 May;42(5):e377. Epub 2011 Mar 17. Comment on Stroke. 2010 Dec;41(12):2908-12.	
Landis CA.	Department of Biobehavioral Nursing and Health System, University of Washington, Seatle, WA 98195-7266, USA. calandis@u.washington.edu	Sleep, pain, fibromyalgia, and chronic fatigue syndrome.	Handb Clin Neurol. 2011;98:613-37.	
Larbcharoensub N, Boonsakan P, Aroonroch R, Rochanawutanon M, Nitiyanant P, Phongkitkarun S, Poonvutikul S, Watchararanan	Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok,	Adrenal histoplasmosis: a case series and review of the literature.	Southeast Asian J Trop Med Public Health. 2011 Jul;42(4):920-5.	Adrenal histoplasmosis is an uncommon mycotic disease typically caused by Histoplasma capsulatum. The objective was to determine the clinicopathological findings in adrenal histoplasmosis. Pathological records were searched from the database at the Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University from 1993 to 2008 for cases of adrenal histoplasmosis. The keywords were "histoplasmosis" and "adrenal gland". Adrenal histoplasmosis was diagnosed by histopathology and Gomori-Grocott methenamine silver staining. Histoplasma capsulatum was confirmed by tissue culture and/or serology. The

SP, Ngarmukos C.	Thailand. Noppadol_l@hotmail.com			authors report seven cases of adrenal histoplasmosis in immunocompetent patients. The mean age at diagnosis was 67 years. All patients presented as chronic fatigue syndrome. The onset of symptoms ranged from one to three months. Addison's disease was found in adrenal histoplasmosis in one case (14.3%). The computed tomography revealed adrenal nodules measuring 1.2 to 7.8 cm in diameter. The histopathology showed granulomatous inflammation with caseous necrosis. Culture of adrenal tissue from two patients revealed Histoplasma capsulatum. Serum Histoplasma antibodies were positive in four cases. A cure was accomplished in 6 out of 7 cases (85.7%). The patients were followed up for 2.5 to 16.5 years.
Larun L, Malterud K.	Research Unit for General Practice, Uni Research, Bergen, Norway. lillebeth.larun@kunnskapssenteret.no	Finding the right balance of physical activity: a focus group study about experiences among patients with chronic fatigue syndrome.	Patient Educ Couns. 2011 May;83(2):222-6. Epub 2010 Jun 26.	OBJECTIVE: To explore contexts of experiences of physical activity perceived as beneficial or harmful for CFS patients. METHODS: A qualitative study with empirical data from two focus groups with purposive sampling. Mean age was 50, two of ten participants were male, and social demographics varied. Participants were invited to share stories of good as well as bad experiences concerning physical activity. Data were analysed with systematic text condensation. RESULTS: Participants were not averse to physical activity, but specific preconditions would determine how the activity was perceived. Physical activity was experienced as helpful and enjoyable, especially related to leisure activities where flexible and individual adaptation was feasible. Non-customized activity may precipitate set-backs giving patients the impression of losing control and being betrayed by their bodies. Strategies to review energy usage in daily life could adjust expectations, diminish stress load and assist in approaching a more appropriate priority and balance. CONCLUSION: Self-management, body awareness and physical activity of choice combined with facilitation and advice from health care professionals is essential to achieve a positive outcome. PRACTICE IMPLICATIONS: Exercise programmes should be adapted, paced, and self-managed in accordance with personal preferences and activity levels to be beneficial and empowering for CFS patients. Copyright © 2010 Elsevier Ireland Ltd. All rights reserved.
Larun L, Malterud K.	Allmennmedisinsk forskningsenhet i Bergen, Uni helse, Kalfarveien 31, Bergen. ela@nokc.no	[Exercise therapy for patients with chronic fatigue syndrome]. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2011 Feb 4;131(3):231-6. Comment in Tidsskr Nor Laegeforen. 2011 May 6;131(8):803.	BACKGROUND: Post-exertional fatigue is the main symptom of chronic fatigue syndrome. Evidence-based guidelines recommend cognitive behavioral therapy and graded exercise therapy. In this article, we present a systematic review of outcome studies and discuss procedures for individualized exercise therapy for patients with chronic fatigue syndrome. MATERIAL AND METHODS: The effect of exercise treatment for these patients was assessed through a meta-analysis of randomized controlled trials which were identified through a systematic literature review. Effect size was calculated for fatigue, pain and health-related quality of life and the GRADE system was used to estimate the documentation level (quality of the evidence and strength of the recommendations). RESULTS: Seven outcome studies were included in the meta-analysis. They demonstrated that exercise therapy seems to reduce fatigue, but the results were inconclusive for pain and health-related quality of life. The

				documentation level is moderate to low and further research can modify the results in positive or negative directions. We found no indications of adverse effects of individualized exercise programs which were adapted to the patients' functional level and included adequate follow-up. INTERPRETATION: In light of general knowledge about positive health effects of exercise therapy and empirically based hypotheses about disease mechanisms in chronic fatigue syndrome, we conclude that further research has a high probability of confirming recommendations on individualized exercise therapy to these patients.
Lee SS, Kim SH, Nah SS, Lee JH, Lee YA, Hong SJ, Kim HS, Lee HS, Kim HA, Joung CI, Choe JY, Kim SK.	Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Republic of Korea.	Smoking habits influence pain and functional and psychiatric features in fibromyalgia.	Joint Bone Spine. 2011 May;78(3):259-65. Epub 2010 Sep 20.	OBJECTIVE: Numerous epidemiologic data have shown that smoking may play a role in the disease manifestations or severity of chronic musculoskeletal pain. The authors of the present study investigated the effect of smoking on clinical features such as pain, fatigue, functional impairment, and psychiatric features in the Korean population with fibromyalgia syndrome (FMS). METHODS: A total of 336 patients with FMS were consecutively enrolled from 10 medical centers which participated in the Korean national fibromyalgia survey. Smoking was divided into current smokers and non-smokers. Instruments of FMS assessment included tender points, Fibromyalgia Impact questionnaire (FIQ), 36-item Medical Outcomes Study Short-Form Health Survey (SF-36), Brief Fatigue Inventory (BFI), Brief Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI)-1 and STAI-2, and social family support and social friend support. Statistical analyses included Chi-square test, Fisher's exact test, Mann-Whitney U test, and multivariate logistic regression analysis. RESULTS: Thirty-three patients (9.8%) out of 336 participants were current smokers. The number of tender points (P=0.037), BFI (P=0.026), general health of SF-36 (P=0.028), BDI (P=0.014), syncope (P=0.024), and reflex sympathetic dystrophy (P=0.003) showing significance between current smokers and non-smokers were not associated with smoking habits after adjustment. The significance of the number of tender points (P=0.009), scores of total tender points (P=0.032), BDI (P=0.038), general weakness (P=0.047), and reflex sympathetic dystrophy (P=0.011) was observed between randomized non-smokers (n=55) and smokers (n=33). In addition, the number of tender points (P=0.027, OR=1.379) was associated with smoking status after adjustment. The analysis between randomized non-smokers (n=45) and smokers (n=22) in female FMS patients showed that BDI in FMS was associated with smoking status (P=0.023, OR=1.077) after logistic regression analysis. CONCLUSIONS: This study revealed that smoking habits may, in part, influence pain or functional and psychiatric features in FMS patients. The impact of smoking on clinical features in FMS should be assessed in a larger study population. Copyright © 2010 Société française de rhumatologie. Published by Elsevier SAS. All rights reserved.
Leone SS, Wessely S, Huibers MJ, Knottnerus JA,	Department of Epidemiology, Maastricht	Two sides of the same coin? On the history and	Psychol Health. 2011 Apr;26(4):449-64. Epub 2010 Apr 29.	BACKGROUND: Burnout and chronic fatigue syndrome (CFS) are two fatigue syndromes which have developed largely independently from each other, yet whose similarities in symptoms can be a source of confusion. We aim to explore the

Kant I.	University, Maastricht, The Netherlands. Stephanie.Leone @epid.unimaas.nl	phenomenology of chronic fatigue and burnout.		phenomenology of burnout and CFS in a historical context as this may provide some insight into the links and relationship between these conditions. METHOD: A narrative review based on literature in the fields of history, social science and medicine. RESULTS: The origins of CFS lie within medicine, whereas burnout developed in a psychological setting. As well as symptoms, burnout and CFS also share similar themes such as an overload process triggering illness onset, the need for restoration of depleted energy, external causal attributions and the characteristics of people suffering from these illnesses. However, these themes are expressed in either psychological or medical terms according to the historical background. CONCLUSION: Despite their similarities, there have been few direct comparisons of the two concepts. Culture, illness perceptions and accountability are important issues in both conditions and could contribute to their differences. Comparing burnout and CFS within one sample frame, thus looking beyond the psychology/medicine divide, could be a useful first step towards understanding their relationship.
Li B, Mahan CM, Kang HK, Eisen SA, Engel CC.	Institute for Clinical Research, Inc., Washington DC, USA.	Longitudinal health study of US 1991 Gulf War veterans: changes in health status at 10-year follow-up.	Am J Epidemiol. 2011 Oct 1;174(7):761-8. Epub 2011 Jul 27.	The authors assessed changes in the health status of US 1991 Gulf War-era veterans from a 1995 baseline survey to a 2005 follow-up survey, using repeated measurement data from 5,469 deployed Gulf War veterans and 3,353 nondeployed Gulf War-era veterans who participated in both surveys. Prevalence differences in health status between the 2 surveys were estimated for adverse health indices and chronic diseases for each veteran group. Persistence risk ratios and incidence risk ratios were calculated after adjustment for demographic and military service characteristics through Mantel-Haenszel stratified analysis. At 10-year follow-up, deployed veterans were more likely to report persistent poor health, as measured by the health indices (functional impairment, limitation of activities, repeated clinic visits, recurrent hospitalizations, perception of health as fair or poor, chronic fatigue syndrome-like illness, and posttraumatic stress disorder), than nondeployed veterans. Additionally, deployed veterans were more likely to experience new onset of adverse health (as measured by the indices) and certain chronic diseases than were nondeployed veterans. During the 10-year period from 1995 to 2005, the health of deployed veterans worsened in comparison with nondeployed veterans because of a higher rate of new onset of various health outcomes and greater persistence of previously reported adverse health on the indices.
Li N, Qiu MY, Hao JR, Zhang QM, Wang SH, Liang F, Yin Y, Luan J, Ge GZ, Qin T, Li BQ.	Wangjing Hospital, China Academy of Chinese Medical Sciences, Beijing 100102, China.	[Randomized controlled trail on moxibustion for maintenance hemodialysis patients in deficiency syndrome]. [Article in Chinese]	Zhongguo Zhen Jiu. 2011 Jan;31(1):15-8.	OBJECTIVE: To explore the effective therapy for maintenance hemodialysis patients in dificiency syndrome in end-stage renal disease. METHODS: Ninety-seven cases were divided into an observation group (51 cases) and a control group (46 cases) randomly, and routine western medicine was used in both of them. On this base, moxibustion was used in Zusanli (ST 36) and Sanyinjiao (SP 6) in paper-tube-moxibustion equipment in the observation group. Evaluate the therapeutic effect on symptoms by comparing the symptom scores in two groups before and after treatment. RESULTS: All the symptom scores in the observation group were improved after treatment, and

				the differences were significant (all P < 0.05). Among all symptoms, the most improved ones included lassitude and fatigue, short breath and aversion to talk, poor appetite, soreness and softness of waist and knees, aversion to cold, cold extremities and so on. In the aspect of therapeutic effect on symptoms, the total effective rate in observation group (64.7%, 33/51) was higher than that in control group (23.9%, 11/46), and the difference was significant (P < 0.05). CONCLUSION: Moxibustion can improve the clinical symptoms of maintenance hemodialysis patients in end-stage renal disease, and can generate some therapeutic effect to the dificiency syndrome of this disease.
Light AR, Bateman L, Jo D, Hughen RW, Vanhaitsma TA, White AT, Light KC.	Department of Anesthesiology The Brain Institute Department of Neurobiology and Anatomy Department of Exercise and Sport Science, University of Utah, Salt Lake City, UT 84132, USA. alan.light@hsc.utah.edu	Gene expression alterations at baseline and following moderate exercise in patients with Chronic Fatigue Syndrome and Fibromyalgia Syndrome.	J Intern Med. 2012 Jan;271(1):64-81. doi: 10.1111/j.1365-2796.2011.02405.x. Epub 2011 Jul 13.	OBJECTIVES: To determine mRNA expression differences in genes involved in signalling and modulating sensory fatigue, and muscle pain in patients with chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FM) at baseline, and following moderate exercise. DESIGN: Forty-eight patients with CFS only, or CFS with comorbid FM, 18 patients with FM that did not meet criteria for CFS, and 49 healthy controls underwent moderate exercise (25 min at 70% maximum age-predicted heart rate). Visual-analogue measures of fatigue and pain were taken before, during and after exercise. Blood samples were taken before and 0.5, 8, 24 and 48 h after exercise. Leucocytes were immediately isolated from blood, number coded for blind processing and analyses and flash frozen. Using real-time, quantitative PCR, the amount of mRNA for 13 genes (relative to control genes) involved in sensory, adrenergic and immune functions was compared between groups at baseline and following exercise. Changes in amounts of mRNA were correlated with behavioural measures and functional clinical assessments. RESULTS: No gene expression changes occurred following exercise in controls. In 71% of patients with CFS, moderate exercise increased most sensory and adrenergic receptor's and one cytokine gene's transcription for 48 h. These postexercise increases correlated with behavioural measures of fatigue and pain. In contrast, for the other 29% of patients with CFS, adrenergic α-2A receptor's transcription was decreased at all time-points after exercise; other genes were not altered. History of orthostatic intolerance was significantly more common in the α-2A decrease subgroup. FM-only patients showed no postexercise alterations in gene expression, but their pre-exercise baseline mRNA for two sensory ion channels and one cytokine were significantly higher than controls. CONCLUSIONS: At least two subgroups of patients with CFS can be identified by gene expression changes following exercise. The larger subgroup showed increases in mRNA for sensory and adrenergic receptors and a cytokine. The smaller subgroup contained most of the patients with CFS with orthostatic intolerance, showed no postexercise increases in any gene and was defined by decreases in mRNA for α-2A. FM-only patients can be identified by baseline increases in three genes. Postexercise increases for four genes meet published criteria as an objective biomarker for CFS and could be useful in guiding treatment selection for different subgroups. © 2011 The

				Association for the Publication of the Journal of Internal Medicine.
Light KC, White AT, Tadler S, Iacob E, Light AR.	Departments of Anesthesiology, Neurobiology and Anatomy, and Exercise and Sport Science, The University of Utah, Salt Lake City, UT 84132, USA.	Genetics and Gene Expression Involving Stress and Distress Pathways in Fibromyalgia with and without Comorbid Chronic Fatigue Syndrome.	Pain Res Treat. 2012;2012:427869. Epub 2011 Sep 29.	In complex multisymptom disorders like fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS) that are defined primarily by subjective symptoms, genetic and gene expression profiles can provide very useful objective information. This paper summarizes research on genes that may be linked to increased susceptibility in developing and maintaining these disorders, and research on resting and stressor-evoked changes in leukocyte gene expression, highlighting physiological pathways linked to stress and distress. These include the adrenergic nervous system, the hypothalamic-pituitary-adrenal axis and serotonergic pathways, and exercise responsive metabolite-detecting ion channels. The findings to date provide some support for both inherited susceptibility and/or physiological dysregulation in all three systems, particularly for catechol-O-methyl transferase (COMT) genes, the glucocorticoid and the related mineralocorticoid receptors (NR3C1, NR3C2), and the purinergic 2X4 (P2X4) ion channel involved as a sensory receptor for muscle pain and fatigue and also in upregulation of spinal microglia in chronic pain models. Methodological concerns for future research, including potential influences of comorbid clinical depression and antidepressants and other medications, on gene expression are also addressed.
Limb M.		Science asks researchers to withdraw paper on chronic fatigue syndrome and infectious retrovirus.	BMJ. 2011 Jun 6;342:d3505. doi: 10.1136/bmj.d3505.	
Lin JM, Resch SC, Brimmer DJ, Johnson A, Kennedy S, Burstein N, Simon CJ.	Chronic Viral Diseases Branch, Mail Stop A-15, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, GA 30333, USA. dwe3@cdc.gov.	The economic impact of chronic fatigue syndrome in Georgia: direct and indirect costs.	Cost Eff Resour Alloc. 2011 Jan 21;9(1):1.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating chronic illness affecting at least 4 million people in the United States. Understanding its cost improves decisions regarding resource allocation that may be directed towards treatment and cure, and guides the evaluation of clinical and community interventions designed to reduce the burden of disease. METHODS: This research estimated direct and indirect costs of CFS and the impact on educational attainment using a population-based, case-control study between September 2004 and July 2005, Georgia, USA. Participants completed a clinical evaluation to confirm CFS, identify other illnesses, and report on socioeconomic factors. We estimated the effect of CFS on direct medical costs (inpatient hospitalizations, provider visits, prescription medication spending, other medical supplies and services) and loss in productivity (employment and earnings) with a stratified sample (n = 500) from metropolitan, urban, and rural Georgia. We adjusted medical costs and earnings for confounders (age, sex, race/ethnicity, education, and geographic strata) using econometric models and weighted estimates to reflect response-rate adjusted sampling rates. RESULTS: Individuals with CFS had mean annual direct medical costs of $5,683. After adjusting

				for confounding factors, CFS accounted for $3,286 of these costs (p < 0.01), which were driven by increased provider visits and prescription medication use. Nearly one-quarter of these expenses were paid directly out-of pocket by those with CFS. Individuals with CFS reported mean annual household income of $23,076. After adjustment, CFS accounted for $8,554 annually in lost household earnings (p < 0.01). Lower educational attainment accounted for 19% of the reduction in earnings associated with CFS. CONCLUSIONS: Study results indicate that chronic fatigue syndrome may lead to substantial increases in healthcare costs and decreases in individual earnings. Studies have estimated up to 2.5% of non-elderly adults may suffer from CFS. In Georgia, a state with roughly 5.5 million people age 18-59, illness could account for $452 million in total healthcare expenditures and $1.2 billion of lost productivity.
Ling H, Braschinsky M, Taba P, Lüüs SM, Doherty K, Hotter A, Poewe W, Lees AJ.	Reta Lila Weston Institute of Neurological Studies, Institute of Neurology, University College London, London, United Kingdom.	Decades of delayed diagnosis in 4 levodopa-responsive young-onset monogenetic parkinsonism patients.	Mov Disord. 2011 Jun;26(7):1337-40. doi: 10.1002/mds.23563. Epub 2011 Mar 29.	BACKGROUND: We report 4 patients with young-onset monogenetic parkinsonism, each of whom was misdiagnosed with either a psychogenic movement disorder or chronic fatigue syndrome for 10 to 23 years after the onset of their first symptoms. RESULTS: Once the diagnosis was eventually made, they all had a rapid and excellent response to levodopa, albeit with the early appearance of interdose dyskinesias in 3. CONCLUSIONS: We discuss possible reasons for the missed diagnosis despite the relentless progression of their motor handicap. DAT scanning supported the revised clinical diagnosis of parkinsonism. © 2011 Movement Disorder Society. Copyright © 2011 Movement Disorder Society.
Lintas C, Guidi F, Manzi B, Mancini A, Curatolo P, Persico AM.	Laboratory of Molecular Psychiatry and Neurogenetics, University Campus Bio-Medico, Rome, Italy.	Lack of infection with XMRV or other MLV-related viruses in blood, post-mortem brains and paternal gametes of autistic individuals.	PLoS One. 2011 Feb 23;6(2):e16609.	BACKGROUND: Autistic spectrum disorder (ASD) is characterized by impaired language, communication and social skills, as well as by repetitive and stereotypic patterns of behavior. Many autistic subjects display a dysregulation of the immune system which is compatible with an unresolved viral infection with prenatal onset, potentially due to vertical viral transmission. Recently, the xenotropic murine leukemia virus-related virus (XMRV) has been implicated in chronic fatigue syndrome (CFS) and in prostate cancer by several, though not all studies. METHODOLOGY/PRINCIPAL FINDINGS: We assessed whether XMRV or other murine leukemia virus (MLV)-related viruses are involved in autistic disorder. Using nested PCR targeted to gag genomic sequences, we screened DNA samples from: (i) peripheral blood of 102 ASD patients and 97 controls, (ii) post-mortem brain samples of 20 ASD patients and 17 sex- and age-matched controls, (iii) semen samples of 11 fathers of ASD children, 25 infertile individuals and 7 fertile controls. No XMRV gag DNA sequences were detected, whereas peripheral blood samples of 3/97 (3.1%) controls were positive for MLV. CONCLUSIONS| SIGNIFICANCE: No MLV-related virus was detected in blood, brain, and semen samples of ASD patients or fathers. Hence infection with XMRV or other MLV-related viruses is unlikely to contribute to autism pathogenesis.
Liu KP, Fang M, Dai	Department of	[A study of median	Zhong Xi Yi Jie He Xue	OBJECTIVE: To study the changes in median frequency (MF) from a surface

DC, Jiang SY, Zuo YZ.	Tuina, Shanghai University of Traditional Chinese Medicine, Shanghai, China. yaotuzheng@126.com	frequencies of skeletal muscle undergoing Tuina intervention in patients with chronic fatigue syndrome]. [Article in Chinese]	Bao. 2011 Oct;9(10):1083-7.	electromyogram of skeletal muscles and functional assessment of chronic illness therapy (FACIT) figure scale scores for patients with chronic fatigue syndrome (CFS) before and after Tuina treatment. METHODS: A controlled clinical trial was adopted. Thirty-two patients suffering from CFS were enrolled according to the inclusion criteria from outpatient department of Shanghai Yueyang Hospital of Integrated Chinese and Western Medicine in China; thirty normal people whose gender, age, height and body mass were concordant with the CFS patients were selected as the normal group. Surface electromyography was used to detect the median frequency (MF) of biceps, quadriceps, and waist and back muscle before and after a 20-day course of treatment. CFS patients also were asked to fill out the figure scale of FACIT to evaluate the degree of fatigue. RESULTS: There was no significant difference in surface electromyography MF of myoelectric signal of biceps and quadriceps between CFS and normal person; however, the waist and back muscle MF of the normal person was significantly lower than that of the CFS patients. Before and after treatment, there were no obvious changes in the MF of myoelectric signals of all muscles. Tuina significantly decreased the scale score of FACIT. CONCLUSION: Tuina can improve the symptom of patients with CFS.
Liu Y, Zhang HG, Li XH.	Institute of Materia Medica and Department of Pharmaceutics, College of Pharmacy, Third Military Medical University, Chongqing, 400038, PR China.	A Chinese herbal decoction, Danggui Buxue Tang, improves chronic fatigue syndrome induced by food restriction and forced swimming in rats.	Phytother Res. 2011 Dec;25(12):1825-32. doi: 10.1002/ptr.3499. Epub 2011 Apr 15.	Danggui Buxue Tang (DBT), a Chinese medicinal decoction that contains Radix Angelicae sinensis (Danggui) and Radix Astragali (Huangqi) at a ratio of 1:5, is used commonly for treating women's ailments. The present study explored the effects of this preparation on chronic fatigue syndrome (CFS). Rats were subjected to a combination of food restriction and forced swimming to induce CFS, and rats were gavaged once daily with either 12 or 24 g/kg DBT for 28 days. Body weights, T-cell subset counts, (3) H-TdR incorporation measurements and mRNA levels of IL-1β, TNF-α, NF-κB, p38MAPK and JNK were determined on days 14 and 28. The swimming endurance capacity was measured on day 28. Rats that received DBT exhibited increased body weight and endurance capacity, corrected T cell subsets counts, increased (3) H-TdR incorporation and decreased mRNA levels of IL-1β, TNF-α, NF-κB, p38MAPK and JNK compared with rats that did not receive DBT. The results indicate that DBT can ameliorate CFS through immune modulation and may act to normalize cytokines and their related signaling pathways. Copyright © 2011 John Wiley & Sons, Ltd.
Lo SC, Pripuzova N, Li B, Komaroff AL, Hung GC, Wang R, Alter HJ.		Retraction for Lo et al., Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood	Proc Natl Acad Sci U S A. 2012 Jan 3;109(1):346. Epub 2011 Dec 27. Retraction of Lo SC, Pripuzova N, Li B, Komaroff AL, Hung GC, Wang R, Alter HJ. Proc	

		donors.	Natl Acad Sci U S A. 2010 Sep 7;107(36):15874-9.	
Lombardi VC, Hagen KS, Hunter KW, Diamond JW, Smith-Gagen J, Yang W, Mikovits JA.	Whittemore Peterson Institute, University of Nevada, Reno MS 0552, 1664 N. Virginia St. Reno, NV 89557-0552, USA. vclombardi@wpinstitute.org	Xenotropic murine leukemia virus-related virus-associated chronic fatigue syndrome reveals a distinct inflammatory signature.	In Vivo. 2011 May-Jun;25(3):307-14.	BACKGROUND: The recent identification of xenotropic murine leukemia virus-related virus (XMRV) in the blood of patients with chronic fatigue syndrome (CFS) establishes that a retrovirus may play a role in the pathology in this disease. Knowledge of the immune response might lead to a better understanding of the role XMRV plays in this syndrome. Our objective was to investigate the cytokine and chemokine response in XMRV-associated CFS. MATERIALS AND METHODS: Using Luminex multi-analyte profiling technology, we measured cytokine and chemokine values in the plasma of XMRV-infected CFS patients and compared these data to those of healthy controls. Analysis was performed using the Gene Expression Pattern Analysis Suite and the Random Forest tree classification algorithm. RESULTS: This study identifies a signature of 10 cytokines and chemokines which correctly identifies XMRV/CFS patients with 93% specificity and 96% sensitivity. CONCLUSION: These data show, for the first time, an immunological pattern associated with XMRV/CFS.
Lommel K, Bamford J, Jhavari M, Martin C, Crofford L.	Division of Rheumatology and College of Public Health, Department of Psychiatry, University of Kentucky, Lexington, KY 40509, USA. karen.lommel@uky.edu	A pilot study: pain, fatigue and stress in maternal relatives of adolescent female psychiatric inpatients assessed for juvenile primary fibromyalgia syndrome.	Int J Adolesc Med Health. 2011;23(1):59-63.	BACKGROUND: This study was designed to assess the presence of pain and impaired functioning in the maternal relatives of adolescent females in an inpatient adolescent psychiatric population. We compared the relatives of adolescents who met the criteria for juvenile primary fibromyalgia syndrome (JPFS) to relatives of adolescents who did not meet the criteria for JPFS. METHODS: A total of 55 biological maternal relatives of adolescent females admitted to a psychiatric unit were recruited to participate in the study. Participants completed four self-administered questionnaires: Multidimensional Fatigue Inventory, Fibromyalgia Impact Questionnaire, Medical Outcomes Survey (SF36v2), and the EPIFUND Health Survey. RESULTS: The maternal relatives of adolescents who met the criteria for JPFS did not score higher than the maternal relatives of adolescents who did not meet the criteria for JPFS. However, all maternal relatives consistently scored higher on self-reported measures of pain, impaired functioning, fatigue, and fibromyalgia symptoms than the average patient diagnosed with fibromyalgia or a chronic pain syndrome. CONCLUSION: Mood disorders and pain disorders share genetic risk factors and vulnerability. Future research is needed to further delineate other factors impacting the maternal caregivers' functioning. These could include stress associated with an adolescent child with psychiatric issues severe enough to warrant hospitalization.
Lopez C, Antoni M, Penedo F, Weiss D, Cruess S, Segotas MC, Helder L, Siegel S, Klimas N, Fletcher MA.	University of Miami, Miami, FL, USA.	A pilot study of cognitive behavioral stress management effects on stress, quality of life, and symptoms in persons	J Psychosom Res. 2011 Apr;70(4):328-34. Epub 2011 Jan 15.	OBJECTIVE: The present pilot study was designed to test the effects of a 12-week group-based cognitive behavioral stress management (CBSM) intervention on stress, quality of life, and symptoms in chronic fatigue syndrome (CFS). We hypothesized that participants randomized to CBSM would report improvements in perceived stress, mood, quality of life, and CFS symptomatology from pre- to postintervention compared to those receiving a psychoeducational (PE) seminar control. METHOD: We

		with chronic fatigue syndrome.		recruited 69 persons with a bona fide diagnosis of CFS and randomized 44 to CBSM and 25 to PE. Participants completed the Perceived Stress Scale (PSS), Profile of Mood States (POMS), Quality of Life Inventory (QOLI), and a Centers for Disease Control (CDC)-based CFS symptom checklist pre- and postintervention. RESULTS: Repeated measures analysis of variance revealed a significant Group×Time interaction for PSS, POMS-total mood disturbance (TMD), and QOLI scores, such that participants in CBSM evidenced greater improvements than those in PE. Participants in CBSM also reported decreases in severity of CFS symptoms vs. those in PE. CONCLUSIONS: Results suggest that CBSM is beneficial for managing distress, improving quality of life, and alleviating CFS symptom severity. Copyright © 2011 Elsevier Inc. All rights reserved.
Luyten P, Kempke S, Van Wambeke P, Claes S, Blatt SJ, Van Houdenhove B.	Department of Psychology at the University of Leuven, in Leuven, Belgium. Patrick.Luyten@psy.kuleuven.be	Self-critical perfectionism, stress generation, and stress sensitivity in patients with chronic fatigue syndrome: relationship with severity of depression.	Psychiatry. 2011 Spring;74(1):21-30.	Chronic Fatigue Syndrome (CFS) is a highly disabling disorder that is part of a broader spectrum of chronic pain and fatigue disorders. Although the etiology and pathogenesis of CFS largely remain unclear, there is increasing evidence that CFS shares important pathophysiological disturbances with mood disorders in terms of disturbances in the stress response and the stress system. From a psycho-dynamic perspective, self-critical perfectionism and related personality factors are hypothesized to explain in part impairments of the stress response in both depression and CFS. Yet, although there is ample evidence that high levels of self-critical perfectionism are associated with stress generation and increased stress sensitivity in depression, evidence supporting this hypothesis in CFS is currently lacking. This study therefore set out to investigate the relationship between self-critical perfectionism, the active generation of stress, stress sensitivity, and levels of depression in a sample of 57 patients diagnosed with CFS using an ecological momentary assessment approach. Results showed, congruent with theoretical assumptions, that self-critical perfectionism was associated with the generation of daily hassles, which in turn predicted higher levels of depression. Moreover, multilevel analyses showed that self-critical perfectionism was related to increased stress sensitivity in CFS patients over a 14-day period, and that increased stress sensitivity in turn was related to increased levels of depression. The implications of these findings for future research and particularly for the development of psychodynamic treatment approaches of CFS and related conditions are discussed.
Maes M, Mihaylova I, Kubera M, Ringel K.	Maes Clinics @ TRIA, Bangkok, Thailand. dr.michaelmaes@hotmail.com	Activation of cell-mediated immunity in depression: association with inflammation, melancholia, clinical staging and the fatigue and somatic	Prog Neuropsychopharmacol Biol Psychiatry. 2012 Jan 10;36(1):169-75. Epub 2011 Sep 16.	BACKGROUND: Depression is characterized by activation of cell-mediated immunity (CMI), including increased neopterin levels, and increased pro-inflammatory cytokines (PICs), such as interleukin-1 (IL-1) and tumor necrosis factor-α (TNFα). These PICs may induce depressive, melancholic and chronic fatigue (CF) symptoms. METHODS: We examined serum neopterin and plasma PIC levels in depressive subgroups in relation to the depressive subtypes and the melancholic and CF symptoms of depression. Participants were 85 patients with depression and in 26 normal controls. Severity of depression was assessed with the Hamilton Depression Rating Scale (HDRS) and

		symptom cluster of depression.		severity of CF with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Serum neopterin was significantly higher in depressed patients and in particular in those with melancholia. There were positive correlations between serum neopterin, the plasma PICs and the number of previous depressive episodes. Neopterin and TNFα were associated with melancholia, while both PICs were associated with CF. Melancholia-group membership was predicted by the HDRS and neopterin, and CF group membership by age, the FF score and serum TNFα. DISCUSSION: Depression and melancholia are accompanied by CMI activation, suggesting that neopterin plays a role in their pathophysiology, e.g. through activation of oxidative and nitrosative stress and apoptosis pathways. The intertwined CMI and inflammatory responses are potentially associated with the onset of depression and with the melancholic and CF symptoms of depression. Exposure to previous depressive episodes may magnify the size of CMI and PIC responses, possibly increasing the likelihood of new depressive episodes. CMI activation and inflammation may contribute to the staging or recurrence of depression. Copyright © 2011 Elsevier Inc. All rights reserved.
Maes M, Twisk FN, Kubera M, Ringel K.	Maes Clinics @ TRIA, Bangkok, Thailand.	Evidence for inflammation and activation of cell-mediated immunity in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): Increased interleukin-1, tumor necrosis factor-α, PMN-elastase, lysozyme and neopterin.	J Affect Disord. 2011 Oct 3. [Epub ahead of print]	BACKGROUND: There is evidence that inflammatory pathways and cell-mediated immunity (CMI) play an important role in the pathophysiology of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Activation of inflammatory and CMI pathways, including increased levels of cytokines, is known to induce fatigue and somatic symptoms. Given the broad spectrum inflammatory state in ME/CFS, the aim of this study was to examine whether inflammatory and CMI biomarkers are increased in individuals with ME/CFS. METHODS: In this study we therefore measured plasma interleukin-(IL)1, tumor necrosis factor (TNF)α, and PMN-elastase, and serum neopterin and lysozyme in 107 patients with ME/CFS, 37 patients with chronic fatigue (CF), and 20 normal controls. The severity of ME/CFS was measured with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Serum IL-1, TNFα, neopterin and lysozyme are significantly higher in patients with ME/CFS than in controls and CF patients. Plasma PMN-elastase is significantly higher in patients with ME/CFS than in controls and CF patients and higher in the latter than in controls. Increased IL-1 and TNFα are significantly correlated with fatigue, sadness, autonomic symptoms, and a flu-like malaise; neopterin is correlated with fatigue, autonomic symptoms, and a flu-like malaise; and increased PMN-elastase is correlated with concentration difficulties, failing memory and a subjective experience of infection. CONCLUSIONS: The findings show that ME/CFS is characterized by low-grade inflammation and activation of CMI. The results suggest that characteristic symptoms of ME/CFS, such as fatigue, autonomic symptoms and a flu-like malaise, may be caused by inflammatory mediators, e.g. IL-1 and TNFα. Copyright © 2011 Elsevier B.V. All rights reserved.
Maes M, Twisk FN,	Maes Clinics @	Increased IgA	J Affect Disord. 2011	BACKGROUND: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is

Kubera M, Ringel K, Leunis JC, Geffard M.	TRIA, Bangkok, Thailand.	responses to the LPS of commensal bacteria is associated with inflammation and activation of cell-mediated immunity in chronic fatigue syndrome.	Oct 1. [Epub ahead of print]	accompanied by a) systemic IgA/IgM responses against the lipopolysaccharides (LPS) of commensal bacteria; b) inflammation, e.g. increased plasma interleukin-(IL)1 and tumor necrosis factor (TNF)α; and c) activation of cell-mediated immunity (CMI), as demonstrated by increased neopterin. METHODS: To study the relationships between the IgA/IgM responses to the LPS of microbiota, inflammation, CMI and the symptoms of ME/CFS we measured the IgA/IgM responses to the LPS of 6 different enterobacteria, serum IL-1, TNFα, neopterin, and elastase in 128 patients with ME/CFS and chronic fatigue (CF). Severity of symptoms was assessed by the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Serum IL-1, TNFα, neopterin and elastase are significantly higher in patients with ME/CFS than in CF patients. There are significant and positive associations between the IgA responses to LPS and serum IL-1, TNFα, neopterin and elastase. Patients with an abnormally high IgA response show increased serum IL-1, TNFα and neopterin levels, and higher ratings on irritable bowel syndrome (IBS) than subjects with a normal IgA response. Serum IL-1, TNFα and neopterin are significantly related to fatigue, a flu-like malaise, autonomic symptoms, neurocognitive disorders, sadness and irritability. CONCLUSIONS: The findings show that increased IgA responses to commensal bacteria in ME/CFS are associated with inflammation and CMI activation, which are associated with symptom severity. It is concluded that increased translocation of commensal bacteria may be responsible for the disease activity in some ME/CFS patients. Copyright © 2011 Elsevier B.V. All rights reserved.
Maes M, Ringel K, Kubera M, Berk M, Rybakowski J.	Maes Clinics @ TRIA, Bangkok, Thailand.	Increased autoimmune activity against 5-HT: A key component of depression that is associated with inflammation and activation of cell-mediated immunity, and with severity and staging of depression.	J Affect Disord. 2011 Dec 12. [Epub ahead of print]	BACKGROUND: Depression is characterized by inflammation and cell-mediated immune (CMI) activation and autoimmune reactions directed against a multitude of self-epitopes. There is evidence that the inflammatory response in depression causes dysfunctions in the metabolism of 5-HT, e.g. lowering the 5-HT precursor tryptophan, and upregulating 5-HT receptor mRNA. This study has been undertaken to examine autoimmune activity directed against 5-HT in relation to CMI activation and inflammation. METHODS: 5-HT antibodies were examined in major depressed patients (n=109) versus normal controls (n=35) in relation to serum neopterin and lysozyme, and plasma pro-inflammatory cytokines (PIC), i.e. interleukin-1 (IL-1) and tumor necrosis factor-α (TNFα). Severity of depression was assessed with the Hamilton Depression Rating Scale (HDRS) and severity of fatigue and somatic symptoms with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: The incidence of anti-5-HT antibody activity was significantly higher in depressed patients (54.1%), and in particular in those with melancholia (82.9%), than in controls (5.7%). Patients with positive 5-HT antibodies showed increased serum neopterin and lysozyme, and plasma TNFα and IL-1; higher scores on the HDRS and FF scales, and more somatic symptoms, including malaise and neurocognitive dysfunctions. There was a significant association between autoimmune activity to 5-HT and the number of previous depressive episodes. DISCUSSION: The autoimmune

				reactions directed against 5-HT might play a role in the pathophysiology of depression and the onset of severe depression. The strong association between autoimmune activity against 5-HT and inflammation/CMI activation is explained by multiple, reciprocal pathways between these factors. Exposure to previous depressive episodes increases the incidence of autoimmune activity directed against 5-HT, which in turn may increase the likelihood to develop new depressive episodes. These findings suggest that sensitization (kindling) and staging of depression are in part based on progressive autoimmune responses. Copyright © 2011 Elsevier B.V. All rights reserved.
Maes M, Mihaylova I, Kubera M, Leunis JC, Geffard M.	Maes Clinics @ TRIA, Bangkok, Thailand. dr.michaelmaes@hotmail.com	IgM-mediated autoimmune responses directed against multiple neoepitopes in depression: new pathways that underpin the inflammatory and neuroprogressive pathophysiology.	J Affect Disord. 2011 Dec;135(1-3):414-8. Epub 2011 Sep 17.	BACKGROUND: There is evidence that depression is accompanied by oxidative and nitrosative stress (O&NS), as indicated by increased free radical levels, lipid peroxidation, and lowered antioxidant levels. The aims of the present study are to examine whether depression is accompanied by autoimmune responses directed against a) neoepitopes that are formed following O&NS damage; and b) the major anchorage molecules, i.e. palmitic and myristic acids and S-farnesyl-L-cysteine. METHODS: We examined serum IgM antibodies to the conjugated fatty acids, palmitic and myristic acids; acetylcholine; S-farnesyl-L-cysteine; and NO-modified adducts in 26 depressed patients and 17 normal controls. Severity of depression was measured with the Hamilton Depression Rating Scale and severity of fatigue and somatic (F&S) symptoms with the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: The prevalences and mean values for the serum IgM levels directed against conjugated palmitic and myristic acids, acetylcholine, S-farnesyl-L-cysteine; and the conjugated NO adducts, NO-tyrosine, NO-phenylalanine, NO-aspartate, NO-histidine, and NO-creatine were significantly higher in depressed patients than in normal controls. The autoimmune responses were significantly related to FF symptoms, such as fatigue and a flu-like malaise, whereas the indicants of nitrosative stress were related to gastro-intestinal and autonomic symptoms. DISCUSSION: Depression is characterized by IgM-related autoimmune responses directed against a) neoepitopes that are normally not detected by the immune system but that due to damage by O&NS have become immunogenic; and b) anchorage epitopes, i.e. palmitic and myristic acids, and S-farnesyl-L-cysteine. These autoimmune responses play a role in the inflammatory and O&NS pathophysiology of depression and may mediate the cellular dysfunctions that contribute to neuroprogression, e.g. aberrations in signal transduction, cellular differentiation and apoptosis. Copyright © 2011 Elsevier B.V. All rights reserved.
Maes M.	Maes Clinics @ TRIA, 998 Rimklongsamsen Road, Bangkok 10310, Thailand.	An intriguing and hitherto unexplained co-occurrence: Depression and chronic fatigue	Prog Neuropsychopharmacol Biol Psychiatry. 2011 Apr 29;35(3):784-94. Epub 2010 Jul 4.	There is a significant 'comorbidity' between depression and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Depressive symptoms frequently occur during the course of ME/CFS. Fatigue and somatic symptoms (F&S), like pain, muscle tension, and a flu-like malaise, are key components of depression. At the same time, depression and ME/CFS show major clinical differences, which allow

	dr.michaelmaes@hotmail.com	syndrome are manifestations of shared inflammatory, oxidative and nitrosative (IO&NS) pathways.		to discriminate them with a 100% accuracy. This paper aims to review the shared pathways that underpin both disorders and the pathways that discriminate them. Numerous studies have shown that depression and ME/CFS are characterized by shared aberrations in inflammatory, oxidative and nitrosative (IO&NS) pathways, like systemic inflammation and its long-term sequels, including O&NS-induced damage to fatty acids, proteins and DNA; dysfunctional mitochondria; lowered antioxidant levels, like zinc and coenzyme Q10; autoimmune responses to neoepitopes formed by O&NS; lowered omega-3 polyunsaturated fatty acid levels; and increased translocation of gram-negative bacteria. Some IO&NS-related pathways, like the induction of indoleamine 2-3-dioxygenase, neurodegeneration and decreased neurogenesis, are more specific to depression, whereas other pathways, like the 2'-5' oligoadenylate synthetase/RNase L pathway, are specific to ME/CFS. Most current animal models of depression, e.g. those induced by cytokines, are not reminiscent of human depression but reflect a mixture of depressive and F&S symptoms. The latter symptoms, sometimes called sickness behavior, differ from depression and ME/CFS because the former is a (sub)acute response to infection-induced pro-inflammatory cytokines that aims to enhance recovery, whereas the latter are characterized by long-term sequels in multiple IO&NS pathways. Depression and ME/CFS are not 'comorbid' disorders, but should be regarded as 'co-associated disorders' that are clinical manifestations of shared pathways. Copyright © 2010 Elsevier Inc. All rights reserved.
Maes M, Kubera M, Uytterhoeven M, Vrydags N, Bosmans E.	Maes Clinics@TRIA, Bangkok, Thailand. dr.michaelmaes@hotmail.com	Increased plasma peroxides as a marker of oxidative stress in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).	Med Sci Monit. 2011 Apr;17(4):SC11-5.	BACKGROUND: There is evidence that myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is characterized by activation of immune, inflammatory, oxidative and nitrosative stress (IO&NS) pathways. The present study was carried out in order to examine whether ME/CFS is accompanied by increased levels of plasma peroxides and serum oxidized LDL (oxLDL) antibodies, two biomarkers of oxidative stress. MATERIAL/METHODS: Blood was collected from 56 patients with ME/CFS and 37 normal volunteers. Severity of ME/CFS was measured using the Fibromyalgia and Chronic Fatigue Syndrome (FF) Rating Scale. RESULTS: Plasma peroxide concentrations were significantly higher in patients with ME/CFS than in normal controls. There was a trend towards significantly higher serum oxLDL antibodies in ME/CFS than in controls. Both biomarkers contributed significantly in discriminating between patients with ME/CFS and normal controls. Plasma peroxide and serum oxLDL antibody levels were both significantly related to one of the FF symptoms. CONCLUSIONS: The results show that ME/CFS is characterized by increased oxidative stress.
Maes M, Mihaylova I, Kubera M, Uytterhoeven M, Vrydags N,	Piyavate Hospital, Bangkok, Thailand, Thailand. dr.michaelmaes@	Lower whole blood glutathione peroxidase (GPX) activity in depression, but not	Neuro Endocrinol Lett. 2011;32(2):133-40.	BAKGROUND: Major depression and myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) are two disorders accompanied by an upregulation of the inflammatory and oxidative and nitrosative (IO&NS) pathways and a decreased antioxidant status. Moreover, depression is accompanied by disorders in inflammatory and neuroprogressive (IN-PRO) pathways.METHODS: This study

Bosmans E.	hotmail.com	in myalgic encephalomyelitis / chronic fatigue syndrome: another pathway that may be associated with coronary artery disease and neuroprogression in depression.		examines whole blood glutathione peroxidase (GPX) in depression and in ME/CFS; GPX is an enzyme that reduces hydroperoxides by oxidizing glutathione and consequently protects the cells from oxidative damage. Blood was sampled in 39 patients with depression, 40 patients with ME/CFS and 24 normal volunteers. Whole blood was analysed for GPX activity using the Ransel assay (Randox). Severity of illness was measured by means of the Hamilton Depression Rating Scale (HDRS) and the Fibromyalgia and Chronic Fatigue Syndrome Rating Scale (FF scale). RESULTS: We found that whole blood GPX activity was significantly (p=0.001) lower in depressed patients than in normal controls and that there were no significant differences between ME/CFS and controls. In depression and ME/CFS, there were significant and inverse relationships between GPX activity and the FF items, depressed mood and autonomic symptoms. In depression, there were significant and negative correlations between whole blood GPX and the HDRS score and autonomic symptoms. DISCUSSION: The results show that lowered whole blood GPX activity contributes to the lowered antioxidant status in depression. Since GPX activity is a predictor of neuroprogression and coronary artery disease (CAD), lowered GPX activity in depression contributes to the IN-PRO pathways and the comorbidity between depression and CAD. Our results suggest that patients with depression would benefit from Ebselen or a supplementation with glutathione, N-Acetyl-l-Cysteine and selenium.
Maes M, Kubera M, Obuchowiczwa E, Goehler L, Brzeszcz J.	Maes Clinics @ TRIA, Bangkok, Thailand, Thailand.	Depression's multiple comorbidities explained by (neuro)inflammatory and oxidative & nitrosative stress pathways.	Neuro Endocrinol Lett. 2011;32(1):7-24.	There is now evidence that depression, as characterized by melancholic symptoms, anxiety, and fatigue and somatic (F&S) symptoms, is the clinical expression of peripheral cell-mediated activation, inflammation and induction of oxidative and nitrosative stress (IO&NS) pathways and of central microglial activation, decreased neurogenesis and increased apoptosis. This review gives an explanation for the multiple "co-morbidities" between depression and a large variety of a) brain disorders related to neurodegeneration, e.g. Alzheimer's, Parkinson's and Huntington's disease, multiple sclerosis and stroke; b) medical disorders, such as cardiovascular disorder, chronic fatigue syndrome, chronic obstructive pulmonary disease, rheumatoid arthritis, psoriasis, systemic lupus erythematosus, inflammatory bowel disease, irritable bowel syndrome, leaky gut, diabetes type 1 and 2, obesity and the metabolic syndrome, and HIV infection; and c) conditions, such as hemodialysis, interferon-α-based immunotherapy, the postnatal period and psychosocial stressors. The common denominator of all those disorders/conditions is the presence of microglial activation and/or activation of peripheral IO&NS pathways. There is evidence that shared peripheral and / or central IO&NS pathways underpin the pathophysiology of depression and the previously mentioned disorders and that activation of these IO&NS pathways contributes to shared risk. The IO&NS pathways function as a smoke sensor that detect threats in the peripheral and central parts of the body and signal these threats as melancholic, anxiety, and fatigue and somatic (F&S) symptoms. The

				presence of concomitant depression is strongly associated with a lower quality of life and increased morbidity and mortality in medical disorders. This may be explained since depression contributes to increased (neuro)inflammatory burden and may therefore drive the inflammatory and degenerative progression. It is concluded that the activation of peripheral and / or central IO&NS pathways may explain the co-occurrence of depression with the above disorders. This shows that depression belongs to the spectrum of inflammatory and degenerative disorders.
Maggi F, Focosi D, Lanini L, Sbranti S, Mazzetti P, Macera L, Davini S, De Donno M, Mariotti ML, Antonelli G, Scatena F, Pistello M.	Virology Unit, Pisa University Hospital U.O. Immunoematologia SSN, Azienda Ospedaliera Universitaria Pisana, Pisa Laboratory of Virology, Department of Molecular Medicine, 'Sapienza' University of Rome, Rome Retrovirus Centre and Virology Section, Department of Experimental Pathology, University of Pisa, Pisa, Italy.	Xenotropic murine leukaemia virus-related virus is not found in peripheral blood cells from treatment-naive human immunodeficiency virus-positive patients.	Clin Microbiol Infect. 2012 Feb;18(2):184-8. doi: 10.1111/j.1469-0691.2011.03580.x. Epub 2011 Jun 14.	Clin Microbiol Infect 2012; 18: 184-188 ABSTRACT: The human pathogen xenotropic murine leukaemia virus-related virus (XMRV) has been tentatively associated with prostate cancer and chronic fatigue syndrome. Unfortunately, subsequent studies failed to identify the virus in various clinical settings. To determine whether XMRV circulates in humans and the relationship with its host, we searched for the virus in 124 human immunodeficiency virus-infected patients who might have been exposed to XMRV, might be prone to infection as a result of progressive immunodeficiency, and had not yet been treated with antiretroviral drugs. Using nested PCR and single-step TaqMan real-time PCR, both designed on the XMRV gag gene, we could not find any positive samples. These findings add to the growing amount of scepticism regarding XMRV. © 2011 The Authors. Clinical Microbiology and Infection © 2011 European Society of Clinical Microbiology and Infectious Diseases.
Magiorkinis G.		Mouse viruses and human disease.	Lancet Infect Dis. 2011 Apr;11(4):264.	
Mahdi AA, Fatima G, Das SK, Verma NS.	Department of Biochemistry, C.S.M. Medical University U.P, Lucknow, 226 003, India. mahdiaa@rediffm	Abnormality of circadian rhythm of serum melatonin and other biochemical parameters in fibromyalgia syndrome.	Indian J Biochem Biophys. 2011 Apr;48(2):82-7.	Fibromyalgia syndrome (FMS) is a complex chronic condition causing widespread pain and variety of other symptoms. It produces pain in the soft tissues located around joints throughout the body. FMS has unknown etiology and its pathophysiology is not fully understood. However, abnormality in circadian rhythm of hormonal profiles and cytokines has been observed in this disorder. Moreover, there are reports of deficiency of serotonin, melatonin, cortisol and cytokines in FMS patients, which are fully regulated by circadian rhythm. Melatonin, the primary hormone of the pineal

	ail.com			gland regulates the body's circadian rhythm and normally its levels begin to rise in the mid-to-late evening, remain high for most of the night, and then decrease in the early morning. FMS patients have lower melatonin secretion during the hours of darkness than the healthy subjects. This may contribute to impaired sleep at night, fatigue during the day and changed pain perception. Studies have shown blunting of normal diurnal cortisol rhythm, with elevated evening serum cortisol level in patients with FMS. Thus, due to perturbed level of cortisol secretion several symptoms of FMS may occur. Moreover, disturbed cytokine levels have also been reported in FMS patients. Therefore, circadian rhythm can be an important factor in the pathophysiology, diagnosis and treatment of FMS. This article explores the circadian pattern of abnormalities in FMS patients, as this may help in better understanding the role of variation in symptoms of FMS and its possible relationship with circadian variations of melatonin, cortisol, cytokines and serotonin levels.
Maher-Edwards L, Fernie BA, Murphy G, Nikcevic AV, Spada MM.	Fatigue Service, Royal Free Hospital, London, UK.	Metacognitive Factors in Chronic Fatigue Syndrome.	Clin Psychol Psychother. 2011 May 12. doi: 10.1002/cpp.757. [Epub ahead of print]	Chronic fatigue syndrome (CFS), which is characterized by fatigue and flu-like symptoms that are not alleviated by rest, is a poorly understood condition and an often controversial diagnosis. Earlier research has indicated that general metacognitions are associated with the severity of symptoms in patients with CFS. In the current study, we aimed to determine whether specific metacognitive factors are implicated in CFS. Using the metacognitive profiling interview template we investigated the following: (1) whether patients held positive or negative metacognitions about conceptual processes; (2) what their goals with respect to engaging in these processes were; and (3) what indicated that it was appropriate to stop. We also examined attention focus when experiencing CFS symptoms, and its advantages and disadvantages. Results showed that patients endorsed positive and negative metacognitions pertaining to conceptual processes. The goals of engaging in these processes were to identify the cause of, and devise strategies to cope with, symptoms. Patients were either unable to identify a stop signal for conceptual processing or identified an improvement in fatigue-related symptoms as representing the stop signal. Finally, patients reported that their attention focus when experiencing symptoms included distraction and monitoring of symptoms. Advantages to these strategies included symptom management, whereas disadvantages included an escalation of negative affect. The present findings provide preliminary evidence that specific metacognitive factors may be involved in CFS. Copyright © 2011 John Wiley & Sons, Ltd. KEY PRACTITIONER MESSAGE: Metacognitive profiling that may aid assessment and conceptualisation of psychological distress in CFS. Copyright © 2011 John Wiley & Sons, Ltd.
Maher-Edwards L, Fernie BA, Murphy G, Wells A, Spada MM.	Fatigue Service, Royal Free Hospital, London, UK.	Metacognitions and negative emotions as predictors of symptom severity in	J Psychosom Res. 2011 Apr;70(4):311-7. Epub 2010 Nov 18.	OBJECTIVE: Chronic fatigue syndrome (CFS) describes a condition that is primarily characterized by fatigue and flu-like symptoms that are not alleviated by rest. This study investigated the relationship among metacognitions, negative emotions, and symptom severity in CFS. METHODS: A total of 96 patients who had received a

		chronic fatigue syndrome.		diagnosis of CFS according to the Oxford Criteria completed a battery of self-report measures that consisted of the Depression Anxiety Stress Scales, the 30-Item Metacognitions Questionnaire, the Chalder Fatigue Questionnaire (CFQ), and the RAND 36-Item Short-Form Health Survey-Physical Functioning. RESULTS: Correlation analyses showed that negative emotions and metacognitions were positively correlated with measures of symptom severity and that metacognitions were a better predictor of symptom severity than anxiety and depression. Hierarchical regression analyses indicated that (1) lack of cognitive confidence predicted both mental and physical factors of the CFQ and physical functioning independently of negative emotions and (2) beliefs about the need to control thoughts predicted the mental factor of the CFQ independently of negative emotions and lack of cognitive confidence. CONCLUSION: The data support the potential application of the metacognitive model of psychological disorder to understanding CFS. Copyright © 2011 Elsevier Inc. All rights reserved.
Makarova N, Zhao C, Zhang Y, Bhosle S, Suppiah S, Rhea JM, Kozyr N, Arnold RS, Ly H, Molinaro RJ, Parslow TG, Hunter E, Liotta D, Petros J, Blackwell JL.	Emory Vaccine Center, Emory University, Atlanta, Georgia, United States of America.	Antibody responses against xenotropic murine leukemia virus-related virus envelope in a murine model.	PLoS One. 2011 Apr 6;6(4):e18272. Erratum in PLoS One. 2011;6(5). doi:10.1371/annotation/913fdc1e-877e-4c70-ac20-761d2d72400d.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) was recently discovered to be the first human gammaretrovirus that is associated with chronic fatigue syndrome and prostate cancer (PC). Although a mechanism for XMRV carcinogenesis is yet to be established, this virus belongs to the family of gammaretroviruses well known for their ability to induce cancer in the infected hosts. Since its original identification XMRV has been detected in several independent investigations; however, at this time significant controversy remains regarding reports of XMRV detection/prevalence in other cohorts and cell type/tissue distribution. The potential risk of human infection, coupled with the lack of knowledge about the basic biology of XMRV, warrants further research, including investigation of adaptive immune responses. To study immunogenicity in vivo, we vaccinated mice with a combination of recombinant vectors expressing codon-optimized sequences of XMRV gag and env genes and virus-like particles (VLP) that had the size and morphology of live infectious XMRV. RESULTS: Immunization elicited Env-specific binding and neutralizing antibodies (NAb) against XMRV in mice. The peak titers for ELISA-binding antibodies and NAb were 1:1024 and 1:464, respectively; however, high ELISA-binding and NAb titers were not sustained and persisted for less than three weeks after immunizations. CONCLUSIONS: Vaccine-induced XMRV Env antibody titers were transiently high, but their duration was short. The relatively rapid diminution in antibody levels may in part explain the differing prevalences reported for XMRV in various prostate cancer and chronic fatigue syndrome cohorts. The low level of immunogenicity observed in the present study may be characteristic of a natural XMRV infection in humans.
Manson AL, Chapman N, Wedatilake Y, Balic	Department of Clinical Immunology, St	Tired with all those supplements?	QJM. 2011 Jun;104(6):531-4. Epub 2010 Aug 13.	

M, Marway H, Seneviratne SL, Holloway P.	Mary's Hospital, Imperial College Healthcare NHS Trust, London W2 1PG, UK. ania.manson@imperial.nhs.uk			
Mariman A, Vogelaers D, Hanoulle I, Delesie L, Tobback E, Pevernagie D.		Validation of the three-factor model of the PSQI in a large sample of chronic fatigue syndrome (CFS) patients.	J Psychosom Res. 2012 Feb;72(2):111-3. Epub 2011 Dec 22.	OBJECTIVE: To evaluate whether a 3-factor model of the Pittsburgh Sleep Quality Index (PSQI) scale would fit the constellation of sleep disturbances in patients with a diagnosis of chronic fatigue syndrome (CFS). METHODS: Consecutive CFS patients filled out the PSQI. Scores from this self-report questionnaire were examined with exploratory and confirmatory factor analysis (CFA). RESULTS: 413 CFS patients were included for analysis in this study. CFA showed that the 7 PSQI component scores clustered into the 3 factors reported by Cole et al. (2006), i.e. Sleep Efficiency, Perceived Sleep Quality and Daily Disturbances. In contrast with the single-factor and all 2-factor models, all factor loadings were significant, and all goodness-of-fit values were acceptable. CONCLUSION: In CFS, the PSQI operates as a 3-factor scoring model as initially seen in healthy and depressed older adults. The separation into 3 discrete factors suggests the limited usefulness of the global PSQI as a single factor for the assessment of subjective sleep quality, as also evidenced by a low Cronbach's alpha (0.64) in this patient sample. Copyright © 2011 Elsevier Inc. All rights reserved.
Markeljević J, Sarac H, Rados M.	University of Zagreb, School of Medicine, Zagreb University Hospital Centre, Department of Internal Medicine, Zagreb, Croatia. Jasenka-markeljevic@gmail.com	Tremor, seizures and psychosis as presenting symptoms in a patient with chronic lyme neuroborreliosis (LNB).	Coll Antropol. 2011 Jan;35 Suppl 1:313-8.	Lyme borreliosis is a multisystem disorder caused by Borrelia burgdorferi (Bb). Neurological symptoms such as lymphocytic meningoradiculoneuritis (Bannwart's syndrome), cranial neuritis (II,III,IV,V,VI), encephalitis, transverse myelitis are found in about 10% of cases during the second phase of the disease. In the chronic stage, many months or years after the initial infection, other neurologic complications may occur, such as encephalomyelitis, epileptic crises, cognitive impairment, peripheral neuropathy and psychiatric disturbances such as depression, anxiety, panicc attacks, catatonia, psychosis etc. Some patient continue to experience symptoms of fatigue, insomnia or psychiatric disorder in the post borrelia syndrome. We describe here a patient with a triad of unusual symptoms in chronic LNB including tremor, seizures and psychosis. Standardized medical interview, neurologic examination, neuroimaging, serum and CSF serology as well as EEG and EMNG evaluation were performed. The patient was treated with intravenous ceftriaxone and doxycycline and responded with rapid clinical and functional improvement.Newertheless, he suffered from multiple systemic and neurologic sequelas that influenced his daily activities in post treatment period. Emphasis is placed on the atypical onset and evolution, the difficulties encountered in formulating diagnosis, early treatment and the uncertainties concerning the sequelae after treatment. In patients with non-specific long lasting symptoms in the absence of overt clinical signs suggesting CNS

				involvement, routine treatment with i.v. ceftriaxone is not to be encouraged.
Marshall R, Paul L, Wood L.	Nursing & Health Care, Faculty of Medicine, University of Glasgow, Glasgow, Scotland, UK. r.marshall@clinmed.gla.ac.uk	The search for pain relief in people with chronic fatigue syndrome: a descriptive study.	Physiother Theory Pract. 2011 Jul;27(5):373-83. Epub 2010 Nov 1.	The purpose of this study was to investigate the use and perceived benefit of complimentary and alternative medicine (CAM) and physiotherapy treatments tried by people with chronic fatigue syndrome (CFS) to ease painful symptoms. This study used a descriptive, cross-sectional design. People with CFS who experienced pain were recruited to this study. Participants were asked during a semistructured interview about the treatments they had tried to relieve their pain. Each interview was conducted in the home of the participant. Fifty participants were recruited, of which, 10 participants were severely disabled by CFS. Eighteen participants were trying different forms of CAM treatment for pain relief at the time of assessment. Three participants were currently receiving physiotherapy. Throughout the duration of their illness 45 participants reported trying 19 different CAM treatments in the search for pain relief. Acupuncture was reported to provide the most pain relief (n=16). Twenty-seven participants reported a total of 16 different interventions prescribed by their physiotherapist. The results of this study suggest some physiotherapy and CAM treatments may help people manage painful CFS symptoms. Future research should be directed to evaluating the effectiveness of interventions such as acupuncture or gentle soft tissue therapies to reduce pain in people with CFS.
Masquelier E, Scaillet N, Luminet O, Desmet A, Grisart J.	Centre de Référence Multidisciplinaire de la Douleur Chronique UCL Mont-Godinne, Belgique. etienne.masquelier@uclouvain.be	[What's about overactive lifestyle in fibromyalgia and chronic fatigue syndrome]. [Article in French]	Rev Med Suisse. 2011 Jun 29;7(301):1421-2, 1424-5.	Fibromyalgia and chronic fatigue syndrome are clinical conditions different but they share common components, particularly multifactorial aetiology. High level of action proneness and "overactive" lifestyle can be considered as predisposing risk factors and perpetuating factors for these somatic functional syndromes. For the clinicians managing complex situations, only a holistic, circular and biopsychosocial approach could restore a new equilibrium (allostasis) with strategies of coping with chronic pain and planification of activities.
McCarberg BH.		Clinical Overview of Fibromyalgia.	Am J Ther. 2011 Feb 15. [Epub ahead of print]	Fibromyalgia (FM) is a complex disorder that affects up to 5% of the general population worldwide, more frequently in women than in men. In addition to chronic widespread pain, patients with FM usually experience other characteristic symptoms, including fatigue, disturbed sleep, stiffness, reduced functioning, dyscognition, and depressed mood. Many patients also have comorbid conditions such as depression, irritable bowel syndrome, temporomandibular disorder, or migraine. Although the etiology of FM remains unclear, evidence suggests that biologic, genetic, and environmental factors are involved. The variability of symptoms and the frequency of comorbidities among patients with FM make this a difficult disorder to diagnose. Diagnosis may be further complicated by the stigmatization of this disorder among treatment providers, the health insurance industry, and the general population. Treating chronic pain disorders such as FM can be time consuming and costly, and other issues such as polypharmacy, treatment adherence, and access to treatment

				often need to be addressed. The aim of this article is to provide physicians with a general overview of FM, including a brief review of the pathophysiology that explains the biologic and genetic bases of this disorder. Also included is a synopsis of new diagnostic criteria and other useful diagnostic tools and a discussion of various treatment challenges and strategies.
McDermott C, Lynch J, Leydon GM.	Primary Medical Care Research Department, University of Southampton, Southampton, UK. crm20@soton.ac.uk	Patients' hopes and expectations of a specialist chronic fatigue syndrome/ME service: a qualitative study.	Fam Pract. 2011 Oct;28(5):572-8. Epub 2011 May 9.	BACKGROUND: The 2007 National Institute for Health and Clinical Excellence guidelines on Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) recommend early management of the condition. Investment by the Department of Health has expanded the number of specialist U.K. CFS/ME services but there has been little research on what patients hope or expect from referral. METHODS: A qualitative study exploring hopes and expectations of patients newly referred to a CFS/ME Service in the South of England. Interviews with 20 patients were analysed using the constant comparative method. RESULTS: Participants hoped referral to a specialist service would clarify diagnosis, give guidance and support, assist in understanding the complexity of the illness and provide hope for the future. While many participants valued the support of their GP, all viewed referral as offering a level of specialist expertise beyond that available in primary care. Many participants expressed high levels of uncertainty about the nature of CFS/ME. While participants hoped that the service would be able to provide information and guidance, many expressed the view that more information earlier in their illness would make the waiting period less stressful and make it possible for them to do more to help themselves. CONCLUSIONS: GP referral to a specialist service appeared to be highly valued by the participants in this study. The levels of uncertainty expressed by many patients about the nature of CFS/ME raises the issue of the role of information on CFS/ME during the early stages of the illness and suggests a need for more reassurance and positive advice during the waiting period.
McGough A.	South Tees Hospitals Foundation Trust.	How to care for patients with chronic fatigue syndrome/ME.	Nurs Times. 2011 Oct 11-17;107(40):16.	
McMahon L, Murray C, Simpson J.	Tees Time to Talk IAPT Service , Middlesbrough , UK.	The potential benefits of applying a narrative analytic approach for understanding the experience of fibromyalgia: a review.	Disabil Rehabil. 2011 Nov 11. [Epub ahead of print]	Purpose: People with fibromyalgia (FM), a medically unexplained illness, habitually experience widespread pain and fatigue. While some qualitative research has aimed to understand the experiences of people with FM, studies from a specific narrative perspective are particularly lacking. This review argues that future research could be significantly enhanced by studies which analyse the narratives of people with FM. Method: This argument is made through reference to an examination of the extant qualitative literature on the experience of FM and theories and narrative studies on chronic illnesses and identity. Results: The empirical literature is reviewed from a narrative perspective; this assumes that the stories people tell reveal much about their identities and social worlds. As such, it is proposed that narrative analysis is

				particularly well suited for exploring issues of self and culture and for appreciating how meanings evolve over time. Further, it is also argued that consideration of these issues is particularly relevant for understanding the experience of FM given the enigmatic nature of the syndrome and its chronic course. Conclusions: The review concludes by emphasizing that narrative analysis is a valuable method which offers the potential for uncovering novel insights about the illness experience for these individuals. [Box: see text].
Meeus M, Ickmans K, De Clerck LS, Moorkens G, Hans G, Grosemans S, Nijs J.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Building L-Mfys, Pleinlaan 2, 1050 Brussels, Belgium. Mira.Meeus@vub.ac.be	Serotonergic descending inhibition in chronic pain: design, preliminary results and early cessation of a randomized controlled trial.	In Vivo. 2011 Nov-Dec;25(6):1019-25.	AIM: We examined whether activation of serotonergic descending pathways improves pain inhibition during exercise in patients with chronic fatigue syndrome (CFS) and comorbid fibromyalgia (FM) in comparison with rheumatoid arthritis (RA) and sedentary, healthy controls in a double-blind randomized controlled trial with cross-over design. PATIENTS AND METHODS: Three female CFS/FM patients, one female RA patient and two healthy women were randomly allocated to the experimental group (2 ml of citalopram intravenously) or the placebo group (2 ml of 0.9% NaCl intravenously). Participants performed a submaximal exercise protocol, preceded and followed by an assessment of endogenous pain inhibition. Seven days later, groups were crossed over. RESULTS: Significant side-effects were observed in all, but one participant immediately after intravenous administration of citalopram. One CFS/FM patient withdrew because of severe post-exertional malaise. CONCLUSION: It was decided that proceeding with the study would be unethical. No conclusion could be made regarding pain inhibition during exercise in CFS/FM compared to RA and controls.
Meeus M, van Eupen I, van Baarle E, De Boeck V, Luyckx A, Kos D, Nijs J.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, Artesis University College Antwerp, Belgium.	Symptom fluctuations and daily physical activity in patients with chronic fatigue syndrome: a case-control study.	Arch Phys Med Rehabil. 2011 Nov;92(11):1820-6.	OBJECTIVES: To compare the activity pattern of patients with chronic fatigue syndrome (CFS) with healthy sedentary subjects and examine the relationship between the different parameters of performed activity (registered by an accelerometer device) and symptom severity and fluctuation (registered by questionnaires) in patients with CFS. DESIGN: Case-control study. Participants were asked to wear an accelerometer device on the nondominant hand for 6 consecutive days. Every morning, afternoon, and evening patients scored the intensity of their pain, fatigue, and concentration difficulties on a visual analog scale. SETTING: Patients were recruited from a specialized chronic fatigue clinic in the university hospital, where all subjects were invited for 2 appointments (for questionnaire and accelerometer adjustments). In between, activity data were collected in the subject's normal home environment. PARTICIPANTS: Female patients (n=67) with CFS and female age-matched healthy sedentary controls. INTERVENTIONS: Not applicable. MAIN OUTCOME MEASURES: Accelerometry (average activity counts, peak activity counts, ratio peak/average, minutes spent per activity category) and symptom severity (intensity of pain, fatigue, and concentration difficulties). RESULTS: Patients with CFS were less active, spent more time sedentary, and less time lightly active (P<.05). The course of the activity level during the registration period (P

				interaction>.05), peak activity, and the staggering of activities (ratio peak/average) on 1 day were not different between groups (P>.05). Negative correlations (-.242 varying to -.307) were observed for sedentary activity and the ratio with symptom severity and variation on the same and the next day. Light, moderate, and vigorous, as well as the average activity and the peak activity, were positively correlated (.242 varying to .421) with symptom severity and variation. CONCLUSIONS: The more patients with CFS are sedentary and the better activity is dispersed, the fewer symptoms and variations they experience on the same and next day. Inversely, more symptoms and variability is experienced when patients were more active that day or the previous day. The direction of these relations cannot be determined in a cross-sectional study and requires further study. Copyright © 2011 American Congress of Rehabilitation Medicine. Published by Elsevier Inc. All rights reserved.
Meeus M, Van Eupen I, Willems J, Kos D, Nijs J.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, Artesis University College Antwerp (AHA), Antwerp, Belgium.	Is the International Physical Activity Questionnaire-short form (IPAQ-SF) valid for assessing physical activity in Chronic Fatigue Syndrome?	Disabil Rehabil. 2011;33(1):9-16. Epub 2010 May 6.	PURPOSE: To evaluate the criterion validity and internal consistency of the International Physical Activity Questionnaire-short form (IPAQ-sf) in Chronic Fatigue Syndrome (CFS) patients. METHOD: Fifty-six CFS patients completed the IPAQ-sf after they wore a tri-axial accelerometer and filled out activity diaries during 1 week. Spearman rank correlation coefficients and Cronbach's Alpha were calculated. RESULTS: The IPAQ-sf correlated significantly with the energy expenditure and Metabolic Equivalents (METs) minutes spent moderately to vigorously active following the activity diary and accelerometer. These correlation coefficients were however low (r varying between 0.282 and 0.426) and rather irrelevant, since CFS patients hardly reach moderate or vigorous activity levels. Internal consistency between the three subitems used for the total score of the IPAQ-sf was 0.337. CONCLUSION: The observed associations between the IPAQ-sf data and the data obtained from the accelerometer (gold standard) and the diaries were too low to be in support of the use of the IPAQ-sf in patients with CFS. The IPAQ-sf does not seem an appropriate tool to assess physical activity in CFS patients. Further study is required to seek for a valid, practical and affordable tool.
Mendoza R, Vaughan AE, Miller AD.	Human Biology Division, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave. N., Seattle, WA 98109-1024, USA.	The left half of the XMRV retrovirus is present in an endogenous retrovirus of NIH/3T3 Swiss mouse cells.	J Virol. 2011 Sep;85(17):9247-8. Epub 2011 Jun 22.	Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus found in association with human prostate cancer and chronic fatigue syndrome, although these associations are controversial. XMRV shows at most 94% identity to known mouse retroviruses. Here we used XMRV-specific PCR to search for a more closely related source of XMRV in mice. While we could not find a complete copy, we did find a 3,600-bp region of XMRV in an endogenous retrovirus present in NIH/3T3 cells. These results show that XMRV has clear ancestors in mice and highlight another possible source of contamination in PCR assays for XMRV.
Menéndez-Arias L.	Consejo Superior de Investigaciones Científicas and	Evidence and controversies on the role of XMRV in prostate cancer and	Rev Med Virol. 2011 Jan;21(1):3-17. doi: 10.1002/rmv.673. Epub 2010 Nov 26.	The recent discovery of xenotropic murine leukaemia virus-related virus (XMRV) in prostate cancer tissues and in the blood of individuals suffering from chronic fatigue syndrome has attracted considerable interest. However, the relevance and significance of XMRV to human disease remain unclear, since the association has not

	Universidad Autónoma de Madrid, Madrid, Spain. lmenendez@cbm.uam.es	chronic fatigue syndrome.		been confirmed in other studies. XMRV is the first gammaretrovirus to be found in humans. XMRV and murine leukaemia viruses share similar structures and genomic organisation. Human restriction factors such as APOBEC3 or tetherin inhibit XMRV replication. Although XMRV induces low rates of transformation in cell culture, it might be able to induce cancer by low-frequency insertional activation of oncogenes or through the generation of highly active transforming viruses. A preference for regulatory regions of transcriptional active genes has been observed after a genomic-wide analysis of XMRV integration sites. Genes related to carcinogenesis and androgen signalling have been identified in the vicinity of integration sites. The XMRV genome contains a glucocorticoid responsive element, and androgens could modulate viral replication in the prostate. Evidence supporting the involvement of XMRV in chronic fatigue syndrome is still very weak, and needs further confirmation and validation. Currently approved anti-retroviral drugs such as zidovudine, tenofovir and raltegravir are efficient inhibitors of XMRV replication in vitro. These drugs might be useful to treat XMRV infection in humans. The identification of XMRV has potentially serious health implications for the implementation of novel techniques including gene therapy or xenotransplantation, while raising concerns on the need for screening donated blood to prevent transmission through transfusion. Copyright © 2010 John Wiley & Sons, Ltd.
Mets MA, Ketzer S, Blom C, van Gerven MH, van Willigenburg GM, Olivier B, Verster JC.	Division of Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht University, P.O. Box 80082, 3508 TB, Utrecht, The Netherlands.	Positive effects of Red Bull® Energy Drink on driving performance during prolonged driving.	Psychopharmacology (Berl). 2011 Apr;214(3):737-45. Epub 2010 Nov 10.	BACKGROUND: The purpose of this study was to examine if Red Bull® Energy Drink can counteract sleepiness and driving impairment during prolonged driving. METHODS: Twenty-four healthy volunteers participated in this double-blind placebo-controlled crossover study. After 2 h of highway driving in the STISIM driving simulator, subjects had a 15-min break and consumed Red Bull® Energy Drink (250 ml) or placebo (Red Bull® Energy Drink without the functional ingredients: caffeine, taurine, glucuronolactone, B vitamins (niacin, pantothenic acid, B6, B12), and inositol) before driving for two additional hours. A third condition comprised 4 h of uninterrupted driving. Primary parameter was the standard deviation of lateral position (SDLP), i.e., the weaving of the car. Secondary parameters included SD speed, subjective driving quality, sleepiness, and mental effort to perform the test. RESULTS: No significant differences were observed during the first 2 h of driving. Red Bull® Energy Drink significantly improved driving relative to placebo: SDLP was significantly reduced during the 3rd ($p < 0.046$) and 4th hour of driving ($p < 0.011$). Red Bull® Energy Drink significantly reduced the standard deviation of speed ($p < 0.004$), improved subjective driving quality ($p < 0.0001$), and reduced mental effort to perform the test ($p < 0.024$) during the 3rd hour of driving. Subjective sleepiness was significantly decreased during both the 3rd and 4th hour of driving after Red Bull® Energy Drink ($p < 0.001$ and $p < 0.009$, respectively). Relative to uninterrupted driving, Red Bull® Energy Drink significantly improved each parameter. CONCLUSION: Red Bull® Energy Drink significantly improves driving performance and reduces driver

				sleepiness during prolonged highway driving.
Mi Z, Lu Y, Zhang S, An X, Wang X, Chen B, Wang Q, Tong Y.	Beijing Institute of Microbiology and Epidemiology and Affiliated Hospital, Academy of Military Medical Sciences, Beijing, China. zhiqiangmi@yahoo.com.cn	Absence of xenotropic murine leukemia virus-related virus in blood donors in China.	Transfusion. 2012 Feb;52(2):326-31. doi: 10.1111/j.1537-2995.2011.03267.x. Epub 2011 Aug 19.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) is a novel human gammaretrovirus that was first identified in patients with prostate cancer in 2006. Subsequent studies have shown that XMRV is also detected in patients with chronic fatigue syndrome (CFS) and even in some healthy controls and blood donors. However, some conflicting findings have been reported by different laboratories or in different regions. The association of XMRV with human diseases and the prevalence of XMRV in different populations needs to be further determined. STUDY DESIGN AND METHODS: XMRV was screened in 391 blood samples from healthy blood donors in China. Nested reverse transcription-polymerase chain reaction (PCR) was used to amplify gag and env genes of XMRV from total RNA of peripheral blood mononuclear cells (PBMNCs) and plasma, respectively. Quantitative PCR was performed to detect XMRV env gene in genomic DNA of PBMNCs. To enhance the detection sensitivity, plasma was added into LNCaP cells to amplify XMRV in the plasma samples. RESULTS: No XMRV was found in the 391 blood donors in China or in the LNCaP cells inoculated with plasma from the blood donors. CONCLUSION: Both PCR and virus isolation in highly permissive LNCaP cells failed to detect XMRV in 391 Chinese blood donors, indicating that XMRV infection might not be present in blood donors in China. © 2012 American Association of Blood Banks.
Minetto MA, Lanfranco F, Botter A, Motta G, Mengozzi G, Giordano R, Picu A, Ghigo E, Arvat E.	Division of Endocrinology, Diabetology and Metabolism, Department of Internal Medicine, Molinette Hospital, University of Turin, C.so Dogliotti 14, 10126 Turin, Italy. marco.minetto@unito.it	Do muscle fiber conduction slowing and decreased levels of circulating muscle proteins represent sensitive markers of steroid myopathy? A pilot study in Cushing's disease.	Eur J Endocrinol. 2011 Jun;164(6):985-93. Epub 2011 Mar 14.	OBJECTIVE: Glucocorticoids are known to decrease protein synthesis and conduction velocity of muscle fibers. However, the degree of impairment of muscle protein synthesis and conduction slowing in patients with Cushing's disease remains poorly characterized. Our objective was to investigate whether and to what extent chronic endogenous hypercortisolism could decrease the circulating levels of muscle proteins and modify myoelectric indexes of sarcolemmal excitability and fatigability. DESIGN: A total of ten patients with Cushing's disease and 30 healthy controls matched for age, sex, and body mass index were compared. METHODS: Blood sampling and electrophysiological tests on vastus lateralis, vastus medialis, and tibialis anterior muscles were performed. RESULTS: Serum creatine kinase (CK) and plasma myoglobin were significantly lower in patients with respect to controls ($P<0.001$ and $P<0.05$ respectively): the mean relative difference between patients and controls was 48.9% for CK and 21.4% for myoglobin. Muscle fiber conduction velocity (MFCV) and myoelectric manifestations of fatigue were significantly decreased in all muscles of the patients with respect to controls. The mean relative difference in MFCV between patients and controls was 26.0% for vastus lateralis, 22.9% for vastus medialis, and 11.6% for tibialis anterior. These differences contrasted with the paucity of signs suggestive of myopathy that were obtained by needle electromyography in the patients. CONCLUSIONS: Slowing of muscle fiber conduction and decreased levels of circulating muscle proteins are sensitive markers of impaired muscle function, which are suitable for use in combination with clinical assessment and standard

				electrodiagnostic tests for accurate identification and follow-up of myopathic patients.
Missen A, Hollingworth W, Eaton N, Crawley E.	School of Social and Community Medicine, University of Bristol School of Health and Social Care, University of West of England, Bristol, UK.	The financial and psychological impacts on mothers of children with chronic fatigue syndrome (CFS/ME).	Child Care Health Dev. 2011 Sep 1. doi: 10.1111/j.1365-2214.2011.01298.x. [Epub ahead of print]	Background Paediatric chronic fatigue syndrome or myalgic encephalopathy (CFS/ME) is relatively common and children can be severely affected attending little or no school for extended periods. There are no studies quantifying the financial impact of having a child with CFS/ME and there is little information of the impact on parental mood. Methods Forty mothers of children with CFS/ME from a regional specialist CFS/ME service completed inventories to assess their psychological well-being (Hospital Anxiety and Depression Scale, General Health Questionnaire-12) loss of earnings and increased expenditure. In addition, eight mothers took part in a semi-structured qualitative interview. Results Most parents of children with CFS/ME experience loss of monthly income (mean =£247) and increase in monthly expenditure (mean =£206). Twenty-eight (72%) mothers were above the cut-off for the General Health Questionnaire-12 compared with 20% in the healthy population (95% CI 55, 85, P < 0.001) suggesting they probably have a mental health problem. This may be explained by the qualitative interviews where mothers described five areas contributing to poor parental health: lack of understanding from others; marital tension; concern about their child's distress; concern about the impact on siblings and emotional distress causing physical symptoms. Conclusions The majority of families of children with CFS/ME experience decreased income and increased expenditure with a marked impact on maternal psychological health. Clinicians need to be aware of this to provide appropriate support to families who care for children with CFS/ME. © 2011 Blackwell Publishing Ltd.
Mitchell JT Jr.		The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1831; author reply 1834-5. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5.	
Miwa K, Fujita M.		Is small heart syndrome a "heart" disease or low output syndrome?	Int J Cardiol. 2011 Jan 7;146(1):95-6. Epub 2010 Nov 12.	
Miwa K, Fujita M.	Department of Internal Medicine, Miwa	Small heart with low cardiac output for orthostatic	Clin Cardiol. 2011 Dec;34(12):782-6. doi: 10.1002/clc.20962.	BACKGROUND: The etiology of chronic fatigue syndrome (CFS) is unknown. Orthostatic intolerance (OI) is common in CFS patients. Recently, small heart with low cardiac output has been postulated to be related to the genesis of both CFS and OI.

	Naika Clinic, Toyama, Japan. info@miwa-naika.com	intolerance in patients with chronic fatigue syndrome.	Epub 2011 Nov 28.	HYPOTHESIS: Small heart is associated with OI in patients with CFS. METHODS: Study CFS patients were divided into groups of 26 (57%) CFSOI(+) and 20 (43%) CFSOI(-) according to the presence or absence of OI. In addition, 11 OI patients and 27 age- and sex-matched control subjects were studied. Left ventricular (LV) dimensions and function were determined echocardiographically. RESULTS: The mean values of cardiothoracic ratio, systemic systolic and diastolic pressures, LV end-diastolic dimension, LV end-systolic dimension, stroke volume index, cardiac index, and LV mass index were all significantly smaller in CFSOI(+) patients than in CFSOI(-) patients and healthy controls, and also in OI patients than in controls. A smaller LV end-diastolic dimension (<40 mm) was significantly (P<0.05) more prevalently noted in CFSOI(+) (54%) and OI (45%) than in CFSOI(-) (5%) and controls (4%). A lower cardiac index (<2 L/min/mm(2)) was more prevalent in CFSOI(+) (65%) than in CFSOI(-) (5%, P<0.01), OI (27%), and controls (11%, P<0.01). CONCLUSIONS: A small size of LV with low cardiac output was noted in OI, and its degree was more pronounced in CFSOI(+). A small heart appears to be related to the genesis of OI and CFS via both cerebral and systemic hypoperfusion. CFSOI(+) seems to constitute a well-defined and predominant subgroup of CFS. © 2011 Wiley Periodicals, Inc.
Moldofsky H, Patcai J.	Sleep Disorders Clinic of the Centre for Sleep and Chronobiology, 340 College St,, Suite 580, Toronto, ON M5T 3A9, Canada. h.moldofsky@utoronto.ca	Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study.	BMC Neurol. 2011 Mar 24;11:37.	BACKGROUND: The long term adverse effects of Severe Acute Respiratory Syndrome (SARS), a viral disease, are poorly understood. METHODS: Sleep physiology, somatic and mood symptoms of 22 Toronto subjects, 21 of whom were healthcare workers, (19 females, 3 males, mean age 46.29 yrs.+/- 11.02) who remained unable to return to their former occupation (mean 19.8 months, range: 13 to 36 months following SARS) were compared to 7 healthy female subjects. Because of their clinical similarities to patients with fibromyalgia syndrome (FMS) these post-SARS subjects were similarly compared to 21 drug free female patients, (mean age 42.4 +/- 11.8 yrs.) who fulfilled criteria for fibromyalgia. RESULTS: Chronic post-SARS is characterized by persistent fatigue, diffuse myalgia, weakness, depression, and nonrestorative sleep with associated REM-related apneas/hypopneas, an elevated sleep EEG cyclical alternating pattern, and alpha EEG sleep anomaly. Post- SARS patients had symptoms of pre and post-sleep fatigue and post sleep sleepiness that were similar to the symptoms of patients with FMS, and similar to symptoms of patients with chronic fatigue syndrome. Both post-SARS and FMS groups had sleep instability as indicated by the high sleep EEG cyclical alternating pattern rate. The post-SARS group had a lower rating of the alpha EEG sleep anomaly as compared to the FMS patients. The post-SARS group also reported less pre-sleep and post-sleep musculoskeletal pain symptoms. CONCLUSIONS: The clinical and sleep features of chronic post-SARS form a syndrome of chronic fatigue, pain, weakness, depression and sleep disturbance, which overlaps with the clinical and sleep features of FMS and chronic fatigue syndrome.
Morell-Dubois S,	Service de	[Complaints, needs	Rev Med Interne. 2011	PURPOSE: Systemic sclerosis (ScS) is very heterogeneous in its clinical presentation

Condette-Wojtasik G, Clerson P, Berezné A, Launay D, Lambert M, Maillard-Lefebvre H, Hatron PY, Hachulla E.	Médecine Interne, Centre de Référence des Maladies Auto-immunes et des Maladies Systémiques Rares, Sclérodermie Systémique, Hôpital Huriez, CHRU de Lille, rue Michel-Polonovski, 59037 Lille cedex, France. sandrine.morell@wanadoo.fr	of patients with systemic sclerosis: a better understanding for a better care]. [Article in French]	Sep;32(9):537-43. Epub 2011 Mar 9.	and its therapeutic care is not codified. A better knowledge of the patients' needs and complaints could improve the patient educational strategies and their global care. METHODS: A self-administered questionnaire aimed to the ScS patient was developed by subspecialty physicians and nurses involved in patient education. It was a cross-sectional study that also included several validated scales: the health control locus scale, the Mactar, HAD and sHAQ scales. RESULTS: One hundred and eight patients (91 women; 18 limited ScS, 71 limited cutaneous ScS, 19 diffuse ScS) filled in the questionnaires. Fatigue was the main complaint in all types of ScS, independently of the ScS type. The aesthetic discomfort mentioned by the patients suffering from cutaneous sclerosis or from telangectasia was important and reached 52±33mm on a 100-mm visual scale. It was more common in the patients presenting a diffuse form of the illness but the difference did not reach a statistical significance (P=0.06). Twenty-seven percent of the patients said they were very or extremely worried because of the degradation of their physical appearance. The functional discomfort linked to the cutaneous sclerosis was rated 50±32mm on a 100-mm visual scale. The intensity of the pain, the importance of the functional discomfort linked to the sclerosis and the intensity of the dyspnea were correlated to the sHAQ (P<0.001). Patients having more frequent recurrent digital ulcers had higher sHAQ scores (P=0.04). The repercussions on the professional life were linked to fatigue first, to the Raynaud's syndrome and to arthralgia. The repercussions on the personal life were mainly linked to the fatigue, the pain and the dyspnea. The patients' compliance was good. CONCLUSION: Fatigue, pain, dyspnea and discomfort linked to sclerosis are major chronic symptoms of the patients with ScS. Identifying the needs and complaints of the patients with ScS should help to improve their care by implementation of an educational program. Copyright © 2011 Société nationale française de médecine interne (SNFMI). Published by Elsevier SAS. All rights reserved.
Morelli V.	Department of Family and Community Medicine, Meharry Medical College, 1005 Dr. D.B. Todd Jr. Boulevard, Nashville, TN 37208, USA. vmorelli@mmc.edu	Fatigue and chronic fatigue in the elderly: definitions, diagnoses, and treatments.	Clin Geriatr Med. 2011 Nov;27(4):673-86.	Because fatigue is so prevalent in the elderly population, it is important that physicians be well versed in the evaluation and management of this complaint. This article discusses the clinical manifestations and predisposing factors for the three major categories of fatigue: recent, prolonged, and chronic. The CDC classification of chronic fatigue syndrome is included. Patient dissatisfaction with the care for their fatigue is a common problem. Several pharmaceutical treatment methods are presented. Non-pharmacologic options, such as use of vitamins, exercise, behavior modification,and diet are also discussed.
Moriya J, Chen R, Yamakawa J,	Department of General	Resveratrol improves hippocampal atrophy	Biol Pharm Bull. 2011 Mar;34(3):354-9.	Neuroimaging evidence showed structural and/or functional abnormalities existing in the central nervous system, especially the hippocampus, in chronic fatigue syndrome

Sasaki K, Ishigaki Y, Takahashi T.	Medicine, Kanazawa Medical University, Ishikawa 920–0293, Japan.	in chronic fatigue mice by enhancing neurogenesis and inhibiting apoptosis of granular cells.		(CFS) patients. However, its pathophysiologic mechanisms are unclear in part due to the lack of an applicable animal model. We established a chronic fatigue murine model by six repeated injections of Brucella abortus antigen to mice, which was manifested as reduced daily running activity and hippocampal atrophy. Thereafter, resveratrol, a polyphenolic activator of sirtuin 1, was used for treatment in this model. Daily running activity was increased by more than 20%, and the hippocampus was enlarged after 4-week resveratrol therapy. Furthermore, resveratrol inhibited neuronal apoptosis and expression of hippocampal acetylated p53 in the fatigue mice. Resveratrol also improved neurogenesis and expression of brain-derived neurotrophic factor mRNA in the hippocampus. We concluded that repeated injection of B. abortus antigen could induce hypoactivity and hippocampal atrophy in mice. Resveratrol may be effective for improving fatigue symptoms and enlarging the atrophic hippocampus by repressing apoptosis and promoting neurogenesis.
Morrissey RP, Czer L, Shah PK.	Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA 90048, USA.	Chronic heart failure: current evidence, challenges to therapy, and future directions.	Am J Cardiovasc Drugs. 2011 Jun 1;11(3):153-71. doi: 10.2165/11592090-000000000-00000.	Heart failure (HF) is a complex syndrome characterized by the inability of the heart to maintain a normal cardiac output without elevated intracardiac filling pressures, resulting in signs of pulmonary and peripheral edema and symptoms of dyspnea and fatigue. Central to the management of HF is a multifaceted pharmacological intervention to abate the harmful counter-regulatory effects of neurohormonal activation and avid salt and water retention. Whereas up to 40 years ago HF was managed with diuretics and leaf of digitalis, the cornerstones of therapy for HF patients with systolic dysfunction now include ACE inhibitors or angiotensin II type 1 receptor antagonists (angiotensin receptor blockers), β-adrenoceptor antagonists (β-blockers), and aldosterone antagonists, which have significantly improved survival. However, with the increasing number of beneficial therapies, there are challenges to implementing all of them. Specific cardiomyopathies also merit specific considerations with respect to treatment, and - unfortunately - there is no therapy for HF with preserved left ventricular ejection fraction that has been shown to improve survival. Although mortality has improved in HF, the biggest challenge to treatment lies in addressing the morbidity of this disease, which is now the most common reason for hospital admission in our aged population. As such, there are many therapies that may serve to improve the quality of life of HF patients. Future HF treatment regimens may include direct cellular therapy via hormone and cytokine signaling or cardiac regeneration through growth factors or cell therapy.
Moss-Morris R, Spence MJ, Hou R.	School of Psychology, University of Southampton, Highfield, Southampton, UK.	The pathway from glandular fever to chronic fatigue syndrome: can the cognitive behavioural model provide the map?	Psychol Med. 2011 May;41(5):1099-107. Epub 2010 Jul 21.	BACKGROUND: The cognitive behavioural model of chronic fatigue syndrome (CFS) suggests that the illness is caused through reciprocal interactions between physiology, cognition, emotion and behaviour. The purpose of this study was to investigate whether the psychological factors operationalized in this model could predict the onset of CFS following an acute episode of infectious mononucleosis commonly known as glandular fever (GF). METHOD: A total of 246 patients with GF were recruited into this prospective cohort study. Standardized self-report measures of

	remm@soton.ac.uk			perceived stress, perfectionism, somatization, mood, illness beliefs and behaviour were completed at the time of their acute illness. Follow-up questionnaires determined the incidence of new-onset chronic fatigue (CF) at 3 months and CFS at 6 months post-infection. RESULTS: Of the participants, 9.4% met the criteria for CF at 3 months and 7.8% met the criteria for CFS at 6 months. Logistic regression revealed that factors proposed to predispose people to CFS including anxiety, depression, somatization and perfectionism were associated with new-onset CFS. Negative illness beliefs including perceiving GF to be a serious, distressing condition, that will last a long time and is uncontrollable, and responding to symptoms in an all-or-nothing behavioural pattern were also significant predictors. All-or-nothing behaviour was the most significant predictor of CFS at 6 months. Perceived stress and consistently limiting activity at the time of GF were not significantly associated with CFS. CONCLUSIONS: The findings from this study provide support for the cognitive behavioural model and a good basis for developing prevention and early intervention strategies for CFS.
Mount DL, Johnson DM, Rego MI, Schofield K, Amponsah A, Graham LF.	Wake Forest University School of Medicine, Winston-Salem, NC 27157, USA. Dmount@wfubmc.edu	Preliminary findings exploring the social determinants of Black males' lay health perspectives.	Am J Mens Health. 2012 Jan;6(1):71-9. Epub 2011 Nov 21.	The unequal discussion of Black males' health is a pressing social problem. This study addressed Black males' lay perspectives regarding their health, illness, and mortality, with attention to the determinants of men's health, prevention, lifestyle, and opportunities for health promotion using an exploratory/qualitative research methodology. Participants were 68 Black males aged 15 to 68 years, with an average age of 44 years (SD = 14.5). The narratives represented a complex interplay of biopsychosocial factors, ranging from intrapersonal attitudes, interpersonal experiences to discussions about community and public policy injustices. Five prominent themes emerged: (a) lack of chronic disease awareness, (b) fatalism, (c) fear and anxiety of academic-medical settings, (d) hyperactive masculinity fatigue, and (e) the gay-straight divide. The term Tired Black Male Health syndrome was coined in the forum. Implications of these findings are discussed in the context of culturally relevant strategies for improving Black male community health engagement.
Nacul LC, Lacerda EM, Campion P, Pheby D, Drachler Mde L, Leite JC, Poland F, Howe A, Fayyaz S, Molokhia M.	Department of Nutrition and Public Health Interventions Research, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. luis.nacul@lshtm.	The functional status and well being of people with myalgic encephalomyelitis/chronic fatigue syndrome and their carers.	BMC Public Health. 2011 May 27;11:402.	BACKGROUND: Diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome or ME/CFS is largely based on clinical history, and exclusion of identifiable causes of chronic fatigue. Characterization of cases and the impact of interventions have been limited due to clinical heterogeneity and a lack of reliable biomarkers for diagnosis and outcome measures. People with ME/CFS (PWME) often report high levels of disability, which are difficult to measure objectively. The well being of family members and those who care for PWME are also likely to be affected. This study aimed to investigate the functional status and well being of PWME and their lay carers, and to compare them with people with other chronic conditions. METHODS: We used a cross sectional design to study 170 people aged between 18 and 64 years with well characterized ME/CFS, and 44 carers, using SF-36 v2™. Mean physical and

	ac.uk			mental domains scores (scales and component summaries) were calculated and compared internally and externally with reference standards for the general population and for population groups with 10 chronic diseases. RESULTS: SF-36 scores in PWME were significantly reduced, especially within the physical domain (mean norm-based Physical Component Summary (PCS) score = 26.8), but also within the mental domain (mean norm-based score for Mental Component Summary (MCS) = 34.1). The lowest and highest scale scores were for "Role-Physical" (mean = 25.4) and "Mental Health" (mean = 36.7) respectively. All scores were in general lower than those for the general population and diseased-specific norms for other diseases. Carers of those with ME/CFS tended to have low scores in relation to population norms, particularly within the mental domain (mean = 45.4). CONCLUSIONS: ME/CFS is disabling and has a greater impact on functional status and well being than other chronic diseases such as cancer. The emotional burden of ME/CFS is felt by lay carers as well as by people with ME/CFS. We suggest the use of generic instruments such as SF-36, in combination of other objective outcome measurements, to describe patients and assess treatments.
Nacul LC, Lacerda EM, Pheby D, Campion P, Molokhia M, Fayyaz S, Leite JC, Poland F, Howe A, Drachler ML.	Department of Nutrition and Public Health Interventions Research, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. Luis.Nacul@lshtm.ac.uk	Prevalence of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in three regions of England: a repeated cross-sectional study in primary care.	BMC Med. 2011 Jul 28;9:91.	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) or chronic fatigue syndrome (CFS) has been used to name a range of chronic conditions characterized by extreme fatigue and other disabling symptoms. Attempts to estimate the burden of disease have been limited by selection bias, and by lack of diagnostic biomarkers and of agreed reproducible case definitions. We estimated the prevalence and incidence of ME/CFS in three regions in England, and discussed the implications of frequency statistics and the use of different case definitions for health and social care planning and for research. METHODS: We compared the clinical presentation, prevalence and incidence of ME/CFS based on a sample of 143,000 individuals aged 18 to 64 years, covered by primary care services in three regions of England. Case ascertainment involved: 1) electronic search for chronic fatigue cases; 2) direct questioning of general practitioners (GPs) on cases not previously identified by the search; and 3) clinical review of identified cases according to CDC-1994, Canadian and Epidemiological Case (ECD) Definitions. This enabled the identification of cases with high validity. RESULTS: The estimated minimum prevalence rate of ME/CFS was 0.2% for cases meeting any of the study case definitions, 0.19% for the CDC-1994 definition, 0.11% for the Canadian definition and 0.03% for the ECD. The overall estimated minimal yearly incidence was 0.015%. The highest rates were found in London and the lowest in East Yorkshire. All but one of the cases conforming to the Canadian criteria also met the CDC-1994 criteria, however presented higher prevalence and severity of symptoms. CONCLUSIONS: ME/CFS is not uncommon in England and represents a significant burden to patients and society. The number of people with chronic fatigue who do not meet specific criteria for ME/CFS is higher still. Both groups have high levels of need for service provision, including health and

				social care. We suggest combining the use of both the CDC-1994 and Canadian criteria for ascertainment of ME/CFS cases, alongside careful clinical phenotyping of study participants. This combination if used systematically will enable international comparisons, minimization of bias, and the identification and investigation of distinct sub-groups of patients with possibly distinct aetiologies and pathophysiologies, standing a better chance of translation into effective specific treatments.
Nas K, Cevik R, Batum S, Sarac AJ, Acar S, Kalkanli S.	Departments of Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey. knas@dicle.edu.tr	Immunologic and psychosocial status in chronic fatigue syndrome.	Bratisl Lek Listy. 2011;112(4):208-12.	OBJECTIVE: The aim of the study was to investigate the immunologic functions and psychosocial status in patients with chronic fatigue syndrome (CFS). METHODS: Twenty-five patients with CFS diagnosed by the international CFS definition criteria and 20 age- and gender-matched healthy controls were recruited. Depression was assessed by Beck Depression Inventory (BDI) and health status was assessed by Nottingham Health Profile (NHP). Monoclonal antibodies (MAbs) were measured to identify the following NK cell subsets: CD3, CD4, CD8 and CD56 and cytokine measurements were performed for IL2r, IL6 and IL8 in both patients and control subjects. RESULTS: The BDI and NHP scores of CFS group were found to be significantly higher than in the control group. The absolute numbers of CD56 cell were also significantly decreased in the patients with CFS compared with the healthy controls. There were no other significant differences of NK cell activity (CD3, CD4 and CD8) and there were significant differences in IL6 and IL2r levels between patients and controls. There were significant correlations between serum IL-6 level and sleep, social isolation and physical ability NHP subscores, and betweenCD56 NK cell activity and emotional reaction NHP sub score in CFS patients. CONCLUSION: Significantly higher ratios of psychological and physical disturbances were found in patients with CFS. Decreased CD56 NK cell activity and increased IL2r levels seem to be important immunopathologic changes in CFS. IL-6 and CD 56 NK cell activity may play an important role in sleep, physical, social, and physicological manifestations of CFS (Tab. 3, Fig. 1, Ref. 36). Full Text in free PDF www.bmj.sk.
Nater UM, Maloney E, Heim C, Reeves WC.	National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control & Prevention, Atlanta, GA, USA.	Cumulative life stress in chronic fatigue syndrome.	Psychiatry Res. 2011 Sep 30;189(2):318-20. Epub 2011 Aug 15.	We studied the impact of cumulative life stress on CFS in a population-based study. We found that exposure to stressors was significantly more common in persons with CFS compared to NF controls; those with CFS reported experiencing significantly higher levels of psychological distress. Also, post-traumatic stress disorder was significantly more common in people with CFS. These results not only corroborate findings from other studies but, importantly, extend those by: a) measuring a comprehensive spectrum of stress variables, b) for the first time presenting data on stress in a population-based study, thus minimizing the effects of recruitment bias, and c) diagnosing CFS by means of standardized, validated scales, thus allowing replication and extension of our findings. Stress may be an important factor in the pathophysiology of CFS. Consequently, future studies should provide a more detailed understanding of the processes that lead from stress to CFS using longitudinal designs. Published by Elsevier Ireland Ltd.

Neu D, Kajosch H, Peigneux P, Verbanck P, Linkowski P, Le Bon O.	Brugmann University Hospital, Sleep Laboratory and Unit for Chronobiology U78, Department of Psychiatry, Université Libre de Bruxelles (U.L.B), Brussels, Belgium. daniel.neu@chu-brugmann.be	Cognitive impairment in fatigue and sleepiness associated conditions.	Psychiatry Res. 2011 Aug 30;189(1):128-34. Epub 2010 Dec 31.	Although relating to very different concepts, sleepiness and fatigue are often confounded. However, both fatigue-associated conditions such as the chronic fatigue syndrome (CFS) and sleepiness-associated conditions such as the sleep apnea-hypopnea syndrome (SAHS) are associated with cognitive impairment with impaired attention, concentration and memory performances. Fifteen pure CFS patients, without primary sleep disorders or clinically relevant sleepiness, were compared to 15 untreated SAHS patients, without clinically relevant fatigue, and to 16 healthy controls of similar age. The auditory verbal learning test (AVLT), digit span, digit symbol and finger tapping test (FTT) were used as cognitive and behavioural measures. In addition we assessed daytime EEG spectral power and P300 evoked potentials. With exception for the digit span, all tests showed lower performances in patient groups. Recall on the AVLT did not differ between the two patient groups, but the digit and symbol spans showed more severe impairment in SAHS patients. Psychomotor performance on the FTT presented with slower hit rates in SAHS than in CFS. EEG theta power was highest in CFS patients. P300 latencies and amplitudes did not differ between groups. Fatigue- and sleepiness-associated conditions can both present with significant and objective impairment of cognitive functioning and behavioural motor performance. In our sample cognitive impairment and psychomotor performance were worse when associated to sleepiness in SAHS than with fatigue in CFS. Copyright © 2010 Elsevier Ltd. All rights reserved.
Newton DJ, Kennedy G, Chan KK, Lang CC, Belch JJ, Khan F.	Vascular and Inflammatory Diseases Research Unit, Institute of Cardiovascular Research, University of Dundee, Dundee, UK.	Large and small artery endothelial dysfunction in chronic fatigue syndrome.	Int J Cardiol. 2012 Feb 9;154(3):335-6. Epub 2011 Nov 10.	
Newton JL, Pairman J, Hallsworth K, Moore S, Plötz T, Trenell MI.	UK National Institute for Health Research Biomedical Research Centre in Ageing & Age-related Disease, Institute for Ageing and Health, Newcastle University,	Physical activity intensity but not sedentary activity is reduced in chronic fatigue syndrome and is associated with autonomic regulation.	QJM. 2011 Aug;104(8):681-7. Epub 2011 Mar 7.	BACKGROUND: Chronic fatigue syndrome (CFS) is a common debilitating condition associated with reduced function and impaired quality of life. The cause is unknown and treatments limited. Studies confirm that CFS is associated with impaired autonomic regulation and impaired muscle function. AIM: Define the relationship between sedentary behaviour, physical activity and autonomic regulation in people with CFS. DESIGN: Cohort study. METHODS: Physical activity was assessed objectively in 107 CFS patients (Fukuda) and age, sex and body mass index (BMI)-matched sedentary controls (n= 107). Fatigue severity was determined using the Fatigue Impact Scale in all participants and heart rate variability performed in the CFS group. RESULTS: The CFS group had levels and patterns of sedentary behaviour similar to non-fatigue controls ($P > 0.05$). Seventy-nine percent of the CFS group did not achieve

	Newcastle, UK. j.l.newton@ncl.ac.uk			the WHO recommended 10,000 steps per day. Active energy expenditure [time >3 METs (metabolic equivalents)] was reduced in CFS when compared with controls (P < 0.0001). Physical activity duration was inversely associated with resting heart rate (P = 0.04; r(2) = 0.03), with reduced activity significantly associating with reduced heart rate variability in CFS. There were no relationships between fatigue severity and any parameter of activity. Thirty-seven percent of the CFS group were overweight (BMI 25-29.9) and 20% obese (BMI ≥ 30). CONCLUSION: Low levels of physical activity reported in CFS represent a significant and potentially modifiable perpetuating factor in CFS and are not attributable to high levels of sedentary activity, rather a decrease in physical activity intensity. The reduction in physical activity can in part be explained by autonomic dysfunction but not fatigue severity.
Neyro JL, Franco R, Rodríguez E, Carrero A, Palacios S.	Servicio de Ginecologia y Obstetricia, Universidad del Pais Vasco, EHU-UPV, Hospital Universitario de Cruces, Baracaldo. jlneyro@sego.es	[Fibromyalgia and menopause. Association or coincidence?]. [Article in Spanish]	Ginecol Obstet Mex. 2011 Sep;79(9):572-8.	Fibromyalgia constitutes today, in the western world, an important problem of health that affects fundamentally in women from 45 years. The studies on the influence of the hormones on the symptomatology of the patients with fibromyalgia have not managed to establish a link of causal union between the hormonal climacteric decline and the development of the painful syndrome. Nevertheless, there are studies that relate the pain, the anxiety and the depression to the level of sexual steroids. It is our aim to check these associations. We will have to expect to the development of the intracrinology and, possibly, to know more the relationship between sexual steroids and neurotransmitters to be able to know the exact relation between fibromyalgia and menopause.
Nijhof SL, Maijer K, Bleijenberg G, Uiterwaal CS, Kimpen JL, van de Putte EM.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht, Netherlands. s.l.nijhof@umcutrecht.nl	Adolescent chronic fatigue syndrome: prevalence, incidence, and morbidity.	Pediatrics. 2011 May;127(5):e1169-75. Epub 2011 Apr 18.	OBJECTIVE: To determine nationwide general practitioner (GP)-diagnosed prevalence and pediatrician-diagnosed incidence rates of adolescent chronic fatigue syndrome (CFS), and to assess CFS morbidity. DESIGN AND SETTING: We collected data from a cross-sectional national sample among GPs and prospective registration of new patients with CFS in all pediatric hospital departments in the Netherlands. PATIENTS AND METHODS: Study participants were adolescents aged 10 to 18 years. A representative sample of GPs completed questionnaires on the prevalence of CFS in their adolescent patients. Pediatric hospital departments prospectively reported new cases of CFS in adolescent patients. For every new reported case, a questionnaire was sent to the reporting pediatrician and the reported patient to assess CFS morbidity. Prevalence was estimated through the data from GP questionnaires and incidence was estimated on the basis of cases newly reported by pediatricians from January to December 2008. RESULTS: Prevalence was calculated as 111 per 100 000 adolescents and incidence as 12 per 100 000 adolescents per year. Of newly reported patients with CFS, 91% scored at or above cutoff points for severe fatigue and 93% at or above the cutoff points for physical impairment. Forty-five percent of patients with CFS reported >50% school absence during the previous 6 months. CONCLUSIONS: Clinically diagnosed incidence and prevalence rates show that adolescent CFS is uncommon compared with chronic fatigue. The primary adverse impact of CFS is

				extreme disability associated with considerable school absence.
Nijhof SL, Bleijenberg G, Uiterwaal CS, Kimpen JL, van de Putte EM.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Centre Utrecht, The Netherlands. s.l.nijhof@umcutrecht.nl	Fatigue In Teenagers on the interNET--the FITNET Trial. A randomized clinical trial of web-based cognitive behavioural therapy for adolescents with chronic fatigue syndrome: study protocol. [ISRCTN59878666].	BMC Neurol. 2011 Feb 19;11:23.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is increasingly recognized as a cause of disability and inactivity in adolescents in the Netherlands. CFS is characterized by unexplained fatigue lasting more than 6 months. Cognitive Behavioural Therapy (CBT) has proven to be effective. However, CBT availability for adolescents with CFS is limited and requires special therapeutic skills not always readily available. An alternative to the face-to-face CBT is FITNET, a web-based therapeutic program designed specifically for adolescents diagnosed with CFS, and their parents. This new CBT approach appeals to the modern youth, who grow up with internet as their main source of information. A web-based program offers the opportunity to lower thresholds for the acceptance and realization of healthcare. This treatment can be activated at any chosen time. The communication between patient and therapist can elapse asynchronously. If effective, this web-based program would greatly increase the therapeutic accessibility. METHODS/DESIGN: A randomized clinical trial is currently conducted. One-hundred-forty adolescents aged 12-18 years diagnosed with CFS will be recruited and randomized to one of two groups: FITNET or usual care. After 6 months, the usual care group will have access to the FITNET program. Outcomes will be assessed at baseline, post intervention, and at 6 months follow-up. Primary outcome measures are school presence, fatigue severity, and physical functioning. DISCUSSION: The FITNET study is the first randomized clinical trial which evaluates the effect of web-based CBT versus usual care in adolescents with CFS. The intervention is based on a theoretical existing model of CBT for patients with CFS. The results of this study will provide information about the possibility and efficacy of web-based CBT for adolescents with CFS and will reveal predictors of efficacy. TRIAL REGISTRATION: ISRCTN: ISRCTN59878666 and ClinicalTrials.gov: NCT00893438.
Nijs J, Meeus M, Van Oosterwijck J, Ickmans K, Moorkens G, Hans G, De Clerck LS.	Department of Human Physiology, Vrije Universiteit Brussel (VUB), Brussels, Belgium. Jo.Nijs@vub.ac.be	In the mind or in the brain? Scientific evidence for central sensitisation in chronic fatigue syndrome.	Eur J Clin Invest. 2012 Feb;42(2):203-12. doi: 10.1111/j.1365-2362.2011.02575.x. Epub 2011 Jul 27.	BACKGROUND: Central sensitisation entails several top-down and bottom-up mechanisms, all contributing to the hyperresponsiveness of the central nervous system to a variety of inputs. In the late nineties, it was first hypothesised that chronic fatigue syndrome (CFS) is characterised by hypersensitivity of the central nervous system (i.e. central sensitisation). Since then, several studies have examined central sensitisation in patients with CFS. This study provides an overview of such studies. MATERIALS AND METHODS: Narrative review. RESULTS: Various studies showed generalised hyperalgesia in CFS for a variety of sensory stimuli, including electrical stimulation, mechanical pressure, heat and histamine. Various tissues are affected by generalised hyperalgesia: the skin, muscle tissue and the lungs. Generalised hyperalgesia in CFS is augmented, rather than decreased, following various types of stressors like exercise and noxious heat pain. Endogenous inhibition is not activated in response to exercise and activation of diffuse noxious inhibitory controls following noxious heat application to the skin is delayed. CONCLUSIONS: The observation of central sensitisation in CFS is in line with our current understanding of CFS. The

				presence of central sensitisation in CFS corroborates with the presence of several psychological influences on the illness, the presence of infectious agents and immune dysfunctions and the dysfunctional hypothalamus-pituitary-adrenal axis as seen in these severely debilitated patients. © 2011 The Authors. European Journal of Clinical Investigation © 2011 Stichting European Society for Clinical Investigation Journal Foundation.
Nijs J, Paul van Wilgen C, Van Oosterwijck J, van Ittersum M, Meeus M.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium. Jo.Nijs@vub.ac.be	How to explain central sensitization to patients with 'unexplained' chronic musculoskeletal pain: practice guidelines.	Man Ther. 2011 Oct;16(5):413-8. Epub 2011 May 31.	Central sensitization provides an evidence-based explanation for many cases of 'unexplained' chronic musculoskeletal pain. Prior to commencing rehabilitation in such cases, it is crucial to change maladaptive illness perceptions, to alter maladaptive pain cognitions and to reconceptualise pain. This can be accomplished by patient education about central sensitization and its role in chronic pain, a strategy known as pain physiology education. Pain physiology education is indicated when: 1) the clinical picture is characterized and dominated by central sensitization; and 2) maladaptive illness perceptions are present. Both are prerequisites for commencing pain physiology education. Face-to-face sessions of pain physiology education, in conjunction with written educational material, are effective for changing pain cognitions and improving health status in patients with various chronic musculoskeletal pain disorders. These include patients with chronic low back pain, chronic whiplash, fibromyalgia and chronic fatigue syndrome. After biopsychosocial assessment pain physiology education comprises of a first face-to-face session explaining basic pain physiology and contrasting acute nociception versus chronic pain (Session 1). Written information about pain physiology should be provided as homework in between session 1 and 2. The second session can be used to correct misunderstandings, and to facilitate the transition from knowledge to adaptive pain coping during daily life. Pain physiology education is a continuous process initiated during the educational sessions and continued within both the active treatment and during the longer term rehabilitation program. Copyright © 2011 Elsevier Ltd. All rights reserved.
Nijs J, Meeus M, Van Oosterwijck J, Roussel N, De Kooning M, Ickmans K, Matic M.	Artesis University College Antwerp, Antwerp, Belgium. Jo.Nijs@vub.ac.be	Treatment of central sensitization in patients with 'unexplained' chronic pain: what options do we have?	Expert Opin Pharmacother. 2011 May;12(7):1087-98. Epub 2011 Jan 22.	INTRODUCTION: Central sensitization accounts for chronic 'unexplained' pain in a wide variety of disorders, including chronic whiplash-associated disorders, temporomandibular disorders, chronic low back pain, osteoarthritis, fibromyalgia, chronic fatigue syndrome and chronic tension-type headache among others. Given the increasing evidence supporting the clinical significance of central sensitization in those with unexplained chronic pain, the awareness is growing that central sensitization should be a treatment target in these patients. AREAS COVERED: This article provides an overview of the treatment options available for desensitizing the CNS in patients with chronic pain due to central sensitization. It focuses on those strategies that specifically target pathophysiological mechanisms known to be involved in central sensitization. In addition, pharmacological options, rehabilitation and neurotechnology options are discussed. EXPERT OPINION: Acetaminophen,

				serotonin-reuptake inhibitor drugs, selective and balanced serototin and norepinephrine-reuptake inhibitor drugs, the serotonin precursor tryptophan, opioids, N-methyl-d-aspartate (NMDA)-receptor antagonists, calcium-channel alpha(2)delta (a2δ) ligands, transcranial magnetic stimulation, transcutaneous electric nerve stimulation (TENS), manual therapy and stress management each target central pain processing mechanisms in animals that - theoretically - desensitize the CNS in humans. To provide a comprehensive treatment for 'unexplained' chronic pain disorders characterized by central sensitization, it is advocated to combine the best evidence available with treatment modalities known to target central sensitization. © 2011 Informa UK, Ltd
Nijs J, Aelbrecht S, Meeus M, Van Oosterwijck J, Zinzen E, Clarys P.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium. jo.nijs@vub.ac.be	Tired of being inactive: a systematic literature review of physical activity, physiological exercise capacity and muscle strength in patients with chronic fatigue syndrome.	Disabil Rehabil. 2011;33(17-18):1493-500. Epub 2010 Dec 20.	A systematic review was undertaken to examine whether patients with chronic fatigue syndrome (CFS) differ from healthy sedentary controls in physiological exercise capacity, physical activity level and muscle strength. From the available literature, it can be concluded that patients with CFS perform less physical activity during daily life, and have less peak isometric muscle strength compared to healthy sedentary control subjects. Conflicting data in relation to physiological exercise capacity of patients with CFS have been reported, but the weighted available evidence points towards a reduced physiological exercise capacity in CFS. Future studies should use a wash-out period for medication use, blinded assessments, a priori power calculation and a sedentary control group comparable for age, gender, body weight, body length and current physical activity level.
Nugraha B, Karst M, Engeli S, Gutenbrunner C.	Department of Rehabilitation Medicine, Hannover Medical School, Carl-Neuberg-Str. 1, Hannover, Germany, Nugraha.Boya@mh-hannover.de.	Brain-derived neurotrophic factor and exercise in fibromyalgia syndrome patients: a mini review.	Rheumatol Int. 2011 Dec 31. [Epub ahead of print]	Fibromyalgia syndrome (FMS) is a common chronic pain condition characterized by chronic widespread pain and decreased pain threshold, with hyperalgesia and allodynia. Associated signs include fatigue, morning stiffness, non-restorative sleep, mood disturbance, depression, irritable bowel syndrome, and headache. In addition to the administration of drugs, psychological therapies treatment of FMS mainly consists of physical therapies. Although the precise pathogenesis of FMS remains elucidated, modern understanding conceptualizes FMS as central sensitization as a consequence of altered endogenous pain- and stress-response system and continuous nociceptive input. Altered brain-derived neurotrophic factor (BDNF) levels in FMS suggest that BDNF-well known for its effects on neuronal plasticity-is involved in this sensitization process. Exercise leads to changes in serum BDNF levels, too. This association highlights the importance of exercise in FMS and other chronic pain conditions.
Núñez M, Fernández-Solà J, Nuñez E, Fernández-Huerta JM, Godás-Sieso T, Gomez-Gil E.	Rheumatology Service, Functional Readaptation Unit, Hospital Clinic, Barcelona,	Health-related quality of life in patients with chronic fatigue syndrome: group cognitive behavioural therapy	Clin Rheumatol. 2011 Mar;30(3):381-9. Epub 2011 Jan 15.	Chronic fatigue syndrome (CFS) produces physical and neurocognitive disability that significantly affects health-related quality of life (HRQL). Multidisciplinary treatment combining graded exercise therapy (GET) cognitive behavioural therapy (CBT) and pharmacological treatment has shown only short-term improvements. To compare the effects on HRQL of (1) multidisciplinary treatment combining CBT, GET, and pharmacological treatment, and (2) usual treatment (exercise counselling and

	Spain. mnunez@clinic.ub.es	and graded exercise versus usual treatment. A randomised controlled trial with 1 year of follow-up.		pharmacological treatment) at 12 months of follow-up. Prospective, randomized controlled trial with a follow-up of 12 months after the end of treatment. Patients consecutively diagnosed with CFS (Fukuda criteria) were randomly assigned to intervention (n = 60) or usual treatment (n = 60) groups. HRQL was assessed at baseline and 12 months by the Medical Outcomes Study Short-Form questionnaire (SF-36). Secondary outcomes included functional capacity for activities of daily living measured by the Stanford Health Assessment Questionnaire (HAQ) and comorbidities. At baseline, the two groups were similar, except for lower SF-36 emotional role scores in the intervention group. At 12 months, the intervention did not improve HRQL scores, with worse SF-36 physical function and bodily pain scores in the intervention group. Multidisciplinary treatment was not superior to usual treatment at 12 months in terms of HRQL. The possible benefits of GET as part of multidisciplinary treatment for CFS should be assessed on an individual patient basis.
Oakes B, Qiu X, Levine S, Hackett J Jr, Huber BT.	Pathology Department, Tufts University School of Medicine, 150 Harrison Avenue, Boston, MA 02111, USA.	Failure to Detect XMRV-Specific Antibodies in the Plasma of CFS Patients Using Highly Sensitive Chemiluminescence Immunoassays.	Adv Virol. 2011;2011:854540. Epub 2011 Jul 27.	In 2009, Lombardi et al. reported their startling finding that the gammaretrovirus xenotropic murine leukemia virus-related retrovirus (XMRV) is present in 67% of blood samples of patients suffering from chronic fatigue syndrome (CFS), as opposed to only 3.7% of samples from healthy individuals. However, we and others could not confirm these results, using a nested PCR assay. An alternative to this highly sensitive, but contamination-prone, technique is to measure the serological response to XMRV. Thus, we tested the plasma samples from our cohorts of CFS patients and healthy controls for the presence of XMRV-specific antibodies. Using two novel chemiluminescence immunoassays (CMIAs), we show that none of our samples have any XMRV-reactive antibodies. Taken together with our previous findings, we conclude that XMRV is not present in any human individual tested by us, regardless of CFS or healthy control.
Okifuji A, Bradshaw DH, Donaldson GW, Turk DC.	Pain Research and Management Center, Department of Anesthesiology, University of Utah, 615 Arapeen Drive, Salt Lake City, UT 84108, USA. Akiko.okifuji@hsc.utah.edu	Sequential analyses of daily symptoms in women with fibromyalgia syndrome.	J Pain. 2011 Jan;12(1):84-93. Epub 2010 Jul 1. Erratum in J Pain. 2011 Apr;12(4):509.	Fibromyalgia syndrome (FMS) is a chronic musculoskeletal pain disorder characterized by generalized pain, chronic fatigue, sleep disturbance, and a range of other symptoms having no definitive pathology. Consequently, patient evaluations rely on self-report. Ecological Momentary Assessment (EMA) allows frequent real-time collection of self-report measures, removing recall bias and increasing external validity. We studied 81 females with FMS aged 18 to 42 years. Participants carried EMA devices (Palm Pilot M100) programmed to request ratings to 8 FMS symptoms/conditions 3 times daily for 30 days. Completeness of response rates varied across participants and over time. Controlling for immediately previous fatigue (ie, fatigue rating from the immediately preceding rating), unit increases in immediately previous pain and immediately previous emotional distress predicted 9 and 7% increases, respectively, in current fatigue. Controlling for immediately previous emotional distress, a unit increase in immediately previous pain predicted 7% increase in current emotional distress. Controlled for immediately previous pain, a unit increase in immediately previous fatigue predicted a 7% increase in current pain,

				enhanced by prior diurnal effects; immediately previous emotional distress was not significant. Collectively these results suggest an asymmetry in which emotional stress and pain may increase fatigue, fatigue but not emotional distress may increase pain, and pain but not fatigue may increase emotional distress. Despite small effects and person-to-person variability, these findings suggest that longitudinal data collection by EMA may reveal sequential or causal explanatory patterns with important clinical implications. PERSPECTIVE: Understanding how multiple symptoms covary in FMS is essential for optimal treatment planning. Our results show small but significant temporal relations among pain, fatigue, and emotional distress. Our results also provide support for the use of EMA as a viable data collection method that allows longitudinal, real-time assessment of multiple FMS symptoms. Copyright © 2011 American Pain Society. Published by Elsevier Inc. All rights reserved.
Oldershaw A, Hambrook D, Rimes KA, Tchanturia K, Treasure J, Richards S, Schmidt U, Chalder T.	Section of Eating Disorders, Division of Psychological Medicine and Psychiatry, Institute of Psychiatry, King's College London, London, UK. anna.oldershaw@kcl.ac.uk	Emotion recognition and emotional theory of mind in chronic fatigue syndrome.	Psychol Health. 2011 Aug;26(8):989-1005. Epub 2011 May 23.	BACKGROUND: Difficulties with social function have been reported in chronic fatigue syndrome (CFS), but underpinning factors are unknown. Emotion recognition, theory of mind (inference of another's mental state) and 'emotional' theory of mind (eToM) (inference of another's emotional state) are important social abilities, facilitating understanding of others. This study examined emotion recognition and eToM in CFS patients and their relationship to self-reported social function. METHODS: CFS patients (n = 45) and healthy controls (HCs; n = 50) completed tasks assessing emotion recognition, basic or advanced eToM (for self and other) and a self-report measure of social function. RESULTS: CFS participants were poorer than HCs at recognising emotion states in the faces of others and at inferring their own emotions. Lower scores on these tasks were associated with poorer self-reported daily and social function. CFS patients demonstrated good eToM and performance on these tasks did not relate to the level of social function. CONCLUSIONS: CFS patients do not have poor eToM, nor does eToM appear to be associated with social functioning in CFS. However, this group of patients experience difficulties in emotion recognition and inferring emotions in themselves and this may impact upon social function.
Oldervoll L.		[Does physical exercise help against fatigue?]. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2011 Feb 4;131(3):221.	
Olivadoti MD, Weinberg JB, Toth LA, Opp MR.	Neuroscience Graduate Program, University of Michigan, USA.	Sleep and fatigue in mice infected with murine gammaherpesvirus 68.	Brain Behav Immun. 2011 May;25(4):696-705. Epub 2011 Jan 24.	Fatigue, a common symptom of many acute and chronic medical conditions, reduces both quality of life and workplace productivity and can be disabling. However, the pathophysiologic mechanisms that underlie fatigue can be difficult to study in human populations due to the patient heterogeneity, the variety of underlying causes and potential triggering events, and an inability to collect samples that may be essential to elucidation of mechanisms (e.g., brain). Although the etiology of chronic fatigue syndrome (CFS) remains elusive, some studies have implicated viral infections, including Epstein-Barr virus (EBV), a human gammaherpesvirus, as a potential factor

				in the pathogenesis of CFS. Murine gammaherpesvirus 68 (γHV68) is a mouse pathogen that shares many similarities with human γHVs, including EBV. In this study, we use γHV68-infected C57BL/6J mice as a model system for studying the impact of chronic viral infection on sleep-wake behavior, activity patterns, and body temperature profiles. Our data show that γHV68 alters sleep, activity, and temperature in a manner suggestive of fatigue. In mice infected with the highest dose used in this study (40,000plaque forming units), food intake, body weight, wheel running, body temperature, and sleep were normal until approximately 7days after infection. These parameters were significantly altered during days 7 through 11, returned to baseline levels at day 12 after infection, and remained within the normal range for the remainder of the 30-day period after inoculation. At that time, both infected and uninfected mice were injected with lipopolysaccharide (LPS), and their responses monitored. Uninfected mice given LPS developed a modest and transient febrile response during the initial light phase (hours 12 through 24) after injection. In contrast, infected mice developed changes in core body temperatures that persisted for at least 5days. Infected mice showed an initial hypothermia that lasted for approximately 12h, followed by a modest fever that persisted for several hours. For the remainder of the 5-day recording period, they showed mild hypothermia during the dark phase. Running wheel activity of infected mice was reduced for at least 5days after injection of LPS, but for only 12h in uninfected mice. Collectively, these observations indicate that (1) physiologic and behavioral processes in mice are altered and recover during an early phase of infection, and (2) mice with latent γHV68 infection have an exacerbated response to challenge with LPS. These findings indicate that laboratory mice with γHV68 infections may provide a useful model for the study of fatigue and other physiologic and behavioral perturbations that may occur during acute and chronic infection with gammaherpesviruses. Copyright © 2011 Elsevier Inc. All rights reserved.
Onlamoon N, Das Gupta J, Sharma P, Rogers K, Suppiah S, Rhea J, Molinaro RJ, Gaughan C, Dong B, Klein EA, Qiu X, Devare S, Schochetman G, Hackett J Jr, Silverman RH, Villinger F.	Department of Pathology and Laboratory Medicine, Emory University School of Medicine, Atlanta, Georgia, USA.	Infection, viral dissemination, and antibody responses of rhesus macaques exposed to the human gammaretrovirus XMRV.	J Virol. 2011 May;85(9):4547-57. Epub 2011 Feb 16.	Xenotropic murine leukemia-related virus (XMRV) was identified in association with human prostate cancer and chronic fatigue syndrome. To examine the infection potential, kinetics, and tissue distribution of XMRV in an animal model, we inoculated five macaques with XMRV intravenously. XMRV established a persistent, chronic disseminated infection, with low transient viremia and provirus in blood lymphocytes during acute infection. Although undetectable in blood after about a month, XMRV viremia was reactivated at 9 months, confirming the chronicity of the infection. Furthermore, XMRV Gag was detected in tissues throughout, with wide dissemination throughout the period of monitoring. Surprisingly, XMRV infection showed organ-specific cell tropism, infecting CD4 T cells in lymphoid organs including the gastrointestinal lamina propria, alveolar macrophages in lung, and epithelial/interstitial cells in other organs, including the reproductive tract. Of note, in spite of the intravenous inoculation, extensive XMRV replication was noted in

				prostate during acute but not chronic infection even though infected cells were still detectable by fluorescence in situ hybridization (FISH) in prostate at 5 and 9 months postinfection. Marked lymphocyte activation occurred immediately postinfection, but antigen-specific cellular responses were undetectable. Antibody responses were elicited and boosted upon reexposure, but titers decreased rapidly, suggesting low antigen stimulation over time. Our findings establish a nonhuman primate model to study XMRV replication/dissemination, transmission, pathogenesis, immune responses, and potential future therapies.
Op De Beeck K, Vermeersch P, Verschueren P, Westhovens R, Mariën G, Blockmans D, Bossuyt X.	Experimental Laboratory Immunology, Department of Medical Diagnostic Sciences, Catholic University Leuven, Belgium.	Detection of antinuclear antibodies by indirect immunofluorescence and by solid phase assay.	Autoimmun Rev. 2011 Oct;10(12):801-8. Epub 2011 Jun 30.	Testing for antinuclear antibodies is useful for the diagnosis of systemic rheumatic diseases. Solid phase assays are increasingly replacing indirect immunofluorescence for detection of antinuclear antibodies. In the most recent generation of solid phase assays, manufacturers attempt to improve the performance of the assays by adding extra antigens. Solid phase assay (EliA CTD Screen, Phadia, in which antibodies to 17 antigens are detected) was compared to indirect immunofluorescence for the detection of antinuclear antibodies in diagnostic samples of 236 patients with autoimmune connective tissue diseases, in 149 healthy blood donors, 139 patients with chronic fatigue syndrome, and 134 diseased controls. The sensitivity of EliA CTD Screen for systemic lupus erythematosus, systemic sclerosis, primary Sjögren's syndrome, mixed connective tissue disease, and inflammatory myopathy was 74%, 72%, 89%, 100%, and 39%, respectively. The reactivity in blood donors, in patients with chronic fatigue syndrome, and in diseased controls was <4%. Likelihood ratios increased with increasing antibody concentrations. Generally, a positive test result by EliA CTD Screen had a higher likelihood ratio for systemic rheumatic disease than a positive test result by indirect immunofluorescence. A negative test result by indirect immunofluorescence, however, had a lower likelihood ratio than a negative test result by EliA CTD Screen, indicating that the negative predictive value was higher for indirect immunofluorescence than for EliA CTD screen. Copyright © 2011 Elsevier B.V. All rights reserved.
Ortega F, Zorzanelli R.	Instituto de Medicina Social, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil. fjortega2@gmail.com	[Neuroimaging and the case of chronic fatigue syndrome]. [Article in Portuguese]	Cien Saude Colet. 2011 Apr;16(4):2123-32.	This article analyzes the use of neuroimaging in research into chronic fatigue syndrome. It reviews some works published in the 1990 s and investigates a specific aspect of these studies, namely the search for a cerebral abnormality, in the form of an altered activation pattern, which could provide a pattern for diagnosis and treatment of the disease. The understanding of chronic fatigue syndrome as a disease reduced to some cerebral findings is analyzed, arguing in favor of a broader vision of this disease that includes psychosocial elements of the patient's life as opposed to entirely somatic explanations.
Papadopoulos AS, Cleare AJ.	Department of Psychological Medicine, Institute of	Hypothalamic-pituitary-adrenal axis dysfunction in chronic fatigue	Nat Rev Endocrinol. 2011 Sep 27;8(1):22-32. doi: 10.1038/nrendo.2011.	The weight of current evidence supports the presence of the following factors related to hypothalamic-pituitary-adrenal (HPA) axis dysfunction in patients with chronic fatigue syndrome (CFS): mild hypocortisolism; attenuated diurnal variation of cortisol; enhanced negative feedback to the HPA axis; and blunted HPA axis responsiveness.

	Psychiatry, Box P074, 103 Denmark Hill, London SE5 8AZ, UK.	syndrome.	153.	Furthermore, HPA axis changes seem clinically relevant, as they are associated with worse symptoms and/or disability and with poorer outcomes to standard treatments for CFS. Regarding etiology, women with CFS are more likely to have reduced cortisol levels. Studies published in the past 8 years provide further support for a multifactorial model in which several factors interact to moderate HPA axis changes. In particular, low activity levels, depression and early-life stress appear to reduce cortisol levels, whereas the use of psychotropic medication can increase cortisol. Addressing these factors-for example, with cognitive behavioral therapy-can increase cortisol levels and is probably the first-line approach for correcting HPA axis dysfunction at present, as steroid replacement is not recommended. Given what is now a fairly consistent pattern of findings for the type of HPA axis changes found in CFS, we recommend that future work focuses on improving our understanding of the cause and relevance of these observed changes.
Paprotka T, Delviks-Frankenberry KA, Cingöz O, Martinez A, Kung HJ, Tepper CG, Hu WS, Fivash MJ Jr, Coffin JM, Pathak VK.	Viral Mutation Section, HIV Drug Resistance Program, National Cancer Institute at Frederick, Frederick, MD 21702, USA.	Recombinant origin of the retrovirus XMRV.	Science. 2011 Jul 1;333(6038):97-101. Epub 2011 May 31. Comment in Nat Rev Urol. 2011 Aug;8(8):409.	The retrovirus XMRV (xenotropic murine leukemia virus-related virus) has been detected in human prostate tumors and in blood samples from patients with chronic fatigue syndrome, but these findings have not been replicated. We hypothesized that an understanding of when and how XMRV first arose might help explain the discrepant results. We studied human prostate cancer cell lines CWR22Rv1 and CWR-R1, which produce XMRV virtually identical to the viruses recently found in patient samples, as well as their progenitor human prostate tumor xenograft (CWR22) that had been passaged in mice. We detected XMRV infection in the two cell lines and in the later passage xenografts, but not in the early passages. In particular, we found that the host mice contained two proviruses, PreXMRV-1 and PreXMRV-2, which share 99.92% identity with XMRV over >3.2-kilobase stretches of their genomes. We conclude that XMRV was not present in the original CWR22 tumor but was generated by recombination of two proviruses during tumor passaging in mice. The probability that an identical recombinant was generated independently is negligible (~10(-12)); our results suggest that the association of XMRV with human disease is due to contamination of human samples with virus originating from this recombination event.
Pardini M, Guida S, Primavera A, Krueger F, Cocito L, Gialloreti LE.	Department of Neurosciences, Ophthalmology and Genetics, University of Genoa, Genoa, Italy. matteo.pardini@gmail.com	Amisulpride vs. fluoxetine treatment of chronic fatigue syndrome: a pilot study.	Eur Neuropsychopharmacol. 2011 Mar;21(3):282-6. Epub 2010 Nov 26.	Different pharmacologic agents have been evaluated in the treatment of Chronic Fatigue Syndrome (CFS), albeit with moderate efficacy. Among the compounds thought to present with potential to be efficacious in CFS patients stands out low-dose amisulpride, a substituted benzamide that has been shown to be an useful treatment for conditions which exhibit some overlap with CFS such as dysthymia and somatoform disorders. We thus recruited forty non-depressed CFS patients that were randomized to receive either amisulpride 25mg bid, or fluoxetine 20mg uid; all subjects were un-blinded to the treatment regimen. At the time of enrollment in the study and after twelve weeks of treatment, enrolled subjects completed the Krupp Fatigue Severity Scale, the Hospital Anxiety and Depression Scale and a visual analog

				scale focused on pain and bodily discomfort. Moreover, all subjects were evaluated by a clinician, blinded to the treatment regimen, using the Clinical Global Impression Severity Scale. Our data revealed a significant improvement both in self-report, and observer-based measures for the amisulpride-treated, but not for the fluoxetine-treated patients. Amisulpride-treated subjects also presented with a significant reduction of somatic complaints, while the amisulpride effect on anxiety and mood levels was not significant. Both drugs were equally well tolerated. Summing up, we showed a positive symptomatic effect of amisulpride, compared to SSRI treatment, in a group of non-depressed CSF patients on self-report and on observer-based measures of fatigue and somatic complaints. If confirmed by larger, blinded studies, amisulpride thus could represent an effective approach to this difficult-to-treat condition. Copyright © 2010 Elsevier B.V. and ECNP. All rights reserved.
Pasi A, Bozzini S, Carlo-Stella N, Martinetti M, Bombardieri S, De Silvestri A, Salvaneschi L, Cuccia M.	HLA Laboratory, Immunohaematology and Transfusion Center, Pavia, Italy.	Excess of activating killer cell immunoglobulin-like receptors and lack of HLA-Bw4 ligands: a two-edged weapon in chronic fatigue syndrome.	Mol Med Report. 2011 May-Jun;4(3):535-40. doi: 10.3892/mmr.2011.447. Epub 2011 Mar 4.	Chronic fatigue syndrome (CFS) is an inflammatory disease of unknown aetiology. Researchers have proposed infectious, neurological and immunological causes of this syndrome. Recently, the xenotropic murine leukemia virus-related virus was detected in 67% of patients with CFS in a US study. This observation is in agreement with one ascertained aspect of the disease: a decreased efficiency in NK cell lytic activity in CFS patients. Here, we analyzed the genomic polymorphism of killer cell immunoglobulin-like receptors (KIRs) and their HLA class I cognate ligands in patients with certified CFS. An excess of KIR3DS1 was found in CFS patients with respect to controls, as well as an increased frequency of the genotype missing KIR2DS5. Forty-four CFS patients and 50 controls also underwent genomic typing for the HLA-ligands. In the patients, a great proportion of KIR3DL1 and KIR3DS1 receptors were found to be missing their HLA-Bw4Ile80 binding motif. We hypothesize that an excess of KIR3DS1, combined with an excess of ligand-free KIR3DL1 and KIR3DS1 receptors, may hamper the clearance of a pathogen via NK cells, thus favouring the chronicity of the infection.
Passeri E, Villa C, Couette M, Itti E, Brugieres P, Cesaro P, Gherardi RK, Bachoud-Levi AC, Authier FJ.	Paris Est-Creteil University & Henri-Mondor University Hospital (APHP): Reference Center for Neuromuscular Diseases Garches-Necker-Mondor-Hendaye, Creteil, F-94010, France.	Long-term follow-up of cognitive dysfunction in patients with aluminum hydroxide-induced macrophagic myofasciitis (MMF).	J Inorg Biochem. 2011 Nov;105(11):1457-63. Epub 2011 Aug 22.	Macrophagic myofasciitis (MMF) is characterized by specific muscle lesions assessing long-term persistence of aluminum hydroxide within macrophages at the site of previous immunization. Affected patients are middle-aged adults, mainly presenting with diffuse arthromyalgias, chronic fatigue, and cognitive dysfunction. Representative features of MMF-associated cognitive dysfunction (MACD) include (i) dysexecutive syndrome; (i) visual memory; (iii) left ear extinction at dichotic listening test. In present study we retrospectively evaluated the progression of MACD in 30 MMF patients. Most patients fulfilled criteria for non-amnestic/dysexecutive mild cognitive impairment, even if some cognitive deficits seemed unusually severe. MACD remained stable over time, although dysexecutive syndrome tended to worsen. Long-term follow-up of a subset of patients with 3 or 4 consecutive neuropsychological evaluations confirmed the stability of MACD with time, despite marked fluctuations. Copyright © 2011 Elsevier Inc. All rights reserved.
Pedersen VH,	King's College	Multi-source	Int J Technol Assess	OBJECTIVES: To propose a new method for comparing and integrating original

Dagenais P, Lehoux P.	London. vibe.pedersen@kcl.ac.uk	synthesis of data to inform health policy.	Health Care. 2011 Jul;27(3):238-46. doi: 10.1017/S0266462311000213. Epub 2011 Jul 8.	qualitative data with systematic reviews of quantitative and qualitative studies, demonstrated by a study of the psychosocial needs of chronic fatigue syndrome (CFS) sufferers in Québec. METHODS: A systematic literature review was performed across various databases for English and French language studies, on the psychosocial aspects of CFS. Qualitative, quantitative, and mixed method studies published between January 1994 and July 2008 were included. Unpublished literature and reference lists of included studies were also searched. Themes identified in the literature were used to guide semi-structured interviews with seventeen CFS-sufferers, mostly recruited from a large specialist practice in Montreal. Interviews were transcribed verbatim and validated by a research assistant. Transcripts were coded using the identified themes. New codes were created when new issues arose. All themes were subsequently synthesized into overall categories using a constant comparative method. RESULTS: The literature search yielded thirty-one papers: twenty-eight primary studies and three systematic reviews. Twelve themes were identified and synthesized into four overall problem categories, such as "Lack of professional recognition." Interviews confirmed findings from the literature, but also revealed unidentified needs specific to CFS-sufferers in Québec. Policy recommendations were provided to address these needs. CONCLUSIONS: Multi-Source Synthesis provides a systematic method for synthesizing data from original studies with literature findings, thereby broadening the knowledge base and the local relevance of decisions concerning specific patient populations.
Peters S, Wearden A, Morriss R, Dowrick CF, Lovell K, Brooks J, Cahill G, Chew-Graham C.	School of Psychological Sciences, University of Manchester, Manchester, UK. Sarah.peters@manchester.ac.uk.	Challenges of nurse delivery of psychological interventions for long-term conditions in primary care: a qualitative exploration of the case of chronic fatigue syndrome/myalgic encephalitis.	Implement Sci. 2011 Dec 22;6(1):132.	ABSTRACT:BACKGROUND: The evidence base for a range of psychosocial and behavioural interventions in managing and supporting patients with long-term conditions (LTCs) is now well-established. With increasing numbers of such patients being managed in primary care, and a shortage of specialists in psychology and behavioural management to deliver interventions, therapeutic interventions are increasingly being delivered by general nurses with limited training in psychological interventions. It is unknown what issues this raises for the nurses or their patients. The purpose of the study was to examine the challenges faced by non-specialist nurses when delivering psychological interventions for an LTC (chronic fatigue syndrome/myalgic encephalomyelitis [CFS/ME]) within a primary care setting. METHODS: A qualitative study nested within a randomised controlled trial [ISRCTN 74156610] explored the experiences and acceptability of two different psychological interventions (pragmatic rehabilitation and supportive listening) from the perspectives of nurses, their supervisors, and patients. Semi structured in-depth interviews were conducted with three nurse therapists, three supervisors, and 46 patients. An iterative approach was used to develop conceptual categories from the dataset. RESULTS: Analyses identified four sets of challenges that were common to both interventions: (i) being a novice therapist, (ii) engaging patients in the therapeutic model, (iii) dealing with emotions, and (iv) the complexity of primary care.

				Each challenge had the potential to cause tension between therapist and patient. A number of strategies were developed by participants to manage the tensions. CONCLUSIONS: Tensions existed for nurses when attempting to deliver psychological interventions for patients with CFS/ME in this primary care trial. Such tensions should be addressed before implementing psychological interventions within routine clinical practice. Similar tensions may be found for other LTCs. Our findings have implications for developing therapeutic alliances and highlight the need for regular supervision.
Petrov D, Marchalik D, Sosin M, Bal A.	UMDNJ/Robert Wood Johnson Medical School, New Brunswick, NJ, USA.	Factors affecting duration of chronic fatigue syndrome in pediatric patients.	Indian J Pediatr. 2012 Jan;79(1):52-5. Epub 2011 May 27.	OBJECTIVE: To determine factors affecting duration of chronic fatigue syndrome (CFS) in pediatric patients. METHODS: This Retrospective cohort consisted of patients with CFS at the regional referral infectious disease clinic for evaluation of fatigue in children and adolescents. Demographic, clinical, and laboratory data were analyzed to identify the impact on duration and severity of pediatric CFS. RESULTS: A total number of 53 predominantly white (98.1%) patients with CFS, aged 9-18 years, were included in the study. Other than fatigue, headaches and sleep disturbance were the most common symptoms of pediatric CFS. Seropositive status for Borrelia burgdorferi (B. burgdorferi) and Epstein-Barr virus (EBV) was identified in 66% of the patients with the diagnosis of CFS by CDC criteria. No association was found between the CFS symptoms, gender, or age at diagnosis and duration of fatigue symptoms. Duration of CFS was associated with high Body-Mass Index (BMI) in a regression model after adjustment for patient's age, gender, and seropositive status for B. burgdorferi and/or EBV (0.34 ± 0.15, $P < 0.04$). CONCLUSIONS: BMI is significantly associated with prolonged duration of CFS.
Pfeffer G, Sirrs S, Wade NK, Mezei MM.	Division of Neurology, University of British Columbia, Vancouver.	Multisystem disorder in late-onset chronic progressive external ophthalmoplegia.	Can J Neurol Sci. 2011 Jan;38(1):119-23.	INTRODUCTION: Chronic progressive external ophthalmoplegia (CPEO) is a mitochondrial syndrome on a disease spectrum with Kearns-Sayre syndrome (KSS). Clinical presentation is variable and our experience suggested that phenotypic differences exist in CPEO with onset after age 20. METHODS: This descriptive study is a retrospective chart review of 40 patients with late-onset CPEO. Clinical features, laboratory and neurophysiology results were reviewed. RESULTS: Multisystem dysfunction was very common in this series. Gastrointestinal dysfunction was more common than expected (60%) as was migraine headache (40%). Clinical characteristics on the KSS disease spectrum were uncommon in this series with only 2.5% having pigmentary retinopathy, 5% with cardiac conduction abnormality, and 22.5% having endocrinopathy (most often thyroid dysfunction rather than diabetes). Neurophysiology abnormalities included length-dependent axonal polyneuropathy in 44% (sometimes subclinical) and myopathic EMG changes in 26%. Exposure to sources of acquired mitochondrial toxicity including cigarette use and hepatitis C infection were more common than expected in this series. DISCUSSION: Phenotype was different in this late-onset series compared with previous reports in CPEO patients. In this series of late-onset patients, multi-organ dysfunction was more common than previously reported in CPEO, and some classical mitochondrial manifestations, such as

				pigmentary retinopathy were rare. We suggest that acquired mitochondrial toxicity may have a role in the pathogenesis of adult-onset CPEO.
Phillips K, Clauw DJ.	University of Michigan, Ann Arbor, MI, United States. kphill@med.umich.edu	Central pain mechanisms in chronic pain states--maybe it is all in their head.	Best Pract Res Clin Rheumatol. 2011 Apr;25(2):141-54.	Mechanisms underlying chronic pain differ from those underlying acute pain. In chronic pain states, central nervous system (CNS) factors appear to play particularly prominent roles. In the absence of anatomical causes of persistent pain, medical sub-specialities have historically applied wide-ranging labels (e.g., fibromyalgia (FM), irritable bowel syndrome, interstitial cystitis and somatisation) for what now is emerging as a single common set of CNS processes. The hallmark of these 'centrally driven' pain conditions is a diffuse hyperalgesic state identifiable using experimental sensory testing, and corroborated by functional neuroimaging. The characteristic symptoms of these central pain conditions include multifocal pain, fatigue, insomnia, memory difficulties and a higher rate of co-morbid mood disorders. In contrast to acute and peripheral pain states that are responsive to non-steroidal anti-inflammatory drugs (NSAIDs) and opioids, central pain conditions respond best to CNS neuromodulating agents, such as serotonin-norepinephrine reuptake inhibitors (SNRIs) and anticonvulsants. Copyright © 2011 Elsevier Ltd. All rights reserved.
Pihur V, Datta S, Datta S.		Meta analysis of Chronic Fatigue Syndrome through integration of clinical, gene expression, SNP and proteomic data.	Bioinformation. 2011 Apr 22;6(3):120-4.	We start by constructing gene-gene association networks based on about 300 genes whose expression values vary between the groups of CFS patients (plus control). Connected components (modules) from these networks are further inspected for their predictive ability for symptom severity, genotypes of two single nucleotide polymorphisms (SNP) known to be associated with symptom severity, and intensity of the ten most discriminative protein features. We use two different network construction methods and choose the common genes identified in both for added validation. Our analysis identified eleven genes which may play important roles in certain aspects of CFS or related symptoms. In particular, the gene WASF3 (aka WAVE3) possibly regulates brain cytokines involved in the mechanism of fatigue through the p38 MAPK regulatory pathway.
Pinquart M, Shen Y.	Department of Psychology, Philipps University, D-35032 Marburg, Germany. pinquart@staff.uni-marburg.de	Behavior problems in children and adolescents with chronic physical illness: a meta-analysis.	J Pediatr Psychol. 2011 Oct;36(9):1003-16. Epub 2011 Aug 1.	OBJECTIVE: To examine the risk of emotional and behavioral problems among children with a chronic physical illness. METHODS: Random-effects meta-analysis was computed to integrate the results of 569 studies that used the Child Behavior Checklist, Youth Self Report, and the Teacher Report Form. RESULTS: Young people with a chronic physical illness have higher levels of internalizing (g = .47 standard mean difference), externalizing (g = .22) and total behavior problems (g = .42) than healthy peers. The largest differences were found in parental ratings and the weakest differences in adolescent self-ratings. Strongest elevations of internalizing problems were found for chronic fatigue syndrome and strongest elevations of externalizing problems were observed for epilepsy and migraine/tension-type headache. Effects also varied by country and, in part, by age, gender, year of publication, and study design. CONCLUSIONS: The results call for regular screens for psychological distress and referrals for mental health services, when needed.

Pinquart M, Shen Y.	Department of Psychology, Philipps University, D-35032 Marburg, Germany. pinquart@staff.uni-marburg.de	Depressive symptoms in children and adolescents with chronic physical illness: an updated meta-analysis.	J Pediatr Psychol. 2011 May;36(4):375-84. Epub 2010 Nov 18.	OBJECTIVE: To integrate results of available studies that compared levels of depressive symptoms of children and adolescents with chronic physical illness to healthy peers or test norms. METHODS: Random-effects meta-analysis was computed with 340 studies and 450 subsamples. RESULTS: Children and adolescents with chronic illness have, on average, higher levels of depressive symptoms than their healthy peers (d = .19 SD units). Differences are strongest for chronic fatigue syndrome (d = .94), fibromyalgia (d = .59), cleft lip and palate (d = .54), migraine/tension head ache (d = .51), and epilepsy (d = .39). Larger effect sizes were found in studies with higher proportion of girls, with a healthy control group, from developing countries, published before 1990, and that used parent rating or clinician ratings rather than child ratings. CONCLUSIONS: Pediatricians and others working with children with chronic illnesses should screen children with chronic physical illness for symptoms of psychological distress and make appropriate referrals for mental health services, when needed.
Pinquart M, Shen Y.	Philipps University, Department of Psychology, Marburg, Germany. pinquart@staff.uni-marburg.de	Anxiety in children and adolescents with chronic physical illnesses: a meta-analysis.	Acta Paediatr. 2011 Aug;100(8):1069-76. doi: 10.1111/j.1651-2227.2011.02223.x. Epub 2011 Mar 15. Comment in Acta Paediatr. 2011 Aug;100(8):1066-8.	To compare levels of anxiety of children with chronic illness with healthy peers and population norms. Meta-analysis integrated results from 332 studies. Children with chronic illness had elevated levels of anxiety (d=0.18 standard deviation units). Strongest elevations were found for chronic fatigue syndrome, migraine/tension headache, sensory impairment and epilepsy. Paediatricians should screen for anxiety symptoms in children at risk and offer interventions, if needed. © 2011 The Author(s)/Acta Paediatrica © 2011 Foundation Acta Paediatrica.
Pizzutelli S.	Pediatric Allergology, Frosinone General Hospital, Frosinone, Italy. sipizzut@tin.it	Systemic nickel hypersensitivity and diet: myth or reality?	Eur Ann Allergy Clin Immunol. 2011 Feb;43(1):5-18.	Nickel is a very common metal contained in many everyday objects and is the leading cause of ACD (Allergic Contact Dermatitis). Nickel is present in most of the constituents of a normal diet, but some food groups are usually considered to be richer. However, the nickel content of specific food can vary widely, depending on many factors. Thus, the daily intake of nickel is also highly variable both among different populations and in a single individual, in different seasons and even in different days. Measuring precisely the daily intake of nickel from food and drinks is extremely difficult, if not impossible. The relationship between ACD and contact with nickel is undisputed and widely confirmed in literature. The situation is different for systemic nickel allergy syndrome (SNAS). The SNAS can have cutaneous signs and symptoms (Systemic Contact Dermatitis or SCD) or extracutaneous signs and symptoms (gastrointestinal, respiratory, neurological, etc.).The occurrence of SCD as a systemic reaction to the nickel normally assumed in the daily diet is very controversial. A rigorous demonstration of the relationship between SCD and nickel is extremely difficult. In particular, further and larger studies are needed to assess the reality and the prevalence of nickel urticaria. With respect to nickel-related gastrointestinal symptoms, as well as chronic fatigue syndrome, fibromyalgia, headache, recurring cold sores and recurrent infections in general, the data available

				in literature are not conclusive and the studies lack the support of clear, first-hand evidence. With respect to respiratory disorders, the role of food nickel and the effectiveness of a dietary treatment have been assumed but not proven. In fact, the usefullness of a therapeutic low-nickel diet is controversial: rare, if not exceptional, and limited to very sporadic cases of SCD. Additionally, the quantitative and qualitative composition of a low-nickel diet presents few certainties and many uncertainties. The low-nickel diets suggested in literature are highly variable, both in the extension of the restrictions and in their details--and the differences are not marginal. CONCLUSION: an evaluation of the data presented by medical literature about SNAS and its relationship with oral nickel does not allow to draw final conclusions. In the absence of genuine certainty we can only conclude that further and broader studies, more rigorously conducted, are needed.
Poppe C, Crombez G, Hanoulle I, Vogelaers D, Petrovic M.	Department of General Internal Medicine, Ghent University Hospital, De Pintelaan 185, 9000, Ghent, Belgium, Carine.Poppe@ugent.be.	Mental quality of life in chronic fatigue is associated with an accommodative coping style and neuroticism: a path analysis.	Qual Life Res. 2011 Oct 29. [Epub ahead of print]	PURPOSE: An accommodative coping style (e.g. acceptance) is related to a better mental health-related quality of life (MHQL) in patients with chronic fatigue syndrome (CFS). We want to explore whether neuroticism is predictive for this coping style and MHQL. Secondly we want to explore the relation between acceptance and physical health-related quality of life (PHQL) and expect that illness-related variables such as fatigue severity and duration are related to PHQL. METHOD: In this cross-sectional study, 117 patients with chronic fatigue syndrome from an outpatient internal medicine clinic completed self-report questionnaires on quality of life (SF-36), acceptance (ICQ), personality traits (NEO-FFI) and fatigue severity (CIS). RESULTS: Regression analyses showed that neuroticism and acceptance are predictors of MHQL (38% of the variance was explained). The path analysis showed that acceptance mediates between neuroticism and MHQL and that PHQL is related to MHQL. PHQL is related to fatigue severity and duration, but not to neuroticism and acceptance. CONCLUSION: Stimulating an 'accepting accommodative coping style' within the treatment for CFS is important in improving mental quality of life. Our results suggest that neuroticism may be negatively related to acceptance and MHQL. This findings support the idea that a psychological diagnostic workout with special attention to personality traits in relation to their coping style is recommended in order to choose the most appropriate therapeutic approach in this population.
Pukhal'skiĭ AL, Shmarina GV, Aleshkin VA.		[Regulatory T-cells: modern approaches to optimization of their numbers]. [Article in Russian]	Vestn Ross Akad Med Nauk. 2011;(8):24-33.	Regulatory T-cells (Tregs) are important components of the complex adaptive system of the body responsive to environmental challenges. Tregs ensure peripheral tolerance and play an important role in control of inflammatory reactions. Several subsets of Tregs have been described. Naturally occurring CD4+CD25+ Tregs are recognized as a major subset of immune cells responsible for peripheral immune self-tolerance. Another subtype of Tregs is inducible. Such Tregs are generated in the periphery and realize their suppressive potential largely in the form of anti-inflammatory activity. The latter plays an important role in cooperation of three principal anti-inflammatory mechanisms that developed in the course of evolution:

				macrophages possessed of suppressive activity, Tregs, and stress hormones. Normally, all the three mechanisms of inflammation control are in equilibrium. However, the balance may be disturbed with ageing due to repeated episodes of stress and HPA axis activation. As a result, secretion of stress hormones coupled to antigen overload leads to Treg accumulation. In the course of time activation of the HPA axis is replaced by its inhibition manifested both as a decrease of the baseline cortisol level and a reduction of stress-induced cortisol response. Cortisol present in blood at low concentrations is no longer capable of controlling inflammation and Tregs become a principal mechanism of anti-inflammatory machinery. Superfluous Treg accumulation results in the development of functional somatic syndromes, such as chronic fatigue syndrome, and (in some patients) in the growth of tumours resulting from the suppression of anticancer immunity. On the other hand, the lack of adequate antigen loading in the childhood may delay Treg maturation. Allergy and asthma manifestations may be a consequence of such Treg insufficiency. Thus, both excess and deficiency of Tregs may be at the bottom of morbid conditions. The advances in modern pharmacology open up opportunities for developing new methods to control the Treg level.
Puri BK, Jakeman PM, Agour M, Gunatilake KD, Fernando KA, Gurusinghe AI, Treasaden IH, Waldman AD, Gishen P.	Department of Imaging, Hammersmith Hospital, London, UK.	Regional grey and white matter volumetric changes in myalgic encephalomyelitis (chronic fatigue syndrome): a voxel-based morphometry 3-T MRI study.	Br J Radiol. 2011 Nov 29. [Epub ahead of print]	Objective: It is not established whether myalgic encephalomyelitis/chronic fatigue syndrome (CFS) is associated with structural brain changes. The aim of this study was to investigate this by conducting the largest voxel-based morphometry study to date in CFS.Methods: High-resolution structural 3-T cerebral MRI scanning was carried out in 26 CFS patients and 26 age- and gender-matched healthy volunteers. Voxel-wise generalised linear modelling was applied to the processed MR data using permutation-based non-parametric testing, forming clusters at t > 2.3 and testing clusters for significance at p < 0.05, corrected for multiple comparisons across space.Results: Significant voxels (p < 0.05, corrected for multiple comparisons) depicting reduced grey matter volume in the CFS group were noted in the occipital lobes (right and left occipital poles; left lateral occipital cortex, superior division; and left supracalcrine cortex), the right angular gyrus and the posterior division of the left parahippocampal gyrus. Significant voxels (p < 0.05, corrected for multiple comparisons) depicting reduced white matter volume in the CFS group were also noted in the left occipital lobe.Conclusion: These data support the hypothesis that significant neuroanatomical changes occur in CFS, and are consistent with the complaint of impaired memory that is common in this illness; they also suggest that subtle abnormalities in visual processing, and discrepancies between intended actions and consequent movements, may occur in CFS.
Puri BK, Gunatilake KD, Fernando KA,	Imaging Department, Hammersmith	Increased tenderness in the left third intercostal space in	J Int Med Res. 2011;39(1):212-4.	A clinical sign has not thus far been associated with myalgic encephalo myelitis (ME). The present study involved systematic clinical examination that included inspection, palpation, percussion and auscultation of the thorax of 42 ME patients and 20 age-

Gurusinghe AI, Agour M, Treasaden IH.	Hospital, Du Cane Road, London W12 0HS, UK. basant.puri@imperial.ac.uk	adult patients with myalgic encephalomyelitis: a controlled study.		matched healthy controls while sitting. Left lateral third intercostal space tenderness was noted in 34 (81%) of the patients and in none of the controls, a difference that was highly statistically significant. This finding may be related to changes in lymphatic function and to the descending course of the thoracic duct. Further studies, preferably blinded and combined with appropriate imaging, are required.
Qiu X, Swanson P, Tang N, Leckie GW, Devare SG, Schochetman G, Hackett J Jr.	Infectious Diseases R&D, Abbott Diagnostics, Abbott Park, Illinois 60064, USA. xiaoxing.qiu@abbott.com	Seroprevalence of xenotropic murine leukemia virus-related virus in normal and retrovirus-infected blood donors.	Transfusion. 2012 Feb;52(2):307-16. doi: 10.1111/j.1537-2995.2011.03395.x. Epub 2011 Oct 24.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV) has been reported in patients with prostate cancer and chronic fatigue syndrome. Although results have been conflicting, the potential of XMRV as an infectious human retrovirus has raised concerns about transfusion safety. To address this issue, normal and retrovirus-infected blood donors were screened for evidence of XMRV infection. STUDY DESIGN AND METHODS: Plasma from 1000 US, 100 human immunodeficiency virus Type 1-infected Cameroonian, and 642 human T-lymphotropic virus Type I (HTLV-I)-infected or uninfected Japanese blood donors as well as 311 sexually transmitted disease diagnostic specimens were screened for antibodies to XMRV gp70 and p15E using chemiluminescent immunoassays (CMIAs). CMIA-reactive samples were evaluated by p30 CMIA, Western blot, and real-time reverse transcriptase polymerase chain reaction. RESULTS: XMRV seroreactivity was low (0%-0.6%) with the exception of the HTLV-I-infected donors (4.9%). Antibody was detected against only a single XMRV protein (p15E or gp70); none of the seroreactive samples had detectable XMRV pol or env sequences. The elevated seroreactivity in HTLV-I-infected donors was due to an increased p15E seroreactive rate (4.1%). Inspection of XMRV and HTLV sequences revealed a high level of conservation within the immunodominant region (IDR) of the transmembrane protein. In some cases, HTLV IDR peptide competitively reduced the XMRV p15E signal. CONCLUSIONS: Based on the low prevalence of seroreactivity, detection of antibody to only a single XMRV protein and the absence of XMRV sequences, this study finds no compelling evidence of XMRV in normal or retrovirus-infected blood donors. The increased p15E seroreactivity observed in HTLV infection is likely due to cross-reactive antibodies. © 2012 American Association of Blood Banks.
Racciatti D, Gorgoretti V, Sepede G, Gambi F, Pizzigallo E.	Clinic of Infectious Diseases, Department of Medicine and Aging, G. d'Annunzio University, Chieti, Italy. racciatt@unich.it	An Italian study on health-related quality of life and fatigue in patients with chronic fatigue syndrome and patients with chronic HCV virus infection: similarities and differences.	Int J Immunopathol Pharmacol. 2011 Jul-Sep;24(3):673-81.	Severe fatigue and a significantly reduced health-related quality of life (HRQoL) have been described in patients with chronic fatigue syndrome (CFS) in comparison with patients affected by chronic hepatitis C (CHC) and other chronic medical conditions. We examined 39 CFS and 49 CHC patients to explore whether fatigue and a poor HRQoL represent a greater medical and social problem in CFS than in CHC. The severity of fatigue and the HRQoL were assessed using the Fatigue Impact Scale (FIS) and the Health Status Questionnaire Short Form-36 (SF-36), respectively. The statistical analysis showed both a higher score of fatigue and a lower HRQoL in CFS than in CHC patients. Furthermore, in CHC patients the FIS evaluation showed a significantly reduced score of the psychosocial domain in comparison with the other domains. Multivariate linear regression analysis revealed female gender as the most

				important positive variable in chronic hepatitis C patients for total score of FIS. In conclusion, CFS was associated with a severe and disabling fatigue and an impaired HRQOL. In particular, both fatigue and all aspects of HRQOL perceived by CFS patients were significantly impaired compared to CHC patients. Consequently, management of fatigue should be considered a priority in order to improve HRQOL in CFS patients. In CHC patients the impact of fatigue on HRQoL was less significant than in CFS patients, even though the FIS evaluation showed a significant impairment of the psychosocial domain.
Rahman K, Burton A, Galbraith S, Lloyd A, Vollmer-Conna U.	School of Psychiatry, University of NSW, Sydney, Australia.	Sleep-wake behavior in chronic fatigue syndrome.	Sleep. 2011 May 1;34(5):671-8.	STUDY OBJECTIVES: Disturbances of the internal biological clock manifest as fatigue, poor concentration, and sleep disturbances-symptoms reminiscent of chronic fatigue syndrome (CFS) and suggestive of a role for circadian rhythm disturbance in CFS. We examined circadian patterns of activity, sleep, and cortisol secretion in patients with CFS. DESIGN: Case-control study, 5-day behavioral observation. SETTING: Natural setting/home environment PARTICIPANTS: 15 patients with CFS and 15 healthy subjects of similar age, sex, body mass index (BMI), and activity levels. INTERVENTIONS: N/A MEASUREMENTS: Self-report questionnaires were used to obtain medical history and demographic information and to assess health behaviors, somatic and psychological symptoms, and sleep quality. An actiwatch accelerometer recorded activity and sleep patterns over 5 days with concurrent activity and symptom logs. Diurnal salivary cortisol secretion was measured. Additionally, overnight heart rate monitoring and pain sensitivity assessment was undertaken. RESULTS: Ratings of symptoms, disability, sleep disturbance, and pain sensitivity were greater in patients with CFS. No between-group differences were found in the pattern or amount of sleep, activity, or cortisol secretion. Afternoon activity levels significantly increased evening fatigue in patients but not control subjects. Low nocturnal heart rate variability was identified as a biological correlate of unrefreshing sleep. CONCLUSIONS: We found no evidence of circadian rhythm disturbance in CFS. However, the role of autonomic activity in the experience of unrefreshing sleep warrants further assessment. The activity symptom-relationship modelled here is of clinical significance in the approach to activity and symptom management in the treatment of CFS.
Ravindran MK, Zheng Y, Timbol C, Merck SJ, Baraniuk JN.	Division of Rheumatology, Immunology and Allergy, Georgetown University, 3800 Reservoir Road NW, Washington, DC 20007-2197,	Migraine headaches in chronic fatigue syndrome (CFS): comparison of two prospective cross-sectional studies.	BMC Neurol. 2011 Mar 5;11:30.	BACKGROUND: Headaches are more frequent in Chronic Fatigue Syndrome (CFS) than healthy control (HC) subjects. The 2004 International Headache Society (IHS) criteria were used to define CFS headache phenotypes. METHODS: Subjects in Cohort 1 (HC = 368; CFS = 203) completed questionnaires about many diverse symptoms by giving nominal (yes/no) answers. Cohort 2 (HC = 21; CFS = 67) had more focused evaluations. They scored symptom severities on 0 to 4 anchored ordinal scales, and had structured headache evaluations. All subjects had history and physical examinations; assessments for exclusion criteria; questionnaires about CFS related symptoms (0 to 4 scale), Multidimensional Fatigue Inventory (MFI) and Medical

	USA.			Outcome Survey Short Form 36 (MOS SF-36). RESULTS: Demographics, trends for the number of diffuse "functional" symptoms present, and severity of CFS case designation criteria symptoms were equivalent between CFS subjects in Cohorts 1 and 2. HC had significantly fewer symptoms, lower MFI and higher SF-36 domain scores than CFS in both cohorts. Migraine headaches were found in 84%, and tension-type headaches in 81% of Cohort 2 CFS. This compared to 5% and 45%, respectively, in HC. The CFS group had migraine without aura (60%; MO; CFS+MO), with aura (24%; CFS+MA), tension headaches only (12%), or no headaches (4%). Co-morbid tension and migraine headaches were found in 67% of CFS. CFS+MA had higher severity scores than CFS+MO for the sum of scores for poor memory, dizziness, balance, and numbness ("Neuro-construct", p = 0.002) and perceived heart rhythm disturbances, palpitations and noncardiac chest pain ("Cardio-construct"; p = 0.045, t-tests after Bonferroni corrections). CFS+MO subjects had lower pressure-induced pain thresholds (2.36 kg [1.95-2.78; 95% C.I.] n = 40) and a higher prevalence of fibromyalgia (47%; 1990 criteria) compared to HC (5.23 kg [3.95-6.52] n = 20; and 0%, respectively). Sumatriptan was beneficial for 13 out of 14 newly diagnosed CFS migraine subjects. CONCLUSIONS: CFS subjects had higher prevalences of MO and MA than HC, suggesting that mechanisms of migraine pathogenesis such as central sensitization may contribute to CFS pathophysiology. CLINICAL TRIAL REGISTRATION: Georgetown University IRB # 2006-481
Reeves RR, Panguluri RL.	G.V. (Sonny) Montgomery VA Medical Center, (11M), 1500 E. Woodrow Wilson Drive, Jackson, MS 29216, USA. roy.reeves@va.gov	Neuropsychiatric complications of traumatic brain injury.	J Psychosoc Nurs Ment Health Serv. 2011 Mar;49(3):42-50. doi: 10.3928/02793695-20110201-03. Epub 2011 Feb 16.	Traumatic brain injury (TBI) may be defined as any extracranial mechanical force to the brain that results in any period of loss of consciousness, any loss of memory for events immediately before or after the event, or any alteration in mental status at the time of the event. The major causes are automobile accidents, falls, sporting injuries, and assaults. Many soldiers returning from combat in Afghanistan and Iraq have also experienced TBI. This article provides an overview of the neuropsychiatric complications of TBI, including impairment of consciousness, posttraumatic amnesia, cognitive disorders and dementia, posttraumatic epilepsy, aphasia, depression, mania, psychosis, anxiety disorders, personality changes, aggression, behavioral dyscontrol, fatigue/apathy, and increased risk of suicide. Discussion will focus primarily on issues affecting mental health clinicians. Because mental health providers are more involved in care of chronic issues related to TBI, these issues will be discussed in more detail, although acute neuropsychiatric complications of TBI will be briefly explained. Copyright 2011, SLACK Incorporated.
Reid S, Chalder T, Cleare A, Hotopf M, Wessely S.	Imperial College, St Mary's Hospital, London, UK.	Chronic fatigue syndrome.	Clin Evid (Online). 2011 May 26;2011. pii: 1101.	INTRODUCTION: Chronic fatigue syndrome (CFS) affects between 0.006% and 3% of the population depending on the criteria of definition used, with women being at higher risk than men. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of treatments for chronic fatigue syndrome? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2010 (Clinical Evidence

				reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 46 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: antidepressants, cognitive behavioural therapy (CBT), corticosteroids, dietary supplements, evening primrose oil, galantamine, graded exercise therapy, homeopathy, immunotherapy, intramuscular magnesium, oral nicotinamide adenine dinucleotide, and prolonged rest.
Reuter SE, Evans AM.	From the School of Pharmacy & Medical Sciences, University of South Australia, Adelaide, SA, Australia. stephanie.reuter@unisa.edu.au	Long-chain acylcarnitine deficiency in patients with chronic fatigue syndrome. Potential involvement of altered carnitine palmitoyltransferase-I activity.	J Intern Med. 2011 Jul;270(1):76-84. doi: 10.1111/j.1365-2796.2010.02341.x. Epub 2011 Jan 19.	OBJECTIVE: The underlying aetiology of chronic fatigue syndrome is currently unknown; however, in the light of carnitine's critical role in mitochondrial energy production, it has been suggested that chronic fatigue syndrome may be associated with altered carnitine homeostasis. This study was conducted to comparatively examine full endogenous carnitine profiles in patients with chronic fatigue syndrome and healthy controls. DESIGN: A cross-sectional, observational study. SETTING AND SUBJECTS: Forty-four patients with chronic fatigue syndrome and 49 age- and gender-matched healthy controls were recruited from the community and studied at the School of Pharmacy & Medical Sciences, University of South Australia. MAIN OUTCOME MEASURES: All participants completed a fatigue severity scale questionnaire and had a single fasting blood sample collected which was analysed for l-carnitine and 35 individual acylcarnitine concentrations in plasma by LC-MS/MS. RESULTS: Patients with chronic fatigue syndrome exhibited significantly altered concentrations of C8:1, C12DC, C14, C16:1, C18, C18:1, C18:2 and C18:1-OH acylcarnitines; of particular note, oleyl-L-carnitine (C18:1) and linoleyl-L-carnitine (C18:2) were, on average, 30-40% lower in patients than controls ($P < 0.0001$). Significant correlations between acylcarnitine concentrations and clinical symptomology were also demonstrated. CONCLUSIONS: It is proposed that this disturbance in carnitine homeostasis is reflective of a reduction in carnitine palmitoyltransferase-I (CPT-I) activity, possibly a result of the accumulation of omega-6 fatty acids previously observed in this patient population. It is hypothesized that the administration of omega-3 fatty acids in combination with l-carnitine would increase CPT-I activity and improve chronic fatigue syndrome symptomology. © 2011 The Association for the Publication of the Journal of Internal Medicine.
Revicki DA, Rentz AM, Luo MP, Wong RL.	Outcomes Research, United BioSource Corporation, Bethesda, MD,	Psychometric characteristics of the short form 36 health survey and functional assessment of	Health Qual Life Outcomes. 2011 May 22;9:36.	BACKGROUND: We evaluated the psychometric characteristics of the Short Form 36 (SF-36) Health Survey and the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue subscale in patients with ankylosing spondylitis (AS). METHODS: We analyzed clinical and patient-reported outcome (PRO) data collected during 12-week, double-blind, placebo-controlled periods of two randomized controlled trials

	USA. dennis.revicki@unitedbiosource.com	chronic illness Therapy-Fatigue subscale for patients with ankylosing spondylitis.		comparing adalimumab and placebo for the treatment of active AS. The Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Functional Index, and other clinical measures were collected during the clinical trial. We evaluated internal consistency/reliability, construct validity, and responsiveness to change for the SF-36 and FACIT-Fatigue. RESULTS: The SF-36 (Cronbach alpha, 0.74-0.92) and FACIT-Fatigue (Cronbach alpha, 0.82-0.86) both had good internal consistency/reliability. At baseline, SF-36 and FACIT-Fatigue scores correlated significantly with Ankylosing Spondylitis Quality of Life scores ($r = -0.36$ to -0.66 and $r = -0.70$, respectively; all $p < 0.0001$). SF-36 scores varied by indicators of clinical severity, with greater impairment observed for more severe degrees of clinical activity (all $p < 0.0001$). FACIT-Fatigue scores correlated significantly with SF-36 scores ($r = 0.42$ to 0.74; all $p < 0.0001$) and varied by clinical severity ($p < 0.05$ to $p < 0.0001$). CONCLUSIONS: The SF-36 is a reliable, valid, and responsive measure of health-related quality of life and the FACIT-Fatigue is a brief and psychometrically sound measure of the effects of fatigue on patients with AS. These PROs may be useful in evaluating effectiveness of new treatments for AS.
Reyes Del Paso GA, Pulgar A, Duschek S, Garrido S.	Department of Psychology, University of Jaén, Jaen, Spain.	Cognitive impairment in fibromyalgia syndrome: The impact of cardiovascular regulation, pain, emotional disorders and medication.	Eur J Pain. 2011 Dec 19. doi: 10.1002/j.1532-2149.2011.00032.x. [Epub ahead of print]	This study investigated cognitive performance in fibromyalgia syndrome (FMS) and its association with cardiovascular and clinical parameters. Thirty-five patients with FMS and 29 matched healthy controls completed a neuropsychological test measuring attention and arithmetic processing. As possible factors underlying the expected cognitive impairment, clinical pain intensity, co-morbid depression and anxiety disorders, sleep complaints, medication use, as well as blood pressure parameters were investigated. The patients' test performance was substantially reduced, particularly in terms of lower speed of cognitive processing and restricted improvement of performance in the course of the task. While the extent of depression, anxiety, fatigue and sleep complaints was unrelated to test performance, better performance was observed in patients showing lower pain ratings and those using opiate medication. The data corroborate the presence of substantial cognitive impairment in FMS. While the experience of chronic pain is crucial in mediating the deficits, co-morbid depression, anxiety, fatigue and sleep complaints play only a subordinate role. In the control group, but not in the patients, blood pressure was inversely associated with mental performance. This finding is in line with the well known cognitive impairment in hypertension. The lack of this association in FMS confirms previous research showing aberrances in the interaction between blood pressure and central nervous function in the affected patients. © 2011 European Federation of International Association for the Study of Pain Chapters.
Rimes KA, Wingrove J.	University of Bath, Department of Psychology, Claverton Down,	Mindfulness-Based Cognitive Therapy for People with Chronic Fatigue Syndrome	Clin Psychol Psychother. 2011 Oct 9. doi: 10.1002/cpp.793.	Cognitive behaviour therapy (CBT) is an effective treatment for chronic fatigue syndrome (CFS; sometimes known as myalgic encephalomyelitis). However, only a minority of patients fully recover after CBT; thus, methods for improving treatment outcomes are required. This pilot study concerned a mindfulness-based cognitive

	Bath, UK. K.A.Rimes@bath.ac.uk.	Still Experiencing Excessive Fatigue after Cognitive Behaviour Therapy: A Pilot Randomized Study.	[Epub ahead of print]	therapy (MBCT) intervention adapted for people with CFS who were still experiencing excessive fatigue after CBT. The study aimed to investigate the acceptability of this new intervention and the feasibility of conducting a larger-scale randomized trial in the future. Preliminary efficacy analyses were also undertaken. Participants were randomly allocated to MBCT or waiting list. Sixteen MBCT participants and 19 waiting-list participants completed the study, with the intervention being delivered in two separate groups. Acceptability, engagement and participant-rated helpfulness of the intervention were high. Analysis of covariance controlling for pre-treatment scores indicated that, at post-treatment, MBCT participants reported lower levels of fatigue (the primary clinical outcome) than the waiting-list group. Similarly, there were significant group differences in fatigue at 2-month follow-up, and when the MBCT group was followed up to 6 months post-treatment, these improvements were maintained. The MBCT group also had superior outcomes on measures of impairment, depressed mood, catastrophic thinking about fatigue, all-or-nothing behavioural responses, unhelpful beliefs about emotions, mindfulness and self-compassion. In conclusion, MBCT is a promising and acceptable additional intervention for people still experiencing excessive fatigue after CBT for CFS, which should be investigated in a larger randomized controlled trial. Copyright © 2011 John Wiley & Sons, Ltd. KEY PRACTITIONER MESSAGE: Only about 30% of people with chronic fatigue syndrome (CFS) recover after cognitive behaviour therapy (CBT); thus, methods for improving treatment outcomes are needed. This is the first pilot randomized study to demonstrate that a mindfulness-based intervention was associated with reduced fatigue and other benefits for people with CFS who were still experiencing excessive fatigue after a course of CBT. Levels of acceptability, engagement in the intervention and rated helpfulness were high. A larger-scale randomized controlled trial is required. Copyright © 2011 John Wiley & Sons, Ltd.
Robinson MJ, Erlwein O, McClure MO.	Section of Infectious Diseases, Jefferiss Research Trust Laboratories, Imperial College London, St Mary's Campus, London, W2 1PG, UK.	Xenotropic murine leukaemia virus-related virus (XMRV) does not cause chronic fatigue.	Trends Microbiol. 2011 Nov;19(11):525-9. Epub 2011 Oct 4.	The xenotropic murine leukaemia virus-related virus (XMRV), a gammaretrovirus, was discovered in prostate cancer tumours by Virochip technology in 2006. It was subsequently detected in chronic fatigue patients in 2009. The association between XMRV and chronic fatigue has proved to be controversial. No study has confirmed these findings and many have refuted them. Here, we present the evidence for our contention that XMRV is not a human pathogen. Copyright © 2011 Elsevier Ltd. All rights reserved.
Robinson MJ, Tuke PW, Erlwein O, Tettmar KI, Kaye S, Naresh KN, Patel A, Walker MM,	Section of Infectious Diseases, Jefferiss Research Trust Laboratories,	No Evidence of XMRV or MuLV Sequences in Prostate Cancer, Diffuse Large B-Cell Lymphoma, or the	Adv Virol. 2011;2011:782353. Epub 2011 Jun 9.	Xenotropic murine leukaemia virus-related virus (XMRV) is a recently described retrovirus which has been claimed to infect humans and cause associated pathology. Initially identified in the US in patients with prostate cancer and subsequently in patients with chronic fatigue syndrome, doubt now exists that XMRV is a human pathogen. We studied the prevalence of genetic sequences of XMRV and related

Kimura T, Gopalakrishnan G, Tedder RS, McClure MO.	Imperial College London, St Mary's Campus, London W2 1PG, UK.	UK Blood Donor Population.		MuLV sequences in human prostate cancer, from B cell lymphoma patients and from UK blood donors. Nucleic acid was extracted from fresh prostate tissue biopsies, formalin-fixed paraffin-embedded (FFPE) prostate tissue and FFPE B-cell lymphoma. The presence of XMRV-specific LTR or MuLV generic gag-like sequences was investigated by nested PCR. To control for mouse DNA contamination, a PCR that detected intracisternal A-type particle (IAP) sequences was included. In addition, DNA and RNA were extracted from whole blood taken from UK blood donors and screened for XMRV sequences by real-time PCR. XMRV or MuLV-like sequences were not amplified from tissue samples. Occasionally MuLV gag and XMRV-LTR sequences were amplified from Indian prostate cancer samples, but were always detected in conjunction with contaminating murine genomic DNA. We found no evidence of XMRV or MuLV infection in the UK blood donors.
Rosenblum H, Shoenfeld Y, Amital H.	Department of Medicine B, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Tel-Hashomer 52621, Israel.	The common immunogenic etiology of chronic fatigue syndrome: from infections to vaccines via adjuvants to the ASIA syndrome.	Infect Dis Clin North Am. 2011 Dec;25(4):851-63. Epub 2011 Sep 9.	Chronic fatigue syndrome (CFS) is characterized by unexplained fatigue that lasts for at least 6 months with a constellation of other symptoms. Most cases start suddenly, and are usually accompanied by a flu-like illness. It is a symptom-based diagnosis of exclusion, the pathogenesis of which is unknown. Studies have examined and hypothesized about the possible biomedical and epidemiologic characteristics of the disease, including genetic predisposition, infections, endocrine abnormalities, and immune dysfunction and psychological and psychosocial factors. Recently, the AISA (autoimmune/inflammatory syndrome induced by adjuvants) syndrome was recognized, indicating the possible contribution of adjuvants and vaccines to the development of autoimmunity. Copyright Â© 2011 Elsevier Inc. All rights reserved.
Ruiz E, Alegre J, García Quintana AM, Aliste L, Blázquez A, Fernández de Sevilla T.	Servicio de Medicina Interna, Unidad de Urgencias, Hospital General Universitario Vall d'Hebron, Barcelona, España. evruiz@vhebron.net	[Chronic fatigue syndrome: study of a consecutive series of 824 cases assessed in two specialized units]. [Article in Spanish]	Rev Clin Esp. 2011 Sep;211(8):385-90. Epub 2011 Jul 27. Comment in Rev Clin Esp. 2011 Sep;211(8):407-9.	BACKGROUND AND OBJECTIVE: The chronic fatigue syndrome (CFS) is a disabling disorder. Few studies are available in our area on the prevalence and characteristics of CFS. Therefore, we carried out a study of a consecutive series of 824 cases diagnosed in two specialized units. PATIENTS AND METHODS: We evaluated all of the CFS patients seen from January 2008 to June 2010. We analyzed social and demographic data, employment status, time of clinical evolution, trigger factors and onset, Fukuda and Canadian criteria, associated comorbidities and treatment. RESULTS: A total of 824 patients were included, 748 (91%) woman, mean age 48±9 years. Average age of onset of symptoms was 35±11 years, time to diagnosis 108±88 month. A precipitating factor was identified in 481 (58%) patients, the onset was gradual in 517 (63%) and 515 (62.5%) were not employed. The most outstanding diagnostic criteria of Fukuda were prolonged generalized fatigue after exercise, sleep disturbance and impairments in concentration and short-term memory. The different groups of symptoms defined by the Canadian consensus showed that CFS is a homogeneous entity. Accompanying comorbidity phenomena were anxiety 691 (83%), sicca syndrome 678 (82%), fibromyalgia 450 (55%). A total of 63% of patients (520) received pharmacological treatment. CONCLUSIONS: CFS is an illness that preferentially affects young women and results in employment absenteeism. The

				most relevant clinical features were prolonged generalized fatigue after exercise, neurocognitive impairment and sleep disturbance. In the evaluation of the patient, it is very important to apply the Canadian criteria and to assess comorbidity. Copyright © 2011 Elsevier España, S.L. All rights reserved.
Rumage C, Falca-Dodson M, Santos SL, Teichman R.	War Related Illness and Injury Study Center, New Jersey.	Medically unexplained symptoms in the veteran population: challenges and opportunities.	MD Advis. 2011 Spring;4(2):34-6.	
Sachdeva AK, Kuhad A, Chopra K.	University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Study, Panjab University, Chandigarh, India.	Epigallocatechin gallate ameliorates behavioral and biochemical deficits in rat model of load-induced chronic fatigue syndrome.	Brain Res Bull. 2011 Oct 10;86(3-4):165-72. Epub 2011 Jul 28.	Chronic fatigue syndrome is a heterogeneous disorder with unknown pathogenesis and etiology, characterized by tiredness, difficulty in concentration and memory, and concomitant skeletal and muscular pain, thus affecting both mental and physical domains. The pathogenesis of chronic fatigue syndrome is multifactorial and involves increased oxido-nitrosative stress along with generation of pro-inflammatory cytokines such as TNF-α. In the present study chronic fatigue was produced in rats by plunging a load of 10 ± 2% body weight and subjecting them to forced swim inside a rectangular jar daily for 28 days. Endurance capacity and post-swim fatigue were assessed on 1st, 7th, 14th, 21st and 28th days. EGCG was administered daily by oral gavage 30 min before forced swim session. On the 29th day, after assessment of various behavioral parameters, blood was collected through tail vein, and animals were sacrificed to harvest the brains, spleens and thymus. Chronic fatigue group exhibited significant behavioral alterations along with enhanced oxido-nitrosative stress and serum TNF-α level as compared to naive group. Chronic treatment with EGCG restored all the behavioral and biochemical alterations associated with chronic fatigue syndrome. The present study signifies the therapeutic potential of EGCG for the treatment of chronic fatigue syndrome. Copyright © 2011 Elsevier Inc. All rights reserved.
Sakakibara S, Sakakibara K, Tosato G.	Laboratory of Cellular Oncology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Building 37, Room 4134, Bethesda, MD 20892-1907, USA. sakakibs@mail.ni	NF-kappaB activation stimulates transcription and replication of retrovirus XMRV in human B-lineage and prostate carcinoma cells.	J Virol. 2011 Apr;85(7):3179-86. Epub 2011 Jan 26.	Xenotropic murine leukemia virus-related virus (XMRV) is a gammaretrovirus linked to prostate carcinoma and chronic fatigue syndrome. Here we report that NF-κB activation can markedly increase XMRV production. The inflammatory cytokine tumor necrosis factor alpha (TNF-α), which activates NF-κB, significantly augmented viral Gag protein production in XMRV-infected cells. Reporter assays showed that TNF-α and Epstein-Barr virus (EBV) latent membrane protein 1 (LMP1), an intrinsic NF-κB activator, increased long terminal repeat (LTR)-dependent XMRV transcription. We identified two NF-κB binding sites (designated κB-1 and κB-2) in the LTR U3 region of XMRV and demonstrated that both sites bind to the NF-κB component p65/RelA. Mutation of the κB-1 site, but not the κB-2 site, impaired responsiveness to TNF-α and LMP1 in reporter assays. A mutant XMRV with a mutation at the κB-1 site replicated significantly less efficiently than the wild-type XMRV in the prostate carcinoma LNCaP,

	h.gov			DU145, and PC-3 cell lines, HEK293 cells, the EBV-immortalized cell line IB4, and the Burkitt's lymphoma cell line BJAB. These results demonstrate that TNF-α and EBV LMP1 enhance XMRV replication in prostate carcinoma and B-lineage cells through the κB-1 site in the XMRV LTR, suggesting that inflammation, EBV infection, and other conditions leading to NF-κB activation may promote XMRV spread in humans.
Sakuma T, Hué S, Squillace KA, Tonne JM, Blackburn PR, Ohmine S, Thatava T, Towers GJ, Ikeda Y.	Department of Molecular Medicine, Mayo Clinic, Rochester, MN 55905, USA.	No evidence of XMRV in prostate cancer cohorts in the Midwestern United States.	Retrovirology. 2011 Mar 29;8:23.	BACKGROUND: Xenotropic murine leukemia virus (MLV)-related virus (XMRV) was initially identified in prostate cancer (PCa) tissue, particularly in the prostatic stromal fibroblasts, of patients homozygous for the RNASEL R462Q mutation. A subsequent study reported XMRV antigens in malignant prostatic epithelium and association of XMRV infection with PCa, especially higher-grade tumors, independently of the RNASEL polymorphism. Further studies showed high prevalence of XMRV or related MLV sequences in chronic fatigue syndrome patients (CFS), while others found no, or low, prevalence of XMRV in a variety of diseases including PCa or CFS. Thus, the etiological link between XMRV and human disease remains elusive. To address the association between XMRV infection and PCa, we have tested prostate tissues and human sera for the presence of viral DNA, viral antigens and anti-XMRV antibodies. RESULTS: Real-time PCR analysis of 110 PCa (Gleason scores >4) and 40 benign and normal prostate tissues identified six positive samples (5 PCa and 1 non-PCa). No statistical link was observed between the presence of proviral DNA and PCa, PCa grades, and the RNASEL R462Q mutation. The amplified viral sequences were distantly related to XMRV, but nearly identical to endogenous MLV sequences in mice. The PCR positive samples were also positive for mouse mitochondrial DNA by nested PCR, suggesting contamination of the samples with mouse DNA. Immuno-histochemistry (IHC) with an anti-XMRV antibody, but not an anti-MLV antibody that recognizes XMRV, sporadically identified antigen-positive cells in prostatic epithelium, irrespectively of the status of viral DNA detection. No serum (159 PCa and 201 age-matched controls) showed strong neutralization of XMRV infection at 1:10 dilution. CONCLUSION: The lack of XMRV sequences or strong anti-XMRV neutralizing antibodies indicates no or very low prevalence of XMRV in our cohorts. We conclude that real-time PCR- and IHC-positive samples were due to laboratory contamination and non-specific immune reactions, respectively.
Santamarina-Perez P, Eiroa-Orosa FJ, Freniche V, Moreno-Mayos A, Alegre J, Saez N, Jacas C.	Hospital Universitari Vall d'Hebron, Barcelona, Spain. psantamarina@vhebron.net	Length of illness does not predict cognitive dysfunction in chronic fatigue syndrome.	Appl Neuropsychol. 2011 Jul;18(3):216-22.	Neuropsychological studies have shown cognitive impairment in chronic fatigue syndrome (CFS), particularly in information-processing speed. The aim of this study was to examine the evolution of cognitive impairment in CFS. The evolution is one of the most disabling aspects of the CFS, and it has received little attention in the literature. Fifty-six women with CFS were assessed with neuropsychological tests. Patients were divided into three groups based on the duration of the disease. There were no differences between groups in terms of cognitive function. The cognitive impairment in CFS was not found to be more severe with longer disease duration. These data suggest that there is no progressive cognitive impairment in patients with

				CFS. Therefore, the cognitive deficits in CFS should be treated with cognitive rehabilitation programs focused on improving emotional distress associated to the illness and on promoting functional abilities.
Santamarina-Pérez P, Freniche V, Eiroa-Orosa FJ, Llobet G, Sáez N, Alegre J, Jacas C.	Servicio de Psiquiatría, Hospital Universitario Vall d'Hebron, Universitat Autònoma de Barcelona, España. psantamarina@vhebron.net	[The role of depression in cognitive impairment in patients with chronic fatigue syndrome]. [Article in Spanish]	Med Clin (Barc). 2011 Mar 12;136(6):239-43. Epub 2010 Dec 9. Comment in Med Clin (Barc). 2011 Nov 12;137(12):572; author reply 572-3.	BACKGROUND AND OBJECTIVE: To analyze the role of depression in cognitive deficits of patients with chronic fatigue syndrome (CFS). PATIENTS AND METHODS: 57 women with CFS were assessed by neuropsychological tests that included measures of attention: CalCap, Mental control of the WMS-III, PASAT, forward and backward digits (WAIS-III), symbol digit modalities test (SDMT); executive functions: Stroop Test, Trail Making Test (TMT A y B), FAS, Tower of London; memory: Auditory-Verbal Learning Test (AVL), Rey Complex Figure (RCF), and psychomotor skills: Grooved Pegboard. The raw scores on the tests were adjusted according to normative data and transformed to T scores. The sample was divided into two groups based on the presence or absence of depression, assessed by clinical interview and administration of the Hospital Anxiety and Depression Scale (HADS). This study compared neuropsychological test scores between the two groups. RESULTS: CFS patients showed cognitive deficit in attention and executive functions, regardless of the presence of depression. There were no significant differences between the two CFS groups. CONCLUSIONS: The cognitive impairments in patients with CFS are not secondary to the presence of depression. These results should be taken into account in the implementation of therapeutic programs in these patients. Copyright © 2010 Elsevier España, S.L. All rights reserved.
Sato E, Yoshikawa R, Miyazawa T.	Laboratory of Signal Transduction, Department of Cell Biology, Institute for Virus Research, Kyoto University.	Quantitative Assays for Xenotropic Murine Leukemia Virus-Related Virus.	J Vet Med Sci. 2011 Sep 30. [Epub ahead of print]	Xenotropic murine leukemia virus-related virus (XMRV), a novel gammaretrovirus in humans, was found in patients with prostate cancer (PC) and chronic fatigue syndrome (CFS). However, there has been controversy whether XMRV is directly associated with human diseases. In this study, we developed a LacZ marker rescue assay using human embryonic kidney 293T cells and a focus assay using a feline fibroblastic sarcoma-positive leukemia-negative QN10S cells. XMRV induced prominent foci in QN10S cells and the viral titer determined by the focus assay was as high as that by the LacZ marker rescue assay. Because the focus assay is simple and sensitive, it will be useful for monitoring infectious XMRVs in CFS and PC patients and virological studies for XMRV.
Satterfield BC, Garcia RA, Jia H, Tang S, Zheng H, Switzer WM.	Cooperative Diagnostics, LLC, Greenwood, SC 29646, USA. brent@codiagnostics.com	Serologic and PCR testing of persons with chronic fatigue syndrome in the United States shows no association with xenotropic or polytropic murine leukemia virus-	Retrovirology. 2011 Feb 22;8:12.	In 2009, a newly discovered human retrovirus, xenotropic murine leukemia virus (MuLV)-related virus (XMRV), was reported by Lombardi et al. in 67% of persons from the US with chronic fatigue syndrome (CFS) by PCR detection of gag sequences. Although six subsequent studies have been negative for XMRV, CFS was defined more broadly using only the CDC or Oxford criteria and samples from the US were limited in geographic diversity, both potentially reducing the chances of identifying XMRV positive CFS cases. A seventh study recently found polytropic MuLV sequences, but not XMRV, in a high proportion of persons with CFS. Here we tested blood specimens from 45 CFS cases and 42 persons without CFS from over 20 states in the United

		related viruses.		States for both XMRV and MuLV. The CFS patients all had a minimum of 6 months of post-exertional malaise and a high degree of disability, the same key symptoms described in the Lombardi et al. study. Using highly sensitive and generic DNA and RNA PCR tests, and a new Western blot assay employing purified whole XMRV as antigen, we found no evidence of XMRV or MuLV in all 45 CFS cases and in the 42 persons without CFS. Our findings, together with previous negative reports, do not suggest an association of XMRV or MuLV in the majority of CFS cases.
Sayburn A.		Study linking chronic fatigue syndrome with retrovirus is partially retracted.	BMJ. 2011 Sep 26;343:d6097. doi: 10.1136/bmj.d6097.	
Schmidt S, Grossman P, Schwarzer B, Jena S, Naumann J, Walach H.	Department of Environmental Health Sciences, University Medical Center, Freiburg, Germany. stefan.schmidt@uniklinik-freiburg.de	Treating fibromyalgia with mindfulness-based stress reduction: results from a 3-armed randomized controlled trial.	Pain. 2011 Feb;152(2):361-9. Epub 2010 Dec 13.	Mindfulness-based stress reduction (MBSR) is a structured 8-week group program teaching mindfulness meditation and mindful yoga exercises. MBSR aims to help participants develop nonjudgmental awareness of moment-to-moment experience. Fibromyalgia is a clinical syndrome with chronic pain, fatigue, and insomnia as major symptoms. Efficacy of MBSR for enhanced well-being of fibromyalgia patients was investigated in a 3-armed trial, which was a follow-up to an earlier quasi-randomized investigation. A total of 177 female patients were randomized to one of the following: (1) MBSR, (2) an active control procedure controlling for nonspecific effects of MBSR, or (3) a wait list. The major outcome was health-related quality of life (HRQoL) 2 months post-treatment. Secondary outcomes were disorder-specific quality of life, depression, pain, anxiety, somatic complaints, and a proposed index of mindfulness. Of the patients, 82% completed the study. There were no significant differences between groups on primary outcome, but patients overall improved in HRQoL at short-term follow-up (P=0.004). Post hoc analyses showed that only MBSR manifested a significant pre-to-post-intervention improvement in HRQoL (P=0.02). Furthermore, multivariate analysis of secondary measures indicated modest benefits for MBSR patients. MBSR yielded significant pre-to-post-intervention improvements in 6 of 8 secondary outcome variables, the active control in 3, and the wait list in 2. In conclusion, primary outcome analyses did not support the efficacy of MBSR in fibromyalgia, although patients in the MBSR arm appeared to benefit most. Effect sizes were small compared to the earlier, quasi-randomized investigation. Several methodological aspects are discussed, e.g., patient burden, treatment preference and motivation, that may provide explanations for differences. In a 3-armed randomized controlled trial in female patients suffering from fibromyalgia, patients benefited modestly from a mindfulness-based stress reduction intervention.
Schneider S, Stone AA, Schwartz JE,	Department of Psychiatry &	Peak and end effects in patients' daily	J Pain. 2011 Feb;12(2):228-35.	Clinical research often relies on retrospective recall of symptom levels, but the information contained in these ratings is not well understood. The "peak-and-end

Broderick JE.	Behavioral Science, Stony Brook University, Stony Brook, New York 11794-8790, USA. Stefan.Schneider@sunysb.edu	recall of pain and fatigue: a within-subjects analysis.		rule" suggests that the most intense (peak) and final (end) moments of an experience disproportionately influence retrospective judgments, which may bias self-reports of somatic symptoms. This study examined the extent to which peak and end symptom levels systematically affect patients' day-to-day recall of pain and fatigue. Rheumatology patients (N = 97) completed 5 to 6 momentary ratings of pain and fatigue per day as well as a daily recall rating of these symptoms for 28 consecutive days. For pain, peak and end momentary ratings predicted daily recall of average pain beyond the actual average of momentary ratings. This effect was small, yet was confirmed in both between-person and within-person (repeated measures) analyses. For fatigue, neither peak nor end momentary symptoms significantly contributed to daily recall. Of note, the evidence for peak- and end-effects in recall of pain and fatigue varied significantly between individual patients. These findings suggest that peak- and end-effects create a small bias in recall reports of pain, but not fatigue. However, there are considerable individual differences in susceptibility to peak and end heuristics. PERSPECTIVE: The peak-end cognitive heuristic could bias end-of-day recall of pain and fatigue. An effect was shown for pain, but not for fatigue. The effects were small and were unlikely to substantially bias end-of-day assessments. Individuals were shown to differ in the degree that the heuristic was associated with recall. Copyright © 2011 American Pain Society. Published by Elsevier Inc. All rights reserved.
Schreurs KM, Veehof MM, Passade L, Vollenbroek-Hutten MM.	University of Twente, Enschede, The Netherlands. k.m.g.schreurs@utwente.nl	Cognitive behavioural treatment for chronic fatigue syndrome in a rehabilitation setting: effectiveness and predictors of outcome.	Behav Res Ther. 2011 Dec;49(12):908-13. Epub 2011 Sep 28.	Cognitive behavioural therapy (CBT) was combined with graded exercise therapy (GET) for patients with chronic fatigue syndrome (CFS) in an uncontrolled implementation study of an inpatient multidisciplinary group therapy. During the intake procedure, 160 CFS patients completed a questionnaire on fatigue related measurements, physical impairment, depression, somatic and psychological attributions, somatic focus, and sense of control over symptoms. Pre-treatment physical activity level was measured with an actometer. At baseline, post-treatment and 6-month follow-up individual strength, subjective fatigue and physical impairment, were reassessed. Large effect sizes were found on subjective fatigue (1.2 post-treatment; 1.2 follow-up) and physical impairment (-.9 post-treatment; -.9 follow-up), Clinically significant improvement was found in 33.8% of the participants at post-treatment and 30.6% at follow-up. Individual strength at post-treatment was predicted by level of physical activity before treatment, and by sense of control over symptoms and physical activity at follow-up. Clinically significant improvement in subjective fatigue was predicted by not receiving a disablement insurance benefit, shorter duration of fatigue, higher sense of control over symptoms and, at follow-up by more pre-treatment physical activity. In conclusion, the intervention was effective for CFS patients. Cognitive behavioural factors that perpetuate fatigue symptoms are also predictors of treatment outcome. Copyright Â© 2011 Elsevier Ltd. All rights reserved.

Schrier M, Amital D, Arnson Y, Rubinow A, Altaman A, Nissenabaum B, Amital H.	Department of Medicine 'B', Sheba Medical Center, 52621, Tel-Hashomer, Ramat-Gan, Israel.	Association of fibromyalgia characteristics in patients with non-metastatic breast cancer and the protective role of resilience.	Rheumatol Int. 2011 Sep 8. [Epub ahead of print]	Cancer patients often complain about weakness, fatigue, and pain. The aim of this study was to assess the features of the fibromyalgia syndrome (FMS) characteristics in patients with non-metastatic breast cancer. The study group included 40 women whose age ranged from 40 to 70 years with Stages 0-3 breast cancer. The control group included 40 healthy women matched by age. A diagnosis of FMS was established based on medical history, physical examination, and the Fibromyalgia Impact Questionnaire (FIQ). Pain measures and functional factors were evaluated by the Brief Pain Inventory and the Sheehan Questionnaire. Resilience was assessed by Antanovsky's Sense of Coherence Questionnaire. Psychiatric disturbances were tested by the MINI Questionnaire and Hamilton questionnaires for depression and anxiety. The prevalence of chronic pain was higher in the study group. Statistically significant differences were also found between the group regarding pain, fatigue, and functional measures. The prevalence of depressive or anxious mood, measured by the Hamilton questionnaires, was strongly related to FMS characteristics reflected by FIQ scores (r = 0.79 between FIQ and the Hamilton Depression Index and r = 0.75 between FIQ and the Hamilton Anxiety Scale). The sense of coherence measure for these patients demonstrated an inverse correlation with pain, fatigue, and functional capability. Women with breast cancer tend to develop chronic widespread pain syndromes more often than do healthy women.
Schutzer SE, Angel TE, Liu T, Schepmoes AA, Clauss TR, Adkins JN, Camp DG, Holland BK, Bergquist J, Coyle PK, Smith RD, Fallon BA, Natelson BH.	Department of Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey, United States of America. schutzer@umdnj.edu	Distinct cerebrospinal fluid proteomes differentiate post-treatment lyme disease from chronic fatigue syndrome.	PLoS One. 2011 Feb 23;6(2):e17287.	BACKGROUND: Neurologic Post Treatment Lyme disease (nPTLS) and Chronic Fatigue (CFS) are syndromes of unknown etiology. They share features of fatigue and cognitive dysfunction, making it difficult to differentiate them. Unresolved is whether nPTLS is a subset of CFS. METHODS AND PRINCIPAL FINDINGS: Pooled cerebrospinal fluid (CSF) samples from nPTLS patients, CFS patients, and healthy volunteers were comprehensively analyzed using high-resolution mass spectrometry (MS), coupled with immunoaffinity depletion methods to reduce protein-masking by abundant proteins. Individual patient and healthy control CSF samples were analyzed directly employing a MS-based label-free quantitative proteomics approach. We found that both groups, and individuals within the groups, could be distinguished from each other and normals based on their specific CSF proteins ($p<0.01$). CFS ($n=43$) had 2,783 non-redundant proteins, nPTLS ($n=25$) contained 2,768 proteins, and healthy normals had 2,630 proteins. Preliminary pathway analysis demonstrated that the data could be useful for hypothesis generation on the pathogenetic mechanisms underlying these two related syndromes. CONCLUSIONS: nPTLS and CFS have distinguishing CSF protein complements. Each condition has a number of CSF proteins that can be useful in providing candidates for future validation studies and insights on the respective mechanisms of pathogenesis. Distinguishing nPTLS and CFS permits more focused study of each condition, and can lead to novel diagnostics and therapeutic interventions.
Schutzer SE,	Departments of	Analysis of	Ann Neurol. 2011	Recent reports showed many patients with chronic fatigue syndrome (CFS) harbor a

Rounds MA, Natelson BH, Ecker DJ, Eshoo MW.	Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, NJ 07103, USA. schutzer@umdnj.edu	cerebrospinal fluid from chronic fatigue syndrome patients for multiple human ubiquitous viruses and xenotropic murine leukemia-related virus.	Apr;69(4):735-8. doi: 10.1002/ana.22389. Epub 2011 Apr 6. Comment in Ann Neurol. 2011 Aug;70(2):341. Ann Neurol. 2011 Apr;69(4):A9-A10.	retrovirus, xenotropic murine leukemia-related virus (XMRV), in blood; other studies could not replicate this finding. A useful next step would be to examine cerebrospinal fluid, because in some patients CFS is thought to be a brain disorder. Finding a microbe in the central nervous system would have greater significance than in blood because of the integrity of the blood-brain barrier. We examined cerebrospinal fluid from 43 CFS patients using polymerase chain reaction techniques, but did not find XMRV or multiple other common viruses, suggesting that exploration of other causes or pathogenetic mechanisms is warranted. Copyright © 2011 American Neurological Association.
Selin LK, Wlodarczyk MF, Kraft AR, Nie S, Kenney LL, Puzone R, Celada F.	Department of Pathology, University of Massachusetts Medical School, Worcester, MA 01655, USA. liisa.selin@umassmed.edu	Heterologous immunity: immunopathology, autoimmunity and protection during viral infections.	Autoimmunity. 2011 Jun;44(4):328-47. Epub 2011 Jan 20.	Heterologous immunity is a common phenomenon present in all infections. Most of the time it is beneficial, mediating protective immunity, but in some individuals that have the wrong crossreactive response it leads to a cascade of events that result in severe immunopathology. Infections have been associated with autoimmune diseases such as diabetes, multiple sclerosis and lupus erythematosis, but also with unusual autoimmune like pathologies where the immune system appears dysregulated, such as, sarcoidosis, colitis, panniculitis, bronchiolitis obliterans, infectious mononucleosis and even chronic fatigue syndrome. Here we review the evidence that to better understand these autoreactive pathologies it requires an evaluation of how T cells are regulated and evolve during sequential infections with different pathogens under the influence of heterologous immunity.
Selmi C, Mix E, Zettl UK.	Division of Rheumatology, Allergy, and Clinical Immunology, University of California, Davis, United States; Autoimmunity and Metabolism Unit, Department of Medicine, IRCCS Istituto Clinico Humanitas, Rozzano, Italy.	A clear look at the neuroimmunology of multiple sclerosis and beyond.	Autoimmun Rev. 2012 Jan;11(3):159-62. Epub 2011 May 23.	The term neuroimmunology was first coined to refer to a generic involvement of the immune system in the pathogenesis of neurological diseases, particularly of the central nervous system. Since then, the neuroimmunology spectrum has steadily grown and currently spans from classical autoimmune diseases of the central and peripheral nervous systems to previously unsuspected conditions such as autism spectrum disorders or chronic fatigue syndrome. Multiple sclerosis remains the predominant entity in terms of research efforts and social pressure as well as a good model of organ-specific autoimmune disease with limited therapeutic options. While the fast-pace genome-wide association studies reported a number of genes to be significantly associated with multiple sclerosis, these currently explain only a minor part of disease susceptibility. Further, clinicians are continuously challenged with the clinical classifications of immune-mediated or autoimmune central and peripheral conditions and with other pragmatic questions such as the roles of vaccination and physical therapy. For these reasons the present collection of Autoimmunity Reviews is timely as it will address these major issues related to neuroimmunology. Copyright © 2011 Elsevier B.V. All rights reserved.
Senel K, Baygutalp F, Baykal T, Erdal A, Ugur M.	Department of Physical Medicine and	Melatonin levels in premenopausal women with	Rheumatol Int. 2011 Dec 23. [Epub ahead of print]	The fibromyalgia syndrome (FMS) is a chronic, widespread pain disorder of unknown etiology. It has been suggest that familial component, environmental factors, endocrine and neurotransmitter alterations, and psychological factors may contribute

	Rehabilitation, Atatürk University Medical Faculty, Erzurum, Turkey, kazimsenel@gmail.com.	fibromyalgia syndrome.		to the development of FMS. The role of melatonin in FMS is unclear. Some studies describe a lower nocturnal peak and a decreased secretion of melatonin in women with FMS when compared with healthy matched controls. The aim of the present study was to determine the possible role of melatonin in FMS patients. We examined the characteristics and levels of melatonin in 25 consecutive premenopausal women with FMS. Serum blood samples were collected from 25 patients and 20 the age and gender matched healthy controls. Melatonin levels were measured by enzyme-linked immunosorbent assay. Then, the results were compared with those from healthy subjects. Serum melatonin levels of FMS patients were not statistically different from those of controls ($P > 0.05$). No association was observed between melatonin levels of patients with FMS and disease duration, sleep disturbances, fatigue, and pain scores. Our results demonstrate that melatonin levels were similar in patients with FMS and healthy controls. Further studies are needed to determine the possible role of melatonin.
Sepede G, Racciatti D, Gorgoretti V, Nacci M, Pizzigallo E, Onofrj M, Di Giannantonio M, Niolu C, Salerno RM, Gambi F.	Department of Neuroscience and Imaging, University of Chieti, Italy. g.sepede@unich.it	Psychophysical distress and alexithymic traits in Chronic Fatigue Syndrome with and without comorbid depression.	Int J Immunopathol Pharmacol. 2011 Oct-Dec;24(4):1017-25.	Patients with Chronic Fatigue Syndrome (CFS) often report a comorbid depressive disorder. Comorbid depression may negatively influence the long-term outcome of CFS therefore it must be correctly diagnosed and treated. The aim of the present study is to provide a clinical and psychometric assessment of CFS patients with and without depressive features. A comparative analysis between 57 CFS subjects (CDC, 1994), 17 of whom with a comorbid depression, and 55 matched healthy volunteers was assessed to evaluate the presence of any psychophysical distress and alexithymic traits, by means of Symptom Checklist-90-R (SCL-90R) and Toronto Alexithymia Scale (TAS-20). The severity of fatigue was also assessed in all CFS patients using the Fatigue Impact Scale (FIS). With regard to psychiatric comorbidity, the SCL-90R scores showed higher levels of somatic complaints in CFS patients than in healthy subjects, whereas augmented depressive and obsessive-compulsive symptoms were observed only in the depressed CFS subgroup. When comparing the TAS-20 scores, we observed a selective impairment in the capacity to identify feelings and emotions, as measured by the Difficulty in Identifying Feelings subscale (DIF), non-depressed CFS patients showing an intermediate score between depressed CFS and healthy controls. Finally, in terms of FIS scores, a statistical trend versus a higher fatigue severity in depressed CFS patients, with respect to non-depressed ones, was observed. In conclusion, comorbid depression in CFS significantly increased the level of psychophysical distress and the severity of alexithymic traits. These findings suggest an urgent need to address and treat depressive disorders in the clinical care of CFS cases, to improve social functioning and quality of life in such patients.
Setty MK, Devadas K, Ragupathy V, Ravichandran V, Tang S, Wood O,	Center for Biologics Evaluation and Research, Food	XMRV: usage of receptors and potential co-receptors.	Virol J. 2011 Sep 6;8:423.	BACKGROUND: XMRV is a gammaretrovirus first identified in prostate tissues of Prostate Cancer (PC) patients and later in the blood cells of patients with Chronic Fatigue Syndrome (CFS). Although XMRV is thought to use XPR1 for cell entry, it infects A549 cells that do not express XPR1, suggesting usage of other receptors or

Gaddam DS, Lee S, Hewlett IK.	and Drug Administration, Bethesda, MD 20892, USA. indira.hewlett@fda.hhs.gov			co-receptors. METHODS: To study the usage of different receptors and co- receptors that could play a role in XMRV infection of lymphoid cells and GHOST (GFP- Human osteosarcoma) cells expressing CD4 along with different chemokine receptors including CCR1, CCR2, etc., were infected with XMRV. Culture supernatants and cells were tested for XMRV replication using real time quantitative PCR. RESULTS: Infection and replication of XMRV was seen in a variety of GHOST cells, LNCaP, DU145, A549 and Caski cell lines. The levels of XMRV replication varied in different cell lines showing differential replication in different cell lines. However, replication in A549 which lacks XPR1 expression was relatively higher than DU145 but lower than, LNCaP. XMRV replication varied in GHOST cell lines expressing CD4 and each of the co-receptors CCR1-CCR8 and bob. There was significant replication of XMRV in CCR3 and Bonzo although it is much lower when compared to DU145, A549 and LNCaP. CONCLUSION: XMRV replication was observed in GHOST cells that express CD4 and each of the chemokine receptors ranging from CCR1- CCR8 and BOB suggesting that infectivity in hematopoietic cells could be mediated by use of these receptors.
Sharpe M.		Chronic fatigue syndrome: neurological, mental or both.	J Psychosom Res. 2011 Jun;70(6):498-9. Epub 2011 Apr 20. Comment on J Psychosom Res. 2011 Jun;70(6):500-4. J Psychosom Res. 2011 Jun;70(6):573-4.	
Shin CH, Bateman L, Schlaberg R, Bunker AM, Leonard CJ, Hughen RW, Light AR, Light KC, Singh IR.	Department of Pathology, University of Utah, 15 North Medical Drive East, Suite 2100, Salt Lake City, UT 84112, USA.	Absence of XMRV retrovirus and other murine leukemia virus-related viruses in patients with chronic fatigue syndrome.	339. J Virol. 2011 Jul;85(14):7195-202. Epub 2011 May 4.	Chronic fatigue syndrome (CFS) is a multisystem disorder characterized by prolonged and severe fatigue that is not relieved by rest. Attempts to treat CFS have been largely ineffective primarily because the etiology of the disorder is unknown. Recently, CFS has been associated with xenotropic murine leukemia virus-related virus (XMRV) as well as other murine leukemia virus (MLV)-related viruses, though not all studies have found these associations. We collected blood samples from 100 CFS patients and 200 self-reported healthy volunteers from the same geographical area. We analyzed these in a blind manner using molecular, serological, and viral replication assays. We also analyzed samples from patients in the original study that reported XMRV in CFS patients. We did not find XMRV or related MLVs either as viral sequences or infectious viruses, nor did we find antibodies to these viruses in any of the patient samples, including those from the original study. We show that at least some of the discrepancy with previous studies is due to the presence of trace amounts of mouse DNA in the Taq polymerase enzymes used in these previous studies. Our findings do not support an association between CFS and MLV-related viruses, including XMRV, and the off-label use of antiretrovirals for the treatment of CFS does not seem justified at present.
Shinohara M.		The PACE trial in	Lancet. 2011 May	

		chronic fatigue syndrome.	28;377(9780):1833-4; author reply 1834-5. Epub 2011 May 16. Erratum in Lancet. 2011 Jul 16;378(9787):228. Comment on Lancet. 2011 Mar 5;377(9768):823-36. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5.	
Silva-Tinoco R, Castillo-Martínez L, Orea-Tejeda A, Orozco-Gutiérrez JJ, Vázquez-Díaz O, Montaño-Hernández P, Flores-Rebollar A, Reza-Albarrán A.		Developing thyroid disorders is associated with poor prognosis factors in patient with stable chronic heart failure.	Int J Cardiol. 2011 Mar 3;147(2):e24-5. Epub 2009 Feb 8.	We sought to assess the developing of thyroid disorders in forty eight patients with chronic stable heart failure and without thyroid abnormalities during six months follow-up. Thyroid function disorders were observed in 27.1% of the subjects: sick euthyroid syndrome (12.5%), subclinical hypothyroidism (10.4%) and overt hypothyroidism (6.2%). Subjects with higher thyroid stimulating hormone (TSH) levels at the end of the study had more hospitalizations. The developing of altered thyroid profile was related to lower hemoglobin levels, smaller phase angle with bioelectrical impedance method and more fatigue perception by the patients. This abnormal thyroid function behavior on stable chronic heart failure and was observed as part of the disease progress and was associated to worse prognosis factors as lower phase angle and anemia. Copyright © 2009 Elsevier Ireland Ltd. All rights reserved.
Silverman RH, Das Gupta J, Lombardi VC, Ruscetti FW, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Mikovits JA.	Department of Cancer Biology, The Lerner Research Institute, The Cleveland Clinic Foundation, Cleveland, OH 44195, USA.	Partial Retraction.	Science. 2011 Sep 22. [Epub ahead of print]	In our 23 October 2009 Report, "Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome," two of the coauthors, Silverman and Das Gupta, analyzed DNA samples from chronic fatigue syndrome (CFS) patients and healthy controls. A reexamination by Silverman and Das Gupta of the samples they used shows that some of the CFS peripheral blood mononuclear cell (PBMC) DNA preparations are contaminated with XMRV plasmid DNA.
Silverman RH, Das Gupta J, Lombardi VC, Ruscetti FW, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-		Partial retraction. Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome.	Science. 2011 Oct 14;334(6053):176. Partial retraction of Lombardi VC, Ruscetti FW, Das Gupta J, Pfost MA, Hagen KS, Peterson DL, Ruscetti	

Sadowski C, Gold B, Dean M, Mikovits JA.			SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA. Science. 2009 Oct 23;326(5952):585-9.	
Silvério R, Laviano A, Rossi Fanelli F, Seelaender M.		l-carnitine and cancer cachexia: Clinical and experimental aspects.	J Cachexia Sarcopenia Muscle. 2011 Mar;2(1):37-44. Epub 2011 Jan 26.	Cancer cachexia is a multifaceted syndrome characterized, among many symptoms, by extensive muscle wasting. Chronic systemic inflammation, partly triggered and sustained by cytokines, as well as increased oxidative stress contributes to the pathogenesis of this complex metabolic disorder. l-carnitine plays a central role in the metabolism of fatty acids and shows important antioxidant and anti-inflammatory properties. Systemic carnitine depletion has been described in several diseases, and it is characterized by fatigue, muscle weakness, and decreased tolerance to metabolic stress. In cachectic cancer patients, low serum carnitine levels have been reported, and this change has been suggested to play an important contributory role in the development of cachexia. Based on these data, carnitine supplementation has been tested in preliminary studies concerning human cachexia, resulting in improved fatigue and quality of life. We present here a review of clinical and experimental evidence regarding the use of carnitine supplementation in the management of cancer cachexia.
Simmons G, Glynn SA, Komaroff AL, Mikovits JA, Tobler LH, Hackett J Jr, Tang N, Switzer WM, Heneine W, Hewlett IK, Zhao J, Lo SC, Alter HJ, Linnen JM, Gao K, Coffin JM, Kearney MF, Ruscetti FW, Pfost MA, Bethel J, Kleinman S, Holmberg JA, Busch MP; Blood XMRV Scientific Research Working Group (SRWG). Collaborators: Glynn S, Holmberg	Blood Systems Research Institute and University of California, San Francisco, San Francisco, CA 94118, USA.	Failure to confirm XMRV/MLVs in the blood of patients with chronic fatigue syndrome: a multi-laboratory study.	Science. 2011 Nov 11;334(6057):814-7. Epub 2011 Sep 22.	Murine leukemia viruses (MLVs), including xenotropic-MLV-related virus (XMRV), have been controversially linked to chronic fatigue syndrome (CFS). To explore this issue in greater depth, we compiled coded replicate samples of blood from 15 subjects previously reported to be XMRV/MLV-positive (14 with CFS) and from 15 healthy donors previously determined to be negative for the viruses. These samples were distributed in a blinded fashion to nine laboratories, which performed assays designed to detect XMRV/MLV nucleic acid, virus replication, and antibody. Only two laboratories reported evidence of XMRV/MLVs; however, replicate sample results showed disagreement, and reactivity was similar among CFS subjects and negative controls. These results indicate that current assays do not reproducibly detect XMRV/MLV in blood samples and that blood donor screening is not warranted.

JA, Bianco C, Busch MP, Dodd RY, Katz LM, Kleinman SH, Komaroff AL, Mikovits JA, Simmons G, Stramer SL, Tobler LH, Vernon SD, Alter H, Coffin J, Mangan DF, Ruscetti F, Kuehnert MJ, Hendry RM, Heneine W, Monroe SS, Switzer WM, Epstein J, Hewlett IK, Lo SC.				
Slatten LA, David Carson K, Carson PP.	Department of Management, University of Louisiana at Lafayette, USA. las3678@louisiana.edu	Compassion fatigue and burnout: what managers should know.	Health Care Manag (Frederick). 2011 Oct;30(4):325-33. doi: 10.1097/HCM.0b013e31823511f7.	Most health care employees experience and are bolstered by compassion satisfaction as they deal with patients in need. However, the more empathetic a health care provider is, the more likely he or she will experience compassion fatigue. Compassion fatigue is a negative syndrome that occurs when dealing with the traumatic experiences of patients, and examples of symptoms include intrusive thoughts, sleeping problems, and depression. Compassion fatigue is different from burnout. Compassion fatigue is a rapidly occurring disorder for primary health care workers who work with suffering patients, whereas burnout, a larger construct, is a slowly progressing disorder for employees who typically are working in burdensome organizational environments. Managers can mitigate problems associated with compassion fatigue with a number of interventions including patient reassignments, formal mentoring programs, employee training, and a compassionate organizational culture. With burnout, health care managers will want to focus primarily on chronic organizational problems.
Smith AK, Fang H, Whistler T, Unger ER, Rajeevan MS.	Division of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, Atlanta, GA	Convergent genomic studies identify association of GRIK2 and NPAS2 with chronic fatigue syndrome.	Neuropsychobiology. 2011;64(4):183-94. Epub 2011 Sep 9.	BACKGROUND: There is no consistent evidence of specific gene(s) or molecular pathways that contribute to the pathogenesis, therapeutic intervention or diagnosis of chronic fatigue syndrome (CFS). While multiple studies support a role for genetic variation in CFS, genome-wide efforts to identify associated loci remain unexplored. We employed a novel convergent functional genomics approach that incorporates the findings from single-nucleotide polymorphism (SNP) and mRNA expression studies to identify associations between CFS and novel candidate genes for further investigation. METHODS: We evaluated 116,204 SNPs in 40 CFS and 40 nonfatigued control subjects

	30333, USA.			along with mRNA expression of 20,160 genes in a subset of these subjects (35 CFS subjects and 27 controls) derived from a population-based study. RESULTS: Sixty-five SNPs were nominally associated with CFS (p<0.001), and 165 genes were differentially expressed (≥4-fold; p≤0.05) in peripheral blood mononuclear cells of CFS subjects. Two genes, glutamate receptor, ionotropic, kinase 2 (GRIK2) and neuronal PAS domain protein 2 (NPAS2), were identified by both SNP and gene expression analyses. Subjects with the G allele of rs2247215 (GRIK2) were more likely to have CFS (p=0.0005), and CFS subjects showed decreased GRIK2 expression (10-fold; p=0.015). Subjects with the T allele of rs356653 (NPAS2) were more likely to have CFS (p=0.0007), and NPAS2 expression was increased (10-fold; p=0.027) in those with CFS. CONCLUSION: Using an integrated genomic strategy, this study suggests a possible role for genes involved in glutamatergic neurotransmission and circadian rhythm in CFS and supports further study of novel candidate genes in independent populations of CFS subjects. Copyright © 2011 S. Karger AG, Basel.
Smith HS, Harris R, Clauw D.	Albany Medical College, Department of Anesthesiology, Albany, NY 12208, USA. smithh@mail.amc.edu	Fibromyalgia: an afferent processing disorder leading to a complex pain generalized syndrome.	Pain Physician. 2011 Mar-Apr;14(2):E217-45.	Fibromyalgia is a condition which appears to involve disordered central afferent processing. The major symptoms of fibromyalgia include multifocal pain, fatigue, sleep disturbances, and cognitive or memory problems. Other symptoms may include psychological distress, impaired functioning, and sexual dysfunction. The pathophysiology of fibromyalgia remains uncertain but is believed to be largely central in nature. In 1990 the American College of Rheumatology (ACR) published diagnostic research criteria for fibromyalgia. The criteria included a history of chronic and widespread pain and the presence of 11 or more out of 18 tender points. Pain was considered chronic widespread when all of the following are present: pain in the left side of the body; pain in the right side of the body; pain above the waist; pain below the waist. In addition, axial skeletal pain must be present and the duration of pain must be more than 3 months. A tender point is considered positive when pain can be elicited by pressures of 4 kg/cm2 or less. For tender points to be considered positive, the patient must perceive the palpation as painful; tenderness to palpation is not sufficient. However, over the next 20 years it became increasingly appreciated that the focus on tender points was not justified. In 2010 a similar group of investigators performed a multicenter study of 829 previously diagnosed fibromyalgia patients and controls using physician physical and interview examinations, including a widespread pain index (WPI), a measure of the number of painful body regions. Random forest and recursive partitioning analyses were used to guide the development of a case definition of fibromyalgia, to develop new preliminary ACR diagnostic criteria, and to construct a symptom severity (SS) scale. The most important diagnostic variables were WPI and categorical scales for cognitive symptoms, un-refreshed sleep, fatigue, and number of somatic symptoms. The categorical scales were summed to create an SS scale. The investigators combined the SS scale and the WPI to recommend a new case definition of fibromyalgia: (WPI > or =

				7 AND SS > or = 5). Although there is no known cure for fibromyalgia, multidisciplinary team efforts using combined treatment approaches, including patient education, aerobic exercise, cognitive behavioral therapy, and pharmacologic therapies (serotonin norepinephrine reuptake inhibitors [e.g., duloxetine, milnacipran] and alpha 2-delta receptor ligands [e.g., pregabalin]) might improve symptoms as well as function in patients with fibromyalgia.
Smits B, van den Heuvel L, Knoop H, Küsters B, Janssen A, Borm G, Bleijenberg G, Rodenburg R, van Engelen B.	Neuromuscular Center Nijmegen, Department of Neurology, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands. b.smits@neuro.umcn.nl	Mitochondrial enzymes discriminate between mitochondrial disorders and chronic fatigue syndrome.	Mitochondrion. 2011 Sep;11(5):735-8. Epub 2011 Jun 2.	We studied the extent of mitochondrial involvement in chronic fatigue syndrome (CFS) and investigated whether measurement of mitochondrial respiratory chain complex (RCC) activities discriminates between CFS and mitochondrial disorders. Mitochondrial content was decreased in CFS compared to healthy controls, whereas RCC activities corrected for mitochondrial content were not. Conversely, mitochondrial content did not discriminate between CFS and two groups of mitochondrial disorders, whereas ATP production rate and complex I, III and IV activity did, all with higher activities in CFS. We conclude that the ATP production rate and RCC activities can reliably discriminate between mitochondrial disorders and CFS.
Smolensky MH, Di Milia L, Ohayon MM, Philip P.	The University of Texas-Houston Health Sciences Center, United States. msmolensky@austin.rr.com	Sleep disorders, medical conditions, and road accident risk.	Accid Anal Prev. 2011 Mar;43(2):533-48.	Sleep disorders and various common acute and chronic medical conditions directly or indirectly affect the quality and quantity of one's sleep or otherwise cause excessive daytime fatigue. This article reviews the potential contribution of several prevalent medical conditions - allergic rhinitis, asthma, chronic obstructive pulmonary disease, rheumatoid arthritis/osteoarthritis - and chronic fatigue syndrome and clinical sleep disorders - insomnia, obstructive sleep apnea, narcolepsy, periodic limb movement of sleep, and restless legs syndrome - to the risk for drowsy-driving road crashes. It also explores the literature on the cost-benefit of preventive interventions, using obstructive sleep apnea as an example. Although numerous investigations have addressed the impact of sleep and medical disorders on quality of life, few have specifically addressed their potential deleterious effect on driving performance and road incidents. Moreover, since past studies have focused on the survivors of driver crashes, they may be biased. Representative population-based prospective multidisciplinary studies are urgently required to clarify the role of the fatigue associated with common ailments and medications on traffic crash risk of both commercial and non-commercial drivers and to comprehensively assess the cost-effectiveness of intervention strategies.
Sommerfeldt L, Portilla H, Jacobsen L, Gjerstad J, Wyller VB.	Oslo University Hospital, Norway.	Polymorphisms of adrenergic cardiovascular control genes are associated with	Acta Paediatr. 2011 Feb;100(2):293-8. doi: 10.1111/j.1651-2227.2010.02072.x. Epub 2010 Nov 18.	AIM: To explore the frequency of polymorphisms in adrenergic cardiovascular control genes in adolescent with chronic fatigue syndrome (CFS) and the relation of such polymorphisms to cardiovascular variables. METHODS: DNA from 53 patients with CFS, 12-18 years old, was analysed for five single nucleotide polymorphisms (SNPs) in the genes catechol-O-methyltransferase (COMT), the β_2 -adrenergic receptor (two

		adolescent chronic fatigue syndrome.		SNPs), the β_1 -adrenergic receptor and the α_2(a) -adrenergic receptor. Frequencies were compared to a reference population constructed from the National Center for Biotechnology Information (NCBI) database, and associations between frequencies and autonomic cardiovascular responses during a 20° head-up tilt-test were explored. RESULTS: For the COMT SNP Rs4680, patients with CFS had a higher frequency of the AA genotype and a lower frequency of the G containing genotypes (AG and GG), when compared to the reference sample (p = 0.046). Also, the AA genotype was associated with a smaller increase in LF/HF ratio (low-frequency:high-frequency heart rate variability ratio, an index of cardiac sympathovagal balance) during head-up tilt when compared to the AG/GG genotypes. For the β_2 -adrenergic receptor SNP Rs1042714, patients with CFS had a lower frequency of the GG genotype and a higher frequency of the genotypes containing C (CG and CC) (p = 0.044). CONCLUSIONS: CFS might be related to polymorphisms of COMT and the β_2 -adrenergic receptor. More details of the molecular mechanisms remain to be investigated. © 2010 The Author(s)/Acta Paediatrica © 2010 Foundation Acta Paediatrica.
Soriano V.		[XMRV, a new human retrovirus for disease]. [Article in Spanish]	Med Clin (Barc). 2011 May 28;136(15):669-70. Epub 2011 Mar 5.	
Spindler J, Hackett J Jr, Qiu X, Wiegand A, Boltz VF, Swanson P, Bream JH, Jacobson LP, Li X, Rinaldo CR, Wolinsky SM, Coffin JM, Mellors JW.	HIV Drug Resistance Program, National Cancer Institute, Frederick, MD 21702-1201, USA.	Prevalence of XMRV Nucleic Acid and Antibody in HIV-1-Infected Men and in Men at Risk for HIV-1 Infection.	Adv Virol. 2011;2011:268214. Epub 2011 Nov 21.	Xenotropic MLV-Related Virus (XMRV) was recently reported to be associated with prostate cancer and chronic fatigue syndrome (CFS). Infection was also reported in 3.7% of healthy individuals. These highly reported frequencies of infection prompted concerns about the possibility of a new, widespread retroviral epidemic. The Multicenter AIDS Cohort Study (MACS) provides an opportunity to assess the prevalence of XMRV infection and its association with HIV-1 infection among men who have sex with men. Reliable detection of XMRV infection requires the application of multiple diagnostic methods, including detection of human antibodies to XMRV and detection of XMRV nucleic acid. We, therefore, tested 332 patient plasma and PBMC samples obtained from recent visits in a subset of patients in the MACS cohort for XMRV antibodies using Abbott prototype ARCHITECT chemiluminescent immunoassays (CMIAs) and for XMRV RNA and proviral DNA using a XMRV single-copy qPCR assay (X-SCA). Although 9 of 332 (2.7%) samples showed low positive reactivity against a single antigen in the CMIA, none of these samples or matched controls were positive for plasma XMRV RNA or PBMC XMRV DNA by X-SCA. Thus, we found no evidence of XMRV infection among men in the MACS regardless of HIV-1 serostatus.
Sprott H.	Rheumaklinik und Institut für Physikalische Medizin,	[Is fibromyalgia a viral disease?]. [Article in German]	Z Rheumatol. 2011 Oct;70(8):637-8.	Are viruses responsible for the pain in patients with fibromyalgia? Are viruses the trigger for rheumatoid arthritis? Is chronic fatigue syndrome a viral disease? There are many open questions with few or controversial answers. According to the current state of knowledge on the origin of the pain in fibromyalgia the varied symptomatic of

	UniversitätsSpital Zürich, Gloriastr. 25, CH-8091, Zürich, Schweiz. haiko.sprott@usz.ch			fibromyalgia is triggered by peripheral as well as central mechanisms. Despite the broad spectrum of symptoms the disease is a specific entity which is mainly treated with dual reuptake inhibitors, anticonvulsives, tramadol, selective serotonin reuptake inhibitors, gamma-hydroxybutyrate and dopamine agonists in individually selected combinations.
Steffen I, Tyrrell DL, Stein E, Montalvo L, Lee TH, Zhou Y, Lu K, Switzer WM, Tang S, Jia H, Hockman D, Santer DM, Logan M, Landi A, Law J, Houghton M, Simmons G.	Blood Systems Research Institute, San Francisco, California, United States of America.	No evidence for XMRV nucleic acids, infectious virus or anti-XMRV antibodies in Canadian patients with chronic fatigue syndrome.	PLoS One. 2011;6(11):e27870. Epub 2011 Nov 17.	The gammaretroviruses xenotropic murine leukemia virus (MLV)-related virus (XMRV) and MLV have been reported to be more prevalent in plasma and peripheral blood mononuclear cells of chronic fatigue syndrome (CFS) patients than in healthy controls. Here, we report the complex analysis of whole blood and plasma samples from 58 CFS patients and 57 controls from Canada for the presence of XMRV/MLV nucleic acids, infectious virus, and XMRV/MLV-specific antibodies. Multiple techniques were employed, including nested and qRT-PCR, cell culture, and immunoblotting. We found no evidence of XMRV or MLV in humans and conclude that CFS is not associated with these gammaretroviruses.
Stewart JM, Medow MS, Messer ZR, Baugham IL, Terilli C, Ocon AJ.	1New York Medical College.	Postural Neurocognitive and Neuronal Activated Cerebral Blood Flow Deficits in Young Chronic Fatigue Syndrome Patients with Postural Tachycardia Syndrome.	Am J Physiol Heart Circ Physiol. 2011 Dec 16. [Epub ahead of print]	Neurocognition is impaired in Chronic Fatigue Syndrome (CFS). We propose that impairment relates to postural cerebral hemodynamics. 25 CFS and 20 control subjects underwent incremental upright tilt at 0°, 15°, 30°, 45°, 60°, and 75° with continuous measurement of arterial blood pressure and cerebral blood flow velocity (CBFv). We used an N-back task with N ranging from 0 to 4 (increased N= increased task difficulty) to test working memory and information processing. We measured N-back outcomes by the number of correct answers and by reaction time. We measured CBFv, critical closing pressure (CCP), and CBFv altered by neuronal activity (activated CBFv) during each N and every tilt angle using transcranial Doppler ultrasound. N-Back outcome in controls decreased with N but was independent of tilt angle. N-Back outcome in CFS decreased with N but deteriorated as orthostasis progressed. Absolute mean CBFv was slightly less than control in CFS at each angle. Activated CBFv in controls was independent of tilt angle and increased with N. In contrast, activated CBFv averaged 0 in CFS, decreased with angle and was less than control. CCP was increased in CFS suggesting increased vasomotor tone and decreased metabolic control of CBFv. CCP did not change with orthostasis in CFS, but decreased monotonically in control subjects, consistent with vasodilation as compensation for the orthostatic reduction of cerebral perfusion pressure. Increasing orthostatic stress impairs neurocognition in CFS. CBFv activation, normally tightly linked to cognitive neuronal activity, is unrelated to cognitive performance in CFS; increased CCP and vasomotor tone may indicate uncoupling of the neurovascular unit during orthostasis.
Stieler K, Schindler S, Schlomm T, Hohn O, Bannert	Institute for Medical Microbiology and	No detection of XMRV in blood samples and tissue	PLoS One. 2011;6(10):e25592. Epub 2011 Oct 12.	BACKGROUND: We recently published the rare detection of xenotropic murine leukemia virus-related virus (XMRV) (1/105) in prostate cancer (PCA) tissue of patients in Northern Europe by PCR. The controversial discussion about the virus

N, Simon R, Minner S, Schindler M, Fischer N.	Virology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.	sections from prostate cancer patients in Northern Europe.		being detected in PCA tissue, blood samples from patients suffering from chronic fatigue syndrome (CFS), as well as from a significant number of healthy controls prompted us to deepen our studies about detection of XMRV infection applying different detection methods (PCR, cocultivation and immunohistochemistry [IHC]). METHODOLOGY/PRINCIPAL FINDINGS: Peripheral blood mononuclear cells (PBMCs) from 92 PCA and 7 healthy controls were isolated, PHA activated and cocultivated with LNCaP cells for up to 8 weeks. Supernatant of these cells was applied to a reporter cell line, DERSE-iGFP. Furthermore, the PBMCs and cocultivated LNCaP cells were tested for the presence of XMRV by PCR as well as Western Blot analysis. While all PCR amplifications and Western Blot analyses were negative for signs of XMRV infection, DERSE-iGFP cells displayed isolated GFP positive cells in three cases. In all three cases XMRV presence could not be confirmed by PCR technology. In addition, we performed XMRV specific IHC on PCA tissue sections. Whole tissue sections (n = 20), as well as tissue microarrays (TMA) including 50 benign prostate hyperplasia (BPH), 50 low grade and 50 high grade PCA sections and TMAs including breast cancer, colon cancer and normal tissues were stained with two XMRV specific antisera. XMRV protein expression was not detected in any cancer sections included. One BPH tissue displayed XMRV specific protein expression in random isolated basal cells. CONCLUSION: We were unable to conclusively detect XMRV in the blood from PCA patients or from healthy controls and there is no conclusive evidence of XMRV protein expression in PCA, breast cancer and colon cancer tissue sections tested by IHC staining.
Stone K.		Paper linking XMRV to chronic fatigue syndrome stirs controversy.	Ann Neurol. 2011 Sep;70(3):A7-8. doi: 10.1002/ana.22599.	
Stouten B, Goudsmit EM, Riley N.		The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1832-3; author reply 1834-5. Epub 2011 May 16. Comment on Lancet. 2011 Mar 5;377(9768):823-36. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5.	
Sullivan PF, Allander T, Lysholm F, Goh S, Persson B, Jacks A,	Department of Genetics, University of North Carolina at	An unbiased metagenomic search for infectious agents using monozygotic	BMC Microbiol. 2011 Jan 2;11:2.	BACKGROUND: Chronic fatigue syndrome is an idiopathic syndrome widely suspected of having an infectious or immune etiology. We applied an unbiased metagenomic approach to try to identify known or novel infectious agents in the serum of 45 cases with chronic fatigue syndrome or idiopathic chronic fatigue. Controls were the

Evengård B, Pedersen NL, Andersson B.	Chapel Hill, Chapel Hill, NC, USA. pfsulliv@med.unc.edu	twins discordant for chronic fatigue.		unaffected monozygotic co-twins of cases, and serum samples were obtained at the same place and time. RESULTS: No novel DNA or RNA viral signatures were confidently identified. Four affected twins and no unaffected twins evidenced viremia with GB virus C (8.9% vs. 0%, p = 0.019), and one affected twin had previously undetected hepatitis C viremia. An excess of GB virus C viremia in cases with chronic fatigue requires confirmation. CONCLUSIONS: Current, impairing chronic fatigue was not robustly associated with viremia detectable in serum.
Swift TR.		Reply to Schutzer et al.	Ann Neurol. 2011 Aug;70(2):341. doi: 10.1002/ana.22492. Comment on Ann Neurol. 2011 Apr;69(4):735-8.	
Switzer WM, Zheng H, Simmons G, Zhou Y, Tang S, Shankar A, Kapusinszky B, Delwart EL, Heneine W.	Laboratory Branch, Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. bswitzer@cdc.gov	No evidence of murine leukemia virus-related viruses in live attenuated human vaccines.	PLoS One. 2011;6(12):e29223. Epub 2011 Dec 22.	BACKGROUND: The association of xenotropic murine leukemia virus (MLV)-related virus (XMRV) in prostate cancer and chronic fatigue syndrome reported in previous studies remains controversial as these results have been questioned by recent data. Nonetheless, concerns have been raised regarding contamination of human vaccines as a possible source of introduction of XMRV and MLV into human populations. To address this possibility, we tested eight live attenuated human vaccines using generic PCR for XMRV and MLV sequences. Viral metagenomics using deep sequencing was also done to identify the possibility of other adventitious agents. RESULTS: All eight live attenuated vaccines, including Japanese encephalitis virus (JEV) (SA-14-14-2), varicella (Varivax), measles, mumps, and rubella (MMR-II), measles (Attenuvax), rubella (Meruvax-II), rotavirus (Rotateq and Rotarix), and yellow fever virus were negative for XMRV and highly related MLV sequences. However, residual hamster DNA, but not RNA, containing novel endogenous gammaretrovirus sequences was detected in the JEV vaccine using PCR. Metagenomics analysis did not detect any adventitious viral sequences of public health concern. Intracisternal A particle sequences closest to those present in Syrian hamsters and not mice were also detected in the JEV SA-14-14-2 vaccine. Combined, these results are consistent with the production of the JEV vaccine in Syrian hamster cells. CONCLUSIONS: We found no evidence of XMRV and MLV in eight live attenuated human vaccines further supporting the safety of these vaccines. Our findings suggest that vaccines are an unlikely source of XMRV and MLV exposure in humans and are consistent with the mounting evidence on the absence of these viruses in humans.
Szu-Ting Fu T, Koutstaal W, Poon L, Cleare AJ.	Institute of Biomedical Sciences, Academia Sinica, 6F, No. 16, Alley	Confidence judgment in depression and dysphoria: The depressive realism vs. negativity	J Behav Ther Exp Psychiatry. 2012 Jun;43(2):699-704. Epub 2011 Oct 5.	BACKGROUND AND OBJECTIVES: According to the negativity hypothesis, depressed individuals are over-pessimistic due to negative self-concepts. In contrast, depressive realism suggests that depressed persons are realistic compared to their nondepressed controls. However, evidence supporting depressive realism predominantly comes from judgment comparisons between controls and nonclinical dysphoric samples

	10, Lane 437, Pa-The Rd Sec 2, Taipei 10552, Taiwan.	hypotheses.		when the controls showed overconfident bias. This study aimed to test the validity of the two accounts in clinical depression and dysphoria. METHODS: Sixty-eight participants, including healthy controls (n = 32), patients with DSM-IV major depression (n = 20), and dysphoric participants with CDC-defined chronic fatigue syndrome (n = 16) performed an adjective recognition task and reported their item-by-item confidence judgments and post-test performance estimate (PTPE). RESULTS: Compared to realistic PTPE made by the controls, patients with major depression showed significant underconfidence. The PTPE of the dysphoric participants was relatively accurate. Both the depressed and dysphoric participants displayed less item-by-item overconfidence as opposed to significant item-by-item overconfidence shown by the controls. LIMITATIONS: The judgment-accuracy patterns of the three groups need to be replicated with larger samples using non-memory task domains. CONCLUSION: The present study confirms depressive realism in dysphoric individuals. However, toward a more severe depressive emotional state, the findings did not support depressive realism but are in line with the prediction of the negativity hypothesis. It is not possible to determine the validity of the two hypotheses when the controls are overconfident. Dissociation between item-by-item and retrospective confidence judgments is discussed. Copyright © 2011 Elsevier Ltd. All rights reserved.
Tak LM, Cleare AJ, Ormel J, Manoharan A, Kok IC, Wessely S, Rosmalen JG.	Interdisciplinary Center for Psychiatric Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.	Meta-analysis and meta-regression of hypothalamic-pituitary-adrenal axis activity in functional somatic disorders.	Biol Psychol. 2011 May;87(2):183-94. Epub 2011 Feb 18.	Dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis is the most investigated biological risk marker in functional somatic disorders (FSDs), such as chronic fatigue syndrome (CFS), fibromyalgia (FM), and irritable bowel syndrome (IBS). Our aim was to assess whether there is an association between basal hypocortisolism and FSD and to identify potential moderators of this association. Meta-analysis on 85 studies revealed that although basal cortisol levels were generally lower in FSD subjects compared to controls, this association did not reach statistical significance (SMD -0.07, 95% CI -0.17 to 0.04, p=0.241). However, when the three FSD were assessed separately, statistically significant basal hypocortisolism was observed in CFS subjects compared to controls (SMD -0.14, 95% CI -0.28 to 0.00, p=0.047), but not in FM or IBS. When all potential moderators were entered into a meta-regression analysis, only type of FSD and female gender were significant independent predictors of basal hypocortisolism. In conclusion, we did not find evidence to consider all three main FSD as hypocortisolemic disorders, as significant reduction in basal cortisol compared to healthy controls was only found in CFS and in females with FM, but not in IBS. Copyright © 2011 Elsevier B.V. All rights reserved.
Tang N, Frank A, Leckie G, Hackett J Jr, Simmons G, Busch M, Abravaya K.	Abbott Molecular Inc., Des Plaines, IL 60018, USA. ning.tang@abbott.com	Development of sensitive single-round pol or env RT-PCR assays to screen for XMRV in multiple sample types.	J Virol Methods. 2012 Jan;179(1):127-34. Epub 2011 Oct 25.	The potential association between xenotropic murine leukemia virus-related virus (XMRV) and prostate cancer and chronic fatigue syndrome (CFS) has been much debated. To help resolve the potential role of XMRV in human disease, it is critical to develop sensitive and accurate reverse transcriptase (RT)-PCR assays to screen for the virus. Single-round RT-PCR assays were developed on the automated m2000™ system for detection of the pol or env regions of XMRV in whole blood, plasma, urine

				cell pellets and urogenital swab samples. Assay performance was assessed by testing two blinded panels, one comprised of whole blood and the other of plasma spiked with serial dilutions of XMRV-infected tissue culture cells and supernatant, respectively, prepared by the Blood XMRV Scientific Research Working Group (SRWG). For both whole blood and plasma panel testing, the assays showed excellent specificity and sensitivity as compared to the other tests included in the SRWG phase I study. Analytical specificity of the assays was also evaluated. Neither pol nor env PCR assays detected a panel of potential cross-reactive microorganisms, although some cross-reaction was observed with mouse genomic DNA. Screening of 196 normal human blood donor plasma, 214 HIV-1 seropositive plasma, 20 formalin-fixed paraffin-embedded (FFPE) prostate cancer specimens, 4 FFPE benign prostate specimens, 400 urine pellets from prostate cancer patients, 166 urine pellets from non-prostate cancer patients, and 135 cervical swab specimens, detected no samples as unequivocally XMRV positive. Copyright © 2011 Elsevier B.V. All rights reserved.
Tang S, Zhao J, Viswanath R, Nyambi PN, Redd AD, Dastyar A, Spacek LA, Quinn TC, Wang X, Wood O, Gaddam D, Devadas K, Hewlett IK.	Laboratory of Molecular Virology, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland 20892, USA. shixing.tang@fda.hhs.gov	Absence of detectable xenotropic murine leukemia virus-related virus in plasma or peripheral blood mononuclear cells of human immunodeficiency virus Type 1-infected blood donors or individuals in Africa.	Transfusion. 2011 Mar;51(3):463-8. doi: 10.1111/j.1537-2995.2010.02932.x. Epub 2010 Nov 15.	BACKGROUND: Since the identification of xenotropic murine leukemia virus-related virus (XMRV) in prostate cancer patients in 2006 and in chronic fatigue syndrome patients in 2009, conflicting findings have been reported regarding its etiologic role in human diseases and prevalence in general populations. In this study, we screened both plasma and peripheral blood mononuclear cells (PBMNCs) collected in Africa from blood donors and human immunodeficiency virus Type 1 (HIV-1)-infected individuals to gain evidence of XMRV infection in this geographic region. STUDY DESIGN AND METHODS: A total of 199 plasma samples, 19 PBMNC samples, and 50 culture supernatants from PBMNCs of blood donors from Cameroon found to be infected with HIV-1 and HIV-1 patients from Uganda were screened for XMRV infection using a sensitive nested polymerase chain reaction (PCR) or reverse transcription (RT)-PCR assay. RESULTS: Using highly sensitive nested PCR or RT-PCR and real-time PCR assays capable of detecting at least 10 copies of XMRV plasmid DNA per reaction, none of the 268 samples tested were found to be XMRV DNA or RNA positive. CONCLUSIONS: Our results failed to demonstrate the presence of XMRV infection in African blood donors or individuals infected with HIV-1. More studies are needed to understand the prevalence, epidemiology, and geographic distribution of XMRV infection worldwide. © 2010 American Association of Blood Banks.
Tang S, Hewlett IK.	Laboratory of Molecular Virology, CBER, Food and Drug Administration, Bethesda, MD 20892, USA.	Testing strategies for detection of xenotropic murine leukemia virus-related virus infection.	Adv Virol. 2011;2011:281425. Epub 2011 Jul 28.	Xenotropic murine leukemia virus-related virus (XMRV) is a newly identified gamma retrovirus and may be associated with prostate cancer- (PC) and chronic fatigue syndrome (CFS). Since its identification in 2006 and detection of polytropic murine lenkemia virus (MLV)-like sequences in CFS patients in 2010, several test methods including nucleic acid testing methods and serological assays have been developed for detection of XMRV and/or MLV-like sequences. However, these research assays have not yet been validated and evaluated due to the lack of well-characterized reference materials. Mouse DNA contamination should be carefully checked when testing

				human specimens in order to avoid false-positive detection of XMRV or MLV-like sequences.
Tang S, Zhao J, Haleyur Giri Setty MK, Devadas K, Gaddam D, Viswanath R, Wood O, Zhang P, Hewlett IK.	Lab of Molecular Virology, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland, United States of America. tangshixing@hotmail.com	Absence of detectable XMRV and other MLV-related viruses in healthy blood donors in the United States.	PLoS One. 2011;6(11):e27391. Epub 2011 Nov 14.	BACKGROUND: Preliminary studies in chronic fatigue syndrome (CFS) patients and XMRV infected animals demonstrated plasma viremia and infection of blood cells with XMRV, indicating the potential risk for transfusion transmission. XMRV and MLV-related virus gene sequences have also been detected in 4-6% of healthy individuals including blood donors in the U.S. These results imply that millions of persons in the U.S. may be carrying the nucleic acid sequences of XMRV and/or MLV-related viruses, which is a serious public health and blood safety concern. METHODOLOGY/PRINCIPAL FINDINGS: To gain evidence of XMRV or MLV-related virus infection in the U.S. blood donors, 110 plasma samples and 71 PBMC samples from blood donors at the NIH blood bank were screened for XMRV and MLV-related virus infection. We employed highly sensitive assays, including nested PCR and real-time PCR, as well as co-culture of plasma with highly sensitive indicator DERSE cells. Using these assays, none of the samples were positive for XMRV or MLV-related virus. CONCLUSIONS/SIGNIFICANCE: Our results are consistent with those from several other studies, and demonstrate the absence of XMRV or MLV-related viruses in the U.S. blood donors that we studied.
Tarello W.	Avian & Exotic Division, Pet Connection Veterinary Clinic, P.O. Box 450288, Dubai, UAE.	Etiologic agents and diseases found associated with clinical aspergillosis in falcons.	Int J Microbiol. 2011;2011:176963. Epub 2011 Jun 7.	The aim of this study was to describe parasitological, microbiological, and pathological findings associated with the isolation of Aspergillus species in 94 clinically diseased captive falcons from Dubai. Concomitant agents and/or diseases were identified in 64 cases, causing either single (n = 36) or multiple coinfections (n = 28). Diagnoses found more often in association with aspergillosis were chronic fatigue and immune dysfunction syndrome (CFIDS) (n = 29), Caryospora sp. (n = 16), Serratospiculum seurati infestation (n = 14), cestodiasis (n = 6), bumblefoot (n = 5), trematodosis due to Strigea falconispalumbi (n = 5), trichomoniasis (n = 4), Babesia shortti (n = 4), Mannheimia (Pastorella) haemolytica (n = 4), interstitial hepatitis (n = 4), Escherichia coli (n = 3), and Clostridium perfringens enterotoxemia (n = 2). Compared with a control group of 2000 diseased falcons without evidence of aspergillosis, the prevalence of Babesia shortti, CFIDS, Mannheimia (Pastorella) haemolytica, Escherichia coli, and falcon herpes virus infection was conspicuously higher in association with aspergillosis. These entities may be considered suitable candidates as predisposing factors for the mycosis.
ter Wolbeek M, van Doornen LJ, Kavelaars A, Tersteeg-Kamperman MD, Heijnen CJ.	Laboratory of Neuroimmunology and Developmental Origins of Disease, University Medical Center	Fatigue, depressive symptoms, and anxiety from adolescence up to young adulthood: a longitudinal study.	Brain Behav Immun. 2011 Aug;25(6):1249-55. Epub 2011 Apr 28.	Fatigue is a common complaint among adolescents. We investigated the course of fatigue in females during the transition from adolescence to young adulthood and examined psychological, immunological, and life style risk factors for development of fatigue and chronic fatigue syndrome (CFS)-related symptoms. Six hundred and thirty-three healthy females (age 14.63±1.37 years) filled out questionnaires measuring fatigue severity, depressive symptoms, anxiety, chronic fatigue syndrome (CFS)-related symptoms, sleep features, and life style characteristics at baseline and 4½ years thereafter. Of 64 participants LPS- and CD2CD28-induced cytokine data at

	Utrecht, Office KC 03.068.0, P.O. Box 85090, 3508 AB Utrecht, The Netherlands.			baseline were available. The best predictor of fatigue in young adulthood was previous fatigue severity. In participants who were non-fatigued during adolescence and who experienced a notable increase in fatigue, fatigue development was preceded by emotional problems and CFS-related complaints during adolescence. Increases as well as decreases in fatigue severity were accompanied by respectively increase and decrease in depressive symptoms and anxiety, suggesting that these symptoms cluster and co-vary over time. Higher interferon (IFN)-γ, higher IFN-γ/interleukin (IL)-4 ratio, lower tumor necrosis factor-α and lower IL-10 at baseline were related to fatigue severity at follow up. The rise in total number of CFS-related symptoms at follow up was predicted by anxiety and decreased physical activity during adolescence. Sleep and substance use were associated with fatigue severity and anxiety and depression. In conclusion, vulnerability to develop fatigue and associated symptoms in young adulthood can to a certain extent be identified already years before the manifestation of complaints. Copyright © 2011 Elsevier Inc. All rights reserved.
Terrada C, Neven B, Boddaert N, Souied EH, Prieur AM, Quartier P, Lehoang P, Bodaghi B.	Department of Ophthalmology, APHP, Pitie-Salpetriere Hospital, 75013, Paris, France, celineterradaoph@gmail.com.	Ocular modifications in a young girl with cryopyrin-associated periodic syndromes responding to interleukin-1 receptor antagonist anakinra.	J Ophthalmic Inflamm Infect. 2011 Sep;1(3):133-6. Epub 2011 Apr 9.	An 8-year-old patient with genetically confirmed chronic infantile neurological cutaneous and articular syndrome was treated with interleukin-1 receptor antagonist, anakinra. She initially presented with recurrent episodes of fever, rash, chronic fatigue, frequent headaches, ocular involvement (corneal infiltrate and papillary edema), and permanent increased biologic inflammatory markers. Following treatment with anakinra, all symptoms and inflammation resolved. Ophthalmologic signs normalized. This ophthalmologic description (optic nerve and cornea) has never been illustrated, even if ocular affections are classic in the cryopyrin-associated periodic syndromes.
Theoharides TC, Asadi S, Weng Z, Zhang B.		Serotonin-selective reuptake inhibitors and nonsteroidal anti-inflammatory drugs-important considerations of adverse interactions especially for the treatment of myalgic encephalomyelitis/chronic fatigue syndrome.	J Clin Psychopharmacol. 2011 Aug;31(4):403-5. Comment in J Clin Psychopharmacol. 2011 Dec;31(6):685-7.	
Tsang BK, Macdonell R.	Department of Neurology, Austin Hospital, Melbourne,	Multiple sclerosis-diagnosis, management and prognosis.	Aust Fam Physician. 2011 Dec;40(12):948-55.	BACKGROUND: Multiple sclerosis is the most common chronic disabling disease of the central nervous system in young adults. OBJECTIVE: This article summarises the diagnosis, management and prognosis of multiple sclerosis. DISCUSSION: Multiple sclerosis usually starts with an acute episode of neurological disturbance, termed a

	Victoria, Australia. bktsang@optusnet.com.au			'clinically isolated syndrome', followed by an illness phase punctuated by relapses and remissions which may transition after 10 years to a phase of progressive accumulation of disability without relapses. Fifteen to 20% of patients will have a progressive course from the onset. There is significant interpatient variability in prognosis. The main diagnostic criteria are clinical, supported by investigations including magnetic resonance imaging and lumbar puncture and evoked potentials. First line disease modifying agents for relapsing remitting multiple sclerosis include interferon-ß and glatiramer. First line treatment for relapses is usually intravenous methylprednisolone for 3 days. Troublesome symptoms may include spasticity, parasthesias, tremor, erectile dysfunction, depression and anxiety, fatigue and pain. After excluding differential diagnoses, symptomatic management includes pharmacological agents, allied health consultation and continence strategies. Although pregnancy reduces disease activity, there is a higher risk of relapse in the postpartum period.
Tsibris AM.		The end of the association between XMRV, MLV-like viruses and chronic fatigue syndrome.	Virulence. 2011 Nov-Dec;2(6):493-4.	
Tucker P, Haig-Ferguson A, Eaton N, Crawley E.	Royal National Hospital for Rheumatic Diseases, Bath, UK.	What to do about attention and memory problems in children with CFS/ME: a neuropsychological approach.	Clin Child Psychol Psychiatry. 2011 Apr;16(2):215-23.	Our recent research has shown that children with chronic fatigue syndrome/myalgic encephalomyopathy (CFS/ME) describe problems with focused attention, sustained attention, recall and stress. Neuropsychological testing demonstrated lower scores for sustained attention, switching attention, divided attention, auditory learning and immediate recall compared to normative data. This paper describes what is currently known about memory and attention problems in children with CFS/ME and suggests a variety of strategies that could be used to overcome these difficulties.
Tuke PW, Tettmar KI, Tamuri A, Stoye JP, Tedder RS.	Transfusion Microbiology Research and Development, National Transfusion Microbiology Laboratories, National Health Service Blood and Transplant, Colindale, London, United Kingdom. philip.tuke@hpa.	PCR master mixes harbour murine DNA sequences. Caveat emptor!	PLoS One. 2011;6(5):e19953. Epub 2011 May 25.	BACKGROUND: XMRV is the most recently described retrovirus to be found in Man, firstly in patients with prostate cancer (PC) and secondly in 67% of patients with chronic fatigue syndrome (CFS) and 3.7% of controls. Both disease associations remain contentious. Indeed, a recent publication has concluded that "XMRV is unlikely to be a human pathogen". Subsequently related but different polytropic MLV (pMLV) sequences were also reported from the blood of 86.5% of patients with CFS. and 6.8% of controls. Consequently we decided to investigate blood donors for evidence of XMRV/pMLV. METHODOLOGY/PRINCIPAL FINDINGS: Testing of cDNA prepared from the whole blood of 80 random blood donors, generated gag PCR signals from two samples (7C and 9C). These had previously tested negative for XMRV by two other PCR based techniques. To test whether the PCR mix was the source of these sequences 88 replicates of water were amplified using Invitrogen Platinum Taq (IPT) and Applied Biosystems Taq Gold LD (ABTG). Four gag sequences (2D, 3F, 7H, 12C) were generated with the IPT, a further sequence (12D) by ABTG re-amplification of an IPT first round product. Sequence comparisons revealed remarkable similarities

	org.uk			between these sequences, endogeous MLVs and the pMLV sequences reported in patients with CFS. CONCLUSIONS/SIGNIFICANCE: Methodologies for the detection of viruses highly homologous to endogenous murine viruses require special caution as the very reagents used in the detection process can be a source of contamination and at a level where it is not immediately apparent. It is suggested that such contamination is likely to explain the apparent presence of pMLV in CFS.
Twisk FN, Maes M, Festvåg L.		[Graded exercise therapy can have harmful effects]. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2011 May 6;131(8):803. Comment on Tidsskr Nor Laegeforen. 2011 Feb 4;131(3):231-6.	
Tófoli LF, Andrade LH, Fortes S.	Medical School/Post-Graduate Program in Family Health, Universidade Federal do Ceará (UFC), Sobral, CE, Brasil. tofoli@ufc.br	Somatization in Latin America: a review of the classification of somatoform disorders, functional syndromes and medically unexplained symptoms. [Article in English, Portuguese]	Rev Bras Psiquiatr. 2011 May;33 Suppl 1:S59-80.	OBJECTIVE: medically unexplained symptoms are common and associated with mental illness in various contexts. Previous studies show that Latin American populations are prone to somatization. Given the reformulation of the International Classification of Diseases towards its 11th edition the peculiarities of the population from this region of the world shall be taken into consideration. The objective of this study is to provide information on somatization in Latin American populations to help the decision making about medically unexplained symptoms diagnostic categories in the 11th edition of the International Classification of Diseases. METHOD: Extensive review of the academic production from 1995 to 2011 on somatization in populations of Latin American origin. RESULTS: The analysis of 106 studies included in this review was divided into 15 categories: systematic reviews, conceptual reviews, prevalence, primary care, depression and anxiety, risk factors, violence, organic conditions, relationship with health care, ethnicity, culture-bound syndromes, chronic fatigue syndrome, fibromyalgia, body dysmorphic disorder, and conversion and dissociation. CONCLUSION: The Latin American studies confirm the difficulty in defining medically unexplained symptoms categories. The supposed "somatizing trace" of Latin cultures may be linked more to cultural and linguistic expression than to an ethnic nature, and these peculiarities must be on the agenda for the new classification of these phenomena in the Classification of Diseases-11th edition.
Umapathi T, Yuki N.	Department of Neurology, National Neuroscience Institute, Singapore. umapathi@nni.com.sg	Pain in Guillain-Barré syndrome.	Expert Rev Neurother. 2011 Mar;11(3):335-9. Comment on Neurology. 2010 Oct 19;75(16):1439-47.	Evaluation of: Ruts L, Drenthen J, Jongen JL et al. Pain in Guillain-Barré syndrome: a long-term follow-up study. Neurology 75, 1439-1447 (2010). Pain has been recognized as an important symptom of Guillain-Barré syndrome (GBS). The article under review prospectively studied the phenomenon of pain in a cohort of 156 GBS patients for a period of 1 year. It confirmed that pain of significant intensity is relatively common in all subtypes of GBS. It may start before the onset of other symptoms. It correlates with sensory loss, severity of the GBS at its nadir and the presence of diarrhea. In the recovery/chronic stages it correlates with weakness, disability and fatigue. Up to a third of patients have pain at 1 year.

Van Den Eede F, Moorkens G, Hulstijn W, Maas Y, Schrijvers D, Stevens SR, Cosyns P, Claes SJ, Sabbe BG.	Department of Psychiatry, Antwerp University Hospital, Antwerp, Belgium. filip.van.den.eede@uza.be	Psychomotor function and response inhibition in chronic fatigue syndrome.	Psychiatry Res. 2011 Apr 30;186(2-3):367-72. Epub 2010 Aug 24.	Most research points to cognitive slowing in chronic fatigue syndrome (CFS), although there have been negative reports. The present study is one of few that examines fine motor processing and the inhibition of automatic responses in a well-characterised CFS population. A total of 35 female CFS patients without current major depression and 25 female controls performed two computerised figure-copying tasks. The cognitive and fine motor processing of visual-spatial information was measured by recording reaction time (RT) and movement time (MT), respectively. The inhibition of automatic responses was assessed by introducing 'conflicting patterns' (i.e., patterns that were difficult to draw from the preferred left to right). A multivariate general linear model was adopted for the statistical analysis of the movement recordings. As a result, CFS was significantly associated with longer RT and MT in the pooled and in the task-specific analyses. However, there was no interaction between disease status and conflicting character of the patterns. In conclusion, these performance data on the figure-copying tasks provide confirmatory evidence for psychomotor slowing in CFS, but not for a disturbed inhibition of automatic responses. Computerised figure-copying tasks may be promising tools for use in neurobiological research and clinical trials in CFS.
van der Kuyl AC, Cornelissen M, Berkhout B.	Laboratory of Experimental Virology, Department of Medical Microbiology, Center for Infection and Immunity Amsterdam, Academic Medical Center, University of Amsterdam Amsterdam, Netherlands.	Of Mice and Men: On the Origin of XMRV.	Front Microbiol. 2010;1:147. Epub 2011 Jan 17.	The novel human retrovirus xenotropic murine leukemia virus-related virus (XMRV) is arguably the most controversial virus of this moment. After its original discovery in prostate cancer tissue from North American patients, it was subsequently detected in individuals with chronic fatigue syndrome from the same continent. However, most other research groups, mainly from Europe, reported negative results. The positive results could possibly be attributed to contamination with mouse products in a number of cases, as XMRV is nearly identical in nucleotide sequence to endogenous retroviruses in the mouse genome. But the detection of integrated XMRV proviruses in prostate cancer tissue proves it to be a genuine virus that replicates in human cells, leaving the question: how did XMRV enter the human population? We will discuss two possible routes: either via direct virus transmission from mouse to human, as repeatedly seen for, e.g., Hantaviruses, or via the use of mouse-related products by humans, including vaccines. We hypothesize that mouse cells or human cell lines used for vaccine production could have been contaminated with a replicating variant of the XMRV precursors encoded by the mouse genome.
van Geelen SM, Fuchs CE, Sinnema G, van de Putte EM, van Geel R, Hermans HJ, Kuis W.	Division of Pediatric Psychology, University Medical Center Utrecht, Utrecht, The Netherlands. S.M.vanGeelen@	Self-investigation in adolescent chronic fatigue syndrome: narrative changes and health improvement.	Patient Educ Couns. 2011 May;83(2):227-33. Epub 2010 Jun 25.	OBJECTIVE: A small-scale intervention study into narrative self-investigation in adolescent chronic fatigue syndrome (CFS). METHOD: The self-confrontation method (SCM) is an instrument to assess and change personal life stories. Forty-two adolescents diagnosed with CFS were included and randomly assigned to either 6 or 12 sessions with the SCM. Twenty-five healthy adolescents were assigned to 6 sessions. Outcome was measured directly after the self-investigation procedure at 4 months. Follow-up measurements were made 10 months later. The Checklist Individual Strength and the Child Health Questionnaire were used to measure

	umcutrecht.nl			changes in fatigue, physical and psychosocial functioning. RESULTS: Self-investigation resulted in significant changes in participants' narratives. Moreover, after self-investigation there was a significant improvement in fatigue, physical and psychosocial functioning for the adolescents with CFS. The patients who completed 12 sessions improved most. At follow-up, the positive effects were maintained. CONCLUSION: Self-investigation enables a move beyond the symptoms of CFS in an individualized, patient centered way. Narrative transformation seems to contribute to improved physical and psychosocial outcome in adolescent CFS. PRACTICE IMPLICATIONS: The SCM allows adolescents to discover (for themselves) factors that might cause or perpetuate their fatigue. The results suggest that self-investigation is a useful instrument in the management of adolescent CFS. Copyright © 2010 Elsevier Ireland Ltd. All rights reserved.
Van Houdenhove B, Luyten P.		Listen to the story: chronic fatigue syndrome patients do not live in a vacuum.	Psychother Psychosom. 2011;80(2):113-5. Epub 2011 Jan 4.	
van Kuppeveld FJ, van der Meer JW.	Department of Medical Microbiology, Radboud University Nijmegen Medical Centre, 6500 HB Nijmegen, Netherlands. f.vankuppeveld@ncmls.ru.nl	XMRV and CFS--the sad end of a story.	Lancet. 2012 Feb 4;379(9814):e27-8. Epub 2011 Jun 21.	
Van Oosterwijck J, Nijs J, Meeus M, Truijen S, Craps J, Van den Keybus N, Paul L.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium.	Pain neurophysiology education improves cognitions, pain thresholds, and movement performance in people with chronic whiplash: a pilot study.	J Rehabil Res Dev. 2011;48(1):43-58.	Chronic whiplash is a debilitating condition characterized by increased sensitivity to painful stimuli, maladaptive illness beliefs, inappropriate attitudes, and movement dysfunctions. Previous work in people with chronic low back pain and chronic fatigue syndrome indicates that pain neurophysiology education is able to improve illness beliefs and attitudes as well as movement performance. This single-case study (A-B-C design) with six patients with chronic whiplash associated disorders (WAD) was aimed at examining whether education about the neurophysiology of pain is accompanied by changes in symptoms, daily functioning, pain beliefs, and behavior. Periods A and C represented assessment periods, while period B consisted of the intervention (pain neurophysiology education). Results showed a significant decrease in kinesiophobia (Tampa Scale for Kinesiophobia), the passive coping strategy of resting (Pain Coping Inventory), self-rated disability (Neck Disability Index), and photophobia (WAD

				Symptom List). At the same time, significantly increased pain pressure thresholds and improved pain-free movement performance (visual analog scale on Neck Extension Test and Brachial Plexus Provocation Test) were established. Although the current results need to be verified in a randomized, controlled trial, they suggest that education about the physiology of pain is able to increase pain thresholds and improve pain behavior and pain-free movement performance in patients with chronic WAD.
Van Oudenhove L, Vandenberghe J, Vos R, Holvoet L, Tack J.	Department of Pathophysiology, Translational Research Center for Gastrointestinal Disorders (TARGID), University of Leuven, Leuven, Belgium. lukas.vanoudenhove@med.kuleuven.be	Factors associated with co-morbid irritable bowel syndrome and chronic fatigue-like symptoms in functional dyspepsia.	Neurogastroenterol Motil. 2011 Jun;23(6):524-e202. doi: 10.1111/j.1365-2982.2010.01667.x. Epub 2011 Jan 24.	BACKGROUND: It is unclear which factors explain the high co-morbidity between functional dyspepsia (FD) and other functional somatic syndromes. The aim of this study is to investigate the association between gastric sensorimotor function, psychosocial factors and 'somatization' on the one hand, and co-morbid irritable bowel syndrome (IBS) and chronic fatigue (CF)-like symptoms on the other, in FD. METHODS: In 259 tertiary care FD patients, we studied gastric sensorimotor function with barostat (sensitivity, accommodation). We measured psychosocial factors (abuse history, alexithymia, trait anxiety, depression, panic disorder) and 'somatization' using self-report questionnaires, and presence of IBS and CF-like symptoms. Hierarchical multiple logistic regression was used to determine which of these factors were independently associated with co-morbid IBS and CF-like symptoms, including testing of potential mediator effects. KEY RESULTS: Co-morbid IBS or CF-like symptoms respectively were found in 142 (56.8%) and 102 (39.4%) patients; both co-morbidities were not significantly associated (P=0.27). Gastric accommodation (β=0.003, P=0.04) and 'somatization' (β=0.17, P= 0.0003) were independent risk factors for IBS (c=0.74, P<0.0001); the effect of adult abuse (β=0.72, P=0.20) was mediated by 'somatization'. Depression (β=0.16, P=0.008) and 'somatization' (β=0.18, P=0.004) were overlapping risk factors for CF-like symptoms (c=0.83, P<0.0001); the effects of alexithymia and lifetime abuse were mediated by depression and 'somatization', respectively. CONCLUSIONS & INFERENCES: 'Somatization' is a common risk factor for co-morbid IBS and CF-like symptoms in FD and mediates the effect of abuse. Gastric sensorimotor function and depression are specific risk factors for co-morbid IBS and CF-like symptoms, respectively. © 2011 Blackwell Publishing Ltd.
Vaughan AE, Mendoza R, Aranda R, Battini JL, Miller AD.	Human Biology Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA.	Xpr1 is an atypical G-protein-coupled receptor that mediates xenotropic and polytropic murine retrovirus neurotoxicity.	J Virol. 2012 Feb;86(3):1661-9. Epub 2011 Nov 16.	Xenotropic murine leukemia virus-related virus (XMRV) was first identified in human prostate cancer tissue and was later found in a high percentage of humans with chronic fatigue syndrome (CFS). While exploring potential disease mechanisms, we found that XMRV infection induced apoptosis in SY5Y human neuroblastoma cells, suggesting a mechanism for the neuromuscular pathology seen in CFS. Several lines of evidence show that the cell entry receptor for XMRV, Xpr1, mediates this effect, and chemical cross-linking studies show that Xpr1 is associated with the Gβ subunit of the G-protein heterotrimer. The activation of adenylate cyclase rescued the cells from XMRV toxicity, indicating that toxicity resulted from reduced G-protein-mediated cyclic AMP (cAMP) signaling. Some proteins with similarity to Xpr1 are

				involved in phosphate uptake into cells, but we found no role of Xpr1 in phosphate uptake or its regulation. Our results indicate that Xpr1 is a novel, atypical G-protein-coupled receptor (GPCR) and that xenotropic or polytropic retrovirus binding can disrupt the cAMP-mediated signaling function of Xpr1, leading to the apoptosis of infected cells. We show that this pathway is also responsible for the classic toxicity of the polytropic mink cell focus-forming (MCF) retrovirus in mink cells. Although it now seems clear that the detection of XMRV in humans was the result of sample contamination with a recombinant mouse virus, our findings may have relevance to neurologic disease induced by MCF retroviruses in mice.
Verhoeven WM, Egger JI, Kuijpers HJ.	Vincent van Gogh Institute for Psychiatry, Centre of Excellence for Neuropsychiatry, Venray, The Netherlands. wverhoeven@vvgi.nl.	Manganese and acute paranoid psychosis: a case report.	J Med Case Reports. 2011 Apr 12;5:146.	INTRODUCTION: Manganese regulates many enzymes and is essential for normal development and body function. Chronic manganese intoxication has an insidious and progressive course and usually starts with complaints of headache, fatigue, sleep disturbances, irritability and emotional instability. Later, several organ systems may be affected and, due to neurotoxicity, an atypical parkinsonian syndrome may emerge. With regard to neuropsychiatry, an array of symptoms may develop up to 30 years after intoxication, of which gait and speech abnormalities, cognitive and motor slowing, mood changes and hallucinations are the most common. Psychotic phenomena are rarely reported. CASE PRESENTATION: We describe the case of a 49-year-old Caucasian man working as a welder who was referred to our facility for evaluation of acute paranoid psychotic behavior. Our patient's medical history made no mention of any somatic complaints or psychiatric symptoms, and he had been involved in a professional career as a metalworker. On magnetic resonance imaging scanning of his brain, a bilateral hyperdensity of the globus pallidus, suggestive for manganese intoxication, was found. His manganese serum level was 52 to 97 nmol/L (range: 7 to 20 nmol/L). A diagnosis of organic psychotic disorder due to manganese overexposure was made. His psychotic symptoms disappeared within two weeks of treatment with low-dose risperidone. At three months later, serum manganese was decreased to slightly elevated levels and the magnetic resonance imaging T1 signal intensity was reduced. No signs of Parkinsonism were found and a definite diagnosis of manganese-induced apathy syndrome was made. CONCLUSION: Although neuropsychiatric and neurological symptoms caused by (chronic) manganese exposure have been reported frequently in the past, in the present day the disorder is rarely diagnosed. In this report we stress that manganese intoxication can still occur, in our case in a confined-space welder, and may present clinically with a paranoid psychotic state that necessitates a rapid diagnostic procedure in order to avoid the permanent structural brain damage that may occur with chronic exposure.
Vierck CJ.	Department of Neuroscience and Comprehensive Center for Pain	A mechanism-based approach to prevention of and therapy for	Pain Res Treat. 2012;2012:951354. Epub 2011 Oct 2.	Fibromyalgia syndrome (FMS) is characterized by pain referred to deep tissues. Diagnosis and treatment of FMS are complicated by a variable coexistence with regional pain, fatigue, sleep disruption, difficulty with mentation, and depression. The widespread, deep pain of FMS can be a consequence of chronic psychological stress

	Research, Colleges of Medicine and Dentistry, University of Florida, P.O. Box 100444, 1600 S.W. Archer Road, Gainesville, FL 32610, USA.	fibromyalgia.		with autonomic dysregulation. Stress acts centrally to facilitate pain and acts peripherally, via sympathetic vasoconstriction, to establish painful muscular ischemia. FMS pain, with or without a coexistent regional pain condition, is stressful, setting up a vicious circle of reciprocal interaction. Also, stress interacts reciprocally with systems of control over depression, mentation, and sleep, establishing FMS as a multiple-system disorder. Thus, stress and the ischemic pain it generates are fundamental to the multiple disorders of FMS, and a therapeutic procedure that attenuates stress and peripheral vasoconstriction should be highly beneficial for FMS. Physical exercise has been shown to counteract peripheral vasoconstriction and to attenuate stress, depression, and fatigue and improve mentation and sleep quality. Thus, exercise can interrupt the reciprocal interactions between psychological stress and each of the multiple-system disorders of FMS. The large literature supporting these conclusions indicates that exercise should be considered strongly as a first-line approach to FMS therapy.
Vlaeyen JW, Karsdorp P, Gatzounis R, Ranson S, Schrooten M.		The PACE trial in chronic fatigue syndrome.	Lancet. 2011 May 28;377(9780):1834; author reply 1834-5. Epub 2011 May 16. Comment in Lancet. 2011 May 28;377(9780):1832-3; author reply 1834-5. Lancet. 2011 May 28;377(9780):1831; author reply 1834-5. Lancet. 2011 May 28;377(9780):1832; author reply 1834-5. Lancet. 2011 May 28;377(9780):1833; author reply 1834-5. Lancet. 2011 May 28;377(9780):1831; author reply 1834-5. Lancet. 2011 May 28;377(9780):1833-4; author reply 1834-5. Comment on Lancet. 2011 Mar 5;377(9768):823-36.	

Vural A, Agacdiken A, Celikyurt U, Culha M, Kahraman G, Kozdag G, Ural D.	Department of Cardiology, Kocaeli University Medical Faculty, Kocaeli, Turkey.	Effect of cardiac resynchronization therapy on libido and erectile dysfunction.	Clin Cardiol. 2011 Jul;34(7):437-41. doi: 10.1002/clc.20918. Epub 2011 Jun 2.	BACKGROUND: Chronic heart failure (HF) is a common, complex clinical syndrome characterized by dyspnea, fatigue and exercise intolerance. HF patients experience decreased libido and erectile dysfunction (ED). The effects of cardiac resynchronization therapy (CRT) on libido and erectile function have not been previously evaluated. We aimed to investigate the effects of CRT on libido and ED. HYPOTHESIS: Cardiac resynchronization therapy improves libido and ED. METHODS: Thirty-one male patients with advanced HF, scheduled for implantation of a CRT device, were included in the study. Left ventricular systolic function, New York Heart Association (NYHA) class, libido, and ED were assessed before and 6 months after CRT. Libido and ED were evaluated with the Aging Male Symptoms (AMS) rating scale and internationally validated Sexual Health Inventory for Men (SHIM) questionnaire, respectively. RESULTS: At the 6-month follow-up, the mean NYHA class improved from 3.4 ± 0.5 to 2.1 ± 0.6 (P<0.001). On echocardiographic examination, an improvement in left ventricular ejection fraction (LVEF) from 18 ± 5% to 32 ± 6% was detected (P<0.001). A significant increase in mean SHIM score and a significant decrease in mean AMS were noted. Changes in SHIM and AMS scores were correlated positively with the increase in LVEF (r = 0.47, P = 0.007 and r = - 0.36, P = 0.04, respectively). Similarly, SHIM scores were correlated negatively (r = - 0.57, P = 0.001) and AMS scores were correlated positively (r = 0.73, P = 0.0001) with the improvement in NYHA class. CONCLUSIONS: CRT results in a significant improvement in libido and erectile function in patients with congestive HF. This improvement is related to the improvements in the LVEF and functional capacity. . © 2011 Wiley Periodicals, Inc.
Wainberg MA, Jeang KT.	McGill University AIDS Centre, Jewish General Hospital, Montreal, Quebec, Canada.	XMRV as a human pathogen?	Cell Host Microbe. 2011 Apr 21;9(4):260-2.	Xenotropic murine leukemia virus-related virus (XMRV) has been proposed to be associated with prostate cancer and chronic fatigue syndrome (CFS). This proposition has been controversial because many investigators have failed to replicate the reported associations. Here, we explore whether XMRV is an authentic human pathogen in the light of recent findings that indicate otherwise. Copyright © 2011 Elsevier Inc. All rights reserved.
Warren JW, Wesselmann U, Morozov V, Langenberg PW.	Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21201, USA. jwarren@medicine.umaryland.edu	Numbers and types of nonbladder syndromes as risk factors for interstitial cystitis/painful bladder syndrome.	Urology. 2011 Feb;77(2):313-9. Comment in Urology. 2011 Feb;77(2):319; author reply 320.	OBJECTIVES: To examine the interaction of types and numbers of antecedent nonbladder syndromes (NBSs) to seek clues to the pathogenesis of interstitial cystitis/painful bladder syndrome (IC/PBS). Numerous case series have shown IC/PBS to be associated with several syndromes that do not include bladder symptoms. In a previously reported case-control study, we confirmed these findings and found that such nonbladder syndromes often preceded the onset of IC/PBS. METHODS: Incident female IC/PBS cases (n = 312) and matched controls were compared for 11 antecedent NBSs. The odds ratios (ORs) for IC/PBS according to the number of antecedent NBSs per person were calculated. From this model, each NBS was serially removed, and the calculations for the ORs were repeated using the remaining 10 NBSs. We assessed the types of NBSs included in each subgroup formed by the

				number of NBSs. RESULTS: The ORs for IC/PBS increased with the increasing number of antecedent NBSs. The types of NBSs were interchangeable in calculating these ORs. The distribution of the types of NBSs was skewed, with allergy overrepresented in those with few NBSs, and the classic functional somatic syndromes of fibromyalgia, chronic fatigue syndrome, and irritable bowel syndrome overrepresented in those with many NBSs. CONCLUSIONS: Two main hypotheses were generated. One was that the incidence of a NBS initiated a process that contributed to the emergence of other NBSs and IC/PBS. The second was that each NBS and IC/PBS was a manifestation of a common, shared pathogenesis. It is likely that a well-designed prospective study will be necessary to distinguish between these 2 hypotheses. Copyright © 2011 Elsevier Inc. All rights reserved.
Waugh EM, Jarrett RF, Shield L, Montgomery D, Dean RT, Mitchell A, Greaves MF, Gallagher A.	LRF Virus Centre, MRC and University of Glasgow Centre for Virus Research, Institute of Infection, Immunity and Inflammation, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow, United Kingdom.	The retrovirus XMRV is not directly involved in the pathogenesis of common types of lymphoid malignancy.	Cancer Epidemiol Biomarkers Prev. 2011 Oct;20(10):2232-6. Epub 2011 Aug 22.	BACKGROUND: A novel retrovirus, xenotropic murine leukemia virus-related virus (XMRV), has been detected in prostate cancer samples and in peripheral blood mononuclear cells (PBMC) from patients with chronic fatigue syndrome. In addition, the virus has been identified in PBMCs from healthy controls. These data suggest that XMRV is circulating in the human population. XMRV is closely related to murine leukemia viruses, which cause lymphoid malignancies in mice. The aim of this study was to determine whether XMRV is directly associated with common forms of human lymphoma or leukemia. METHODS: DNA samples from 368 patients with lymphoid malignancies and 139 patients with benign lymphadenopathy or other malignant disease were screened for XMRV, using three specific and sensitive quantitative PCR assays. RESULTS: XMRV was not detected in any sample using any of the three assays. CONCLUSIONS: The data suggest that this virus is not directly involved in the pathogenesis of common types of lymphoid malignancy and that XMRV is not a prevalent blood borne infection, at least in the United Kingdom. IMPACT: There is no evidence that XMRV is associated with lymphoid malignancies, and further studies should resolve inconsistencies in results of studies examining XMRV prevalence. ©2011 AACR
Webb CM, Collin SM, Deave T, Haig-Ferguson A, Spatz A, Crawley E.	St George's University of London, Cranmer Terrace, London, UK.	What stops children with a chronic illness accessing health care: a mixed methods study in children with Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME).	BMC Health Serv Res. 2011 Nov 11;11:308.	BACKGROUND: Paediatric Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) is relatively common and disabling with a mean time out of school of more than one academic year. NICE guidelines recommend referral to specialist services immediately if severely affected, within 3 months if moderately affected and within 6 months if mildly affected. However, the median time-to-assessment by a specialist service in the UK is 18 months. This study used a mixed-methods approach to examine factors associated with time taken to access specialist services. METHODS: Time-to-assessment was analysed as a continuous "survival-time" variable in Cox regression models using data from self-completed assessment forms for children attending a regional specialist CFS/ME service between January 2006 and December 2009. Semi-structured interviews about barriers experienced in accessing healthcare

				for their child were conducted with nine parents of children aged < 17 years (8 individual and one parent couple). Interviews were digitally recorded and analysed using "thematic analysis". RESULTS: 405 children were assessed between 2006 and 2009 and information on school attendance was available on 388. Only 1/125 with severe CFS/ME and 49/263 (19%) with mild to moderate CFS/ME were seen within NICE recommended timeframe. Increased fatigue was associated with shorter time to assessment (HR = 1.15; 95% CI 1.03, 1.29 per unit increase in Chalder fatigue score; P = 0.01). Time-to-assessment was not associated with disability, mood, age or gender. Parents described difficulties accessing specialist services because of their own as well as their GP's and Paediatrician's lack of knowledge. They experienced negative attitudes and beliefs towards the child's condition when they consulted GPs, Paediatricians and Child Psychiatrists. Parents struggled to communicate an invisible illness that their child and not themselves were experiencing. CONCLUSIONS: GPs, Child Psychiatrists and Paediatricians need more knowledge about CFS/ME and the appropriate referral pathways to ensure timeliness in referral to specialist services.
Wensaas KA, Langeland N, Hanevik K, Mørch K, Eide GE, Rortveit G.	Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway. knut-arne.wensaas@uni.no	Irritable bowel syndrome and chronic fatigue 3 years after acute giardiasis: historic cohort study.	Gut. 2012 Feb;61(2):214-9. Epub 2011 Sep 12.	BACKGROUND: Giardia lamblia is a common cause of gastroenteritis worldwide, but there is limited knowledge about the long-term complications. OBJECTIVE: To estimate the relative risk of irritable bowel syndrome (IBS) and chronic fatigue 3 years after acute giardiasis. DESIGN: Controlled historic cohort study with 3 years' follow-up. Data collected by mailed questionnaire. SETTING: Waterborne outbreak of giardiasis in the city of Bergen, Norway. PARTICIPANTS: 817 patients exposed to Giardia lamblia infection verified by detection of cysts in stool samples and 1128 matched controls. MAIN OUTCOME MEASURES: IBS and chronic fatigue. RESULTS: The prevalence of IBS in the exposed group was 46.1%, compared with 14.0% in the control group, and the adjusted RR=3.4 (95% CI 2.9 to 3.8). Chronic fatigue was reported by 46.1% of the exposed group and 12.0% of the controls, the adjusted RR was 4.0 (95% CI 3.5 to 4.5). IBS and chronic fatigue were associated and the RR for the exposed group of having a combination of the two outcomes was 6.8 (95% CI 5.3 to 8.5). The RR was also increased for having just one of the two syndromes, 1.8 for IBS (95% CI 1.4 to 2.3) and 2.2 for chronic fatigue (95% CI 1.7 to 2.8). CONCLUSIONS: Infection with Giardia lamblia in a non-endemic area was associated with a high prevalence of IBS and chronic fatigue 3 years after acute illness, and the risk was significantly higher than in the control group. This shows that the potential consequences of giardiasis are more serious than previously known. Further studies are needed, especially in areas where giardiasis is endemic.
White AT, Light AR, Hughen RW, Vanhaitsma TA, Light KC.	Department of Anesthesiology, University of Utah, 30 N 1900 E, Room 3C444,	Differences in metabolite-detecting, adrenergic, and immune gene	Psychosom Med. 2012 Jan;74(1):46-54. Epub 2011 Dec 30.	OBJECTIVE: Chronic fatigue syndrome (CFS) and multiple sclerosis (MS) are characterized by debilitating fatigue, yet evaluation of this symptom is subjective. We examined metabolite-detecting, adrenergic, and immune gene expression (messenger ribonucleic acid [mRNA]) in patients with CFS (n = 22) versus patients with MS (n = 20) versus healthy controls (n = 23) and determined their relationship to fatigue and pain

	Salt Lake City, UT 84132-2501, USA.	expression after moderate exercise in patients with chronic fatigue syndrome, patients with multiple sclerosis, and healthy controls.		before and after exercise. METHODS: Blood samples and fatigue and pain ratings were obtained at baseline and 0.5, 8, 24, and 48 hours after sustained moderate exercise. Leukocyte mRNA of four metabolite-detecting receptors (acid-sensing ion channel 3, purinergic type 2X4 and 2X5 receptors, and transient receptor potential vanilloid type 1) and four adrenergic (α-2a, β-1, and β-2 receptors and catechol-O-methyltransferase) and five immune markers (CD14, toll-like receptor 4 [TLR4], interleukin [IL] 6, IL-10, and lymphotoxin α) was examined using quantitative polymerase chain reaction. RESULTS: Patients with CFS had greater postexercise increases in fatigue and pain (10-29 points above baseline, $p < .001$) and greater mRNA increases in purinergic type 2X4 receptor, transient receptor potential vanilloid type 1, CD14, and all adrenergic receptors than controls (mean ± standard error = 1.3 ± 0.14- to 3.4 ± 0.90-fold increase above baseline, $p = .04$-$.005$). Patients with CFS with comorbid fibromyalgia ($n = 18$) also showed greater increases in acid-sensing ion channel 3 and purinergic type 2X5 receptors ($p < .05$). Patients with MS had greater postexercise increases than controls in β-1 and β-2 adrenergic receptor expressions (1.4 ± 0.27- and 1.3 ± 0.06-fold increases, respectively, $p = .02$ and $p < .001$) and greater decreases in TLR4 ($p = .02$). In MS, IL-10 and TLR4 decreases correlated with higher fatigue scores. CONCLUSIONS: Postexercise mRNA increases in metabolite-detecting receptors were unique to patients with CFS, whereas both patients with MS and patients with CFS showed abnormal increases in adrenergic receptors. Among patients with MS, greater fatigue was correlated with blunted immune marker expression.
White PD, Goldsmith KA, Johnson AL, Potts L, Walwyn R, DeCesare JC, Baber HL, Burgess M, Clark LV, Cox DL, Bavinton J, Angus BJ, Murphy G, Murphy M, O'Dowd H, Wilks D, McCrone P, Chalder T, Sharpe M; PACE trial management group. Collaborators: Darbyshire J,	Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine, Queen Mary University of London, UK. p.d.white@qmul.ac.uk	Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial.	Lancet. 2011 Mar 5;377(9768):823-36. Epub 2011 Feb 18. Comment in Lancet. 2011 Mar 5;377(9768):786-8. Lancet. 2011 May 28;377(9780):1808. Lancet. 2011 May 28;377(9780):1833; author reply 1834-5. Lancet. 2011 May 28;377(9780):1831; author reply 1834-5. Lancet. 2011 May 28;377(9780):1831; author reply 1834-5. Lancet. 2011 May	BACKGROUND: Trial findings show cognitive behaviour therapy (CBT) and graded exercise therapy (GET) can be effective treatments for chronic fatigue syndrome, but patients' organisations have reported that these treatments can be harmful and favour pacing and specialist health care. We aimed to assess effectiveness and safety of all four treatments. METHODS: In our parallel-group randomised trial, patients meeting Oxford criteria for chronic fatigue syndrome were recruited from six secondary-care clinics in the UK and randomly allocated by computer-generated sequence to receive specialist medical care (SMC) alone or with adaptive pacing therapy (APT), CBT, or GET. Primary outcomes were fatigue (measured by Chalder fatigue questionnaire score) and physical function (measured by short form-36 subscale score) up to 52 weeks after randomisation, and safety was assessed primarily by recording all serious adverse events, including serious adverse reactions to trial treatments. Primary outcomes were rated by participants, who were necessarily unmasked to treatment assignment; the statistician was masked to treatment assignment for the analysis of primary outcomes. We used longitudinal regression models to compare SMC alone with other treatments, APT with CBT, and APT with GET. The final analysis included all participants for whom we had data for primary outcomes. This trial is registered at http://isrctn.org, number

Butler J, Doherty P, Law S, Llewelyn M, Sensky T, Aylward M, Spencer P, Clark C, Stansfeld S, Wearden A, Dieppe P, Fletcher A, Feinmann C, Akagi H, Miller A, Spickett G, Bowman B, Fleetwood D.			28;377(9780):1831-2. Lancet. 2011 May 28;377(9780):1834; author reply 1834-5. Lancet. 2011 May 28;377(9780):1833-4; author reply 1834-5. Lancet. 2011 May 28;377(9780):1832; author reply 1834-5. Lancet. 2011 May 28;377(9780):1832-3; author reply 1834-5.	ISRCTN54285094. FINDINGS: We recruited 641 eligible patients, of whom 160 were assigned to the APT group, 161 to the CBT group, 160 to the GET group, and 160 to the SMC-alone group. Compared with SMC alone, mean fatigue scores at 52 weeks were 3·4 (95% CI 1·8 to 5·0) points lower for CBT (p = 0·0001) and 3·2 (1·7 to 4·8) points lower for GET (p = 0·0003), but did not differ for APT (0·7 [-0·9 to 2·3] points lower; p = 0·38). Compared with SMC alone, mean physical function scores were 7·1 (2·0 to 12·1) points higher for CBT (p = 0·0068) and 9·4 (4·4 to 14·4) points higher for GET (p = 0·0005), but did not differ for APT (3·4 [-1·6 to 8·4] points lower; p=0·18). Compared with APT, CBT and GET were associated with less fatigue (CBT p = 0·0027; GET p = 0·0059) and better physical function (CBT p=0·0002; GET p<0·0001). Subgroup analysis of 427 participants meeting international criteria for chronic fatigue syndrome and 329 participants meeting London criteria for myalgic encephalomyelitis yielded equivalent results. Serious adverse reactions were recorded in two (1%) of 159 participants in the APT group, three (2%) of 161 in the CBT group, two (1%) of 160 in the GET group, and two (1%) of 160 in the SMC-alone group. INTERPRETATION: CBT and GET can safely be added to SMC to moderately improve outcomes for chronic fatigue syndrome, but APT is not an effective addition. FUNDING: UK Medical Research Council, Department of Health for England, Scottish Chief Scientist Office, Department for Work and Pensions. Copyright © 2011 Elsevier Ltd. All rights reserved.
Wiborg JF, Knoop H, Prins JB, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, the Netherlands. j.wiborg@nkcv.umcn.nl	Does a decrease in avoidance behavior and focusing on fatigue mediate the effect of cognitive behavior therapy for chronic fatigue syndrome?	J Psychosom Res. 2011 Apr;70(4):306-10. Epub 2011 Feb 12.	OBJECTIVE: Cognitive behavior therapy (CBT) leads to a significant reduction in fatigue severity and impairment in patients with chronic fatigue syndrome (CFS). The purpose of the present study was to determine whether the effect of CBT for CFS on fatigue and impairment is mediated by a decrease in avoidance behavior and focusing on fatigue. METHODS: For this purpose, we reanalyzed a randomized controlled trial which was previously conducted to test the efficacy of CBT for CFS. Two hundred nineteen patients completed assessment prior and subsequent to treatment or a control group period. RESULTS: Mediation analysis revealed that a decrease in focusing on fatigue mediated the effect of CBT for CFS on fatigue and impairment. Avoidance of activity and avoidance of aversive stimuli were not significantly changed by treatment and were therefore excluded from mediation analysis. CONCLUSION: A decrease in the focus on fatigue seems to contribute to the treatment effect of CBT for CFS. Copyright © 2011 Elsevier Inc. All rights reserved.
Williams AM, Kitchen P, Eby J.	Department of Geography and Earth Sciences, McMaster University, Hamilton, Ontario, Canada.	Alternative health care consultations in Ontario, Canada: A geographic and socio-demographic analysis.	BMC Complement Altern Med. 2011 Jun 22;11:47.	BACKGROUND: An important but understudied component of Canada's health system is alternative care. The objective of this paper is to examine the geographic and socio-demographic characteristics of alternative care consultation in Ontario, Canada's largest province. METHODS: Data is drawn from the Canadian Community Health Survey (CCHS Cycle 3.1, 2005) for people aged 18 or over (n = 32,598) who had a consultation with an alternative health care provider. Four groups of consultations are examined: (1) all consultations (2) massage therapy (3) acupuncture, and (4)

				homeopath/naturopath. Descriptive statistics, mapping and logistic regression modeling are employed to analyze the data and to compare modalities of alternative health care use. RESULTS: In 2005, more than 1.2 million adults aged 18 or over consulted an alternative health care provider, representing about 13% of the total population of Ontario. The analysis revealed a varied geographic pattern of consultations across the province. Consultations were fairly even across the urban to rural continuum and rural residents were just as likely to consult a provider as their urban counterparts. From a health perspective, people with a chronic condition, lower health status and self-perceived unmet health care needs were more likely to see an alternative health provider. Women with chronic conditions such as fibromyalgia, high blood pressure, chronic fatigue syndrome and chemical sensitivities were more likely to see an alternative provider if they felt their health care needs were not being met. CONCLUSIONS: The analysis revealed that geography is not a factor in determining alternative health care consultations in Ontario. By contrast, there is a strong association between these consultations and socio-demographic characteristics particularly age, sex, education, health and self-perceived unmet health care needs. The results underscore the importance of women's health needs as related to alternative care use. The paper concludes that there is a need for more place-specific research that explores the reasons why people use specific types of alternative health care as tied to socio-economic status, health, place of residence, and knowledge of these treatments.
Williams DK, Galvin TA, Ma H, Khan AS.	Laboratory of Retroviruses, Division of Viral Products, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, 8800 Rockville Pike, Bethesda, MD 20892, USA.	Investigation of xenotropic murine leukemia virus-related virus (XMRV) in human and other cell lines.	Biologicals. 2011 Nov;39(6):378-83. Epub 2011 Oct 12.	Xenotropic murine leukemia virus-related virus (XMRV) was discovered in human prostate tumors and later in some chronic fatigue syndrome (CFS) patients. However, subsequent studies have identified various sources of potential contamination with XMRV and other murine leukemia virus (MLV)-related sequences in test samples. Biological and nucleotide sequence analysis indicates that XMRV is distinct from known xenotropic MLVs and has a broad host range and cell tropism including human cells. Therefore, it is prudent to minimize the risk of human exposure to infection by evaluating XMRV contamination in cell lines handled in laboratory research and particularly those used in the manufacture of biological products. Nested DNA PCR assays were optimized for investigating XMRV gag and env sequences in various cell lines, which included MRC-5, Vero, HEK-293, MDCK, HeLa, and A549, that may be used in the development of some vaccines and other cell lines broadly used in research. The sensitivity of the DNA PCR assays was <10 copies in approximately 1.8 x 10(5) cells equivalent of human DNA. The results indicated the absence of XMRV in the cell lines tested; although in some cases DNA fragments identified as cellular sequences were seen following the first round of PCR amplification with the env primer pair. Published by Elsevier Ltd.
Wojcik W, Armstrong D,		Is chronic fatigue syndrome a	J Psychosom Res. 2011 Jun;70(6):573-4. Epub	

Kanaan R.		neurological condition? A survey of UK neurologists.	2011 Apr 8. Comment in J Psychosom Res. 2011 Jun;70(6):498-9.	
Wojcik W, Armstrong D, Kanaan R.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK.	Chronic fatigue syndrome: labels, meanings and consequences.	J Psychosom Res. 2011 Jun;70(6):500-4. Epub 2011 Apr 9. Comment in J Psychosom Res. 2011 Jun;70(6):498-9.	In this month's issue, we report a survey of members of the Association of British Neurologists, which asked if they viewed chronic fatigue syndrome (CFS) as a neurological condition--84% of respondents did not. This is at odds with current classification in ICD-10. We discuss the difficulties of classifying CFS and myalgic encephalopmeylitis (ME), including historical and sociological factors, the pitfalls of the physical/psychological dichotomy and why classification matters to doctors and patients. Copyright © 2011 Elsevier Inc. All rights reserved.
Wolff D, Gerritzen A.	Medical Laboratory Bremen, Bremen, Germany. dietmar.wolff@mlhb.de	Presence of murine leukemia virus (MLV)-related virus gene sequences in a commercial RT-PCR reagent.	Clin Lab. 2011;57(7-8):631-4.	BACKGROUND: The recent identification of murine leukemia virus (MLV)-related viruses in patients with chronic fatigue syndrome (CFS) has aroused much interest, not least among sufferers. However, other studies failed to detect these viruses in CFS patients. METHODS: We wanted to establish a MLV-related virus real-time PCR for routine diagnostics. RESULTS: Our study identified false positive MLV-related virus results due to a contamination of Superscript III Platinum One-Step Quantitative RT-PCR System (Invitrogen). CONCLUSIONS: This observation may be helpful to elucidate discrepant results for the detection of MLV-related virus like xenotropic MLV-related virus (XMRV) in recently published studies.
Wyller VB, Barbieri R, Saul JP.	Department of Pediatrics, Rikshospitalet University Hospital, 0027, Oslo, Norway. brwylle@online.no	Blood pressure variability and closed-loop baroreflex assessment in adolescent chronic fatigue syndrome during supine rest and orthostatic stress.	Eur J Appl Physiol. 2011 Mar;111(3):497-507. Epub 2010 Oct 2.	Hemodynamic abnormalities have been documented in the chronic fatigue syndrome (CFS), indicating functional disturbances of the autonomic nervous system responsible for cardiovascular regulation. The aim of this study was to explore blood pressure variability and closed-loop baroreflex function at rest and during mild orthostatic stress in adolescents with CFS. We included a consecutive sample of 14 adolescents 12-18 years old with CFS diagnosed according to a thorough and standardized set of investigations and 56 healthy control subjects of equal sex and age distribution. Heart rate and blood pressure were recorded continuously and non-invasively during supine rest and during lower body negative pressure (LBNP) of -20 mmHg to simulate mild orthostatic stress. Indices of blood pressure variability and baroreflex function (α-gain) were computed from monovariate and bivariate spectra in the low-frequency (LF) band (0.04-0.15 Hz) and the high-frequency (HF) band (0.15-0.50 Hz), using an autoregressive algorithm. Variability of systolic blood pressure in the HF range was lower among CFS patients as compared to controls both at rest and during LBNP. During LBNP, compared to controls, α-gain HF decreased more, and α-gain LF and the ratio of α-gain LF/α-gain HF increased more in CFS patients, all suggesting greater shift from parasympathetic to sympathetic baroreflex control. CFS in adolescents is characterized by reduced systolic blood pressure variability and a sympathetic predominance of baroreflex heart rate control during orthostatic stress. These findings may have implications for the pathophysiology of CFS in adolescents.
Yoldi B.		[Cognitive disorder: a	Med Clin (Barc). 2011	

		reality in the chronic fatigue syndrome]. [Article in Spanish]	Nov 12;137(12):572; author reply 572-3. Epub 2011 Jun 23. Comment on Med Clin (Barc). 2011 Mar 12;136(6):239-43. Med Clin (Barc). 2011 Mar 12;136(6):248-9.	
Yuan JP, Peng J, Yin K, Wang JH.	Guangdong Provincial Key Laboratory of Marine Resources and Coastal Engineering, School of Marine Sciences, Sun Yat-Sen University, Guangzhou, PR China. yuanjp@mail.sysu.edu.cn	Potential health-promoting effects of astaxanthin: a high-value carotenoid mostly from microalgae.	Mol Nutr Food Res. 2011 Jan;55(1):150-65. doi: 10.1002/mnfr.201000414. Epub 2010 Nov 18.	The ketocarotenoid astaxanthin can be found in the microalgae Haematococcus pluvialis, Chlorella zofingiensis, and Chlorococcum sp., and the red yeast Phaffia rhodozyma. The microalga H. pluvialis has the highest capacity to accumulate astaxanthin up to 4-5% of cell dry weight. Astaxanthin has been attributed with extraordinary potential for protecting the organism against a wide range of diseases, and has considerable potential and promising applications in human health. Numerous studies have shown that astaxanthin has potential health-promoting effects in the prevention and treatment of various diseases, such as cancers, chronic inflammatory diseases, metabolic syndrome, diabetes, diabetic nephropathy, cardiovascular diseases, gastrointestinal diseases, liver diseases, neurodegenerative diseases, eye diseases, skin diseases, exercise-induced fatigue, male infertility, and $HgCl_2$-induced acute renal failure. In this article, the currently available scientific literature regarding the most significant activities of astaxanthin is reviewed. Copyright © 2011 WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim.
Yunus MB.	Section of Rheumatology, Department of Medicine, University of Illinois College of Medicine at Peoria, One Illini Drive, Peoria, IL 61605, USA.	The prevalence of fibromyalgia in other chronic pain conditions.	Pain Res Treat. 2012;2012:584573. Epub 2011 Nov 17.	Central sensitivity syndromes (CSS) include fibromyalgia syndrome (FMS), irritable bowel syndrome, temporomandibular disorder, restless legs syndrome, chronic fatigue syndrome, and other similar chronic painful conditions that are based on central sensitization (CS). CSS are mutually associated. In this paper, prevalence of FMS among other members of CSS has been described. An important recent recognition is an increased prevalence of FMS in other chronic pain conditions with structural pathology, for example, rheumatoid arthritis, systemic lupus, ankylosing spondylitis, osteoarthritis, diabetes mellitus, and inflammatory bowel disease. Diagnosis and proper management of FMS among these diseases are of crucial importance so that unwarranted use of such medications as corticosteroids can be avoided, since FMS often occurs when RA or SLE is relatively mild.
Zadrazil J.	III. interní nefrologická, revmatologická a endokrinologcá klinika Lékaiské fakulty UP a FN Olomouc.	[Aetiology and a clinical picture of chronic renal failure]. [Article in Czech]	Vnitr Lek. 2011 Jul-Aug;57(7-8):607-13.	The term chronic renal failure (CRF) usually means the final stage of chronic kidney disease (CKD) with a decline in glomerular filtration rate (GF) below 0.25 mL/s. CRF is a world-wide serious health and economic issue with an increasing incidence and prevalence. CRF patients are, in comparison to other patients, hospitalized more often and for longer and, despite improvements in care, their quality of life is usually low and morbidity and mortality high. We present an overview of the most important CKD risk factors and the diseases most likely to result in CRF. Diabetic nephropathy,

	josef.zadrazil@fnol.cz			followed by various forms ofischemic renal disease and primary and secondary glomerulopathy, chronic tubulointerstitial nephritis and autosomal dominant polycystic kidney disease are the leading causes of CRF. We provide a brief overview of other disease states that may result in renal failure. Clinical manifestations of CRF are discussed, mainly cardiovascular, gastrointestinal, haematological and neurological symptoms. Breathlessness is a consequence of hypervolaemia, metabolic acidosis and anaemia. The disease often presents with symptoms, such as headache and visual disturbances, resulting from arterial hypertension. Gastrointestinal symptoms and fatigue, usually caused by anaemia, are frequent. Platelet dysfunction is manifested as an increased bleeding time. Paradoxically, apart form tendency to abnormal bleeding, CRF also tends to be associated with thromboembolic complications. Patients may experience itching, bone, joint and muscle aches, are more prone to infections. They may suffer from insomnia, concentration disorders and apathy. The signs of peripheral mixed sensory-motor neuropathy include paraesthesia, paresis and restless leg syndrome. However, renal failure may also be oligosymptomatic or asymptomatic. Cardiovascular complications are the most frequent cause of morbidity and mortality of CRF patients.
Zeller L, Abu-Shakra M, Weitzman D, Buskila D.	Department of Medicine F, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel.	The effect of exercise cessation on non-articular tenderness measures and quality of life in well-trained athletes.	Isr Med Assoc J. 2011 Jan;13(1):44-7.	BACKGROUND: The term chronic multi-symptom illness (CMI) refers to a spectrum of pain disorders, such as fibromyalgia and chronic fatigue syndrome, that are characterized by unexplained chronic pain, fatigue, and cognitive and mood complaints OBJECTIVES: To examine the hypothesis that exercise cessation is associated with symptoms similar to CMI in well-trained amateur athletes. METHODS: The study, conducted in running and triathlon clubs in Israel, involved 26 asymptomatic healthy athletes who regularly exercise 6.75 +/- 3.65 hours a week. All athletes were instructed to refrain from physical activity for 7 days. All underwent a complete physical exam, rheumatological assessment including non-articular tenderness threshold (using dolorimeter) and tender points. In addition they completed the SF-36 quality of life questionnaire. Assessments were conducted before exercise cessation and 7 days later. RESULTS: Seven days after sports deprivation all subjects were significantly more tender by all tender measures ($P < 0.001$) (dolorimeter thresholds and tender point count). There was also a significant reduction in the scores for physical role function ($P < 0.001$), emotional role function ($P < 0.001$) and summary subscales of the SF-36 questionnaire after exercise cessation. CONCLUSIONS: Exercise deprivation is associated with change in non-articular tenderness threshold and reduction in quality of life scores. This may be associated with the development of chronic multi-symptom illness.
Zhang HY, Liu ZD, Hu CJ, Wang DX, Zhang YB, Li YZ.	Department of Rheumatology and Clinical Immunology,	Up-regulation of TGF-β1 mRNA expression in peripheral blood mononuclear cells of	J Formos Med Assoc. 2011 Nov;110(11):701-4. Epub 2011 Oct 22.	BACKGROUND/PURPOSE: It has been shown that the abnormality in immune cells in chronic fatigue syndrome (CFS) patients is closely associated with the participation of TGF-β. In order to study the relationship between TGF-β1 and CFS, we investigated the mRNA levels of TGF-β1 in peripheral blood mononuclear cells (PBMCs) in patients

	Peking Union Medical College Hospital, Chinese Academy of Medical Science, No. 1 Shuaifuyuan, Beijing, China.	patients with chronic fatigue syndrome.		with CFS. METHODS: Fluorescent quantitative real time reverse-transcription polymerase chain reaction (FQ-RT-PCR) was performed to test TGF-β1 mRNA expression in PBMCs in 63 cases of CFS, 50 cases of disease controls, and 50 cases of healthy controls. RESULTS: The mean value of TGF-β1 mRNA expression in CFS patients was ΔΔCt=1.17±0.58, which was significantly higher than the disease controls (ΔΔCt=0.07±1.08, df=111, $p < 0.01$) and the healthy controls (ΔΔCt=0.00±1.63, df=111, $p < 0.01$). No significant difference was detected between disease and healthy controls ($p > 0.05$). CONCLUSION: The expression of TGF-β1 in PBMCs is significantly elevated in patients with CFS. It might be correlated to the pathogenesis of the disease. Copyright © 2011. Published by Elsevier B.V.
Zhang ZZ, Guo BF, Feng Z, Zhang L, Zhao XJ.	Department of Epidemiology, Michigan State University, East Lansing, MI 48224, USA.	Is XMRV a causal virus for prostate cancer?	Asian J Androl. 2011 Sep;13(5):698-701. doi: 10.1038/aja.2011.32. Epub 2011 Jul 18.	The potential association between xenotropic murine leukaemia virus-related gammaretrovirus (XMRV) and prostate cancer (PCa) has been documented since 2006. It is important for furthering our understanding of the biological mechanisms of PCa to ascertain whether this association is causal. To summarize the available information on the epidemiological and laboratory findings of the association, we conducted a literature search of the PubMed electronic database (from March 2006 to February 2011) to identify relevant published studies that examined the association between XMRV and PCa. Although several studies showed the positive association between XMRV and PCa, more recent studies did not support this conclusion. The positive findings might be due to contamination of human samples. Further studies are needed to clarify this association.
Zheng H, Jia H, Shankar A, Heneine W, Switzer WM.	Laboratory Branch, Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America.	Detection of murine leukemia virus or mouse DNA in commercial RT-PCR reagents and human DNAs.	PLoS One. 2011;6(12):e29050. Epub 2011 Dec 20.	The xenotropic murine leukemia virus (MLV)-related viruses (XMRV) have been reported in persons with prostate cancer, chronic fatigue syndrome, and less frequently in blood donors. Polytropic MLVs have also been described in persons with CFS and blood donors. However, many studies have failed to confirm these findings, raising the possibility of contamination as a source of the positive results. One PCR reagent, Platinum Taq polymerase (pol) has been reported to contain mouse DNA that produces false-positive MLV PCR results. We report here the finding of a large number of PCR reagents that have low levels of MLV sequences. We found that recombinant reverse-transcriptase (RT) enzymes from six companies derived from either MLV or avian myeloblastosis virus contained MLV pol DNA sequences but not gag or mouse DNA sequences. Sequence and phylogenetic analysis showed high relatedness to Moloney MLV, suggesting residual contamination with an RT-containing plasmid. In addition, we identified contamination with mouse DNA and a variety of MLV sequences in commercially available human DNAs from leukocytes, brain tissues, and cell lines. These results identify new sources of MLV contamination and highlight the importance of careful pre-screening of commercial specimens and diagnostic reagents to avoid false-positive MLV PCR results.
Şimşek I.	Medicine Faculty, Department of	Irritable bowel syndrome and other	J Clin Gastroenterol. 2011 Aug;45	Irritable bowel syndrome is one of several highly prevalent functional gastrointestinal disorders (FGID) displaying symptoms of gastrointestinal dysmotility and visceral

	Gastroenterology, Dokuz Eylul University, Izmir, Turkey. ilkay.simsek@deu.edu.tr	functional gastrointestinal disorders.	Suppl:S86-8.	hypersensitivity. Substantial overlap of symptoms and comorbidities occur not only between irritable bowel syndrome and other FGID but also with gastrointestinal disorders that are not related to motility (eg, celiac disease and lactose intolerance) and to somatic conditions (eg, fibromyalgia and chronic fatigue syndrome). Pathogenic mechanisms common among FGIDs may include alternations in intestinal and colonic microflora. Evidence is also emerging of an interplay between gut immune cells/activity and alternations in motility, secretion, and sensation. The role of cytokine activity and inflammation is important in this regard. As recommended by Rome III, diagnostic testing should be guided by the patient's age, primary symptom characteristics, and other clinical and laboratory features. The high prevalence of coexisting conditions suggests the need to routinely assess patients for related disorders. Treatment should be based on an individualized evaluation, explanation, and reassurance.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No authors listed]		Chronic fatigue syndrome: going viral?	Lancet. 2010 Sep 18;376(9745):930.	
[No authors listed]	Medicinska Lliniken, Falu Lasarettet. johannes.lindh@ltdalarna.se	[Stress, mental illness and our cultural diseases. Don't wink at the pathogenesis!]. [Article in Swedish]	Lakartidningen. 2010 Sep 15-21;107(37):2141.	
[No authors listed]		My wife has been diagnosed with chronic fatigue syndrome (CFS). What is this condition, and what is the treatment for it?	Duke Med Health News. 2010 Mar;16(3):8.	
[No authors listed]		Wiped out: new findings on chronic fatigue syndrome.	Johns Hopkins Med Lett Health After 50. 2010 Apr;22(2):1-2, 7.	
Ablin JN, Odes L, Neumann L, Buskila D.	Institute of Rheumatology and Internal Medicine 6, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel. ajacob@post.tau.ac.il	The Hebrew version of the FibroFatigue scale: validation of a questionnaire for assessment of fibromyalgia and chronic fatigue syndrome.	Rheumatol Int. 2010 Jul;30(9):1173-6. Epub 2009 Sep 25.	The objective of this study is to validate a translated Hebrew version of the FibroFatigue Scale (FFS). The Hebrew version of the FFS was administered to 100 patients fulfilling ACR criteria for classification of FM together with the validated Hebrew version of the Fibromyalgia Impact Questionnaire (FIQ), the validated Hebrew version of the Short Form-36 (SF-36) and a Visual Analogue Scale (VAS) measurement of pain, anxiety, depression, morning stiffness and global well being. Test-retest reliability was assessed using Spearman correlations. Internal consistency was evaluated with Cronbach's alpha of reliability. Construct validity of the FFS was evaluated by correlations among the FFS, the FIQ and the subscales of the SF-36. Mean duration of symptoms was 10.7 years, and mean age of participants was 53.5 years. Test-retest reliability was between 0.46 and 0.85 for the various FFS items. Internal consistency was 0.89 for the overall FFS. Significant correlations were obtained between the FFS items and the SF-36. These results support the reliability and validity of the data obtained with the Hebrew version of the FSS for detecting and measuring symptom severity in Hebrew speaking patients with FM.
Ahlborg G Jr, Glise K, Ellbin S, Nordin-Johansson A, Birgander LS,		[New health insurance rules no obstacles for good prognosis in	Lakartidningen. 2010 Jul 21-Aug 10;107(29-31):1789-90.	

Stenlund T.		fatigue syndrome]. [Article in Swedish]		
Alegre J, Rosés JM, Javierre C, Ruiz-Baqués A, Segundo MJ, de Sevilla TF.	Servicio de Medicina Interna, Hospital Vall d'Hebrón, Barcelona, España.	[Nicotinamide adenine dinucleotide (NADH) in patients with chronic fatigue syndrome]. [Article in Spanish]	Rev Clin Esp. 2010 Jun;210(6):284-8. Epub 2010 May 5.	BACKGROUND: Nicotinamide adenine dinucleotide (NADH) may be depleted in chronic fatigue syndrome (SFC). The purpose of the study was to evaluate the efficacy of supplementation with NADH in these patients. MATERIAL AND METHODS: A double blind, placebo controlled, 3 month long clinical trial was conducted. The patients were randomized to oral NADH oral 20mg or placebo during the first two months. The intensity of the fatigue, functional performance, mood state, functional impact of the fatigue, quality of life, sleep quality, exercise capacity and functional reserve as well as the investigator's and patient's opinion on the efficacy of the intervention prior to and at 30, 60 and 90 days of the onset of the treatment were evaluated. A stress test was performed in the baseline visit and at 60 days (last day of the double blind treatment). RESULTS: A total of 86 patients, 77 of whom completed the study (mean age, 47 years, 72 women) were enrolled. No significant differences were found in most of the variable studied at the end of the study. Administration of NADH was associated to a decrease in anxiety condition of -1.0 points ($p<0.05$) and of -0.2 points (p=NS) in the placebo assigned group. Maximum heart rate after the stress test decreased a mean of -8.1l/min ($p<0.05$) in the NADH group and increased by +1.7l/min in the placebo group (p=0.73). No differences were found in the perception of efficacy with NADH and placebo, by the investigator and patients. CONCLUSIONS: Administration of oral NADH was associated to a decrease in anxiety and maximum heart rate, after a stress test in patients with CFS. On the contrary, this treatment did not modify other clinical variables and the global functional performance.
Armes J.	Florence Nightingale School of Nursing & Midwifery, King's College London, London, UK. jo.armes@kcl.ac.uk	Nurse-delivered, home-based pragmatic rehabilitation has a short-term effect on improving fatigue in people with chronic fatigue syndrome compared with usual GP care, but effects were not sustained at 1 year.	Evid Based Nurs. 2010 Oct;13(4):125-6. Comment on: BMJ. 2010;340:c1777.	
Asberg M, Grape T, Krakau I, Nygren A, Rohde M, Wahlberg A, Währborg P.	Karolinska Institutet/Danderyds Sjukhus, Stockholm. marie.asberg@ki.se	[Stress as the cause of mental illness]. [Article in Swedish]	Lakartidningen. 2010 May 12-25;107(19-20):1307-10.	

Atkinson W.		Chronic fatigue syndrome poses management challenge.	Manag Care. 2010 Oct;19(10):24-6.	
Avellaneda Fernández A, Izquierdo Martínez M.	CS los Cármenes, Madrid, Cátedra de Salud Pública y Gestión Sanitaria, Universidad Europea de Madrid, Madrid, España.	[Cognitive impairment: a reality in chronic fatigue syndrome.] [Article in Spanish]	Med Clin (Barc). 2010 Dec 17. [Epub ahead of print]	
Bakker RJ, van de Putte EM, Kuis W, Sinnema G.	Department of Pediatrics, Antonius Ziekenhuis, Sneek, The Netherlands.	Effects of an educational video film in fatigued children and adolescents: a randomised controlled trial.	Arch Dis Child. 2010 Sep 22. [Epub ahead of print]	Background In many cases standard management for chronic fatigue syndrome (CFS) in children and adolescents is ineffective. Objective To evaluate the efficacy of a video film intervention in preventing the development of persistent fatigue and significant school absence in fatigued children and adolescents. Design Randomised controlled trial. Participants 91 patients with fatigue; 50 were randomly assigned to receive the intervention (video film plus usual care) and 41 to usual care only. Intervention A video film on CFS and coping behaviour. Main outcome measures Self-reported fatigue severity, physical activity, motivation, concentration and school absence. Results 79 patients had complete data at 12 months (42 in the video film and 37 in the usual care group). Mean fatigue severity and school absenteeism scores did not differ significantly, but in the intervention group the score for reduced motivation was higher (difference 2.9 (CI 0.1 to 5.7), p=0.038). 18% more patients in the intervention compared to the usual care group also had persistent fatigue with significant school absence. The odds of developing persistent fatigue and of missing >50% of school classes was 3.3 times higher in the intervention than in the usual care group (OR 3.3 (CI 1.0 to 11.3), p=0.046). Conclusion This particular video film intervention plus usual care in children and adolescents with unexplained fatigue did not prevent an unfavourable outcome and possibly had an adverse effect in that it reduced motivation and increased the incidence of persistent fatigue with significant school absence. The use of this particular film is not recommended.
Bannert N.		Is a novel human retrovirus associated with prostate cancer and chronic fatigue syndrome?	Future Microbiol. 2010 May;5(5):689-91.	
Baraniuk JN, Zheng Y.	Division of Rheumatology, Immunology and Allergy, Georgetown	Relationships among rhinitis, fibromyalgia, and chronic fatigue.	Allergy Asthma Proc. 2010 May-Jun;31(3):169-78.	New information about the pathophysiology of idiopathic nonallergic rhinopathy indicates a high prevalence in chronic fatigue syndrome (CFS). This article shows the relevance of CFS and allied disorders to allergy practice. CFS has significant overlap with systemic hyperalgesia (fibromyalgia), autonomic dysfunction (irritable bowel syndrome and migraine headaches), sensory hypersensitivity (dyspnea; congestion; rhinorrhea; and appreciation of visceral nociception in the esophagus,

	University, PHC Building, 3800 Reservoir Road, NW, Washington, DC 20007-2197, USA. baraniuj@georgetown.edu			gastrointestinal tract, bladder, and other organs), and central nervous system maladaptations (central sensitization) recorded by functional magnetic resonance imaging (fMRI). Neurological dysfunction may account for the overlap of CFS with idiopathic nonallergic rhinopathy. Scientific advances are in fMRI, nociceptive sensor expression, and, potentially, infection with xenotropic murine leukemia-related virus provide additional insights to novel pathophysiological mechanisms of the "functional" complaints of these patients that are mistakenly interpreted as allergic syndromes. As allergists, we must accept the clinical challenges posed by these complex patients and provide proper diagnoses, assurance, and optimum care even though current treatment algorithms are lacking.
Baraniuk JN.	Georgetown University, 3800 Reservoir Road NW, Washington, DC 20007-2197, USA. baraniuj@georgetown.edu	Xenotropic murine leukemia virus-related virus in chronic fatigue syndrome and prostate cancer.	Curr Allergy Asthma Rep. 2010 May;10(3):210-4.	Xenotropic murine leukemia virus-related virus (XMRV) is a gamma retrovirus that has been associated with chronic fatigue syndrome (CFS) and prostate cancer. The search for viral causes of these syndromes was reignited by the finding that RNase L activity was low in hereditary prostate cancer and some CFS patients. The six strains of XMRV that have been sequenced have greater than 99% identity, indicating a new human infection rather than laboratory contamination. DNA, RNA, and proteins from XMRV have been detected in 50% to 67% of CFS patients and in about 3.7% of healthy controls. XMRV infections could be transmitted to permissive cell lines from CFS plasma, suggesting the potential for communicable and blood-borne spread of the virus and potentially CFS. This troubling concept is currently under intense evaluation. The most important steps now are to independently confirm the initial findings; develop reliable assays of biomarkers; and to move on to investigations of XMRV pathophysiology and treatment in CFS, prostate cancer, and potentially other virus-related syndromes, if they exist.
Barnes E, Flanagan P, Brown A, Robinson N, Brown H, McClure M, Oxenius A, Collier J, Weber J, Günthard HF, Hirschel B, Fidler S, Phillips R, Frater J.	Nuffield Department of Clinical Medicine, Peter Medawar Building for Pathogen Research, Oxford University, and Oxford NIHR Biomedical Research Centre, Oxford, United Kingdom.	Failure to detect xenotropic murine leukemia virus-related virus in blood of individuals at high risk of blood-borne viral infections.	J Infect Dis. 2010 Nov 15;202(10):1482-5. Epub 2010 Oct 11. Comment in: J Infect Dis. 2010 Nov 15;202(10):1463-6.	A xenotropic murine leukemia virus-related virus (XMRV) has recently been reported in association with prostate cancer and chronic fatigue syndrome, with a prevalence of up to 3.7% in the healthy population. We looked for XMRV in 230 patients with human immunodeficiency virus type 1 or hepatitis C infection. XMRV was undetectable in plasma or peripheral blood mononuclear cells by polymerase chain reaction targeting XMRV gag or env. T cell responses to XMRV Gag were undetectable in peripheral blood mononuclear cells by ex vivo gamma interferon enzyme-linked immunospot assay. In our cohorts, XMRV was not enriched in patients with blood-borne or sexually transmitted infections from the United Kingdom and Western Europe.
Basseri B, Yamini D, Chee G, Enayati PD, Tran T, Poordad F.	Hepatology Section, Division of Gastroenterology, Cedars-Sinai Medical Center, Los Angeles, CA, USA.	Comorbidities associated with the increasing burden of hepatitis C infection.	Liver Int. 2010 Aug;30(7):1012-8. Epub 2010 Apr 8.	BACKGROUND: Hepatitis C virus (HCV) infection is implicated in an increasing number of liver transplantations, hospitalizations and healthcare costs. AIMS: We present an updated assessment of comorbidities associated with HCV in comparison to the general US population. METHODS: Cross-sectional retrospective review of data from 800 patients with HCV evaluated between January 1998 and November 2007. Patient data were prospectively collected using a standardized questionnaire completed at the first encounter and was compared with general US epidemiological data. Odds ratios and 95% confidence intervals (CI) are reported. RESULTS: HCV conferred a 44% (CI 1.16-1.78) and 25%

				(CI 1.01-1.54) increased risk of diabetes (12.5 vs. 7.3-8.4%; P=0.001) and obesity (23.9 vs. 19.8-33.1%; P=0.041), respectively, compared with the US population. Human immunodeficiency virus (HIV) (5.3 vs. 0.3%; P<0.001) and end-stage renal disease (ESRD) (4.5 vs. 0.2%; P<0.001) were 16- and 13-fold more prevalent in HCV. Interestingly, HCV bestowed 90% decreased odds (CI 0.09-0.15) for hyperlipidaemia (12.3 vs. 53.2-56.1%; P<0.001). The HCV population had a higher prevalence of significant alcohol consumption (41.5 vs. 4.7%; P<0.001), current smoking (57.7 vs. 18.8-20.8%; P<0.001), drug use (46.8 vs. 14.6-15.6%; P<0.001), incarceration (6.6 vs. 2.7%; P<0.001) and tattoos (20.3 vs. 14%; P=0.011), as well as chronic fatigue (44.6 vs. 11.3-19%; P<0.001) and depression (29.3 vs. 5.0-10.3%; P<0.001). CONCLUSION: HCV poses an increasing healthcare burden associated with increased prevalence of diabetes, obesity, HIV, ESRD, maladaptive lifestyle habits and poor quality of life. Practitioners should be cognizant of these trends in order to appropriately manage these comorbidities.
Beever R.	Department of Family Medicine, University of British Columbia, British Columbia, Canada. Richard.beever@northernhealth.ca	The effects of repeated thermal therapy on quality of life in patients with type II diabetes mellitus.	J Altern Complement Med. 2010 Jun;16(6):677-81.	OBJECTIVES: Decreased quality of life in diabetes is associated with poor health outcomes. Far-infrared sauna treatments improve the quality of life for those with chronic pain, chronic fatigue syndrome, depression, and congestive heart failure. The objective of this study is to determine whether far-infrared saunas have a beneficial effect on quality of life in those with type II diabetes. DESIGN: This was a sequential, longitudinal, interrupted time series design study. SETTING/LOCATION: The setting was Fraser Lake BC, a rural village in central British Columbia, Canada. SUBJECTS: All patients of the Fraser Lake Community Health Center with type II diabetes were invited to participate in this study. INTERVENTIONS: The study consisted of 20-minute, 3 times weekly infrared sauna sessions, over a period of 3 months. OUTCOME MEASURES: To assess quality of life, subjects completed the 36-item Short-form Health Survey Version 2 (SF-36v2) questionnaire as well as "Zero-to-Ten" Visual Analogue Scales. Baseline study parameters were measured within 1 week prior to commencing sauna sessions. Postintervention measurements were collected between 1 and 3 days after the last sauna session. RESULTS: Physical health, general health, and social functioning indices of the SF-36v2 improved. Visual Analogue Scales for stress and fatigue improved. CONCLUSIONS: Far-infrared sauna use maybe associated with improved quality of life in people with type II diabetes mellitus. Uptake of infrared saunas use is greater than the uptake of other lifestyle interventions.
Biswal B, Kunwar P, Natelson BH.	Departments of Radiology, UMDNJ-New Jersey Medical School, Newark NJ, United States.	Cerebral blood flow is reduced in chronic fatigue syndrome as assessed by arterial spin labeling.	J Neurol Sci. 2010 Dec 15. [Epub ahead of print]	BACKGROUND: Chronic fatigue syndrome is diagnosed by a set of clinical criteria and therefore is probably heterogeneous. Earlier reports tested the hypothesis that the syndrome had a neurological substrate by doing studies of cerebral blood flow (CBF) but with discrepant results. One possible reason for the discrepancy was that relative CBF was assessed. We found reduced CBF in an earlier study of absolute CBF using xenon-CT. The purpose of this study was to use a second method of assessing CBF and to look within the study group for heterogeneity of responses. METHOD: Eleven CFS patients and 10 age matched healthy controls underwent neuroimaging using arterial spin labeling to determine their regional and global absolute CBF. A template was constructed based on the control data, and individual patient montages were compared on a case by case basis to determine if differences in regions of interest occurred. RESULTS: The patients as a group had significantly lower global CBF than the controls. The reduction in CBF occurred across nearly every region assessed. Nine of the 11 patients showed these reductions compared to the average control data, while two patients

				showed actual increases relative to the controls. CONCLUSION: The data extend our earlier observation that CFS patients as a group have broad decreases in CBF compared to healthy controls. However, as expected, the effect was not homogeneous in that 2 of the 11 patients studied showed actual increases in CBF relative to controls.
Bjerregaard P, Nallapaneni H, Gussak I.	Division of Cardiology, VA Medical Center and Washington University in St. Louis, St. Louis, MO 63106, USA. preben.bjerregaard@va.gov	Short QT interval in clinical practice.	J Electrocardiol. 2010 Sep-Oct;43(5):390-5. Epub 2010 Jul 27.	The last ten years have seen a growing interest in clinical scenarios, where a short QT interval may play a role, especially because of an increased risk of sudden cardiac death in some situations. One such entity is Short QT Syndrome, which has emerged as a rare, but very malignant disease, in particular when the QT interval is very short. A short QT interval has also been noticed in some patients with other arrhythmic syndromes such as Idiopathic Ventricular Fibrillation, Brugade Syndrome and Early Repolarization Syndrome, but the role of a short QT interval in these settings is so far not known. Hypercalcemia often leads to shortening of the QT interval, but there are no data in humans to suggest an increased risk of sudden cardiac death in this setting. In addition, a shorter-than-usual QT interval has been reported in patients with Chronic Fatigue Syndrome and in response to atropine, catecholamine and Hyperthermia. When a short QT interval is encountered in daily clinical practice, these various scenarios needs to be considered, but it is still not possible to come up with clear guidelines for how to work up and risk stratify such individuals. Genetic testing is only useful in very few and the value of an electrophysiologic study, Holter monitoring or stress testing to assess QT adaptation to heart rate and T wave morphology analysis may all be helpful, but not well-established, tests in this setting.
Boneva RS, Maloney EM, Lin JM, Jones JF, Wieser F, Nater UM, Heim CM, Reeves WC.	1 Centers for Disease Control and Prevention , Atlanta, Georgia .	Gynecological History in Chronic Fatigue Syndrome: A Population-Based Case-Control Study.	J Womens Health (Larchmt). 2010 Nov 20. [Epub ahead of print]	Abstract Background: Chronic fatigue syndrome (CFS) affects disproportionately more women than men, and the condition is more common at perimenopause. We examined gynecological history events as risk factors for CFS. Methods: In a case-control study from a randomly selected population sample from Wichita, Kansas, 36 women with CFS and 48 nonfatigued controls, of similar age, race, and body mass index (BMI), answered a structured gynecological history questionnaire. Results: CFS cases and controls had the same mean age (51 years) and age at menarche (12 years). Overall, a greater proportion of women with CFS than controls reported pelvic pain unrelated to menstruation (22.2% vs. 1.7%, p = 0.004), endometriosis (36.1% vs. 16.7, %, p = 0.046), and periods of amenorrhea (53.9 % vs. 46.2%, p = 0.06). Compared to controls, women in the CFS group had a higher mean number of pregnancies (2.8 vs 2.0, p = 0.05) and gynecological surgeries (1.8 vs. 1.1, p = 0.05). Similar proportions of the CFS (69.4%) and control (72.9%) groups were menopausal. Although menopausal women in the CFS and control groups had similar mean age (55.5 and 55.8, respectively), menopause occurred about 4.4 years earlier in the CFS group (41.7 years vs. 46.1 years, respectively, p = 0.11). Among menopausal women, 76% of the CFS group reported hysterectomy vs. 54.6% of controls (p = 0.09), and 56% of women with CFS reported oophorectomy vs. 34.3% of controls (p = 0.11). Conclusions: The higher prevalence of gynecological conditions and gynecological surgeries in women with CFS highlights the importance of evaluating gynecological health in these patients and the need for more research to clarify the chronologic and the pathophysiological relationships between these conditions and CFS.
Brenu EW, Staines DR, Baskurt OK,	Faculty of Health Science and	Immune and hemorheological	J Transl Med. 2010 Jan 11;8:1.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is a multifactorial disorder that affects various physiological systems including immune and neurological systems. The immune system has been

Ashton KJ, Ramos SB, Christy RM, Marshall-Gradisnik SM.	Medicine, Population Health and Neuroimmunology Unit, Bond University, Robina, Queensland, Australia. ebrenu@student.bond.edu.au	changes in chronic fatigue syndrome.		substantially examined in CFS with equivocal results, however, little is known about the role of neutrophils and natural killer (NK) phenotypes in the pathomechanism of this disorder. Additionally the role of erythrocyte rheological characteristics in CFS has not been fully expounded. The objective of this present study was to determine deficiencies in lymphocyte function and erythrocyte rheology in CFS patients. METHODS: Flow cytometric measurements were performed for neutrophil function, lymphocyte numbers, NK phenotypes (CD56(dim)CD16(+) and CD56(bright)CD16(-)) and NK cytotoxic activity. Erythrocyte aggregation, deformability and fibrinogen levels were also assessed. RESULTS: CFS patients (n = 10) had significant decreases in neutrophil respiratory burst, NK cytotoxic activity and CD56(bright)CD16(-) NK phenotypes in comparison to healthy controls (n = 10). However, hemorheological characteristic, aggregation, deformability, fibrinogen, lymphocyte numbers and CD56(dim)CD16(+) NK cells were similar between the two groups. CONCLUSION: These results indicate immune dysfunction as potential contributors to the mechanism of CFS, as indicated by decreases in neutrophil respiratory burst, NK cell activity and NK phenotypes. Thus, immune cell function and phenotypes may be important diagnostic markers for CFS. The absence of rheological changes may indicate no abnormalities in erythrocytes of CFS patients.
Brimmer DJ, Fridinger F, Lin JM, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. dyv4@cdc.gov	U.S. healthcare providers' knowledge, attitudes, beliefs, and perceptions concerning Chronic Fatigue Syndrome.	BMC Fam Pract. 2010 Apr 21;11:28.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating illness with particular difficulties for healthcare providers because there are no diagnostic signs or laboratory tests and because management aims to merely improve symptoms. Further complicating management, healthcare providers' awareness concerning CFS has not been rigorously assessed. The present study aimed to ascertain United States (U.S.) healthcare providers' awareness of CFS and to assess their knowledge, attitudes, and beliefs (KAB) related to diagnosis and management of the illness. This information forms the foundation for developing CFS educational strategies. METHODS: We combined convenience and probability samples to measure CFS KAB among healthcare providers. In the convenience sample, 1,255 healthcare providers (81% response rate) from 13 professional conferences completed a 12-item form. Descriptive statistics were reported for 9 KAB item responses and chi-square tests were performed for examining their association with giving a diagnosis of CFS. We used principal component analysis to construct multidimensional subscales and perform a general linear model to examine factors associated with subscales. The probability sample involved data on 15 CFS-specific questions from 2006 and 2007 DocStyles web-based panel surveys collected from 2,750 physicians (average response rate 55%). We calculated descriptive and chi-square statistics. The significance was set at two-tailed with the alpha level of 0.05. RESULTS: Healthcare providers in both samples were aware of CFS and exhibited a high level of knowledge. Overall, 96% of respondents in the DocStyles (probability) sample had heard about CFS. Healthcare providers in the conference (convenience) sample demonstrated good KAB scores; physicians' scores were highest on KAB scales and lowest in perception. Nurses' scores were lowest in knowledge. More than 40% of physicians reported ever giving a CFS diagnosis and in the DocStyles (probability) sample more than 80% of physicians correctly identified CFS symptoms. Physicians reported professional journals, the Internet, and continuing education programs as the top 3 sources from which they obtain CFS information. CONCLUSIONS: Findings from these combined samples fill a gap in the evidence-base of U.S. healthcare providers' and knowledge, attitudes, and beliefs concerning CFS. Importantly, respondents

				in both samples expressed similar knowledge, attitudes, beliefs and perceptions. Awareness was high and negative attitudes were low. The primary areas for future education should address diagnosis and management of CFS and should be delivered through those venues providers indicated they primarily use. Data from this study provide a benchmark for evaluation the success of these future efforts.
Brkic S, Tomic S, Maric D, Novakov Mikic A, Turkulov V.	Clinic for Infectious Diseases, Clinical Center Vojvodina, Novi Sad, Serbia. tomkis@eunet.rs	Lipid peroxidation is elevated in female patients with chronic fatigue syndrome.	Med Sci Monit. 2010 Nov 30;16(12):CR628-32.	BACKGROUND: Chronic fatigue syndrome is a debilitating disease of unclear cause and pathogenesis. It affects mostly women from lower socioeconomic classes. There is mounting evidence that oxidative stress, specifically lipid peroxidation (LPO) contributes to the disease process. We investigated levels of LPO and its possible consequences for these patients. MATERIAL/METHODS: Forty women aged 15-45 years who fulfilled the 1994 Centers for Disease Control's diagnostic criteria for chronic fatigue syndrome (CFS) with no comorbidities were recruited and were age matched to a control group of 40 healthy women. Levels of total cholesterol (TC), triglycerides (TG), LDL cholesterol (LDLc), HDL cholesterol (HDLc), and malondialdehyde (MDA) levels were measured. RESULTS: Although initial statistical analyses showed no differences between groups (P=.345), when subdivided according to the level of MDA, a difference was found in the subgroup of high-level MDA (P=.034). There was a negative correlation between HDLc and MDA levels (r=0.3; P=.046), a positive correlation between TG and MDA levels (r=0.4; P=.006), and lower levels of HDL cholesterol in the CFS group (P=.036). CONCLUSIONS: High levels of MDA, positively correlated with TG and lower HDL levels, might be indicative of proatherogenic events in female CFS patients, a group not otherwise considered a risk for atherosclerosis.
Broderick G, Fuite J, Kreitz A, Vernon SD, Klimas N, Fletcher MA.	Division of Pulmonary Medicine, Department of Medicine, University of Alberta, College Plaza, 8215 112 Street NW, Edmonton, Alberta, Canada. gordon.broderick @ualberta.ca	A formal analysis of cytokine networks in chronic fatigue syndrome.	Brain Behav Immun. 2010 Oct;24(7):1209-17. Epub 2010 May 4. Comment in: Brain Behav Immun. 2010 Oct;24(7):1218; author reply 1219.	Chronic Fatigue Syndrome (CFS) is a complex illness affecting 4 million Americans for which no characteristic lesion has been identified. Instead of searching for a deficiency in any single marker, we propose that CFS is associated with a profound imbalance in the regulation of immune function forcing a departure from standard pre-programmed responses. To identify these imbalances we apply network analysis to the co-expression of 16 cytokines in CFS subjects and healthy controls. Concentrations of IL-1a, 1b, 2, 4, 5, 6, 8, 10, 12, 13, 15, 17 and 23, IFN-γ, lymphotoxin-α (LT-α) and TNF-α were measured in the plasma of 40 female CFS and 59 case-matched controls. Cytokine co-expression networks were constructed from the pair-wise mutual information (MI) patterns found within each subject group. These networks differed in topology significantly more than expected by chance with the CFS network being more hub-like in design. Analysis of local modularity isolated statistically distinct cytokine communities recognizable as pre-programmed immune functional components. These showed highly attenuated Th1 and Th17 immune responses in CFS. High Th2 marker expression but weak interaction patterns pointed to an established Th2 inflammatory milieu. Similarly, altered associations in CFS provided indirect evidence of diminished NK cell responsiveness to IL-12 and LT-α stimulus. These observations are consistent with several processes active in latent viral infection and would not have been uncovered by assessing marker expression alone. Furthermore this analysis identifies key sub-networks such as IL-2:IFN-γ:TNF-α that might be targeted in restoring normal immune function.
Brown M, Khorana N, Jason LA.	DePaul University.	The role of changes in activity as a function of	J Clin Psychol. 2010 Oct 25. [Epub ahead of print]	Nonpharmacological interventions for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) often emphasize gradual increases in activity to promote improvement in physical functioning and fatigue. The energy envelope theory may provide a framework for understanding the relationship

		perceived available and expended energy in nonpharmacological treatment outcomes for ME/CFS.		between changes in activity level and outcomes for patients with ME/CFS. This study examined the relationship between energy envelope and changes in activity after nonpharmacological interventions in a sample of 44 adults with ME/CFS. Results showed that those who were within their energy envelope before treatment showed more improvement in physical functioning and fatigue compared with those outside of their energy envelope. These findings suggest that an assessment of perceived available and expended energy could help guide the development of individualized nonpharmacological interventions for people with ME/CFS. © 2010 Wiley Periodicals, Inc. J Clin Psychol 00:1-8, 2010.
Brown MM, Brown AA, Jason LA.	Center for Community Research, DePaul University, Chicago, IL 60614, USA. mbrown59@depaul.edu	Illness duration and coping style in chronic fatigue syndrome.	Psychol Rep. 2010 Apr;106(2):383-93.	A sample of patients with chronic fatigue syndrome was recruited to assess coping strategies and illness duration. It was hypothesized that adaptive coping strategies would be higher among those with longer illness duration. Those in the longer illness duration group reported higher use of active coping, positive reframing, planning, and acceptance, and lower use of behavioral disengagement than those in the shorter illness duration group. No significant differences were found between the two illness duration groups for physical impairment or symptom severity, but the long duration group revealed a lower percentage of participants who were working than the short duration group. These findings suggest that individuals with longer or shorter duration of the illness have differences in coping styles but not differences in physical impairment or symptom severity.
Burton AR, Rahman K, Kadota Y, Lloyd A, Vollmer-Conna U.	School of Psychiatry, University of NSW, Sydney, Australia.	Reduced heart rate variability predicts poor sleep quality in a case-control study of chronic fatigue syndrome.	Exp Brain Res. 2010 Jul;204(1):71-8. Epub 2010 May 26.	Parasympathetic function is important in the induction and maintenance of sleep. We examined whether nocturnal vagal modulation of heart rate is related to the poor sleep quality commonly reported in chronic fatigue syndrome (CFS). Heart rate (HR, as R-R intervals) was continuously monitored during sleep in 20 patients with CFS and 20 matched control subjects. Questionnaires assessed demographic information, symptoms, functional impairment, and subjective sleep quality. CFS was associated with more sleep problems in general and poorer subjective sleep quality on the study night (all $p < 0.003$), and reports of repeated awakening during the night were 7 times more likely compared to healthy subjects ($p = 0.017$). Time and frequency-domain parameters of HR variability during sleep were significantly lower in patients with CFS (all $p < 0.006$). Multiple regression analyses revealed that heart rate variability (HRV) parameters were the best predictors of subjective sleep measures. This study identified significant reductions in vagal modulation of heart rate during sleep in CFS. Low HRV strongly predicted sleep quality-suggesting a pervasive state of nocturnal sympathetic hypervigilance in CFS.
Bürgel B, Friesland M, Koch A, Manns MP, Wedemeyer H, Weissenborn K, Schulz-Schaeffer WJ, Pietschmann T, Steinmann E, Ciesek S.	Division of Experimental Virology, TWINCORE, Centre for Experimental and Clinical Infection Research; a joint venture between the Medical School	Hepatitis C virus enters human peripheral neuroblastoma cells - evidence for extra-hepatic cells sustaining hepatitis C virus penetration.	J Viral Hepat. 2010 Jun 23. [Epub ahead of print]	Summary. Patients with chronic hepatitis C virus (HCV) infection show an increased incidence of nervous system disorders such as chronic fatigue syndrome, depression and cognitive dysfunction. It is unclear whether this is because of HCV replication in the brain and in peripheral neuronal cells or to more indirect effects of HCV infection on the central or peripheral nervous system. The aim of this study was to investigate whether cells originating from these tissues are permissive for HCV cell entry, RNA replication and virus assembly. Among eight cell lines analysed, the human peripheral neuroblastoma cell line SKNMC expressed all HCV entry factors and was efficiently infected with HCV pseudoparticles (HCVpp) independent of the HCV genotype. All remaining cell types including human neuroblastoma and glioblastoma cell lines and microglial cells lacked expression of at least one host factor essential for HCV entry. When transfected with HCV luciferase reporter virus RNA, inoculated

	Hannover (MHH) and the Helmholtz Centre for Infection Research (HZI), Hannover, Germany.			with HCV reporter viruses or challenged with high-titre cell culture-derived HCV, none of these cells supported detectable HCV RNA replication. Thus, in conclusion, this comprehensive screening did not reveal evidence directly strengthening the notion that HCV enters and replicates in the central nervous system. However, productive viral entry into the peripheral neuroblastoma cell line SKNMC indicates that HCV may penetrate into certain nonhepatic cell types which may serve as viral reservoirs and could modulate viral pathogenesis.
Cameron B, Flamand L, Juwana H, Middeldorp J, Naing Z, Rawlinson W, Ablashi D, Lloyd A.	Center for Infection and Inflammation Research, School of Medical Sciences, University of New South Wales, Sydney, New South Wales, Australia. b.cameron@unsw.edu.au	Serological and virological investigation of the role of the herpesviruses EBV, CMV and HHV-6 in post-infective fatigue syndrome.	J Med Virol. 2010 Oct;82(10):1684-8.	Multiple previous studies have sought evidence for ongoing, active infection with, or reactivation of, Herpesviruses in patients with chronic fatigue syndrome (CFS), with conflicting results. This study aimed to clarify this by studying 20 patients enrolled in a well-characterized model of the onset and evolution of CFS, the prospective cohort of the Dubbo Infection Outcomes Study (DIOS). The patients selected for examination included five CFS patients with primary Epstein-Barr virus (EBV) infection; five CFS patients with acute viral infection not caused by EBV; and 10 matched controls with prompt resolution of primary EBV infection. Serum samples from three timepoints were assayed using a comprehensive range of serological assays for EBV, HHV-6, and CMV. Viral genomes were assessed using quantitative PCR assays. All patients were seropositive for HHV-6, and 10 were seropositive for CMV at infection baseline (five patients and five controls). Low titer CMV IgM antibodies were found at infection baseline in two of these cases and three control patients. HHV-6 IgG antibody titers were highest at infection baseline but did not differ between the CFS cases and the control patients. There were increases in EBV IgG VCA p18, EBNA-1 IgG, and EA IgG titers over time, but these did not differ between CFS cases and control patients. EBV and HHV6 DNA levels were at control levels in a minority of samples, and CMV was undetectable in all samples. These data do not support the hypothesis of ongoing or reactivated EBV, HHV-6, or CMV infection in the pathogenesis of CFS.
Cameron B, Hirschberg DL, Rosenberg-Hassan Y, Ablashi D, Lloyd AR.		Serum cytokine levels in postinfective fatigue syndrome.	Clin Infect Dis. 2010 Jan 15;50(2):278-9.	
Carlo-Stella N.		Letter to the editor re: "A formal analysis of cytokine networks in chronic fatigue syndrome" by Broderick et al.	Brain Behav Immun. 2010 Oct;24(7):1218; author reply 1219. Epub 2010 Jun 16. Comment on: Brain Behav Immun. 2010 Oct;24(7):1209-17.	
Carlowe J.		Chronic fatigue syndrome is not caused by XMRV virus, study shows.	BMJ. 2010 Dec 22;341:c7358. doi: 10.1136/bmj.c7358.	

Carter S.		FINE trial for CFS. Both significant and small?	BMJ. 2010 Jun 9;340:c2988. doi: 10.1136/bmj.c2988.	
Cella M, Chalder T.	Institute of Psychiatry, King's College London, London, United Kingdom. matteo.cella@kcl.ac.uk	Measuring fatigue in clinical and community settings.	J Psychosom Res. 2010 Jul;69(1):17-22. Epub 2009 Dec 11.	OBJECTIVE: The Chalder Fatigue Scale (CFQ) is a widely used instrument to assess fatigue in both clinical and nonclinical settings. Psychometric properties of the scale and discriminative abilities were examined. METHODS: A total of 361 patients with CFS and 1615 individuals in the community were assessed with the CFQ. Principal component analysis (PCA) was used to explore the structure of the scale. Receiver-operating characteristic curve (ROC) was used to investigate the discriminative properties. RESULTS: Two components, physical and mental fatigue, were identified in the CFS patient group and in the general population samples. Area under the curve for ROC was .91. The fatigue scale effectively discriminates, at high scores, between CFS patients and the general population. CONCLUSION: Physical and mental fatigue are clearly separable components of fatigue. The CFQ can discriminate reliably between clinical and nonclinical conditions.
Chalder T, Deary V, Husain K, Walwyn R.	Department of Psychological Medicine and Psychiatry, King's College London, Weston Education Centre, London, UK. trudie.chalder@kcl.ac.uk	Family-focused cognitive behaviour therapy versus psycho-education for chronic fatigue syndrome in 11- to 18-year-olds: a randomized controlled treatment trial.	Psychol Med. 2010 Aug;40(8):1269-79. Epub 2009 Nov 6.	BACKGROUND: Only one previous randomized controlled trial (RCT) has examined the efficacy of cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) in children. The aim of this study was to compare family-focused CBT with psycho-education for CFS in adolescents. METHOD: Sixty-three 11- to 18-year-olds (43 girls, 20 boys) with CFS were randomly assigned to either family-focused CBT or psycho-education delivered over 6 months. School attendance was the main outcome, which was assessed at the end of treatment and at 3, 6 and 12 months follow-up. RESULTS: At the main outcome point (the 6-month follow-up) both groups had improved similarly. However, although those who received family-focused CBT were attending school for longer than those who received psycho-education, at discharge from treatment and at 3 months follow-up, they improved less quickly across the follow-up period. CONCLUSIONS: Adolescents with CFS get back to school more quickly after family-focused CBT. This is important as they are at a crucial stage of their development. However, the finding that psycho-education was as effective as family-focused CBT at 6 and 12 months follow-up has important implications for health service delivery.
Chastin SF, Granat MH.	Glasgow Caledonian University, School of Health and Social Care, Cowcaddens Road, Glasgow G4 0BA, Scotland, UK. Sebastien.Chastin@gcal.ac.uk	Methods for objective measure, quantification and analysis of sedentary behaviour and inactivity.	Gait Posture. 2010 Jan;31(1):82-6. Epub 2009 Oct 24.	The purpose of this study was to develop and test a generic technique to robustly quantify the pattern of sedentary behaviour from objective records. The technique was applied to four groups of subjects: a healthy group with an active occupation (N=54), a healthy group with a sedentary occupation (N=53), a group of subjects with chronic low back pain (N=5) and a group of subjects with chronic fatigue syndrome (N=14). This study presents the first evidence that bouts of sedentary activity are power law distributed. Results showed that there was no significant difference in total sedentary time between the groups, however, the patterns of accumulation of sedentary time were significantly different for the groups. Sedentary groups accumulated their total sedentary time from a small number of longer sedentary bouts. Active groups tended to break their sedentary time into a greater number of shorter bouts. This suggests that the power law exponent alpha and the GINI index G, used to describe the pattern of accumulation of sedentary time, could be used to evaluate and quantify sedentary behaviour.
Chelimsky G,	Department of	A comparison of	Gastroenterol Res	Cyclic vomiting syndrome (CVS) shares many features with migraine headache, including auras,

Madan S, Alshekhlee A, Heller E, McNeeley K, Chelimsky T.	Pediatrics, University Hospitals of Cleveland, Cleveland, OH 44106, USA. gisela.chelimsky@uhhospitals.org	dysautonomias comorbid with cyclic vomiting syndrome and with migraine.	Pract. 2009;2009:701019. Epub 2010 Jan 6.	photophobia, and antimigrainous treatment response being traditionally viewed as a migraine variant. Aims. To determine whether CVS is associated with the same disorders as migraine headache, and compare these associations to those in healthy control subjects.METHODS: Cross-sectional study of patients utilizing the ODYSA instrument, evaluating the probability of 12 functional/autonomic diagnoses, CVS, migraine, orthostatic intolerance (OI), reflex syncope, interstitial cystitis, Raynaud's syndrome, complex regional pain syndrome (CRPS), irritable bowel syndrome, functional dyspepsia, functional abdominal pain, fibromyalgia, and chronic fatigue syndrome. Control subjects were age-matched gender-matched friends. Patients had to fulfill criteria for CVS or migraine, while control subjects could not. RESULTS: 103 subjects were studied, 21 with CVS, 46 with migraine and 36 healthy controls. CVS and migraine did not differ in the relative frequencies of fibromyalgia, OI, syncope, and functional dyspepsia. However, CVS patients did demonstrate a significantly elevated frequency of CRPS. CONCLUSIONS: Although CVS and migraine clearly share many of the same comorbidities, they do differ in one important association, suggesting that they may not be identical in pathophysiology. Since OI is common in CVS, treatment strategies could also target this abnormality.
Chen XH, Li LQ, Zhang W, Yang J, Dai YS, Xu DH, Tang CZ.	Department of Acupuncture and Moxibustion, The First Affiliated Hospital of Guangzhou University of TCM, Guangzhou 510405, China. dr_xinghua@yahoo.com.cn	[Randomized controlled study on acupuncture treatment for chronic fatigue syndrome]. [Article in Chinese]	Zhongguo Zhen Jiu. 2010 Jul;30(7):533-6.	OBJECTIVE: To observe the therapeutic effect of acpuncture treatment for chronic fatigue syndrome (CFS). METHODS: Nighty cases of CFS were randomly divided into an observation group and a control group, 45 cases in each group. The observation group was treated with acupunture at Renying (ST 9), Fengfu (GV 16), Baihui (GV 20); the control group was treated with 250 mL 5% Glucose injectio combined with 20 mL Shenmai injectio. Fatigue Scale (FS) was used to compare the scores between the two groups after treatment. RESULTS: The total scores in the observation group were 9.37 +/- 2.33 and 5.41 +/- 1.96 before and after treatment respectively, and in the control group, they were 9.08 +/- 2.27 and 7.34 +/- 2.03 respectively. FS brainwork integral, physical fatigue integral, and total integral all decreased after treatment in two groups (all $P < 0.001$), and it decreased much more obviously in the observation group ($P < 0.05$, $P < 0.01$). CONCLUSION: Both of the acpuncture treatment and Shenmai injectio are able to decrease fatigue scale score, improve the fatigue symptoms of CFS patients, and the effect of acupucture treatment is obviously superior to that of Shenmai injectio.
Cheng CS, Zhu YH, Liang FR, Wu X, Jin SG, Wu FP.	Acupuncture and Massage College, Chengdu University of TCM, Chengdu 610075, China. ccstcm@163.com	[Effect of electroacupuncture at Shenshu (BL 23) and Zusanli (ST 36) on the event-related potentials of chronic fatigue syndrome]. [Article in Chinese]	Zhongguo Zhen Jiu. 2010 Apr;30(4):309-12.	OBJECTIVE: To observe the effective mechanism of electroacupuncture for chronic fatigue syndrome (CFS). METHODS: The dynamic detection of chronobiology was used to test the event-related potentials in 20 healthy subjects and 20 CFS patients. P3a and P3b latencies at 4 equidistant time points (8:00, 14:00, 20:00, 2:00) within 24 hours were collected and analyzed. RESULTS: (1) Latency of P3a in CFS group was obviously prolonged at 14:00 compared to health group with statistical significance ($P < 0.05$), latency of P3b was decreased at 14:00 after electroacupuncture treatment with statistical significance compared to that of pre-treatment ($P < 0.01$). (2) There were obviously circadian rhythm in latency of P3a and P3b in health group ($P < 0.05$), which were not seen in CFS group ($P > 0.05$); the circadian rhythm latency of P3b restored after treatment ($P < 0.05$). (3) The latency acrophase of P3a and P3b pre-treatment obviously shifted backward compared to that of healthy subjects ($P < 0.05$), shifted forward after electroacupuncture treatment ($P < 0.05$). CONCLUSION: The event-related potential circadian rhythms are lost in CFS patients. Electroacupuncture at Shenshu (BL 23) and Zusanli (ST 36) can regulate the circadian rhythm of P3a

				and P3b latency and improve the cognition of the patients in daytime.
Chew-Graham C, Dowrick C, Wearden A, Richardson V, Peters S.	Primary Care Research Group, School of Community-Based Medicine, University of Manchester, Manchester, UK.	Making the diagnosis of Chronic Fatigue Syndrome/Myalgic Encephalitis in primary care: a qualitative study.	BMC Fam Pract. 2010 Feb 23;11:16.	BACKGROUND: NICE guidelines emphasise the role of the primary care team in the management of patients with Chronic Fatigue Syndrome/Myalgic Encephalitis (CFS/ME). A key stage in effective management is making an accurate early diagnosis, supported by appropriate referral. METHODS: A nested qualitative study within a multi-centre randomised controlled trial which aimed to explore GPs' views on their role in making the diagnosis of CFS/ME and subsequent management of patients in primary care. Semi-structured interviews with 22 GPs. Interviews were transcribed verbatim and an iterative approach used to develop themes from the dataset. RESULTS: GPs described difficulties in defining CFS/ME and suggested that their role in making a diagnosis was to exclude physical causes for the patient's symptoms, but they reported little confidence in positively attributing the label of CFS/ME to a patient and their symptoms. GPs suggested that the label of CFS/ME could be potentially harmful for the patient. The role of referral to secondary care was debated and GPs struggled defining their own role in management of this group of patients. CONCLUSIONS: Until GPs feel comfortable making the diagnosis of CFS/ME and facilitating initial management, and have appropriate services to refer patients to, there will continue to be delays in confirming the diagnosis and patients presenting in primary care with fatigue may not receive appropriate care. TRIAL REGISTRATION: ISRCTN 74156610.
Chia J, Chia A, Voeller M, Lee T, Chang R.	EV Med Research, Torrance, California, USA. evmed@sbcglobal.net	Acute enterovirus infection followed by myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) and viral persistence.	J Clin Pathol. 2010 Feb;63(2):165-8. Epub 2009 Oct 14.	AIMS: Enteroviruses are well-known causes of acute respiratory and/or gastrointestinal infections and non-specific flu-like illness. Although enterovirus protein, RNA and non-cytopathic viruses have been demonstrated in the stomach biopsies of patients with myalgia encephalomyelitis/chronic fatigue syndrome (ME/CFS), causality for chronic diseases is difficult to establish without having well-documented cases of acute enterovirus infections. The aim of this study was to link acute enteroviral infection to viral persistence in patients with ME/CFS. METHOD: Patients admitted to the hospital with acute febrile illnesses were screened for enteroviral infections. Acutely infected patients were followed longitudinally, and those who developed symptoms of ME/CFS underwent oesophagogastroduodenoscopy and biopsies of the antrum to document viral persistence by immunoperoxidase staining for viral protein and viral RNA assay. RESULTS: Three representative patients with different manifestations of acute enterovirus infections progressed to have chronic symptoms of ME/CFS. Persistent viral infection was demonstrated in the antrum years later. CONCLUSION: After acute infections, enteroviruses can persist in patients resulting in manifestation of ME/CFS. Chronic enterovirus infection in an immunocompetent host may be an example of a stalemate between attenuated, intracellular viruses and an ineffective immune response.
Christley Y, Duffy T, Martin CR.	Lecturer, Research and International Project Manager, Chair in Mental Health, School of Health, Nursing and Midwifery, University of the	A review of the definitional criteria for chronic fatigue syndrome.	J Eval Clin Pract. 2010 Oct 4. doi: 10.1111/j.1365-2753.2010.01512.x. [Epub ahead of print]	Rationale, aims and objectives The research community has for more than three decades tried to unravel the diagnostic mystery that is Chronic Fatigue Syndrome (CFS). This has resulted in considerable amounts of time and money being invested in attempts aimed at establishing the aetiology and pathogenesis of CFS. All of this investment has produced evidence of an interesting variety of endocrine, immune, infectious, muscular and neurological abnormalities in CFS; however, the cause remains elusive. The absence of a known causative agent or diagnostic test for CFS has resulted in the development of a number of CFS case definitions. As such, the main objectives of this paper are to provide a critical review of the similarities and differences between the varying

	West of Scotland, Ayr Campus, UK.			approaches to CFS case definition. The conflicts and controversies that have emerged as a result of the differing definitional criterion for CFS are highlighted and the potential impact on future research is identified. Methods, results and conclusions This paper presents a critical review of the most frequently used case definitions in CFS. There are currently five case definitions of CFS; however, the most prominent and widely used of these definitions is the 1994 Centre for Disease Control and Prevention Case Definitions. However, the pre-eminence of this definition over the others has never been substantiated and it has been widely criticized for its lack of specificity. Furthermore, none of the above case definitions have produced evidence to demonstrate their accuracy or precision at defining cases of CFS. A summary description of the symptom profile included in each of the case definitions is provided. The inconsistencies that have emerged in CFS research as a consequence of differing approaches to case definition are also highlighted and discussed.
Ciccone DS, Chandler HK, Natelson BH.	Department of Psychiatry, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, NJ 07103, USA. cicconds@umdnj.edu	Illness trajectories in the chronic fatigue syndrome: a longitudinal study of improvers versus non-improvers.	J Nerv Ment Dis. 2010 Jul;198(7):486-93.	The natural progression of chronic fatigue syndrome (CFS) in adults is not well established. The aims of this longitudinal study were to (a) compare CFS Improvers and Non-Improvers; (b) determine whether an initial diagnosis of fibromyalgia (FM) was associated with CFS nonimprovement; and (c) determine whether this effect could be explained by the presence of nonspecific physical symptoms. Consecutive referrals to a tertiary clinic that satisfied case criteria for CFS were invited to enroll in a longitudinal study. After an initial on-site physical examination and psychiatric interview, a total of 94 female care-seekers completed biannual telephone surveys, including the Short Form-36 physical functioning (PF) scale, over a period of 2(1/2) years. There were very few differences between Improvers and Non-Improvers at baseline but at final assessment Improvers had less disability, less fatigue, lower levels of pain, fewer symptoms of depressed mood, and fewer nonspecific physical complaints. Participants with FM at baseline were 3.23 times ($p < 0.05$) more likely to become Non-Improvers than those without FM. Participants identified initially as Somatizers were 3.33 times ($p < 0.05$) more likely to become Non-Improvers. Patients with CFS who bear the added burden of FM are at greater risk of a negative outcome than patients with CFS alone. This effect could not be explained by the presence of multiple, nonspecific symptoms.
Clauson KA, Zeng-Treitler Q, Kandula S.	Department of Pharmacy Practice, Nova Southeastern University, College of Pharmacy, Palm Beach Gardens, FL 33410, USA. clauson@nova.edu	Readability of patient and health care professional targeted dietary supplement leaflets used for diabetes and chronic fatigue syndrome.	J Altern Complement Med. 2010 Jan;16(1):119-24.	OBJECTIVES: The purpose of this study was to assess readability of patient and health care professional targeted dietary supplement (DS) leaflets used for diabetes mellitus (DM) and chronic fatigue syndrome (CFS) with a novel measurement tool and Flesch-Kincaid Grade Level (FKGL). METHODS: Patient and professional leaflets for DS used to treat DM and CFS from the Natural Medicines Comprehensive Database (NMCD) and Natural Standard (NS) databases were evaluated. Leaflets were analyzed using FKGL and the author-developed health information readability analyzer (HIReA). HIReA integrates lexical, semantic, syntactic, cohesion, and style features and yields values of -1 (very hard) to 1 (very easy). RESULTS: Patient-targeted leaflets substantially exceeded the consensus readability level (6th grade) as assessed by both FKGL (grade 13.0767) and HIReA (-0.2360). Professional leaflets were similarly more difficult to read as scored by HIReA (-0.7065) and FKGL (grade 14.7429). Most and least difficult-to-read sections in patient leaflets (NS/NMCD) were Related Terms (-0.8863)/Other Names (-0.8146), and Safety Concerns (0.0821)/Scientific Evidence (0.0629), respectively. Overall, leaflets in NS (-0.5721) were more difficult to read than those in NMCD (-0.3704). These differences appeared to be less pronounced when FKGL was used to assess

				the readability, indicating its lack of preciseness. CONCLUSIONS: Readability for patient targeted DS leaflets is far more difficult than recommended levels. HIReA is a more precise method to measure readability than FKGL. The disparity between targeted levels of readability and measured levels may contribute to a lack of understanding by patients, with a resulting negative impact on adherence and outcomes.
Clauw DJ.	Chronic Pain and Fatigue Research Center, The University of Michigan, 24 Frank Lloyd Wright Drive, Ann Arbor, MI 48106, USA. dclauw@umich.edu	Perspectives on fatigue from the study of chronic fatigue syndrome and related conditions.	PM R. 2010 May;2(5):414-30.	Fatigue is a symptom whose causes are protean and whose phenotype includes physical, mood, and behavioral components. Chronic fatigue syndrome (CFS) is an illness that has strong biological underpinnings and no definite etiology. Diagnostic criteria established by the Centers for Disease Control and Prevention have helped classify CFS as an overlap of mood, behavioral, and biological components. These include the presence of fatigue for more than 6 months associated with a diminution of functional activity and somatic symptoms, and pain not attributable to a specific diagnosis or disease. Four of the following criteria need to be present: sore throat, impaired memory or cognition, unrefreshing sleep, postexertional fatigue, tender glands, aching stiff muscles, joint pain, and headaches. Many researchers have observed that CFS shares features in common with other somatic syndromes, including irritable bowel syndrome, fibromyalgia, and temporomandibular joint dysfunction. Correlations between inflammation and infection, augmented sensory processing, abnormalities of neurotransmitters, nerve growth factors, low levels of serotonin and norepinephrine, abnormalities of homeostasis of the stress system, and autonomic dysfunction may be hallmarks of CFS. The relative contributions of each of these abnormalities to the profound fatigue associated with CFS need to be explored further to better evaluate and treat the syndrome.
Cockshell SJ, Mathias JL.	School of Psychology, The University of Adelaide, Adelaide, South Australia, Australia.	Cognitive functioning in chronic fatigue syndrome: a meta-analysis.	Psychol Med. 2010 Aug;40(8):1253-67. Epub 2010 Jan 5. Comment in: Psychol Med. 2010 Jul;40(7):1230-1.	BACKGROUND: Cognitive problems are commonly reported in persons with chronic fatigue syndrome (CFS) and are one of the most disabling symptoms of this condition. A number of cognitive deficits have been identified, although the findings are inconsistent and hindered by methodological differences. The current study therefore conducted a meta-analysis of research examining cognitive functioning in persons with CFS in order to identify the pattern and magnitude of any deficits that are associated with this condition. METHOD: A comprehensive search of the PubMed and PsycINFO databases for studies that examined cognitive functioning in CFS between 1988 and 2008 identified 50 eligible studies. Weighted Cohen's d effect sizes, 95% confidence intervals and fail-safe Ns were calculated for each cognitive score. RESULTS: Evidence of cognitive deficits in persons with CFS was found primarily in the domains of attention, memory and reaction time. Deficits were not apparent on tests of fine motor speed, vocabulary, reasoning and global functioning. CONCLUSIONS: Persons with CFS demonstrate moderate to large impairments in simple and complex information processing speed and in tasks requiring working memory over a sustained period of time.
Comiskey C, Larkan F.	School of Nursing and Midwifery, Trinity College Dublin, 24 D'Olier St, Dublin 2, Ireland. Catherine.comiske	A national cross-sectional survey of diagnosed sufferers of myalgic encephalomyelitis/ chronic fatigue	Ir J Med Sci. 2010 Dec;179(4):501-5. Epub 2010 Sep 26.	BACKGROUND: The diagnosis and treatment of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is subject to debate. AIMS: To measure the time to diagnosis and services accessed. METHOD: A national cross-sectional study. A profile and service utilisation questionnaire, information on the pathways to diagnosis, the WHOQoL Brief and a listing of priorities of the needs of participants were used. Individuals were invited to participate if they had a medical diagnosis of ME/CFS. RESULTS: A total of 211 surveys were returned. Prior to diagnosis sufferers accessed on average 4.5 services after their initial consultation. The mean time to diagnosis was 3.7 years but time ranged from 0 to 34

	y@tcd.ie	syndrome: pathways to diagnosis, changes in quality of life and service priorities.		years. Quality of life deteriorated post-onset. The priority for future service provision was increased understanding and diagnosis of ME/CFS by the medical profession. CONCLUSION: In order to alleviate the burden on the sufferer there is a greater need for education on this condition.
Costigan A, Elliott C, McDonald C, Newton JL.	NIHR Biomedical Research Centre in Ageing-Cardiovascular Theme, Newcastle University, Newcastle, UK.	Orthostatic symptoms predict functional capacity in chronic fatigue syndrome: implications for management.	QJM. 2010 Aug;103(8):589-95. Epub 2010 Jun 9.	OBJECTIVES: To establish the relationship between the functional impairment experienced by Chronic fatigue syndrome (CFS) patients and the symptoms frequently experienced by those with CFS; specifically cognitive impairment, fatigue and orthostatic symptoms. DESIGN: Cross sectional questionnaire survey. SETTING: Specialist CFS Clinical Service. SUBJECTS: Ninety-nine Fukuda diagnosed CFS and 64-matched controls. MAIN OUTCOME MEASURES: Symptom and functional assessment tools completed and returned by post included; PROMIS HAQ (Patient-Reported Outcomes Measurement Information System, Health Assessment Questionnaire), CFQ (Cognitive Failures Questionnaire), FIS (Fatigue Impact Scale) and OGS (Orthostatic Grading Scale) assessment tools. RESULTS: CFS patients experience greater functional impairment than controls [mean (95% CI) PROMIS HAQ scores CFS 36 (31-42) vs. controls 6 (2-10); P < 0.0001], especially in the functional domains of activities and reach. Poorer functional ability impairment is significantly associated with greater cognitive impairment (P = 0.0002, r = 0.4), fatigue (P < 0.0001, r = 0.5) and orthostatic symptoms (P < 0.0001, r = 0.6). However, only orthostatic symptoms (OGS) independently associated with functional impairment (beta = 0.4, P = 0.01). CONCLUSION: Treatment of orthostatic symptoms in CFS has the potential to improve functional capacity and so improve quality of life.
Courgnaud V, Battini JL, Sitbon M, Mason AL.	Institut de Génétique Moléculaire de Montpellier, Centre National de la Recherche Scientifique, Universite Montpellier, France.	Mouse retroviruses and chronic fatigue syndrome: Does X (or P) mark the spot?	Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15666-7. Epub 2010 Aug 23. Comment on: Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15874-9.	
Creavin ST, Dunn KM, Mallen CD, Nijrolder I, van der Windt DA.	Arthritis Research Campaign National Primary Care Centre, Keele University, Staffordshire ST5 5BG, United Kingdom. samcreavin@gmail	Co-occurrence and associations of pain and fatigue in a community sample of Dutch adults.	Eur J Pain. 2010 Mar;14(3):327-34. Epub 2009 Jun 18.	Widespread pain and chronic fatigue are common in the general population. Previous research has demonstrated co-occurrence of syndromes that are associated with pain and fatigue (fibromyalgia and chronic fatigue syndrome), but there is limited existing data on the co-occurrence of these symptoms in general. This study investigates the co-occurrence of pain and fatigue, and characterises people with these symptoms individually, and in combination. A postal questionnaire was sent to a random sample of 4741 community dwelling Dutch adults registered with five general practices. There were 2447 participants (adjusted response=53.5%). Persistent fatigue was reported by 60% of the 451 subjects with chronic widespread pain. Chronic widespread pain was reported by 33% of the 809 responders with persistent fatigue. Anxiety and depression were more common in subjects who

	.com			reported both symptoms than those who reported either one or neither. Participants who had chronic disease, high body mass index, low activity levels or did not perceive ability to influence health had higher adjusted odds of reporting both symptoms (but not one alone) than subjects not having these characteristics. Pain and fatigue occur more often than would be expected by chance and there are a number of reasons for this. Clinicians should be aware that co-occurrence of the symptoms is common, especially in people who have high BMI or chronic disease, and that people with both symptoms are often anxious or depressed. Further work should address longitudinal associations of pain and fatigue.
Creti L, Libman E, Baltzan M, Rizzo D, Bailes S, Fichten CS.	Department of Psychiatry, SMBD Jewish General Hospital, 4333 Cote Ste Catherine Road, B-28, Montreal, Quebec, H3T 1E4, Canada. laura.creti@mail.mcgill.ca	Impaired sleep in chronic fatigue syndrome: how is it best measured?	J Health Psychol. 2010 May;15(4):596-607.	The goal was to examine comparative efficacy of polysomnography, actigraphy, and self-report in evaluating the sleep/wake experience of individuals with chronic fatigue syndrome (CFS). Sleep parameters were evaluated by the three measurement modalities for the same night in 49 participants with CFS. Psychological and daytime functioning were measured by self-report. Results indicate that: (a) objectively measured nocturnal sleep time effectively approximated subjective experience although nocturnal wakefulness did not; (b) total sleep time and sleep efficiency differentiated individuals with and without insomnia complaints; (c) daytime sleepiness, fatigue, and non-refreshing sleep were not reflected by the objective sleep-related measures (polysomnography and actigraphy).
Crowhurst G.		XMRV: does this virus hold the key to myalgic encephalomyelitis/ CFS?	Br J Nurs. 2010 Jul 22-Aug 11;19(14):919-22.	In October 2009 a team of researchers from the Whittemore Peterson Institute, in association with the National Cancer Institute and the Cleveland Clinic in the USA, made a discovery that could potentially open the door to useful treatments for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). The researchers, led by Judy Mikovits, discovered a significant correlation between ME/CFS and an infectious retrovirus called xenotropic murine leukaemia virus-related virus (XMRV). XMRV is classified as a gammaretrovirus, belonging to the same broad family as HIV, but more closely related to a group of viruses that cause cancers such as leukaemia. XMRV is the first member of the gammaretrovirus genus of retroviruses to be found in humans; the research to fully understand the connection between ME/CFS and XMRV, as well as what it means to have the virus, is ongoing. The disastrous impact of AIDS on human health has significantly raised the profile of retroviruses as human pathogens, and XMRV has potentially serious health implications not only for patients, but also for those caring for people with ME/CFS.
Daniels J, Wearden AJ.	University of Bath, UK.	Socialization to the model: the active component in the therapeutic alliance? A preliminary study.	Behav Cogn Psychother. 2011 Mar;39(2):221-7. Epub 2010 Nov 22.	Background: Therapeutic alliance has been found to be a significant predictor of outcome in psychotherapy yet what constitutes therapeutic alliance remains unclear. Examining the common constructs of therapeutic alliance, it is possible that there may be a conceptual overlap between active components of therapeutic alliance and socialization to the treatment model. Aim: To investigate the relationship between socialization to the model and therapeutic alliance. Method: Participants (N = 43) were taken from the active treatment arm in a RCT for the treatment of chronic fatigue syndrome (CFS/ME). Therapeutic alliance was measured using a 5-item questionnaire (brief CALPAS) and socialization to the model was extracted from therapy tapes using a novel coding system. Results: Key findings were that when patients and therapists agreed about goals of treatment, there were higher levels of concordance, less evidence of applying principles incongruent to the model, and

				less resistance during the treatment sessions. Conclusions: The outcome of this preliminary study contributes to the potential understanding of active components in the therapeutic alliance, and supports further research to achieve a more detailed picture of "non-specific" factors in therapy, including the active process of socialization in therapeutic alliance.
Davenport TE, Stevens SR, VanNess MJ, Snell CR, Little T.	Department of Physical Therapy, Thomas J Long School of Pharmacy and Health Sciences, University of the Pacific, 3601 Pacific Ave, Stockton, CA 95211, USA. tdavenport@pacific.edu	Conceptual model for physical therapist management of chronic fatigue syndrome/myalgic encephalomyelitis.	Phys Ther. 2010 Apr;90(4):602-14. Epub 2010 Feb 25.	Fatigue is one of the most common reasons why people consult health care providers. Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is one cause of clinically debilitating fatigue. The underdiagnosis of CFS/ME, along with the spectrum of symptoms that represent multiple reasons for entry into physical therapy settings, places physical therapists in a unique position to identify this health condition and direct its appropriate management. The diagnosis and clinical correlates of CFS/ME are becoming better understood, although the optimal clinical management of this condition remains controversial. The 4 aims of this perspective article are: (1) to summarize the diagnosis of CFS/ME with the goal of promoting the optimal recognition of this condition by physical therapists; (2) to discuss aerobic system and cognitive deficits that may lead to the clinical presentation of CFS/ME; (3) to review the evidence for graded exercise with the goal of addressing limitations in body structures and functions, activity, and participation in people with CFS/ME; and (4) to present a conceptual model for the clinical management of CFS/ME by physical therapists.
De Luca C, Scordo G, Cesareo E, Raskovic D, Genovesi G, Korkina L.	Laboratory of Tissue Engineering & Cutaneous Pathophysiology, Istituto Dermopatico dell'Immacolata, Rome, Italy.	Idiopathic environmental intolerances (IEI): from molecular epidemiology to molecular medicine.	Indian J Exp Biol. 2010 Jul;48(7):625-35.	Inherited or acquired impairment of xenobiotics metabolism is a postulated mechanism underlying environment-associated pathologies such as multiple chemical sensitivity, fibromyalgia, chronic fatigue syndrome, dental amalgam disease, and others, also collectively named idiopathic environmental intolerances (IEI). In view of the poor current knowledge of their etiology and pathogenesis, and the absence of recognised genetic and metabolic markers of the diseases. They are often considered "medically unexplained syndromes",. These disabling conditions share the features of polysymptomatic multi-organ syndromes, considered by part of the medical community to be aberrant responses triggered by exposure to low-dose organic and inorganic chemicals and metals, in concentrations far below average reference levels admitted for environmental toxicants. A genetic predisposition to altered biotransformation of environmental chemicals, drugs, and metals, and of endogenous low-molecular weight metabolites, caused by polymorphisms of genes coding for xenobiotic metabolizing enzymes, their receptors and transcription factors appears to be involved in the susceptibility to these environment-associated pathologies, along with epigenetic factors. Free radical/antioxidant homeostasis may also be heavily implicated, indirectly by affecting the regulation of xenobiotic metabolizing enzymes, and directly by causing increased levels of oxidative products, implicated in the chronic damage of cells and tissues, which is in part correlated with clinical symptoms. More systematic studies of molecular epidemiology, toxico- and pharmaco-genomics, elucidating the mechanisms of regulation, expression, induction, and activity of antioxidant/detoxifying enzymes, and the possible role of inflammatory mediators, promise a better understanding of this pathologically increased sensitivity to low-level chemical stimuli, and a solid basis for effective individualized antioxidant- and/or chelator-based treatments.
Deary V, Chalder T.	Institute of Health and Society,	Personality and perfectionism in	Psychol Health. 2010	OBJECTIVE: To test the hypothesis that people with chronic fatigue syndrome (CFS) would differ significantly from a healthy control group on measures of general personality and perfectionism,

	Newcastle University, UK. vincent.deary@ncl.ac.uk	chronic fatigue syndrome: a closer look.	Apr;25(4):465-75.	specifically on measures of neuroticism and unhealthy perfectionism. METHOD: A total of 27 female CFS outpatients and 30 female healthy controls completed questionnaires, including the NEO Personality Inventory-Revised, the Multi-dimensional Perfectionism Scale and measures of anxiety and depression. RESULTS: The CFS group was significantly more fatigued, anxious and depressed than healthy controls. They scored significantly higher on neuroticism and unhealthy perfectionism. Healthy and unhealthy perfectionism were positively correlated in the CFS group, but not in the control group. CONCLUSION: The present study confirms the link between neuroticism and fatigue and finds a link between unhealthy perfectionism and fatigue. A 'healthy trait', such as healthy perfectionism, when coupled with evaluative concerns is not necessarily healthy in a fatigued population. Researchers and clinicians should note the context in which apparently benign traits are expressed, and how they interact with other traits.
Decker MJ, Eyal S, Shinar Z, Fuxman Y, Cahan C, Reeves WC, Baharav A.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. mdecker@cdc.gov	Validation of ECG-derived sleep architecture and ventilation in sleep apnea and chronic fatigue syndrome.	Sleep Breath. 2010 Sep;14(3):233-9. Epub 2009 Oct 9.	PURPOSE: Newly developed algorithms putatively derive measures of sleep, wakefulness, and respiratory disturbance index (RDI) through detailed analysis of heart rate variability (HRV). Here, we establish levels of agreement for one such algorithm through comparative analysis of HRV-derived values of sleep-wake architecture and RDI with those calculated from manually scored polysomnographic (PSG) recordings. METHODS: Archived PSG data collected from 234 subjects who participated in a 3-day, 2-night study characterizing polysomnographic traits of chronic fatigue syndrome were scored manually. The electrocardiogram and pulse oximetry channels were scored separately with a novel scoring algorithm to derive values for wakefulness, sleep architecture, and RDI. RESULTS: Four hundred fifty-four whole-night PSG recordings were acquired, of which, 410 were technically acceptable. Comparative analyses demonstrated no difference for total minutes of sleep, wake, NREM, REM, nor sleep efficiency generated through manual scoring with those derived through HRV analyses. When NREM sleep was further partitioned into slow-wave sleep (stages 3-4) and light sleep (stages 1-2), values calculated through manual scoring differed significantly from those derived through HRV analyses. Levels of agreement between RDIs derived through the two methods revealed an R = 0.89. The Bland-Altman approach for determining levels of agreement between RDIs generated through manual scoring with those derived through HRV analysis revealed a mean difference of -0.7 +/- 8.8 (mean +/- two standard deviations). CONCLUSION: We found no difference between values of wakefulness, sleep, NREM, REM sleep, and RDI calculated from manually scored PSG recordings with those derived through analyses of HRV.
Den Eede FV, Moorkens G, Hulstijn W, Maas Y, Schrijvers D, Stevens SR, Cosyns P, Claes SJ, Sabbe BG.	Department of Psychiatry, Antwerp University Hospital (UZA), Antwerp, Belgium; Collaborative Antwerp Psychiatric Research Institute (CAPRI), Faculty of	Psychomotor function and response inhibition in chronic fatigue syndrome.	Psychiatry Res. 2010 Aug 24. [Epub ahead of print]	Most research points to cognitive slowing in chronic fatigue syndrome (CFS), although there have been negative reports. The present study is one of few that examines fine motor processing and the inhibition of automatic responses in a well-characterised CFS population. A total of 35 female CFS patients without current major depression and 25 female controls performed two computerised figure-copying tasks. The cognitive and fine motor processing of visual-spatial information was measured by recording reaction time (RT) and movement time (MT), respectively. The inhibition of automatic responses was assessed by introducing 'conflicting patterns' (i.e., patterns that were difficult to draw from the preferred left to right). A multivariate general linear model was adopted for the statistical analysis of the movement recordings. As a result, CFS was significantly associated with longer RT and MT in the pooled and in the task-specific analyses. However, there was no interaction

	Medicine, University of Antwerp (UA), Antwerp, Belgium.			between disease status and conflicting character of the patterns. In conclusion, these performance data on the figure-copying tasks provide confirmatory evidence for psychomotor slowing in CFS, but not for a disturbed inhibition of automatic responses. Computerised figure-copying tasks may be promising tools for use in neurobiological research and clinical trials in CFS.
Denner J.	Retrovirus induced immunosuppressio n, Robert Koch Institute, Nordufer 20, D-13353 Berlin, Germany. DennerJ@rki.de	Detection of a gammaretrovirus, XMRV, in the human population: open questions and implications for xenotransplantatio n.	Retrovirology. 2010 Mar 10;7:16.	XMRV (xenotropic murine leukaemia virus-related virus) is a gammaretrovirus that has been detected in human patients with prostate carcinoma, chronic fatigue syndrome (CFS) and also in a small percentage of clinically healthy individuals. It is not yet clear whether the distribution of this virus is primarily limited to the USA or whether it is causally associated with human disease. If future investigations confirm a broad distribution of XMRV and its association with disease, this would have an impact on xenotransplantation of porcine tissues and organs. Xenotransplantation is currently being developed to compensate for the increasing shortage of human material for the treatment of tissue and organ failure but could result in the transmission of porcine pathogens. Maintenance of pathogen-free donor animals will dramatically reduce this risk, but some of the porcine endogenous retroviruses (PERVs) found in the genome of all pigs, can produce infectious virus and infect cultured human cells. PERVs are closely related to XMRV so it is critical to develop tests that discriminate between them. Since recombination can occur between viruses, and recombinants can exhibit synergism, recipients should be tested for XMRV before xenotransplantation.
Dennison L, Stanbrook R, Moss-Morris R, Yardley L, Chalder T.	Centre for Clinical Applications of Health Psychology, University of Southampton, UK.	Cognitive behavioural therapy and psycho-education for chronic fatigue syndrome in young people: reflections from the families' perspective.	Br J Health Psychol. 2010 Feb;15(Pt 1):167-83. Epub 2009 May 6.	OBJECTIVES: Recent trials have produced optimistic results for family-focussed cognitive behavioural therapy (CBT) for chronic fatigue syndrome (CFS) in young people. This study sought to examine the under-researched question of the views and experiences of patients and families who take part. DESIGN: Semi-structured interviews and qualitative analysis were chosen in order to address clients' perspectives in depth. METHODS: Sixteen young people and sixteen parents who participated in a trial of CBT versus psycho-education (PE) for CFS were interviewed. Key themes were discerned using inductive thematic analysis. RESULTS: Most families had low expectations of a cure but hope for improvement. Generally speaking, participants found both CBT and PE acceptable and helpful. Behavioural aspects of CBT (e.g. goal-setting, graded activity) were found helpful. The opportunity to gain support, recognition and validation was important. Cognitive elements of therapy were sometimes deemed inappropriate and some felt emotional aspects of CFS were not adequately addressed. Participants were ambivalent towards the extent of family involvement. Negative experiences related to the therapy setting and feeling inappropriately labeled. Most participants felt therapy was a stepping-stone towards normal life, although many felt recovery was incomplete. Very few differences were found between themes from CBT and PE participants. A notable exception was that every young person who experienced CBT described therapy as helpful, whereas the participants who strongly opposed the therapy approach had all experienced PE. CONCLUSIONS: The detailed insights regarding families' therapy experiences suggest areas of improvement for service delivery and topics for further investigation.
Dittner AJ, Rimes K, Thorpe S.	South London & Maudsley NHS Trust, Chronic Fatigue Syndrome	Negative perfectionism increases the risk of fatigue following	Psychol Health. 2010 Feb 18:1-16. [Epub ahead of print]	Cognitive-behavioural models of excessive fatigue suggest that people who believe that failure to meet high standards indicates unacceptability to others (a form of 'negative perfectionism') are at risk of fatigue after a period of illness or stress. The present study investigates this using a prospective design and possible mediating factors between such beliefs and fatigue were also investigated.

	Unit, London, SE5 8AZ UK.	a period of stress.		Undergraduate students completed questionnaires at the beginning of the academic year (time 1; n = 436) and again following a time of academic pressure, 16 weeks later (time 2; n = 206). Participants were significantly more fatigued at time 2 than at time 1. Negative perfectionism was positively associated with all measures of fatigue and predicted subsequent levels of physical fatigue after controlling for time 1 fatigue. Time 1 negative perfectionism was not associated with time 2 perfectionist studying behaviours, distress about academic work or specific health behaviours, but was associated with time 2 depression. Results also indicated that time 2 depression may account for the relationship between baseline negative perfectionism and subsequent fatigue. This is the first prospective study to demonstrate a significant relationship between perfectionism and subsequent fatigue.
Dolgin E.		Chronic controversy continues over mysterious XMRV virus.	Nat Med. 2010 Aug;16(8):832.	
Egge C, Wyller VB.	Division of Pediatrics, Oslo University Hospital Rikshospitalet, Oslo, Norway. brwylle@online.no.	No differences in cardiovascular autonomic responses to mental stress in chronic fatigue syndrome adolescents as compared to healthy controls.	Biopsychosoc Med. 2010 Dec 14;4:22.	ABSTRACT: Chronic fatigue syndrome (CFS) is a disabling disease with unknown etiology. There is accumulating evidence of altered cardiovascular autonomic responses to different somatic stressors, in particular orthostatic stress, whereas autonomic responses to mental stress remain to be investigated. In this study, we explored cardiovascular autonomic responses to a simple mental stress test in CFS patients and healthy controls.A consecutive sample of 13 patients with CFS, aged 12 to 18 years, and a volunteer sample of 53 healthy control subjects of equal age and gender distribution were included. Blood pressure, heart rate and acral skin blood flow were continuously recorded during an arithmetic exercise.At baseline, heart rate was significantly higher among CFS patients than controls (p = 0.02). During the arithmetic exercise, however, there were no significant differences in the responses between the two groups.In conclusion, CFS patients have unaltered autonomic responses to simple mental stress as compared to healthy control subjects.
Enserink M.		Chronic fatigue syndrome. Conflicting papers on hold as XMRV frenzy reaches new heights.	Science. 2010 Jul 2;329(5987):18-9.	
Enserink M.		Chronic fatigue syndrome. New XMRV paper looks good, skeptics admit--yet doubts linger.	Science. 2010 Aug 27;329(5995):1000.	
Erlwein O, Kaye S, McClure MO,	Jefferiss Research Trust Laboratories,	Failure to detect the novel	PLoS One. 2010 Jan 6;5(1):e8519.	BACKGROUND: In October 2009 it was reported that 68 of 101 patients with chronic fatigue syndrome (CFS) in the US were infected with a novel gamma retrovirus, xenotropic murine leukaemia

Weber J, Wills G, Collier D, Wessely S, Cleare A.	Section of Infectious Diseases, Wright-Fleming Institute, Faculty of Medicine, Imperial College London, St Mary's Campus, Norfolk Place, London, United Kingdom.	retrovirus XMRV in chronic fatigue syndrome.		virus-related virus (XMRV), a virus previously linked to prostate cancer. This finding, if confirmed, would have a profound effect on the understanding and treatment of an incapacitating disease affecting millions worldwide. We have investigated CFS sufferers in the UK to determine if they are carriers of XMRV. METHODOLOGY: Patients in our CFS cohort had undergone medical screening to exclude detectable organic illness and met the CDC criteria for CFS. DNA extracted from blood samples of 186 CFS patients were screened for XMRV provirus and for the closely related murine leukaemia virus by nested PCR using specific oligonucleotide primers. To control for the integrity of the DNA, the cellular beta-globin gene was amplified. Negative controls (water) and a positive control (XMRV infectious molecular clone DNA) were included. While the beta-globin gene was amplified in all 186 samples, neither XMRV nor MLV sequences were detected. CONCLUSION: XMRV or MLV sequences were not amplified from DNA originating from CFS patients in the UK. Although we found no evidence that XMRV is associated with CFS in the UK, this may be a result of population differences between North America and Europe regarding the general prevalence of XMRV infection, and might also explain the fact that two US groups found XMRV in prostate cancer tissue, while two European studies did not.
Erlwein O, Kaye S, Robinson M, McClure M.		Chronic fatigue syndrome: xenotropic murine leukemia virus-related virus, murine leukemia virus, both, or neither?	Proc Natl Acad Sci U S A. 2010 Oct 26;107(43):E161; author reply E163-4. Epub 2010 Sep 30. Comment on: Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15874-9.	
Evering RM, van Weering MG, Groothuis-Oudshoorn KC, Vollenbroek-Hutten MM.	Roessingh Research and Development, Enschede, The Netherlands.	Daily physical activity of patients with the chronic fatigue syndrome: a systematic review.	Clin Rehabil. 2010 Oct 13. [Epub ahead of print]	Objective: To give an overview of the physical activity level of patients with chronic fatigue syndrome in comparison with asymptomatic controls. Data sources: MEDLINE, Web of Science, EMBASE, PsycINFO, Picarta, the Cochrane Controlled Trial Register that is included in the Cochrane Library and reference tracking. Review methods: A systematic literature search was conducted focusing on studies concerning physical activity levels of patients with chronic fatigue syndrome compared to controls. A meta-analysis was performed to pool data of the studies. Results: Seventeen studies were included with 22 different comparisons between patients with chronic fatigue syndrome and controls. Fourteen studies, including 18 comparisons, showed lower physical activity levels in patients with chronic fatigue syndrome as compared to controls. Four studies, including four comparisons, showed no differences between both groups. The meta-analysis included seven studies and showed a daily physical activity level in patients with chronic fatigue syndrome of only 68% of the physical activity level observed in control subjects. The pooled mean coefficient of variation in patients with chronic fatigue syndrome was higher as compared to control subjects (34.3% versus 31.5%), but this difference did not reach significance. Conclusion: Patients with chronic fatigue syndrome appear to be less physically active compared with asymptomatic controls. There is no difference in variation of physical activity levels between patients with chronic fatigue syndrome and healthy control subjects,

				but the validity and reliability of some methods of measuring physical activity is questionable or unknown.
Falkenberg VR, Gurbaxani BM, Unger ER, Rajeevan MS.	Division of Viral and Rickettsial Diseases, Centers for Disease Control & Prevention, Atlanta, GA, 30333, USA.	Functional Genomics of Serotonin Receptor 2A (HTR2A): Interaction of Polymorphism, Methylation, Expression and Disease Association.	Neuromolecular Med. 2010 Oct 13. [Epub ahead of print]	Serotonergic neurotransmission plays a key role in the pathophysiology of neuropsychiatric illnesses. The functional significance of a promoter polymorphism, -1438G/A (rs6311), in one of the major genes of this system (serotonin receptor 2A, HTR2A) remains poorly understood in the context of epigenetic factors, transcription factors and endocrine influences. We used functional and structural equation modeling (SEM) approaches to assess the contributions of the polymorphism (rs6311), DNA methylation and clinical variables to HTR2A expression in chronic fatigue syndrome (CFS) subjects from a population-based study. HTR2A was up-regulated in CFS through allele-specific expression modulated by transcription factors at critical sites in its promoter: an E47 binding site at position -1,438, (created by the A-allele of rs6311 polymorphism), a glucocorticoid receptor (GR) binding site encompassing a CpG at position -1,420, and Sp1 binding at CpG methylation site -1,224. Methylation at -1,420 was strongly correlated with methylation at -1,439, a CpG site that is dependent upon the G-allele of rs6311 at position -1,438. SEM revealed a strong negative interaction between E47 and GR binding (in conjunction with cortisol level) on HTR2A expression. This study suggests that the promoter polymorphism (rs6311) can affect both transcription factor binding and promoter methylation, and this along with an individual's stress response can impact the rate of HTR2A transcription in a genotype and methylation-dependent manner. This study can serve as an example for deciphering the molecular determinants of transcriptional regulation of major genes of medical importance by integrating functional genomics and SEM approaches. Confirmation in an independent study population is required.
Fernell E, Landgren M.		Chronic fatigue could be a marker of ADHD in children and adolescents.	Acta Paediatr. 2010 Jan;99(1):5; author reply 5-6. Comment in: Acta Paediatr. 2010 Mar;99(3):324. Comment on: Acta Paediatr. 2009 Aug;98(8):1313-8.	
Fiest KM, Currie SR, Williams JV, Wang J.	Department of Psychiatry, University of Calgary, Canada.	Chronic conditions and major depression in community-dwelling older adults.	J Affect Disord. 2010 Dec 17. [Epub ahead of print]	OBJECTIVES: To estimate (1) the prevalence of long-term medical conditions and of comorbid major depression, and (2) the associations between major depression and various chronic medical conditions in a general population of older adults (over 50years of age) and in persons who are traditionally classified as seniors (65years and older). METHODS: Data from the Canadian Community Health Survey- Mental Health and Wellbeing (CCHS-1.2) were analyzed. Non-institutionalized individuals over 15years of age in the 10 Canadian provinces were sampled in the CCHS-1.2. The entire sample of the CCHS-1.2 consisted of 36,894 individuals, for the main analyses in this study the dataset was restricted to those aged 50 and over (n=15,591). Chronic health conditions were assessed using a self-report method of doctor diagnosis. The World Mental Health-Composite Diagnostic Interview was used to asses major depressive episodes based on DSM-IV criteria. RESULTS: The overall

				prevalence of having at least one chronic condition in those over 50years of age was 82.4%, compared to 62.0% in those under 50. The prevalence of a major depressive episode in those over 50 with one chronic condition was 3.7%, compared with 1.0% in those without a long-term medical condition. The top 3 chronic health conditions in seniors aged 65 or older were arthritis/rheumatism, high blood pressure and back problems. Chronic Fatigue Syndrome, fibromyalgia and migraine headache had the highest comorbidity with major depression in the senior population. LIMITATIONS: The use of self-report data on chronic health conditions, potential diagnostic overlap between conditions, and the inability to make causal inferences due to the cross-sectional nature of the data are all limitations of the current study. CONCLUSIONS: Differences were found between rates of chronic conditions and major depression between the general population, older adults and seniors in this study. Further research is needed to delineate the direction of these relationships in seniors. Primary and secondary prevention efforts should target seniors who exhibit symptoms of depression or highly prevalent chronic health conditions.
Fink P, Rosendal M, Dam ML, Schröder A.	Forskningsklinikken for Funktionelle Lidelser og Psykosomatik, Arhus Universitetshospital, Arhus Sygehus, 8000 Arhus C, Denmark. per.fink@aarhus.rm.dk	[New unifying diagnosis of functional diseases]. [Article in Danish]	Ugeskr Laeger. 2010 Jun 14;172(24):1835-8. Comment in: Ugeskr Laeger. 2010 Aug 23;172(34):2327; author reply 2327.	Functional somatic symptoms are prevalent in all medical settings, but their management is hampered by an obsolete theoretical framework and inadequate classification systems. Epidemiological and neurobiological studies suggest that the functional somatic syndromes, e.g. fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome and somatoform disorders belong to the same family of disorders. An empirically based diagnosis including different subtypes and severities is proposed as a unifying diagnostic construct: bodily distress syndrome. This construct provides a common language for functional disorders across medical specialties.
Fink P, Schröder A.	The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital, 8000 Aarhus, Denmark. per.fink@aarhus.rm.dk	One single diagnosis, bodily distress syndrome, succeeded to capture 10 diagnostic categories of functional somatic syndromes and somatoform disorders.	J Psychosom Res. 2010 May;68(5):415-26.	BACKGROUND: In order to clarify the classification of physical complaints not attributable to verifiable, conventionally defined diseases, a new diagnosis of bodily distress syndrome was introduced. The aim of this study was to test if patients diagnosed with one of six different functional somatic syndromes or a DSM-IV somatoform disorder characterized by physical symptoms were captured by the new diagnosis. METHOD: A stratified sample of 978 consecutive patients from neurological (n=120) and medical (n=157) departments and from primary care (n=701) was examined applying post-hoc diagnoses based on the Schedules for Clinical Assessment in Neuropsychiatry diagnostic instrument. Diagnoses were assigned only to clinically relevant cases, i.e., patients with impairing illness. RESULTS: Bodily distress syndrome included all patients with fibromyalgia (n=58); chronic fatigue syndrome (n=54) and hyperventilation syndrome (n=49); 98% of those with irritable bowel syndrome (n=43); and at least 90% of patients with noncardiac chest pain (n=129), pain syndrome (n=130), or any somatoform disorder (n=178). The overall agreement of bodily distress syndrome with any of these diagnostic categories was 95% (95% CI 93.1-96.0; kappa 0.86, P<.0001). Symptom profiles of bodily distress syndrome organ subtypes were similar to those of the corresponding functional somatic syndromes with diagnostic agreement ranging from 90% to 95%. CONCLUSION: Bodily distress syndrome seem to cover most of the relevant "somatoform" or

				"functional" syndromes presenting with physical symptoms, not explained by well-recognized medical illness, thereby offering a common ground for the understanding of functional somatic symptoms. This may help unifying research efforts across medical disciplines and facilitate delivery of evidence-based care.
Fischer N, Schulz C, Stieler K, Hohn O, Lange C, Drosten C, Aepfelbacher M.	Institute for Medical Microbiology and Virology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany. nfischer@uke.de	Xenotropic murine leukemia virus-related gammaretrovirus in respiratory tract.	Emerg Infect Dis. 2010 Jun;16(6):1000-2.	Xenotropic murine leukemia virus-related gammaretrovirus (XMRV) has been recently associated with prostate cancer and chronic fatigue syndrome. To identify nucleic acid sequences, we examined respiratory secretions by using PCR. XMRV-specific sequences were detected in 2%-3% of samples from 168 immunocompetent carriers and approximately 10% of samples from 161 immunocompromised patients.
Fletcher MA, Rosenthal M, Antoni M, Ironson G, Zeng XR, Barnes Z, Harvey JM, Hurwitz B, Levis S, Broderick G, Klimas NG.	a	Plasma neuropeptide Y: a biomarker for symptom severity in chronic fatigue syndrome.	Behav Brain Funct. 2010 Dec 29;6(1):76. [Epub ahead of print]	ABSTRACT: BACKGROUND: Chronic fatigue syndrome (CFS) is a complex, multi-symptom illness with a multisystem pathogenesis involving alterations in the nervous, endocrine and immune systems. Abnormalities in stress responses have been identified as potential triggers or mediators of CFS symptoms. This study focused on the stress mediator neuropeptide Y (NPY). We hypothesized that NPY would be a useful biomarker for CFS. METHODS: The CFS patients (n = 93) were from the Chronic Fatigue and Related Disorders Clinic at the University of Miami and met the 1994 case definition of Fukuda and colleagues. Healthy sedentary controls (n = 100)) were from NIH or VA funded studies. Another fatiguing, multi-symptom illness, Gulf War Illness (GWI), was also compared to CFS. We measured NPY in plasma using a radioimmunoassay (RIA). Psychometric measures, available for a subset of CFS patients included: Perceived Stress Scale, Profile of Mood States, ATQ Positive & Negative Self-Talk Scores, the COPE, the Beck Depression Inventory, Fatigue Symptom Inventory, Cognitive Capacity Screening Examination, Medical Outcomes Survey Short Form-36, and the Quality of Life Scale. RESULTS: Plasma NPY was elevated in CFS subjects, compared to controls (p=.000) and to GWI cases (p=.000). Receiver operating characteristics (ROC) curve analyses indicated that the predictive ability of plasma NPY to distinguish CFS patients from healthy controls and from GWI was significantly better than chance alone. In 42 patients with CFS, plasma NPY had significant correlations (<0.05) with perceived stress, depression, anger/hostility, confusion, negative thoughts, positive thoughts, general health, and cognitive status. In each case the correlation (+ or -) was in the anticipated direction. CONCLUSIONS: This study is the first in the CFS literature to report that plasma NPY is elevated compared to healthy controls and to a fatigued comparison group, GWI patients. The significant correlations of NPY with stress, negative mood, general health, depression and cognitive function strongly suggest that this peptide be considered as a biomarker to distinguish subsets of CFS.
Fletcher MA, Zeng XR, Maher K, Levis S, Hurwitz B, Antoni M,	Department of Medicine, University of Miami Miller	Biomarkers in chronic fatigue syndrome: evaluation of	PLoS One. 2010 May 25;5(5):e10817.	BACKGROUND: Chronic Fatigue Syndrome (CFS) studies from our laboratory and others described decreased natural killer cell cytotoxicity (NKCC) and elevated proportion of lymphocytes expressing the activation marker, dipeptidyl peptidase IV (DPPIV) also known as CD26. However, neither these assays nor other laboratory tests are widely accepted for the diagnosis or prognosis of CFS. This study

Broderick G, Klimas NG.	School of Medicine, Miami, Florida, USA. mfletche@med.miami.edu	natural killer cell function and dipeptidyl peptidase IV/CD26.		sought to determine if NKCC or DPPIV/CD26 have diagnostic accuracy for CFS. METHODS/RESULTS: Subjects included female and male CFS cases and healthy controls. NK cell function was measured with a bioassay, using K562 cells and (51)Cr release. Lymphocyte associated DPPIV/CD26 was assayed by qualitative and quantitative flow cytometry. Serum DPPIV/CD26 was measured by ELISA. Analysis by receiver operating characteristic (ROC) curve assessed biomarker potential. Cytotoxic function of NK cells for 176 CFS subjects was significantly lower than in the 230 controls. According to ROC analysis, NKCC was a good predictor of CFS status. There was no significant difference in NK cell counts between cases and controls. Percent CD2+ lymphocytes (T cells and NK cells) positive for DPPIV/C26 was elevated in CFS cases, but there was a decrease in the number of molecules (rMol) of DPPIV/C26 expressed on T cells and NK cells and a decrease in the soluble form of the enzyme in serum. Analyses by ROC curves indicated that all three measurements of DPPIV/CD26 demonstrated potential as biomarkers for CFS. None of the DPPIV/C26 assays were significantly correlated with NKCC. CONCLUSIONS: By ROC analysis, NKCC and three methods of measuring DPPIV/C26 examined in this study had potential as biomarkers for CFS. Of these, NKCC, %CD2+CD26+ lymphocytes and rMol CD26/CD2+ lymphocyte, required flow cytometry, fresh blood and access to a high complexity laboratory. Soluble DPPIV/C26 in serum is done with a standard ELISA assay, or with other soluble factors in a multiplex type of ELISA. Dipeptidyl peptidase IV on lymphocytes or in serum was not predictive of NKCC suggesting that these should be considered as non-redundant biomarkers. Abnormalities in DPPIV/CD26 and in NK cell function have particular relevance to the possible role of infection in the initiation and/or the persistence of CFS.
Flor-Henry P, Lind JC, Koles ZJ.	Alberta Hospital Edmonton, Box 307, Edmonton, Edmonton, Alberta, Canada T5J 2J7. Pierre.Flor-Henry@capitalhealth.ca	EEG source analysis of chronic fatigue syndrome.	Psychiatry Res. 2010 Feb 28;181(2):155-64. Epub 2009 Dec 16.	Sixty-one dextral, unmedicated women with chronic fatigue syndrome (CFS) diagnosed according to the Fukuda criteria (1994) and referred for investigation by rheumatologists and internists were studied with quantitative EEG (43 channels) at rest with eyes open and during verbal and spatial cognitive activation. The EEGs from the patients were compared with recordings from 80 dextral healthy female controls. Only those subjects who could provide 20 1-s artefact-free segments of EEG were admitted into the study. The analysis consisted of the identification of the spatial patterns in the EEGs that maximally differentiated the two groups and the estimation of the cortical source distributions underlying these patterns. Spatial patterns were analyzed in the alpha (8-13Hz) and beta (14-20Hz) bands and the source distributions were estimated using the Borgiotti-Kaplan BEAMFORMER algorithm. The results indicate that the spatial patterns identified were effective in separating the two groups, providing a minimum correct retrospective classification rate of 72% in both frequency bands while the subjects were at rest to a maximum of 83% in the alpha band during the verbal cognitive condition. Underlying cortical source distributions showed significant differences between the two groups in both frequency bands and in all cognitive conditions. Lateralized cortical differences were evident between the two groups in the both frequency bands during both the verbal and spatial cognitive conditions. During these active cognitive conditions, the CFS group showed significantly greater source-current activity than the controls in the left frontal-temporal-parietal regions of the cortex.
Fomicheva EE, Filatenkova TA,	State Science Research Institute	Activity in the hypothalamo-	Neurosci Behav Physiol. 2010	Changes in the activity of the hypothalamo-hypophyseal-adrenocortical system (HHACS) were studied in an experimental model of chronic fatigue syndrome induced by i.p. administration of synthetic

Rybakina EG.	of Experimental Medicine, Russian Academy of Medical Sciences, 12 Academician Pavlov Street, 197376, St. Petersburg, Russia. eefomicheva@rambler.ru	hypophyseal-adrenocortical system on experimental induction of chronic fatigue syndrome.	Mar;40(3):245-50. Epub 2010 Feb 10.	doublestranded RNA (polyriboinosinic:polyribocytidylic acid, Poly I:C) at a dose of 3 mg/kg. Functional changes in the different components of the HHACS were detected using standard tests with i.p. ACTH or hydrocortisone on the background of cold stress and injections of Poly I:C. Single doses of Poly I:C were followed by the development of impairments to HHACS function, with decreases in the ACTH sensitivity of adrenal cells and suppression of the negative feedback mechanism, resulting in significant decreases in corticosterone concentrations in standard tests with administration of ACTH and hydrocortisone.
Friedberg F.	Putnam Hall/South Campus, Stony Brook University, Stony Brook, NY 11794-8790, USA. fred.friedberg@stonybrook.edu	Chronic fatigue syndrome, fibromyalgia, and related illnesses: a clinical model of assessment and intervention.	J Clin Psychol. 2010 Jun;66(6):641-65.	A clinically informative behavioral literature on chronic fatigue syndrome (CFS) and fibromyalgia (FM) has emerged over the past decade. The purpose of this article is to (a) define these conditions and their less severe counterparts, i.e., unexplained chronic fatigue (UCF) and chronic widespread pain; (b) briefly review the behavioral theory and intervention literature on CFS and FM; and (c) describe a user-friendly clinical model of assessment and intervention for these illnesses. The assessments described will facilitate understanding of the somewhat unusual and puzzling somatic presentations that characterize these patients. Using an individualized cognitive-behavioral approach the mental health clinician can offer significant help to these often stigmatized and medically underserved patients.
Fukuda S, Hashimoto R, Ohi K, Yamaguti K, Nakatomi Y, Yasuda Y, Kamino K, Takeda M, Tajima S, Kuratsune H, Nishizawa Y, Watanabe Y.	Department of Biomarker and Molecular Biophysics, Osaka City University Graduate School of Medicine, Osaka, Japan.	A functional polymorphism in the disrupted-in schizophrenia 1 gene is associated with chronic fatigue syndrome.	Life Sci. 2010 May 8;86(19-20):722-5. Epub 2010 Mar 20.	AIMS: Disrupted-in schizophrenia 1 (DISC1), identified in a pedigree with a familial psychosis with the chromosome translocation (1:11), is a putative susceptibility gene for psychoses such as schizophrenia and major depressive disorder (MDD). Patients with chronic fatigue syndrome (CFS) report having continuous severe fatigue and many overlapping symptoms with MDD; however, the mechanism and effective treatment of CFS are still unclear. We focused on the overlapping symptoms between CFS and MDD and performed an association study of the functional single-nucleotide polymorphism (SNP) in the DISC1 gene with CFS. MAIN METHODS: Venous blood was drawn from CFS patients and controls and genomic DNA was extracted from the whole blood according to standard procedures. Ser704Cys DISC1 SNP was genotyped using the TaqMan 5'-exonuclease allelic discrimination assay. KEY FINDINGS: We found that the Cys704 allele of Ser704Cys SNP was associated with an increased risk of CFS development compared with the Ser704 allele. SIGNIFICANCE: DISC1 Ser704Cys might be a functional variant that affects one of the mechanisms implicated in the biology of CFS. Some patients with CFS showed a phenotype similar to that of patients with MDD, but further studies are needed to clarify the biological mechanism, because this study is of a rather preliminary nature. Despite the variety of patients with CFS, DISC1 Ser704Cys has an association with CFS, which may also suggest that DISC1 plays a central role in the induction of various psychiatric diseases.
Fukuda S, Kuratsune H, Tajima S, Takashima S, Yamagutchi K,	Department of Physiology, Osaka City University Graduate School of Medicine, Osaka	Premorbid personality in chronic fatigue syndrome as determined by the	Compr Psychiatry. 2010 Jan-Feb;51(1):78-85. Epub 2009 Mar 12.	BACKGROUND: Using the Temperament and Character Inventory (TCI), we examined personality characteristics in patients with chronic fatigue syndrome (CFS) compared with healthy control subjects, and CFS patients with and without psychiatric diseases. There have been no previous reports assessing personality in CFS patients using the TCI. METHODS: A total of 211 CFS patients and 90 control subjects completed the TCI and the Chalder Fatigue Scale questionnaires. RESULTS: Compared

Nishizawa Y, Watanabe Y.	545-8585, Japan. fukuda@med.osaka-cu.ac.jp	Temperament and Character Inventory.		with control subjects, CFS patients demonstrated significantly lower premorbid Novelty Seeking, and higher Harm Avoidance and persistence. The fatigue score for CFS patients with psychiatric diseases was higher than that for CFS patients without psychiatric diseases. Patients with CFS with psychiatric diseases showed lower premorbid Self-Directedness when compared with CFS patients without psychiatric diseases. The fatigue score was negatively correlated with premorbid Self-Directedness and Cooperativeness, and positively correlated with Harm Avoidance among CFS patients. CONCLUSION: This study supported the stereotyped image of CFS patients as perfectionists, which is similar to the Persistence score, and neurotics, which is similar to the Harm Avoidance score. Patients displaying greater neuroticisms and poorer social and communication skills, similar to the Self-Directedness and Cooperativeness scores, tend to have intercurrent psychiatry diseases and show more severe symptoms of CFS.
Gagliardi L, Ho JT, Torpy DJ.	School of Medicine, University of Adelaide, Adelaide, SA 5005, Australia.	Corticosteroid-binding globulin: the clinical significance of altered levels and heritable mutations.	Mol Cell Endocrinol. 2010 Mar 5;316(1):24-34. Epub 2009 Jul 28.	Corticosteroid-binding globulin (CBG) is the specific high-affinity plasma transport glycoprotein for cortisol. Stress-induced falls in CBG levels may heighten hypothalamic-pituitary-adrenal axis responses and CBG:tissue interactions may allow targeted cortisol delivery. Three genetic variants of CBG have been identified that reduce cortisol binding affinity and/or CBG levels. These include the Leuven and Lyon mutations which reduce CBG:cortisol binding affinity 3- and 4-fold, respectively, and the null mutation resulting in a 50% (heterozygote) or 100% (homozygote) reduction in CBG levels. The three reported null homozygotes demonstrate that complete CBG deficiency is not lethal, although it may be associated with hypotension and fatigue. The phenotype of a CBG null murine model included fatigue and immune defects. One community-based study revealed that severe CBG mutations are rare in idiopathic fatigue disorders. The mechanisms by which CBG mutations may cause fatigue are unknown. There are preliminary data of altered CBG levels in hypertension and in the metabolic syndrome; however, the nature of these associations is uncertain. Further studies may clarify the functions of CBG, and clinical observations may validate and/or extend the phenotypic features of various CBG mutations.
Gardner A, Boles RG.	Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden.	Beyond the serotonin hypothesis: Mitochondria, inflammation and neurodegeneration in major depression and affective spectrum disorders.	Prog Neuropsychopharmacol Biol Psychiatry. 2010 Aug 5. [Epub ahead of print]	For many years, a deficiency of monoamines including serotonin has been the prevailing hypothesis on depression, yet research has failed to confirm consistent relations between brain serotonin and depression. High degrees of overlapping comorbidities and common drug efficacies suggest that depression is one of a family of related conditions sometimes referred to as the "affective spectrum disorders", and variably including migraine, irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia and generalized anxiety disorder, among many others. Herein, we present data from many different experimental modalities that strongly suggest components of mitochondrial dysfunction and inflammation in the pathogenesis of depression and other affective spectrum disorders. The three concepts of monoamines, energy metabolism and inflammatory pathways are inter-related in many complex manners. For example, the major categories of drugs used to treat depression have been demonstrated to exert effects on mitochondria and inflammation, as well as on monoamines. Furthermore, commonly-used mitochondrial-targeted treatments exert effects on mitochondria and inflammation, and are increasingly being shown to demonstrate efficacy in the affective spectrum disorders. We propose that interactions among monoamines, mitochondrial dysfunction and inflammation can inspire explanatory, rather than mere descriptive, models of these

				disorders.
Ghanizadeh A.	Shiraz University of Medical Sciences, Hafez Hospital, Shiraz, Iran. ghanizad@sina.tums.ac.ir	Could chronic fatigue be a marker of ADHD in children and adolescents?	Acta Paediatr. 2010 Mar;99(3):324. Epub 2009 Nov 20. Comment on: Acta Paediatr. 2009 Aug;98(8):1313-8. Acta Paediatr. 2010 Jan;99(1):5; author reply 5-6.	
Ghio M, Contini P, Setti M, Ubezio G, Mazzei C, Tripodi G.	Division of Clinical Immunology, Department of Internal Medicine, University of Genoa Medical School, 16132, Genoa, Italy. mghio@unige.it	sHLA-I Contamination, a novel mechanism to explain ex vivo/in vitro modulation of IL-10 synthesis and release in CD8(+) T lymphocytes and in neutrophils following intravenous immunoglobulin infusion.	J Clin Immunol. 2010 May;30(3):384-92. Epub 2010 Feb 2.	BACKGROUND: Numerous mechanisms have been proposed to explain the beneficial action of intravenous immune globulin (IVIG) in autoimmune and systemic inflammatory disorders; among others, they could decrease pro-inflammatory cytokine levels and also induce anti-inflammatory cytokines. MATERIALS AND METHODS: Ex vivo analysis of cells from ten IVIG recipients showed significant increase of IL-10 mRNA and intra-cellular IL-10 molecules in both leukotypes. RESULTS: In vitro comparable results were obtained incubating CD8(+) T lymphocytes and neutrophils from healthy donors with IVIG. sHLA-I and/or sFasL immunodepletion abolished IL-10 modulation. Co-culture with contaminant-free IgM or MabThera did not exert any mRNA modulation. Finally, IgM or MabThera plus purified sHLA-I molecules enhanced IL-10-mRNA in both leukotypes to levels comparable to those obtained with IVIG incubation. CONCLUSION: As IVIG infusion involves administration of soluble contaminants, these data consent to speculate that IVIG might modulate IL-10 via the immunomodulatory activities of sHLA-I contaminant molecules inducing transcriptional and post-transcriptional modulation of IL-10 in CD8(+) T lymphocytes and neutrophils.
Gordon BA, Knapman LM, Lubitz L.	Physiotherapy Department, Austin Health and Discipline of Exercise Science, RMIT University, Australia. brett.gordon@austin.org.au	Graduated exercise training and progressive resistance training in adolescents with chronic fatigue syndrome: a randomized controlled pilot study.	Clin Rehabil. 2010 Dec;24(12):1072-9. Epub 2010 Jul 6.	OBJECTIVE: to investigate the differential effects of aerobic graded exercise and progressive resistance training on exercise tolerance, fatigue and quality of life in adolescent patients with chronic fatigue syndrome (CFS). DESIGN: single-blind, randomized controlled pilot trial. SETTING: a major metropolitan hospital in Melbourne, Australia. SUBJECTS: twenty-two adolescents aged 13-18 years diagnosed with CFS and admitted to the inpatient chronic fatigue rehabilitation programme. INTERVENTION: patients were randomized to either graded aerobic exercise training or a progressive resistance training programme, for five days/week for four weeks. The graded aerobic training consisted of 20-40 minutes of stationary cycling and treadmill exercise. The progressive resistance training involved 16 exercises performed with single set, moderate load and high repetitions. MAIN MEASURES: exercise tolerance (time to fatigue) measured on a graded sub-maximal treadmill test, metabolic equivalents and quality of life, along with muscular strength (maximium push-ups) and endurance (sit-to-stand) and questionnaires evaluating depressive symptoms and fatigue severity. RESULTS: no intervention was significantly better than the other for any outcome. However, physical capacity and quality of life significantly improved in both groups, while fatigue severity and symptoms of depression improved only with aerobic training. CONCLUSIONS: resistance and aerobic training

				resulted in similar changes to physical capacity, quality of life and fatigue severity. Generally, patients who completed resistance training or aerobic training experienced significant improvements in outcomes from baseline when they entered the programme. Whether these improvements can be attributed to the treatment is unknown.
Groom HC, Boucherit VC, Makinson K, Randal E, Baptista S, Hagan S, Gow JW, Mattes FM, Breuer J, Kerr JR, Stoye JP, Bishop KN.	Division of Virology, MRC National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, UK.	Absence of xenotropic murine leukaemia virus-related virus in UK patients with chronic fatigue syndrome.	Retrovirology. 2010 Feb 15;7:10.	BACKGROUND: Detection of a retrovirus, xenotropic murine leukaemia virus-related virus (XMRV), has recently been reported in 67% of patients with chronic fatigue syndrome. We have studied a total of 170 samples from chronic fatigue syndrome patients from two UK cohorts and 395 controls for evidence of XMRV infection by looking either for the presence of viral nucleic acids using quantitative PCR (limit of detection <16 viral copies) or for the presence of serological responses using a virus neutralisation assay. RESULTS: We have not identified XMRV DNA in any samples by PCR (0/299). Some serum samples showed XMRV neutralising activity (26/565) but only one of these positive sera came from a CFS patient. Most of the positive sera were also able to neutralise MLV particles pseudotyped with envelope proteins from other viruses, including vesicular stomatitis virus, indicating significant cross-reactivity in serological responses. Four positive samples were specific for XMRV. CONCLUSIONS: No association between XMRV infection and CFS was observed in the samples tested, either by PCR or serological methodologies. The non-specific neutralisation observed in multiple serum samples suggests that it is unlikely that these responses were elicited by XMRV and highlights the danger of over-estimating XMRV frequency based on serological assays. In spite of this, we believe that the detection of neutralising activity that did not inhibit VSV-G pseudotyped MLV in at least four human serum samples indicates that XMRV infection may occur in the general population, although with currently uncertain outcomes.
Groom HC, Yap MW, Galão RP, Neil SJ, Bishop KN.	Division of Virology, MRC National Institute for Medical Research, London NW7 1AA, United Kingdom.	Susceptibility of xenotropic murine leukemia virus-related virus (XMRV) to retroviral restriction factors.	Proc Natl Acad Sci U S A. 2010 Mar 16;107(11):5166-71. Epub 2010 Mar 1.	Xenotropic murine leukemia virus-related virus (XMRV) is a recently discovered gammaretrovirus that has been linked to prostate cancer and chronic fatigue syndrome. This virus is therefore an important potential human pathogen and, as such, it is essential to understand its host cell tropism. Intriguingly, infectious virus has been recovered from patient-derived peripheral blood mononuclear cells. These cells express several antiviral restriction factors that are capable of inhibiting the replication of a wide range of retroviruses, including other gamma retroviruses. This raises the possibility that, similar to HIV, XMRV may have acquired resistance to restriction. We therefore investigated the susceptibility of XMRV to a panel of different restriction factors. We found that both human APOBEC3 and tetherin proteins are able to block XMRV replication. Expression of human TRIM5alpha, however, had no effect on viral infectivity. There was no evidence that XMRV expressed countermeasures to overcome restriction. In addition, the virus was inhibited by factors from nonhuman species, including mouse Apobec3, tetherin, and Fv1 proteins. These results have important implications for predicting the natural target cells for XMRV replication, for relating infection to viral pathogenicity and pathology, and for the design of model systems with which to study XMRV-related diseases.
Guise J, McVittie C, McKinlay A.	Tayside Institute for Health Studies, University of Abertay Dundee, Level 3, Kydd	A discourse analytic study of ME/CFS (Chronic Fatigue Syndrome) sufferers'	J Health Psychol. 2010 Apr;15(3):426-35.	The aetiology, symptoms, diagnosis and treatment of ME/CFS are controversial. Doctors and sufferers often have opposing perspectives, leading to problematic clinical interactions. We use discourse analysis to explore ME/CFS sufferers' descriptions of interactions with medical professionals taken from an asynchronous, online sufferers' support group. Participants described themselves as experiencing limited medical care and attention but restricted criticisms to 'legitimate', pragmatic or

	Building, Bell St., Dundee DD11HG, UK. j.guise@abertay.ac.uk	experiences of interactions with doctors.		ancillary matters such as a clinicians' unwillingness to prescribe untested treatments. Participants also described themselves as active in seeking a resolution to their problems. They thus attended to possible negative attributions of being 'complaining' or unmotivated to seek recovery.
Gupta A, Vij G, Chopra K.	Pharmacology Division, University Institute of Pharmaceutical Sciences, UGC Center of Advanced Study, Panjab University, Chandigarh 160014, India.	Possible role of oxidative stress and immunological activation in mouse model of chronic fatigue syndrome and its attenuation by olive extract.	J Neuroimmunol. 2010 Sep 14;226(1-2):3-7. Epub 2010 May 26.	Various putative theories involved in the development of chronic fatigue syndrome revolve around the role of stress, infection and oxidative stress. Scientific evidence highlighting the protective role of nutritional supplements in chronic fatigue syndrome is lacking. Based on these assumptions, the present study was designed to evaluate the effect of olive extract in a mouse model of immunologically-induced fatigue, wherein purified lipopolysaccharide (LPS) and Brucella abortus (BA) antigen were used as immunogens. The assessment of chronic fatigue syndrome was based on immobility period during chronic water-immersion stress test for 10 min daily. The stress-induced hyperalgesia was measured by tail withdrawal latency. Mice challenged with LPS or BA for 19 days showed significant increase in the immobility time, hyperalgesia and oxidative stress on the 19th day. Serum tumor necrosis factor-alpha (TNF-α) levels were also markedly increased with LPS or BA challenge. Concurrent treatment with olive extract resulted in a significant decrease in the immobility time as well as hyperalgesia. There was significant attenuation of oxidative stress as well as serum TNF-α levels. The results of the present study strongly indicate the role of oxidative stress and immunological activation in the pathophysiology of chronic fatigue syndrome and highlight the valuable role of olive extract in combating chronic fatigue syndrome.
Hambrook D, Oldershaw A, Rimes K, Schmidt U, Tchanturia K, Treasure J, Richards S, Chalder T.		Emotional expression, self-silencing, and distress tolerance in anorexia nervosa and chronic fatigue syndrome.	Br J Clin Psychol. 2010 Aug 10. [Epub ahead of print]	Objectives Difficulties in processing emotional states are implicated in the aetiology and maintenance of diverse health conditions, including anorexia nervosa (AN) and chronic fatigue syndrome (CFS). This study sought to explore distress tolerance, self-silencing, and beliefs regarding the experience and expression of emotions in individuals diagnosed with AN and CFS. These conditions were chosen for this study because their clinical presentation is characterized by physical symptoms, yet cognitive behavioural models suggest that emotional processing difficulties contribute to the aetiology and maintenance of both. Design A between-subjects cross-sectional design was employed. Methods Forty people with AN, 45 with CFS, and 48 healthy controls (HCs) completed the Distress Tolerance Scale (DTS), Silencing the Self Scale (STSS), Beliefs about Emotions Scale (BES), and measures of clinical symptomatology. Results Initial group comparisons found that both AN and CFS participants scored higher than HCs on a subscale measuring difficulties in distress tolerance. AN and CFS participants were also more likely to judge themselves by external standards, endorse statements reflecting a tendency to put the needs of others before themselves, and present an outwardly socially compliant image of themselves whilst feeling hostile within. Relative to HCs, AN participants reported more maladaptive beliefs regarding the experience of having negative thoughts and feelings and revealing these emotions to others, with CFS participants showing a non-significant trend in the same direction. After controlling for differences in age, anxiety, and depression the only significant difference to remain was that observed for the STSS care as self-sacrifice subscale. More maladaptive beliefs about the experience and expression of emotions were associated with greater degree of eating disorder symptomatology in the AN group. Conclusions Differences in emotional processing are present in AN

				and CFS compared to HCs, with some disorder-specific variation, and may be associated with greater clinical symptomatology. These findings support current explanatory models of both AN and CFS, and suggest that emotional processing should be addressed in the assessment and treatment of individuals with these illnesses.
Heins MJ, Knoop H, Prins JB, Stulemeijer M, van der Meer JW, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. m.heins@nkcv.umcn.nl	Possible detrimental effects of cognitive behaviour therapy for chronic fatigue syndrome.	Psychother Psychosom. 2010 Jun;79(4):249-56. Epub 2010 May 25.	BACKGROUND: Cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) can decrease the level of fatigue and disabilities, but it has been suggested that during therapy some patients experience a deterioration of their symptoms rather than an improvement. The aim of this study is to examine the frequency and severity of symptom deterioration during CBT for CFS. METHODS: Data from 3 randomised controlled trials on CBT for CFS were pooled and reanalysed. Symptom deterioration during the trial was rated by patients and measured as deterioration in fatigue, pain, functional impairment and psychological distress. Both the frequency and severity of deterioration in these domains were compared between the patients receiving CBT and those in the control group. Predictors of symptom deterioration were identified by comparing their means in patients with and without an increase in fatigue. Statistically significant predictors were then combined in a logistic regression model. RESULTS: The frequency of symptom deterioration varied from 2 to 12% in patients receiving CBT and from 7 to 17% in the control group. None of the measures showed a significantly higher frequency of symptom deterioration in the CBT group. The severity of deterioration was also comparable in the CBT and in the control group. No predictors of symptom deterioration specific to CBT were found. CONCLUSION: Patients receiving CBT do not experience more frequent or more severe symptom deterioration than untreated patients. The reported deterioration during CBT seems to reflect the natural variation in symptoms. Thus, CBT is not only a helpful, but also a safe treatment for CFS.
Henrich TJ, Li JZ, Felsenstein D, Kotton CN, Plenge RM, Pereyra F, Marty FM, Lin NH, Grazioso P, Crochiere DM, Eggers D, Kuritzkes DR, Tsibris AM.	Division of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts, USA.	Xenotropic murine leukemia virus-related virus prevalence in patients with chronic fatigue syndrome or chronic immunomodulatory conditions.	J Infect Dis. 2010 Nov 15;202(10):1478-81. Epub 2010 Oct 11. Comment in: J Infect Dis. 2010 Nov 15;202(10):1463-6.	We investigated the prevalence of xenotropic murine leukemia virus-related virus (XMRV) among 293 participants seen at academic hospitals in Boston, Massachusetts. Participants were recruited from the following 5 groups of patients: chronic fatigue syndrome (n = 32), human immunodeficiency virus infection (n = 43), rheumatoid arthritis (n = 97), hematopoietic stem-cell or solid organ transplant (n = 26), or a general cohort of patients presenting for medical care (n = 95). XMRV DNA was not detected in any participant samples. We found no association between XMRV and patients with chronic fatigue syndrome or chronic immunomodulatory conditions.
Hoeck AD, Pall ML.	Mariawald str. 750935, Cologne, Germany.	Will vitamin D supplementation ameliorate diseases characterized by chronic inflammation and fatigue?	Med Hypotheses. 2011 Feb;76(2):208-13. Epub 2010 Oct 25.	Chronic NF-κB activation has been supposed as a key event in chronic fatigue syndrome (CFS) and many other better-defined pro-inflammatory diseases. Knowledge about the impact of deficiency vitamin D on chronic NF-κB activation could open a new disease approach. Whereas NF-κB activation leads at first to a pro-inflammatory immune response, later on a vitamin D-dependent anti-inflammatory response ensues. Binding of the active vitamin D metabolite 1,25(OH)(2)D(3) to vitamin D receptor (VDR) yields a transcription factor which represses NF-κB activation, and additionally modulates and down-regulates adaptive, but enhances innate immune responses, and improves redox balance, thus counterbalancing inflammation on multiple levels. However, this built-in late

				counterbalance against inflammation works only when stores of calcium and 25(OH)D(3) are abundant. Therefore a connection between lowered vitamin D-metabolism and persistent NF-κB activation, augmented nitrosative-oxidative stress, redox imbalance, chronic inflammation, and concomitant fatigue can be postulated. In order to confirm this hypothesis, randomized controlled clinical studies about the clinical effects of supplementation of calcium and vitamin D(3) would be necessary in diseases characterized by persistent NF-κB activation and chronic inflammation and fatigue.
Hohn O, Strohschein K, Brandt AU, Seeher S, Klein S, Kurth R, Paul F, Meisel C, Scheibenbogen C, Bannert N.	Centre for Biological Security 4, Robert Koch-Institute, Berlin, Germany.	No Evidence for XMRV in German CFS and MS Patients with Fatigue Despite the Ability of the Virus to Infect Human Blood Cells In Vitro.	PLoS One. 2010 Dec 22;5(12):e15632.	BACKGROUND: Xenotropic murine leukemia virus-related virus (XMRV), a novel human retrovirus originally identified in prostate cancer tissues, has recently been associated with chronic fatigue syndrome (CFS), a disabling disease of unknown etiology affecting millions of people worldwide. However, several subsequent studies failed to detect the virus in patients suffering from these illnesses or in healthy subjects. Here we report the results of efforts to detect antibody responses and viral sequences in samples from a cohort of German CFS and relapsing remitting multiple sclerosis (MS) patients with fatigue symptoms. METHODOLOGY: Blood samples were taken from a cohort of 39 patients fulfilling the Fukuda/CDC criteria (CFS), from 112 patients with an established MS diagnosis and from 40 healthy donors. Fatigue severity in MS patients was assessed using the Fatigue Severity Scale (FSS). Validated Gag- and Env-ELISA assays were used to screen sera for XMRV antibodies. PHA-activated PBMC were cultured for seven days in the presence of IL-2 and DNA isolated from these cultures as well as from co-cultures of PBMC and highly permissive LNCaP cells was analyzed by nested PCR for the presence of the XMRV gag gene. In addition, PBMC cultures were exposed to 22Rv1-derived XMRV to assess infectivity and virus production. CONCLUSION: None of the screened sera from CFS and MS patients or healthy blood donors tested positive for XMRV specific antibodies and all PBMC (and PBMC plus LNCaP) cultures remained negative for XMRV sequences by nested PCR. These results argue against an association between XMRV infection and CFS and MS in Germany. However, we could confirm that PBMC cultures from healthy donors and from CFS patients can be experimentally infected by XMRV, resulting in the release of low levels of transmittable virus.
Hollingsworth KG, Jones DE, Taylor R, Blamire AM, Newton JL.	Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK.	Impaired cardiovascular response to standing in chronic fatigue syndrome.	Eur J Clin Invest. 2010 Jul;40(7):608-15. Epub 2010 May 23.	BACKGROUND: Impaired skeletal muscle metabolism is recognized in chronic fatigue syndrome (CFS). This study examined the relationship between skeletal and cardiac muscle function and symptoms on standing in CFS using magnetic resonance spectroscopy (MRS) and impedance cardiography. MATERIALS AND METHODS: Phosphocreatine (PCr)/adenosine triphosphate (ATP) ratio by cardiac MRS, PCr/ADP and proton efflux by muscle MRS were performed in 12 CFS (Fukuda) and 8 controls. Head up tilt (HUT) and cardiac contractility (left ventricular work index, LVWI) (n = 64 CFS and matched controls) were found. Fatigue impact was accessed by Fatigue Impact Scale and orthostatic symptoms by Orthostatic Grading Scale (OGS). RESULTS: Cardiac PCr/ATP correlated with measures of muscle bioenergetic function (half-time PCr recovery [kappa = -0.71, P = 0.005] and half-time ADP recovery [kappa = -0.60, P = 0.02]) suggesting that the muscle and cardiac bioenergetic function correlate in CFS. Four of 12 (33.3%) CFS patients had PCr/ATP values consistent with significant cardiac impairment. Those with impaired cardiac energy metabolism had significantly reduced maximal and initial proton efflux rates (P < 0.05). Cardiac PCr/ATP ratio correlated with myocardial contractility (LVWI) in response to standing (P = 0.03). On HUT, LVWI on standing was significantly higher in CFS (P

				= 0.05) with symptoms on standing (OGS) occurring in 61/64 (95%) (vs. 25/64 [39%] controls; P < 0.0001). OGS scores were significantly higher in those with abnormal LVWI responses to standing (P = 0.04), with the LVWI on standing correlating with OGS scores (r(2) = 0.1; P = 0.03). HUT was positive in 19 (32%). CONCLUSIONS: Skeletal muscle and cardiac bioenergetic abnormalities associate in CFS. Cardiac bioenergetic metabolism associates with increase in cardiac contractility on standing. Haemodynamic assessment in CFS is well tolerated and safe with a high diagnostic yield comparable with unexplained syncope.
Hong P, Li J, Li Y.	Graduate School, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, People's Republic of China.	Failure to detect Xenotropic murine leukaemia virus-related virus in Chinese patients with chronic fatigue syndrome.	Virol J. 2010 Sep 13;7:224.	BACKGROUND: Recent controversy has surrounded the question of whether xenotropic murine leukaemia virus-related virus (XMRV) contributes to the pathogenesis of chronic fatigue syndrome (CFS). To investigate the question in a Chinese population, 65 CFS patients and 85 blood donor controls were enrolled and multiplex real-time PCR or reverse transcriptase PCR (RT-PCR) was developed to analyze the XMRV infection status of the study participants. The assay was standardized by constructing plasmid DNAs and armored RNAs as XMRV standards and competitive internal controls (CICs), respectively. RESULTS: The sensitivities of the multiplex real-time PCR and RT-PCR assays were 20 copies/reaction and 10 IU/ml, respectively, with 100% specificity. The within-run precision coefficient of variation (CV) ranged from 1.76% to 2.80% and 1.70% to 2.59%, while the between-run CV ranged from 1.07% to 2.56% and 1.06% to 2.74%. XMRV was not detected in the 65 CFS patients and 65 normal individuals out of 85 controls. CONCLUSIONS: This study failed to show XMRV in peripheral blood mononuclear cells (PBMCs) and plasma of Chinese patients with CFS. The absence of XMRV nucleic acids does not support an association between XMRV infection and the development of CFS in Chinese.
Horton SM, Poland F, Kale S, Drachler Mde L, de Carvalho Leite JC, McArthur MA, Campion PD, Pheby D, Nacul L.	University of East Anglia, Norwich, UK. s.horton@uea.ac.uk	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) in adults: a qualitative study of perspectives from professional practice.	BMC Fam Pract. 2010 Nov 15;11:89.	BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) can cause profound and prolonged illness and disability, and poses significant problems of uncertainty for healthcare professionals in its diagnosis and management. The aim of this qualitative study was to explore the nature of professional 'best practice' in working with people with CFS/ME. METHODS: The views and experiences of health care practitioners (HCPs) were sought, who had been judged by people with CFS/ME themselves to have been particularly helpful and effective. Qualitative semi-structured interviews following a topic guide were carried out with six health care practitioners. Interviews were audio-recorded, transcribed and subject to thematic analysis. RESULTS: Five main themes were developed: 1) Diagnosis; 2) Professional perspectives on living with CFS/ME; 3) Interventions for treatment and management; 4) Professional values and support for people with CFS/ME and their families; 5) Health professional roles and working practices. Key findings related to: the diagnostic process, especially the degree of uncertainty which may be shared by primary care physicians and patients alike; the continued denial in some quarters of the existence of CFS/ME as a condition; the variability, complexity, and serious impact of the condition on life and living; the onus on the person with CFS/ME to manage their condition, supported by HCPs; the wealth of often conflicting and confusing information on the condition and options for treatment; and the vital role of extended listening and trustful relationships with patients. CONCLUSIONS: While professional frustrations were clearly expressed about the variability of services both in primary and specialist care and continuing equivocal attitudes to CFS/ME as a condition, there were also strong positive messages for people

				with CFS/ME where the right services are in place. Many of the findings from these practitioners seen by their patients as helping them more effectively, accord with the existing literature identifying the particular importance of listening skills, respect and trust for establishing a therapeutic relationship which recognises key features of the patient trajectory and promotes effective person-centred management of this complex condition. These findings indicate the need to build such skills and knowledge more systematically into professional training informed by the experience of specialist services and those living with the condition.
Houghton CA, Steels EL, Fassett RG, Coombes JS.	School of Human Movement Studies, University of Queensland, St Lucia, Qld 4067, Australia.	Effects of a gliadin-combined plant superoxide dismutase extract on self-perceived fatigue in women aged 50-65 years.	Phytomedicine. 2010 Oct 31. [Epub ahead of print]	Fatigue syndromes exist on a continuum of severity from mild and transient to the disabling chronic fatigue syndrome, with oxidative stress linked to its pathogenesis. A thermolabile gliadin-combined plant superoxide dismutase (SOD) extract has shown potential in clinical trials as a therapeutic antioxidant. This study investigated the effects of 12 weeks of 500mg/day of a SOD/gliadin supplement on fatigue. Thirty-eight women aged 50-65 years with self-perceived fatigue entered this randomized, double-blind, placebo-controlled trial. The primary outcome measure was general fatigue determined by the Multidimensional Fatigue Inventory (MFI). Secondary outcome measures included other measures of fatigue from the MFI and blood measures of oxidative stress, antioxidant status and hormones. There were no significant (P>0.05) differences between, or within groups, for decreases in general fatigue (active=1.6%, placebo=4.1%). There were no within or between group differences (P>0.05) in other measures of fatigue (physical fatigue, reduced activity, reduced motivation, mental fatigue and total fatigue score). In regard to the biochemical measures, there were non-significant (P>0.05) differences in increases in plasma SOD activity (active=7.1%, placebo=12.2%), plasma GPx activity (active=2.4%, placebo=0.7%), red blood cell GPx activity (active=9.8%, placebo=4.4%). Markers of oxidative stress were decreased but there were no differences (P>0.05) within or between groups; malondialdehyde (active=4.1%, placebo=1.6%), F-2 isoprostanes (active=14.7%, placebo=22.4%). There was a trend (P=0.08) for a decrease in cortisol in the active group (24.6%), however this was not significantly different from the decrease in the placebo participants (4.1%). DHEA differences were not significant (P<0.05) and declined 1.3% in the active group and 14.4% in the placebo group. In summary, the thermolabile SOD/gliadin supplement had no significant effect on self-perceived fatigue, antioxidants, oxidative stress or hormones in women aged 50-65 years.
Huang Y, Katz BZ, Mears C, Kielhofner GW, Taylor R.	Department of Occupational Therapy, University of Illinois at Chicago, College of Applied Health Sciences, 1919 W Taylor Street, Chicago, IL 60612, USA.	Postinfectious fatigue in adolescents and physical activity.	Arch Pediatr Adolesc Med. 2010 Sep;164(9):803-9. Comment in: Arch Pediatr Adolesc Med. 2010 Sep;164(9):880-1.	OBJECTIVE: To compare adolescents who do and do not recover from acute infectious mononucleosis in terms of fatigue severity and activity levels before, during, and in the 2 years following infection. DESIGN: Prospective case-control study. SETTING: The baseline and 12- and 24-month evaluations occurred in the subjects' homes. The 6-month outpatient visit occurred at Children's Memorial Hospital in Chicago, Illinois. PARTICIPANTS: Three hundred one adolescents (aged 12-18 years) with acute infectious mononucleosis. MAIN EXPOSURES: All participants were evaluated at baseline (during active infection). Six months following infection, 39 of them met criteria for chronic fatigue syndrome. These subjects were matched by sex and Tanner stage to 39 randomly selected screened-negative subjects. Both groups were reevaluated at 12- and 24-month follow-ups. OUTCOME MEASURES: Scores from the Fatigue Severity Scale and the Modifiable Activity Questionnaire. RESULTS: For both groups, physical activity levels declined and sleep increased as a result of having mononucleosis.

				Compared with their matched controls, adolescents with chronic fatigue syndrome reported significantly higher levels of fatigue at all points and spent significantly more time sleeping during the day 6 and 12 months following infection. The 2 groups did not differ significantly in terms of physical activity levels before, during, or after infection. There was a consistent trend for decreased physical activity in the chronic fatigue syndrome group. CONCLUSIONS: Adolescents with chronic fatigue syndrome appear to be pushing themselves in an attempt to maintain similar activity levels as their peers, but paying for it in terms of fatigue severity and an increased need for sleep, particularly during the day.
Hurum H, Sulheim D, Thaulow E, Wyller VB.	Division of Paediatrics, Oslo University Hospital, Oslo, Norway Department of Pediatrics, Østfold Hospital, Fredrikstad, Norway Department of Pediatrics, Innlandet Hospital, Lillehammer, Norway.	Elevated nocturnal blood pressure and heart rate in adolescent chronic fatigue syndrome.	Acta Paediatr. 2011 Feb;100(2):289-92. doi: 10.1111/j.1651-2227.2010.02073.x . Epub 2010 Nov 17.	Aim: To compare ambulatory recordings of heart rate (HR) and blood pressure in adolescents with chronic fatigue syndrome (CFS) and healthy controls. We hypothesized both HR and blood pressure to be elevated among CFS patients. Methods: Forty-four CFS patients aged 12-18 years were recruited from our paediatric outpatient clinic. The controls were 52 healthy adolescents having similar distribution of age and gender. 24-h ambulatory blood pressure and HR were recorded using a validated, portable oscillometric device. Results: At night (sleep), HR, mean arterial blood pressure and diastolic blood pressure were significantly higher in CFS patients as compared with controls ($p < 0.01$). During daytime, HR was significantly higher among CFS patients ($p < 0.05$), whereas blood pressures were equal among the two groups. Conclusions: The findings support previous experimental evidence of sympathetic predominance of cardiovascular control in adolescent CFS patients. Also, the findings prompt increased focus on cardiovascular risk assessment and suggest a possible target for therapeutic intervention.
Hué S, Gray ER, Gall A, Katzourakis A, Tan CP, Houldcroft CJ, McLaren S, Pillay D, Futreal A, Garson JA, Pybus OG, Kellam P, Towers GJ.	MRC Centre for Medical Molecular Virology, Division of Infection and Immunity, University College London, 46 Cleveland St, London W1T 4JF, UK. pk5@sanger.ac.uk.	Disease-associated XMRV sequences are consistent with laboratory contamination.	Retrovirology. 2010 Dec 20;7(1):111.	ABSTRACT:BACKGROUND: Xenotropic murine leukaemia viruses (MLV-X) are endogenous gammaretroviruses that infect cells from many species, including humans. Xenotropic murine leukaemia virus-related virus (XMRV) is a retrovirus that has been the subject of intense debate since its detection in samples from humans with prostate cancer (PC) and chronic fatigue syndrome (CFS). Controversy has arisen from the failure of some studies to detect XMRV in PC or CFS patients and from inconsistent detection of XMRV in healthy controls. RESULTS: Here we demonstrate that Taqman PCR primers previously described as XMRV-specific can amplify common murine endogenous viral sequences from mouse suggesting that mouse DNA can contaminate patient samples and confound specific XMRV detection. To consider the provenance of XMRV we sequenced XMRV from the cell line 22Rv1, which is infected with an MLV-X that is indistinguishable from patient derived XMRV. Bayesian phylogenies clearly show that XMRV sequences reportedly derived from unlinked patients form a monophyletic clade with interspersed 22Rv1 clones (posterior probability >0.99). The cell line-derived sequences are ancestral to the patient-derived sequences (posterior probability >0.99). Furthermore, pol sequences apparently amplified from PC patient material (VP29 and VP184) are recombinants of XMRV and Moloney MLV (MoMLV) a virus with an envelope that lacks tropism for human cells. Considering the diversity of XMRV we show that the mean pairwise genetic distance among env and pol 22Rv1-derived sequences exceeds that of patient-associated sequences (Wilcoxon rank sum test:

				p = 0.005 and p < 0.001 for pol and env, respectively). Thus XMRV sequences acquire diversity in a cell line but not in patient samples. These observations are difficult to reconcile with the hypothesis that published XMRV sequences are related by a process of infectious transmission. CONCLUSIONS: We provide several independent lines of evidence that XMRV detected by sensitive PCR methods in patient samples is the likely result of PCR contamination with mouse DNA and that the described clones of XMRV arose from the tumour cell line 22Rv1, which was probably infected with XMRV during xenografting in mice. We propose that XMRV might not be a genuine human pathogen.
Israeli E, Pardo A.	The Chaim Zabludowicz Center for Autoimmune Diseases, Chaim Sheba Medical Center, 52621, Tel-Hashomer, Israel, eitanister@gmail.com.	The sick building syndrome as a part of the autoimmune (auto-inflammatory) syndrome induced by adjuvants.	Mod Rheumatol. 2010 Dec 29. [Epub ahead of print]	Sick building syndrome (SBS) is a term coined for a set of clinically recognizable symptoms and ailments without a clear cause reported by occupants of a building. In the 1990s the term "functional somatic syndromes" was applied to several syndromes, including SBS, multiple chemical sensitivity, repetition stress injury, the side effects of silicone breast implants, the Gulf War syndrome (GWS), chronic fatigue syndrome, the irritable bowel syndrome, and fibromyalgia. Recently, Shoenfeld and Agmon-Levin suggested that four conditions-siliconosis, macrophagic myofascitis, the GWS, and post-vaccination phenomena-which share clinical and pathogenic resemblances, may be included under a common syndrome entitled the "autoimmune (auto-inflammatory) syndrome induced by adjuvants". Comparison of the clinical manifestations, symptoms, and signs of the four conditions described by Shoenfeld and Agmon-Levin with those described for SBS shows that nine out of ten main symptoms are present in all 5 conditions. Shoenfeld and Agmon-Levin further propose several major and minor criteria, which, although requiring further validation, may aid in the diagnosis of this newly defined syndrome. We propose here that SBS may also be included as a part of "Shoenfeld's syndrome".
Jason L, Brown M, Evans M, Anderson V, Lerch A, Brown A, Hunnell J, Porter N.	Center for Community Research, DePaul University, Chicago, IL 60614, USA.	Measuring substantial reductions in functioning in patients with chronic fatigue syndrome.	Disabil Rehabil. 2010 Jul 9. [Epub ahead of print]	Purpose. All the major current case definitions for chronic fatigue syndrome (CFS) specify substantial reductions in previous levels of occupational, educational, social, or personal activities to meet criteria. Difficulties have been encountered in operationalizing 'substantial reductions.' For example, the Medical Outcomes Study Short Form-36 Health Survey (SF-36) has been used to determine whether individuals met the CFS disability criterion. However, previous methods of using the SF-36 have been prone to including people without substantial reductions in key areas of physical functioning when diagnosing CFS. This study sought to empirically identify the most appropriate SF-36 subscales for measuring substantial reductions in patients with CFS. Method. The SF-36 was administered to two samples of patients with CFS: one recruited from tertiary care and the other a community-based sample; as well as a non-fatigued control group. Receiver operating characteristics were used to determine the optimal cutoff scores for identifying patients with CFS. Results. The SF-36 Role-Emotional subscale had the worst sensitivity and specificity, whereas the Vitality, Role-Physical, and Social Functioning subscales had the best sensitivity and specificity. Conclusion. Based on the evidence from this study, the potential criteria for defining substantial reductions in functioning and diagnosing CFS is provided.
Jason LA, Boulton A, Porter NS, Jessen T, Njoku MG, Friedberg F.	Center for Community Research, 990 W. Fullerton Ave., Suite 3100,	Classification of myalgic encephalomyelitis/ chronic fatigue syndrome by types	Behav Med. 2010 Jan-Mar;36(1):24-31.	Persons with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) often complain of fatigue states (eg, postexertional malaise, brain fog) that are qualitatively different than normal, daily fatigue. Given the heterogeneous nature of ME/CFS, it is likely that individuals with this illness experience these fatigue types differently in terms of severity and frequency. It is also possible that meaningful subgroups of patients exist that exhibit different patterns of the fatigue experience. The purpose of

	Chicago, IL 60614, USA. ljason@depaul.edu	of fatigue.		this study was to investigate whether individuals with ME/CFS can be classified in a meaningful way according to the different types of fatigue they experience. One hundred individuals with ME/CFS participated in the study. Individuals that met inclusion criteria were administered the Multiple Fatigue Types Questionnaire (MFTQ), a 5-factor instrument that distinguishes between different types of fatigue. A cluster analysis was used to classify patients into various clusters based on factor subscale scores. Using a 3-factor solution, individuals were classified according to illness severity (low, moderate, severe) across the different fatigue factors. However, a 5-cluster solution enabled participants with moderate to severe fatigue levels to fall into more differentiated clusters and demonstrate distinct fatigue state patterns. These results suggest that fatigue patterns of individuals with ME/CFS are heterogeneous, and that patients may be classified into meaningful subgroups.
Jason LA, Evans M, Brown M, Porter N.	Center for Community Research, DePaul University, 990 W. Fullerton Ave., Chicago, IL 60614, USA. Ljason@depaul.edu	What is fatigue? Pathological and nonpathological fatigue.	PM R. 2010 May;2(5):327-31.	Aid in understanding issues surrounding the construct validity of fatigue including the distinction between pathological versus nonpathological fatigue. Fatigue is a universal symptom reported by individuals in the general population as well as by those suffering from different medical and psychological illnesses, including cancer, multiple sclerosis, chronic fatigue syndrome, depression, and anxiety. Chronic fatigue is a significant problem in many primary care settings, and the debilitating and prolonged nature of fatigue can pose significant economic consequences for society. Researchers have struggled to better assess and understand the etiology and classification of fatigue within different illness groups.
Jason LA, Paavola E, Porter N, Morello ML.	DePaul University, Center for Community Research, 990 W. Fullerton Avenue, Suite 3100, Chicago, IL 60614, USA. ljason@depaul.edu	Frequency and content analysis of chronic fatigue syndrome in medical text books.	Aust J Prim Health. 2010;16(2):174-8.	Text books are a cornerstone in the training of medical staff and students, and they are an important source of references and reviews for these professionals. The objective of this study was to determine both the quantity and quality of chronic fatigue syndrome (CFS) information included in medical texts. After reviewing 119 medical text books from various medical specialties, we found that 48 (40.3%) of the medical text books included information on CFS. However, among the 129 527 total pages within these medical text books, the CFS content was presented on only 116.3 (0.090%) pages. Other illnesses that are less prevalent, such as multiple sclerosis and Lyme disease, were more frequently represented in medical text books. These findings suggest that the topic ofCFS is underreported in published medical text books.
Jason LA, Roesner N, Porter N, Parenti B, Mortensen J, Till L.	DePaul University. Ljason@depaul.edu	Provision of social support to individuals with chronic fatigue syndrome.	J Clin Psychol. 2010 Mar;66(3):249-58.	The present study evaluated a buddy program designed to provide support for individuals with chronic fatigue syndrome (CFS). The intervention involved weekly visits by a student paraprofessional, who helped out with tasks that needed to be done in an effort to reduce some of the taxing demands and responsibilities that participants regularly encountered. This model of rehabilitation focused on avoiding overexertion in persons with CFS, aiming to avoid setbacks and relapses while increasing their tolerance for activity. Participants with CFS were randomly assigned to either a 4-month buddy intervention or a control condition. Posttest results showed that individuals who received a student buddy intervention had significantly greater reductions in fatigue severity and increases in vitality than individuals in the control condition. There were no significant changes between groups for physical functioning and stress. Buddy interventions that help patients with CFS reduce overexertion and possibly remain within their energy envelopes can be thought of as representing a different paradigm than nonpharmacologic interventions that focus only on increasing levels of activity through

				graded exercise.
Jelbert R, Stedmon J, Stephens A.	University of Plymouth, UK. beckyjelbert@yahoo.co.uk	A qualitative exploration of adolescents' experiences of chronic fatigue syndrome.	Clin Child Psychol Psychiatry. 2010 Apr;15(2):267-83. Epub 2010 Feb 23.	The aim of this study is to provide a qualitative perspective of adolescents' experiences of Chronic Fatigue Syndrome (CFS). Five adolescents who were considered to have recovered from CFS participated in semistructured interviews regarding their experience. The transcripts were then analysed using interpretative phenomenological analysis. Five main themes were identified to represent common shared experiences across participants.These related to seeking understanding around the illness, experiences of loss, perceived influences on the illness, difficult emotional experiences, and adolescents' status post recovery. While significant efforts are being made to increase knowledge and understanding of CFS within the child and adolescent population there is still much to be learned, as is evident from this direct account of adolescents' experiences. We identify implications for clinical practice and suggestions for future research in light of listening to the adolescents' stories.
Jensen OM.		[Myalgic encephalomyelitis-chronic fatigue syndrome is not a functional disease]. [Article in Danish]	Ugeskr Laeger. 2010 Aug 23;172(34):2328; author reply 2328. Comment on: Ugeskr Laeger. 2010 Jun 14;172(24):1811.	
Jeziorski E, Foulongne V, Ludwig C, Louhaem D, Chiocchia G, Segondy M, Rodière M, Sitbon M, Courgnaud V.	Institut de Génétique Moléculaire de Montpellier UMR 5535 CNRS, 1919 route de Mende, 34293 Montpellier cedex 5, France.	No evidence for XMRV association in pediatric idiopathic diseases in France.	Retrovirology. 2010 Aug 2;7:63.	Retroviruses have been linked to a variety of diseases such as neoplastic and immunodeficiency disorders and neurologic and respiratory diseases. Recently, a novel infectious human retrovirus, the xenotropic murine leukemia virus-related virus (XMRV), has been identified in cohorts of patients with either a familial type of prostate cancer or chronic fatigue syndrome. The apparent unrelatedness of these diseases raised the question of the potential involvement of XMRV in other diseases.Here, we investigated the presence of XMRV in a selection of pediatric idiopathic infectious diseases with symptoms that are suggestive of a retroviral infection, as well as in children with respiratory diseases and in adult patients with spondyloarthritis (SpA). Using a XMRV env-nested PCR, we screened 72 DNA samples obtained from 62 children hospitalized in the Montpellier university hospital (France) for hematological, neurological or inflammatory pathologies, 80 DNA samples from nasopharyngeal aspirates from children with respiratory diseases and 19 DNA samples from SpA. None of the samples tested was positive for XMRV or MLV-like env sequences, indicating that XMRV is not involved in these pathologies.
Johnson SK, Schmaling KB, Dmochowski J, Bernstein D.	University of North Carolina at Charlotte, 9201 University City Blvd, Charlotte, NC 28223, USA. skjohnso@uncc.ed	An investigation of victimization and the clinical course of chronic fatigue syndrome.	J Health Psychol. 2010 Apr;15(3):351-61.	Medically unexplained syndromes, including chronic fatigue syndrome (CFS), have been associated with victimization in childhood and adulthood. The purpose of this study was to examine the associations of victimization experiences in childhood and adulthood with functional status and illness severity in a sample of patients with CFS using longitudinal data. In the sample of 93 patients with CFS, childhood abuse and neglect had greater impact than adulthood victimization. Overall, victimization experiences in childhood demonstrated modest associations with clinical outcomes in CFS, although several victimization experiences were in the opposite direction of expectations. Victimization

	u			predicted worse outcomes, but not worsening outcomes over time.
Jones DE, Gray J, Frith J, Newton JL.	UK NIHR Biomedical Centre in Ageing, Institute of Cellular Medicine, Institute for Ageing and Health, Newcastle University, Newcastle, UK.	Fatigue severity remains stable over time and independently associated with orthostatic symptoms in chronic fatigue syndrome: a longitudinal study.	J Intern Med. 2011 Feb;269(2):182-8. doi: 10.1111/j.1365-2796.2010.02306.x . Epub 2010 Nov 14.	Abstract. Jones DEJ, Gray J, Frith J, Newton JL (UK NIHR Biomedical Centre in Ageing, Institute of Cellular Medicine, Institute for Ageing and Health, Newcastle University, Newcastle, UK) Fatigue severity remains stable over time and independently associated with orthostatic symptoms in chronic fatigue syndrome: a longitudinal study. J Intern Med 2011; 269: 182-188. Objectives: To examine fatigue variability over time in chronic fatigue syndrome (CFS) and the effect of other symptoms on its predictability. Design: Longitudinal cohort study of patients with CFS (Fukuda criteria). Setting: Specialist CFS clinical service. Subjects: Phase 1: 100 patients who participated in a study of CFS symptoms in 2005 were revisited in 2009. Phase 2: 25 patients completed fatigue diaries to address intra- and inter-day variability in perceived fatigue. Main outcome measures: Phase 1: subjects completed fatigue impact scale (FIS), Epworth sleepiness scale (ESS), orthostatic grading scale (OGS) and hospital anxiety and depression scale (HADS). Changes in variables represented the differences between 2005 and 2009. Phase 2: subjects rated fatigue on a scale of 0 (no fatigue) to 10 (severe fatigue) four times a day for 5 weeks. Results: Symptom assessment tools were available in both 2005 and 2009 for 74% of patients. FIS and HADS depression (HAD-D) and anxiety (HAD-A) scores significantly improved during follow-up whereas ESS and OGS remained stable. FIS improved in 29/74 (39%) subjects, and by ≥10 points in 19 (26%). FIS worsened by ≥10 points in 33/74 (45%) subjects. On multivariate analysis, independent predictors of current fatigue (FIS in 2009) were FIS in 2005, HAD-D in 2009, OGS in 2009 and change in HAD-A. Reported fatigue was stable from week to week and from day to day. Patients reported higher fatigue in the morning (mean ± SD; 6.4 ± 2), becoming significantly lower at lunchtime (6.2 ± 2; P < 0.05) and increasing again to 7 ± 2 at bedtime. Conclusions: Current fatigue is independently associated with current autonomic symptom burden, current depression and change in anxiety during follow-up. These findings have implications for targeted symptom management in CFS.
Jones DE, Hollingsworth KG, Taylor R, Blamire AM, Newton JL.	Institute of Cellular Medicine, Newcastle University, Newcastle-upon-Tyne, UK.	Abnormalities in pH handling by peripheral muscle and potential regulation by the autonomic nervous system in chronic fatigue syndrome.	J Intern Med. 2010 Apr;267(4):394-401.	OBJECTIVES: To examine muscle acid handling following exercise in chronic fatigue syndrome (CFS/ME) and the relationship with autonomic dysfunction. DESIGN: Observational study. SETTING: Regional fatigue service. SUBJECTS & INTERVENTIONS: Chronic fatigue syndrome (n = 16) and age and sex matched normal controls (n = 8) underwent phosphorus magnetic resonance spectroscopy (MRS) to evaluate pH handling during exercise. Subjects performed plantar flexion at fixed 35% load maximum voluntary contraction. Heart rate variability was performed during 10 min supine rest using digital photophlethysmography as a measure of autonomic function. RESULTS: Compared to normal controls, the CFS/ME group had significant suppression of proton efflux both immediately postexercise (CFS: 1.1 +/- 0.5 mmol L(-1) min(-1) vs. normal: 3.6 +/- 1.5 mmol L(-1) min(-1), P < 0.001) and maximally (CFS: 2.7 +/- 3.4 mmol L(-1) min(-1) vs. control: 3.8 +/- 1.6 mmol L(-1) min(-1), P < 0.05). Furthermore, the time taken to reach maximum proton efflux was significantly prolonged in patients (CFS: 25.6 +/- 36.1 s vs. normal: 3.8 +/- 5.2 s, P < 0.05). In controls the rate of maximum proton efflux showed a strong inverse correlation with nadir muscle pH following exercise (r(2) = 0.6; P < 0.01). In CFS patients, in contrast, this significant normal relationship was lost (r(2) = 0.003; P = ns). In normal individuals, the maximum proton efflux following exercise were closely correlated with total heart rate variability (r(2) = 0.7; P = 0.007) this relationship was lost in CFS/ME patients (r(2) < 0.001; P = ns).

				CONCLUSION: Patients with CFS/ME have abnormalities in recovery of intramuscular pH following standardised exercise degree of which is related to autonomic dysfunction. This study identifies a novel biological abnormality in patients with CFS/ME which is potentially open to modification.
Kadota Y, Cooper G, Burton AR, Lemon J, Schall U, Lloyd A, Vollmer-Conna U.	School of Psychiatry, University of NSW, Sydney, Australia.	Autonomic hyper-vigilance in post-infective fatigue syndrome.	Biol Psychol. 2010 Sep;85(1):97-103. Epub 2010 Jun 2.	This study examined whether post-infective fatigue syndrome (PIFS) is associated with a disturbance in bidirectional autonomic signalling resulting in heightened perception of symptoms and sensations from the body in conjunction with autonomic hyper-reactivity to perceived challenges. We studied 23 patients with PIFS and 25 healthy matched control subjects. A heartbeat discrimination task and a pressure pain threshold test were used to assess interoceptive sensitivity. Cardiac response was assessed over a 4-min Stroop task. PIFS was associated with higher accuracy in heartbeat discrimination and a lower pressure pain threshold. Increased interoceptive sensitivity correlated strongly with current symptoms and potentiated differences in the cardiac response to the Stroop task, which in PIFS was characterized by insensitivity to task difficulty and lack of habituation. Our results provide the first evidence of heightened interoceptive sensitivity in PIFS. Together with the distinct pattern in cardiac responsivity these findings present a picture of physiological hyper-vigilance and response inflexibility.
Kaiser J.		Virology. No meeting of minds on XMRV's role in chronic fatigue, cancer.	Science. 2010 Sep 17;329(5998):1454.	
Kato K, Sullivan PF, Pedersen NL.	School of Nursing and Rehabilitation, International University of Health and Welfare, Odawara, Japan. kenji-kato@umin.ac.jp	Latent class analysis of functional somatic symptoms in a population-based sample of twins.	J Psychosom Res. 2010 May;68(5):447-53. Epub 2010 Mar 1.	OBJECTIVE: This study aimed to investigate empirically how and in what way individuals with symptoms of functional somatic syndromes should be classified. We also aimed to look into genetic and environmental influences on the classification. METHOD: A total of 28,531 twins aged 41-64 underwent screening interviews via a computer-assisted data collection system from 1998 to 2002. Nine functional somatic symptoms (abnormal tiredness, general muscular pain, recurrent abdominal discomfort, back pain, gastroesophageal reflux, recurrent headache, recurrent urinary problem, dizziness, breathlessness at rest) were assessed using structured questions in a blinded manner. Latent class analysis was applied to the data. Structural equation modeling was further performed in order to estimate the relative importance of genetic and environmental influences on class probability. RESULTS: Latent class analysis resulted in a five-class solution. Individuals in the first class did not show any health problems. Those assigned to the second, third, and fourth classes tended to have abnormal tiredness, gastrointestinal problems, and pain-related symptoms, respectively. Individuals in the fifth class had multiple symptoms to a greater extent than the other classes. All the five classes showed modest genetic influences (7-29% of the total variation) with gender differences except Class 3; however, the majority of influences on the class membership derived from unique environmental effects. CONCLUSION: The findings suggested the necessity of redefining the existing classification criteria for functional somatic syndromes in terms of single (uncomplicated) or multiple (complicated) syndromes. Environmental influences are important for the etiology of functional somatic syndromes.
Katz BZ, Boas S,	Department of	Exercise tolerance	J Pediatr. 2010	OBJECTIVE: Six months after acute infectious mononucleosis (IM), 13% of adolescents meet criteria

Shiraishi Y, Mears CJ, Taylor R.	Pediatrics, Northwestern University, Feinberg School of Medicine and Children's Memorial Hospital, Chicago, IL 60614, USA. bkatz@northwestern.edu	testing in a prospective cohort of adolescents with chronic fatigue syndrome and recovered controls following infectious mononucleosis.	Sep;157(3):468-72, 472.e1. Epub 2010 May 6.	for chronic fatigue syndrome (CFS). We measured exercise tolerance in adolescents with CFS and control subjects 6 months after IM. STUDY DESIGN: Twenty-one adolescents with CFS 6 months after IM and 21 recovered control subjects performed a maximal incremental exercise tolerance test with breath-by-breath gas analysis. Values expressed are mean+/-standard deviation. RESULTS: The adolescents diagnosed with CFS and control subjects did not differ in age, weight, body mass index, or peak work capacity. Lower oxygen consumption peak percent of predicted was seen in adolescents with CFS compared with control subjects (CFS 99.3+/-16.6 vs control subject 110.7+/-19.9, P=.05). Peak oxygen pulse also was lower in adolescents with CFS compared with recovered control subjects (CFS 12.4+/-2.9 vs control subjects 14.9+/-4.3, P=.03). CONCLUSIONS: Adolescents with CFS 6 months after IM have a lower degree of fitness and efficiency of exercise than recovered adolescents. Whether these abnormal exercise findings are a cause or effect of CFS is unknown. IM can lead to both fatigue and measurable changes in exercise testing in a subset of adolescents.
Kean S.		Virology. An indefatigable debate over chronic fatigue syndrome.	Science. 2010 Jan 15;327(5963):254-5.	
Kearney M, Maldarelli F.		Current status of xenotropic murine leukemia virus-related retrovirus in chronic fatigue syndrome and prostate cancer: reach for a scorecard, not a prescription pad.	J Infect Dis. 2010 Nov 15;202(10):1463-6. Epub 2010 Oct 11. Comment on: J Infect Dis. 2010 Nov 15;202(10):1470-7. J Infect Dis. 2010 Nov 15;202(10):1478-81. J Infect Dis. 2010 Nov 15;202(10):1482-5.	
Kempke S, Goossens L, Luyten P, Bekaert P, Van Houdenhove B, Van Wambeke P.	Department of Psychology, University of Leuven, Leuven, Belgium. stefan.kempke@psy.kuleuven.be	Predictors of outcome in a multi-component treatment program for chronic fatigue syndrome.	J Affect Disord. 2010 Oct;126(1-2):174-9. Epub 2010 Feb 18.	BACKGROUND: Little is known about factors predicting treatment outcome in chronic fatigue syndrome (CFS). METHODS: Based on Vercoulen et al.'s (1998) cognitive-behavioral model of perpetuating factors in CFS, the predictive value of the following patient characteristics were examined in a sample of 178 CFS patients who followed a multi-component treatment program: (1) somatic attributions, (2) psychological attributions, (3) sense of control over symptoms, (4) physical activity, (5) functional impairment, (6) somatic focus, and (7) severity of depression. RESULTS: Only pre-treatment severity of depression was associated with negative treatment outcome defined in terms of post-treatment fatigue and improvement in fatigue. LIMITATIONS: The study was conducted at a tertiary care centre and did not include a control group or a long-term follow-up. CONCLUSIONS:

				Level of depression may be the most important factor of the cognitive-behavioral model predicting post-treatment fatigue in CFS. Hence, findings suggest that treatment of CFS should include a focus on severity of depression.
Kempke S, Van Houdenhove B, Luyten P, Goossens L, Bekaert P, Van Wambeke P.	Department of Psychology, University of Leuven, Leuven, Belgium.	Unraveling the role of perfectionism in chronic fatigue syndrome: Is there a distinction between adaptive and maladaptive perfectionism?	Psychiatry Res. 2010 Oct 18. [Epub ahead of print]	In the current study, we investigated whether the distinction between adaptive (i.e. high personal standards) and maladaptive (i.e. concern over mistakes and doubt about actions) perfectionism that has been found in the literature, is also valid in patients with chronic fatigue syndrome (CFS). We hypothesized that maladaptive, but not adaptive, perfectionism would be significantly and positively related to severity of fatigue and depression in CFS. We examined this hypothesis in a sample of 192 CFS patients using structural equation modelling (SEM). Although the two perfectionism dimensions were related to each other, results supported a model in which only maladaptive perfectionism was positively related to severity of fatigue and depression. Further, we found that depression fully mediated the effect of maladaptive perfectionism on fatigue. The results suggest that adaptive and maladaptive perfectionism are two distinct, albeit related, dimensions in CFS. Findings of this study have important implications for theory and treatment of CFS, particularly for cognitive-behavioral treatment.
Kennedy G, Khan F, Hill A, Underwood C, Belch JJ.	Vascular and Inflammatory Diseases Research Unit, The Institute of Cardiovascular Research, Centre for Cardiovascular and Lung Biology, Division of Medical Sciences, Ninewells Hospital and Medical School, Dundee, Scotland, United Kingdom. g.y.kennedy@dundee.ac.uk	Biochemical and vascular aspects of pediatric chronic fatigue syndrome.	Arch Pediatr Adolesc Med. 2010 Sep;164(9):817-23. Comment in: Arch Pediatr Adolesc Med. 2010 Sep;164(9):880-1.	OBJECTIVE: To evaluate the biochemical and vascular aspects of pediatric chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). DESIGN: Cross-sectional clinical study. SETTING: Tayside, Scotland, United Kingdom. PARTICIPANTS: Twenty-five children with CFS/ME and 23 healthy children recruited from throughout the United Kingdom. INTERVENTIONS: Participants underwent a full clinical examination to establish a diagnosis of CFS/ME and were asked to describe and score their CFS/ME symptoms. Biochemical markers were measured. Arterial wave reflection was estimated to assess systemic arterial stiffness. MAIN OUTCOME MEASURES: Markers of oxidative stress and free radicals, C-reactive protein level, white blood cell apoptosis, and arterial wave reflection. RESULTS: Children with CFS/ME had increased oxidative stress compared with control individuals (isoprostanes: 252.30 vs 215.60 pg/mL, P = .007; vitamin C, mean [SD]: 0.84 [0.26] vs 1.15 [0.28] mg/dL, P < .001; vitamin E, 8.72 [2.39] vs 10.94 [3.46] microg/mL, P = .01) and increased white blood cell apoptosis (neutrophils: 53.7% vs 35.7%, P = .005; lymphocytes: 40.1% vs 24.6%, P = .009). Arterial stiffness variables did not differ significantly between groups (mean augmentation index, -0.57% vs -0.47%, P = .09); however, the derived variables significantly correlated with total (r = 0.543, P = .02) and low-density lipoprotein (r = 0.631, P = .004) cholesterol in patients with CFS/ME but not in controls. CONCLUSIONS: Biomedical anomalies seen in adults with CFS/ME-increased oxidative stress and increased white blood cell apoptosis-can also be observed in children with clinically diagnosed CFS/ME compared with matched controls. Unlike in their adult counterparts, however, arterial stiffness remained within the reference range in these pediatric patients.
Kennedy G, Underwood C, Belch JJ.	Ninewells Hospital and Medical School, Division of Medical Sciences, Mail Box 1, Centre for Cardiovascular	Physical and functional impact of chronic fatigue syndrome/myalgic encephalomyelitis in childhood.	Pediatrics. 2010 Jun;125(6):e1324-30. Epub 2010 May 17.	OBJECTIVE: The aim of this study was to compare self-reported and parent-reported quality of life for a group of pediatric patients with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) and age- and gender-matched healthy control children, to determine the extent of functional and physical impairment. METHODS: The Child Health Questionnaire was completed by 25 children with CFS/ME, who were recruited throughout the United Kingdom, and by 23 age-, gender-, and Tanner scale-matched control children. In addition, patients were asked questions about the background to their

	and Lung Biology, Vascular and Inflammatory Diseases Research Unit, Dundee DD1 9SY, United Kingdom. g.y.kennedy@dundee.ac.uk			illness (ie, precipitating factors), the status of their illness, and school attendance. RESULTS: The median illness duration for patients was 3 years. Sixty-eight percent of the children said that their illness developed quickly, and the illness had an infectious onset for 88%. Only 1 child (4%) attended school full-time, whereas 12 (48%) attended school part-time and 8 (32%) received home tuition only. Children with CFS/ME scored significantly lower for 10 of 14 Child Health Questionnaire concepts; the lowest scores were observed for global health (scores of 21.4 and 84.1 for patients and control subjects, respectively; P < .0001) and role/social limitations attributable to physical health problems (scores of 24.9 and 100, respectively; P < .0001). Quality of life for the children with CFS/ME compared unfavorably with previously published results for pediatric patients with type 1 diabetes mellitus or asthma. CONCLUSION: The quality of life of children with CFS/ME was profoundly reduced, compared with that of their healthy counterparts.
Kermode-Scott B.		Canada bans blood donations from people with history of chronic fatigue syndrome.	BMJ. 2010 Apr 9;340:c1974. doi: 10.1136/bmj.c1974.	
Kerr JR, Gough J, Richards SC, Main J, Enlander D, McCreary M, Komaroff AL, Chia JK.	Department of Cellular & Molecular Medicine, St George's University of London, London, UK. jkerr@sgul.ac.uk	Antibody to parvovirus B19 nonstructural protein is associated with chronic arthralgia in patients with chronic fatigue syndrome/myalgic encephalomyelitis.	J Gen Virol. 2010 Apr;91(Pt 4):893-7. Epub 2009 Dec 9.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a neuro-immune disease of uncertain pathogenesis. Human parvovirus B19 infection has been shown to occur just prior to development of the onset of CFS/ME in several cases, although B19 seroprevalence studies do not show any significant differences between CFS/ME and controls. In this study, we analysed parvovirus B19 markers in CFS/ME patients (n=200), diagnosed according to Fukuda CDC criteria, and normal blood donors (n=200). Serum from each subject was tested for anti-B19 VP2 IgM and IgG (by Biotrin ELISA), anti-B19 NS1 IgM and IgG (by immunofluorescence), and B19 DNA (by real-time PCR). CFS/ME patients and normal blood donors had a similar B19 seroprevalence (75 % versus 78 %, respectively). Eighty-three CFS patients (41.5 %) as compared with fourteen (7 %) normal blood donors tested positive for anti-B19 NS1 IgG (chi(2)=64.8; P<0.0001; odds ratio=9.42, CI 5.11-17.38). Of these 83 patients, 61 complained of chronic joint pain, while 22 did not. Parvovirus B19 DNA was detected in serum of 11 CFS patients and none of the controls by Taqman real-time PCR (chi(2)=9.35, P<0.002). Positivity for anti-B19 NS1 IgG was associated with higher expression levels of the human CFS-associated genes NHLH1 and GABPA. As NS1 antibodies are thought to indicate chronic or severe courses of B19 infection, these findings suggest that although the seroprevalence of B19 in CFS patients is similar to controls, the immune control of the virus in these patients may not be efficient.
Kim S, Rusmevichientong A, Dong B, Remenyi R, Silverman RH, Chow SA.	Biomedical Engineering Interdepartmental Program, University of California Los Angeles, Los Angeles, California,	Fidelity of target site duplication and sequence preference during integration of xenotropic murine leukemia virus-related virus.	PLoS One. 2010 Apr 20;5(4):e10255.	Xenotropic murine leukemia virus (MLV)-related virus (XMRV) is a new human retrovirus associated with prostate cancer and chronic fatigue syndrome. The causal relationship of XMRV infection to human disease and the mechanism of pathogenicity have not been established. During retrovirus replication, integration of the cDNA copy of the viral RNA genome into the host cell chromosome is an essential step and involves coordinated joining of the two ends of the linear viral DNA into staggered sites on target DNA. Correct integration produces proviruses that are flanked by a short direct repeat, which varies from 4 to 6 bp among the retroviruses but is invariant for each particular retrovirus. Uncoordinated joining of the two viral DNA ends into target DNA can cause insertions, deletions, or

	United States of America.			other genomic alterations at the integration site. To determine the fidelity of XMRV integration, cells infected with XMRV were clonally expanded and DNA sequences at the viral-host DNA junctions were determined and analyzed. We found that a majority of the provirus ends were correctly processed and flanked by a 4-bp direct repeat of host DNA. A weak consensus sequence was also detected at the XMRV integration sites. We conclude that integration of XMRV DNA involves a coordinated joining of two viral DNA ends that are spaced 4 bp apart on the target DNA and proceeds with high fidelity.
Kindlon T, Goudsmit EM.		Graded exercise for chronic fatigue syndrome: too soon to dismiss reports of adverse reactions.	J Rehabil Med. 2010 Feb;42(2):184; author reply 184-6. Comment on: J Rehabil Med. 2008 Nov;40(10):882-3; author reply 883-5.	
Kindlon T.		FINE trial for CFS. Missing data.	BMJ. 2010 Jun 9;340:c2990. doi: 10.1136/bmj.c2990.	
Kindlon T.		Criteria used to define chronic fatigue syndrome questioned.	Psychosom Med. 2010 Jun;72(5):506-7; author reply 507-9. Comment on: Psychosom Med. 2009 Jun;71(5):557-65.	
Kindlon T.		Stratification using biological factors should be performed in more CFS studies.	Psychol Med. 2010 Feb;40(2):352. Epub 2009 Oct 12.	
Kishi A, Natelson BH, Togo F, Struzik ZR, Rapoport DM, Yamamoto Y.	Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, 113-0033, Japan.	Sleep stage transitions in chronic fatigue syndrome patients with or without fibromyalgia.	Conf Proc IEEE Eng Med Biol Soc. 2010;1:5391-4.	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained conditions that share considerable overlapping symptoms, including sleep-related complaints. However, differences between the two conditions have been reported, and we hypothesized that dynamic aspects of sleep, recently attracting scientific interests, would be different in the two groups of patients. We thus study transition probabilities between sleep stages of CFS patients with or without FM. Subjects were 26 healthy controls, 14 CFS patients without FM (CFS alone) and 12 CFS patients with FM (CFS+FM) - all women. We studied transition probabilities between sleep stages (waking, REM sleep and Stage I, Stage II and slow-wave sleep (Stage III+IV)). We found that probabilities of transition from REM sleep to waking were significantly greater in CFS alone than in controls; we have reported previously this

				sleep disruption as the specific sleep problem for CFS alone [Kishi et al., 2008]. Probabilities of transitions from waking, REM sleep and Stage I to Stage II, and those from slow-wave sleep to Stage I, were significantly greater in CFS+FM than in controls; the former might indicate increased sleep pressure in CFS+FM and the latter may be the specific sleep problem of CFS+FM. These results suggest that CFS and FM are different illnesses associated with different problems of sleep regulation.
Knoop H, Prins JB, Moss-Morris R, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, 6500 HB Nijmegen, The Netherlands. j.knoop@nkcv.umcn.nl	The central role of cognitive processes in the perpetuation of chronic fatigue syndrome.	J Psychosom Res. 2010 May;68(5):489-94. Epub 2010 Mar 16.	OBJECTIVE: Chronic fatigue syndrome (CFS) is considered to be one of the functional somatic syndromes (FSS). Cognitions and behavior are thought to perpetuate the symptoms of CFS. Behavioral interventions based on the existing models of perpetuating factors are quite successful in reducing fatigue and disabilities. The evidence is reviewed that cognitive processes, particularly those that determine the perception of fatigue and its effect on behavior, play a central role in the maintenance of symptoms. METHOD: Narrative review. RESULTS: Findings from treatment studies suggest that cognitive factors mediate the positive effect of behavioral interventions on fatigue. Increased fitness or increased physical activity does not seem to mediate the treatment response. Additional evidence for the role of cognitive processes is found in studies comparing the subjective beliefs patients have of their functioning with their actual performance and in neurobiological research. CONCLUSION: Three different cognitive processes may play a role in the perpetuation of CFS symptoms. The first is a general cognitive representation in which fatigue is perceived as something negative and aversive and CFS is seen as an illness that is difficult to influence. The second process involved is the focusing on fatigue. The third element is formed by specific dysfunctional beliefs about activity and fatigue.
Krisciukaitis A, Simoliuniene R, Tamosiunas M, Saferis V, Vainoras A, Gargasas L.	Institute for Biomedical Research, Kaunas University of Medicine, Eiveniu 4, 50009 Kaunas, Lithuania. akri@kmu.lt	Efficiency evaluation of autonomic heart control by using the principal component analysis of ECG P-wave.	Methods Inf Med. 2010;49(2):161-7. Epub 2010 Feb 22.	BACKGROUND: Cardiac output is controlled by the autonomic nervous system by changing the heart rate and/or the contractions of the heart muscle in response to the hemodynamic needs of the whole body. Malfunction of these mechanisms causes the postural orthostatic tachycardia syndrome and/or the chronic fatigue syndrome. Evaluation of functionality and efficiency of the control mechanisms could give valuable diagnostic information in the early stages of dysfunction of the heart control systems and help to monitor the healing process in rehabilitation period after interventions. OBJECTIVES: In this study we demonstrate how P-wave changes evoked by an orthostatic test could be quantitatively evaluated by using the method based on the principal component analysis. METHODS: ECG signals were recorded during an orthostatic test performed according to the typical protocol in three groups of volunteer subjects representing healthy young and older persons, part of which had transient periods of supraventricular arrhythmias. Quantitative evaluation of P-wave morphology changes was performed by means of principal component analysis-based method. RESULTS: Principal component-based estimates showed certain variety of P-wave shape during orthostatic test, what revealed a possibility to evaluate the properties of parasympathetic heart control. CONCLUSIONS: Quantitative evaluation of ECG P-wave changes evoked by an orthostatic test by using a newly developed method provides a quantitative estimate for functionality and efficiency of the heart rate control mechanisms. The method could be used in eHealth systems.
Kuehn BM.		Study reignites debate about viral agent in patients with chronic	JAMA. 2010 Oct 20;304(15):1653-4, 1656.	

		fatigue syndrome.		
Kumar A, Vashist A, Kumar P.	Pharmacology Division, University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Study, Panjab University, Chandigarh, India. kumaruips@yahoo.com	Potential role of pioglitazone, caffeic acid and their combination against fatigue syndrome-induced behavioural, biochemical and mitochondrial alterations in mice.	Inflammopharmacology. 2010 Oct;18(5):241-51. Epub 2010 Jul 3.	Chronic fatigue is an illness characterised by persistent and relapsing fatigue, often accompanied by numerous neuropsychiatric problems, such as anxiety and depression. The aetiology of chronic fatigue remains unclear so far. However, recent studies suggested the involvement of oxidative stress in this chronic debilitating disease. Alternatively, antioxidants have also been reported to have beneficial effect against chronic fatigue-like conditions. Therefore, present study has been designed to explore the potential role of pioglitazone, caffeic acid and their combination against chronic fatigue-like condition in mice. In the experimental protocol, the mice were put on the running wheel apparatus for 6 min test session daily for 21 days which produced fatigue-like condition. The locomotor activity and anxiety levels were measured on 0, 8th, 15th and 22nd days. The brains were isolated on 22nd day immediately after the behavioural assessments, oxidative damage and mitochondrial enzyme complexes were then estimated subsequently. Three weeks pioglitazone (5 and 10 mg/kg) and caffeic acid (5 and 10 mg/kg) pretreatment significantly attenuated the chronic fatigue-like condition (restored running wheel activity, locomotor activity and reduced anxiety-like behaviour) as compared to that in control (chronic fatigue) animals. Further, pioglitazone (5 and 10 mg/kg) and caffeic acid (5 and 10 mg/kg) drug treatments for 3 weeks significantly attenuated oxidative damage (decreased lipid peroxidation, nitrite concentration, restored reduction in glutathione and catalase levels), altered mitochondrial enzymes complex (I, II and IV) activities and mitochondrial redox activity (MTT assay) when compared with control. Further, combination of lower dose of pioglitazone (5 mg/kg) and caffeic acid (5 mg/kg) showed significant synergism in their protective effect which was significant as compared to their effect per se. The present study highlights the potential role of pioglitazone, caffeic acid and their combination in the pathophysiology of chronic fatigue-like condition in mice.
Kunstman KJ, Bhattacharya T, Flaherty J, Phair JP, Wolinsky SM.	Northwestern University, Chicago, Illinois 60611, USA.	Absence of xenotropic murine leukemia virus-related virus in blood cells of men at risk for and infected with HIV.	AIDS. 2010 Jul 17;24(11):1784-5.	Xenotropic murine leukemia virus-related virus has been detected in blood cells of patients with chronic fatigue syndrome and in 3.7% of healthy controls from the same geographic region. We evaluated 996 men who were participants in the Multicenter AIDS Cohort Study for xenotropic murine leukemia virus-related virus sequences in blood cells by means of a real-time quantitative PCR assay. Xenotropic murine leukemia virus-related virus was detected in none of the men on the basis of the absence of xenotropic murine leukemia virus-related virus DNA, suggesting that infection may be population-specific.
Lacerda EM, Nacul L, Pheby D, Shepherd C, Spencer P.	London School of Hygiene & Tropical Medicine, EPH/NPHIRU/CFS/ME Observatory, London, UK. Eliana.Lacerda@lshtm.ac.uk	Exploring the feasibility of establishing a disease-specific post-mortem tissue bank in the UK: a case study in ME/CFS.	J Clin Pathol. 2010 Nov;63(11):1032-4. Epub 2010 Oct 5.	BACKGROUND: Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) is a condition, the aetiology of which remains controversial, and there is still no consensus on its nature and determination. It has rarely been studied in post-mortem examinations, despite increasing evidence of abnormalities from neuroimaging studies. AIM: To ascertain the feasibility of developing a national post-mortem ME/CFS tissue bank in the UK, to enhance studies on aetiology and pathogenesis, including cell and tissue abnormalities associated with the condition. METHODS: The case study was carried out combining qualitative methods, ie, key informant interviews, focus group discussions with people with ME/CFS, and a workshop with experts in ME/CFS or in tissue banking. RESULTS AND CONCLUSIONS: The study results suggest that the establishment of the post-mortem ME/CFS tissue bank is both desirable and feasible, and would be acceptable to the possible tissue donors, provided that some issues were explicitly addressed.

Lakhan SE, Kirchgessner A.	Global Neuroscience Initiative Foundation, Los Angeles, CA, USA. slakhan@gnif.org.	Gut inflammation in chronic fatigue syndrome.	Nutr Metab (Lond). 2010 Oct 12;7:79.	ABSTRACT: Chronic fatigue syndrome (CFS) is a debilitating disease characterized by unexplained disabling fatigue and a combination of accompanying symptoms the pathology of which is incompletely understood. Many CFS patients complain of gut dysfunction. In fact, patients with CFS are more likely to report a previous diagnosis of irritable bowel syndrome (IBS), a common functional disorder of the gut, and experience IBS-related symptoms. Recently, evidence for interactions between the intestinal microbiota, mucosal barrier function, and the immune system have been shown to play a role in the disorder's pathogenesis.Studies examining the microecology of the gastrointestinal (GI) tract have identified specific microorganisms whose presence appears related to disease; in CFS, a role for altered intestinal microbiota in the pathogenesis of the disease has recently been suggested. Mucosal barrier dysfunction promoting bacterial translocation has also been observed. Finally, an altered mucosal immune system has been associated with the disease. In this article, we discuss the interplay between these factors in CFS and how they could play a significant role in GI dysfunction by modulating the activity of the enteric nervous system, the intrinsic innervation of the gut.If an altered intestinal microbiota, mucosal barrier dysfunction, and aberrant intestinal immunity contribute to the pathogenesis of CFS, therapeutic efforts to modify gut microbiota could be a means to modulate the development and/or progression of this disorder. For example, the administration of probiotics could alter the gut microbiota, improve mucosal barrier function, decrease pro-inflammatory cytokines, and have the potential to positively influence mood in patients where both emotional symptoms and inflammatory immune signals are elevated. Probiotics also have the potential to improve gut motility, which is dysfunctional in many CFS patients.
Landmark-Høyvik H, Reinertsen KV, Loge JH, Kristensen VN, Dumeaux V, Fosså SD, Børresen-Dale AL, Edvardsen H.	Department of Genetics, Institute for Cancer Research, Oslo University Hospital Radiumhospitalet, Oslo, Montebello, Norway.	The genetics and epigenetics of fatigue.	PM R. 2010 May;2(5):456-65.	Fatigue is a common symptom and includes both physical and mental components. It can be associated with a variety of different syndromes and diseases, but in many cases is not associated with other comorbid conditions. Most humans have experienced acute fatigue in relation to different stressors. Acute fatigue typically decreases as the effect of the triggering factor is reduced and a normal homeostatic balance is restored. Fatigue that persists for 6 months or more is termed chronic fatigue. Chronic fatigue (CF) in combination with a minimum of 4 of 8 symptoms and the absence of diseases that could explain these symptoms, constitute the case definition for chronic fatigue syndrome. In spite of its prevalence, the biology of fatigue is relatively poorly understood and biological markers have not yet been identified. This literature search was performed in PubMed to identify research on the genetics and epigenetics of fatigue. Publications were included if fatigue was a major topic and the topic was combined with genetic and/or epigenetic measurements in adult humans. A total of 40 publications were identified. Although altered functioning in the hypothalamic-pituitary-adrenal axis, the serotonergic system, and associations with infectious agents have been identified, the search for genetic or epigenetic markers of fatigue, either in the context of CF or chronic fatigue syndrome (CFS) has been relatively unproductive or, in the case of epigenetics, nonexistent. Although several studies, both hypothesis-testing and hypothesis-generating, have been performed to search for biomarkers, they have mostly been underpowered, restricted by the heterogeneity of the phenotype, or limited by an unsystematic study design. To be able to confirm the hypothesis that risk for, or levels of, fatigue are influenced by the genetic or epigenetic background of an individual, studies need to be based on larger sample sizes with a more clearly defined phenotype.

				Studies need to focus not only on the influence of a single aspect such as single nucleotide polymorphisms (SNPs) or differential gene expression on disease risk or state, but also on the systems biology behind the disease in combination with information on environmental influences and validation of findings in functional studies.
Langenberg PW, Wallach EE, Clauw DJ, Howard FM, Diggs CM, Wesselmann U, Greenberg P, Warren JW.	Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD, USA.	Pelvic pain and surgeries in women before interstitial cystitis/painful bladder syndrome.	Am J Obstet Gynecol. 2010 Mar;202(3):286.e1 -6. Epub 2009 Dec 22.	OBJECTIVE: The objective of the study was to compare subjects with interstitial cystitis/painful bladder syndrome (IC/PBS) with controls on prior surgeries. STUDY DESIGN: IC/PBS subjects were compared with matched controls on surgeries and possible surgical indications prior to their index dates. RESULTS: Adjusted for demographic variables, logistic regression showed subjects exceeded controls in surgeries longer than 12 months and less than 1 month before the index date. However, addition of possible surgical indications showed chronic pelvic pain (CPP) to have a strong association with IC/PBS, whereas associations with surgeries were reduced to nonsignificance. CONCLUSION: Although women with IC/PBS were more likely to have experienced prior surgeries than controls, the apparent indications for surgeries, not the surgeries themselves, were stronger risk factors for IC/PBS. In particular, a prior history of CPP had a strong association with IC/PBS. Several features of study design, including extensive medical record review, suggest that prior CPP was not undiagnosed IC/PBS. Further investigation of CPP may yield insight into the pathogenesis of IC/PBS.
Larun L, Malterud K.	Research Unit for General Practice, Uni Research, Bergen, Norway; Norwegian Knowledge Centre for the Health Services, Oslo, Norway.	Finding the right balance of physical activity A focus group study about experiences among patients with chronic fatigue syndrome.	Patient Educ Couns. 2010 Jun 25. [Epub ahead of print]	OBJECTIVE: To explore contexts of experiences of physical activity perceived as beneficial or harmful for CFS patients. METHODS: A qualitative study with empirical data from two focus groups with purposive sampling. Mean age was 50, two of ten participants were male, and social demographics varied. Participants were invited to share stories of good as well as bad experiences concerning physical activity. Data were analysed with systematic text condensation. RESULTS: Participants were not averse to physical activity, but specific preconditions would determine how the activity was perceived. Physical activity was experienced as helpful and enjoyable, especially related to leisure activities where flexible and individual adaptation was feasible. Non-customized activity may precipitate set-backs giving patients the impression of losing control and being betrayed by their bodies. Strategies to review energy usage in daily life could adjust expectations, diminish stress load and assist in approaching a more appropriate priority and balance. CONCLUSION: Self-management, body awareness and physical activity of choice combined with facilitation and advice from health care professionals is essential to achieve a positive outcome. PRACTICE IMPLICATIONS: Exercise programmes should be adapted, paced, and self-managed in accordance with personal preferences and activity levels to be beneficial and empowering for CFS patients.
Lavergne MR, Cole DC, Kerr K, Marshall LM.	Women's College Hospital, Family and Community Medicine, Toronto, ON M5S 1B2.	Functional impairment in chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity.	Can Fam Physician. 2010 Feb;56(2):e57-65.	OBJECTIVE: To characterize patients diagnosed with multiple chemical sensitivity (MCS), chronic fatigue syndrome (CFS), or fibromyalgia (FM), to compare their level of function with Canadian population average values, and to assess factors associated with function. DESIGN: Chart review and abstraction of clinical information. SETTING: The Environmental Health Clinic (EHC) at Women's College Hospital in Toronto, Ont, which is a provincial referral centre for patients with illnesses with suspected environmental links, especially MCS, CFS, and FM. PARTICPANTS: A total of 128 consecutive patients diagnosed with 1 or more of MCS, CFS, or FM, seen between January 2005 and March 2006 at the EHC. MAIN OUTCOME MEASURES: Demographic and socioeconomic characteristics, comorbid diagnoses, duration of illness, health services usage, life stresses, helpful therapeutic strategies, and

				functional impairment measured by the Short Form-36, compared with Canadian population average values. Factors significantly associated with function in bivariate analyses were included in multiple linear and logistic regression models. RESULTS: The patient population was predominantly female (86.7%), with a mean age of 44.6 years. Seventy-eight patients had discrete diagnoses of 1 of MCS, CFS, or FM, while the remainder had 2 or 3 overlapping diagnoses. Most (68.8%) had stopped work, and on average this had occurred 3 years after symptom onset. On every Short Form-36 subscale, patients had markedly lower functional scores than population average values, more so when they had 2 or 3 of these diagnoses. Having FM, younger age at onset, and lower socioeconomic status were most consistently associated with poor function. CONCLUSION: Patients seen at the EHC demonstrated marked functional impairment, consistent with their reported difficulties working and caring for their homes and families during what should be their peak productive years. Early comprehensive assessment, medical management, and social and financial support might avoid the deterioration of function associated with prolonged illness. Education and information resources are required for health care professionals and the public, along with further etiologic and prognostic research.
Lawn T, Kumar P, Knight B, Sharpe M, White PD.	East London Foundation Trust , St Bartholomew's Hospital , London EC1A 7BE , UK.	Psychiatric misdiagnoses in patients with chronic fatigue syndrome.	JRSM Short Rep. 2010 Sep 6;1(4):28.	OBJECTIVES: The aim of this study was to examine the accuracy of doctors at diagnosing co-morbid psychiatric disorders in patients with chronic fatigue syndrome (CFS). DESIGN: Case series comparing clinical diagnoses with a standardized structured psychiatric interview. SETTING: Secondary care specialist chronic fatigue syndrome clinic. PARTICIPANTS: One hundred and thirty-five participants of a randomized controlled trial of non-pharmacological treatments at one centre in the PACE trial. MAIN OUTCOME MEASURES: Current psychiatric diagnoses made by CFS specialist doctors, compared with current psychiatric diagnoses made independently using a structured psychiatric interview. RESULTS: Clinicians identified 59 (44%, 95% CI 39-56%) of patients as suffering from a co-morbid psychiatric disorder compared to 76 (56%, CI 53-69%) by structured interview. Depressive and anxiety disorders were most common. Clinicians were twice as likely to miss diagnoses (30 patients, 22%) than misdiagnose them (13, 10%). Psychiatrists were less likely to miss diagnoses than other clinicians, but were as likely to misdiagnose them. CONCLUSIONS: Doctors assessing patients in a chronic fatigue syndrome clinic miss psychiatric diagnoses more often than misdiagnosing them. Missed diagnoses are common. CFS clinic doctors should be trained to diagnose psychiatric disorders.
Lee AK, Miller WC, Townson AF, Anton HA; F2N2 Research Group.	Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada.	Medication use is associated with fatigue in a sample of community-living individuals who have a spinal cord injury: a chart review.	Spinal Cord. 2010 May;48(5):429-33. Epub 2009 Nov 17.	OBJECTIVES: To investigate the relationship between medications known to cause fatigue in spinal cord injury (SCI) and fatigue severity and to describe the pattern of prescription of these medications. STUDY DESIGN: Retrospective chart review. SETTING: GF Strong Rehabilitation Centre, Vancouver, British Columbia, Canada. METHODS: Medical charts of 136 individuals admitted to the GF Strong Outpatient SCI Program between December 2004 and May 2007 were reviewed. Data collected included information on medications, clinical and demographic characteristics and Fatigue Severity Scale (FSS) scores. Multiple linear regression techniques were used to analyse the data. RESULTS: Fifty-two percent of the subjects had clinically relevant fatigue. As a group, the subjects were taking 147 different medications; 41/147 medications were identified as causing fatigue. The two most commonly prescribed categories of medications were antispasticity medications (75 subjects) and analgesic medications (61 subjects). Although several variables were found to contribute to the FSS

				scores including the use of fatigue-causing medications, the presence of pain (7.6% of variance) and the use of fatigue-causing analgesics (4.2% of variance) explained the most variance in the scores. CONCLUSION: Fatigue is prevalent in outpatients with SCI. Fatigue-causing medications contribute to a higher FSS score. Clinicians treating persons with SCI should be aware that fatigue is a common and significant problem. Clinicians should be aware that fatigue may be exacerbated by the use of medication and should enquire about the effects of medication on fatigue when assessing and prescribing new medications.
Lee K, Jones KS.	Model Development Section, HIV Drug Resistance Program, Center for Cancer Research, National Cancer Institute-Frederick, Frederick, Maryland 21702, USA. joneska@mail.nih.gov	The path well traveled: using mammalian retroviruses to guide research on XMRV.	Mol Interv. 2010 Feb;10(1):20-4.	
Leone SS, Wessely S, Huibers MJ, Knottnerus JA, Kant I.	Department of Epidemiology, Maastricht University, Maastricht, The Netherlands.	Two sides of the same coin? On the history and phenomenology of chronic fatigue and burnout.	Psychol Health. 2010 Apr 29:1-16. [Epub ahead of print]	Background: Burnout and chronic fatigue syndrome (CFS) are two fatigue syndromes which have developed largely independently from each other, yet whose similarities in symptoms can be a source of confusion. We aim to explore the phenomenology of burnout and CFS in a historical context as this may provide some insight into the links and relationship between these conditions. Method: A narrative review based on literature in the fields of history, social science and medicine. Results: The origins of CFS lie within medicine, whereas burnout developed in a psychological setting. As well as symptoms, burnout and CFS also share similar themes such as an overload process triggering illness onset, the need for restoration of depleted energy, external causal attributions and the characteristics of people suffering from these illnesses. However, these themes are expressed in either psychological or medical terms according to the historical background. Conclusion: Despite their similarities, there have been few direct comparisons of the two concepts. Culture, illness perceptions and accountability are important issues in both conditions and could contribute to their differences. Comparing burnout and CFS within one sample frame, thus looking beyond the psychology/medicine divide, could be a useful first step towards understanding their relationship.
Leone SS.		A disabling combination: fatigue and depression.	Br J Psychiatry. 2010 Aug;197:86-7. Comment on: Br J Psychiatry. 2010 Aug;197:106-13.	Fatigue and common psychiatric symptoms - depression in particular - have consistently been found to be strongly associated. All have a negative impact on functional status, but evidence suggests that functional impairment is especially marked when they co-occur. Therefore, it is pertinent to understand the relationship between fatigue and depression.

Limonard GJ, Peters JB, Nabuurs-Franssen MH, Weers-Pothoff G, Besselink R, Groot CA, Dekhuijzen PN, Vercoulen JH.	Department of Pulmonary Diseases, Canisius-Wilhelmina Hospital, Weg door Jonkerbos 100, 6525 SZ Nijmegen, The Netherlands. gjmlimonard@gmail.com	Detailed analysis of health status of Q fever patients 1 year after the first Dutch outbreak: a case-control study.	QJM. 2010 Dec;103(12):953-8. Epub 2010 Aug 27.	BACKGROUND: Q fever is a zoonosis caused by the obligate intracellular bacterium Coxiella burnetii. The two long-term complications, after primary infection, are chronic Q fever in ~1% of patients, and a chronic fatigue syndrome in 10-20%. However, the existence of a protracted decreased health status after Q fever remains controversial. AIM: To determine the health status of the patients of the Q fever outbreak in The Netherlands in 2007, 1 year after primary infection. DESIGN: Cross-sectional case-control study. METHODS: Health status of the patients from the 2007 Dutch Q fever outbreak was compared to age-, sex- and geographically matched and Q fever seronegative controls. Health status of both patients and controls was assessed with the Nijmegen Clinical Screening Instrument (NCSI). RESULTS: Fifty-four Q fever patients provided 34 years of age- and sex-matched controls from the same neighbourhood. Eleven controls had positive Q fever serology and were excluded. Q fever patients had significantly more problems on the subdomains of symptoms and functional impairment. Overall quality of life was decreased in both patients and controls, 59% vs. 39%, respectively, ns). Severe fatigue levels were present in 52% of patients vs. 26% in controls ($P < 0.05$). CONCLUSION: These data support a sustained decrease in many aspects of health status in Q fever patients in The Netherlands, 1 year after primary infection.
Lloyd A, White P, Wessely S, Sharpe M, Buchwald D.	Centre for Infection and Inflammation Research, University of New South Wales, Sydney, Australia 2052. a.lloyd@unsw.edu.au	Comment on "Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome".	Science. 2010 May 14;328(5980):825; author reply 825. Comment on: Science. 2009 Oct 23;326(5952):585-9.	Lombardi et al. (Reports, 23 October 2009, p. 585) reported a significant association between the human retrovirus XMRV and chronic fatigue syndrome (CFS). However, the cases with CFS and the control subjects in their study are poorly described and unlikely to be representative. Independent replication is a critical first step before accepting the validity of this finding.
Lo SC, Pripuzova N, Li B, Komaroff AL, Hung GC, Wang R, Alter HJ.	Center for Biologics Evaluation and Research, Bethesda, MD 20892, USA. shyhching.lo@FDA.hhs.gov	Detection of MLV-related virus gene sequences in blood of patients with chronic fatigue syndrome and healthy blood donors.	Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15874-9. Epub 2010 Aug 23. Erratum in: Proc Natl Acad Sci U S A. 2010 Nov 2;107(44):19132. Comment in: Proc Natl Acad Sci U S A. 2010 Oct 26;107(43):E161; author reply E163-4. Proc Natl Acad Sci U S A. 2010 Sep	Chronic fatigue syndrome (CFS) is a serious systemic illness of unknown cause. A recent study identified DNA from a xenotropic murine leukemia virus-related virus (XMRV) in peripheral blood mononuclear cells (PBMCs) from 68 of 101 patients (67%) by nested PCR, as compared with 8 of 218 (3.7%) healthy controls. However, four subsequent reports failed to detect any murine leukemia virus (MLV)-related virus gene sequences in blood of CFS patients. We examined 41 PBMC-derived DNA samples from 37 patients meeting accepted diagnostic criteria for CFS and found MLV-like virus gag gene sequences in 32 of 37 (86.5%) compared with only 3 of 44 (6.8%) healthy volunteer blood donors. No evidence of mouse DNA contamination was detected in the PCR assay system or the clinical samples. Seven of 8 gag-positive patients tested again positive in a sample obtained nearly 15 y later. In contrast to the reported findings of near-genetic identity of all XMRVs, we identified a genetically diverse group of MLV-related viruses. The gag and env sequences from CFS patients were more closely related to those of polytropic mouse endogenous retroviruses than to those of XMRVs and were even less closely related to those of ecotropic MLVs. Further studies are needed to determine whether the same strong association with MLV-related viruses is found in other groups of patients with CFS, whether these viruses play a causative role in the development of CFS, and whether

			7;107(36):15666-7. Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15661. Proc Natl Acad Sci U S A. 2010 Oct 26;107(43):E162; author reply E163-4.	they represent a threat to the blood supply.
Maes M, Mihaylova I, Kubera M, Uytterhoeven M, Vrydags N, Bosmans E.	Maes Clinics, Belgium. crc.mh@telenet.be	Increased plasma peroxides and serum oxidized low density lipoprotein antibodies in major depression: markers that further explain the higher incidence of neurodegeneration and coronary artery disease.	J Affect Disord. 2010 Sep;125(1-3):287-94. Epub 2010 Jan 18.	BACKGROUND: Major depression is characterized by a decreased antioxidant status, an induction of the inflammatory and oxidative and nitrosative (IO&NS) pathways and inflammatory-neurodegenerative (I&ND) pathways. This study examines two markers of oxidative stress in depression, i.e. plasma peroxides and serum oxidized LDL (oxLDL) antibodies. METHODS: Blood was sampled in 54 patients with major depression (mean+/-SD age=43.5+/-11.6 years) and 37 normal volunteers (43.6+/-11.1 years). The severity of illness was measured by means of the Hamilton Depression Rating Scale. The Fibromyalgia and Chronic Fatigue Syndrome Rating Scale was used to measure severity of "psychosomatic" symptoms in depression. RESULTS: We found significantly higher plasma peroxides (p=0.002) and serum oxLDL antibodies (p=0.0002) in depressed patients as compared to normal controls. There was no significant correlation between both markers and both independently from each other predicted major depression. There were significant correlations between the oxLDL antibodies and the scores on two items of the FF scale, i.e. gastro-intestinal symptoms and headache. DISCUSSION: The results show that major depression is accompanied by increased oxidative stress and lipid peroxidation. These results further extend the IO&NS pathophysiology of major depression. Since increased peroxides and oxLDL antibodies are predictors of coronary artery disease (CAD) and neurodegeneration, our findings suggest that IO&NS pathways are involved in the increased incidence of both CAD and neurodegeneration in depression.
Maes M, Twisk FN.	Maes Clinics @ TRIA, Piyavate Hospital, Bangkok, Thailand. crc.mh@telenet.be	Chronic fatigue syndrome: Harvey and Wessely's (bio)psychosocial model versus a bio(psychosocial) model based on inflammatory and oxidative and nitrosative stress pathways.	BMC Med. 2010 Jun 15;8:35.	BACKGROUND: In a recently published paper, Harvey and Wessely put forward a 'biopsychosocial' explanatory model for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), which is proposed to be applicable to (chronic) fatigue even when apparent medical causes are present. METHODS: Here, we review the model proposed by Harvey and Wessely, which is the rationale for behaviourally oriented interventions, such as cognitive behaviour therapy (CBT) and graded exercise therapy (GET), and compare this model with a biological model, in which inflammatory, immune, oxidative and nitrosative (IO&NS) pathways are key elements. DISCUSSION: Although human and animal studies have established that the pathophysiology of ME/CFS includes IO&NS pathways, these abnormalities are not included in the model proposed by Harvey and Wessely. Activation of IO&NS pathways is known to induce fatigue and somatic (F&S) symptoms and can be induced or maintained by viral and bacterial infections, physical and psychosocial stressors, or organic disorders such as (auto)immune disorders. Studies have shown that ME/CFS and major depression are both clinical manifestations of shared IO&NS pathways, and that both disorders can be discriminated by specific symptoms and unshared or differentiating pathways. Interventions with CBT/GET are potentially

				harmful for many patients with ME/CFS, since the underlying pathophysiological abnormalities may be intensified by physical stressors. CONCLUSIONS: In contrast to Harvey and Wessely's (bio)psychosocial model for ME/CFS a bio(psychosocial) model based upon IO&NS abnormalities is likely more appropriate to this complex disorder. In clinical practice, we suggest physicians should also explore the IO&NS pathophysiology by applying laboratory tests that examine the pathways involved.
Maes M, Twisk FN.		Treatment of myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS), a multisystem disease, should target the pathophysiological aberrations (inflammatory and oxidative and nitrosative stress pathways), not the psychosocial "barriers" for a new equilibrium.	Patient Educ Couns. 2010 Jul;80(1):148-9; author reply 147. Epub 2010 Mar 29. Comment on: Patient Educ Couns. 2009 Nov;77(2):153-4.	
Maes M.		An intriguing and hitherto unexplained co-occurrence: Depression and chronic fatigue syndrome are manifestations of shared inflammatory, oxidative and nitrosative (IO&NS) pathways.	Prog Neuropsychopharmacol Biol Psychiatry. 2010 Jul 4. [Epub ahead of print]	There is a significant 'comorbidity' between depression and myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Depressive symptoms frequently occur during the course of ME/CFS. Fatigue and somatic symptoms (F&S), like pain, muscle tension, and a flu-like malaise, are key components of depression. At the same time, depression and ME/CFS show major clinical differences, which allow to discriminate them with a 100% accuracy. This paper aims to review the shared pathways that underpin both disorders and the pathways that discriminate them. Numerous studies have shown that depression and ME/CFS are characterized by shared aberrations in inflammatory, oxidative and nitrosative (IO&NS) pathways, like systemic inflammation and its long-term sequels, including O&NS-induced damage to fatty acids, proteins and DNA; dysfunctional mitochondria; lowered antioxidant levels, like zinc and coenzyme Q10; autoimmune responses to neoepitopes formed by O&NS; lowered omega-3 polyunsaturated fatty acid levels; and increased translocation of gram-negative bacteria. Some IO&NS-related pathways, like the induction of indoleamine 2-3-dioxygenase, neurodegeneration and decreased neurogenesis, are more specific to depression, whereas other pathways, like the 2'-5' oligoadenylate synthetase/RNase L pathway, are specific to ME/CFS. Most current animal models of depression, e.g. those induced by cytokines, are not reminiscent of human depression but reflect a mixture of depressive and F&S symptoms. The latter symptoms, sometimes called sickness behavior, differ from depression and ME/CFS because the former is a (sub)acute

				response to infection-induced pro-inflammatory cytokines that aims to enhance recovery, whereas the latter are characterized by long-term sequels in multiple IO&NS pathways. Depression and ME/CFS are not 'comorbid' disorders, but should be regarded as 'co-associated disorders' that are clinical manifestations of shared pathways.
Maloney EM, Boneva RS, Lin JM, Reeves WC.	Centers for Disease Control and Prevention, Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne and Enteric Diseases, MS-A15, 1600 Clifton Rd, Atlanta, GA 30333, USA. evm3@cdc.gov	Chronic fatigue syndrome is associated with metabolic syndrome: results from a case-control study in Georgia.	Metabolism. 2010 Sep;59(9):1351-7. Epub 2010 Jan 27.	We hypothesized that persons with chronic fatigue syndrome (CFS) would have a higher prevalence of metabolic syndrome compared with well controls, and that unwell persons with insufficient symptoms or fatigue for CFS (termed ISF) would have a prevalence of metabolic syndrome intermediate between those with CFS and the controls. We also sought to examine the relationship between metabolic syndrome and measures of functional impairment, fatigue, and other symptoms. Our analysis was based on a population-based case-control study conducted in metropolitan, urban, and rural areas of Georgia, United States, between September 2004 and July 2005. There were 111 persons with CFS, 259 with ISF, and 123 controls. Metabolic syndrome was determined based on having at least 3 of 5 standard risk components (abdominal obesity, high triglycerides, high blood pressure, elevated fasting glucose, and decreased high-density lipids) according to the National Cholesterol Education Program Adult Treatment Panel III definition. Persons with CFS were 2-fold as likely to have metabolic syndrome (odds ratio = 2.12, confidence interval = 1.06, 4.23) compared with the controls. There was a significant graded relationship between the number of metabolic syndrome factors and CFS; each additional factor was associated with a 37% increase in likelihood of having CFS. The association of ISF with metabolic syndrome was weaker (odds ratio = 1.72, confidence interval = 0.94-3.16). Among persons with CFS, the number of metabolic syndrome factors was significantly correlated with worse fatigue on a standardized summary measure of fatigue (r = 0.20, P = .04). In conclusion, CFS was associated with metabolic syndrome, which further exacerbated fatigue.
Maquet D, Croisier JL, Dupont C, Moutschen M, Ansseau M, Zeevaert B, Crielaard JM.	Department of Motricity Sciences, University of Liege, University Hospital Centre of Liege, ISEPK, B21, 4, allée des Sports, 4000 Liege, Belgium. d.maquet@ulg.ac.be	Fibromyalgia and related conditions: electromyogram profile during isometric muscle contraction.	Joint Bone Spine. 2010 May;77(3):264-7. Epub 2010 Apr 22.	OBJECTIVES: To evaluate electromyogram (EMG) profiles in patients with three related conditions: fibromyalgia, chronic fatigue syndrome, and depression. METHODS: We studied 44 healthy volunteers, 22 patients with fibromyalgia, 11 patients with chronic fatigue syndrome, and 10 patients admitted for depression. The trapezius electromyogram was recorded during maximally sustained, bilateral, 90 degrees abduction of the shoulders. EMG signal frequency and amplitude were measured throughout the test. RESULTS: In the fibromyalgia group, isometric contraction duration was significantly shorter than in the other two patient groups (P<0.001) and the EMG frequency and amplitude pattern indicated premature discontinuation of the muscle contraction. Findings in the chronic fatigue patients were similar to those in the healthy controls. The patients with depression had a distinctive EMG profile characterized by excessive initial motor-unit recruitment with a shift in the frequency spectrum. CONCLUSIONS: Fibromyalgia was associated with a specific EMG pattern indicating premature discontinuation of the muscle contraction. Therefore, maximal voluntary muscle contraction tests may be of limited value for assessing function in fibromyalgia patients. Chronic fatigue syndrome patients had similar EMG findings to those in the healthy controls. The EMG alterations in the patients with depression were consistent with manifestations of psychomotor retardation.
Marshall R, Paul L, Wood L.	Physiotherapist, Research Assistant,	The search for pain relief in people	Physiother Theory Pract. 2010 Nov 1.	The purpose of this study was to investigate the use and perceived benefit of complimentary and alternative medicine (CAM) and physiotherapy treatments tried by people with chronic fatigue

	Nursing & Health Care, Faculty of Medicine, University of Glasgow, Glasgow, Scotland, United Kingdom.	with chronic fatigue syndrome: A descriptive study.	[Epub ahead of print]	syndrome (CFS) to ease painful symptoms. This study used a descriptive, cross-sectional design. People with CFS who experienced pain were recruited to this study. Participants were asked during a semistructured interview about the treatments they had tried to relieve their pain. Each interview was conducted in the home of the participant. Fifty participants were recruited, of which, 10 participants were severely disabled by CFS. Eighteen participants were trying different forms of CAM treatment for pain relief at the time of assessment. Three participants were currently receiving physiotherapy. Throughout the duration of their illness 45 participants reported trying 19 different CAM treatments in the search for pain relief. Acupuncture was reported to provide the most pain relief (n=16). Twenty-seven participants reported a total of 16 different interventions prescribed by their physiotherapist. The results of this study suggest some physiotherapy and CAM treatments may help people manage painful CFS symptoms. Future research should be directed to evaluating the effectiveness of interventions such as acupuncture or gentle soft tissue therapies to reduce pain in people with CFS.
Martin M, Alexeeva I.	Department of Experimental Psychology, University of Oxford, UK.	Mood volatility with rumination but neither attentional nor interpretation biases in chronic fatigue syndrome.	Br J Health Psychol. 2010 Nov;15(Pt 4):779-96. Epub 2010 Jan 22.	OBJECTIVES: This study tested whether (1) chronic fatigue syndrome (CFS) individuals have a bias in the initial orientation of attention to illness-related information, which is enhanced by rumination. (2) CFS individuals have an illness interpretation bias (IB) in their early automatic processing of ambiguous information. (3) CFS individuals experience a greater degree of mood fluctuation following rumination and distraction inductions. DESIGN: Thirty-three CFS participants who had received a medical practitioner's diagnosis of CFS were compared to 33 healthy matched controls on an exogenous cueing task and a lexical decision task. METHOD: All participants underwent either a rumination or distraction induction. They then completed an exogenous cueing task to assess bias to illness and social threat compared with neutral stimuli, as well as a lexical decision task to assess their interpretation of ambiguous words having illness, social threat, or neutral interpretations. RESULTS: Reaction time data revealed that CFS individuals did not have an attentional bias (AB) in the initial orientation of attention to illness-related material. Nor was there an IB towards illness in CFS individual's automatic response to ambiguous information. However, as hypothesized, CFS individuals showed a greater degree of mood fluctuation following the rumination/distraction induction. CONCLUSION: Rumination and distraction lead to greater mood volatility in CFS individuals than in controls, but not to attentional nor interpretation biases in the early automatic stages of information processing in CFS individuals.
Martin WJ.	A	Possible widespread low-level occurrence of murine leukemia virus-related gene sequences in humans.	Proc Natl Acad Sci U S A. 2010 Oct 26;107(43):E162; author reply E163-4. Epub 2010 Sep 30. Comment on: Proc Natl Acad Sci U S A. 2010 Sep 7;107(36):15874-9.	a
Masruha MR, Lin J, de Souza Vieira	Department of Neurology and	Urinary 6-sulphatoxymelaton	Headache. 2010 Mar;50(3):413-9.	OBJECTIVE: To assess urinary 6-sulphatoxymelatonin levels in a large consecutive series of patients with migraine and several comorbidities (chronic fatigue, fibromyalgia, insomnia, anxiety, and

DS, Minett TS, Cipolla-Neto J, Zukerman E, Vilanova LC, Peres MF.	Neurosurgery - Federal University of São Paulo, São Paulo - Brazil.	in levels are depressed in chronic migraine and several comorbidities.	Epub 2009 Oct 8.	depression) as compared with controls. BACKGROUND: Urine analysis is widely used as a measure of melatonin secretion, as it is correlated with the nocturnal profile of plasma melatonin secretion. Melatonin has critical functions in human physiology and substantial evidence points to its importance in the regulation of circadian rhythms, sleep, and headache disorders. METHODS: Urine samples were collected into a single plastic container over a 12-hour period from 8:00 pm to 8:00 am of the next day, and 6-sulphatoxymelatonin was measured by quantitative ELISA. All of the patients were given a detailed questionnaire about headaches and additionally answered the following questionnaires: Chalder fatigue questionnaire, Epworth somnolence questionnaire, State-Trait Anxiety Inventory, and the Beck Depression Inventory. RESULTS: A total of 220 subjects were evaluated - 73 (33%) had episodic migraine, 73 (33%) had chronic migraine, and 74 (34%) were enrolled as control subjects. There was a strong correlation between the concentration of 6-sulphatoxymelatonin detected and chronic migraine. Regarding the comorbidities, this study objectively demonstrates an inverse relationship between 6-sulphatoxymelatonin levels and depression, anxiety, and fatigue. CONCLUSIONS: To our knowledge, this is the first study to evaluate the relationship between the urinary concentration of melatonin and migraine comorbidities. These results support hypothalamic involvement in migraine pathophysiology.
Matalliotakis IM, Cakmak H, Ziogos MD, Kalogeraki A, Kappou D, Arici A.	Department of Obstetrics and Gynecology, University of Crete, Heraklion, Crete, Greece. matakgr@yahoo.com	Endometriosis-associated Lyme disease.	J Obstet Gynaecol. 2010 Feb;30(2):184-6.	The aim of this study is to report three cases of patients with endometriosis and infertility, and associated with Lyme disease. The medical files of 405 women with endometriosis and 200 without endometriosis were studied retrospectively. We report 3 cases with endometriosis and Lyme disease. Of 405 patients with endometriosis treated in our study over a 6-year period, 3(0.8%) had Lyme disease. All cases presented with typical erythema migraines, fever and fatigue. The serological findings were positive for Borrelia burgdorferi, for 3 cases. Two out of 3 women underwent IVF-ET procedures and one of them conceived in the first cycle without complication during pregnancy or after childbirth recorded. We concluded that women with endometriosis are more likely to have chronic fatigue syndrome, systemic lupus erythematous, Sjögren's syndrome, rheumatoid arthritis, multiple sclerosis, and other autoimmune inflammatory and endocrine diseases. A review of the literature confirms the uniqueness of the co-existence of Lyme disease in women with endometriosis in these cases.
May M, Emond A, Crawley E.	Centre for Child and Adolescent Health, Hampton House, Cotham Hill, Bristol BS6 6JS, UK.	Phenotypes of chronic fatigue syndrome in children and young people.	Arch Dis Child. 2010 Apr;95(4):245-9. Epub 2009 Oct 19.	OBJECTIVE: To investigate the heterogeneity of chronic fatigue syndrome (CFS/ME) in children and young people. SETTING: Regional specialist CFS/ME service Patients Children and young people aged <19 years old. METHODS: Exploratory factor analysis was performed on symptoms present at assessment in 333 children and young people with CFS/ME. Linear and logistic regression analysis of data from self-completed assessment forms was used to explore the associations between the retained factors and sex, age, length of illness, depression, anxiety and markers of severity (fatigue, physical function, pain and school attendance). RESULTS: Three phenotypes were identified using factor analysis: muscoloskeletal (factor 1) had loadings on muscle and joint pain and hypersensitivity to touch, and was associated with worse fatigue (regression coefficient 0.47, 95% CI 0.25 to 0.68, p<0.001), physical function (regression coefficient -0.52, 95% CI -0.83 to -0.22, p=0.001) and pain. Factor 2 (migraine) loaded on noise and light hypersensitivity, headaches, nausea, abdominal pain and dizziness and was most strongly associated with physical function and pain. Sore throat phenotype

				(factor 3) had loadings on sore throat and tender lymph nodes and was not associated with fatigue or pain. There was no evidence that phenotypes were associated with age, length of illness or symptoms of depression (regression coefficient for association of depression with musculoskeletal pain -0.02, 95% CI -0.27 to 0.23, p=0.87). The migraine phenotype was associated with anxiety (0.40, 95% CI 0.06 to 0.74, p=0.02). IMPLICATIONS: CFS/ME is heterogeneous in children with three phenotypes at presentation that are differentially associated with severity and are unlikely to be due to age or length of illness.
Mayor S.		Study fails to show link previously found between virus and chronic fatigue syndrome.	BMJ. 2010 Feb 19;340:c1033. doi: 10.1136/bmj.c1033.	
McClure M, Kaye S.		Can detection of xenotropic murine leukemia virus-related virus be linked to chronic fatigue syndrome?	Expert Rev Mol Diagn. 2010 Jul;10(5):537-9.	
McClure M, Wessely S.		Chronic fatigue syndrome and human retrovirus XMRV.	BMJ. 2010 Feb 25;340:c1099. doi: 10.1136/bmj.c1099. Erratum in: BMJ. 2010;340. doi: 10.1136/bmj.c1284. Comment on: BMJ. 2010;340:c1018.	
McEwen BS, Kalia M.	Laboratory of Neuroendocrinology, The Rockefeller University, New York, NY 10065, USA. mcewen@rockefeller.edu	The role of corticosteroids and stress in chronic pain conditions.	Metabolism. 2010 Oct;59 Suppl 1:S9-15.	The relationship between corticosteroids (endogenous and exogenous) and stress is well known, as is the use of steroids as concomitant treatment in pain management during acute inflammation. In the past, steroids have not been considered the first line of treatment in pain management. In this review, we examine new scientific and clinical evidence that demonstrates the direct role that steroids play in the generation and clinical management of chronic pain. We will discuss the new findings demonstrating the fact that steroids and related mediators produce paradoxical effects on pain such as analgesia, hyperalgesia, and even placebo analgesia. In addition, we will examine the physiologic effect of stress, high allostatic load, and idiopathic disease states such as chronic fatigue syndrome, fibromyalgia, irritable bowel syndrome, and burnout. The recently observed positive relationship between glutaminergic activity in the insula and clinical pain will be examined in the context of understanding the central role of steroids in chronic pain. The complex role of the hypothalamic-pituitary-adrenal axis in pain will be discussed as well as other heterogeneous forms of chronic pain that involve many components of the central nervous system. Components of the hypothalamic-

				pituitary-adrenal axis have paradoxical effects on certain types of pain that are dependent on dose and on site (whether peripheral or central) and mode of application. Recent studies on glia have shown that they prolong a state of neuronal hypersensitization in the dorsal root ganglia by releasing growth factors and other substances that act on the immune system. We will discuss the implication of these new findings directly linking pain to steroids, stress, and key higher brain regions in the context of future therapeutic targets.
Meeus M, Nijs J, Huybrechts S, Truijen S.	Department of Health Sciences, Division of Musculoskeletal Physiotherapy, Artesis Hogeschool Antwerpen (AHA), Merksem, Belgium.	Evidence for generalized hyperalgesia in chronic fatigue syndrome: a case control study.	Clin Rheumatol. 2010 Apr;29(4):393-8.	Several studies provided evidence for generalized hyperalgesia in fibromyalgia or whiplash-associated disorders. In chronic fatigue syndrome, however, pain is a frequently reported complaint, but up to now, evidence for generalized hyperalgesia is lacking. The aim of this study is to examine whether the pressure pain thresholds (PPTs) at both symptomatic and asymptomatic sites differ in chronic fatigue syndrome (CFS) patients with chronic pain, compared to healthy controls. Therefore, 30 CFS patients with chronic pain and 30 age- and gender-matched healthy controls indicated on a Margolis Pain Diagram where they felt pain lasting longer than 24 h in the past 4 weeks. After completing a test battery of questionnaires evaluating pain cognitions, functional status and symptomatology, a blinded researcher assessed PPTs bilaterally at seven nonspecific sites on both trunk and extremities. PPTs were compared for the two complete groups. In addition, PPTs of patients and controls who did not report pain in a respective zone were compared. PPTs of the patients were significantly lower ($p<0.001$) compared to those of the control group, also when pain-free samples per zone were compared ($p<0.001$). The mean PPT was 3.30 kg/cm2 in all CFS patients and 8.09 kg/cm2 in the controls. No confounding factors responsible for the observed differences, as, e.g., catastrophizing and depression, could be revealed. These findings provide evidence for the existence of hyperalgesia even in asymptomatic areas (generalized secondary hyperalgesia). The generalized hyperalgesia may represent the involvement of a sensitized central nervous system.
Meeus M, Nijs J, Van Oosterwijck J, Van Alsenoy V, Truijen S.	Department of Health Sciences, Artesis University College, Antwerp, Belgium.	Pain physiology education improves pain beliefs in patients with chronic fatigue syndrome compared with pacing and self-management education: a double-blind randomized controlled trial.	Arch Phys Med Rehabil. 2010 Aug;91(8):1153-9.	OBJECTIVE: To examine whether pain physiology education was capable of changing pain cognitions and pain thresholds in patients with chronic fatigue syndrome (CFS) and chronic widespread pain. DESIGN: Double-blind randomized controlled trial. SETTING: Specialized chronic fatigue clinic in university hospital. PARTICIPANTS: A random sample of patients (N=48) with CFS patients (8 men, 40 women) experiencing chronic pain, randomly allocated to the control group (n=24) or experimental group (n=24). Two women in the experimental group did not complete the study because of practical issues (lack of time and restricted mobility). INTERVENTIONS: One individual pain physiology education session (experimental) or 1 pacing and self-management education session (control). MAIN OUTCOME MEASURES: Algometry, the Neurophysiology of Pain Test, and questionnaires evaluating pain cognitions-the Pain Coping Inventory, the Pain Catastrophizing Scale, and the Tampa Scale for Kinesiophobia-version CFS-were completed immediately before and immediately after the intervention. RESULTS: After the intervention, the experimental group demonstrated a significantly better understanding of the neurophysiology of pain ($P<.001$) and a reduction of the Pain Catastrophizing Scale subscale "ruminating" ($P=.009$) compared with controls. For these variables, moderate to large Cohen d effect sizes were revealed (.79-2.53). CONCLUSIONS: A 30-minute educational session on pain physiology imparts a better understanding of pain and brings about less rumination in the short term. Pain physiology education can be an important therapeutic modality in

				the approach of patients with CFS and chronic pain, given the clinical relevance of inappropriate pain cognitions.
Meeus M, Roussel NA, Truijen S, Nijs J.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, Artesis University College Antwerp, Merksem, Belgium.	Reduced pressure pain thresholds in response to exercise in chronic fatigue syndrome but not in chronic low back pain: an experimental study.	J Rehabil Med. 2010 Oct;42(9):884-90.	OBJECTIVE: The aims of this study were to examine: (i) baseline pressure pain thresholds in patients with chronic fatigue syndrome and those with chronic low back pain compared with healthy subjects; (ii) the change in mean pain threshold in response to exercise; and (iii) associations with exercise-induced increase in nitric oxide. PARTICIPANTS: Twenty-six patients with chronic fatigue syndrome suffering of chronic pain, 21 patients with chronic low back pain and 31 healthy subjects. METHODS: Participants underwent a submaximal aerobic exercise protocol on a bicycle ergometer, preceded and followed by venous blood sampling (nitric oxide) and algometry (hand, arm, calf, low back). RESULTS: Patients with chronic fatigue syndrome presented overall lower pain thresholds compared with healthy subjects and patients with chronic low back pain ($p < 0.05$). No significant differences were found between healthy subjects and patients with chronic low back pain. After submaximal aerobic exercise, mean pain thresholds decreased in patients with chronic fatigue syndrome, and increased in the others ($p < 0.01$). At baseline, nitric oxide levels were significantly higher in the chronic low back pain group. After controlling for body mass index, no significant differences were seen between the groups at baseline or in response to exercise. Nitric oxide was not related to pain thresholds in either group. CONCLUSION: The results suggest hyperalgesia and abnormal central pain processing during submaximal aerobic exercise in chronic fatigue syndrome, but not in chronic low back pain. Nitric oxide appeared to be unrelated to pain processing.
Meeus M, VAN Eupen I, Hondequin J, DE Hauwere L, Kos D, Nijs J.	Division of Musculoskeletal Physiotherapy, Artesis University College (AHA), Department of Health Sciences, Van Aertselaerstraat 31, 2170 Merksem, Belgium.	Nitric oxide concentrations are normal and unrelated to activity level in chronic fatigue syndrome: a case-control study.	In Vivo. 2010 Nov-Dec;24(6):865-9.	AIM: since patients with chronic fatigue syndrome (CFS) often present elevated levels of nitric oxide (NO) and low levels of physical activity, this study aimed at revealing possible correlations between NO concentration and physical activity. PATIENTS AND METHODS: thirty CFS patients and 29 age- and gender-matched sedentary controls wore an accelerometer for one week and underwent venous blood sampling at the beginning and the end of the week. RESULTS: CFS patients were significantly less active ($p=0.001$), but no significant differences in the amounts of NO ($p=0.464$ and 0.569) or interaction between NO levels and activity levels in either the CFS patients or controls were revealed. CONCLUSION: these results provide further evidence for reduced activity levels in CFS patients, but refute there being any interaction between the amount of blood NO and activity level in both groups. The blood NO was neither predictive of, nor dependent on the activity level in CFS.
Meeus M, Van Eupen I, Willems J, Kos D, Nijs J.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, Artesis University College Antwerp (AHA), Antwerp, Belgium.	Is the International Physical Activity Questionnaire-short form (IPAQ-SF) valid for assessing physical activity in Chronic Fatigue Syndrome?	Disabil Rehabil. 2011;33(1):9-16. Epub 2010 May 6.	PURPOSE: To evaluate the criterion validity and internal consistency of the International Physical Activity Questionnaire-short form (IPAQ-sf) in Chronic Fatigue Syndrome (CFS) patients. METHOD: Fifty-six CFS patients completed the IPAQ-sf after they wore a tri-axial accelerometer and filled out activity diaries during 1 week. Spearman rank correlation coefficients and Cronbach's Alpha were calculated. RESULTS: The IPAQ-sf correlated significantly with the energy expenditure and Metabolic Equivalents (METs) minutes spent moderately to vigorously active following the activity diary and accelerometer. These correlation coefficients were however low (r varying between 0.282 and 0.426) and rather irrelevant, since CFS patients hardly reach moderate or vigorous activity levels. Internal consistency between the three subitems used for the total score of the IPAQ-sf was 0.337. CONCLUSION: The observed associations between the IPAQ-sf data and the data obtained from the

				accelerometer (gold standard) and the diaries were too low to be in support of the use of the IPAQ-sf in patients with CFS. The IPAQ-sf does not seem an appropriate tool to assess physical activity in CFS patients. Further study is required to seek for a valid, practical and affordable tool.
Menéndez-Arias L.	Centro de Biología Molecular "Severo Ochoa" (Consejo Superior de Investigaciones Científicas and Universidad Autónoma de Madrid), Madrid, Spain.	Evidence and controversies on the role of XMRV in prostate cancer and chronic fatigue syndrome.	Rev Med Virol. 2010 Nov 26. [Epub ahead of print]	The recent discovery of xenotropic murine leukaemia virus-related virus (XMRV) in prostate cancer tissues and in the blood of individuals suffering from chronic fatigue syndrome has attracted considerable interest. However, the relevance and significance of XMRV to human disease remain unclear, since the association has not been confirmed in other studies. XMRV is the first gammaretrovirus to be found in humans. XMRV and murine leukaemia viruses share similar structures and genomic organisation. Human restriction factors such as APOBEC3 or tetherin inhibit XMRV replication. Although XMRV induces low rates of transformation in cell culture, it might be able to induce cancer by low-frequency insertional activation of oncogenes or through the generation of highly active transforming viruses. A preference for regulatory regions of transcriptional active genes has been observed after a genomic-wide analysis of XMRV integration sites. Genes related to carcinogenesis and androgen signalling have been identified in the vicinity of integration sites. The XMRV genome contains a glucocorticoid responsive element, and androgens could modulate viral replication in the prostate. Evidence supporting the involvement of XMRV in chronic fatigue syndrome is still very weak, and needs further confirmation and validation. Currently approved anti-retroviral drugs such as zidovudine, tenofovir and raltegravir are efficient inhibitors of XMRV replication in vitro. These drugs might be useful to treat XMRV infection in humans. The identification of XMRV has potentially serious health implications for the implementation of novel techniques including gene therapy or xenotransplantation, while raising concerns on the need for screening donated blood to prevent transmission through transfusion. Copyright © 2010 John Wiley & Sons, Ltd.
Merkes M.	Australian Institute for Primary Care, La Trobe University, Bundoora, Vic. 3086, Australia. m.merkes@latrobe.edu.au	Mindfulness-based stress reduction for people with chronic diseases.	Aust J Prim Health. 2010;16(3):200-10.	Mindfulness-based stress reduction (MBSR) is a structured group program that uses mindfulness meditation to improve well-being and alleviate suffering. This article reviews the impact of MBSR for people with chronic diseases. The review includes original research that was published in English and peer-reviewed and reported outcomes for adults with chronic diseases who had participated in an MBSR program. Fifteen studies were identified. Outcomes related to mental and physical health, well-being, and quality of life. The studies included different research designs, and used self-report and physiological outcome measures. Participants' clinical diagnoses included fibromyalgia, chronic pain, rheumatoid arthritis, type 2 diabetes, chronic fatigue syndrome, multiple chemical sensitivity, and cardiovascular diagnoses. All 15 studies found that participation in an MBSR program resulted in improvements. No negative change was reported between baseline and follow up. Outcomes in regard to specific variables were difficult to compare and equivocal. Overall, positive change predominated. Chronic diseases are associated with a range of unwelcome psychological and physical consequences. Participation in an MBSR program is likely to result in coping better with symptoms, improved overall well-being and quality of life, and enhanced health outcomes. As an adjunct to standard care, MBSR has potential for much wider application in Australian primary care settings.
Mikovits JA, Huang Y, Pfost MA, Lombardi VC,	Whittemore-Peterson Institute for Neuroimmune	Distribution of xenotropic murine leukemia virus-	AIDS Rev. 2010 Jul-Sep;12(3):149-52.	In 2006, sequences described as xenotropic murine leukemia virus-related virus (XMRV) were discovered in prostate cancer patients. In October 2009, we published the first direct isolation of infectious XMRV from humans and the detection of infectious XMRV in patients with chronic fatigue

Bertolette DC, Hagen KS, Ruscetti FW.	Diseases, University of Nevada, Reno, NV 89557, USA. judym@wpinstitute.org	related virus (XMRV) infection in chronic fatigue syndrome and prostate cancer.		syndrome. In that study, a combination of classic retroviral methods were used including: DNA polymerase chain reaction and reverse transcriptase polymerase chain reaction for gag and env, full length genomic sequencing, immunoblotting for viral protein expression in activated peripheral blood mononuclear cells, passage of infectious virus in both plasma and peripheral blood mononuclear cells to indicator cell lines, and detection of antibodies to XMRV in plasma. A combination of these methods has since allowed us to confirm infection by XMRV in 85% of the 101 patients that were originally studied. Since 2009, seven studies, predominantly using DNA polymerase chain reaction of blood products or tumor tissue, have reported failures to detect XMRV infection in patients with either prostate cancer or chronic fatigue syndrome. A review of the current literature on XMRV supports the importance of applying multiple independent techniques in order to determine the presence of this virus. Detection methods based upon the biological and molecular amplification of XMRV, which is usually present at low levels in unstimulated blood cells and plasma, are more sensitive than assays for the virus by DNA polymerase chain reaction of unstimulated peripheral blood mononuclear cells. When we examined patient blood samples that had originally tested negative by DNA polymerase chain reaction by more sensitive methods, we observed that they were infected with XMRV; thus, the DNA polymerase chain reaction tests provided false negative results. Therefore, we conclude that molecular analyses using DNA from unstimulated peripheral blood mononuclear cells or from whole blood are not yet sufficient as stand-alone assays for the identification of XMRV-infected individuals. Complementary methods are reviewed, that if rigorously followed, will likely show a more accurate snapshot of the actual distribution of XMRV infection in humans.
Mikovits JA, Lombardi VC, Pfost MA, Hagen KS, Ruscetti FW.	Whittemore Peterson Institute, Reno, Nevada, USA. judym@wpinstitute.org	Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome.	Virulence. 2010 Sep-Oct;1(5):386-90.	In October 2009, we reported the first direct isolation of infectious xenotropic murine leukemia virus-related virus (XMRV). In that study, we used a combination of biological amplification and molecular enhancement techniques to detect XMRV in more than 75% of 101 patients with chronic fatigue syndrome (CFS). Since our report, controversy arose after the publication of several studies that failed to detect XMRV infection in their CFS patient populations. In this addenda, we further detail the multiple detection methods we used in order to observe XMRV infection in our CFS cohort. Our results indicate that PCR from DNA of unstimulated peripheral blood mononuclear cells is the least sensitive method for detection of XMRV in subjects' blood. We advocate the use of more than one type of assay in order to determine the frequency of XMRV infection in patient cohorts in future studies of the relevance of XMRV to human disease.
Miller E.	Oddział Rehabilitacji III Miejskiego Szpitala w Łodzi. betty.miller@interia.pl	[Cryostimulation factor supporting rehabilitation patients with multiple sclerosis and fatigue syndrome]. [Article in Polish]	Wiad Lek. 2010;63(2):41-5.	INTRODUCTION: Fatigue is considered to be one of the most prevalent and disabling symptoms among individuals with multiple sclerosis (MS). According to different studies, fatigue is reported by 75-95% of patients. Fatigue syndrome considerably affects quality of life. Characteristic feature of fatigue syndrome in multiple sclerosis is its relapse caused by warmth. There are only a few researches into fatigue in multiple sclerosis. The most commonly used scale to estimate fatigue is Fatigue Severity Scale (FSS). Cryostimulation has been applied to treat depression. AIM OF THE STUDY: Comparison of the influence of cryostimulation as a supporting factor of kinesytherapy on increasing strength of selected muscle groups of inferior extremities and degree of disability in case of patients with multiple sclerosis and fatigue syndrome and without the latter. MATERIAL AND METHODS: The examination included 60 randomized patients with diagnosed multiple sclerosis (ICD10-G35). To

				assess the results scales: EDSS, FSS and widespread Lovett scale (punctation with accuracy of measurement 0.5 point) were used. Interpretation of the FSS scale results was made according to Krupp and comp. Fatigue syndrome was diagnosed where results reached 6.5 and higher. Evaluaton of muscle strength concerning chosen muscles groups of inferior extremities: quadriceps femoris, illopsoas, biceps femoris. When the strength of leg muscles was asymmetric, lower values of Lovett scale were used. Patients were divided into 2 groups with regard to positive or negative fatigue syndrome. In the examined group (n = 24) fatigue syndrome was positive (FSS under 6.5) and control (n = 36) negative (FSS under 6.5). All patients were treated with cryostimulation and individual program of exercises adapted to their degree of disability. RESULTS: The use of cryostimulation and kinesytherapy to patients with MS and fatigue syndrome indicates statistically important (p = 0.05) decrease of disability degree in EDSS scale and improvement of muscle strength of quadriceps femoris and illiopsoas compared to MS patients without fatigue syndrome. CONCLUSIONS: Cryostimulation is a factor supporting rehabilitation patients with multiple sclerosis and fatigue syndrome.
Miwa K, Fujita M.	Department of Internal Medicine, Nanto Family and Community Medical Center, 577 Matsubara, Nanto, Toyama 939-1518, Japan. k-3wa@pm.ctt.ne.jp	Fluctuation of serum vitamin E (alpha-tocopherol) concentrations during exacerbation and remission phases in patients with chronic fatigue syndrome.	Heart Vessels. 2010 Jul;25(4):319-23. Epub 2010 Jul 31.	The etiology of chronic fatigue syndrome remains unknown. Oxidative stress may be involved in its pathogenesis. Vitamin E is a major endogenous lipid-soluble antioxidative substance, and is consumed during the lipid peroxidation process. We studied a population comprising 27 patients with chronic fatigue syndrome (10 men and 17 women, 29 +/- 6 years of age) and 27 age- and sex-matched control subjects. Serum vitamin E (alpha-tocopherol) concentrations were determined and expressed as mg/g total lipids (total cholesterol and triglyceride) to evaluate oxidative stress. Serum alpha-tocopherol concentrations (mg/g lipids) were significantly (P < 0.001) lower in the patients with chronic fatigue syndrome (2.81 +/- 0.73) than in the control subjects (3.88 +/- 0.65). The patients with chronic fatigue syndrome were re-examined during a follow-up interval. After 8 +/- 2 months, 16 patients exhibited a status that warranted re-examination during remission of the symptoms at a regular visit to our hospital (Group 1), while the remaining 11 did not (Group 2). The serum alpha-tocopherol levels were significantly elevated during remission as compared with those at baseline in Group 1 (2.71 +/- 0.62 --> 3.24 +/- 0.83, P < 0.001). The levels did not significantly change after the interval in Group 2 (2.97 +/- 0.86 --> 2.85 +/- 0.73, not significant). In conclusion, serum alpha-tocopherol concentrations were significantly lower in the patients with chronic fatigue syndrome as compared with the control subjects, suggesting increased oxidative stress in the former. The low level of serum alpha-tocopherol was ameliorated during the remission phase as compared with the exacerbation phase in the patients with chronic fatigue syndrome, suggesting that increased oxidative stress may be involved in the pathogenesis of chronic fatigue syndrome and might also be directly related to the severity of the symptoms of chronic fatigue syndrome.
Miyazawa T.	Laboratory of Signal Transduction, Department of Cell Biology, Institute for Virus Research,	Endogenous retroviruses as potential hazards for vaccines.	Biologicals. 2010 May;38(3):371-6. Epub 2010 Apr 8.	Retroviruses are classified as exogenous or endogenous according to their mode of transmission. Generally, endogenous retroviruses (ERVs) are not pathogenic in their original hosts; however, some ERVs induce diseases. In humans, a novel gammaretrovirus was discovered in patients with prostate cancer or chronic fatigue syndrome. This virus was closely related to xenotropic murine leukemia virus (X-MLV) and designated as xenotropic murine leukemia virus-related virus (XMRV). The origin and transmission route of XMRV are still unknown at present; however, XMRV may be derived from ERVs

	Kyoto University, 53 Shogoin-Kawaracho, Sakyo-ku, Kyoto 606-8507, Japan. takavet@gmail.com			of rodents because X-MLVs are ERVs of inbred and wild mice. Many live attenuated vaccines for animals are manufactured by using cell lines from animals, which are known to produce infectious ERVs; however, the risks of infection by ERVs from xenospecies through vaccination have been ignored. This brief review gives an overview of ERVs in cats, the potential risks of ERV infection by vaccination, the biological characteristics of RD-114 virus (a feline ERV), which possibly contaminates vaccines for companion animals, and the methods for detection of infectious RD-114 virus.
Mohammed RH, ElMakhzangy HI, Gamal A, Mekky F, El Kassas M, Mohammed N, Abdel Hamid M, Esmat G.	Department of Rheumatology and Rehabilitation, Faculty of Medicine, Cairo University Hospitals, Cairo, Egypt. rmhamdy@yahoo.com	Prevalence of rheumatologic manifestations of chronic hepatitis C virus infection among Egyptians.	Clin Rheumatol. 2010 Dec;29(12):1373-80. Epub 2010 Apr 22.	Chronic hepatitis C virus (HCV) viremia has been known to provoke a plethora of autoimmune syndromes referred to as extrahepatic manifestations of chronic HCV infection. Aim of the current study was to assess the prevalence of rheumatologic manifestations among Egyptians with hepatitis C infection and its' association with cryoglobulin profile. The current research represents a cross-sectional study where patients with chronic HCV infection attending the outpatient clinic of the National Hepatology and Tropical Medicine Research Institute over a period of 1 year were interviewed. Patients with decompensated liver disease, on interferon therapy, having end-stage renal disease or coexisting viral infection like hepatitis B surface antibody positive patients were all excluded from the research. Laboratory investigations as well as serological assay including cryoglobulin profile, rheumatoid factor, antinuclear antibody, HCV-PCR were performed. Three hundred and six patients having chronic HCV infection were interviewed in this research. The overall estimated prevalence of rheumatologic manifestations in the current research was 16.39%, chronic fatigue syndrome 9.5%, sicca symptoms 8.8%, arthralgia 6.5%, fibromyalgia 1.9%, myalgia 1.3%, arthritis 0.7%, cryoglobulinemic vasculitis 0.7%, autoimmune hemolytic anemia 0.7%, thrombocytopenia 0.7%. Xerophthalmia was significantly present in male population ($p = 0.04$), whereas fibromyalgia, cryoglobulinemic vasculitis, arthritis, and autoimmune hemolytic anemia were significantly present in female population under study ($p < 0.05$). In chronic HCV genotype 4 infection, the prevalence of rheumatologic manifestations was 16.3% with chronic fatigue syndrome and sicca symptoms being the most common with no significant correlation to the degree of elevation of liver disease or viral load.
Mokina TV, Antipenko EA, Gustov AV.	Department of Neurology, Neurosurgery, and Psychiatry, Nizhnii Novgorod State Medical Academy, Nizhnii Novgorod, Russia. tv_mokina@mail.ru	Use of adaptol in the treatment of chronic fatigue syndrome in patients with chronic cerebral ischemia.	Neurosci Behav Physiol. 2010 Sep;40(7):757-9.	
Moore RA, Straube S, Paine J, Phillips CJ, Derry S,	Pain Research and Nuffield Department of	Fibromyalgia: Moderate and substantial pain	Pain. 2010 May;149(2):360-4. Epub 2010 Mar 26.	Chronic pain is associated with a range of other problems, including disturbed sleep, depression, anxiety, fatigue, reduced quality of life, and an inability to work or socialise. We investigated whether good symptom control of pain (using definitions of moderate and substantial benefit) is associated

McQuay HJ.	Anaesthetics, University of Oxford, John Radcliffe Hospital, Oxford, UK. andrew.moore@pru.ox.ac.uk	intensity reduction predicts improvement in other outcomes and substantial quality of life gain.		with improvement in other symptoms. Individual patient data from four randomised trials in fibromyalgia (2575 patients) lasting 8-14weeks were used to calculate percentage pain reduction for each completing patient (1858), divided into one of five groups according to pain reduction, irrespective of treatment: substantial benefit - 50% pain reduction; moderate - 30% to <50%; minimal - 15% to <30%; marginal - 0% to <15%; worse - <0% (increased pain intensity). We then calculated change from baseline to end of trial for measures of fatigue, function, sleep, depression, anxiety, ability to work, general health status, and quality-adjusted life year (QALY) gain over a 12-month period. Substantial and moderate pain intensity reductions were associated with statistically significant reduction from baseline by end of trial in all measures, with values by trial end at or approaching normative values. Substantial pain intensity reduction resulted in 0.11 QALYs gained, and moderate pain intensity reduction in 0.07 QALYs gained over a 12-month period. Substantial and moderate pain intensity reduction predicts broad beneficial outcomes and improved quality of life that do not occur without pain relief. Pain intensity reduction is a simple and effective predictor of which patients should continue treatment, and which should discontinue and try an alternative therapy.
Moss-Morris R, Hamilton W.		Pragmatic rehabilitation for chronic fatigue syndrome.	BMJ. 2010 Apr 23;340:c1799. doi: 10.1136/bmj.c1799. Comment on: BMJ. 2010;340:c1777.	
Moss-Morris R, Spence MJ, Hou R.	School of Psychology, University of Southampton, UK.	The pathway from glandular fever to chronic fatigue syndrome: can the cognitive behavioural model provide the map?	Psychol Med. 2010 Jul 21:1-9. [Epub ahead of print]	BACKGROUND: The cognitive behavioural model of chronic fatigue syndrome (CFS) suggests that the illness is caused through reciprocal interactions between physiology, cognition, emotion and behaviour. The purpose of this study was to investigate whether the psychological factors operationalized in this model could predict the onset of CFS following an acute episode of infectious mononucleosis commonly known as glandular fever (GF).MethodA total of 246 patients with GF were recruited into this prospective cohort study. Standardized self-report measures of perceived stress, perfectionism, somatization, mood, illness beliefs and behaviour were completed at the time of their acute illness. Follow-up questionnaires determined the incidence of new-onset chronic fatigue (CF) at 3 months and CFS at 6 months post-infection. RESULTS: Of the participants, 9.4% met the criteria for CF at 3 months and 7.8% met the criteria for CFS at 6 months. Logistic regression revealed that factors proposed to predispose people to CFS including anxiety, depression, somatization and perfectionism were associated with new-onset CFS. Negative illness beliefs including perceiving GF to be a serious, distressing condition, that will last a long time and is uncontrollable, and responding to symptoms in an all-or-nothing behavioural pattern were also significant predictors. All-or-nothing behaviour was the most significant predictor of CFS at 6 months. Perceived stress and consistently limiting activity at the time of GF were not significantly associated with CFS. CONCLUSIONS: The findings from this study provide support for the cognitive behavioural model and a good basis for developing prevention and early intervention strategies for CFS.
Munn SE.		Chronic fatigue	BMJ. 2010 Mar	

		syndrome. More than defeatism greets patients with ME.	2;340:c1179. doi: 10.1136/bmj.c1179.	
Murrough JW, Mao X, Collins KA, Kelly C, Andrade G, Nestadt P, Levine SM, Mathew SJ, Shungu DC.	Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, USA.	Increased ventricular lactate in chronic fatigue syndrome measured by 1H MRS imaging at 3.0 T. II: comparison with major depressive disorder.	NMR Biomed. 2010 Jul;23(6):643-50.	Chronic fatigue syndrome (CFS), a complex illness characterized by fatigue, impaired concentration, and musculoskeletal pain, is often misdiagnosed as a psychiatric illness due to the overlap of its symptoms with mood and anxiety disorders. Using proton magnetic resonance spectroscopic imaging ((1)H MRSI), we previously measured levels of the major brain metabolites in CFS, in generalized anxiety disorder (GAD), and in healthy control subjects, and found significantly higher levels of ventricular cerebrospinal fluid (CSF) lactate in CFS compared to the other two groups. In the present study, we sought to assess the specificity of this observation for CFS by comparing ventricular lactate levels in a new cohort of 17 CFS subjects with those in 19 healthy volunteers and in 21 subjects with major depressive disorder (MDD), which, like GAD, is a neuropsychiatric disorder that has significant symptom overlap with CFS. Ventricular CSF lactate was significantly elevated in CFS compared to healthy volunteers, replicating the major result of our previous study. Ventricular lactate measures in MDD did not differ from those in either CFS or healthy volunteers. We found a significant correlation between ventricular CSF lactate and severity of mental fatigue that was specific to the CFS group. In an exploratory analysis, we did not find evidence for altered levels of the amino acid neurotransmitters, gamma-aminobutyric acid (GABA) and glutamate + glutamine ('Glx'), in CFS compared to MDD or healthy controls. Future (1)H MRS studies with larger sample sizes and well-characterized populations will be necessary to further clarify the sensitivity and specificity of neurometabolic abnormalities in CFS and MDD.
Naess H, Sundal E, Myhr KM, Nyland HI.	Department of Neurology, Haukeland University Hospital, University of Bergen, Bergen, Norway. halvor.naess@haukeland.no	Postinfectious and chronic fatigue syndromes: clinical experience from a tertiary-referral centre in Norway.	In Vivo. 2010 Mar-Apr;24(2):185-8.	BACKGROUND: We aimed to compare patients reporting acute infection with those reporting no infection at onset of chronic fatigue syndrome (CFS). PATIENTS AND METHODS: This study includes 873 patients with CFS referred to a tertiary centre on average 4.8 years after symptom onset. Assessment was by both observer query and self-reports. Antibody analyses against infectious agents including Epstein-Barr virus and enterovirus were performed in a majority of patients. RESULTS: Females comprised 75.3% of the patient group, and the mean age was 33 years. Initial infection was reported by 77%. There was no difference as to antibody analyses. Logistic regression showed that initial infection was independently associated with acute onset of fatigue, improvement of fatigue at referral, and the following symptoms at referral: fever, tender lymph nodes, and myalgia. CONCLUSION: CFS patients with initial infection as a precipitating factor more often report acute onset of fatigue, more frequent accompanying symptoms, and more frequent improvement on referral than do patients without initial infection.
Nakamura T, Schwander SK, Donnelly R, Ortega F, Togo F, Broderick G, Yamamoto Y,	Pain & Fatigue Study Center, UMDNJ--New Jersey Medical School, Newark, New Jersey 07103,	Cytokines across the night in chronic fatigue syndrome with and without fibromyalgia.	Clin Vaccine Immunol. 2010 Apr;17(4):582-7. Epub 2010 Feb 24.	The symptoms of chronic fatigue syndrome (CFS) are consistent with cytokine dysregulation. This has led to the hypothesis of immune dysregulation as the cause of this illness. To further test this hypothesis, we did repeated blood sampling for cytokines while patients and matched healthy controls slept in the sleep lab. Because no one method for assaying cytokines is acknowledged to be better than another, we assayed for protein in serum, message in peripheral blood lymphocytes (PBLs), and function in resting and stimulated PBLs. We found no evidence of proinflammatory

Cherniack NS, Rapoport D, Natelson BH.	USA.			cytokine upregulation. Instead, in line with some of our earlier studies, we did find some evidence to support a role for an increase in interleukin-10, an anti-inflammatory cytokine. Although the changes were small, they may contribute to the common complaint in CFS patients of disrupted sleep.
Nater UM, Jones JF, Lin JM, Maloney E, Reeves WC, Heim C.	Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Ga., USA.	Personality features and personality disorders in chronic fatigue syndrome: a population-based study.	Psychother Psychosom. 2010;79(5):312-8. Epub 2010 Jul 28.	BACKGROUND: Chronic fatigue syndrome (CFS) presents unique diagnostic and management challenges. Personality may be a risk factor for CFS and may contribute to the maintenance of the illness. METHODS: 501 study participants were identified from the general population of Georgia: 113 people with CFS, 264 with unexplained unwellness but not CFS (insufficient fatigue, ISF) and 124 well controls. We used the Personality Diagnostic Questionnaire, 4th edition, to evaluate DSM-IV personality disorders. We used the NEO Five-Factor Inventory to assess personality features (neuroticism, extraversion, openness, agreeableness and conscientiousness). The Multidimensional Fatigue Inventory measured 5 dimensions of fatigue, and the Medical Outcomes Survey Short Form 36 measured 8 dimensions of functional impairment. RESULTS: Twenty-nine percent of the CFS cases had at least 1 personality disorder, compared to 28% of the ISF cases and 7% of the well controls. The prevalence of paranoid, schizoid, avoidant, obsessive-compulsive and depressive personality disorders were significantly higher in CFS and ISF compared to the well controls. The CFS cases had significantly higher scores on neuroticism, and significantly lower scores on extraversion than those with ISF or the well controls. Personality features were correlated with selected composite characteristics of fatigue. CONCLUSIONS: Our results suggest that CFS is associated with an increased prevalence of maladaptive personality features and personality disorders. This might be associated with being noncompliant with treatment suggestions, displaying unhealthy behavioral strategies and lacking a stable social environment. Since maladaptive personality is not specific to CFS, it might be associated with illness per se rather than with a specific condition.
Neu D, Kajosch H, Peigneux P, Verbanck P, Linkowski P, Le Bon O.	Brugmann University Hospital, Sleep Laboratory and Unit for Chronobiology U78, Department of Psychiatry, Université Libre de Bruxelles (U.L.B), Brussels, Belgium.	Cognitive impairment in fatigue and sleepiness associated conditions.	Psychiatry Res. 2010 Dec 31. [Epub ahead of print]	Although relating to very different concepts, sleepiness and fatigue are often confounded. However, both fatigue associated conditions as the chronic fatigue syndrome (CFS) and sleepiness associated conditions as the sleep apnea-hypopnea syndrome (SAHS) reported cognitive impairment with lowered attention, concentration and memory performances. Fifteen pure CFS patients, without primary sleep disorders or clinically relevant sleepiness, were compared to 15 untreated SAHS patients, without clinically relevant fatigue, and to 16 healthy controls of similar age. Auditory verbal learning test (AVLT), digit span, digit symbol and finger tapping test (FTT) were used as cognitive and behavioural measures. In addition we assessed daytime EEG spectral power and P300 evoked potentials. With exception for the digit span, all tests showed lower performances in patient groups. Recall on the AVLT did not differ between the two patient groups, but the digit and symbol spans showed more severe impairment in SAHS patients. Psychomotor performance on the FTT presented with slower hit rates in SAHS than in CFS. EEG theta power was highest in CFS patients. P300 latencies and amplitudes did not differ between groups. Fatigue and sleepiness associated conditions can both present with significant and objective impairment of cognitive functioning and behavioural motor performance. In our sample cognitive impairment and psychomotor performance were worse when associated to sleepiness in SAHS than to fatigue in CFS.
Newton JL, Mabillard H, Scott	NIHR Biomedical Research Centre in	The Newcastle NHS Chronic	J R Coll Physicians Edinb. 2010	In England the Department of Health has funded specialist clinical services aimed at diagnosing and managing the symptoms of chronic fatigue syndrome (CFS). These services are not available to those

A, Hoad A, Spickett G.	Ageing and Institute for Ageing & Health, Newcastle University, Newcastle upon Tyne NE1 4LP, UK. julia.newton@nuth.nhs.uk.	Fatigue Syndrome Service: not all fatigue is the same.	Dec;40(4):304-7.	who do not fulfil the diagnostic criteria for CFS. This service evaluation examined the proportion of those referred to a specialist CFS service fulfilling the Fukuda diagnostic criteria for CFS and the alternative fatigue-associated diagnoses. The CFS database was interrogated to include every patient referred to the Newcastle service from November 2008 to December 2009. All medical notes were reviewed and the diagnosis, sex and age recorded. Data were compared to a previous service evaluation (2005-07). In 2008-09, 260 subjects were referred: 19 referrals per month (260/14), compared with 17 referrals per month in 2005-07 (375/24). The proportion of patients diagnosed with CFS increased significantly compared with 2007 (36% [20/56] vs 60% [157/260]; p<0.0001). Of the 40% of patients subsequently found not to have CFS the most common diagnosis was fatigue associated with a chronic disease (47% of all alternative diagnoses); 20% had primary sleep disorders, 15% psychological/psychiatric illnesses and 4% a cardiovascular disorder. Thirteen per cent remained unexplained (5.2% of the total referrals). This study found a significant increase in the proportion of patients referred to National Health Service (NHS) CFS services diagnosed with CFS. A large proportion of patients presenting with fatigue are not eligible for referral to the Department of Health specialist fatigue services, which represents an unmet need in terms of symptom management in current NHS services.
Nickel JC, Tripp DA, Pontari M, Moldwin R, Mayer R, Carr LK, Doggweiler R, Yang CC, Mishra N, Nordling J.	Department of Urology, Queen's University, Kingston General Hospital, Kingston, Ontario, Canada. jcn@queensu.ca	Interstitial cystitis/painful bladder syndrome and associated medical conditions with an emphasis on irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome.	J Urol. 2010 Oct;184(4):1358-63. Epub 2010 Aug 17.	PURPOSE: We characterized and compared the impact of clinical phenotypic associations between interstitial cystitis/painful bladder syndrome and controls in relation to potentially related conditions, particularly irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome. MATERIALS AND METHODS: Female patients with interstitial cystitis/painful bladder syndrome and controls with no interstitial cystitis/painful bladder syndrome completed a biopsychosocial phenotyping questionnaire battery which included demographics/history form, self-reported history of associated conditions, and 10 validated questionnaires focused on symptoms, suffering/coping and behavioral/social factors. RESULTS: Questionnaires were completed by 205 patients with interstitial cystitis/painful bladder syndrome and 117 controls matched for age. Prevalence of self-reported associated condition diagnosis in interstitial cystitis/painful bladder syndrome vs controls was irritable bowel syndrome 38.6% vs 5.2%, fibromyalgia 17.7% vs 2.6% and chronic fatigue syndrome 9.5% vs 1.7% (all p <0.001). In the interstitial cystitis/painful bladder syndrome cohort 50.3% reported no other associated condition, 24.4% had interstitial cystitis/painful bladder syndrome + irritable bowel syndrome only, 2.5% had interstitial cystitis/painful bladder syndrome + fibromyalgia only, 1.5% had interstitial cystitis/painful bladder syndrome + chronic fatigue syndrome only, while 20.2% had multiple associated conditions. As the number of associated conditions increased (ie localized, regional, systemic), pain, stress, depression and sleep disturbance increased while social support, sexual functioning and quality of life deteriorated. Anxiety and catastrophizing remained increased in all groups. Symptom duration was associated with this apparent phenotypic progression. CONCLUSIONS: Irritable bowel syndrome, fibromyalgia and chronic fatigue syndrome are more prevalent in patients with interstitial cystitis/painful bladder syndrome than in asymptomatic control subjects, and result in significant impact. There are at least 3 distinct clinical phenotypes based on identification of overlapping syndrome patterns. A suggestion that remains to be proven with longitudinal studies is that there may be progression over time from an organ centric to a regional and finally to a systemic

				pain syndrome with progression of symptom severity, and deterioration of cognitive and psychosocial parameters.
Nicodemus CF, Berek JS.		TLR3 agonists as immunotherapeutic agents.	Immunotherapy. 2010 Mar;2(2):137-40.	
Nijs J, Aelbrecht S, Meeus M, Van Oosterwijck J, Zinzen E, Clarys P.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium.	Tired of being inactive: a systematic literature review of physical activity, physiological exercise capacity and muscle strength in patients with chronic fatigue syndrome.	Disabil Rehabil. 2010 Dec 20. [Epub ahead of print]	A systematic review was undertaken to examine whether patients with chronic fatigue syndrome (CFS) differ from healthy sedentary controls in physiological exercise capacity, physical activity level and muscle strength. From the available literature, it can be concluded that patients with CFS perform less physical activity during daily life, and have less peak isometric muscle strength compared to healthy sedentary control subjects. Conflicting data in relation to physiological exercise capacity of patients with CFS have been reported, but the weighted available evidence points towards a reduced physiological exercise capacity in CFS. Future studies should use a wash-out period for medication use, blinded assessments, a priori power calculation and a sedentary control group comparable for age, gender, body weight, body length and current physical activity level.
Nijs J, Van Oosterwijck J, Meeus M, Lambrecht L, Metzger K, Frémont M, Paul L.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium. jo.nijs@vub.ac.be	Unravelling the nature of postexertional malaise in myalgic encephalomyelitis/ chronic fatigue syndrome: the role of elastase, complement C4a and interleukin-1beta.	J Intern Med. 2010 Apr;267(4):418-35.	OBJECTIVES: Too vigorous exercise or activity increase frequently triggers postexertional malaise in people with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), a primary characteristic evident in up to 95% of people with ME/CFS. The present study aimed at examining whether two different types of exercise results in changes in health status, circulating elastase activity, interleukin (IL)-1beta and complement C4a levels. DESIGN: Comparative experimental design. SETTING: University. SUBJECTS: Twenty-two women with ME/CFS and 22 healthy sedentary controls Interventions: participants were subjected to a submaximal exercise (day 8) and a self-paced, physiologically limited exercise (day 16). Each bout of exercise was preceded and followed by blood sampling, actigraphy and assessment of their health status. RESULTS: Both submaximal exercise and self-paced, physiologically limited exercise resulted in postexertional malaise in people with ME/CFS. However, neither exercise bout altered elastase activity, IL-1beta or complement C4a split product levels in people with ME/CFS or healthy sedentary control subjects ($P > 0.05$). Postexercise complement C4a level was identified as a clinically important biomarker for postexertional malaise in people with ME/CFS. CONCLUSIONS: Submaximal exercise as well as self-paced, physiologically limited exercise triggers postexertional malaise in people with ME/CFS, but neither types of exercise alter acute circulating levels of IL-1beta, complement C4a split product or elastase activity. Further studying of immune alterations in relation to postexertional malaise in people with ME/CFS using multiple measurement points postexercise is required.
Nogué Xarau S, Alarcón Romay M, Martínez Martínez JM, Delclós Clanchet J, Rovira	Unidad de Toxicología Clínica, Hospital Clínic, Barcelona, España.	[Multiple chemical sensitivity: Epidemiological, clinical and prognostic	Med Clin (Barc). 2010 Jun 12;135(2):52-8. Epub 2010 Mar 19.	BACKGROUND AND OBJECTIVE: The progressive increase in cases of multiple chemical sensitivity (MCS) syndrome and the lack of studies which associate the syndrome with possible occupational origins means that further research in this field is required. The objective of this study was to compare the epidemiological, clinical and prognostic aspects of cases of MCS of occupational and non-occupational origin. PATIENTS AND METHOD: Observational study of patients diagnosed with MCS by

Prat E, Fernández Solà J.		differences between occupational and non-occupational cases.]. [Article in Spanish]		the toxicology outpatients clinic of the Hospital Clinic of Barcelona between 2002 and 2007. The occupational and non-occupational origin of MCS was considered as an independent variable. The dependant variables were occupational activity, triggering agents of MCS, chemical agents associated with the development of clinical manifestations, severity of the symptoms, comorbidities and work disability. Percentages were compared between groups. RESULTS: A total of 165 patients were included: The mean age was 47.7 years and 90.9% were women. There were significant differences between patients of occupational and non-occupational origin with respect to comorbidities such as chronic fatigue syndrome (68.1% versus 88.5%; p=0.002) and fibromyalgia (49.3% versus 73.9%; p=0.002), temporary disability (60.9% versus 39.6%; p=0.006) and permanent disability (8.7% versus 22.9%; p=0.006). CONCLUSIONS: Cases of MCS attributed to an occupational origin had fewer comorbidities and less permanent disability than those of non-occupational origin.
Oakes B, Tai AK, Cingoz O, Henefield MH, Levine S, Coffin JM, Huber BT.		Contamination of human DNA samples with mouse DNA can lead to false detection of XMRV-like sequences.	Retrovirology. 2010 Dec 20;7(1):109. [Epub ahead of print]	ABSTRACT: BACKGROUND: In 2006, a novel gammaretrovirus, XMRV (xenotropic murine leukemia virus-related virus), was discovered in some prostate tumors. A more recent study indicated that this infectious retrovirus can be detected in 67% of patients suffering from chronic fatigue syndrome (CFS), but only very few healthy controls (4%). However, several groups have published to date that they could not identify XMRV RNA or DNA sequences in other cohorts of CFS patients, while another group detected murine leukemia virus (MLV)-like sequences in 87% of such patients, but only 7% of healthy controls. Since there is a high degree of similarity between XMRV and abundant endogenous MLV proviruses, it is important to distinguish contaminating mouse sequences from true infections. RESULTS: DNA from the peripheral blood of 112 CFS patients and 36 healthy controls was tested for XMRV with two different PCR assays. A TaqMan qPCR assay specific for XMRV pol sequences was able to detect viral DNA from 2 XMRV-infected cells (~ 10-12 pg DNA) in up to 5 g of human genomic DNA, but yielded negative results in the test of 600 ng genomic DNA from 100,000 peripheral blood cells of all samples tested. However, positive results were obtained with some of these samples, using a less specific nested PCR assay for a different XMRV sequence. DNA sequencing of the PCR products revealed a wide variety of virus-related sequences, some identical to those found in prostate cancer and CFS patients, others more closely related to known endogenous MLVs. However, all samples that tested positive for XMRV and/or MLV DNA were also positive for the highly abundant intracisternal A-type particle (IAP) long terminal repeat and most were positive for murine mitochondrial cytochrome oxidase sequences. No contamination was observed in any of the negative control samples, containing those with no DNA template, which were included in each assay. CONCLUSIONS: Mouse cells contain upwards of 100 copies each of endogenous MLV DNA. Even much less than one cell's worth of DNA can yield a detectable product using highly sensitive PCR technology. It is, therefore, vital that contamination by mouse DNA be monitored with adequately sensitive assays in all samples tested.
Ongrádi J, Kövesdi V, Medveczky GP.	Semmelweis Egyetem, Altalános Orvostudományi Kar, Közegészségtani	[Human herpesvirus 6]. [Article in Hungarian]	Orv Hetil. 2010 Mar 28;151(13):523-32.	Human herpesvirus 6 discovered in 1986 is the most ancient human herpesvirus shown by molecular characteristics. Variant B infects children under the age of 2 years by droplets from asymptomatic virus shedding adults occasionally causing exanthema subitum. The virus infects CD4+ macrophages and lymphocytes; subsequently establishes lifelong latency and persistence with occasional shedding through the saliva. This variant frequently reactivates in bone marrow and organ transplant recipients

	Intézet, Budapest, Nagyvárad tér 4. 1089. ongjos@hotmail.com			with concomitant immunosuppression causing even fatal complications. It is a cofactor in the pathogenesis of multiple sclerosis, chronic fatigue syndrome, Hodgkin and non-Hodgkin lymphomas. The direct consequences of variant A infection and latency in CD4+ cells are not known. It transactivates HIV infection in vitro and in humans, and facilitates tumor progression induced by human papilloma viruses. Pathogenic effects of both variants are mediated by altered cytokine and chemokine profiles. Serological differentiation of the two variants is unreliable; however, it is possible by using PCR. Ganciclovir, foscarnet and cidofovir can be used for treatment and chemoprophylaxis of severe complications.
Paprotka T, Venkatachari NJ, Chaipan C, Burdick R, Delviks-Frankenberry KA, Hu WS, Pathak VK.	Viral Mutation Section, National Cancer Institute-Frederick, P.O. Box B, Frederick, MD 21702-1201, USA.	Inhibition of xenotropic murine leukemia virus-related virus by APOBEC3 proteins and antiviral drugs.	J Virol. 2010 Jun;84(11):5719-29. Epub 2010 Mar 24.	Xenotropic murine leukemia virus-related virus (XMRV), a gammaretrovirus, has been isolated from human prostate cancer tissue and from activated CD4(+) T cells and B cells of patients with chronic fatigue syndrome, suggesting an association between XMRV infection and these two diseases. Since APOBEC3G (A3G) and APOBEC3F (A3F), which are potent inhibitors of murine leukemia virus and Vif-deficient human immunodeficiency virus type 1 (HIV-1), are expressed in human CD4(+) T cells and B cells, we sought to determine how XMRV evades suppression of replication by APOBEC3 proteins. We found that expression of A3G, A3F, or murine A3 in virus-producing cells resulted in their virion incorporation, inhibition of XMRV replication, and G-to-A hypermutation of the viral DNA with all three APOBEC3 proteins. Quantitation of A3G and A3F mRNAs indicated that, compared to the human T-cell lines CEM and H9, prostate cell lines LNCaP and DU145 exhibited 50% lower A3F mRNA levels, whereas A3G expression in 22Rv1, LNCaP, and DU145 cells was nearly undetectable. XMRV proviral genomes in LNCaP and DU145 cells were hypermutated at low frequency with mutation patterns consistent with A3F activity. XMRV proviral genomes were extensively hypermutated upon replication in A3G/A3F-positive T cells (CEM and H9), but not in A3G/A3F-negative cells (CEM-SS). We also observed that XMRV replication was susceptible to the nucleoside reverse transcriptase (RT) inhibitors zidovudine (AZT) and tenofovir and the integrase inhibitor raltegravir. In summary, the establishment of XMRV infection in patients may be dependent on infection of A3G/A3F-deficient cells, and cells expressing low levels of A3G/A3F, such as prostate cancer cells, may be ideal producers of infectious XMRV. Furthermore, the anti-HIV-1 drugs AZT, tenofovir, and raltegravir may be useful for treatment of XMRV infection.
Pardini M, Guida S, Primavera A, Krueger F, Cocito L, Gialloreti LE.	Department of Neurosciences, Ophthalmology and Genetics, University of Genoa, Genoa, Italy; Magnetic Resonance Research Centre on Nervous System Diseases, University of	Amisulpride vs. fluoxetine treatment of Chronic Fatigue Syndrome: A pilot study.	Eur Neuropsychopharmacol. 2010 Nov 26. [Epub ahead of print]	Different pharmacologic agents have been evaluated in the treatment of Chronic Fatigue Syndrome (CFS), albeit with moderate efficacy. Among the compounds thought to present with potential to be efficacious in CFS patients stands out low-dose amisulpride, a substituted benzamide that has been shown to be an useful treatment for conditions which exhibit some overlap with CFS such as dysthymia and somatoform disorders. We thus recruited forty non-depressed CFS patients that were randomized to receive either amisulpride 25mg bid, or fluoxetine 20mg uid; all subjects were un-blinded to the treatment regimen. At the time of enrollment in the study and after twelve weeks of treatment, enrolled subjects completed the Krupp Fatigue Severity Scale, the Hospital Anxiety and Depression Scale and a visual analog scale focused on pain and bodily discomfort. Moreover, all subjects were evaluated by a clinician, blinded to the treatment regimen, using the Clinical Global Impression Severity Scale. Our data revealed a significant improvement both in self-report, and observer-based measures for the amisulpride-treated, but not for the fluoxetine-treated patients.

	Genoa, Genoa, Italy; Centre for Communication and Neurorehabilitation Research-CNAPP, Rome, Italy.			Amisulpride-treated subjects also presented with a significant reduction of somatic complaints, while the amisulpride effect on anxiety and mood levels was not significant. Both drugs were equally well tolerated. Summing up, we showed a positive symptomatic effect of amisulpride, compared to SSRI treatment, in a group of non-depressed CSF patients on self-report and on observer-based measures of fatigue and somatic complaints. If confirmed by larger, blinded studies, amisulpride thus could represent an effective approach to this difficult-to-treat condition.
Pellicano C, Gallo A, Li X, Ikonomidou VN, Evangelou IE, Ohayon JM, Stern SK, Ehrmantraut M, Cantor F, McFarland HF, Bagnato F.	Neuroimmunology Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, 10 Center Dr, Bethesda, MD 20892-1400, USA.	Relationship of cortical atrophy to fatigue in patients with multiple sclerosis.	Arch Neurol. 2010 Apr;67(4):447-53.	BACKGROUND: Fatigue is a common and disabling symptom of multiple sclerosis (MS). Previous studies reported that damage of the corticostriatothalamocortical circuit is critical in its occurrence. OBJECTIVE: To investigate the relationship between fatigue in MS and regional cortical and subcortical gray matter atrophy. DESIGN: Case-control study. SETTING: National Institutes of Health. PARTICIPANTS: Twenty-four patients with MS and 24 matched healthy volunteers who underwent 3.0-T magnetic resonance imaging and evaluations of fatigue (Modified Fatigue Impact Scale) and depression (Center for Epidemiologic Studies Depression Scale). MAIN OUTCOME MEASURES: Relationship between thalamic and basal ganglia volume, cortical thickness of frontal and parietal lobes, and, in patients, T2 lesion volume and normal-appearing white matter volume and the extent of fatigue. RESULTS: Patients were more fatigued than healthy volunteers (P = .04), while controlling for the effect of depression. Modified Fatigue Impact Scale score correlated with cortical thickness of the parietal lobe (r = -0.50, P = .01), explaining 25% of its variance. The posterior parietal cortex was the only parietal area significantly associated with the Modified Fatigue Impact Scale scores. CONCLUSIONS: Cortical atrophy of the parietal lobe had the strongest relationship with fatigue. Given the implications of the posterior parietal cortex in motor planning and integration of information from different sources, our preliminary results suggest that dysfunctions in higher-order aspects of motor control may have a role in determining fatigue in MS.
Perrin R, Embleton K, Pentreath VW, Jackson A.	Department of Medicine, University of Manchester, UK.	Longitudinal MRI shows no cerebral abnormality in chronic fatigue syndrome.	Br J Radiol. 2010 May;83(989):419-23. Epub 2010 Mar 11.	MRI has previously provided conflicting results when used to search for brain abnormalities in sufferers of chronic fatigue syndrome (CFS). Eighteen CFS patients and nine healthy volunteers each underwent MRI on two occasions, one year apart. The resulting images were examined for abnormalities in brain atrophy, deep white matter hyperintensities (WMH) and cerebral blood and cerebrospinal fluid (CSF) flow. Mean proportionate CSF volume was not significantly different between subject groups. All participants showed a slight increase in CSF between scans, but no significant difference was found between those with CFS and those without. Between-group comparisons of ventricular volume revealed no significant differences at study commencement and no significant change over the year. No significant inter-group differences were found for any of the cerebral blood and CSF flow parameters. Low levels of WMH were found in all participants. Objective scoring of WMH using Scheltens' scale revealed no change in summary components (prosencephalic deep white matter hyperintensities, basal ganglia hyperintensities and infratentorial hyperintensities) or in individual component variables between the baseline and 1 year follow-up scans. No abnormal patterns in rate and extent of brain atrophy, ventricle volume, white matter lesions, cerebral blood flow or aqueductal CSF flow were detected in the CFS population. These results throw open the debate into whether MRI scanning can reveal diagnostic signs of CFS and clinically questions the

				diagnoses of CFS made on the basis of previous research conclusions.
Pinquart M, Shen Y.	Department of Psychology, Philipps University.	Depressive Symptoms in Children and Adolescents with Chronic Physical Illness: An Updated Meta-Analysis.	J Pediatr Psychol. 2010 Nov 18. [Epub ahead of print]	OBJECTIVE: To integrate results of available studies that compared levels of depressive symptoms of children and adolescents with chronic physical illness to healthy peers or test norms. METHODS: Random-effects meta-analysis was computed with 340 studies and 450 subsamples. RESULTS: Children and adolescents with chronic illness have, on average, higher levels of depressive symptoms than their healthy peers (d = .19 SD units). Differences are strongest for chronic fatigue syndrome (d = .94), fibromyalgia (d = .59), cleft lip and palate (d = .54), migraine/tension head ache (d = .51), and epilepsy (d = .39). Larger effect sizes were found in studies with higher proportion of girls, with a healthy control group, from developing countries, published before 1990, and that used parent rating or clinician ratings rather than child ratings. CONCLUSIONS: Pediatricians and others working with children with chronic illnesses should screen children with chronic physical illness for symptoms of psychological distress and make appropriate referrals for mental health services, when needed.
Popova NF, Kamchatnov PR, Riabukhina OV, Batysheva TT, Zaĭtsev KA, Boĭko AN.	Rossiĭskiĭ gosudarstvennyĭ meditsinskiĭ universitet.	[Omaron in the complex treatment of patients with multiple sclerosis.] [Article in Russian]	Zh Nevrol Psikhiatr Im S S Korsakova. 2010;110(11):17-20.	We studied efficacy and tolerability of the combined drug omaron (25 mg of cinnarizine and 400 mg of piracetam in one tablet) in patients with multiple sclerosis. The dosage of the drug was 1 tablet 3 times a day during 12 weeks in 33 patients (mean age 35.3±4.2 years) of the index group. A comparison group consisted of 27 patients matched for demographic and clinical characteristics who did not receive nootropics during the study. None of patients included in the study received disease modifying drugs. The significant ($p<0.05$) decrease in the severity of chronic fatigue syndrome (by 28.6% compared to baseline), improvement ($p<0.05$) of cognitive functions (increase of MMSE scores by 9.4%) were found in the index group compared to the comparison one. The statistically significant changes in the severity of disability assessed by EDSS were not observed. Omaron was well-tolerated with no serious adverse-effects.
Porter NS, Jason LA, Boulton A, Bothne N, Coleman B.	Center for Community Research, DePaul University, Chicago, IL 60614, USA.	Alternative medical interventions used in the treatment and management of myalgic encephalomyelitis/ chronic fatigue syndrome and fibromyalgia.	J Altern Complement Med. 2010 Mar;16(3):235-49.	BACKGROUND: There have been several systematic reviews attempting to evaluate the efficacy of possible treatments for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and fibromyalgia (FM). However, information regarding the efficacy of complementary and alternative medicine (CAM) has not been comprehensively or systematically covered in these reviews, despite its frequent use in the patient community. PURPOSE: The purpose of this study was to systematically review and evaluate the current literature related to alternative and complementary treatments for ME/CFS and FM. It should be stressed that the treatments evaluated in this review do not reflect the clinical approach used by most practitioners to treat these illnesses, which include a mix of natural and unconventionally used medications and natural hormones tailored to each individual case. However, nearly all clinical research has focused on the utility of single CAM interventions, and thus is the primary focus of this review. METHODS: Several databases (e.g., PubMed, MEDLINE,((R)) PsychInfo) were systematically searched for randomized and nonrandomized controlled trials of alternative treatments and nonpharmacological supplements. Included studies were checked for references and several experts were contacted for referred articles. Two leading subspecialty journals were also searched by hand. Data were then extracted from included studies and quality assessments were conducted using the Jadad scale. RESULTS: Upon completion of the literature search and the exclusion of studies not meeting criterion, a total of 70 controlled clinical trials were included in the review. Sixty (60) of the 70 studies found at least one positive effect of the intervention (86%), and 52

				studies also found improvement in an illness-specific symptom (74%). The methodological quality of reporting was generally poor. CONCLUSIONS: Several types of alternative medicine have some potential for future clinical research. However, due to methodological inconsistencies across studies and the small body of evidence, no firm conclusions can be made at this time. Regarding alternative treatments, acupuncture and several types of meditative practice show the most promise for future scientific investigation. Likewise, magnesium, l-carnitine, and S-adenosylmethionine are nonpharmacological supplements with the most potential for further research. Individualized treatment plans that involve several pharmacological agents and natural remedies appear promising as well.
Prior KN, Bond MJ.	Discipline of General Practice, School of Medicine, Flinders University, Adelaide, Australia.	New dimensions of abnormal illness behaviour derived from the Illness Behaviour Questionnaire.	Psychol Health. 2010 Dec;25(10):1209-27.	The primary aim was to explore the factor structure of the Illness Behaviour Questionnaire (IBQ) and the generalisability of the derived dimensions to both general community members and four chronic illness groups. A questionnaire was administered to 675 participants, comprising 344 from the community, 80 with asthma, 95 with diabetes, 79 with chronic pain and 77 with chronic fatigue syndrome (CFS). Illness severity was calculated for all chronic illness participants (self-rated health for community members). Three IBQ scales were derived following an exploratory factor analysis for the whole sample: Affirmation of Illness (α = 0.71 (CFS)-0.79 (asthma, diabetes)), Concern for Health (α = 0.71 (asthma)-0.78 (pain)) and General Affective State (α = 0.70 (CFS)-0.80 (asthma)). Patterns of response across the five samples, and intercorrelations among the new scales and the original seven scales, were largely in accord with expectation. Long-standing criticisms of the IBQ were addressed by using systematic statistical principles to identify meaningful and psychometrically sound IBQ dimensions. The derived structure offers a more parsimonious account of possible illness responses, with the availability of a more concise yet informative index of abnormal illness behaviour having practical utility for researchers and clinicians alike.
Qiu X, Swanson P, Luk KC, Tu B, Villinger F, Das Gupta J, Silverman RH, Klein EA, Devare S, Schochetman G, Hackett J Jr.	Infectious Diseases R&D, Abbott Diagnostics, 100 Abbott Park Rd, Abbott Park, IL 60064, USA. xiaoxing.qiu@abbott.com	Characterization of antibodies elicited by XMRV infection and development of immunoassays useful for epidemiologic studies.	Retrovirology. 2010 Aug 17;7:68.	BACKGROUND: Xenotropic Murine Leukemia Virus-related Virus (XMRV) is a human gammaretrovirus recently identified in prostate cancer tissue and in lymphocytes of patients with chronic fatigue syndrome. To establish the etiologic role of XMRV infection in human disease requires large scale epidemiologic studies. Development of assays to detect XMRV-specific antibodies would greatly facilitate such studies. However, the nature and kinetics of the antibody response to XMRV infection have yet to be determined. RESULTS: Three rhesus macaques were infected with XMRV to determine the dynamics of the antibody responses elicited by infection with XMRV. All macaques developed antibodies to XMRV during the second week of infection, and the predominant responses were to the envelope protein gp70, transmembrane protein p15E, and capsid protein p30. In general, antibody responses to gp70 and p15E appeared early with higher titers than to p30, especially in the early period of seroconversion. Antibodies to gp70, p15E and p30 persisted to 158 days and were substantially boosted by re-infection, thus, were identified as useful serologic markers. Three high-throughput prototype assays were developed using recombinant proteins to detect antibodies to these viral proteins. Both gp70 and p15E prototype assays demonstrated 100% sensitivity by detecting all Western blot (WB) positive serial bleeds from the XMRV-infected macaques and good specificity (99.5-99.9%) with blood donors. Seroconversion sensitivity and specificity of the p30 prototype assay were 92% and 99.4% respectively. CONCLUSIONS: This study provides the first demonstration of

				seroconversion patterns elicited by XMRV infection. The nature and kinetics of antibody responses to XMRV in primates were fully characterized. Moreover, key serologic markers useful for detection of XMRV infection were identified. Three prototype immunoassays were developed to detect XMRV-specific antibodies. These assays demonstrated good sensitivity and specificity; thus, they will facilitate large scale epidemiologic studies of XMRV infection in humans.
Quinn C.		A mystery no more.	Nurs Stand. 2010 Sep 29-Oct 5;25(4):22-3.	New research has solved one of the puzzles surrounding chronic fatigue syndrome, which could help in its future treatment.
Rasmussen LB.		[Maharishi Ayurveda and unclear conditions]. [Article in Norwegian]	Tidsskr Nor Laegeforen. 2010 Apr 8;130(7):721. Comment on: Tidsskr Nor Laegeforen. 2009 Aug 13;129(15):1481-3.	
Reuter SE, Evans AM.	School of Pharmacy & Medical Sciences Sansom Institute for Health Research, University of South Australia, Adelaide, SA, AUSTRALIA.	Long-chain acylcarnitine deficiency in chronic fatigue syndrome patients. Potential involvement of altered carnitine palmitoyltransferase-I activity.	J Intern Med. 2010 Dec 22. doi: 10.1111/j.1365-2796.2010.02341.x. [Epub ahead of print]	Objective. The underlying aetiology of chronic fatigue syndrome is currently unknown; however, in light of carnitine's critical role in mitochondrial energy production, it has been suggested that chronic fatigue syndrome may be associated with altered carnitine homeostasis. This study was conducted to comparatively examine full endogenous carnitine profiles in chronic fatigue syndrome patients and healthy controls. Design. A cross-sectional, observational study. Setting and subjects. Forty-four patients with chronic fatigue syndrome and 49 age- and gender-matched healthy controls were recruited from the community and studied at the School of Pharmacy & Medical Sciences, University of South Australia. Main outcome measures. All participants completed a fatigue severity scale questionnaire and had a single fasting blood sample collected which was analysed for L-carnitine and 35 individual acylcarnitine concentrations in plasma by LC-MS/MS. Results. Chronic fatigue syndrome patients exhibited significantly altered concentrations of C8:1, C12DC, C14, C16:1, C18, C18:1, C18:2 and C18:1-OH acylcarnitines; of particular note, oleyl-L-carnitine (C18:1) and linoleyl-L-carnitine (C18:2) were, on average, 30-40% lower in patients than controls ($p<0.0001$). Significant correlations between acylcarnitine concentrations and clinical symptomology were also demonstrated. Conclusions. It is proposed that this disturbance in carnitine homeostasis is a result of a reduction in carnitine palmitoyltransferase-I (CPT-I) activity, possibly due to the accumulation of omega-6 fatty acids previously observed in this patient population. It is hypothesised that the administration of omega-3 fatty acids in combination with L-carnitine would increase CPT-I activity and improve chronic fatigue syndrome symptomology.
Rimes KA, Chalder T.	Department of Psychological Medicine, King's College London, Institute of	The Beliefs about Emotions Scale: validity, reliability and sensitivity to change.	J Psychosom Res. 2010 Mar;68(3):285-92. Epub 2009 Dec 9.	OBJECTIVE: Beliefs about the unacceptability of experiencing or expressing negative emotions have been noted in individuals with a range of problems, including chronic fatigue syndrome (CFS), irritable bowel syndrome, somatization disorder, depression, eating disorders, social phobia, posttraumatic stress disorder, and borderline personality disorder. These beliefs are likely to have implications for emotion regulation and processing, and are addressed explicitly or implicitly within many therapies

	Psychiatry, London, UK. katharine.rimes@kcl.ac.uk			including cognitive behavior therapy (CBT), mindfulness-based cognitive therapy (MBCT), and Acceptance and Commitment Therapy (ACT). This article describes the development, validation, and internal reliability of the Beliefs about Emotions Scale (BES), a self-report questionnaire to assess such beliefs. METHODS: The new scale was completed by people with CFS (n=121) and healthy controls (n=73). Twenty-two individuals with CFS completed the scale before and after CBT. RESULTS: People with CFS had significantly higher scores on this new questionnaire than healthy controls. Principal components analysis identified one factor, and the scale had high internal consistency (0.91). Scores on the BES were most highly correlated with a measure of negative perfectionism (r=0.59) and also showed significant correlations with measures of dysfunctional attitudes, self-sacrifice, depression, anxiety, and fatigue. When completed before and after CBT for CFS, the questionnaire was sufficiently sensitive to detect a significant reduction in endorsement of unhelpful beliefs about emotions. CONCLUSION: The new Beliefs about Emotions Scale showed good internal reliability, validity and sensitivity to change.
Roberts AD, Charler ML, Papadopoulos A, Wessely S, Chalder T, Cleare AJ.	King's College London, Institute of Psychiatry, Department of Psychological Medicine, London, UK.	Does hypocortisolism predict a poor response to cognitive behavioural therapy in chronic fatigue syndrome?	Psychol Med. 2010 Mar;40(3):515-22. Epub 2009 Jul 17.	BACKGROUND: There is evidence that patients with chronic fatigue syndrome (CFS) have mild hypocortisolism. The clinical significance of this is unclear. We aimed to determine whether hypocortisolism exerted any effect on the response of CFS to cognitive behavioural therapy (CBT). METHOD: We measured 24-h urinary free cortisol (UFC) in 84 patients with Centers for Disease Control and Prevention (CDC)-defined CFS (of whom 64 were free from psychotropic medication) who then received CBT in a specialist, tertiary out-patient clinic as part of their usual clinical care. We also measured salivary cortisol output from 0800 to 2000 h in a subsample of 56 psychotropic medication-free patients. RESULTS: Overall, 39% of patients responded to CBT after 6 months of treatment. Lower 24-h UFC output was associated with a poorer response to CBT but only in psychotropic medication-free patients. A flattened diurnal profile of salivary cortisol was also associated with a poor response to CBT. CONCLUSIONS: Low cortisol is of clinical relevance in CFS, as it is associated with a poorer response to CBT. Hypocortisolism could be one of several maintaining factors that interact in the persistence of CFS.
Robinson M, Gray SR, Watson MS, Kennedy G, Hill A, Belch JJ, Nimmo MA.	Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK.	Plasma IL-6, its soluble receptors and F2-isoprostanes at rest and during exercise in chronic fatigue syndrome.	Scand J Med Sci Sports. 2010 Apr;20(2):282-90. Epub 2009 Apr 13.	The aim of the current study was to investigate the levels of interleukin-6 (IL-6), its soluble receptors (sIL-6R and sgp130) and F(2)-isoprostanes, at rest and during exercise, in patients with chronic fatigue syndrome (CFS). Six male CFS patients and six healthy controls performed an incremental exercise test to exhaustion and a submaximal exercise bout to exhaustion. Blood samples taken in the submaximal test at rest, immediately post-exercise and 24 h post-exercise were analyzed for IL-6, sIL-6R, sgp130 and F(2)-isoprostanes. A further 33 CFS and 33 healthy control participants gave a resting blood sample for IL-6 and sIL-6R measurement. During the incremental exercise test only power output at the lactate threshold was lower ($P<0.05$) in the CFS group. F(2)-isoprostanes were higher ($P<0.05$) in CFS patients at rest and this difference persisted immediately and 24 h post-exercise. The exercise study found no differences in IL-6, sIL-6R or sgp130 at any time point between groups. In the larger resting group, there were no differences in IL-6 and sIL-6R between CFS and control groups. This investigation has demonstrated that patients with CFS do not have altered plasma levels of IL-6, sIL-6R or sgp130 either at rest or following exercise. F(2)-isoprostanes, however, were consistently higher in CFS patients.

Robinson MJ, Erlwein OW, Kaye S, Weber J, Cingoz O, Patel A, Walker MM, Kim WJ, Uiprasertkul M, Coffin JM, McClure MO.		Mouse DNA contamination in human tissue tested for XMRV.	Retrovirology. 2010 Dec 20;7(1):108. [Epub ahead of print]	ABSTRACT: BACKGROUND: We used a PCR-based approach to study the prevalence of genetic sequences related to a gammaretrovirus, xenotropic murine leukemia virus-related virus, XMRV, in human prostate cancer. This virus has been identified in the US in prostate cancer patients and in those with chronic fatigue syndrome. However, with the exception of two patients in Germany, XMRV has not been identified in prostate cancer tissue in Europe. Most putative associations of new or old human retroviruses with diseases have turned out to be due to contamination. We have looked for XMRV sequences in DNA extracted from formalin-fixed paraffin- embedded prostate tissues. To control for contamination, PCR assays to detect either mouse mitochondrial DNA (mtDNA) or intracisternal A particle (IAP) long terminal repeat DNA were run on all samples, owing to their very high copy number in mouse cells. RESULTS: In general agreement with the US prevalence, XMRV-like sequences were found in 4.8% of prostate cancers. However, these were also positive, as were 21.5% of XMRV-negative cases, for IAP sequences, and many, but not all were positive for mtDNA sequences. CONCLUSIONS: These results show that contamination with mouse DNA is widespread and detectable by the highly sensitive IAP assay, but not always with less sensitive assays, such as murine mtDNA PCR. This study highlights the ubiquitous presence of mouse DNA in laboratory specimens and offers a means of rigorous validation for future studies of murine retroviruses in human disease.
Rusmevichientong A, Chow SA.	Department of Molecular and Medical Pharmacology, Molecular Biology Institute, 650 Charles E. Young Drive, Los Angeles, CA 90095, USA.	Biology and pathophysiology of the new human retrovirus XMRV and its association with human disease.	Immunol Res. 2010 Dec;48(1-3):27-39.	Xenotropic murine leukemia virus-related virus (XMRV) is a new human retrovirus originally identified in prostate cancer patients with a deficiency in the antiviral enzyme RNase L. XMRV has been detected with varying frequencies in cases of prostate cancer and chronic fatigue syndrome (CFS), as well as in a small proportion of healthy individuals. An etiologic link between XMRV infection and human disease, however, has yet to be established. Here, we summarize existing knowledge regarding the characteristics of XMRV replication, association of XMRV with prostate cancer and CFS, and potential mechanisms of XMRV pathophysiology. We also highlight several areas, such as the establishment of standardized assays and the development of animal models, as future directions to advance our current understanding of XMRV and its relevance to human disease.
Sachdeva AK, Kuhad A, Tiwari V, Arora V, Chopra K.	Pharmacology Research Laboratory, University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Study, Panjab University, Chandigarh, India.	Protective effect of epigallocatechin gallate in murine water-immersion stress model of chronic fatigue syndrome.	Basic Clin Pharmacol Toxicol. 2010 Jun;106(6):490-6. Epub 2010 Jan 18.	Chronic fatigue syndrome (CFS) is a specific clinical condition that characterizes unexplained disabling fatigue. In the present study, chronic fatigue was produced in mice by subjecting them to forced swim inside a rectangular jar of specific dimensions for 6 min. daily for 15 days. Epigallocatechin gallate (EGCG; 25, 50 and 100 mg/kg, p.o.) was administered daily 30 min. before forced swim session. Immobility period and post-swim fatigue was assessed on alternate days. On the 16th day, after assessment of various behavioural parameters, mice were killed to harvest the brain, spleen and thymus. There was significant increase in oxidative-nitrosative stress and tumour necrosis factor-alpha levels in the brain of mice subjected to water-immersion stress as compared with naive group. These behavioural and biochemical alterations were restored after chronic treatment with EGCG. The present study points out that EGCG could be of therapeutic potential in the treatment of chronic fatigue.
Santamarina-Pérez P, Freniche V, Eiroa-Orosa FJ,	Servicio de Psiquiatría, Hospital	[The role of depression in cognitive	Med Clin (Barc). 2010 Dec 8. [Epub ahead of print]	BACKGROUND AND OBJECTIVE: To analyze the role of depression in cognitive deficits of patients with chronic fatigue syndrome (CFS). PATIENTS AND METHODS: 57 women with CFS were assessed by neuropsychological tests that included measures of attention: CalCap, Mental control of the WMS-III,

Llobet G, Sáez N, Alegre J, Jacas C.	Universitario Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, España.	inpairment in patients with chronic fatigue syndrome.] [Article in Spanish]		PASAT, forward and backward digits (WAIS-III), symbol digit modalities test (SDMT); executive functions: Stroop Test, Trail Making Test (TMT A y B), FAS, Tower of London; memory: Auditory-Verbal Learning Test (AVL), Rey Complex Figure (RCF), and psychomotor skills: Grooved Pegboard. The raw scores on the tests were adjusted according to normative data and transformed to T scores. The sample was divided into two groups based on the presence or absence of depression, assessed by clinical interview and administration of the Hospital Anxiety and Depression Scale (HADS). This study compared neuropsychological test scores between the two groups. RESULTS: CFS patients showed cognitive deficit in attention and executive functions, regardless of the presence of depression. There were no significant differences between the two CFS groups. CONCLUSIONS: The cognitive impairments in patients with CFS are not secondary to the presence of depression. These results should be taken into account in the implementation of therapeutic programs in these patients.
Santhouse AM, Hotopf M, David AS.		Chronic fatigue syndrome.	BMJ. 2010 Feb 11;340:c738. doi: 10.1136/bmj.c738. Comment in: BMJ. 2010;340:c1181.	
Sathyapalan T, Beckett S, Rigby AS, Mellor DD, Atkin SL.	Department of Endocrinology, Diabetes and Metabolism, Hull York Medical School, Michael White Diabetes Centre, Hull Royal Infirmary, 220-236 Anlaby Road, Hull, HU32RW UK. thozhukat.sathyapalan@hyms.ac.uk	High cocoa polyphenol rich chocolate may reduce the burden of the symptoms in chronic fatigue syndrome.	Nutr J. 2010 Nov 22;9:55.	BACKGROUND: Chocolate is rich in flavonoids that have been shown to be of benefit in disparate conditions including cardiovascular disease and cancer. The effect of polyphenol rich chocolate in subjects with chronic fatigue syndrome (CFS) has not been studied previously. METHODS: We conducted a double blinded, randomised, clinical pilot crossover study comparing high cocoa liquor/polyphenol rich chocolate (HCL/PR) in comparison to simulated iso-calorific chocolate (cocoa liquor free/low polyphenols(CLF/LP)) on fatigue and residual function in subjects with chronic fatigue syndrome. Subjects with CFS having severe fatigue of at least 10 out of 11 on the Chalder Fatigue Scale were enrolled. Subjects had either 8 weeks of intervention in the form of HCL/PR or CLF/LP, with a 2 week wash out period followed by 8 weeks of intervention with the other chocolate. RESULTS: Ten subjects were enrolled in the study. The Chalder Fatigue Scale score improved significantly after 8 weeks of the HCL/PR chocolate arm [median (range) Exact Sig. (2-tailed)] [33 (25 - 38) vs. 21.5 (6 - 35) 0.01], but that deteriorated significantly when subjects were given simulated iso-calorific chocolate (CLF/CP) [28.5 (17 - 20) vs. 34.5 (13-26) 0.03]. The residual function, as assessed by the London Handicap scale, also improved significantly after the HCL/PR arm [0.49 (0.33 - 0.62) vs. 0.64 (0.44 - 0.83) 0.01] and deteriorated after iso-calorific chocolate [00.44 (0.43 - 0.68) vs. 0.36 (0.33 - 0.62)0.03]. Likewise the Hospital Anxiety and Depression score also improved after the HCL/PR arm, but deteriorated after CLF/CP. Mean weight remained unchanged throughout the trial. CONCLUSION: This study suggests that HCL/PR chocolate may improve symptoms in subjects with chronic fatigue syndrome.
Sato E, Furuta RA, Miyazawa T.		An endogenous murine leukemia viral genome contaminant in a commercial RT-	Retrovirology. 2010 Dec 20;7(1):110. [Epub ahead of print]	ABSTRACT: During pilot studies to investigate the presence of viral RNA of xenotropic murine leukemia virus (MLV)-related virus (XMRV) infection in sera from chronic fatigue syndrome (CFS) patients in Japan, a positive band was frequently detected at the expected product size in negative control samples when detecting a partial gag region of XMRV using a one-step RT-PCR kit. We suspected that the kit itself might have been contaminated with small traces of endogenous MLV

		PCR Kit is amplified using standard primers for XMRV.		genome or XMRV and attempted to evaluate the quality of the kit in two independent laboratories. We purchased four one-step RT-PCR kits from Invitrogen, TaKaRa, Promega and QIAGEN in Japan. To amplify the partial gag gene of XMRV or other MLV-related viruses, primer sets (419F and 1154R, and GAG-I-F and GAG-I-R) which have been widely used in XMRV studies were employed. The nucleotide sequences of the amplicons were determined and compared with deposited sequences of a polytropic endogenous MLV (PmERV), XMRV and endogenous MLV-related viruses derived from CFS patients. We found that the enzyme mixtures of the one-step RT-PCR kit from Invitrogen were contaminated with RNA derived from PmERV. The nucleotide sequence of a partial gag region of the contaminant amplified by RT-PCR was nearly identical (99.4 % identity) to a PmERV on chromosome 7 and highly similar (96.9 to 97.6 %) to recently identified MLV-like viruses derived from CFS patients. We also determined the nucleotide sequence of a partial env region of the contaminant and found that it was almost identical (99.6 %) to the PmERV. In the investigation of XMRV infection in patients of CFS and prostate cancer, researchers should prudently evaluate the test kits for the presence of endogenous MLV as well as XMRV genomes prior to PCR and RT-PCR tests.
Satterfield BC, Garcia RA, Gurrieri F, Schwartz CE.	Cooperative Diagnostics, LLC, Greenwood, SC 29646, USA. brent@codiagnostics.com.	PCR and serology find no association between xenotropic murine leukemia virus-related virus (XMRV) and autism.	Mol Autism. 2010 Oct 14;1(1):14.	ABSTRACT: Xenotropic murine leukemia virus-related virus (XMRV) is a retrovirus implicated in prostate cancer and chronic fatigue syndrome (CFS). Press releases have suggested that it could contribute to autism spectrum disorder (ASD). In this study we used two PCR assays and one antibody assay to screen 25 blood samples from autistic children born to mothers with CFS and from 20 mixed controls including family members of the children assayed, people with fibromyalgia and people with chronic Lyme disease. Using a real-time PCR assay, we screened an additional 48 South Carolina autism disorder samples, 96 Italian ASD samples, 61 South Carolina ASD samples and 184 healthy controls. Despite having the ability to detect low copy number XMRV DNA in a large background of cellular DNA, none of the PCR assays found any evidence of XMRV infection in blood cells from patients or controls. Further, no anti-XMRV antibodies were detected, ruling out possible low level or abortive infections in blood or in other reservoirs. These results imply that XMRV is not associated with autism.
Scully P, McKernan DP, Keohane J, Groeger D, Shanahan F, Dinan TG, Quigley EM.	Alimentary Pharmabiotic Centre, University College Cork, Ireland.	Plasma cytokine profiles in females with irritable bowel syndrome and extra-intestinal co-morbidity.	Am J Gastroenterol. 2010 Oct;105(10):2235-43. Epub 2010 Apr 20.	OBJECTIVES: Irritable bowel syndrome (IBS) is a functional disorder that is associated with a number of extra-intestinal co-morbidities and a pro-inflammatory profile. This study was designed to examine the cytokine profile among a group of IBS patients with the extra-intestinal co-morbidities fibromyalgia, premenstrual dysmorphic disorder, and chronic fatigue syndrome. METHODS: In all, 100 female IBS patients with these co-morbidities, 21 IBS subjects without co-morbidity ("pure" IBS; Rome II), and 54 age-matched female controls took part in the study. Blood was drawn for measurement of the plasma cytokines interleukin (IL)-1β, IL-6, IL-8, IL-10, IL-12p70, IL-13, tumor necrosis factor (TNF)α, and interferon γ. The presence of the selected extra-intestinal manifestations was assessed using standard international criteria. RESULTS: Patients with IBS have increased plasma levels of IL-6 and IL-8; those with these extra-intestinal co-morbidities were found to have, in addition, increased levels of IL-1β and TNFα. No associations were evident between cytokine profiles and the nature of the co-morbidity or number of extra-intestinal co-morbidities present. CONCLUSIONS: Although IBS is characterized by a pro-inflammatory profile featuring the pro-inflammatory cytokines IL-6 and IL-8, IBS patients with certain extra-intestinal co-morbid conditions are distinguished by additional

				elevations in IL-1β and TNFα.
Sharp NC.	Centre for Sports Medicine and Human Performance, Brunel University, Uxbridge, West London, UK.	The human genome and sport, including epigenetics, gene doping, and athleticogenomics.	Endocrinol Metab Clin North Am. 2010 Mar;39(1):201-15, xi.	Hugh Montgomery's discovery of the first of more than 239 fitness genes together with rapid advances in human gene therapy have created a prospect of using genes, genetic elements, and cells that have the capacity to enhance athletic performance (to paraphrase the World Anti-Doping Agency's definition of gene doping). This brief overview covers the main areas of interface between genetics and sport, attempts to provide a context against which gene doping may be viewed, and predicts a futuristic legitimate use of genomic (and possibly epigenetic) information in sport.
Shepherd CB.		Chronic fatigue syndrome. Severely affected, severely neglected.	BMJ. 2010 Mar 2;340:c1181. doi: 10.1136/bmj.c1181. Comment on: BMJ. 2010;340:c738.	
Shishioh-Ikejima N, Ogawa T, Yamaguti K, Watanabe Y, Kuratsune H, Kiyama H.	Department of Anatomy & Neurobiology, Osaka City University, Graduate School of Medicine, Osaka 545-8585, Japan.	The increase of alpha-melanocyte-stimulating hormone in the plasma of chronic fatigue syndrome patients.	BMC Neurol. 2010 Aug 23;10:73.	BACKGROUND: Despite extensive research, no reliable biological marker for chronic fatigue syndrome (CFS) has yet been identified. However, hyperactivation of melanotrophs in the pituitary gland and increased levels of plasma alpha-melanocyte-stimulating hormone (alpha-MSH) have recently been detected in an animal model of chronic stress. Because CFS is considered to be caused partly by chronic stress events, increased alpha-MSH plasma levels may also occur in CFS patients. We therefore examined alpha-MSH levels in CFS patients. METHODS: Fifty-five CFS patients, who were previously diagnosed within 10 years of with the disease, were enrolled in this study. Thirty healthy volunteers were studied as controls. Fasting bloods samples were collected in the morning and evaluated for their plasma levels of alpha-MSH, adrenocorticotropic hormone (ACTH), serum cortisol and dehydroepiandrosterone sulfate (DHEA-S). Mean levels of alpha-MSH were compared between the CFS and control groups using Welch's t test. RESULTS: The mean plasma alpha-MSH concentration in the CFS group (17.9 +/- 1.0 pg/mL) was significantly higher than that in healthy controls (14.5 +/- 1.0 pg/mL, p = 0.02). However, there was a wide range of values in the CFS group. The factors correlated with the plasma alpha-MSH values were analyzed using Spearman's rank correlation. A negative correlation was found between the duration of the CFS and the plasma alpha-MSH values (p = 0.04, rs = -0.28), but no correlations with ACTH, cortisol or DHEA-S levels were identified (p = 0.55, 0.26, 0.33, respectively). The CFS patients were divided into two groups: patients diagnosed for <or= 5 years' duration, and those diagnosed for 5-10 years' duration. They were compared with the healthy controls using one-way ANOVA and Tukey-Kramer multiple comparison tests. The mean alpha-MSH concentration in the <or= 5 years group was 20.8 +/- 1.2 pg/mL, which was significantly higher than that in the healthy controls (p < 0.01). There was no significant difference between the 5-10 year group (15.6 +/- 1.4 pg/mL) and the healthy controls. CONCLUSIONS: CFS patients with a disease duration of <or= 5 years had significantly higher levels of alpha-MSH in their peripheral blood. alpha-MSH could be a potent biological marker for the diagnosis of CFS, at least during the first 5 years after onset of the disease.
Silverman MN,	Section on	Neuroendocrine	PM R. 2010	Central fatigue, a persistent and subjective sense of tiredness, generally correlates poorly with

Heim CM, Nater UM, Marques AH, Sternberg EM.	Neuroendocrine Immunology and Behavior, National Institute of Mental Health, National Institutes of Health, Rockville, MD(dagger).	and immune contributors to fatigue.	May;2(5):338-46.	traditional markers of disease. It is frequently associated with psychosocial factors, such as depression, sleep disorder, anxiety, and coping style, which suggest that dysregulation of the body's stress systems may serve as an underlying mechanism in the maintenance of chronic fatigue (CF). This article addresses the endocrine, neural, and immune factors that contribute to fatigue and describes research regarding the role of these factors in chronic fatigue syndrome as a model for addressing the biology of CF. In general, hypoactivity of the hypothalamic-pituitary-adrenal axis, autonomic nervous system alterations characterized by sympathetic overactivity and low vagal tone, as well as immune abnormalities, may contribute to the expression of CF. Noninvasive methods for evaluating endocrine, neural, and immune function are also discussed. Simultaneous evaluation of neuroendocrine and immune systems with noninvasive techniques will help elucidate the underlying interactions of these systems, their role in disease susceptibility, and progression of stress-related disorders.
Silverman RH, Nguyen C, Weight CJ, Klein EA.	Department of Cancer Biology, Lerner Research Institute, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA. silverr@ccf.org	The human retrovirus XMRV in prostate cancer and chronic fatigue syndrome.	Nat Rev Urol. 2010 Jul;7(7):392-402. Epub 2010 Jun 1.	Xenotropic murine leukemia virus-related virus (XMRV) is an authentic, newly recognized human retrovirus first identified in prostate cancer tissues from men with a deficiency in the innate immunity gene RNASEL. At present, studies have detected XMRV at widely different rates in prostate cancer cases (0-27%) and in patients with chronic fatigue syndrome (CFS; 0-67%). Indirect or direct modes of carcinogenesis by XMRV have been suggested depending on whether the virus was found in stroma or malignant epithelium. Viral replication in the prostate might be affected by androgens, which stimulate XMRV through a transcriptional enhancer site in viral DNA. By contrast, host restriction factors, such as APOBEC3 and tetherin, inhibit virus replication. Immune dysfunction mediated by XMRV has been suggested as a possible factor in CFS. Recent studies show that some existing antiretroviral drugs suppress XMRV infections and diagnostic assays are under development. Although other retroviruses of the same genus as XMRV (gammaretroviruses) cause cancer and neurological disease in animals, whether XMRV is a cause of either prostate cancer or CFS remains unknown. Emerging science surrounding XMRV is contributing to our knowledge of retroviral infections while focusing intense interest on two major human diseases.
Singh IR, Gorzynski JE, Drobysheva D, Bassit L, Schinazi RF.	Department of Pathology, University of Utah, Salt Lake City, Utah, United States of America. ila.singh@path.utah.edu	Raltegravir is a potent inhibitor of XMRV, a virus implicated in prostate cancer and chronic fatigue syndrome.	PLoS One. 2010 Apr 1;5(4):e9948.	BACKGROUND: Xenotropic murine leukemia-related retrovirus (XMRV) is a recently discovered retrovirus that has been linked to human prostate cancer and chronic fatigue syndrome (CFS). Both diseases affect a large fraction of the world population, with prostate cancer affecting one in six men, and CFS affecting an estimated 0.4 to 1% of the population. PRINCIPAL FINDINGS: Forty-five compounds, including twenty-eight drugs approved for use in humans, were evaluated against XMRV replication in vitro. We found that the retroviral integrase inhibitor, raltegravir, was potent and selective against XMRV at submicromolar concentrations, in MCF-7 and LNCaP cells, a breast cancer and prostate cancer cell line, respectively. Another integrase inhibitor, L-000870812, and two nucleoside reverse transcriptase inhibitors, zidovudine (ZDV), and tenofovir disoproxil fumarate (TDF) also inhibited XMRV replication. When combined, these drugs displayed mostly synergistic effects against this virus, suggesting that combination therapy may delay or prevent the selection of resistant viruses. CONCLUSIONS: If XMRV proves to be a causal factor in prostate cancer or CFS, these discoveries may allow for rational design of clinical trials.
Smith HS, Barkin	Albany Medical	Fibromyalgia	Am J Ther. 2010	Fibromyalgia is a complex condition that is characterized by chronic widespread pain and multiple

RL.	College, Department of Anesthesiology, Albany, NY 12208, USA. smithh@mail.amc.edu	syndrome: a discussion of the syndrome and pharmacotherapy.	Jul-Aug;17(4):418-39.	other symptoms, including fatigue, sleep disturbances, cognitive dysfunction, stiffness, and depressive episodes. Fibromyalgia may coexist and/or overlap with other conditions that may involve central sensitivity, including chronic fatigue syndrome, irritable bowel syndrome, irritable bladder syndrome or interstitial cystitis, and temporomandibular disorder. The pathophysiology of fibromyalgia remains uncertain but is believed to be partly the result of central systems affecting afferent processing as well as impaired endogenous pain-inhibitory systems. Abnormal central nociceptive processing may contribute to fibromyalgia, producing heightened responses to various noxious stimuli with resulting mechanical hyperalgesia. Fibromyalgia remains a clinical diagnosis. There has been a recent paradigm shift away from requiring 11 or more out of 18 tender points and instead focusing on the presence of chronic widespread pain as well as symptoms of fatigue, unrefreshed sleep, and other somatic complaints. Although there is no known cure for fibromyalgia, multidisciplinary team efforts using combined treatment approaches, including patient education, aerobic exercise, cognitive behavioral therapy, and pharmacologic therapies (serotonin norepinephrine reuptake inhibitors [eg, duloxetine, milnacipran] and alpha 2-delta receptor ligands [eg, pregabalin]) may improve symptoms as well as function of patients with fibromyalgia.
Smith MS, Buchwald DS, Bogart A, Goldberg J, Smith WR, Afari N.	Department of Pediatrics, University of Washington, Seattle, Washington, USA.	Adolescent offspring of mothers with chronic fatigue syndrome.	J Adolesc Health. 2010 Mar;46(3):284-91. Epub 2009 Oct 13.	PURPOSE: The goal of this study was to determine whether adolescent offspring of mothers with chronic fatigue syndrome (CFS) have higher prevalence of CFS and report more fatigue, greater pain sensitivity, more sleep problems, and poorer cardiopulmonary fitness in comparison with offspring with no exposure to maternal CFS. METHODS: A total of 26 adolescent offspring of 20 mothers diagnosed with CFS were compared with 45 adolescent offspring of 30 age-matched healthy control mothers. Study measures included structured interviews and medical and laboratory examinations for CFS; tender point examination; maximum oxygen uptake and perceived exertion; dolorimetry pain ratings; and questionnaires on fatigue severity and sleepiness. RESULTS: In comparison with offspring of healthy mothers, those exposed to mothers with CFS reported higher prevalence of fatigue of at least 1-month duration (23% vs. 4%), fatigue of 6 months or longer (15% vs. 2%), and met criteria for CFS (12% vs. 2%), although these differences only approached statistical significance. CFS and healthy mothers differed on almost all study outcomes, but offspring groups did not differ on measures of current fatigue severity, pain sensitivity, sleep, mean number of tender points, and cardiopulmonary fitness. CONCLUSIONS: The higher prevalence of fatiguing states in offspring of CFS mothers, despite the lack of statistical significance, suggests that familial factors may potentially play a role in developing chronically fatiguing states. Alternately, perturbations in pain sensitivity and cardiopulmonary fitness may be consequences of CFS. Future studies should focus on examining the impact of maternal CFS and associated disability on psychosocial functioning of offspring.
Smith RA.		Contamination of clinical specimens with MLV-encoding nucleic acids: implications for XMRV and other candidate	Retrovirology. 2010 Dec 20;7(1):112. [Epub ahead of print]	ABSTRACT: Efforts to assess the prevalence of xenotropic murine leukemia virus-related virus (XMRV) in patients with prostate cancer and chronic fatigue syndrome have relied heavily on PCR-based testing of clinical samples and have yielded widely divergent findings. This week in Retrovirology, reports from four independent research groups illustrate the extreme care needed to exclude DNA or RNA contamination in PCR analyses of XMRV. In addition, phylogenetic evidence suggesting that previously-published XMRV sequences originated from a commonly-used prostate carcinoma cell line (22Rv1) is presented. These findings raise important questions regarding the provenance of XMRV and

		human retroviruses.		its potential connection to human disease.
Sommerfeldt L, Portilla H, Jacobsen L, Gjerstad J, Wyller VB.	Division of Paediatrics, Oslo University Hospital, Oslo, Norway STAMI, The National Institute of Occupational Health, Oslo, Norway Department of Molecular Biosciences, University of Oslo, Norway.	Polymorphisms of adrenergic cardiovascular control genes are associated with adolescent chronic fatigue syndrome.	Acta Paediatr. 2011 Feb;100(2):293-8. doi: 10.1111/j.1651-2227.2010.02072.x. Epub 2010 Nov 18.	Aim: To explore the frequency of polymorphisms in adrenergic cardiovascular control genes in adolescent with chronic fatigue syndrome (CFS) and the relation of such polymorphisms to cardiovascular variables. Methods: DNA from 53 patients with CFS, 12-18 years old, was analysed for five single nucleotide polymorphisms (SNPs) in the genes catechol-O-methyltransferase (COMT), the β(2) -adrenergic receptor (two SNPs), the β(1) -adrenergic receptor and the α(2a) -adrenergic receptor. Frequencies were compared to a reference population constructed from the National Center for Biotechnology Information (NCBI) database, and associations between frequencies and autonomic cardiovascular responses during a 20° head-uptilt-test were explored. Results: For the COMT SNP Rs4680, patients with CFS had a higher frequency of the AA genotype and a lower frequency of the G containing genotypes (AG and GG), when compared to the reference sample (p = 0.046). Also, the AA genotype was associated with a smaller increase in LF/HF ratio (low-frequency:high-frequency heart rate variability ratio, an index of cardiac sympathovagal balance) during head-up tilt when compared to the AG/GG genotypes. For the β(2) -adrenergic receptor SNP Rs1042714, patients with CFS had a lower frequency of the GG genotype and a higher frequency of the genotypes containing C (CG and CC) (p = 0.044). Conclusions: CFS might be related to polymorphisms of COMT and the β(2) -adrenergic receptor. More details of the molecular mechanisms remain to be investigated.
Sperber AD, Dekel R.	Department of Gastroenterology, Tel-Aviv Medical Center, Tel-Aviv, Israel.	Irritable Bowel Syndrome and Co-morbid Gastrointestinal and Extra-gastrointestinal Functional Syndromes.	J Neurogastroenterol Motil. 2010 Apr;16(2):113-9. Epub 2010 Apr 27.	The irritable bowel syndrome (IBS) is the best known of the functional gastrointestinal tract disorders. Many IBS patients have at least one co-morbid somatic complaint and many meet diagnostic criteria for other functional disorders. Patients with IBS and another functional disorder, in comparison with patients with IBS only, have more severe IBS symptoms, a higher rate of psychopathology, greater impairment of quality of life, and more illness-related work absenteeism. Estimates of the prevalence of IBS in patients with fibromyalgia range from 30-35% to as high as 70%. Studies of IBS among patients with chronic fatigue syndrome have reported a prevalence ranging from 35-92%. The prevalence of IBS among patients with chronic fatigue syndrome is reported to be 14%. IBS patients with other co-morbid functional disorders appear to manifest a greater degree of somatization. It has been suggested that the presence of multiple co-morbid disorders may be a marker for psychological influences on etiology. This raises the question of whether the functional syndromes represent the same pathophysiological process, i.e., are the same entity that has been separated into different clinical entities because of medical sub-specialization, or are indeed separate disorders. While the answer to this question awaits further research, it would appear that most functional patients who meet formal diagnostic criteria for more than one functional disorder manifest one disorder clinically more that the others and seek consultation differentially for that set of symptoms.
Spitzer AR, Broadman M.	Wayne State University School of Medicine, Detroit, Michigan, USA.	A retrospective review of the sleep characteristics in patients with chronic fatigue	Pain Pract. 2010 Jul-Aug;10(4):294-300. Epub 2010 Mar 2.	This study characterizes findings on sleep testing and Human Leukocyte Antigen (HLA) markers in a group of patients with fibromyalgia (FM) and chronic fatigue syndrome (CFS). One hundred eighteen patients seen in a general neurology practice over 5 years meeting standard clinical criteria for FM or CFS were analyzed retrospectively. Cases of untreated sleep apnea or restless legs syndrome were excluded prior to inclusion in this study. Ninety-two patients had multiple sleep latency testing

	raidl@ieee.org	syndrome and fibromyalgia.		(MSLT). Seventy-three (80%) were abnormal by standard criteria. Of 57 females having positive MSLTs, 22 (39%) had one or more periods of sleep onset rapid eye movement (SOREM), and 5 of 16 (31%) males with positive MSLTs had one or more SOREM. Highly fragmented sleep, as previously described in FM, was seen but not analyzed quantitatively. HLA DQB1*0602 was obtained in 74 patients, and positive in 32 (43%), P < 0.0001 compared with published values in 228 populations. In our patients, who presented with neuromuscular fatigue or generalized pain, we found a sleep disorder characterized by objective hypersomnia. Some patients had characteristics of narcolepsy. Objective assessment by sleep studies can assist the diagnostic process, aid future research, and provide rationale for treatment.
Spitzer AR, Broadman M.	Neurology Department, Wayne State University School of Medicine, Detroit, Michigan, USA. raidl@ieee.org	Treatment of the narcoleptiform sleep disorder in chronic fatigue syndrome and fibromyalgia with sodium oxybate.	Pain Pract. 2010 Jan-Feb;10(1):54-9.	This study investigates the response of the underlying sleep disorder associated with Chronic Fatigue Syndrome (CFS) and fibromyalgia (FM) to treatment. We retrospectively reviewed 118 cases clinically consistent with CFS or FM, treated in a neurology practice. Abnormal findings on sleep studies and associated human leukocyte antigen markers, and a clinical pattern suggestive of narcolepsy, are present in a high proportion of patients. When considered appropriate based on the clinical picture and test results, treatment with sodium oxybate was offered to these patients. Sixty percent of patients treated with oxybate experienced significant relief of pain, while 75% experienced significant relief of fatigue. We postulate that the response to oxybate in CFS and FM suggests a disturbance of sleep similar to narcolepsy. These findings support this novel approach to intervention and further research. The inability to distinguish CFS and FM by testing and response to treatment suggests that they may represent variations of the same disorder or may be closely related disorders.
Staniszewska S, Crowe S, Badenoch D, Edwards C, Savage J, Norman W.	RCN Research Institute, School of Health & Social Studies University of Warwick, Coventry, UK. Sophie.Staniszewska@warwick.ac.uk	The PRIME project: developing a patient evidence-base.	Health Expect. 2010 Sep;13(3):312-22. Epub 2010 Jun 23.	BACKGROUND: The concept of evidence has become firmly rooted in health care, with most importance placed on the outcome of research in clinical and economic spheres. Much less emphasis is placed on the patient's contribution to evidence which remains relatively vague, of low status and often difficult to integrate with other forms of knowledge. AIM: This article proposes a concept of patient-based evidence, to complement clinical and economic forms of evidence, and demonstrates one way in which it has been operationalized. The PRIME project developed a patient evidence-base to capture the lived experience of individuals with myalgic encephalitis (ME) or chronic fatigue syndrome (CFS). DESIGN: Interviews were performed with 40 individuals with ME/CFS who varied in a range of demographic characteristics, including age, gender, and how severely affected individuals were. RESULTS: PRIME has developed a patient evidence-base which has an extensive array of experiences data to provide researchers, clinicians and others with an in-depth insight into the lived experience of ME/CFS that can be used and analysed. Data are grouped into a wide range of themes, which can be downloaded and used in a variety of ways as a source of evidence to enable understanding of the lived experience of ME/CFS and so contribute to the development of a more patient-focused research agenda in ME/CFS. CONCLUSIONS: While patient-based evidence used in the PRIME Project provides a useful start, further work is required to develop this area conceptually and methodologically, particularly in relation to how patient-based evidence can be considered alongside clinical and economic evidence.
Stieler K, Fischer N.	Institute for Medical	Apobec 3G efficiently reduces	PLoS One. 2010 Jul 23;5(7):e11738.	BACKGROUND: The human exogenous gammaretrovirus XMRV is thought to be implicated in prostate cancer and chronic fatigue syndrome. Besides pressing epidemiologic questions, the elucidation of the

	Microbiology, Virology and Hygiene, University Medical Center Eppendorf, Hamburg, Germany.	infectivity of the human exogenous gammaretrovirus XMRV.		tissue and cell tropism of the virus, as well as its sensitivity to retroviral restriction factors is of fundamental importance. The Apobec3 (A3) proteins, a family of cytidine deaminases, are one important group of host proteins that control primary infection and efficient viral spread. METHODOLOGY/PRINCIPAL FINDINGS: Here we demonstrate that XMRV is resistant to human Apobec 3B, 3C and 3F, while being highly susceptible to the human A3G protein, a factor which is known to confer antiviral activity against most retroviruses. We show that XMRV as well as MoMLV virions package Apobec proteins independent of their specific restriction activity. hA3G was found to be a potent inhibitor of XMRV as well as of MoMLV infectivity. In contrast to MoMLV, XMRV infection can also be partially reduced by low concentrations of mA3. Interestingly, established prostate cancer cell lines, which are highly susceptible to XMRV infection, do not or only weakly express hA3G. CONCLUSIONS: Our findings confirm and extend recently published data that show restriction of XMRV infection by hA3G. The results will be of value to explore which cells are infected with XMRV and efficiently support viral spread in vivo. Furthermore, the observation that XMRV infection can be reduced by mA3 is of interest with regard to the current natural reservoir of XMRV infection.
Stieler K, Schulz C, Lavanya M, Aepfelbacher M, Stocking C, Fischer N.	Institute for Medical Microbiology and Virology, University Medical Center Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany.	Host range and cellular tropism of the human exogenous gammaretrovirus XMRV.	Virology. 2010 Mar 30;399(1):23-30. Epub 2010 Jan 27.	Recently, the first human infection with an exogenous gammaretrovirus (XMRV) was reported. In its initial description, XMRV was confined to prostate stromal fibroblasts, although subsequent reports demonstrated XMRV protein expression in prostate epithelial cells. Most recently, XMRV has been detected in blood cells of patients with chronic fatigue syndrome. The aim of this study was to elucidate the transmission routes and tissue tropism of XMRV by comparing its host range, receptor usage and LTR functionality with other MLV isolates. We demonstrate using pseudotype experiments that XMRV Env mediates efficient infection of cells from different species. We show that replication competent XMRV infects various human cell types, including hematopoietic cell lines and prostate stromal fibroblasts. XMRV-LTR activity is significantly higher in the prostate cancer cell line LNCaP and in prostate stromal fibroblasts, compared to other cell types tested and could be one factor contributing to efficient viral spread in prostate tissue.
Stoye JP, Silverman RH, Boucher CA, Le Grice SF.		The Xenotropic Murine Leukemia Virus-Related Retrovirus Debate Continues at First International Workshop.	Retrovirology. 2010 Dec 22;7(1):113. [Epub ahead of print]	ABSTRACT: The 1st International Workshop on Xenotropic Murine Leukemia Virus-Related Retrovirus (XMRV), co-sponsored by the National Institutes of Health, The Department of Health and Human Services and Abbott Diagnostics, was convened on September 7/8 on the NIH campus, Bethesda, MD. Attracting an international audience of over 200 participants, the 2-day event combined a series of plenary talks with updates on different aspects of XMRV research, addressing basic gammaretrovirus biology, host response, association of XMRV with chronic fatigue syndrome and prostate cancer, assay development and epidemiology. The current status of XMRV research, concerns among the scientific community and suggestions for future actions are summarized in this meeting report.
Sudlow C, Macleod M, Al-Shahi Salman R, Stone J.	Division of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Edinburgh EH4	Comment on "Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue	Science. 2010 May 14;328(5980):825; author reply 825. Comment on: Science. 2009 Oct 23;326(5952):585-9.	Lombardi et al. (Reports, 23 October 2009, p. 585) reported an association between the human gammaretrovirus XMRV and chronic fatigue syndrome. However, their results may be misleading because of various potential sources of bias and confounding. If real, the association may lack generalizability because of the specific characteristics of the cases studied and could be due to reverse causality.

	2XU, UK. cathie.sudlow@ed.ac.uk	syndrome".		
Sutcliffe K, Gray J, Tan MP, Pairman J, Wilton K, Parry SW, Newton JL.	UK NIHR Biomedical Research Centre in Ageing - Cardiovascular Theme, Newcastle, UK.	Home orthostatic training in chronic fatigue syndrome--a randomized, placebo-controlled feasibility study.	Eur J Clin Invest. 2010 Jan;40(1):18-24. Epub 2009 Nov 12.	BACKGROUND: Orthostatic (Tilt)-training is an effective treatment for neurally mediated hypotension (NMH). NMH is a frequent finding in chronic fatigue syndrome (CFS). We evaluated home orthostatic training (HOT) in CFS in a randomized placebo-controlled feasibility study. METHODS: Thirty-eight patients with CFS (Fukuda Criteria) were randomly allocated to daily tilt training (n = 19) or sham training (n = 19) for 6 months. Haemodynamic responses to standing were performed in all subjects using continuous technology (Taskforce) at enrolment, week 1, 4 and 24. Symptom response and compliance were assessed using diaries. RESULTS: Two patients (one from each arm) withdrew from the study. Fourteen patients in each group complied completely or partially, and patients found the training manageable and achievable. Compared to the sham group, blood pressure while standing dropped to 8.0 mmHg less in the HOT group at 4 weeks (95% CI: 1.0 to 15.0, P = 0.03). At 4 weeks, the HOT group had higher total peripheral resistance compared to the sham group; mean difference 70.2, 95% CI: -371.4 to 511.8. Changes were maintained at 6 months. There was no significant difference in fatigue between groups at 4 weeks (mean difference 1.4, 95% CI: -13.5 to 16.2), but there was a trend towards improvement in fatigue at 6 months. Compliers had lower fatigue compared to non-compliers. CONCLUSIONS: A placebo-controlled study of HOT in CFS is feasible. HOT is well tolerated and generally complied with. A likely physiological rationale for HOT in CFS is related to reductions in orthostatic intolerance. An adequately powered study including strategies to enhance compliance is warranted.
Suárez A, Guillamó E, Roig T, Blázquez A, Alegre J, Bermúdez J, Ventura JL, García-Quintana AM, Comella A, Segura R, Javierre C.	Department of Physiological Sciences II, Medical School, University of Barcelona, L'Hospitalet, Barcelona, Spain.	Nitric oxide metabolite production during exercise in chronic fatigue syndrome: a case-control study.	J Womens Health (Larchmt). 2010 Jun;19(6):1073-7.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disabling illness of unknown etiology that is characterized by fatigue associated with a reduced ability to work, lasting for more than 6 months, and accompanied by a specific set of symptoms. The diagnosis remains difficult because of the absence of laboratory tests and is, therefore, made largely on the basis of the symptoms reported by the patient. The aim of this study was to analyze differences in blood nitrate levels in CFS patients and a matched control group after a physical exercise test. METHODS: Forty-four consecutive female patients with CFS and 25 healthy women performed an exercise test using a cycle ergometer with monitoring of cardiopulmonary response. Blood samples were obtained for biochemical analyses of glucose, lactate, and nitrates at the beginning (under resting conditions) and after the maximal and supramaximal tests. RESULTS: Plasma nitrates differed between the groups, with higher values in the CFS group ($F = 6.93$, $p = 0.003$). Nitrate concentration increased in relation to workload and reached higher values in the CFS group, the maximum difference with respect to the control group being 295% ($t = 4.88$, $p < 0.001$). CONCLUSIONS: The main result of the present study is that nitric oxide (NO) metabolites (nitrates) showed a much higher increase after a maximal physical test in CFS patients than in a group of matched subjects. This combination (exercise plus NO response evaluation) may be useful in the assessment of CFS.
Switzer WM, Jia H, Hohn O, Zheng H, Tang S, Shankar A,	Laboratory Branch, Division of HIV/AIDS	Absence of evidence of xenotropic murine	Retrovirology. 2010 Jul 1;7:57.	BACKGROUND: XMRV, a xenotropic murine leukemia virus (MuLV)-related virus, was recently identified by PCR testing in 67% of persons with chronic fatigue syndrome (CFS) and in 3.7% of healthy persons from the United States. To investigate the association of XMRV with CFS we tested blood

Bannert N, Simmons G, Hendry RM, Falkenberg VR, Reeves WC, Heneine W.	Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. bswitzer@cdc.gov	leukemia virus-related virus infection in persons with chronic fatigue syndrome and healthy controls in the United States.		specimens from 51 persons with CFS and 56 healthy persons from the US for evidence of XMRV infection by using serologic and molecular assays. Blinded PCR and serologic testing were performed at the US Centers for Disease Control and Prevention (CDC) and at two additional laboratories. RESULTS: Archived blood specimens were tested from persons with CFS defined by the 1994 international research case definition and matched healthy controls from Wichita, Kansas and metropolitan, urban, and rural Georgia populations. Serologic testing at CDC utilized a Western blot (WB) assay that showed excellent sensitivity to MuLV and XMRV polyclonal or monoclonal antibodies, and no reactivity on sera from 121 US blood donors or 26 HTLV-and HIV-infected sera. Plasma from 51 CFS cases and plasma from 53 controls were all WB negative. Additional blinded screening of the 51 cases and 53 controls at the Robert Koch Institute using an ELISA employing recombinant Gag and Env XMRV proteins identified weak seroreactivity in one CFS case and a healthy control, which was not confirmed by immunofluorescence. PCR testing at CDC employed a gag and a pol nested PCR assay with a detection threshold of 10 copies in 1 ug of human DNA. DNA specimens from 50 CFS patients and 56 controls and 41 US blood donors were all PCR-negative. Blinded testing by a second nested gag PCR assay at the Blood Systems Research Institute was also negative for DNA specimens from the 50 CFS cases and 56 controls. CONCLUSIONS: We did not find any evidence of infection with XMRV in our U.S. study population of CFS patients or healthy controls by using multiple molecular and serologic assays. These data do not support an association of XMRV with CFS.
Sánchez-Barceló EJ, Mediavilla MD, Tan DX, Reiter RJ.	Department of Physiology & Pharmacology, School of Medicine, University of Cantabria, 39011 Santander, Spain. barcelo@unican.es	Clinical uses of melatonin: evaluation of human trials.	Curr Med Chem. 2010;17(19):2070-95.	During the last 20 years, numerous clinical trials have examined the therapeutic usefulness of melatonin in different fields of medicine. The objective of this article is to review, in depth, the science regarding clinical trials performed to date. The efficacy of melatonin has been assessed as a treatment of ocular diseases, blood diseases, gastrointestinal tract diseases, cardiovascular diseases, diabetes, rheumatoid arthritis, fibromyalgia, chronic fatigue syndrome, infectious diseases, neurological diseases, sleep disturbances, aging and depression. Melatonin has been also used as a complementary treatment in anaesthesia, hemodialysis, in vitro fertilization and neonatal care. The conclusion of the current review is that the use of melatonin as an adjuvant therapy seems to be well funded for macular degeneration, glaucoma, protection of the gastric mucosa, irritable bowel syndrome, arterial hypertension, diabetes, side effects of chemotherapy and radiation in cancer patients or hemodialysis in patients with renal insufficiency and, especially, for sleep disorders of circadian etiology (jet lag, delayed sleep phase syndrome, sleep deterioration associated with aging, etc.) as well as in those related with neurological degenerative diseases (Alzheimer, etc.,) or Smith-Magenis syndrome. The utility of melatonin in anesthetic procedures has been also confirmed. More clinical studies are required to clarify whether, as the preliminary data suggest, melatonin is useful for treatment of fibromyalgia, chronic fatigue syndrome, infectious diseases, neoplasias or neonatal care. Preliminary data regarding the utility of melatonin in the treatment of ulcerative colitis, Crohn's disease, rheumatoid arthritis are either ambiguous or negative. Although in a few cases melatonin seems to aggravate some conditions, the vast majority of studies document the very low toxicity of melatonin over a wide range of doses.
Tanaka M, Watanabe Y.	Department of Physiology, Osaka	A new hypothesis of chronic fatigue	Med Hypotheses. 2010	Chronic fatigue syndrome is an illness characterized by a profound, disabling, and unexplained sensation of fatigue lasting at least 6 months, which severely impairs daily functioning and is

	City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan. masa-t@msic.med.osaka-cu.ac.jp	syndrome: co-conditioning theory.	Aug;75(2):244-9. Epub 2010 Mar 24.	accompanied by a combination of non-specific symptoms. Many potential causes of chronic fatigue syndrome have been investigated, including viral infections, immune dysfunctions, abnormal neuroendocrine responses, central nervous system abnormalities, autonomic dysfunctions, impaired exercise capacities, sleep disruptions, genetic backgrounds, psychiatric abnormalities, personality, and abnormal psychological processes. However, no etiology, specific physical signs or laboratory test abnormalities have been found. It is essential to establish a conceptual theory of chronic fatigue syndrome that can explain its pathophysiology in order to identify the clinical entity and to develop effective treatment methods. In this article, a new conceptual hypothesis about the pathophysiology of chronic fatigue syndrome, the co-conditioning theory, is presented: after repetitive overwork and/or stress, alarm signal to rest and fatigue sensation may cause in response to an unconditioned stimulus (impaired homeostasis and function) that has been paired with a conditioned stimulus (overwork and/or stress). In the future, a new treatment strategy for patients with chronic fatigue syndrome, re-co-conditioning therapy, may be developed on the basis of the co-conditioning theory. In addition, this theory will likely contribute to a better understanding of the pathophysiology of chronic fatigue syndrome.
Tang S, Zhao J, Viswanath R, Nyambi PN, Redd AD, Dastyar A, Spacek LA, Quinn TC, Wang X, Wood O, Gaddam D, Devadas K, Hewlett IK.	From the Laboratory of Molecular Virology, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland; the Department of Pathology, New York University School of Medicine, New York, New York; and the Division of Intramural Research, NIAID, NIH, Johns Hopkins University School of Medicine, Baltimore, Maryland.	Absence of detectable xenotropic murine leukemia virus-related virus in plasma or peripheral blood mononuclear cells of human immunodeficiency virus Type 1-infected blood donors or individuals in Africa.	Transfusion. 2010 Nov 15. doi: 10.1111/j.1537-2995.2010.02932.x. [Epub ahead of print]	BACKGROUND: Since the identification of xenotropic murine leukemia virus-related virus (XMRV) in prostate cancer patients in 2006 and in chronic fatigue syndrome patients in 2009, conflicting findings have been reported regarding its etiologic role in human diseases and prevalence in general populations. In this study, we screened both plasma and peripheral blood mononuclear cells (PBMNCs) collected in Africa from blood donors and human immunodeficiency virus Type 1 (HIV-1)-infected individuals to gain evidence of XMRV infection in this geographic region. STUDY DESIGN AND METHODS: A total of 199 plasma samples, 19 PBMNC samples, and 50 culture supernatants from PBMNCs of blood donors from Cameroon found to be infected with HIV-1 and HIV-1 patients from Uganda were screened for XMRV infection using a sensitive nested polymerase chain reaction (PCR) or reverse transcription (RT)-PCR assay. RESULTS: Using highly sensitive nested PCR or RT-PCR and real-time PCR assays capable of detecting at least 10 copies of XMRV plasmid DNA per reaction, none of the 268 samples tested were found to be XMRV DNA or RNA positive. CONCLUSIONS: Our results failed to demonstrate the presence of XMRV infection in African blood donors or individuals infected with HIV-1. More studies are needed to understand the prevalence, epidemiology, and geographic distribution of XMRV infection worldwide.

The GK, Bleijenberg G, Buitelaar JK, van der Meer JW.	Radboud University Nijmegen Medical Centre, Department of Psychiatry, 966, Reinier Postlaan 10, 6525 GC Nijmegen, The Netherlands. g.the@aig.umcn.nl	The effect of ondansetron, a 5-HT3 receptor antagonist, in chronic fatigue syndrome: a randomized controlled trial.	J Clin Psychiatry. 2010 May;71(5):528-33. Epub 2010 Jan 26.	BACKGROUND: Accumulating data support the involvement of the serotonin (5-hydroxytryptamine [5-HT]) system in the pathophysiology of chronic fatigue syndrome. Neuropharmacologic studies point to a hyperactive 5-HT system, and open-label treatment studies with 5-HT(3) receptor antagonists have shown promising results. In this randomized controlled clinical trial, the effect of ondansetron, a 5-HT(3) receptor antagonist, was assessed on fatigue severity and functional impairment in adult patients with chronic fatigue syndrome. METHOD: A randomized, placebo-controlled, double-blind clinical trial was conducted at Radboud University Nijmegen Medical Centre, The Netherlands. Sixty-seven adult patients who fulfilled the US Centers for Disease Control and Prevention (CDC) criteria for chronic fatigue syndrome and who were free from current psychiatric comorbidity participated in the clinical trial. Participants received either ondansetron 16 mg per day or placebo for 10 weeks. The primary outcome variables were fatigue severity (Checklist Individual Strength fatigue severity subscale [CIS-fatigue]) and functional impairment (Sickness Impact Profile-8 [SIP-8]). The effect of ondansetron was assessed by analysis of covariance. Data were analyzed on an intention-to-treat basis. All patients were recruited between June 2003 and March 2006. RESULTS: Thirty-three patients were allocated to the ondansetron condition, 34 to the placebo condition. The 2 groups were well matched in terms of age, sex, fatigue severity, functional impairment, and CDC symptoms. Analysis of covariance showed no significant differences between the ondansetron- and placebo-treated groups during the 10-week treatment period in fatigue severity and functional impairment. CONCLUSIONS: This clinical trial demonstrates no benefit of ondansetron compared to placebo in the treatment of chronic fatigue syndrome. TRIAL REGISTRATION: www.trialregister.nl: ISRCTN02536681.
Thomas PW, Thomas S, Kersten P, Jones R, Nock A, Slingsby V, Green C, Baker R, Galvin K, Hillier C.	Dorset Research and Development Support Unit, Poole Hospital NHS Foundation Trust, Poole, Dorset, UK.	Multi-centre parallel arm randomised controlled trial to assess the effectiveness and cost-effectiveness of a group-based cognitive behavioural approach to managing fatigue in people with multiple sclerosis.	BMC Neurol. 2010 Jun 16;10:43.	BACKGROUND: Fatigue is one of the most commonly reported and debilitating symptoms of multiple sclerosis (MS); approximately two-thirds of people with MS consider it to be one of their three most troubling symptoms. It may limit or prevent participation in everyday activities, work, leisure, and social pursuits, reduce psychological well-being and is one of the key precipitants of early retirement. Energy effectiveness approaches have been shown to be effective in reducing MS-fatigue, increasing self-efficacy and improving quality of life. Cognitive behavioural approaches have been found to be effective for managing fatigue in other conditions, such as chronic fatigue syndrome, and more recently, in MS. The aim of this pragmatic trial is to evaluate the clinical and cost-effectiveness of a recently developed group-based fatigue management intervention (that blends cognitive behavioural and energy effectiveness approaches) compared with current local practice. METHODS/DESIGN: This is a multi-centre parallel arm block-randomised controlled trial (RCT) of a six session group-based fatigue management intervention, delivered by health professionals, compared with current local practice. 180 consenting adults with a confirmed diagnosis of MS and significant fatigue levels, recruited via secondary/primary care or newsletters/websites, will be randomised to receive the fatigue management intervention or current local practice. An economic evaluation will be undertaken alongside the trial. Primary outcomes are fatigue severity, self-efficacy and disease-specific quality of life. Secondary outcomes include fatigue impact, general quality of life, mood, activity patterns, and cost-effectiveness. Outcomes in those receiving the fatigue management intervention will be measured 1 week prior to, and 1, 4, and 12 months after the intervention (and at equivalent times in those receiving current local practice). A qualitative component will examine what

				aspects of the fatigue management intervention participants found helpful/unhelpful and barriers to change. DISCUSSION: This trial is the fourth stage of a research programme that has followed the Medical Research Council guidance for developing and evaluating complex interventions. What makes the intervention unique is that it blends cognitive behavioural and energy effectiveness approaches. A potential strength of the intervention is that it could be integrated into existing service delivery models as it has been designed to be delivered by staff already working with people with MS. Service users will be involved throughout this research. TRIAL REGISTRATION: Current Controlled Trials ISRCTN76517470.
Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, Stein MR, Drexler E, Martin VT, Hutchinson S, Aurora SK, Recober A, Herial NA, Utley C, White L, Khuder SA.	University of Toledo College of Medicine, Toledo, OH, USA.	Childhood maltreatment and migraine (part III). Association with comorbid pain conditions.	Headache. 2010 Jan;50(1):42-51. Epub 2009 Oct 21.	OBJECTIVE: To evaluate in a headache clinic population the relationship of childhood maltreatment on the prevalence of pain conditions comorbid with migraine. BACKGROUND: Childhood maltreatment is highly prevalent and has been frequently associated with recurrent headache. The relationship of maltreatment and pain has, however, been a subject of some debate. METHODS: Cross-sectional data on self-reported physician-diagnosed pain conditions were electronically collected from persons with migraine (diagnosed according to International Classification of Headache Disorders-2), seeking treatment in headache clinics at 11 centers across the US and Canada. These included irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), fibromyalgia (FM), interstitial cystitis (IC), arthritis, endometriosis, and uterine fibroids. Other information included demographics, migraine characteristics (frequency, headache-related disability), remote and current depression (The Patient Health Questionnaire-9), and remote and current anxiety (The Beck Anxiety Inventory). Patients also completed the Childhood Trauma Questionnaire regarding sexual, emotional, and physical abuse, and emotional and physical neglect under the age of 18 years old. Statistical analyses accounted for the survey design and appropriate procedures in SAS such as surveymeans, surveyfreq, and surveylogistic were applied to the weighted data. RESULTS: A total of 1348 migraineurs (88% women) were included in this study (mean age 41 years). Based on physician diagnosis or validated criteria, 31% had IBS, 16% had CFS, and 10% had FM. Diagnosis of IC was reported by 6.5%, arthritis by 25%, and in women, endometriosis was reported by 15% and uterine fibroids by 14%. At least 1 comorbid pain condition was reported by 61%, 2 conditions by 18%, and 3 or more by 13%. Childhood maltreatment was reported by 58% of the patients. Emotional abuse was associated with increased prevalence of IBS, CFS, arthritis, and physical neglect with arthritis. In women, physical abuse was associated with endometriosis and physical neglect with uterine fibroids. Emotional abuse, and physical abuse and neglect ($P < .0001$ for all) were also associated with increased total number of comorbid conditions. In ordinal logistic regression models, adjusted for sociodemographics and current depression (prevalence 28%) and anxiety (prevalence 56%), emotional abuse (odds ratios [OR] = 1.69, 95% confidence intervals [CI]: 1.224-2.33) and physical neglect (OR = 1.73, 95% CI: 1.22-2.46) were independently associated with an increased number of pain conditions. The cohort of women, similarly, had associations of emotional abuse (OR = 1.94, 95% CI: 1.40-2.72) and physical neglect (OR = 1.90, 95% CI: 1.34-2.68) with an increased number of pain comorbidities. CONCLUSION: The association of childhood maltreatment and pain was stronger in those reporting multiple pain conditions and multiple maltreatment types. This finding suggests that in migraineurs childhood maltreatment may be a risk factor for development of comorbid pain disorders.

Toft M, Bendixen A, Hansen R, Hemdorff S, Egeriis E.		[Should fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity be treated in psychiatric services? 3]. [Article in Danish]	Ugeskr Laeger. 2010 Oct 25;172(43):2977; author reply 2977.	
Toft M.		[Should fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity be treated in psychiatric services?]. [Article in Danish]	Ugeskr Laeger. 2010 Aug 23;172(34):2327; author reply 2327. Comment on: Ugeskr Laeger. 2010 Jun 14;172(24):1835-8.	
Togo F, Natelson BH, Cherniack NS, Klapholz M, Rapoport DM, Cook DB.	Pain & Fatigue Study Center, Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark, NJ 07103, USA.	Sleep is not disrupted by exercise in patients with chronic fatigue syndromes.	Med Sci Sports Exerc. 2010 Jan;42(1):16-22.	PURPOSE: Patients with chronic fatigue syndrome (CFS) report that exertion produces dramatic symptom worsening. We hypothesized this might be due to the exacerbation of an underlying sleep disorder, which we have previously demonstrated to exist. METHODS: Female patients with CFS and matched healthy controls with no evidence of major depressive disorder were studied with overnight polysomnography on a baseline night and on a night after their performance of a maximal exercise test. RESULTS: CFS patients as a group had evidence for disturbed sleep compared with controls. Although exercise improved sleep for healthy subjects, it did not do this for the group as a whole. When we stratified the sample on the basis of self-reported sleepiness after a night's sleep, the patient group with reduced morning sleepiness showed improvement in sleep structure, whereas those with increased morning sleepiness continued to show evidence for sleep disruption. CONCLUSIONS: Sleep is disturbed in CFS patients as a group, but exercise does not exacerbate this sleep disturbance. Approximately half the patients studied actually sleep better after exercise. Therefore, activity-related symptom worsening is not caused by worsened sleep.
Toms C, Robson-Ansley P, St Clair Gibson A.		Chronic fatigue syndrome: a hormonal origin? A rare case of dysmenorrhoea membranacea-alternative	Arch Gynecol Obstet. 2010 Oct;282(4):467-8. Epub 2010 Apr 3.	

		pathology.		
Toussaint L, Overvold-Ronningen M, Vincent A, Luedtke C, Whipple M, Schriever T, Luskin F.	Department of Psychology, Luther College, Decorah, Iowa 52101, USA. touslo01@luther.edu	Implications of forgiveness enhancement in patients with fibromyalgia and chronic fatigue syndrome.	J Health Care Chaplain. 2010 Jul;16(3-4):123-39.	The purpose of this review is to examine forgiveness as a means to enhance coping with the emotional sequelae of two disorders, fibromyalgia and chronic fatigue. As with many chronic illnesses, fibromyalgia and chronic fatigue often result in a host of negative emotions including, anger, stress, fear, and depression. We contend that learning to become more forgiving may be a complementary treatment to cope with the ongoing stress, frustration, and negative emotions that result from these two conditions. Our review includes descriptive information on fibromyalgia and chronic fatigue, a brief review of the literature on anger and its influence on health, a review of the connections between forgiveness and well-being, and methods to enhance forgiveness in patients' lives. We conclude with a conceptual model that we hope will be useful to design and/or evaluate work on forgiveness in these patients.
Tovbushenko MP, Merkulova GA, Anashkin VV, Vagaĭtseva EA.		[Effectiveness of medical rehabilitation in patients with chronic fatigue syndrome at a health resort]. [Article in Russian]	Vopr Kurortol Fizioter Lech Fiz Kult. 2010 Mar-Apr;(2):16-8.	The possibility to apply natural medicinal factors of a spa-and-resort facility along with targeted physiotherapeutic exposure (succinic acid electrophoresis, reflexo-segmental peloidotherapy) and polyoxidonium injections was evaluated. The study demonstrated high effectiveness of the proposed approach to medical rehabilitation of patients with chronic fatigue syndrome.
Tummers M, Knoop H, Bleijenberg G.	Radboud University Nijmegen Medical Centre, Expert Centre for Chronic Fatigue, 4628, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. m.tummers@nkcv.umcn.nl	Effectiveness of stepped care for chronic fatigue syndrome: a randomized noninferiority trial.	J Consult Clin Psychol. 2010 Oct;78(5):724-31.	OBJECTIVE: In this randomized noninferiority study, the effectiveness and efficiency of stepped care for chronic fatigue syndrome (CFS) was compared to care as usual. Stepped care was formed by guided self-instruction, followed by cognitive behavior therapy (CBT) if the patient desired it. Care as usual encompassed CBT after a waiting period. METHOD: A total of 171 CFS patients were randomly allocated to stepped care or care as usual. Patients in both conditions were assessed 3 times: at baseline, after guided self-instruction or the waiting period, and after CBT. The primary outcome variables were fatigue severity (Checklist Individual Strength) and disabilities (Sickness Impact Profile and Medical Outcomes Survey Short Form-36). RESULTS: An intention to treat analysis showed that stepped care (N = 84) for CFS is noninferior to care as usual (N = 85). Both conditions were equivalent in reducing fatigue severity, reducing disabilities, and increasing physical functioning. The treatment results of both conditions were in accordance with those of previous randomized controlled trials testing the effectiveness of CBT for CFS. The total therapist time needed to treat a patient was significantly less in the stepped care condition. CONCLUSIONS: Stepped care is as effective as CBT and is more time efficient for the therapist.
Twisk FN, Arnoldus RJ, Maes M.		Letter to the Editor: Plausible explanations for neurocognitive deficits in ME/CFS, aggravation of neurocognitive	Psychol Med. 2010 Jul;40(7):1230-1. Epub 2010 Apr 12. Comment on: Psychol Med. 2010 Aug;40(8):1253-67.	

		impairment induced by exertion.		
Tyne HL, Taylor J, Baker GA, Steiger MJ.	Department of Neurological Sciences, University of Liverpool, The Walton Centre for Neurology and Neurosurgery, Lower Lane, Liverpool, L9 7LJ, UK. htyne@ukonline.co.uk	Modafinil for Parkinson's disease fatigue.	J Neurol. 2010 Mar;257(3):452-6. Epub 2009 Oct 20.	Fatigue is common in Parkinson's disease (PD), occurring in up to 42% of patients (2). There is no recognized treatment. This is a study of modafinil for Parkinson's disease related fatigue. Ethical approval was given. Patients with idiopathic PD were recruited from a Movement Disorders clinic. Those with depression, dementia, and other causes for fatigue were excluded. Patients were assessed using the Fatigue Severity Scale (FSS), Hospital Anxiety and Depression Scale (HADS), self-rating of improvement, Epworth Sleepiness Scale (ESS), and UPDRS. Modafinil was titrated up over 4 weeks to maximum of 400 mg/day. There followed a 5 week maintenance phase before reassessment. Thirteen patients participated. No significant change was seen in any safety measure. The FSS did not change significantly, however those on modafinil rated an improvement in their fatigue compared to placebo. The Modafinil group had a statistically significant improvement on ESS ($p < 0.05$). This is a small study of modafinil in selected PD patients. There is a suggestion of improvement on the global clinical impression scale for fatigue, but no significant change on FSS. A larger study is needed to further evaluate this drug in PD fatigue. This study highlights the problems with recruitment when trialing treatments of non-motor symptoms in PD. A significant improvement in EDS was seen.
Ulas UH, Chelimsky TC, Chelimsky G, Mandawat A, McNeeley K, Alshekhlee A.	Autonomic Laboratory, Neurological Institute, University Hospitals Case Medical Center, Case Western Reserve University, Cleveland, OH 44106-5040, USA. Umit.Ulas@uhhospitals.org	Comorbid health conditions in women with syncope.	Clin Auton Res. 2010 Aug;20(4):223-7. Epub 2010 May 11.	OBJECTIVE: We determine the comorbid conditions associated with syncope in women. In addition, we hypothesize a higher proportion of autonomic comorbid conditions during the female reproductive age. METHODS: We identified a cohort of patients admitted to US hospitals with the principal diagnosis of syncope. We compare patient demographics stratified by gender as well as syncope associated comorbidities. We compared these comorbidities in female of reproductive age (15-45) to men as control. RESULTS: From a total sample of 305,932, females constituted 56.7% (n = 173,434). Females were slightly older (mean age 70.9 +/- 17.9 vs. 66.7 +/- 17.3; $P < 0.0001$); with similar racial distribution (white 57.8 vs. 57.5%), and similar length of hospital stay (mean 2.66 +/- 2.63 vs. 2.68 +/- 2.72 days; $P > 0.05$). Females had higher proportion of migraine (1.65 vs. 1.29%; odds ratio 'OR' 1.29; 95% confidence interval 'CI' 1.21, 1.36); chronic fatigue syndrome (1.73 vs. 1.3%; OR 1.32; 95% CI 1.25, 1.4); gastroparesis (0.2 vs. 0.12%; OR 1.64; 95% CI 1.35, 1.98); interstitial cystitis (0.07 vs. 0.01%; OR 7.44; 95% CI 4.10, 13.5); and postural tachycardia syndrome (0.49 vs. 0.44%; OR 1.1; 95% CI 1.001, 1.23). Orthostatic hypotension was not different between the groups ($P = 0.24$). When the sample was stratified by age category, the odds ratio for gastroparesis, orthostatic hypotension, and postural tachycardia syndrome was increased ($P < 0.05$). INTERPRETATION: A higher proportion of autonomic dysfunction was present in women compared to men. In addition, these comorbid autonomic conditions were especially prominent during the female reproductive age.
Ursini F, Succurro E, Grembiale A, Gagliardi DA, Arturi F.	Dipartimento di Medicina Interna Unità di Medicina Sperimentale e Clinica dell'Università di	[The HPA axis in the pathogenesis of chronic fatigue syndrome]. [Article in Italian]	Clin Ter. 2010 Sep-Oct;161(5):461-4.	Chronic fatigue syndrome (CFS) is a clinical syndrome characterized by profound disabling chronic fatigue associated with a wide array of other physical symptoms. Its etiology is currently unknown. Among the various hypotheses, considerable interest has been placed in the hypothalamus-pituitary-adrenal axis as a possible target of the pathogenesis of CFS. This article reviews the available scientific evidence about a role of hypothalamic-pituitary-adrenal axis in the pathogenesis of chronic fatigue syndrome.

	Catanzaro Magna Graecia, Catanzaro, Italia. francesco.ursini@yahoo.it			
Vallings R.	Howick Health and Medical Clinic, 140 North Road, R.D.2, Papakura 2582, New Zealand. vallings@xtra.co.nz	A case of chronic fatigue syndrome triggered by influenza H1N1 (swine influenza).	J Clin Pathol. 2010 Feb;63(2):184-5. Epub 2009 Oct 26.	This case report describes an adolescent boy who was diagnosed as suffering from chronic fatigue syndrome 5 months after infection with H1N1 influenza.
van der Meer JW, Netea MG, Galama JM, van Kuppeveld FJ.	Department of Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands. j.vandermeer@aig.umcn.nl	Comment on "Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome".	Science. 2010 May 14;328(5980):825; author reply 825. Comment on: Science. 2009 Oct 23;326(5952):585-9.	Lombardi et al. (Reports, 23 October 2009, p. 585) reported detection of the human gammaretrovirus XMRV in the blood cells of patients with chronic fatigue syndrome (CFS). However, the patient description provided was incomplete. The inclusion of patients from a "CFS outbreak" previously linked with a viral infection, without confirmation in sporadic CFS cases, casts doubt on the role of XMRV in the pathogenesis of CFS.
van Geelen SM, Bakker RJ, Kuis W, van de Putte EM.	Department of Pediatrics, University Medical Center Utrecht, Lundlaan 6, Utrecht, the Netherlands. s.m.vangeelen@umcutrecht.nl	Adolescent chronic fatigue syndrome: a follow-up study.	Arch Pediatr Adolesc Med. 2010 Sep;164(9):810-4.	OBJECTIVE: To describe the symptomatic and educational long-term outcomes, health care use, and risk factors of nonrecovery in adolescent chronic fatigue syndrome (CFS). DESIGN: Follow-up study. SETTING: Academic pediatric hospital. PARTICIPANTS: Sixty adolescents with CFS. INTERVENTIONS: Regular care. OUTCOME MEASURES: The Checklist Individual Strength, Child Health Questionnaire, and a general questionnaire regarding further symptoms, school attendance, work attendance, and treatment. RESULTS: Complete measurements were returned for 54 adolescents (90%). At initial assessment, their mean (SD) age was 16.0 (1.5) years and 20.4% were male. The mean follow-up duration was 2.2 years. At follow-up, the mean (SD) age was 18.2 (1.5) years; 28 adolescents (51.9%) had nearly complete improvement of symptoms but 26 (48.1%) did not experience improvement. Adolescents who attended school (n = 41) had missed an average of 33% of classes during the last month. The rest (n = 13) had worked an average of 38.7% of a full-time job during the last month. A total of 66.7% of subjects were treated by a physiotherapist, 38.9% were clinically treated in rehabilitation, 48.1% had received psychological support, and 53.7% had used alternative treatment. CONCLUSIONS: About half of the adolescents had recovered from CFS at follow-up. The other half was still severely fatigued and physically impaired. Health care use had been high, and school and work attendance were low. Older age at inclusion was a risk factor, and pain, poor mental health, self-esteem, and general health perception at outcome were associated with an unfavorable outcome. Future research should focus on customizing existing treatment and studying additional treatment options.
van Geelen SM,	Division of	Self-investigation	Patient Educ	OBJECTIVE: A small-scale intervention study into narrative self-investigation in adolescent chronic

Fuchs CE, Sinnema G, van de Putte EM, van Geel R, Hermans HJ, Kuis W.	Pediatric Psychology, University Medical Center Utrecht, Utrecht, The Netherlands.	in adolescent chronic fatigue syndrome: Narrative changes and health improvement.	Couns. 2010 Jun 23. [Epub ahead of print]	fatigue syndrome (CFS). METHOD: The self-confrontation method (SCM) is an instrument to assess and change personal life stories. Forty-two adolescents diagnosed with CFS were included and randomly assigned to either 6 or 12 sessions with the SCM. Twenty-five healthy adolescents were assigned to 6 sessions. Outcome was measured directly after the self-investigation procedure at 4 months. Follow-up measurements were made 10 months later. The Checklist Individual Strength and the Child Health Questionnaire were used to measure changes in fatigue, physical and psychosocial functioning. RESULTS: Self-investigation resulted in significant changes in participants' narratives. Moreover, after self-investigation there was a significant improvement in fatigue, physical and psychosocial functioning for the adolescents with CFS. The patients who completed 12 sessions improved most. At follow-up, the positive effects were maintained. CONCLUSION: Self-investigation enables a move beyond the symptoms of CFS in an individualized, patient centered way. Narrative transformation seems to contribute to improved physical and psychosocial outcome in adolescent CFS. PRACTICE IMPLICATIONS: The SCM allows adolescents to discover (for themselves) factors that might cause or perpetuate their fatigue. The results suggest that self-investigation is a useful instrument in the management of adolescent CFS.
van Hoogmoed D, Fransen J, Bleijenberg G, van Riel P.	Nijmegen Expert Centre of Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. d.vanhoogmoed@reuma.umcn.nl	Physical and psychosocial correlates of severe fatigue in rheumatoid arthritis.	Rheumatology (Oxford). 2010 Jul;49(7):1294-302. Epub 2010 Mar 29.	OBJECTIVES: Fatigue is a frequently experienced and patient-relevant complaint in RA. Disease activity, anaemia and pain are regarded as disease-related factors that may lead to fatigue in RA. However, psychosocial factors may also play a role in maintaining severe fatigue. The objectives of this study were to determine the prevalence of severe fatigue in RA patients, to study patient perceptions of fatigue and to determine which disease-related factors and psychosocial factors are independently associated with fatigue severity. METHODS: For this study consecutive RA outpatients were enrolled (n = 228). The patients filled out questionnaires regarding fatigue using the Checklist Individual Strength (CIS), including psychosocial factors, pain and disability. The clinical data that were collected included ESR, CRP, haemoglobin level and 28-joint disease activity score (DAS-28). Chunk-wise backward linear regression was used for analysis. RESULTS: Severe fatigue (CIS > or = 35) was experienced by 42% of the RA patients, and they perceived their fatigue as frustrating or exhausting. The severely fatigued RA patients scored worse on all measured psychosocial items, compared with patients without severe fatigue. Pain severity, role functioning, depressive mood, self-efficacy on fatigue, worrying, helplessness and non-restorative sleep were the factors most strongly associated with fatigue level. CONCLUSIONS: A considerable proportion of RA patients had severe fatigue, with fatigue levels similar to chronic fatigue syndrome. Fatigue in RA was related to pain and functioning, not inflammation, as disease-related factors and to several psychosocial factors including coping and cognitions concerning fatigue.
Van Houdenhove B, Kempke S, Luyten P.	Dienst Liaisonpsychiatrie, UZ Leuven, Herestraat 49, Leuven 3000, Belgium. boudewijn.vanhou	Psychiatric aspects of chronic fatigue syndrome and fibromyalgia.	Curr Psychiatry Rep. 2010 Jun;12(3):208-14.	Chronic fatigue syndrome and/or fibromyalgia (CFS/FM) consists of highly overlapping, medically unexplained symptoms, including long-lasting fatigue, effort intolerance, cognitive dysfunction, and widespread pain and tenderness. CFS/FM often seems to be triggered by infections and physical trauma, but depression, sleep disturbances, and personality may also be involved. Moreover, dysregulation of the stress system, the immune system, and central pain mechanisms may determine the pathophysiology of the illness, leading to a loss of capacity to adapt to all kind of stressors. CFS/FM patients can be best helped by a pragmatic and individualized approach aimed at adjusting

	denhove@uz.kuleuven.ac.be			lifestyle and optimizing self-care, which in the long run may contribute to a restoration of physical and mental adaptability. Future psychiatric research into CFS/FM should focus on the complex interrelationships among pain/fatigue, stress/depression, and personality, as well as on processes of therapeutic change and the advantages of customized treatment.
Van Houdenhove B, Luyten P.		Chronic fatigue syndrome reflects loss of adaptability.	J Intern Med. 2010 Sep;268(3):249-51. Comment on: J Intern Med. 2010 Sep;268(3):265-78.	
Van Houdenhove B, Pae CU, Luyten P.	University Hospitals Leuven and Chronic Fatigue Reference Centre, UZ Leuven, Herestraat 49, B-3000 Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Chronic fatigue syndrome: is there a role for non-antidepressant pharmacotherapy?	Expert Opin Pharmacother. 2010 Feb;11(2):215-23.	IMPORTANCE OF THE FIELD: Chronic fatigue syndrome (CFS) is a prevalent but poorly understood condition mainly characterized by debilitating, persistent or recurrent fatigue; increased physical and mental fatigability; cognitive impairment and widespread musculoskeletal pain. Despite intensive treatment research, the role of pharmacotherapy in the illness remains uncertain. AREAS COVERED IN THIS REVIEW: An updated review is given of pharmacotherapy in CFS, with a focus on non-antidepressant, controlled drug trials performed between 1988 and August 2009. WHAT THE READER WILL GAIN: Antiviral, immunological and antibiotic therapies, although sometimes associated with symptom amelioration, can be more harmful than beneficial in CFS. Stimulants seem to benefit some CFS patients but their long-term effects is uncertain. Although antidepressants are not curative for the illness, they might be useful for some symptomatic aspects and co-morbid anxiety and depression. There is little or no evidence that CFS patients benefit from other pharmacological agents (e.g., steroids) or from dietary supplements and complementary medicine products. Future research into treatment should take specific subgroups into account and should target immunological aspects of the illness as well as the complex relationships between CFS, stress and depression. TAKE HOME MESSAGE: Pharmacotherapy can currently not be considered first-line treatment in CFS and should always be used in a context of self-management and rehabilitation.
van Kuppeveld FJ, de Jong AS, Lanke KH, Verhaegh GW, Melchers WJ, Swanink CM, Bleijenberg G, Netea MG, Galama JM, van der Meer JW.	Department of Medical Microbiology, Radboud University Nijmegen Medical Centre, 6500 HB Nijmegen, Netherlands. f.vankuppeveld@ncmls.ru.nl	Prevalence of xenotropic murine leukaemia virus-related virus in patients with chronic fatigue syndrome in the Netherlands: retrospective analysis of samples from an established cohort.	BMJ. 2010 Feb 25;340:c1018. doi: 10.1136/bmj.c1018. Comment in: BMJ. 2010;340:c1099.	OBJECTIVE: The presence of the retrovirus xenotropic murine leukaemia virus-related virus (XMRV) has been reported in peripheral blood mononuclear cells of patients with chronic fatigue syndrome. Considering the potentially great medical and social relevance of such a discovery, we investigated whether this finding could be confirmed in an independent European cohort of patients with chronic fatigue syndrome. DESIGN: Analysis of a well defined cohort of patients and matched neighbourhood controls by polymerase chain reaction. SETTING: Certified (ISO 15189) laboratory of clinical virology in a university hospital in the Netherlands. Population Between December 1991 and April 1992, peripheral blood mononuclear cells were isolated from 76 patients and 69 matched neighbourhood controls. In this study we tested cells from 32 patients and 43 controls from whom original cryopreserved phials were still available. MAIN OUTCOME MEASURES: Detection of XMRV in peripheral blood mononuclear cells by real time polymerase chain reaction assay targeting the XMRV integrase gene and/or a nested polymerase chain reaction assay targeting the XMRV gag gene. RESULTS: We detected no XMRV sequences in any of the patients or controls in either of the assays, in which relevant positive and negative isolation controls and polymerase chain reaction controls were included. Spiking experiments showed that we were able to detect at least 10 copies of XMRV

				sequences per 10(5) peripheral blood mononuclear cells by real time as well as by nested polymerase chain reaction, demonstrating high sensitivity of both assays. CONCLUSIONS: This study failed to show the presence of XMRV in peripheral blood mononuclear cells of patients with chronic fatigue syndrome from a Dutch cohort. These data cast doubt on the claim that XMRV is associated with chronic fatigue syndrome in the majority of patients.
van Luijtelaar G, Verbraak M, van den Bunt M, Keijsers G, Arns M.	Radboud University Nijmegen, PO Box 9104, 6500 HE, Nijmegen, The Netherlands. g.vanluijtelaar@donders.ru.nl	EEG findings in burnout patients.	J Neuropsychiatry Clin Neurosci. 2010 Spring;22(2):208-17.	The concept of burnout remains enigmatic since it is only determined by behavioral characteristics. Moreover, the differential diagnosis with depression and chronic fatigue syndrome is difficult. EEG-related variables in 13 patients diagnosed with burnout syndrome were compared with 13 healthy comparison subjects in order to explore the existence of neurobiological markers for burnout. Burnout patients showed reduced P300 amplitude, a lower alpha peak frequency and reduced beta power. These EEG-related differences in burnout patients differ from those described in the literature in depression and chronic fatigue patients. Our preliminary findings suggest that burnout might be considered as a separate clinical syndrome.
Van Oosterwijck J, Nijs J, Meeus M, Lefever I, Huybrechts L, Lambrecht L, Paul L.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit Brussel, Belgium.	Pain inhibition and postexertional malaise in myalgic encephalomyelitis/ chronic fatigue syndrome: an experimental study.	J Intern Med. 2010 Sep;268(3):265-78. Epub 2010 Mar 3. Comment in: J Intern Med. 2010 Sep;268(3):249-51.	OBJECTIVES: To examine the efficacy of the pain inhibitory systems in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) during two different types of exercise and to examine whether the (mal)functioning of pain inhibitory systems is associated with symptom increases following exercise. DESIGN: A controlled experimental study. SETTING AND SUBJECTS: Twenty-two women with ME/CFS and 22 healthy sedentary controls were studied at the Department of Human Physiology, Vrije Universiteit Brussel. INTERVENTIONS: All subjects performed a submaximal exercise test and a self-paced, physiologically limited exercise test on a cycle ergometer. The exercise tests were undertaken with continuous cardiorespiratory monitoring. Before and after the exercise bouts, subjects filled out questionnaires to assess health status, and underwent pressure pain threshold measurements. Throughout the study, subjects' activity levels were assessed using accelerometry. RESULTS: In patients with ME/CFS, pain thresholds decreased following both types of exercise, whereas they increased in healthy subjects. This was accompanied by a worsening of the ME/CFS symptom complex post-exercise. Decreased pressure thresholds during submaximal exercise were associated with postexertional fatigue in the ME/CFS group ($r = 0.454$; $P = 0.034$). CONCLUSIONS: These observations indicate the presence of abnormal central pain processing during exercise in patients with ME/CFS and demonstrate that both submaximal exercise and self-paced, physiologically limited exercise trigger postexertional malaise in these patients. Further study is required to identify specific modes and intensity of exercise that can be performed in people with ME/CFS without exacerbating symptoms.
van't Leven M, Zielhuis GA, van der Meer JW, Verbeek AL, Bleijenberg G.	Department of Epidemiology, Biostatistics and HTA, Radboud University Nijmegen Medical Centre, the Netherlands.	Fatigue and chronic fatigue syndrome-like complaints in the general population.	Eur J Public Health. 2010 Jun;20(3):251-7. Epub 2009 Aug 18.	BACKGROUND: Most knowledge on chronic fatigue (CF) and chronic fatigue syndrome (CFS) is based on clinical studies, not representative of the general population. This study aimed to assess the prevalence of fatigue in an adult general population and to identify associations with lifestyle factors. METHODS: Total 22,500 residents of Nijmegen were selected at random and interviewed by questionnaire. Data on 9062 respondents (43% response) were analysed, taken into account age, gender and concomitant disease. Subjects were classified into four groups: not fatigued (NF, reference group), short-term fatigue (SF, <6 months), chronic fatigue (CF, >or=6 months) and CFS-like fatigue (in accordance with the Center for Disease Control criteria for CFS, without clinical confirmation).

				RESULTS: Our study population showed the following breakdown: NF 64.4% (95% CI 63.6-65.6%), SF 4.9% (95% CI 4.5-5.4%), CF 30.5% (95% CI 29.5-31.4%) and CFS-like fatigue 1.0% (95% CI 0.8-1.2%). Compared with the NF group, more of the CFS respondents were female [odds ratio (OR) = 1.9], obese (OR = 4.1), using analgesics (OR = 7.8), had a low alcohol intake (OR = 0.4), were eating less healthy food (OR = 0.5) and were physically less active (OR = 0.1). These associations largely applied to the SF and CF group. The fatigue could have been due to a concomitant disease in 34 and 55.5% of the SF and CF cases, respectively. CONCLUSION: The prevalence of CF in the general population appears to be much higher than previously indicated. Even with strict criteria for CFS, it is estimated that approximately 1% of the adult population experiences this condition. Interestingly, a large part of this group remains unrecognized by the general practitioner. A striking similarity in lifestyle pattern between SF, CF and CFS calls for further research.
Vanheule S, Vandenbergen J, Verhaeghe P, Desmet M.		Interpersonal problems in alexithymia: A study in three primary care groups.	Psychol Psychother. 2010 Feb 11. [Epub ahead of print]	Objectives The present study investigated the relation between alexithymia and interpersonal problems in a sample of primary care patients with either chronic fatigue syndrome (CFS); a chronic cardiovascular or auto-immune disease; or a minor medical condition. It was hypothesized that the relation between cold interpersonal functioning would account for the differences in alexithymia scores between the patient groups. Design and methods Participants were 155 primary care patients that were recruited through 52 general practitioners: 52 CFS patients; 52 patients with a chronic cardiovascular or auto-immune disease; 51 patients with a minor medical condition. Interpersonal problems were assessed by means of the Inventory of Interpersonal Problems and alexithymia was assessed by means of the Toronto Alexithymia Scale. Results CFS patients and patients with a chronic cardiovascular or auto-immune disease have substantially higher alexithymia scores than patients with a minor medical condition. Alexithymia is positively related to cold and distant interpersonal functioning; negatively related to self-sacrificing and overly accommodating in relation to others; and positively related to vindictiveness and self-centredness. The relation between alexithymia and these interpersonal problems accounts for the differences in alexithymia scores between the patient groups. Conclusions Alexithymia and interpersonal problems should be considered together, in terms of one deficient affect regulatory system, and the relation between alexithymia and specific illness conditions is secondary to this. Clinical assessment of patients with problems in naming and discussing affective states should never be isolated from an examination of their interpersonal problems, and vice versa. Mentalization-based therapy is recommended for patients with problems in naming affective states, interpersonal problems, and concomitant CFS or other alexithymia-related diseases.
VanNess JM, Stevens SR, Bateman L, Stiles TL, Snell CR.	Pacific Fatigue Laboratory, University of the Pacific, Stockton, California 95211, USA. mvanness@pacific.edu	Postexertional malaise in women with chronic fatigue syndrome.	J Womens Health (Larchmt). 2010 Feb;19(2):239-44.	OBJECTIVE: Postexertional malaise (PEM) is a defining characteristic of chronic fatigue syndrome (CFS) that remains a source of some controversy. The purpose of this study was to explore the effects of an exercise challenge on CFS symptoms from a patient perspective. METHODS: This study included 25 female CFS patients and 23 age-matched sedentary controls. All participants underwent a maximal cardiopulmonary exercise test. Subjects completed a health and well-being survey (SF-36) 7 days postexercise. Subjects also provided, approximately 7 days after testing, written answers to open-ended questions pertaining to physical and cognitive responses to the test and length of recovery. SF-36 data were compared using multivariate analyses. Written questionnaire responses were used to determine recovery time as well as number and type of symptoms experienced. RESULTS: Written

				questionnaires revealed that within 24 hours of the test, 85% of controls indicated full recovery, in contrast to 0 CFS patients. The remaining 15% of controls recovered within 48 hours of the test. In contrast, only 1 CFS patient recovered within 48 hours. Symptoms reported after the exercise test included fatigue, light-headedness, muscular/joint pain, cognitive dysfunction, headache, nausea, physical weakness, trembling/instability, insomnia, and sore throat/glands. A significant multivariate effect for the SF-36 responses ($p < 0.001$) indicated lower functioning among the CFS patients, which was most pronounced for items measuring physiological function. CONCLUSIONS: The results of this study suggest that PEM is both a real and an incapacitating condition for women with CFS and that their responses to exercise are distinctively different from those of sedentary controls.
Vermeulen RC, Kurk RM, Visser FC, Sluiter W, Scholte HR.	CFS/ME and Pain Research Center Amsterdam, Waalstraat 25-31, 1078 BR Amsterdam, The Netherlands. rv@cvscentrum.nl	Patients with chronic fatigue syndrome performed worse than controls in a controlled repeated exercise study despite a normal oxidative phosphorylation capacity.	J Transl Med. 2010 Oct 11;8:93.	BACKGROUND: The aim of this study was to investigate the possibility that a decreased mitochondrial ATP synthesis causes muscular and mental fatigue and plays a role in the pathophysiology of the chronic fatigue syndrome (CFS/ME). METHODS: Female patients (n = 15) and controls (n = 15) performed a cardiopulmonary exercise test (CPET) by cycling at a continuously increased work rate till maximal exertion. The CPET was repeated 24 h later. Before the tests, blood was taken for the isolation of peripheral blood mononuclear cells (PBMC), which were processed in a special way to preserve their oxidative phosphorylation, which was tested later in the presence of ADP and phosphate in permeabilized cells with glutamate, malate and malonate plus or minus the complex I inhibitor rotenone, and succinate with rotenone plus or minus the complex II inhibitor malonate in order to measure the ATP production via Complex I and II, respectively. Plasma CK was determined as a surrogate measure of a decreased oxidative phosphorylation in muscle, since the previous finding that in a group of patients with external ophthalmoplegia the oxygen consumption by isolated muscle mitochondria correlated negatively with plasma creatine kinase, 24 h after exercise. RESULTS: At both exercise tests the patients reached the anaerobic threshold and the maximal exercise at a much lower oxygen consumption than the controls and this worsened in the second test. This implies an increase of lactate, the product of anaerobic glycolysis, and a decrease of the mitochondrial ATP production in the patients. In the past this was also found in patients with defects in the mitochondrial oxidative phosphorylation. However the oxidative phosphorylation in PBMC was similar in CFS/ME patients and controls. The plasma creatine kinase levels before and 24 h after exercise were low in patients and controls, suggesting normality of the muscular mitochondrial oxidative phosphorylation. CONCLUSION: The decrease in mitochondrial ATP synthesis in the CFS/ME patients is not caused by a defect in the enzyme complexes catalyzing oxidative phosphorylation, but in another factor. TRIAL REGISTRATION: Clinical trials registration number: NL16031.040.07.
Voet NB, Bleijenberg G, Padberg GW, van Engelen BG, Geurts AC.	Nijmegen Centre for Evidence Based Practice; Department of Rehabilitation, Radboud University Nijmegen Medical	Effect of aerobic exercise training and cognitive behavioural therapy on reduction of chronic fatigue in patients with	BMC Neurol. 2010 Jun 30;10:56.	BACKGROUND: In facioscapulohumeral dystrophy (FSHD) muscle function is impaired and declines over time. Currently there is no effective treatment available to slow down this decline. We have previously reported that loss of muscle strength contributes to chronic fatigue through a decreased level of physical activity, while fatigue and physical inactivity both determine loss of societal participation. To decrease chronic fatigue, two distinctly different therapeutic approaches can be proposed: aerobic exercise training (AET) to improve physical capacity and cognitive behavioural therapy (CBT) to stimulate an active life-style yet avoiding excessive physical strain. The primary aim of the FACTS-2-FSHD (acronym for Fitness And Cognitive behavioural TherapieS/for Fatigue and

	Centre, Nijmegen, The Netherlands. N.Voet@reval.umcn.nl	facioscapulohumeral dystrophy: protocol of the FACTS-2-FSHD trial.		ACTivitieS in FSHD) trial is to study the effect of AET and CBT on the reduction of chronic fatigue as assessed with the Checklist Individual Strength subscale fatigue (CIS-fatigue) in patients with FSHD. Additionally, possible working mechanisms and the effects on various secondary outcome measures at all levels of the International Classification of Functioning, Disability and Health (ICF) are evaluated. METHODS/DESIGN: A multi-centre, assessor-blinded, randomized controlled trial is conducted. A sample of 75 FSHD patients with severe chronic fatigue (CIS-fatigue > or = 35) will be recruited and randomized to one of three groups: (1) AET + usual care, (2) CBT + usual care or (3) usual care alone, which consists of no therapy at all or occasional (conventional) physical therapy. After an intervention period of 16 weeks and a follow-up of 3 months, the third (control) group will as yet be randomized to either AET or CBT (approximately 7 months after inclusion). Outcomes will be assessed at baseline, immediately post intervention and at 3 and 6 months follow up. DISCUSSION: The FACTS-2-FSHD study is the first theory-based randomized clinical trial which evaluates the effect and the maintenance of effects of AET and CBT on the reduction of chronic fatigue in patients with FSHD. The interventions are based on a theoretical model of chronic fatigue in patients with FSHD. The study will provide a unique set of data with which the relationships between outcome measures at all levels of the ICF could be assessed. TRIAL REGISTRATION: Dutch Trial Register, NTR1447.
Vollmer-Conna U.		Chronic fatigue syndrome in adolescence: where to from here?	Arch Pediatr Adolesc Med. 2010 Sep;164(9):880-1. Comment on: Arch Pediatr Adolesc Med. 2010 Sep;164(9):803-9. Arch Pediatr Adolesc Med. 2010 Sep;164(9):817-23.	
Walters SJ.	Medical Statistics Group, School of Health and Related Research, University of Sheffield, Sheffield S1 4DA, UK. s.j.walters@sheffield.ac.uk	Therapist effects in randomised controlled trials: what to do about them.	J Clin Nurs. 2010 Apr;19(7-8):1102-12.	AIMS AND OBJECTIVES: The aim of this study is to describe and compare three statistical methods to allow for therapist effects in individually randomised controlled trials. BACKGROUND: In an individually randomised controlled trial where the intervention is delivered by a health professional it seems likely that the effectiveness of the intervention, independent of any treatment effect, could depend on the skill of the health professional delivering it. This leads to a potential clustering of the outcomes for the patients being treated by the same health professional. DESIGN: Retrospective statistical analysis of outcomes from four example randomised controlled trial datasets with potential clustering by health professional. METHODS: Three methods to allow for clustering are described: cluster level analysis; random effects models and marginal models. These models were fitted to continuous outcome data from four example randomised controlled trial datasets with potential clustering by health professional. RESULTS: The cluster level models produced the widest confidence intervals. Little difference was found between the estimates of the regression coefficients for the treatment effect and confidence intervals between the individual patient level models for the datasets. The conclusions reached for each dataset match those published in the original papers. The

				intracluster correlation coefficient ranged from <0.001-0.04 for the outcomes, which shows only minor levels of clustering within the datasets. CONCLUSIONS: The models, which use individual level data are to be preferred. Treatment coefficients from these models have different interpretations. The choice of model should depend on the scientific question being asked. RELEVANCE TO CLINICAL PRACTICE: We recommend that researchers should be aware of any potential clustering, by health professional, in their randomised controlled trial and use appropriate methods to account for this clustering in the statistical analysis of the data.
Wearden AJ, Dowrick C, Chew-Graham C, Bentall RP, Morriss RK, Peters S, Riste L, Richardson G, Lovell K, Dunn G; Fatigue Intervention by Nurses Evaluation (FINE) trial writing group and the FINE trial group. Collaborators: Bennett C, Bentall R, Booth L, Brocki J, Cahill G, Chapman A, Chew-Graham C, Connell S, Dowrick C, Dunn G, Fleetwood D, Ibbotson L, Jerman D, Lovell K, Mann J, Morriss R, Peters S, Powell P, Quarmby D, Richardson G, Riste L, Wearden A, Williams J.	School of Psychological Sciences, University of Manchester, Manchester. alison.wearden@manchester.ac.uk	Nurse led, home based self help treatment for patients in primary care with chronic fatigue syndrome: randomised controlled trial.	BMJ. 2010 Apr 23;340:c1777. doi: 10.1136/bmj.c1777. Comment in: BMJ. 2010;340:c1799. Evid Based Nurs. 2010 Oct;13(4):125-6.	OBJECTIVE: To evaluate the effectiveness of home delivered pragmatic rehabilitation-a programme of gradually increasing activity designed collaboratively by the patient and the therapist-and supportive listening-an approach based on non-directive counselling-for patients in primary care with chronic fatigue syndrome/myalgic encephalomyelitis or encephalitis (CFS/ME). DESIGN: Single blind, randomised, controlled trial. SETTING: 186 general practices across the north west of England between February 2005 and May 2007. PARTICIPANTS: 296 patients aged 18 or over with CFS/ME (median illness duration seven years) diagnosed using the Oxford criteria. INTERVENTIONS: Participants were randomly allocated to pragmatic rehabilitation, supportive listening, or general practitioner treatment as usual. Both therapies were delivered at home in 10 sessions over 18 weeks by one of three adult specialty general nurses who had received four months' training, including supervised practice, in each of the interventions. GP treatment as usual was unconstrained except that patients were not to be referred for systematic psychological therapies during the treatment period. Main outcome measures The primary clinical outcomes were fatigue and physical functioning at the end of treatment (20 weeks) and 70 weeks from recruitment compared with GP treatment as usual. Lower fatigue scores and higher physical functioning scores denote better outcomes. RESULTS: A total of 257 (87%) of the 296 patients who entered the trial were assessed at 70 weeks, the primary outcome point. Analysis was on an intention to treat basis, with robust treatment effects estimated after adjustment for missing data using probability weights. Immediately after treatment (at 20 weeks), patients allocated to pragmatic rehabilitation (n=95) had significantly improved fatigue (effect estimate -1.18, 95% confidence interval -2.18 to -0.18; P=0.021) but not physical functioning (-0.18, 95% CI -5.88 to +5.52; P=0.950) compared with patients allocated to treatment as usual (n=100). At one year after finishing treatment (70 weeks), there were no statistically significant differences in fatigue or physical functioning between patients allocated to pragmatic rehabilitation and those on treatment as usual (-1.00, 95% CI -2.10 to +0.11; P=0.076 and +2.57, 95% CI 3.90 to +9.03; P=0.435). At 20 weeks, patients allocated to supportive listening (n=101) had poorer physical functioning than those allocated to treatment as usual (-7.54, 95% CI -12.76 to -2.33; P=0.005) and no difference in fatigue. At 70 weeks, patients allocated to supportive listening did not differ significantly from those allocated to treatment as usual on either primary outcome. CONCLUSIONS: For patients with CFS/ME in primary care, pragmatic rehabilitation delivered by trained nurse therapists improves fatigue in the short term compared with unconstrained GP treatment as usual, but the effect is small and not statistically significant at one year follow-up. Supportive listening delivered by trained nurse therapists is not an effective treatment for CFS/ME. Trial registration International Standard Randomised Controlled Trial Number IRCTN74156610.

Weaver SA, Janal MN, Aktan N, Ottenweller JE, Natelson BH.	Department of Neurology & Neurosciences, UMDNJ-New Jersey Medical School, Newark, New Jersey, USA.	Sex differences in plasma prolactin response to tryptophan in chronic fatigue syndrome patients with and without comorbid fibromyalgia.	J Womens Health (Larchmt). 2010 May;19(5):951-8.	BACKGROUND: Some think chronic fatigue syndrome (CFS) and fibromyalgia (FM) are variants of the same illness process. This would imply that CFS patients with and without comorbid FM have similar biological underpinnings. To test this, we compared serotonergic-based responses, plasma prolactin (PRL), and self-reported measures of fatigue to intravenous infusion of tryptophan among patients with CFS alone, CFS + FM, and healthy controls. METHODS: Men and women with CFS alone or CFS + FM and healthy subjects, none with current major depressive disorder (MDD), were given 120 mg of L-tryptophan per kg lean body mass intravenously (i.v.). Before and after tryptophan infusion, blood samples were collected, and plasma PRL, tryptophan, and kynurenine concentrations were determined. RESULTS: Women with CFS alone, but not CFS + FM, showed upregulated plasma PRL responses compared with controls. There were no differences among groups of men. Plasma tryptophan and kynurenine concentrations did not differ among groups. CONCLUSIONS: These results indicate that women with CFS alone have upregulated serotonergic tone that is not seen in those with comorbid FM. The lack of effect in men suggests a mechanism that might explain, in part, the increased prevalence of CFS in women. The data support the interpretation that CFS in women is a different illness from FM.
Weiss RA.	Division of Infection and Immunity, University College London, 46 Cleveland Street, London W1T 4JF, UK. r.weiss@ucl.ac.uk	A cautionary tale of virus and disease.	BMC Biol. 2010 Sep 27;8:124.	The recent identification of the gammaretrovirus XMRV and a second gammaretrovirus of a different subtype in chronic fatigue syndrome has aroused much interest, not least among sufferers. However, it remains highly controversial whether the detection of these viruses represents true infection or laboratory artifacts.
White AT, Light AR, Hughen RW, Bateman L, Martins TB, Hill HR, Light KC.	Department of Exercise and Sport Science, University of Utah, Salt Lake City, Utah, USA.	Severity of symptom flare after moderate exercise is linked to cytokine activity in chronic fatigue syndrome.	Psychophysiology. 2010 Jul 1;47(4):615-24. Epub 2010 Mar 4.	Chronic fatigue syndrome (CFS) patients often report symptom flare (SF) for >24 h after moderate exercise (post-ex). We hypothesized that SF is linked to increases in circulating cytokines and CD40 Ligand (CD40L). In 19 CFS patients and 17 controls, mental and physical fatigue and pain symptom ratings were obtained together with serum for 11 cytokines and CD40L before and at 0.5, 8, 24, and 48 h post-ex. Before exercise, CFS had lower CD40L ($p<.05$) but similar cytokines versus controls. In subgroups based on SF at 48 h, high SF patients (n=11) increased in IL-1beta, IL-12, IL-6, IL-8, IL-10, and IL-13 ($p<.05$) 8 h post-ex. Low SF patients (n=8) showed post-ex decreases in IL-10, IL-13, and CD40L, and controls decreased in IL-10, CD40L, and TNFalpha ($p<.05$). Thus, in CFS, cytokine activity may vary directly with SF, which may explain prior inconsistent findings.
White PD.	Wolfson Institute of Preventive Health, Barts and The London School of Medicine and Dentistry, Queen Mary University of	Chronic fatigue syndrome: Is it one discrete syndrome or many? Implications for the "one vs. many" functional somatic	J Psychosom Res. 2010 May;68(5):455-9. Epub 2010 Mar 17.	There is a current debate as to whether "functional somatic syndromes" (FSSs) are more similar to or different from each other. While at the same time, there is evidence of heterogeneity within single syndromes. So, it could be that these syndromes are all part of one big process/illness, are discrete in their own right, or that they are heterogeneous collections of different illnesses lumped together by common symptoms but separated by uncommon pathophysiologies. The example of chronic fatigue syndrome (CFS) is instructive. There is evidence to support all three models of understanding. Three recent large studies have suggested that FSSs are both similar and dissimilar at the same time. The

	London, London, UK. p.d.white@qmul.ac.uk	syndromes debate.		solution to the debate is that we need to both "lump" and "split." We need to study both the similarities between syndromes and their dissimilarities to better understand what we currently call the FSSs.
Whittemore A.		The Whittemore Peterson Institute: building bridges through private and public sector collaboration.	Mol Interv. 2010 Jun;10(3):120-6.	
Wiborg JF, Knoop H, Stulemeijer M, Prins JB, Bleijenberg G.	Department of Medical Psychology, Radboud University Nijmegen Medical Centre, Expert Centre Chronic Fatigue, The Netherlands. j.wiborg@nkcv.umcn.nl	How does cognitive behaviour therapy reduce fatigue in patients with chronic fatigue syndrome? The role of physical activity.	Psychol Med. 2010 Aug;40(8):1281-7. Epub 2010 Jan 5.	BACKGROUND: Cognitive behaviour therapy (CBT) is known to reduce fatigue severity in chronic fatigue syndrome (CFS). How this change in symptomatology is accomplished is not yet understood. The purpose of the present study was to determine whether the effect of CBT on fatigue is mediated by an increase in physical activity. METHOD: Three randomized controlled trials were reanalysed, previously conducted to evaluate the efficacy of CBT for CFS. In all samples, actigraphy was used to assess the level of physical activity prior and subsequent to treatment or a control group period. The mediation hypothesis was analysed according to guidelines of Baron & Kenny [Journal of Personality and Social Psychology (1986)51, 1173-1182]. A non-parametric bootstrap approach was used to test statistical significance of the mediation effect. RESULTS: Although CBT effectively reduced fatigue, it did not change the level of physical activity. Furthermore, changes in physical activity were not related to changes in fatigue. Across the samples, the mean mediation effect of physical activity averaged about 1% of the total treatment effect. This effect did not yield significance in any of the samples. CONCLUSIONS: The effect of CBT on fatigue in CFS is not mediated by a persistent increase in physical activity.
Wiborg JF, van der Werf S, Prins JB, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen, Medical Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands. j.wiborg@nkcv.umcn.nl	Being homebound with chronic fatigue syndrome: A multidimensional comparison with outpatients.	Psychiatry Res. 2010 May 15;177(1-2):246-9. Epub 2010 Mar 5.	Many patients with chronic fatigue syndrome (CFS) seem to experience periods in which they are homebound due to their symptomatology. Despite a growing body of research about CFS, little is known about patients who no longer feel able to leave their homes. The purpose of the present study was to examine whether homebound patients differ from other CFS patients on illness-specific characteristics. Besides experiencing more impairment in daily functioning than participants of an outpatient intervention study, homebound patients were characterised by extremely high levels of daily fatigue, predominant somatic attributions, and pervasively passive activity patterns. The course of symptomatology was similarly stable in both groups. Our findings suggest that homebound patients form a distinct subgroup of CFS patients who might profit from a treatment approach that is tailored to their specific needs. The exploratory nature of this first systematic investigation of homebound CFS patients is stressed, and suggestions for future research are made.
Wyller VB, Barbieri R, Saul JP.	Department of Pediatrics, Rikshospitalet University Hospital, 0027,	Blood pressure variability and closed-loop baroreflex assessment in	Eur J Appl Physiol. 2010 Oct 2. [Epub ahead of print]	Hemodynamic abnormalities have been documented in the chronic fatigue syndrome (CFS), indicating functional disturbances of the autonomic nervous system responsible for cardiovascular regulation. The aim of this study was to explore blood pressure variability and closed-loop baroreflex function at rest and during mild orthostatic stress in adolescents with CFS. We included a consecutive sample of 14 adolescents 12-18 years old with CFS diagnosed according to a thorough and standardized set of

	Oslo, Norway, brwylle@online.no.	adolescent chronic fatigue syndrome during supine rest and orthostatic stress.		investigations and 56 healthy control subjects of equal sex and age distribution. Heart rate and blood pressure were recorded continuously and non-invasively during supine rest and during lower body negative pressure (LBNP) of -20 mmHg to simulate mild orthostatic stress. Indices of blood pressure variability and baroreflex function (α-gain) were computed from monovariate and bivariate spectra in the low-frequency (LF) band (0.04-0.15 Hz) and the high-frequency (HF) band (0.15-0.50 Hz), using an autoregressive algorithm. Variability of systolic blood pressure in the HF range was lower among CFS patients as compared to controls both at rest and during LBNP. During LBNP, compared to controls, α-gain HF decreased more, and α-gain LF and the ratio of α-gain LF/α-gain HF increased more in CFS patients, all suggesting greater shift from parasympathetic to sympathetic baroreflex control. CFS in adolescents is characterized by reduced systolic blood pressure variability and a sympathetic predominance of baroreflex heart rate control during orthostatic stress. These findings may have implications for the pathophysiology of CFS in adolescents.
Wyller VB, Evang JA, Godang K, Solhjell KK, Bollerslev J.	Division of Paediatrics, Oslo University Hospital, Oslo, Norway. asa.myrelid@kbh.uu.se	Hormonal alterations in adolescent chronic fatigue syndrome.	Acta Paediatr. 2010 May;99(5):770-3. Epub 2010 Mar 1.	AIM: The chronic fatigue syndrome is associated with alterations in the hypothalamus-pituitary-adrenal axis and cardiovascular autonomic nervous activity, suggesting a central dysregulation. This study explored differences among adolescent chronic fatigue syndrome patients and healthy controls regarding antidiuretic hormone, the renin-angiotensin-aldosterone-system, sex hormones and cardiac peptides. METHODS: We included a consecutive sample of 67 adolescents aged 12-18 years with chronic fatigue syndrome diagnosed according to a thorough and standardized set of investigations, and a volunteer sample of 55 healthy control subjects of equal gender and age distribution. Hormones were assayed with standard laboratory methods. RESULTS: Among patients, plasma antidiuretic hormone was significantly decreased and serum osmolality and plasma renin activity were significantly increased ($p <$ or $= 0.001$). Serum concentration of aldosterone, cortisol, NT-proBNP and sex hormones were not significantly different in the two groups. CONCLUSION: Chronic fatigue syndrome in adolescents is associated with alterations in hormonal systems controlling osmolality and blood volume, possibly supporting a theory of central dysregulation.
Yan Y, Liu Q, Wollenberg K, Martin C, Buckler-White A, Kozak CA.	NIH, NIAID, LMM, Bldg. 4, Room 329, 4 Center Drive MSC 0460, Bethesda, MD 20892-0460. ckozak@niaid.nih.gov.	Evolution of functional and sequence variants of the mammalian XPR1 receptor for mouse xenotropic gammaretroviruses and the human-derived retrovirus XMRV.	J Virol. 2010 Nov;84(22):11970-80. Epub 2010 Sep 15.	Genetic conflicts between retroviruses and their receptors result in the evolution of novel host entry restrictions and novel virus envelopes, and such variants can influence trans-species transmission. We screened rodents and other mammals for sequence variation in the Xpr1 receptor for the mouse xenotropic or polytropic mouse leukemia viruses (X-MLVs or P-MLVs, respectively) of the gammaretrovirus family and for susceptibility to mouse-derived X/P-MLVs and to XMRV (xenotropic murine leukemia virus-related virus), an X-MLV-like virus isolated from humans with prostate cancer and chronic fatigue syndrome. We identified multiple distinct susceptibility phenotypes; these include the four known Xpr1 variants in Mus and a novel fifth Xpr1 gene found in Mus molossinus and Mus musculus. We describe the geographic and species distribution of the Mus Xpr1 variants but failed to find the X-MLV-restrictive laboratory mouse allele in any wild mouse. We used mutagenesis and phylogenetic analysis to evaluate the functional contributions made by constrained, variable, and deleted residues. Rodent Xpr1 is under positive selection, indicating a history of host-pathogen conflicts; several codons under selection have known roles in virus entry. All non-Mus mammals are susceptible to mouse X-MLVs, but some restrict other members of the X/P-MLV family, and the resistance of hamster and gerbil cells to XMRV indicates that XMRV has unique receptor

				requirements. We show that the hypervariable fourth extracellular XPR1 loop (ECL4) contains three evolutionarily constrained residues that do not contribute to receptor function, we identify two novel residues important for virus entry (I579 and T583), and we describe a unique pattern of ECL4 variation in the three virus-restrictive Xpr1 variants found in MLV-infected house mice; these mice carry different deletions in ECL4, suggesting either that these sites or loop size affects receptor function.
Yao K, Crawford JR, Komaroff AL, Ablashi DV, Jacobson S.	Viral Immunology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892, USA.	Review part 2: Human herpesvirus-6 in central nervous system diseases.	J Med Virol. 2010 Oct;82(10):1669-78.	
Yap KY, Kuo EY, Lee JJ, Chui WK, Chan A.	Department of Pharmacy, Faculty of Science, National University of Singapore, Singapore.	An onco-informatics database for anticancer drug interactions with complementary and alternative medicines used in cancer treatment and supportive care: an overview of the OncoRx project.	Support Care Cancer. 2010 Jul;18(7):883-91. Epub 2009 Sep 9.	PURPOSE: Cancer patients are at high risk of manifesting interactions from use of anticancer drugs (ACDs) and complementary and alternative medicines (CAMs). These interactions can result in sub-therapeutic effects or increased toxicities which may compromise the outcome of chemotherapy. It is important for practitioners to gain convenient access to ACD-CAM interaction information so as to make better-informed decisions in daily practice. This paper describes the creation of an oncology database (OncoRx) that documents ACD-CAM interactions, including traditional Chinese medicines (TCMs) that are commonly used for cancer treatment, prevention, and supportive care therapy. METHODS: Information regarding ACDs, CAMs, and drug interactions were collated from 14 sources, inclusive of hardcopy and online resources, and input into a modified web server with a database engine and a programming interface using a combination of software and programming scripts. RESULTS: OncoRx currently contains a total of 117 ACDs and 166 CAMs. Users are able to search for interactions based on various CAM uses: cancer treatment or prevention, immune-system-related, alopecia, nausea, and vomiting, peripheral neuropathy and pain, inflammation, fatigue, and non-cancer related. Pharmacokinetic data on ACDs and CAMs, characteristics of CAMs based on TCM principles, and drug interaction parameters such as effects, mechanisms, evidences, and proposed management plans, are shown in the search results. CONCLUSION: OncoRx is an oncology database which detects ACD interactions. It is currently able to detect interactions with CAMs. It is hoped that OncoRx will serve as a useful resource to clinicians, educators, trainers, and students working in the oncology setting.
Young P, Finn BC, Bruetman J, Pellegrini D, Kremer A.	Servicios de Clínica Médica, Hospital Británico de Buenos Aires, Argentina. pabloyoung2003@	[The chronic asthenia syndrome: a clinical approach]. [Article in Spanish]	Medicina (B Aires). 2010;70(3):284-92.	The term asthenia comes from the Greek (centsqsneia, a: privation, without; esthénos: vigor, force), it means absence of strength, vigor or force. It is a symptom, difficult to define, with a set of vague sensations, different for each patient. It is a frequent cause of consult, almost 30% in ambulatory settings. The chronic fatigue represents up to 10% of these cases, and the 0.2-0.7% belongs to the chronic fatigue syndrome. It is very important to differentiate asthenia from weakness, dizziness or dyspnoea, since patients may confuse them. The factor time in asthenia is very useful for its

	yahoo.com.ar			characterization, it was defined to the prolonged fatigue when it lasts for more than a month and chronic when the duration is greater than 6 months. The depression is the commonest fatigue cause, representing approximately half of the cases. The most effective treatment of the asthenia is to solve the underlying cause, although up to 20% of the patients remain without diagnosis. The diagnosis of the chronic fatigue syndrome is of exclusion and the criteria of the international consensus of year 1994 are due to use. The high frequency of the symptom entails an enormous social and economic cost and it is for that reason so important for physicians to have a correct manage of this symptom.
Zhang L, Gough J, Christmas D, Mattey DL, Richards SC, Main J, Enlander D, Honeybourne D, Ayres JG, Nutt DJ, Kerr JR.	Department of Cellular & Molecular Medicine, St George's University of London, London, UK.	Microbial infections in eight genomic subtypes of chronic fatigue syndrome/myalgic encephalomyelitis.	J Clin Pathol. 2010 Feb;63(2):156-64. Epub 2009 Dec 2.	BACKGROUND: The authors have previously reported genomic subtypes of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) based on expression of 88 human genes. AIM: To attempt to reproduce these findings, determine the specificity of this signature to CFS/ME, and test for associations between CFS/ME subtype and infection. METHODS: Expression levels of 88 human genes were determined in blood of 62 new patients with idiopathic CFS/ME (according to Fukuda criteria), six patients with Q-fever-associated CFS/ME from the Birmingham Q-fever outbreak (according to Fukuda criteria), 14 patients with endogenous depression (according to DSM-IV criteria) and 29 normal blood donors. RESULTS: In patients with CFS/ME, differential expression was confirmed for all 88 genes. Q-CFS/ME had similar patterns of gene expression to idiopathic CFS/ME. Gene expression in patients with endogenous depression was similar to that in the normal controls, except for upregulation of five genes (APP, CREBBP, GNAS, PDCD2 and PDCD6). Clustering of combined gene data in CFS/ME patients for this and the authors' previous study (117 CFS/ME patients) revealed genomic subtypes with distinct differences in SF36 scores, clinical phenotypes, severity and geographical distribution. Antibody testing for Epstein-Barr virus, enterovirus, Coxiella burnetii and parvovirus B19 revealed evidence of subtype-specific relationships for Epstein-Barr virus and enterovirus, the two most common infectious triggers of CFS/ME. CONCLUSIONS: This study confirms the involvement of these genes in CFS/ME.
Zou J, Yuan J, Lv S, Tu J.	Scientific Research Department, Shanghai University of Sports, Shanghai, 200438, China. zoujun777@126.com	Effects of exercise on behavior and peripheral blood lymphocyte apoptosis in a rat model of chronic fatigue syndrome.	J Huazhong Univ Sci Technolog Med Sci. 2010 Apr;30(2):258-64. Epub 2010 Apr 21.	This study examined the effects of exercise on behavior and peripheral blood leukocyte apoptosis in a rat model of chronic fatigue syndrome (CFS). Thirty-six healthy male Sprague-Dawley rats were equally randomized into 3 groups: the control group, CFS model group and the exercise group in terms of body weight. A total of 25 rats entered the final statistical analysis due to 11 deaths during the study. CFS model was established by subjecting the rats in CFS model group and exercise group to electric shock, chronic restraint stress and cold water swim. Besides, rats in the exercise group took running wheel exercise. After a week of conditioning feeding, model construction and running wheel exercise were performed simultaneously, and lasted for 23 consecutive days. The behavior experiments, including running wheel exercise, open-field test, tail suspension test and Morris water maze test, were conducted, either before or after the model establishment. Rats were sacrificed and peripheral blood was obtained for the assessment of lymphocyte apoptosis index by flow cytometry (FCM). It was found that as compared with those in the control group, the weight of the rats was decreased obviously ($P<0.01$), the mobility time in the open-field and the tail suspension tests was shortened significantly ($P<0.01$), the time to locate the platform was enhanced ($P<0.01$) and the cell apoptosis index was increased substantially ($P<0.01$) in the CSF model group. Meanwhile, in comparison to the model group, the behavior in the open-field and the tail suspension tests was

				improved significantly (P<0.05), and the apoptosis index decreased remarkably (P<0.01) in the exercise group. It is concluded that sport intervention can prevent lymphocyte apoptosis and improve animal behavior rather than the memory.
Zou N, Kubota M, Kuruma E, Kojima C, Nagai A.	Department of Human Life and Environment, Nara Women's University, Kitauoya-nishimachi, Nara 630-8506, Japan.	Fatigue status in relation to lifestyle in healthy Japanese adolescents.	Int J Pediatr. 2010;2010. pii: 520320. Epub 2010 Sep 19.	In order to investigate the prevalence of physical, mental, and chronic fatigue syndrome-(CFS-) related fatigue and its relation to lifestyle, 1,225 adolescents (591 males, 634 females) aged 11 to 16 years were asked to complete a self-reported questionnaire on fatigue status and lifestyle in the past one month. There was no gender difference in physical and mental fatigue scores, but CFS-related scores were significantly higher in females than in males. These scores were found to increase with the increase of age. After adjusting for age and gender, multiple regression analysis showed that physical and mental fatigue scores were associated with sleeping hours, extracurricular sports activity, food balance, the frequencies of snacks between regular meals, intake of sugar-sweetened beverages, and visits to the nurse's room. This paper is the first large cross-sectional study on fatigue in healthy adolescents in Japan, albeit there were numerous such studies in Western countries.

2009				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Ablin JN, Buskila D, Clauw DJ.	University of Michigan Chronic Pain and Fatigue Research Center, Ann Arbor, MI 48106, USA.	Biomarkers in fibromyalgia.	Curr Pain Headache Rep. 2009 Oct;13(5):343-9.	Fibromyalgia is a common pain syndrome characterized by widespread pain, tenderness, and a number of other somatic symptoms and syndromes. Although there was original skepticism that any objective abnormalities would be identified in these individuals, at present there are many that have been reproducibly identified, and most point to dysregulation of central nervous system function as a key underlying pathogenic mechanism in this and related illnesses. This article reviews several objective abnormalities or measures that have been identified or used in fibromyalgia, and indicates which of these may be most promising to eventually use as biomarkers to follow the response to treatment or progress of disease over time.
Ablin JN, Odes L, Neumann L, Buskila D.	Institute of Rheumatology and Internal Medicine 6, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, ajacob@post.tau.ac.il.	The Hebrew version of the FibroFatigue scale: validation of a questionnaire for assessment of fibromyalgia and chronic fatigue syndrome.	Rheumatol Int. 2009 Sep 25. [Epub ahead of print]	The objective of this study is to validate a translated Hebrew version of the FibroFatigue Scale (FFS). The Hebrew version of the FFS was administered to 100 patients fulfilling ACR criteria for classification of FM together with the validated Hebrew version of the Fibromyalgia Impact Questionnaire (FIQ), the validated Hebrew version of the Short Form-36 (SF-36) and a Visual Analogue Scale (VAS) measurement of pain, anxiety, depression, morning stiffness and global well being. Test-retest reliability was assessed using Spearman correlations. Internal consistency was evaluated with Cronbach's alpha of reliability. Construct validity of the FFS was evaluated by correlations among the FFS, the FIQ and the subscales of the SF-36. Mean duration of symptoms was 10.7 years, and mean age of participants was 53.5 years. Test-retest reliability was between 0.46 and 0.85 for the various FFS items. Internal consistency was 0.89 for the overall FFS. Significant correlations were obtained between the FFS items and the SF-36. These results support the reliability and validity of the data obtained with the Hebrew version of the FSS for detecting and measuring symptom severity in Hebrew speaking patients with FM.
Adams D, Wu T, Yang X, Tai S, Vohra S.	CARE Program, Department of Pediatrics, University of Alberta, 8B19 11111 Jasper Avenue, Edmonton, Alberta, Canada, T5K 0L4.	Traditional Chinese medicinal herbs for the treatment of idiopathic chronic fatigue and chronic fatigue syndrome.	Cochrane Database Syst Rev. 2009 Oct 7;(4):CD006348.	BACKGROUND: Chronic fatigue is increasingly common. Conventional medical care is limited in treating chronic fatigue, leading some patients to use traditional Chinese medicine therapies, including herbal medicine. OBJECTIVES: To assess the effectiveness of traditional Chinese medicine herbal products in treating idiopathic chronic fatigue and chronic fatigue syndrome. SEARCH STRATEGY: The following databases were searched for terms related to traditional Chinese medicine, chronic fatigue, and clinical trials: CCDAN Controlled Trials Register (July 2009), MEDLINE (1966-2008), EMBASE (1980-2008), AMED (1985-2008), CINAHL (1982-2008), PSYCHINFO (1985-2008), CENTRAL (Issue 2 2008), the Chalmers Research Group PedCAM Database (2004), VIP Information (1989-2008), CNKI (1976-2008), OCLC Proceedings First (1992-2008), Conference Papers Index (1982-2008), and Dissertation Abstracts (1980-2008). Reference lists of included studies and review articles were examined and experts in the field were contacted for knowledge of additional studies. SELECTION CRITERIA: Selection criteria included published or unpublished randomized controlled trials (RCTs) of participants diagnosed with idiopathic chronic fatigue or chronic fatigue syndrome comparing traditional Chinese medicinal herbs with placebo, conventional standard of care (SOC), or no treatment/wait lists. The outcome of interest was fatigue. DATA COLLECTION AND ANALYSIS: 13 databases were searched for RCTs investigating TCM herbal products for the treatment of chronic fatigue. Over 2400 references were located. Studies were screened and assessed for inclusion criteria

				by two authors. MAIN RESULTS: No studies that met all inclusion criteria were identified. AUTHORS' CONCLUSIONS: Although studies examining the use of TCM herbal products for chronic fatigue were located, methodologic limitations resulted in the exclusion of all studies. Of note, many of the studies labelled as RCTs and conducted in China did not utilize rigorous randomization procedures. Improvements in methodology in future studies is required for meaningful synthesis of data.
Ament W, Verkerke GJ.	Department of Biometrics, Faculty of Health and Technology, Zuyd University, Heerlen, the Netherlands. wim.ament@xendo.com	Exercise and fatigue.	Sports Med. 2009;39(5):389-422. doi: 10.2165/00007256-200939050-00005.	Physical exercise affects the equilibrium of the internal environment. During exercise the contracting muscles generate force or power and heat. So physical exercise is in fact a form of mechanical energy. This generated energy will deplete the energy stocks within the body. During exercise, metabolites and heat are generated, which affect the steady state of the internal environment. Depending on the form of exercise, sooner or later sensations of fatigue and exhaustion will occur. The physiological role of these sensations is protection of the exercising subject from the deleterious effects of exercise. Because of these sensations the subject will adapt his or her exercise strategy. The relationship between physical exercise and fatigue has been the scope of interest of many researchers for more than a century and is very complex. The exercise intensity, exercise endurance time and type of exercise are all variables that cause different effects within the body systems, which in turn create different types of sensation within the subject's mind during the exercise. Physical exercise affects the biochemical equilibrium within the exercising muscle cells. Among others, inorganic phosphate, protons, lactate and free Mg2+ accumulate within these cells. They directly affect the mechanical machinery of the muscle cell. Furthermore, they negatively affect the different muscle cell organelles that are involved in the transmission of neuronal signals. The muscle metabolites produced and the generated heat of muscle contraction are released into the internal environment, putting stress on its steady state. The tremendous increase in muscle metabolism compared with rest conditions induces an immense increase in muscle blood supply, causing an increase in the blood circulatory system and gas exchange. Nutrients have to be supplied to the exercising muscle, emptying the energy stocks elsewhere in body. Furthermore, the contracting muscle fibres release cytokines, which in their turn create many effects in other organs, including the brain. All these different mechanisms sooner or later create sensations of fatigue and exhaustion in the mind of the exercising subject. The final effect is a reduction or complete cessation of the exercise. Many diseases speed up the depletion of the energy stocks within the body. So diseases amplify the effect of energy stock depletion that accompanies exercise. In addition, many diseases produce a change of mind-set before exercise. These changes of mind-set can create sensations of fatigue and exercise-avoiding behaviour at the onset of an exercise. One might consider these sensations during disease as a feed-forward mechanism to protect the subject from an excessive depletion of their energy stocks, to enhance the survival of the individual during disease.
Armitage R, Landis C, Hoffmann R, Lentz M, Watson N, Goldberg J, Buchwald D.	Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA. rosearmi@umich.e	Power spectral analysis of sleep EEG in twins discordant for chronic fatigue syndrome.	J Psychosom Res. 2009 Jan;66(1):51-7. Epub 2008 Nov 25.	OBJECTIVE: The purpose of the study was to evaluate quantitative sleep electroencephalogram (EEG) frequencies in monozygotic twins discordant for chronic fatigue syndrome. METHODS: Thirteen pairs of female twins underwent polysomnography. During the first night, they adapted to the sleep laboratory, and during the second night, their baseline sleep was assessed. Visual stage scoring was conducted on sleep electroencephalographic records according to standard criteria, and power spectral analysis was used to quantify delta through beta frequency bands, processed in 6-s blocks.

	du			Data were averaged across sleep stage within each twin and coded for sleep stage and the presence or absence of chronic fatigue syndrome (CFS). A completely within-subjects repeated measure multivariate analysis of variance evaluated twin pairs by frequency band by sleep stage interactions and simple effects. The relationship between alpha and delta EEG was also assessed across twin pairs. RESULTS: No significant differences in spectral power in any frequency band were found between those with CFS and their nonfatigued cotwins. Phasic alpha activity, coupled with delta was noted in five subjects with CFS but was also present in 4/5 healthy twins, indicating this finding likely reflects genetic influences on the sleep electroencephalogram rather than disease-specific sleep pathology. CONCLUSIONS: The genetic influences on sleep polysomnography and microarchitecture appear to be stronger than the disease influence of chronic fatigue syndrome, despite greater subjective sleep complaint among the CFS twins. EEG techniques that focus on short duration events or paradigms that probe sleep regulation may provide a better description of sleep abnormalities in CFS.
Arnold LM.	Department of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA.	Pain and the brain: chronic widespread pain.	J Clin Psychiatry. 2009 Apr;70(4):e10.	Chronic widespread pain is associated with several medical and psychiatric disorders including, but not limited to, chronic fatigue syndrome, fibromyalgia, mood disorders, hepatitis, endocrine disorders such as hypothyroidism, and rheumatologic disorders such as rheumatoid arthritis. Careful and comprehensive differential diagnosis must be performed to ensure a correct diagnosis before an appropriate treatment can be selected. Fibromyalgia, in particular, is challenging to diagnose and treat because it shares many characteristics with other disorders and is commonly concurrent with major mood disorders. A comprehensive disease management strategy including patient education, pharmacotherapy, cognitivebehavioral therapy, and aerobic and other forms of exercise can be beneficial for many patients with fibromyalgia. 2009 Physicians Postgraduate Press, Inc.
Aslakson E, Vollmer-Conna U, Reeves WC, White PD.	Centers for Disease Control and Prevention, Atlanta, Georgia, USA. wcr1@cdc.gov.	Replication of an empirical approach to delineate the heterogeneity of chronic unexplained fatigue.	Popul Health Metr. 2009 Oct 5;7:17.	ABSTRACT: BACKGROUND: Chronic fatigue syndrome (CFS) is defined by self-reported symptoms. There are no diagnostic signs or laboratory markers, and the pathophysiology remains inchoate. In part, difficulties identifying and replicating biomarkers and elucidating the pathophysiology reflect the heterogeneous nature of the syndromic illness CFS. We conducted this analysis of people from defined metropolitan, urban, and rural populations to replicate our earlier empirical delineation of medically unexplained chronic fatigue and CFS into discrete endophenotypes. Both the earlier and current analyses utilized quantitative measures of functional impairment and symptoms as well as laboratory data. This study and the earlier one enrolled participants from defined populations and measured the internal milieu, which differentiates them from studies of clinic referrals that examine only clinical phenotypes. METHODS: This analysis evaluated 386 women identified in a population-based survey of chronic fatigue and unwellness in metropolitan, urban, and rural populations of the state of Georgia, USA. We used variables previously demonstrated to effectively delineate endophenotypes in an attempt to replicate identification of these endophenotypes. Latent class analyses were used to derive the classes, and these were compared and contrasted to those described in the previous study based in Wichita, Kansas. RESULTS: We identified five classes in the best fit analysis. Participants in Class 1 (25%) were polysymptomatic, with sleep problems and depressed mood. Class 2 (24%) was also polysymptomatic, with insomnia and depression, but participants were also obese with associated metabolic strain. Class 3 (20%) had more selective symptoms but was equally obese with metabolic strain. Class 4 (20%) and Class 5 (11%) consisted of nonfatigued, less

				symptomatic individuals, Class 4 being older and Class 5 younger. The classes were generally validated by independent variables. People with CFS fell equally into Classes 1 and 2. Similarities to the Wichita findings included the same four main defining variables of obesity, sleep problems, depression, and the multiplicity of symptoms. Four out of five classes were similar across both studies. CONCLUSION: These data support the hypothesis that chronic medically unexplained fatigue is heterogeneous and can be delineated into discrete endophenotypes that can be replicated. The data do not support the current perception that CFS represents a unique homogeneous disease and suggests broader criteria may be more explanatory. This replication suggests that delineation of endophenotypes of CFS and associated ill health may be necessary in order to better understand etiology and provide more patient-focused treatments.
Attree EA, Dancey CP, Pope AL.	University of East London, School of Psychology, London, United Kingdom. e.a.attree@uel.ac.uk	An assessment of prospective memory retrieval in women with chronic fatigue syndrome using a virtual-reality environment: an initial study.	Cyberpsychol Behav. 2009 Aug;12(4):379-85.	People with chronic fatigue syndrome (CFS) have increased rates of depression, anxiety, and illness intrusiveness; they may also suffer from cognitive problems such as retrospective memory (RM) deficits and concentration difficulties that can stem from diminished information-processing capability. We predicted that this diminished capacity may also lead to deficits in other cognitive functions, such as prospective memory (ProM). Event-, time-, and activity-based ProM was assessed in 11 women with CFS and 12 healthy women using a computer-generated virtual environment (VE). RM was assessed using a free-recall test, and subjective assessment of both ProM and RM was assessed by questionnaire. Groups were equivalent in age and measures of IQ. People with CFS performed slightly worse than healthy controls on both the event- and time-based ProM measures, although these were not statistically significant. However, the CFS group performed significantly worse than the healthy controls on both the free recall-task and on subjective assessment of both RM and ProM. Women with CFS do have some subtle decrements in memory, particularly RM. However, it is possible that the decrements found in the present sample would be greater in real life. Further studies utilizing both healthy controls and illness controls are now needed to ascertain how sensitive the VE measure is and to inform the development of tasks in the VE that place progressively increasing demands on working memory capacity.
Avellaneda Fernández A, Pérez Martín A, Izquierdo Martínez M, Arruti Bustillo M, Barbado Hernández FJ, de la Cruz Labrado J, Díaz-Delgado Peñas R, Gutiérrez Rivas E, Palacín Delgado C, Rivera Redondo J, Ramón	Carlos III Health Institute, Sinesio Delgado, n degrees 6, 28029, Madrid, Spanish Society of Primary Care Physicians, Narváez, 15 1 degrees Izda, 28009, Madrid, Spain. alfavel@gmail.com	Chronic fatigue syndrome: aetiology, diagnosis and treatment.	BMC Psychiatry. 2009 Oct 23;9 Suppl 1:S1.	Chronic fatigue syndrome is characterised by intense fatigue, with duration of over six months and associated to other related symptoms. The latter include asthenia and easily induced tiredness that is not recovered after a night's sleep. The fatigue becomes so severe that it forces a 50% reduction in daily activities. Given its unknown aetiology, different hypotheses have been considered to explain the origin of the condition (from immunological disorders to the presence of post-traumatic oxidative stress), although there are no conclusive diagnostic tests. Diagnosis is established through the exclusion of other diseases causing fatigue. This syndrome is rare in childhood and adolescence, although the fatigue symptom per se is quite common in paediatric patients. Currently, no curative treatment exists for patients with chronic fatigue syndrome. The therapeutic approach to this syndrome requires a combination of different therapeutic modalities. The specific characteristics of the symptomatology of patients with chronic fatigue require a rapid adaptation of the educational, healthcare and social systems to prevent the problems derived from current systems. Such patients require multidisciplinary management due to the multiple and different issues affecting them. This document was realized by one of the Interdisciplinary Work Groups from the Institute for Rare

Giménez JR.				Diseases, and its aim is to point out the main social and care needs for people affected with Chronic Fatigue Syndrome. For this, it includes not only the view of representatives for different scientific societies, but also the patient associations view, because they know the true history of their social and sanitary needs. In an interdisciplinary approach, this work also reviews the principal scientific, medical, socio-sanitary and psychological aspects of Chronic Fatigue Syndrome.
Avellaneda Fernández A, Pérez Martín A, Izquierdo Martínez M, Arruti Bustillo M, Barbado Hernández FJ, de la Cruz Labrado J, Díaz-Delgado Peñas R, Gutiérrez Rivas E, Palacín Delgado C, Ramón Giménez JR, Rivera Redondo J.	Instituto de Investigación de Enfermedades Raras, Instituto de Salud Carlos III, Madrid, España; Sociedad Española de Medicos de Atención Primaria, Madrid, España.	[Chronic fatigue syndrome. Summary of the consensus document.] [Article in Spanish]	Aten Primaria. 2009 Oct;41(10):e1-5. Epub 2009 Sep 18.	
Avellaneda Fernández A, Pérez Martín A, Izquierdo Martínez M.	Instituto de Salud Carlos III, CS Los Cármenes, Madrid, España.	[Chronic fatigue syndrome. Consensus document.] [Article in Spanish]	Aten Primaria. 2009 Oct;41(10):529-31. Epub 2009 Sep 9.	
Bartley EJ, Rhudy JL, Williams AE.	Department of Psychology, The University of Tulsa, Oklahoma 74104, USA.	Experimental assessment of affective processing in fibromyalgia.	J Pain. 2009 Nov;10(11):1151-60. Epub 2009 Jul 24.	Fibromyalgia syndrome (FMS) is a chronic pain disorder associated with widespread musculoskeletal pain, tenderness, and fatigue. Additionally, correlational research suggests negative affect (eg, depression, anxiety) and deficits in positive affect may contribute to FMS symptomatology. However, well-controlled, experimental research is necessary to ascertain whether patients with FMS have problems in affective processing. The present study used a well-validated picture-viewing paradigm to evoke emotional responses in 17 patients with FMS and 17 sex- and age-matched healthy control participants. Each participant viewed pleasant (erotica), neutral, and unpleasant (attack related) pictures, and abrupt white noises were delivered during two-thirds of the pictures to evoke startle eyeblinks. Appetitive and defensive responding was assessed from subjective (valence/pleasure and arousal ratings) and physiological (corrugator EMG, heart rate, skin-conductance response, startle-reflex modulation) reactions to pictures. Results suggested FMS was associated with greater defensive activation (displeasure, subjective arousal, corrugator EMG) to the unpleasant, threat-related pictures, but not deficits in appetitive activation to erotic pictures. Although preliminary, these data suggest individuals with FMS have deficits in affective processing, but this dysregulation may be limited to defensive activation. Implications for treatment and future research are discussed.

				PERSPECTIVE: Fibromyalgia is a debilitating disease associated with affective distress. Results from the present study suggest that FMS is associated with enhanced defensive activation to nonpainful threat-related stimuli, but not deficits in appetitive reactions to erotic stimuli. These findings have implications for the treatment and study of FMS.
Baumann K, Krayenbühl P.	Klinik und Poliklinik für Innere Medizin, Universitätsspital Zürich.	[Fatigue][Article in German]	Praxis (Bern 1994). 2009 Apr 29;98(9):465-71.	
Beever R.	Richard.beever@northernhealth.ca	Far-infrared saunas for treatment of cardiovascular risk factors: summary of published evidence.	Can Fam Physician. 2009 Jul;55(7):691-6.	OBJECTIVE: To review the literature about the health benefits of far-infrared sauna (FIRS) use. QUALITY OF EVIDENCE: A search of Web of Science, EBSCO, Ovid MEDLINE, Ovid HealthSTAR, and EMBASE using the terms far-infrared and sauna, refined by limiting the search to studies of humans published in English, yielded 9 relevant papers (level I or level II evidence). MAIN MESSAGE: Far-infrared saunas are approved by the Canadian Standards Association and are sold to the public. The manufacturers claim numerous health benefits; however, the published evidence to substantiate these claims is limited. Four papers support the use of FIRS therapy for those with congestive heart failure and 5 papers support its use for those with coronary risk factors. CONCLUSION: There is limited moderate evidence supporting FIRS efficacy in normalizing blood pressure and treating congestive heart failure; fair evidence, from a single study, supporting FIRS therapy in chronic pain; weak evidence, from a single study, supporting FIRS therapy in chronic fatigue syndrome; weak evidence, from a single study, supporting FIRS therapy for obesity; and consistent fair evidence to refute claims regarding the role of FIRSs in cholesterol reduction.
Ben-Zvi A, Vernon SD, Broderick G.	Department of Chemical and Materials Engineering, University of Alberta, Edmonton, Alberta, Canada.	Model-based therapeutic correction of hypothalamic-pituitary-adrenal axis dysfunction.	PLoS Comput Biol. 2009 Jan;5(1):e1000273. Epub 2009 Jan 23.	The hypothalamic-pituitary-adrenal (HPA) axis is a major system maintaining body homeostasis by regulating the neuroendocrine and sympathetic nervous systems as well modulating immune function. Recent work has shown that the complex dynamics of this system accommodate several stable steady states, one of which corresponds to the hypocortisol state observed in patients with chronic fatigue syndrome (CFS). At present these dynamics are not formally considered in the development of treatment strategies. Here we use model-based predictive control (MPC) methodology to estimate robust treatment courses for displacing the HPA axis from an abnormal hypocortisol steady state back to a healthy cortisol level. This approach was applied to a recent model of HPA axis dynamics incorporating glucocorticoid receptor kinetics. A candidate treatment that displays robust properties in the face of significant biological variability and measurement uncertainty requires that cortisol be further suppressed for a short period until adrenocorticotropic hormone levels exceed 30% of baseline. Treatment may then be discontinued, and the HPA axis will naturally progress to a stable attractor defined by normal hormone levels. Suppression of biologically available cortisol may be achieved through the use of binding proteins such as CBG and certain metabolizing enzymes, thus offering possible avenues for deployment in a clinical setting. Treatment strategies can therefore be designed that maximally exploit system dynamics to provide a robust response to treatment and ensure a positive outcome over a wide range of conditions. Perhaps most importantly, a treatment course involving further reduction in cortisol, even transient, is quite counterintuitive and challenges the conventional strategy of supplementing cortisol levels, an approach based on steady-

				state reasoning.
Bito S.	Department of Clinical Education, National Hospital Organization Tokyo Medical Center.	[Functional somatic syndrome in general practice] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1715-9.	General practitioners (GPs) see many patients with various symptoms such as dizziness, general fatigue, chronic headache, numbness, chronic upper abdominal pain and chronic diarrhea and these patients often have no abnormal findings in diagnostic tests. Even some specific conditions are categorized as "diseases" such as "fibromyalgia" and "non-ulcer dyspepsia", the patients actually suffer from various illnesses and have common questions. One is "Why am I suffering from such illness?" and the other is "How can I waive from the suffering?". GPs should usually face with these patients' questions. Even without categorization by "functional somatic syndrome", GPs provide continuity of care and sometimes provide prescriptions for such patients. The concept of postmodern is essential in management of functional somatic syndrome.
Bjørkum T, Wang CE, Waterloo K.	Sogndal BUP, Postboks 184, 6851 Sogndal. torunn.bjoerkum@helse-forde.no	[Patients' experience with treatment of chronic fatigue syndrome][Article in Norwegian]	Tidsskr Nor Laegeforen. 2009 Jun 11;129(12):1214-6.	BACKGROUND: Chronic fatigue syndrome is a highly debated condition. Little is known about causes and treatment. Patients" experience is important in this context. MATERIAL AND METHODS:828 persons with chronic fatigue syndrome (ICD-10 code: G93.3) were included in the study. They were recruited through two Norwegian patient organizations (ME-association and MENiN). The participants filled in a questionnaire on their experience with various approaches to alleviate their condition. RESULTS: Pacing was evaluated as useful by 96% of the participants, rest by 97%, and 96% of the participants considered complete shielding and quietness to be useful. 57% of the participants who had received help to identify and challenge negative thought patterns regarded this useful. 79% of the participants with experience from graded training regarded this to worsen their health status. Overall, the results were similar, irrelevant of the severity of the condition. INTERPRETATION:Most participants in this study evaluated pacing, rest and complete shielding and quietness to be useful. The experience of the participants indicate that cognitive behaviour therapy can be useful for some patients, but that graded training may cause deterioration of the condition in many patients. The results must, however, be interpreted with care, as the participants are not a representative sample, and we do not know the specific content of the approaches.
Blaney GP, Albert PJ, Proal AD.	Stillpoint Centre, Vancouver, British Columbia, Canada. gregblaney@shaw.ca	Vitamin D metabolites as clinical markers in autoimmune and chronic disease.	Ann N Y Acad Sci. 2009 Sep;1173:384-90.	Recent research has implicated vitamin D deficiency (serum levels of 25-hydroxyvitamin D <50 nmol/L) with a number of chronic conditions, including autoimmune conditions such as multiple sclerosis, lupus, and psoriasis, and chronic conditions such as osteoporosis, osteoarthritis, metabolic syndrome, fibromyalgia and chronic fatigue syndrome. It has been assumed that low levels of 25-hydroxyvitamin D (25-D) accurately indicate vitamin D storage and vitamin D receptor (VDR)-mediated control of calcium metabolism and innate immunity. To evaluate this assumption, 25-D and 1,25-dihydroxyvitamin D3 (1,25-D) levels were measured in 100 Canadian patients with these conditions. Additionally, other inflammatory markers (CK, CRP) were measured. Results showed a strong positive association between these autoimmune conditions and levels of 1,25-D >110 pmol/L. However, there was little association with vitamin D deficiency or the other inflammatory markers, meaning that the results challenge the assumption that serum levels of 25-D are a sensitive measure of the autoimmune disease state. Rather, these findings support the use of 1,25-D as a clinical marker in autoimmune conditions. High levels of 1,25-D may result when dysregulation of the VDR by bacterial ligands prevents the receptor from expressing enzymes necessary to keep 1,25-D in a normal range.
Bol Y, Duits AA,	Department of	The psychology of	J Psychosom Res.	Fatigue is a frequent and disabling symptom in patients with multiple sclerosis (MS), but it is difficult

Hupperts RM, Vlaeyen JW, Verhey FR.	Psychology, Maastricht University Medical Center, Maastricht, The Netherlands. y.bol@np.unimaas.nl	fatigue in patients with multiple sclerosis: a review.	2009 Jan;66(1):3-11. Epub 2008 Sep 24.	to define and measure. Today, MS-related fatigue is not fully understood, and evidence related to explanatory pathophysiological factors are conflicting. Here, we evaluate the contribution of psychological factors to MS-related fatigue. Insight into the possible underlying psychological mechanisms might help us to develop adequate psychological interventions and to improve the overall management of fatigue. Conceptual issues and the relationships between MS-related fatigue and mood, anxiety, cognition, personality, and cognitive-behavioral factors are discussed, and the implications for clinical practice and research are presented.
Boneva RS, Lin JM, Maloney EM, Jones JF, Reeves WC.	Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. rboneva@cdc.gov	Use of medications by people with chronic fatigue syndrome and healthy persons: a population-based study of fatiguing illness in Georgia.	Health Qual Life Outcomes. 2009 Jul 20;7:67.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating condition of unknown etiology and no definitive pharmacotherapy. Patients are usually prescribed symptomatic treatment or self-medicate. We evaluated prescription and non-prescription drug use among persons with CFS in Georgia and compared it to that in non-fatigued Well controls and also to chronically Unwell individuals not fully meeting criteria for CFS. METHODS: A population-based, case-control study. To identify persons with possible CFS-like illness and controls, we conducted a random-digit dialing telephone screening of 19,807 Georgia residents, followed by a detailed telephone interview of 5,630 to identify subjects with CFS-like illness, other chronically Unwell, and Well subjects. All those with CFS-like illness (n = 469), a random sample of chronically Unwell subjects (n = 505), and Well individuals (n = 641) who were age-, sex-, race-, and geographically matched to those with CFS-like illness were invited for a clinical evaluation and 783 participated (48% overall response rate). Clinical evaluation identified 113 persons with CFS, 264 Unwell subjects with insufficient symptoms for CFS (named ISF), and 124 Well controls; the remaining 280 subjects had exclusionary medical or psychiatric conditions, and 2 subjects could not be classified. Subjects were asked to bring all medications taken in the past 2 weeks to the clinic where a research nurse viewed and recorded the name and the dose of each medication. RESULTS: More than 90% of persons with CFS used at least one drug or supplement within the preceding two weeks. Among users, people with CFS used an average of 5.8 drugs or supplements, compared to 4.1 by ISF and 3.7 by Well controls. Persons with CFS were significantly more likely to use antidepressants, sedatives, muscle relaxants, and anti-acids than either Well controls or the ISF group. In addition, persons with CFS were significantly more likely to use pain-relievers, anti-histamines and cold/sinus medications than were Well controls. CONCLUSION: Medical care providers of patients with chronic fatigue syndrome should be aware of polypharmacy as a problem in such patients, and the related potential iatrogenic effects and drug interactions.
Boone KB.	Center for Forensic Studies, Alliant International University - LA, 1000 South Fremont Avenue, Alhambra, CA91803, USA. kboone@labiomed.org	Fixed belief in cognitive dysfunction despite normal neuropsychological scores: neurocognitive hypochondriasis?	Clin Neuropsychol. 2009 Aug;23(6):1016-36.	A subset of patients who present for neuropsychological testing report dysfunction in daily life activities secondary to cognitive deficits, but are found on formal testing to have no objective abnormalities, raising the possibility of "neurocognitive hypochondriasis." Such a case is presented, and the factors that appear to give rise to this presentation are explored. Cases of hypochondriacal overconcern regarding cognitive function are likely not rare, particularly given research showing there is little correlation between objective report of cognitive dysfunction and actual test scores in such conditions as mild traumatic brain injury, chronic fatigue syndrome, fibromyalgia, toxic mold exposure, and post-polio syndrome.

Bramsen I.		Can CBT substantially change grey matter volume in chronic fatigue syndrome? Comment in: Brain. 2009 Jul;132(Pt 7):e119; author reply e120.Comment on: Brain. 2008 Aug;131(Pt 8):2172-80.	Brain. 2009 Jun;132(Pt 6):e110; author reply e111. Epub 2008 Aug 29.	
Brimmer DJ, McCleary KK, Lupton TA, Faryna KM, Reeves WC.	Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. dyv4@cdc.gov	Continuing medical education challenges in chronic fatigue syndrome.	BMC Med Educ. 2009 Dec 2;9:70.	BACKGROUND: Chronic fatigue syndrome (CFS) affects at least 4 million people in the United States, yet only 16% of people with CFS have received a diagnosis or medical care for their illness. Educating health care professionals about the diagnosis and management of CFS may help to reduce population morbidity associated with CFS. METHODS: This report presents findings over a 5-year period from May 2000 to June 2006 during which we developed and implemented a health care professional educational program. The objective of the program was to distribute CFS continuing education materials to providers at professional conferences, offer online continuing education credits in different formats (e.g., print, video, and online), and evaluate the number of accreditation certificates awarded. RESULTS: We found that smaller conference size (OR = 80.17; 95% CI 8.80, 730.25), CFS illness related target audiences (OR = 36.0; 95% CI 2.94, 436.34), and conferences in which CFS research was highlighted (OR = 4.15; 95% CI 1.16, 14.83) significantly contributed to higher dissemination levels, as measured by visit rates to the education booth. While print and online courses were equally requested for continuing education credit opportunities, the online course resulted in 84% of the overall award certificates, compared to 14% for the print course. This remained consistent across all provider occupations: physicians, nurses, physician assistants, and allied health professionals. CONCLUSION: These findings suggest that educational programs promoting materials at conferences may increase dissemination efforts by targeting audiences, examining conference characteristics, and promoting online continuing education forums.
Bruusgaard D, Natvig B.	Seksjon for arbeids- og trygdemedisin, Universitetet i Oslo, Postboks 1130, Blindern 0318 Oslo, Norway.	[Unclear conditions--common mechanisms?] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2009 Aug 13;129(15):1481-3.	

	dag.bruusgaard@medisin.uio.no			
Burkhard B, Kittel R.	Medizinischen Dienst der Krankenversicherung in Bayern, München.	[Visualisation methods for etheric formative forces] [Article in German]	Versicherungsmedizin. 2009 Sep 1;61(3):126-8.	Rudolf Steiner, the founder of anthroposophy, suggested the development of visualisation methods for "etheric formative forces". The essential methods, their "spiritual scientific" basis and indications are described and their claims critically tested. Summary: The methods are not validated, the key criteria for diagnostic tests (reproducibility, sensitivity, specifity) are not given.
Burton C, Knoop H, Popovic N, Sharpe M, Bleijenberg G.	Division of Community Health Sciences, General Practice Section, University of Edinburgh, West Richmond Street, Edinburgh, UK. chris.burton@ed.ac.uk.	Reduced complexity of activity patterns in patients with Chronic Fatigue Syndrome: a case control study.	Biopsychosoc Med. 2009 Jun 2;3:7.	ABSTRACT: BACKGROUND: Chronic fatigue syndrome (CFS) is an illness characterised by pervasive physical and mental fatigue without specific identified pathological changes. Many patients with CFS show reduced physical activity which, though quantifiable, has yielded little information to date. Nonlinear dynamic analysis of physiological data can be used to measure complexity in terms of dissimilarity within timescales and similarity across timescales. A reduction in these objective measures has been associated with disease and ageing. We aimed to test the hypothesis that activity patterns of patients with CFS would show reduced complexity compared to healthy controls. METHODS: We analysed continuous activity data over 12 days from 42 patients with CFS and 21 matched healthy controls. We estimated complexity in two ways, measuring dissimilarity within timescales by calculating entropy after a symbolic dynamic transformation of the data and similarity across timescales by calculating the fractal dimension using allometric aggregation. RESULTS: CFS cases showed reduced complexity compared to controls, as evidenced by reduced dissimilarity within timescales (mean (SD) Renyi(3) entropy 4.05 (0.21) vs. 4.30 (0.09), $t = -6.6$, $p < 0.001$) and reduced similarity across timescales (fractal dimension 1.19 (0.04) vs. 1.14 (0.04), $t = 4.2$, $p < 0.001$). This reduction in complexity persisted after adjustment for total activity. CONCLUSION: Patients with CFS show evidence of reduced complexity of activity patterns. Measures of complexity applied to activity have potential value as objective indicators for CFS.
Byrnes A, Jacks A, Dahlman-Wright K, Evengard B, Wright FA, Pedersen NL, Sullivan PF.	Department of Genetics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, United States of America.	Gene expression in peripheral blood leukocytes in monozygotic twins discordant for chronic fatigue: no evidence of a biomarker.	PLoS One. 2009 Jun 5;4(6):e5805.	BACKGROUND: Chronic fatiguing illness remains a poorly understood syndrome of unknown pathogenesis. We attempted to identify biomarkers for chronic fatiguing illness using microarrays to query the transcriptome in peripheral blood leukocytes. METHODS: Cases were 44 individuals who were clinically evaluated and found to meet standard international criteria for chronic fatigue syndrome or idiopathic chronic fatigue, and controls were their monozygotic co-twins who were clinically evaluated and never had even one month of impairing fatigue. Biological sampling conditions were standardized and RNA stabilizing media were used. These methodological features provide rigorous control for bias resulting from case-control mismatched ancestry and experimental error. Individual gene expression profiles were assessed using Affymetrix Human Genome U133 Plus 2.0 arrays. FINDINGS: There were no significant differences in gene expression for any transcript. CONCLUSIONS: Contrary to our expectations, we were unable to identify a biomarker for chronic fatiguing illness in the transcriptome of peripheral blood leukocytes suggesting that positive findings in prior studies may have resulted from experimental bias.
Carlo-Stella N, Bozzini S, De Silvestri A, Sbarsi I,	Genetics and Microbiology Department,	Molecular study of receptor for advanced glycation	Int J Immunopathol Pharmacol. 2009	The receptor for advanced glycation end product (RAGE) is thought to play an important role in inflammation. Chronic fatigue syndrome (CFS) is a long-lasting fatigue that compromises at least 50% of a subject's daily activities without other known cause. Immune dysfunction has been implicated

Pizzochero C, Lorusso L, Martinetti M, Cuccia M.	University of Pavia, Pavia, Italy.	endproduct gene promoter and identification of specific HLA haplotypes possibly involved in chronic fatigue syndrome.	Jul-Sep;22(3):745-54.	and an association with a peculiar genetic cytokine profile, predisposing to an immunomodulatory response of inflammatory nature, was found. The aim of this study is to analyse RAGE polymorphisms and HLA-DRB1 alleles in seventy-five Italian CFS patients and 141 controls matched for age, sex and ethnicity. These two groups underwent genomic study for RAGE 374T/A and 429C/T promoter polymorphisms; moreover, 46 patients and 186 controls were typed for HLA-DRB1 at low resolution molecular level. Of these, 31 patients and 99 controls also underwent high resolution analysis to define the HLA-DRB1*11 and DRB1*13 alleles. The haplotypes RAGE-374T, DRB1*04; RAGE-374T, DRB1*09; RAGE-374T, DRB1*11; RAGE-374A, DRB1*13; RAGE-429T, DRB1*04 and RAGE-429C, DRB1*11 were significantly more frequent in CFS patients, whereas RAGE-429C, DRB1*07 would seem protective. A significantly lower frequency of DRB1*1104 (5.4% vs 12.9% p=0.04, OR=0.39) and a significantly higher frequency of HLA-DRB1*1301 (13.0% vs 5.1% p=0.006, OR= 2.79) were found in CFS patients. A synergic effect was observed with RAGE polymorphism. The OR values strengthened in the following cis combinations: RAGE-374A, HLA-DRB1*1104 (OR=0.27) and RAGE-374A, HLADRB1*1301 (OR=6.23). HLA haplotypes rather than single alleles of RAGE or of DRB1 genes seem to be involved in CFS, probably including a subregion of major interest.
Cathébras P, Lauwers A.	Service de médecine interne, hôpital Nord, CHU de Saint-Etienne, 42055 Saint-Etienne Cedex 2, France. pascal.cathebras@chu-st-etienne.fr	[Should we make the diagnosis of fibromyalgia?][Article in French]	Rev Prat. 2009 Jan 20;59(1):25-31.	Fibromyalgia is a functional somatic syndrome characterized by widespread musculoskeletal pain, fatigue, poor sleep, and exercise intolerance, frequently (but inconstantly) associated with psychological distress. Fibromyalgia is a common condition, affecting predominantly middle-aged women, with a chronic course. Fibromaylgia should be differentiated from, and may be associated with, a number of metabolic, rheumatic, neurological or psychiatric conditions. The most plausible pathophysiologic mechanism involves an alteration of pain modulation at the peripheral and central levels of the nervous system ("sensitization"). Psychosocial factors play an important role in precipitating and maintaining symptoms, health care utilization, and disablement. Treatments of fibromyalgia rely mainly on the acknowledgement of pain and distress, patient education, analgesics, balneotherapy and physiotherapy, physical reconditioning (aerobic exercise), and certain antidepressants.
Chalder T, Deary V, Husain K, Walwyn R.	Department of Psychological Medicine and Psychiatry, King's College London, Weston Education Centre, London, UK.	Family-focused cognitive behaviour therapy versus psycho-education for chronic fatigue syndrome in 11- to 18-year-olds: a randomized controlled treatment trial.	Psychol Med. 2009 Nov 6:1-11. [Epub ahead of print]	BACKGROUND: Only one previous randomized controlled trial (RCT) has examined the efficacy of cognitive behaviour therapy (CBT) for chronic fatigue syndrome (CFS) in children. The aim of this study was to compare family-focused CBT with psycho-education for CFS in adolescents.MethodSixty-three 11- to 18-year-olds (43 girls, 20 boys) with CFS were randomly assigned to either family-focused CBT or psycho-education delivered over 6 months. School attendance was the main outcome, which was assessed at the end of treatment and at 3, 6 and 12 months follow-up. RESULTS: At the main outcome point (the 6-month follow-up) both groups had improved similarly. However, although those who received family-focused CBT were attending school for longer than those who received psycho-education, at discharge from treatment and at 3 months follow-up, they improved less quickly across the follow-up period. CONCLUSIONS: Adolescents with CFS get back to school more quickly after family-focused CBT. This is important as they are at a crucial stage of their development. However, the finding that psycho-education was as effective as family-focused CBT at 6 and 12 months follow-up has important implications for health service delivery.
Chastin SF, Granat	Glasgow	Methods for	Gait Posture. 2009	The purpose of this study was to develop and test a generic technique to robustly quantify the pattern

MH.	Caledonian University, School of Health and Social Care, Cowcaddens Road, Glasgow G4 0BA, Scotland, UK.	objective measure, quantification and analysis of sedentary behaviour and inactivity.	Oct 23. [Epub ahead of print]	of sedentary behaviour from objective records. The technique was applied to four groups of subjects: a healthy group with an active occupation (N=54), a healthy group with a sedentary occupation (N=53), a group of subjects with chronic low back pain (N=5) and a group of subjects with chronic fatigue syndrome (N=14). This study presents the first evidence that bouts of sedentary activity are power law distributed. Results showed that there was no significant difference in total sedentary time between the groups, however, the patterns of accumulation of sedentary time were significantly different for the groups. Sedentary groups accumulated their total sedentary time from a small number of longer sedentary bouts. Active groups tended to break their sedentary time into a greater number of shorter bouts. This suggests that the power law exponent alpha and the GINI index G, used to describe the pattern of accumulation of sedentary time, could be used to evaluate and quantify sedentary behaviour.
Chen LH, Wilson ME, Davis X, Loutan L, Schwartz E, Keystone J, Hale D, Lim PL, McCarthy A, Gkrania-Klotsas E, Schlagenhauf P; GeoSentinel Surveillance Network. Collaborators: von Sonnenburg F, Gelman SS, Chappuis F, Kain KC, Field V, Burchard GD, Libman MD, Maclean JD, Leder K, Torresi J, Brown G, Parola P, Simon F, Delmont J, Kass R, Carosi G, Castelli F, Pandey P, Shaw M, Kozarsky PE, Franco-Paredes C, Piyaphanee W, Silachamroon U,	Harvard University, Boston, Massachusetts, USA. lchen@hms.harvard.edu	Illness in long-term travelers visiting GeoSentinel clinics.	Emerg Infect Dis. 2009 Nov;15(11):1773-82.	Length of travel appears to be associated with health risks. GeoSentinel Surveillance Network data for 4,039 long-term travelers (trip duration >6 months) seen after travel during June 1, 1996, through December 31, 2008, were compared with data for 24,807 short-term travelers (trip duration <1 month). Long-term travelers traveled more often than short-term travelers for volunteer activities (39.7% vs. 7.0%) and business (25.2% vs. 13.8%). More long-term travelers were men (57.2% vs. 50.1%) and expatriates (54.0% vs. 8.9%); most had pretravel medical advice (70.3% vs. 48.9%). Per 1,000 travelers, long-term travelers more often experienced chronic diarrhea, giardiasis, Plasmodium falciparum and P. vivax malaria, irritable bowel syndrome (postinfectious), fatigue >1 month, eosinophilia, cutaneous leishmaniasis, schistosomiasis, and Entamoeba histolytica diarrhea. Areas of concern for long-term travelers were vector-borne diseases, contact-transmitted diseases, and psychological problems. Our results can help prioritize screening for and diagnosis of illness in long-term travelers and provide evidence-based pretravel advice.

Tachikawa N, Sagara H, Connor BA, Kanagawa S, Kato Y, Jensenius M, Haulman NJ, Roesel D, Jong EC, Coyle CM, Wittner M, López-Vélez R, Pérez-Molina JA, Nutman TB, Klion AD, Hagmann S, Miller A, Weber R, Steffen R, Stauffer WM, Walker PF, Freedman DO, Ansdell V, Wilder-Smith A, Sack B, McKenzie R, Caumes E, Pérignon A, Licitra C, Crespo A, Barnett ED, Gurtman A, Perret C, Valdivieso F, Muller R, Cahill JD, McKinley G, McLellan S, MacDonald S, Lynch MW, Borwein S, Anglim A.				
Chew-Graham C, Dixon R, Shaw JW, Smyth N, Lovell K, Peters S.	School of Community-Based Medicine, University of Manchester, Manchester, M13 9PL, UK. cchew@manchester.ac.uk.	Practice Nurses' views of their role in the management of Chronic Fatigue Syndrome/Myalagic Encephalitis: a qualitative study.	BMC Nurs. 2009 Jan 22;8:2.	ABSTRACT: BACKGROUND: NICE guidelines suggest that patients with Chronic Fatigue Syndrome/Myalgic Encephalitis (CFS/ME) should be managed in Primary Care. Practice Nurses are increasingly being involved in the management of long-term conditions, so are likely to also have a growing role in managing CFS/ME. However their attitudes to, and experiences of patients with CFS/ME and its management must be explored to understand what barriers may exist in developing their role for this group of patients. The aim of this study was to explore Practice Nurses' understanding and beliefs about CFS/ME and its management. METHODS: Semi-structured interviews with 29 Practice Nurses. Interviews were transcribed verbatim and an iterative approach used to develop themes from the dataset. RESULTS: Practice nurses had limited understanding about CFS/ME

				which had been largely gained through contact with patients, friends, personal experiences and the media rather than formal training. They had difficulty seeing CFS/ME as a long term condition. They did identify a potential role they could have in management of CFS/ME but devalued their own skills in psychological intervention, and suggested counselling would be an appropriate therapeutic option. They recognised a need for further training and on going supervision from both medical and psychological colleagues. Some viewed the condition as contentious and held pejorative views about CFS/ME. Such scepticism and negative attitudes will be a significant barrier to the management of patients with CFS/ME in primary care. CONCLUSION: The current role of Practice Nurses in the ongoing management of patients with CFS/ME is limited. Practice Nurses have little understanding of the evidence-base for treatment of CFS/ME, particularly psychological therapies, describing management options in terms of advice giving, self-help or counselling. Practice Nurses largely welcomed the potential development of their role in this area, but identified barriers and training needs which must be addressed to enable them to feel confident managing of patients with this condition. Training must begin by addressing negative attitudes to patients with CFS/ME.
Chia JK, Chia AY, Voeller M, Lee TM, Chang R.	EV Med Research, United States;	Acute enterovirus infection followed by myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) and viral persistence.	J Clin Pathol. 2009 Oct 14. [Epub ahead of print]	A number of infections have been associated with myalgia encephalomyelitis/chronic fatigue syndrome (ME/CFS). Often occurring in epidemics, enteroviruses are significant causes of respiratory, gastrointestinal infections, non-specific flu-like illnesses, and many disseminated infections. It has been difficult to demonstrate causality for chronic diseases without having well-documented cases of acute enterovirus infections. In this report, we described 3 patients presenting with acute enterovirus infections, which were followed by ME/CFS, and the persistent viral infections were demonstrated by finding enterovirus VP1 protein and RNA in the stomach.
Cho HJ, Menezes PR, Hotopf M, Bhugra D, Wessely S.	Department of Preventive Medicine, University of São Paulo Medical School, University Hospital, University of São Paulo, Brazil. h.cho@iop.kcl.ac.uk	Comparative epidemiology of chronic fatigue syndrome in Brazilian and British primary care: prevalence and recognition.	Br J Psychiatry. 2009 Feb;194(2):117-22.	BACKGROUND: Although fatigue is a ubiquitous symptom across countries, clinical descriptions of chronic fatigue syndrome have arisen from a limited number of high-income countries. This might reflect differences in true prevalence or clinical recognition influenced by sociocultural factors. AIMS: To compare the prevalence, physician recognition and diagnosis of chronic fatigue syndrome in London and São Paulo. METHOD: Primary care patients in London (n=2459) and São Paulo (n=3914) were surveyed for the prevalence of chronic fatigue syndrome. Medical records were reviewed for the physician recognition and diagnosis. RESULTS: The prevalence of chronic fatigue syndrome according to Centers for Disease Control 1994 criteria was comparable in Britain and Brazil: 2.1% v. 1.6% (P=0.20). Medical records review identified 11 diagnosed cases of chronic fatigue syndrome in Britain, but none in Brazil (P<0.001). CONCLUSIONS: The primary care prevalence of chronic fatigue syndrome was similar in two culturally and economically distinct nations. However, doctors are unlikely to recognise and label chronic fatigue syndrome as a discrete disorder in Brazil. The recognition of this illness rather than the illness itself may be culturally induced.
Cho JH, Cho CK, Shin JW, Son JY, Kang W, Son CG.	East-West Cancer Center, Dunsan Oriental Hospital of Oriental Medical College of Daejeon	Myelophil, an extract mix of Astragali Radix and Salviae Radix, ameliorates	Complement Ther Med. 2009 Jun;17(3):141-6. Epub 2009 Jan 23.	OBJECTIVES: To investigate the anti-fatigue effects of Myelophil, an extract of a mix of Astragali Radix and Salviae Radix, which has been used to treat patients with chronic fatigue. SUBJECTS AND DESIGN: A randomised, double-blind, controlled clinical trial was performed with 36 adults who complained of chronic fatigue. The subjects were divided among a control group and low- and high-dose groups (3 or 6g of oral Myelophil per day, respectively) and were monitored for 4 weeks. Fatigue severity was

	University, Seo-gu, Daejeon, South Korea.	chronic fatigue: a randomised, double-blind, controlled pilot study.		subjectively characterised, and the expression of 42 cytokines was evaluated using an antibody array. RESULTS: Myelophil administration (3g per day) significantly decreased the fatigue severity score compared with the control ($p<0.05$). No changes were noted in cytokine expression. CONCLUSIONS: Myelophil appears to have a pharmacological effect against fatigue, suggesting the clinical relevance of the traditional medicinal plants, Astragalus membranaceus and Salvia miltiorrhiza.
Chong YY, Ng BY.	Department of Rheumatology and Immunology, Singapore General Hospital, Singapore. chong.yong.yeow@sgh.com.sg	Clinical aspects and management of fibromyalgia syndrome.	Ann Acad Med Singapore. 2009 Nov;38(11):967-73.	Fibromyalgia syndrome (FMS) is a chronic and debilitating musculoskeletal pain disorder of unknown aetiology with usual accompanying features of fatigue, sleep disturbances and stiffness. Its place in medical textbooks was controversial with rheumatologists holding the helm of its management for many years. Over the last decade, abnormalities have been identified at multiple levels in the peripheral, central, and sympathetic nervous systems as well as the hypothalomo-pituitary-adrenal axis stress response system. With the elucidation of these pathways of pain, FMS is known more as a central sensitivity syndrome. This led to tremendous increment in interest in both pharmacological and non-pharmacological treatment of FMS. The United States Food and Drug Administration (FDA) has also successively approved 3 drugs for the management of fibromyalgia--pregabalin, duloxetine and milnacipran. Non-pharmacological modalities showed aerobic exercise, patient education and cognitive behavioural therapy to be most effective. Overall, management of FMS requires a multi-disciplinary approach.
Chrousos GP, Kino T.	First Department of Pediatrics, Athens University Medical School, Athens, Greece. chrousge@med.uoa.gr	Glucocorticoid signaling in the cell. Expanding clinical implications to complex human behavioral and somatic disorders.	Ann N Y Acad Sci. 2009 Oct;1179:153-66.	Glucocorticoids contribute to the maintenance of basal and stress-related homeostasis in all higher organisms, and influence a large proportion of the expressed human genome, and their effects spare almost no organs or tissues. Glucocorticoids regulate many functions of the central nervous system, such as arousal, cognition, mood, sleep, the activity and direction of intermediary metabolism, the maintenance of a proper cardiovascular tone, the activity and quality of the immune and inflammatory reaction, including the manifestations of the sickness syndrome, and growth and reproduction. The numerous actions of glucocorticoids are mediated by a set of at least 16 glucocorticoid receptor (GR) isoforms forming homo- or hetero-dimers. The GRs consist of multifunctional domain proteins operating as ligand-dependent transcription factors that interact with many other cell signaling systems, including large and small G proteins. The presence of multiple GR monomers and homo- or hetero-dimers expressed in a cell-specific fashion at different quantities with quantitatively and qualitatively different transcriptional activities suggest that the glucocorticoid signaling system is highly stochastic. Glucocorticoids are heavily involved in human pathophysiology and influence life expectancy. Common behavioral and/or somatic complex disorders, such as anxiety, depression, insomnia, chronic pain and fatigue syndromes, obesity, the metabolic syndrome, essential hypertension, diabetes type 2, atherosclerosis with its cardiovascular sequelae, and osteoporosis, as well as autoimmune inflammatory and allergic disorders, all appear to have a glucocorticoid-regulated component.
Clauw DJ.	Chronic Pain & Fatigue Research Center, Department of Anesthesiology,	Fibromyalgia: an overview.	Am J Med. 2009 Dec;122(12 Suppl):S3-S13.	Fibromyalgia is the diagnosis given to individuals with chronic widespread musculoskeletal pain for which no alternative cause, such as tissue inflammation or damage, can be identified. Fibromyalgia is now believed to be, at least in part, a disorder of central pain processing that produces heightened responses to painful stimuli (hyperalgesia) and painful responses to nonpainful stimuli (allodynia). Aberrations in central pain processing may also be partly responsible for symptoms experienced in

	University of Michigan, Ann Arbor, Michigan 48106, USA. dclauw@med.umich.edu			several chronic pain disorders that coaggregate with fibromyalgia, which is itself a product of genetic and environmental factors. Thus, aberrational central pain processing is implicated in irritable bowel syndrome, temporomandibular disorder, chronic low back pain, and certain other chronic pain disorders. Fibromyalgia and related disorders appear to reflect deficiencies in serotonergic and noradrenergic, but not opioidergic, transmission in the central nervous system. The heightened state of pain transmission may also be owing to increases in pronociceptive neurotransmitters such as glutamate and substance P. In some cases, psychological and behavioral factors are also in play. Although the overlapping symptomatology between fibromyalgia and related disorders may present diagnostic challenges, proper examination and observation can help clinicians make an accurate diagnosis. In recent years, the vastly improved understanding of the mechanism underlying fibromyalgia and the related spectrum of diseases has fostered rapid advances in the therapy of these chronic pain disorders by both pharmacologic and nonpharmacologic interventions. (c) 2009 Elsevier Inc.
Coffin JM, Stoye JP.	Department of Molecular Microbiology, Tufts University, Boston, MA 02111, USA. john.coffin@tufts.edu	Virology. A new virus for old diseases?	Science. 2009 Oct 23;326(5952):530-1. Epub 2009 Oct 8. Comment on: Science. 2009 Oct 23;326(5952):585-9.	
Courjaret J, Schotte CK, Wijnants H, Moorkens G, Cosyns P.	Department of Psychiatry, University Hospital Antwerp, Edegem, Belgium. kim.courjaret@uza.be	Chronic fatigue syndrome and DSM-IV personality disorders.	J Psychosom Res. 2009 Jan;66(1):13-20. Epub 2008 Nov 22.	OBJECTIVE: Personality is an important factor in the research of the chronic fatigue syndrome (CFS). Although some studies report a high rate of personality disorders--around the 40% level--in samples of patients with CFS, the generalizability of these findings can be questioned. The present study evaluates the prevalence of Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) personality disorders in a sample of female CFS patients and in two control groups. METHOD: The ADP-IV questionnaire (Assessment of DSM Personality Disorders IV) was used to assess the DSM-IV-TR personality disorders at a dimensional and categorical level in a sample of 50 female CFS patients and in two matched control samples of Flemish civilians (n=50) and psychiatric patients (n=50). RESULTS: The results indicate a striking lack of statistical significant differences between the CFS sample and the Flemish control group at the level of dimensional Trait scores, number of criteria, and prevalence rates of personality disorder diagnoses. Unsurprisingly, higher scores at these levels were obtained within the psychiatric sample. The prevalence of an Axis II disorder was 12% in the Flemish and CFS samples, whereas the psychiatric sample obtained a prevalence of 54%. CONCLUSION: The prominent absence of any significant difference in personality disorder characteristics between the female Flemish general population and the CFS samples seems to suggest only a minor etiological role for personality pathology, as defined by the DSM-IV Axis II, within CFS.
Crawley E, Hunt L, Stallard P.	Centre of Child and Adolescent Health, Hampton House,	Anxiety in children with CFS/ME.	Eur Child Adolesc Psychiatry. 2009 Nov;18(11):683-9.	Anxiety symptoms are commonly described in children with chronic fatigue syndrome or myalgic encephalopathy (CFS/ME) but to date there has been little information on the type of anxiety children experience or the relationship between anxiety and school attendance, disability or fatigue. The aim

	Cotham Hill, Bristol BS6 6JS, UK. esther.crawley@bristol.ac.uk		Epub 2009 May 19.	of this study was to first describe the prevalence and type of anxiety symptoms in children with CFS/ME compared with a normal European population, and secondly to investigate the association of anxiety symptoms with age, gender, school attendance, fatigue, and physical function in paediatric CFS/ME. Data were prospectively collected on children and young people with CFS/ME referred to a large specialist CFS/ME service. One hundred and sixty-four children with CFS/ME had complete data for the Spence Children's Anxiety Scale. Teenage girls had the highest rates of total anxiety symptoms with 38% (95% CI 27-49) over the cut off (top 10% of normal European population) and significantly higher rates of symptoms in each subscale. Younger girls were more likely to score over the cut off in separation anxiety (37%, 19-40) and social phobia (39%, 25-47). There was no evidence of association between total anxiety symptoms and: time at school, time to assessment, pain or age. Associations with fatigue and physical function were attenuated when adjusted for other variables. Although anxiety symptoms are high in CFS/ME, particularly in teenage girls, it does not appear to be associated with school attendance or other measures of disability. Separation anxiety and social phobia were the most clearly elevated in paediatric CFS/ME.
Crawley E, Sterne JA.	Centre for Child and Adolescent Health, University of Bristol, Bristol, UK. esther.crawley@bristol.ac.uk	Association between school absence and physical function in paediatric chronic fatigue syndrome/myalgic encephalopathy.	Arch Dis Child. 2009 Oct;94(10):752-6. Epub 2008 Nov 11.	OBJECTIVE: To investigate factors associated with school attendance and physical function in paediatric chronic fatigue syndrome/myalgic encephalopathy (CFS/ME). DESIGN: Cross-sectional study. SETTING: Regional specialist CFS/ME service. PATIENTS: Children and young people aged under 18 years. OUTCOME MEASURES: Self-reported school attendance and physical function measured using the physical function subscale of the Short Form 36. METHODS: Linear and logistic regression analysis of data from self-completed assessment forms on children attending a regional specialist service between 2004 and 2007. Analyses were done in two groups of children: with a completed Spence Children's Anxiety Scale (SCAS) and with a completed Hospital Anxiety and Depression Scale (HADS). RESULTS: Of 211 children with CFS/ME, 62% attended 40% of school or less. In children with completed SCAS, those with better physical function were more likely to attend school (adjusted odds ratio (OR) 1.70; 95% CI 1.36 to 2.13). This was also true for those with completed HADS (adjusted OR 2.05; 95% CI 1.4 to 3.01). Increasing fatigue and pain and low mood were associated with worse physical function. There was no evidence that anxiety, gender, age at assessment, family history of CFS/ME or time from onset of symptoms to assessment in clinic were associated with school attendance or physical function. IMPLICATIONS: Paediatricians should recognise that reduced school attendance is associated with reduced physical function rather than anxiety. Improving school attendance in children with CFS/ME should focus on evidence-based interventions to improve physical function, particularly concentrating on interventions that are likely to reduce pain and fatigue.
Creavin ST, Dunn KM, Mallen CD, Nijrolder I, van der Windt DA.	Arthritis Research Campaign National Primary Care Centre, Keele University, Staffordshire ST5 5BG, United Kingdom.	Co-occurrence and associations of pain and fatigue in a community sample of Dutch adults.	Eur J Pain. 2009 Jun 17. [Epub ahead of print]	Widespread pain and chronic fatigue are common in the general population. Previous research has demonstrated co-occurrence of syndromes that are associated with pain and fatigue (fibromyalgia and chronic fatigue syndrome), but there is limited existing data on the co-occurrence of these symptoms in general. This study investigates the co-occurrence of pain and fatigue, and characterises people with these symptoms individually, and in combination. A postal questionnaire was sent to a random sample of 4741 community dwelling Dutch adults registered with five general practices. There were 2447 participants (adjusted response=53.5%). Persistent fatigue was reported by 60% of the 451 subjects with chronic widespread pain. Chronic widespread pain was reported by 33% of the 809

				responders with persistent fatigue. Anxiety and depression were more common in subjects who reported both symptoms than those who reported either one or neither. Participants who had chronic disease, high body mass index, low activity levels or did not perceive ability to influence health had higher adjusted odds of reporting both symptoms (but not one alone) than subjects not having these characteristics. Pain and fatigue occur more often than would be expected by chance and there are a number of reasons for this. Clinicians should be aware that co-occurrence of the symptoms is common, especially in people who have high BMI or chronic disease, and that people with both symptoms are often anxious or depressed. Further work should address longitudinal associations of pain and fatigue.
Cuadros J, Vargas M.	jcuadros@fivmadrid.es	A new mind-body approach for a total healing of fibromyalgia: a case report.	Am J Clin Hypn. 2009 Jul;52(1):3-12.	Fibromyalgia is a severe, chronic and widespread pain syndrome with no definite treatment protocol. Several medications are currently in use to treat this condition. Various pharmacological treatments, as well as alternative mind-body therapies, have been directed towards reducing fatigue and pain, but these treatments have only resulted in a partial relief of symptoms with no long-term or permanent effects. This study shows the results obtained from four female patients suffering from fibromyalgia after undergoing a mind-body treatment in which psychosocial genomic postulates as well as ideodynamic hand movements were the main tools employed in their healing. It is suggested that a mind-body oriented treatment could generate stable and permanent changes that enable patients to experience a total recovery from fibromyalgia.
Daley M, Morin CM, LeBlanc M, Grégoire JP, Savard J, Baillargeon L.	Ecole de Psychologie, Université Laval, Quebec, Canada G1K 0A6.	Insomnia and its relationship to health-care utilization, work absenteeism, productivity and accidents.	Sleep Med. 2009 Apr;10(4):427-38. Epub 2008 Aug 26.	BACKGROUND AND PURPOSE: To document and provide a micro analysis of the relationship between insomnia and health problems, health-care use, absenteeism, productivity and accidents. PARTICIPANTS AND METHODS: A population-based sample of 953 French-speaking adults from Québec, Canada. Participants were categorized as having insomnia syndrome (SYND) or insomnia symptoms (SYMPT) or as good sleepers (GS). They completed questionnaires on sleep, health, use of health-care services and products, accidents, work absences and reduced work productivity. Data were also obtained from the Québec-government-administered health insurance board on selected variables (e.g., consultations with health-care professionals, diagnoses). RESULTS: There were significantly more individuals in the SYND group relative to the GS group reporting at least one chronic health problem (83% vs. 53%; OR: 2.78) and who had consulted a health-care professional in the past year (81% vs. 60%; OR: 2.8). There were also higher proportions of individuals in the SYND group than in the GS group who had used prescription medications (57% vs. 30.7%; OR: 2.8), most notably to treat insomnia, mood and anxiety disorders, or who had used over-the-counter products (75.6% vs. 62.0%; OR: 1.8) and alcohol as a sleep aid (17.8% vs. 3.9%; OR: 4.6). In terms of daytime function, 25.0% of the SYND had been absent from work relative to 17.1% of GS (OR: 1.7), 40.6% reported having experienced reduced productivity compared to 12.3% of GS (OR: 4.8) and non-motor-vehicle accidents occurred at higher rates in the SYND group (12.5% vs. 6.4% for GS; OR: 2.4). No differences were found for hospitalisations or motor-vehicle accidents. Most of the associations remained significant even after controlling for psychiatric comorbidity. Rates for the SYMPT group were situated between SYND and GS on all major dependent variables. Furthermore, insomnia and fatigue were perceived as contributing significantly to accidents, absences and decreased work productivity, regardless of insomnia status. CONCLUSIONS: This study indicates that insomnia is

				associated with significant morbidity in terms of health problems and health-care utilization, work absenteeism and reduced productivity, and risk of non-motor-vehicle accidents. Future studies should evaluate whether treating insomnia can reverse this morbidity.
De Lange FP, Knoop H, Bleijenberg G, Van der Meer JW, Hagoort P, Toni I.		The experience of fatigue in the brain.Comment on: Psychol Med. 2008 Jul;38(7):941-51.	Psychol Med. 2009 Mar;39(3):523-4. Epub 2008 Dec 18.	
de Tommaso M, Sardaro M, Serpino C, Costantini F, Vecchio E, Prudenzano MP, Lamberti P, Livrea P.	Neurological and Psychiatric Sciences Department, Neurophysiopathology of Pain Unit, University of Bari, Bari, Italy. m.detommaso@neurol.uniba.it	Fibromyalgia comorbidity in primary headaches.	Cephalalgia. 2009 Apr;29(4):453-64. Epub 2009 Dec 15.	Fibromyalgia syndrome (FMS) is a chronic pain condition of unknown aetiology characterized by diffuse pain and tenderness at tender points. The aim of the study was to assess the prevalence and clinical features of FMS in the different forms of primary headaches, in a tertiary headache centre. Primary headache patients (n = 217) were selected and submitted to the Total Tenderness Score, anxiety and depression scales, Migraine Disability Assessment, allodynia questionnaire, Short Form 36 Health Survey and the Medical Outcomes Study-Sleep Scale. In patients with FMS, the Multidimensional Assessment of Fatigue, the Pain Visual Analog Scale, the Manual Tender Point Survey and the Fibromyalgia Impact Questionnaire were employed. FMS was present in 36.4% of patients and prevailed significantly in tension-type headache and in patients with higher headache frequency. Headache frequency, pericranial muscle tenderness, anxiety and sleep inadequacy were especially associated with FMS comorbidity. In the FMS patients, fatigue and pain at tender points were significantly correlated with headache frequency. FMS seems increasingly prevalent with increased headache frequency, for the facilitation of central sensitization phenomena favoured by anxiety and sleep disturbances.
Deangelis TM, Shen L.	Mount Sinai School of Medicine, New York, NY, USA.	Outbreak of progressive inflammatory neuropathy following exposure to aerosolized porcine neural tissue.	Mt Sinai J Med. 2009 Oct;76(5):442-7.	In the fall of 2007, the Minnesota Department of Health was notified of 11 cases of an unexplained neurological illness, all linked to a pork processing plant, Quality Pork Processors, Inc., in Austin, MN. The cluster of workers had been experiencing similar symptoms, including fatigue, pain, numbness, and tingling in their extremities as well as weakness. The symptoms were described as more sensory than motor, and all patients had evidence of polyradiculoneuropathy with signs of nerve root irritation. An epidemiological investigation revealed that the only commonality between cases was their exposure to a pork brain extraction procedure involving compressed air. As relatives of the cases remained asymptomatic and all cultures for known pathogens were negative, the etiology of the syndrome seemed not to be infectious. Clinically, the syndrome was most akin to chronic inflammatory demyelinating polyneuropathy. Laboratory tests corroborated the clinical findings, revealing inflammation of peripheral nerves and nerve roots; however, these cases also had features clinically distinct from chronic inflammatory demyelinating polyneuropathy as well as laboratory testing revealing a novel immunoglobulin G immunostaining pattern. This suggested that the observed inflammation was the result of 1 or more unidentified antigens. This syndrome was ultimately dubbed progressive inflammatory neuropathy and was theorized to be an autoimmune reaction to aerosolized porcine neural tissue. Since the investigation's outset, 18 cases of progressive inflammatory neuropathy have been identified at the Minnesota pork processing plant, with 5 similar

				cases at an Indiana plant and 1 case at a Nebraskan plant. The plants in which cases have been identified have since stopped the use of compressed air in removing pork brains. All cases have stabilized or improved, with some requiring immunosuppressive and analgesic treatment. The study of progressive inflammatory neuropathy is ongoing, and the details of this investigation highlight the value of epidemiological principles in the identification and containment of outbreaks while researchers attempt to uncover the unique pathophysiology and potential etiology of the illness. Mt Sinai J Med 76:442-447, 2009. (c) 2009 Mount Sinai School of Medicine.
Decker MJ, Eyal S, Shinar Z, Fuxman Y, Cahan C, Reeves WC, Baharav A.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne Enteric Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail Stop A-15, Atlanta, GA, 30333, USA, mdecker@cdc.gov.	Validation of ECG-derived sleep architecture and ventilation in sleep apnea and chronic fatigue syndrome.	Sleep Breath. 2009 Oct 9. [Epub ahead of print]	PURPOSE: Newly developed algorithms putatively derive measures of sleep, wakefulness, and respiratory disturbance index (RDI) through detailed analysis of heart rate variability (HRV). Here, we establish levels of agreement for one such algorithm through comparative analysis of HRV-derived values of sleep-wake architecture and RDI with those calculated from manually scored polysomnographic (PSG) recordings. METHODS: Archived PSG data collected from 234 subjects who participated in a 3-day, 2-night study characterizing polysomnographic traits of chronic fatigue syndrome were scored manually. The electrocardiogram and pulse oximetry channels were scored separately with a novel scoring algorithm to derive values for wakefulness, sleep architecture, and RDI. RESULTS: Four hundred fifty-four whole-night PSG recordings were acquired, of which, 410 were technically acceptable. Comparative analyses demonstrated no difference for total minutes of sleep, wake, NREM, REM, nor sleep efficiency generated through manual scoring with those derived through HRV analyses. When NREM sleep was further partitioned into slow-wave sleep (stages 3-4) and light sleep (stages 1-2), values calculated through manual scoring differed significantly from those derived through HRV analyses. Levels of agreement between RDIs derived through the two methods revealed an R = 0.89. The Bland-Altman approach for determining levels of agreement between RDIs generated through manual scoring with those derived through HRV analysis revealed a mean difference of -0.7 +/- 8.8 (mean +/- two standard deviations). CONCLUSION: We found no difference between values of wakefulness, sleep, NREM, REM sleep, and RDI calculated from manually scored PSG recordings with those derived through analyses of HRV.
Decker MJ, Tabassum H, Lin JM, Reeves WC.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne Enteric Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail Stop A-15, Atlanta, Georgia, USA. mdecker@cdc.gov.	Electroencephalographic correlates of Chronic Fatigue Syndrome.	Behav Brain Funct. 2009 Oct 6;5:43.	ABSTRACT: BACKGROUND: Unremitting fatigue and unrefreshing sleep, hallmark traits of Chronic Fatigue Syndrome (CFS), are also pathognomonic of sleep disorders. Yet, no reproducible perturbations of sleep architecture, multiple sleep latency times or Epworth Sleepiness Scores are found to be associated consistently with CFS. This led us to hypothesize that sleep homeostasis, rather than sleep architecture, may be perturbed in CFS. To probe this hypothesis, we measured and compared EEG frequencies associated with restorative sleep between persons with CFS and matched controls, both derived from a population-based sample. METHODS: We evaluated overnight polysomnography (PSG) in 35 CFS and 40 control subjects. PSG records were manually scored and epochs containing artifact removed. Fast Fourier Transformation was utilized to deconstruct individual EEG signals into primary frequency bands of alpha, delta, theta, sigma, and beta frequency domains. The spectral power of each frequency domain for each sleep state was compared between persons with CFS and matched controls. RESULTS: In persons with CFS, delta power was diminished during slow wave sleep, but elevated during both stage 1 and REM. Alpha power was reduced during stage 2, slow wave, and REM sleep. Those with CFS also had significantly lower theta, sigma, and beta spectral

				power during stage 2, Slow Wave Sleep, and REM. DISCUSSION: Employing quantitative EEG analysis we demonstrate reduced spectral power of cortical delta activity during SWS. We also establish reduced spectral power of cortical alpha activity, with the greatest reduction occurring during REM sleep. Reductions in theta, beta, and sigma spectral power were also apparent. CONCLUSION: Unremitting fatigue and unrefreshing sleep, the waking manifestations of CFS, may be the consequence of impaired sleep homeostasis rather than a primary sleep disorder.
Dennis D, Robertson D, Curtis L, Black J.	Northside Hospital, USA. ddennis@mindspring.com	Fungal exposure endocrinopathy in sinusitis with growth hormone deficiency: Dennis-Robertson syndrome.	Toxicol Ind Health. 2009 Oct-Nov;25(9-10):669-80. Epub 2009 Oct 6.	A retrospective study was carried out on 79 patients with a history of mold exposure, fatigue, and chronic rhinosinusitis (CRS) to determine whether there is a causal relationship between fungal exposure and chronic sinusitis, fatigue, and anterior hypopituitarism, especially growth hormone deficiency (GHD). Of the patients, 94% had a history of CRS, endoscopically and/or computed tomography (CT) confirmed; 100% had chronic fatigue and 100% had either significant history of indoor mold exposure and/or positive mold plate testing as measured by settle plates, with an average colony count of 21 (0-4 normal). A total of 62 had positive mold plate testing and 17 had positive history of mold exposure. Of 75, 73 (97.3%) had positive serum immunoglobulin G (IgG)-specific antibodies to fungal antigens. Out of 8, 7 were positive for urinary trichothecenes. Resting levels of insulin-like growth factor 1 (IGF-1) averaged 123 ng/mL (range 43-285, normal 88-249 ng/mL). Despite normal resting levels of IGF-1, significant deficiency of serum human growth hormone (GH) was confirmed by insulin tolerance test (ITT) in 40 of 50 tested. In all, 51% (40/79) were GH deficient. Primary or secondary hypothyroidism in T3 and/or T4 was seen in 81% (64/79) patients; 75% (59/79) had adrenocorticotrophic hormone (ACTH) deficiency. Fungal exposure endocrinopathy likely represents the major cause of GHD, affecting approximately 4.8 million people compared to approximately known 60,000 cases from all other causes. A literature review indicates a possible mechanism of GHD in fungal exposure is that the fungal glucan receptors in the lenticulostellate cells of the anterior pituitary bind to fungal cells wall glucans and activate the innate immune system, which activates macrophages that destroy the fungus and lenticulostellate tissue. Treatment of patients included normal saline nasal irrigations, antifungal and antibiotic nasal sprays, appropriate use of oral antibiotics and antifungals, facial steamer with CitriDrops. Thymate and/or Intramax vitamin supplements, hormone replacement, and reduction of indoor mold levels. Resolution of rhinosinusitis was seen in 93% (41 of 45) of the patients who achieved a mold count by settling plates of 0-4 colonies. Thirty patients were unable to lower their mold counts below four colonies and had various degrees of mucosal disease and fatigue remaining. Fatigue was improved in all 37 patients who received GH and cortisol and/or thyroid hormone, which were deficient. Fatigue was partially relieved in 7 of the 37 who did not achieve mold counts of fewer than four colonies.
Dennison L, Stanbrook R, Moss-Morris R, Yardley L, Chalder T.		Cognitive behavioural therapy and psycho-education for chronic fatigue syndrome in young people: Reflections	Br J Health Psychol. 2009 May 6. [Epub ahead of print]	Objectives Recent trials have produced optimistic results for family-focussed cognitive behavioural therapy (CBT) for chronic fatigue syndrome (CFS) in young people. This study sought to examine the under-researched question of the views and experiences of patients and families who take part. Design Semi-structured interviews and qualitative analysis were chosen in order to address clients' perspectives in depth. Methods Sixteen young people and sixteen parents who participated in a trial of CBT versus psycho-education (PE) for CFS were interviewed. Key themes were discerned using inductive thematic analysis. Results Most families had low expectations of a cure but hope for

		from the families' perspective.		improvement. Generally speaking, participants found both CBT and PE acceptable and helpful. Behavioural aspects of CBT (e.g. goal-setting, graded activity) were found helpful. The opportunity to gain support, recognition and validation was important. Cognitive elements of therapy were sometimes deemed inappropriate and some felt emotional aspects of CFS were not adequately addressed. Participants were ambivalent towards the extent of family involvement. Negative experiences related to the therapy setting and feeling inappropriately labeled. Most participants felt therapy was a stepping-stone towards normal life, although many felt recovery was incomplete. Very few differences were found between themes from CBT and PE participants. A notable exception was that every young person who experienced CBT described therapy as helpful, whereas the participants who strongly opposed the therapy approach had all experienced PE. Conclusions The detailed insights regarding families' therapy experiences suggest areas of improvement for service delivery and topics for further investigation.
Dickson A, Toft A, O'Carroll RE.	School of Health and Social Sciences, Napier University, Edinburgh, UK. a.dickson@napier.ac.uk	Neuropsychological functioning, illness perception, mood and quality of life in chronic fatigue syndrome, autoimmune thyroid disease and healthy participants.	Psychol Med. 2009 Sep;39(9):1567-76. Epub 2009 Jan 15.	BACKGROUND: This study attempted to longitudinally investigate neuropsychological function, illness representations, self-esteem, mood and quality of life (QoL) in individuals with chronic fatigue syndrome (CFS) and compared them with both healthy participants and a clinical comparison group of individuals with autoimmune thyroid disease (AITD). METHOD: Neuropsychological evaluation was administered at two time points, five weeks apart. Twenty-one individuals with CFS, 20 individuals with AITD and 21 healthy participants were matched for age, pre-morbid intelligence, education level and socio-economic status (SES). All groups also completed measures of illness perceptions, mood, self-esteem and QoL at both time points. RESULTS: The CFS group showed significantly greater impairment on measures of immediate and delayed memory, attention and visuo-constructional ability, and reported significantly higher levels of anxiety and depression. After controlling for the effects of mood, the CFS group still demonstrated significant impairment in attention. The CFS group also reported significantly lower self-reported QoL than the AITD and healthy participants. In terms of illness perceptions, the AITD group believed that their condition would last longer, that they had more treatment control over their condition, and reported less concern than the CFS group. CONCLUSIONS: These results suggest that the primary cognitive impairment in CFS is attention and that this is not secondary to affective status. The lower treatment control perceptions and greater illness concerns that CFS patients report may be causally related to their affective status.
Dinos S, Khoshaba B, Ashby D, White PD, Nazroo J, Wessely S, Bhui KS.	Centre for Psychiatry, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK. s.dinos@qmul.ac.uk	A systematic review of chronic fatigue, its syndromes and ethnicity: prevalence, severity, co-morbidity and coping.	Int J Epidemiol. 2009 Dec;38(6):1554-70. Epub 2009 Apr 6.	BACKGROUND: Chronic Fatigue Syndrome (CFS) is characterized by unexplained fatigue that lasts for at least 6 months alongside a constellation of other symptoms. CFS was historically thought to be most common among White women of higher socio-economic status. However, some recent studies in the USA suggest that the prevalence is actually higher in some minority ethnic groups. If there are convincing differences in prevalence and risk factors across all or some ethnic groups, investigating the causes of these can help unravel the pathophysiology of CFS. METHODS: A systematic review was conducted to explore the relationship between fatigue, chronic fatigue (CF--fatigue lasting for 6 months), CFS and ethnicity. Studies were population-based and health service-based. Meta-analysis was also conducted to examine the population prevalence of CF and CFS across ethnic groups. RESULTS: Meta-analysis showed that compared with the White American majority, African Americans and Native Americans have a higher risk of CFS [Odds Ratio (OR) 2.95, 95% confidence interval (CI):

				0.69-10.4; OR = 11.5, CI: 1.1-56.4, respectively] and CF (OR = 1.56, CI: 1.03-2.24; OR = 3.28, CI: 1.63-5.88, respectively). Minority ethnic groups with CF and CFS experience more severe symptoms and may be more likely to use religion, denial and behavioural disengagement to cope with their condition compared with the White majority. CONCLUSIONS: Although available studies and data are limited, it does appear that some ethnic minority groups are more likely to suffer from CF and CFS compared with White people. Ethnic minority status alone is insufficient to explain ethnic variation of prevalence. Psychosocial risk factors found in high-risk groups and ethnicity warrant further investigation to improve our understanding of aetiology and the management of this complex condition.
Donalek JG.	Department of Nursing, DePaul University, Chicago, IL 60614, USA. jdonalek@depaul.edu	When a parent is chronically ill: chronic fatigue syndrome.	Nurs Res. 2009 Sep-Oct;58(5):332-9.	BACKGROUND: Chronic illness may reshape not only the life of the ill parent but also that of the entire family, but research in this area remains limited. More specifically, little is known about how an ill parent and the family respond to a particularly devastating and controversial chronic illness, chronic fatigue syndrome (CFS). OBJECTIVES: The objective of this study was to describe the responses of the parent and the ensuing family system responses to the presence of chronic fatigue syndrome as a chronic parental illness. METHODS: Parents were interviewed individually, and then the ill parent and as many immediate family members as possible were interviewed collectively. After consent or assent, interviews were audiotaped and transcribed. Thematic analyses at the individual, intrafamily, and across-family levels were used to explore these phenomena. RESULTS: Eight ill parents first described the onset of illness, an ongoing struggle to receive diagnosis and care, and the significance of the illness in transforming present and future roles. Multiple members of the family together with the ill parent described how they struggled with the reality of the illness, the shifting roles and responsibilities, the reduced family income, and the frequent social isolation that could be exacerbated by the controversial nature of the illness. Families described and demonstrated their struggles to maintain normal family life and plans in the face of continuing uncertainty. DISCUSSION: This study is situated within current scholarship on family responses to chronic parental illness. The value of the family research interview is affirmed. Recommendations are made for future directions in family nursing research exploring responses of families in which a parent is chronically ill.
Drachler Mde L, Leite JC, Hooper L, Hong CS, Pheby D, Nacul L, Lacerda E, Campion P, Killett A, McArthur M, Poland F.	School of Allied Health Professions, University of East Anglia, Norwich, NR4 7TJ, UK. malu.drachler@gmail.com	The expressed needs of people with chronic fatigue syndrome/myalgic encephalomyelitis: a systematic review.	BMC Public Health. 2009 Dec 11;9:458.	BACKGROUND: We aimed to review systematically the needs for support in managing illness and maintaining social inclusion expressed by people with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) METHODS: We carried out a systematic review of primary research and personal ('own') stories expressing the needs of people with CFS/ME. Structured searches were carried out on Medline, AMED, CINAHL, EMBASE, ASSIA, CENTRAL, and other health, social and legal databases from inception to November 2007. Study inclusion, data extraction and risk of bias were assessed independently in duplicate. Expressed needs were tabulated and a conceptual framework developed through an iterative process. RESULTS: Thirty two quantitative and qualitative studies, including the views of over 2500 people with CFS/ME with mainly moderate or severe illness severity, met the inclusion criteria. The following major support needs emerged: 1) The need to make sense of symptoms and gain diagnosis, 2) for respect and empathy from service providers, 3) for positive attitudes and support from family and friends, 4) for information on CFS/ME, 5) to adjust views and priorities, 6) to develop strategies to manage impairments and activity limitations, and 7) to develop

				strategies to maintain/regain social participation. CONCLUSIONS: Although the studies were heterogeneous, there was consistent evidence that substantial support is needed to rebuild lives. Gaining support depends - most importantly - on the ability of providers of health and social care, colleagues, friends and relatives, and those providing educational and leisure services, to understand and respond to those needs.
Dworzańska E, Mitosek-Szewczyk K, Stelmasiak Z.	Katedra i Klinika Neurologii, Uniwersytet Medyczny w Lublinie, Samodzielny Publiczny Szpital Kliniczny nr 4, ul. Jaczewskiego 8, 20-954 Lublin, Poland. cieckoewa@interia.pl	[Fatigue in multiple sclerosis][Article in Polish]	Neurol Neurochir Pol. 2009 Jan-Feb;43(1):71-6.	Fatigue is one of the most common symptoms of multiple sclerosis (MS) and is associated with reduced quality of life. The fatigue syndrome is characterized by uncontrollable apathy, exhaustion, fatigability and lack of energy. The mechanisms underlying fatigue in MS are still poorly understood but studies suggest that immune and neuroendocrine factors may play a causative role in the development of fatigue. The first step in management of MS-related fatigue is identifying and eliminating any secondary causes (adverse effects of drugs, infections, sleep disorders, metabolic diseases). As the fatigue syndrome in patients with MS cannot be evaluated objectively in the routine clinical setting, a number of scales have been developed. The Fatigue Severity Scale is a general scale. Additional scales that have been tested in MS include the Fatigue Impact Scale. Therapy of fatigue syndrome consists of modafinil, amantadine, pemoline and non-pharmacological management.
Dyer C.		High court rejects challenge to NICE guidelines on chronic fatigue syndrome.	BMJ. 2009 Mar 17;338:b1110. doi: 10.1136/bmj.b1110.	
Edd EM, Flores S.	College of Nursing, New York University, John A. Hartford Institute for Geriatric Nursing, New York University, New York, NY, USA.	Sleepiness or excessive daytime somnolence.	Geriatr Nurs. 2009 Jan-Feb;30(1):53-60.	Excessive daytime somnolence (EDS) is associated with age-related changes, environment, circadian rhythm or sleep pattern disorder, insomnia, medications, lifestyle factors, depression, pain, and illness. The notion of "sleep architecture" connotes a structure that describes the sleep cycle (i.e., stages) and wakefulness during a single sleep period-that is, rapid eye movement (REM) and non-REM sleep. Circadian rhythms perform a variety of functions including regulation of the quality and distribution of the stages of sleep. Insomnia includes delayed sleep onset as well as premature wakening; sleep is nonrestorative. Comorbidities associated with insomnia are Alzheimer's disease and other dementias, delirium, depression, congestive heart failure, chronic obstructive pulmonary disease, gastroesophageal reflux disease, pain, degenerative diseases of the neurological system, and sleep apnea. Continuous inadequate sleep affects cognitive function, physical performance, overall well-being, and quality of life. There is a greater risk of falls from insomnia than is the use of hypnotics to manage it. Sleep disruption among older adults is underrecognized and undertreated. Assessment using valid tools can be performed rapidly. There are a variety of treatment options, including sleep hygiene and pharmacological and alternative modalities.
Evans KM, Flanagan DE, Wilkin TJ.	Department of Endocrinology and Metabolism,	Chronic fatigue: is it endocrinology?	Clin Med. 2009 Feb;9(1):34-8.	Fatigue and stress-related illnesses often become diagnoses of exclusion after extensive investigation. 'Tired all the time' is a frequent reason for referral to the endocrine clinic, the implicit question being--is there a subtle endocrine pathology contributing to the patient's symptoms? Often initial

	Peninsula Medical School, Plymouth and Derriford Hospital, Plymouth. kme@doctors.org.uk			assessment suggests not but there are no clear data to address the question of whether overt pathology will develop in the future. This study observed outcomes after five years in 101 consecutive and unselected referrals to secondary care for 'fatigue?cause', where initial assessment did not suggest treatable endocrine pathology. The findings suggest that the clinical diagnosis of fatigue, based on history and tests to exclude anaemia, hypothyroidism and diabetes, is secure: these patients do not subsequently demonstrate excess morbidity and mortality, and their presenting symptoms are not early features of significant endocrine pathology.
Exley C, Swarbrick L, Gherardi RK, Authier FJ.	Birchall Centre for Inorganic Chemistry and Materials Science, Keele University, Staffordshire ST5 5BG, UK. c.exley@chem.keele.ac.uk	A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome.	Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11.	Macrophagic myofasciitis and chronic fatigue syndrome are severely disabling conditions which may be caused by adverse reactions to aluminium-containing adjuvants in vaccines. While a little is known of disease aetiology both conditions are characterised by an aberrant immune response, have a number of prominent symptoms in common and are coincident in many individuals. Herein, we have described a case of vaccine-associated chronic fatigue syndrome and macrophagic myofasciitis in an individual demonstrating aluminium overload. This is the first report linking the latter with either of these two conditions and the possibility is considered that the coincident aluminium overload contributed significantly to the severity of these conditions in this individual. This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis.
Fletcher MA, Zeng XR, Barnes Z, Levis S, Klimas NG.	Department of Medicine, University of Miami Miller School of Medicine, 1600 NW 10th Ave, Miami, FL, USA. mfletche@med.miami.edu	Plasma cytokines in women with chronic fatigue syndrome.	J Transl Med. 2009 Nov 12;7:96.	BACKGROUND: Chronic Fatigue Syndrome (CFS) studies from our laboratory and others have described cytokine abnormalities. Other studies reported no difference between CFS and controls. However, methodologies varied widely and few studies measured more than 4 or 5 cytokines. Multiplex technology permits the determination of cytokines for a large panel of cytokines simultaneously with high sensitivity and with only 30 ul of plasma per sample. No widely accepted laboratory test or marker is available for the diagnosis or prognosis of CFS. This study screened plasma factors to identify circulating biomarkers associated with CFS. METHODS: Cytokines were measured in plasma from female CFS cases and female healthy controls. Multiplex technology provided profiles of 16 plasma factors including the pro -inflammatory cytokines: tumor necrosis factor alpha (TNFalpha), lymphotoxin alpha (LTalpha), interleukin (IL) - IL-Ialpha, IL-1beta, IL-6; TH1 cytokines: interferon gamma (IFNgamma), IL-12p70, IL-2, IL-15; TH2: IL-4, IL-5; TH17 cytokines, IL-17 and IL-23; anti-inflammatory cytokines IL-10, IL-13; the inflammatory mediator and neutrophil attracting chemokine IL-8 (CXCL8). Analysis by receiver operating characteristic (ROC) curve assessed the biomarker potential of each cytokine. RESULTS: The following cytokines were elevated in CFS compared to controls: LTalpha, IL-1alpha, IL-1beta, IL-4, IL-5, IL-6 and IL-12. The following cytokines were decreased in CFS: IL-8, IL-13 and IL-15. The following cytokines were not different: TNFalpha, IFNgamma, IL-2, IL-10, IL-23 and IL-17. Applying (ROC) curve analyses, areas under the curves (AUC) for IL-5 (0. 84), LTalpha (0.77), IL-4 (0.77), IL-12 (0.76) indicated good biomarker potential. The AUC of IL-6 (0.73), IL-15 (0.73), IL-8 (0.69), IL-13 (0.68) IL-1alpha (0.62), IL-1beta (0.62) showed fair potential as biomarkers. CONCLUSION: Cytokine abnormalities are common in CFS. In this study, 10 of 16 cytokines examined showed good to fair promise as biomarkers. However, the cytokine changes observed are likely to

				more indicative of immune activation and inflammation, rather than specific for CFS. As such, they are targets for herapeutic strategies. Newer techniques allow evaluation of large panels of cytokines in a cost effective fashion.
Flor-Henry P, Lind JC, Koles ZJ.	Alberta Hospital Edmonton, Box 307, Edmonton, Edmonton, Alberta, Canada T5J 2J7.	EEG source analysis of chronic fatigue syndrome.	Psychiatry Res.. [Epub ahead of print]	Sixty-one dextral, unmedicated women with chronic fatigue syndrome (CFS) diagnosed according to the Fukuda criteria (1994) and referred for investigation by rheumatologists and internists were studied with quantitative EEG (43 channels) at rest with eyes open and during verbal and spatial cognitive activation. The EEGs from the patients were compared with recordings from 80 dextral healthy female controls. Only those subjects who could provide 20 1-s artefact-free segments of EEG were admitted into the study. The analysis consisted of the identification of the spatial patterns in the EEGs that maximally differentiated the two groups and the estimation of the cortical source distributions underlying these patterns. Spatial patterns were analyzed in the alpha (8-13Hz) and beta (14-20Hz) bands and the source distributions were estimated using the Borgiotti-Kaplan BEAMFORMER algorithm. The results indicate that the spatial patterns identified were effective in separating the two groups, providing a minimum correct retrospective classification rate of 72% in both frequency bands while the subjects were at rest to a maximum of 83% in the alpha band during the verbal cognitive condition. Underlying cortical source distributions showed significant differences between the two groups in both frequency bands and in all cognitive conditions. Lateralized cortical differences were evident between the two groups in the both frequency bands during both the verbal and spatial cognitive conditions. During these active cognitive conditions, the CFS group showed significantly greater source-current activity than the controls in the left frontal-temporal-parietal regions of the cortex.
Fluge Ø, Mella O.	Department of Oncology and Medical Physics, Haukeland University Hospital, N-5021 Bergen, Norway. oystein.fluge@gmail.com	Clinical impact of B-cell depletion with the anti-CD20 antibody rituximab in chronic fatigue syndrome: a preliminary case series.	BMC Neurol. 2009 Jul 1;9:28.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disease of unknown aetiology. A patient with CFS had unexpected, marked recovery of CFS symptoms lasting for five months during and after cytotoxic chemotherapy for Hodgkin's disease. We reasoned that the transient CFS recovery was related to methotrexate treatment, which induces immunomodulation in part through B-cell depletion. METHODS: In a case series, this patient and two additional CFS patients were B-cell depleted by infusion of the monoclonal anti-CD20 antibody rituximab. RESULTS: All three had improvement of all CFS symptoms. Patients 1 and 2 had major amelioration from 6 weeks after intervention, patient 3 slight improvement from the same time, but then improved markedly from 26 weeks after intervention. The symptomatic effect lasted until weeks 16, 18 and 44, respectively. At relapse, all were retreated with a single (patient 1) or double rituximab infusion (patients 2 and 3). Again, all three had marked symptom improvement, mimicking their first response. After new symptom recurrence, patients 1 and 2 were given weekly oral methotrexate, patient 1 having effect also from this agent. Patients 1 and 2 were again treated for a third rituximab infusion after new relapse, again with a marked clinical benefit. No unexpected toxicity was seen. CONCLUSION: These observations suggest that B-lymphocytes are involved in CFS pathogenesis for a subset of patients. Benefit for all CFS symptoms, the delayed symptom relief following B-cell depletion, the kinetics of relapses, and the effect also from methotrexate treatment, provide suggestive evidence that B-cells play a significant role in the ongoing clinical features, and that CFS may be amenable to therapeutic interventions aimed at modifying B-cell number and function. More systematic investigations of this therapeutic

				strategy, and of its biological basis, are now needed.
Fluge Ø, Mella O.	Department of Oncology and Medical Physics, Haukeland University Hospital, N-5021 Bergen, Norway. oystein.fluge@gmail.com	Clinical impact of B-cell depletion with the anti-CD20 antibody rituximab in chronic fatigue syndrome: a preliminary case series.	BMC Neurol. 2009 Jul 1;9:28.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disease of unknown aetiology. A patient with CFS had unexpected, marked recovery of CFS symptoms lasting for five months during and after cytotoxic chemotherapy for Hodgkin's disease. We reasoned that the transient CFS recovery was related to methotrexate treatment, which induces immunomodulation in part through B-cell depletion. METHODS: In a case series, this patient and two additional CFS patients were B-cell depleted by infusion of the monoclonal anti-CD20 antibody rituximab. RESULTS: All three had improvement of all CFS symptoms. Patients 1 and 2 had major amelioration from 6 weeks after intervention, patient 3 slight improvement from the same time, but then improved markedly from 26 weeks after intervention. The symptomatic effect lasted until weeks 16, 18 and 44, respectively. At relapse, all were retreated with a single (patient 1) or double rituximab infusion (patients 2 and 3). Again, all three had marked symptom improvement, mimicking their first response. After new symptom recurrence, patients 1 and 2 were given weekly oral methotrexate, patient 1 having effect also from this agent. Patients 1 and 2 were again treated for a third rituximab infusion after new relapse, again with a marked clinical benefit. No unexpected toxicity was seen. CONCLUSION: These observations suggest that B-lymphocytes are involved in CFS pathogenesis for a subset of patients. Benefit for all CFS symptoms, the delayed symptom relief following B-cell depletion, the kinetics of relapses, and the effect also from methotrexate treatment, provide suggestive evidence that B-cells play a significant role in the ongoing clinical features, and that CFS may be amenable to therapeutic interventions aimed at modifying B-cell number and function. More systematic investigations of this therapeutic strategy, and of its biological basis, are now needed.
Fomicheva EE, Filatenkova TA, Rybakina EG.		[Activity of hypotnalamic-pituitary-adrenal axis by induction of experimental chronic fatigue syndrom][Article in Russian]	Ross Fiziol Zh Im I M Sechenova. 2009 Jan;95(1):11-8.	Changes in the activity of hypothalamic-pituitary adrenal (HPA) axis were investigated in experimental model of chronic fatigue syndrome (CFS) induced by intraperitoneal administration of synthetic double-stranded RNA (polyriboinosinic: polyribocytidylic acid, Poly I : C) to rats in the dose of 3 mg/kg body weight. In order to reveal functional changes in different links of the HPA axis, standard probes with intraperitoneal administration of ACTH and hydrocortisone against the background of cold stress application and Poly I : C injections were performed. A single injection of Poly I : C led to disordered HPA axis functions which was manifested by decreased sensitivity of the cells in the adrenal gland in response to ACTH, and suppression of the mechanism of negative feedback resulting in significant fall of cortisocterone concentration in standard assays with ACTH and hydrocortisone administration.
Forstenius L, Helmfrid S.		[Chronic fatigue syndrome--more than just chronic fatigue] [Article in Swedish]	Lakartidningen. 2009 Sep 9-15;106(37):2298-9.	
Frémont M, Metzger K, Rady H, Hulstaert J, De Meirleir K.	Protea Biopharma, Z.1-Researchpark 100, 1731 Zellik, Belgium. mfremont@protea	Detection of herpesviruses and parvovirus B19 in gastric and intestinal mucosa	In Vivo. 2009 Mar-Apr;23(2):209-13.	BACKGROUND: Human herpesvirus-6 (HHV-6), Epstein-Barr virus and parvovirus B19 have been suggested as etiological agents of chronic fatigue syndrome but none of these viruses is consistently detected in all patients. However, active viral infections may be localized in specific tissues, and, therefore, are not easily detectable. The aim of this study was to investigate the presence of HHV-6, HHV-7, EBV and parvovirus B19 in the gastro-intestinal tract of CFS patients. PATIENTS AND

	biopharma.com	of chronic fatigue syndrome patients.		METHODS: Using real-time PCR, viral DNA loads were quantified in gastro-intestinal biopsies of 48 CFS patients and 35 controls. RESULTS: High loads of HHV-7 DNA were detected in most CFS and control biopsies. EBV and HHV-6 were detected in 15-30% of all biopsies. Parvovirus B19 DNA was detected in 40% of the patients versus less than 15% of the controls. CONCLUSION: Parvovirus B19 may be involved in the pathogenesis of CFS, at least for a subset of patients. The gastro-intestinal tract appears as an important reservoir of infection for several potentially pathogenic viruses.
Frenger P.	A Working Hypothesis, Inc., Houston, TX.	Multi-system fibromyalgia syndrome emulator - biomed 2009.	Biomed Sci Instrum. 2009;45:292-8.	Fibromyalgia Syndrome is a chronic disorder characterized by abnormal pain, fatigue, depression, cognitive dysfunction and sleep disturbance. The body's immune, hormonal, and nervous systems are involved. The author proposes a model from his clinical practice where a relapsing human Herpesvirus 4 infection of ss-lymphocytes causes inappropriate activation of immune system components, thus leading to typical FMS signs and symptoms. This clinical model was subsequently embodied in a computer based on the author's human nervous system function emulator, which imitates the brain's biochemicalneural-cognitive operations. This Forth language emulator program runs on a multiprocessor network recently enhanced with 8-core 32-bit CPUs. Supplemental analog circuit boards provide support for an artificial neural network, synthetic emotion and cellular substrate-receptor binding activity simulation. The effects of antiviral antibiotics and other chemicals on this disease are included in the emulator.
Friedberg F, Sohl S.	Stony Brook University. Fred.Friedberg@stonybrook.edu	Cognitive-behavior therapy in chronic fatigue syndrome: is improvement related to increased physical activity?	J Clin Psychol. 2009 Apr;65(4):423-42.	This multiple case study of cognitive-behavioral treatment (CBT) for chronic fatigue syndrome (CFS) compared self-report and behavioral outcomes. Eleven relatively high-functioning participants with CFS received 6-32 sessions of outpatient graded-activity oriented CBT. Self-report outcomes included measures of fatigue impact, physical function, depression, anxiety, and global change. Behavioral outcomes included actigraphy and the 6-minute walking test. Global change ratings were very much improved (n=2), much improved (n=2), improved (n=5), and no change (n=2). Of those reporting improvement, clinically significant actigraphy increases (n=3) and decreases (n=4) were found, as well as no significant change (n=2). The nature of clinical improvement in CBT trials for high-functioning CFS patients may be more ambiguous than that postulated by the cognitive-behavioral model.
Friedberg F, Sohl SJ.	Department of Psychiatry and Behavioral Science Putnam Hall, Stony Brook University, NY 11794-8790, USA. fred.friedberg@stonybrook.edu	Longitudinal change in chronic fatigue syndrome: what home-based assessments reveal.	J Behav Med. 2009 Apr;32(2):209-18. Epub 2008 Dec 20.	The purpose of this 2-year prospective study was to compare standard self-report and ecologically-based outcome measures in patients with chronic fatigue syndrome (CFS). Standard measures assessed physical function, fatigue impact, psychological variables, and global impression of change ratings. Ecological measures included actigraphy, a structured activity record, and an electronic fatigue/energy diary. Results for this high functioning sample (N = 75) revealed that self-report global improvement was significantly associated with lower momentary fatigue and fatigue impact, and a higher frequency of standing up (at home), but not with actigraphy or psychological variables. However, actigraphy change was significantly correlated with change in self-report physical function. At follow-up, only a small minority (<20%) scored in the healthy adult range for fatigue impact and physical function. The findings suggest that home-based measures of symptom severity and physical functioning may provide evidence of change (or lack of change) that is important for interpreting standard self-report outcomes in CFS.
Frykholm BO.	aion.terapi@yahoo.com	On the question of infectious	Med Hypotheses. 2009	Close similarities in the courses of multiple sclerosis and schizophrenia laid the theoretical ground for attempting to find a common infectious aetiology for the two diseases. Chlamydia pneumoniae, which

		aetiologies for multiple sclerosis, schizophrenia and the chronic fatigue syndrome and their treatment with antibiotics.	Jun;72(6):736-9. Epub 2009 Mar 6.	belongs to the rickettsial family of microorganisms has been linked to both diseases. It is postulated that since rickettsial microorganisms are ubiquitous in human populations they and the human species normally live in peaceful coexistence. In rare cases, for unknown reasons, varieties of them may become aggressive and pathogenic. The kynurenic acid hypothesis of schizophrenia has attracted much attention. It also seems to have initiated a paradigmatic shift from the hitherto prevailing serological research approach to one which focuses on immunological factors. An open clinical pilot study in which, during 2006, eight female and five male patients with psychotic symptoms were treated with a combination of antibiotics is presented, to which, in the beginning of 2007 two female patients suffering from severe and long standing chronic fatigue syndrome were added. On one year follow-up, six out of the eight female patients showed stable excellent treatment results, whereas two were rated as showing significant treatment results. Four of the five men who entered the study were suffering from chronic schizophrenia, whereas the fifth, was a case of severe acute catatonic schizophrenia. Two of the male patients showed significant treatment results, whereas three of them were rated as having had a slight to moderate improvement. No less than three of the women had suffered their first episode of psychosis after giving birth to their first (and only) child. This finding, as these women all responded excellently to treatment with antibiotics, indicates that post partum psychosis could be regarded as an infectious complication of childbirth of, as to the causative agent, unknown aetiology. High priority ought therefore be given to initiate controlled clinical trials with antibiotic treatment of this serious condition. The otherwise promising results of the pilot study seem to warrant further and controlled clinical trials with treatment with antibiotics of patients with psychotic symptoms. As the second patient with psychotic symptoms to enter the study, had a long standing history of chronic fatigue, where an initial treatment with the antidepressant fluoxetine had only worsened her condition, whereas ninety days of treatment with antibiotics, combined with vitamin B injections, effected a complete recovery, the author decided, when two patients with long standing and incapacitating chronic fatigue syndromes sought the clinic in February and March 2007, to include them in the study. The first of them, after sixty days of treatment with antibiotics showed excellent treatment results on follow-up one year later, whereas the second, who also took the combination of antibiotics for sixty days, was rated as having shown a significant improvement.
Fukunaga M.	Department of Psychosomatic Medicine, Faculty of Medicine, Kansai Medical University.	[Overview of functional somatic syndromes] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1644-5.	
Godás Sieso T, Gómez Gil E, Salamero Baró M, Fernandez-Huerta JM, Fernandez-Solá J.	Instituto de Neurociencias, Servicio de Psicología, Unidad de fatiga crónica, Hospital Clínic de	[Relationship between chronic fatigue syndrome and type A behaviour] [Article in Spanish]	Med Clin (Barc). 2009 Oct 17;133(14):539-41. Epub 2009 Jul 10.	BACKGROUND AND OBJECTIVE: To quantify the relationship between Chronic Fatigue Syndrome (CFS) and Type A Behaviour Pattern (TABP) PATIENTS AND METHOD: The Jenkins Activity Survey (JAS) was administered to 82 patients diagnosed with CFS to determine the prevalence of TABP. Subjects' mean z scores on the JAS were compared with those from the general population (healthy controls) and from patients with ischemic cardiopathy (pathologic controls). RESULTS: CFS patients' mean score on the JAS was 5 points higher than that of the general population (healthy controls) and 2 points higher

	Barcelona, Barcelona, España.			than that of patients with ischemic cardiopathy. CONCLUSIONS: TABP appears to be related with CFS and should be taken into account in the treatment of these patients.
Godfrey E, Cleare A, Coddington A, Roberts A, Weinman J, Chalder T.	Department of Psychology, Kings College London, London, UK.	Chronic fatigue syndrome in adolescents: do parental expectations of their child's intellectual ability match the child's ability?	J Psychosom Res. 2009 Aug;67(2):165-8. Epub 2009 Apr 16.	OBJECTIVE: This cross-sectional study aimed to measure the discrepancy between actual and perceived IQ in a sample of adolescents with CFS compared to healthy controls. We hypothesized that adolescents with CFS and their parent would have higher expectations of the adolescent's intellectual ability than healthy adolescents and their parent. METHODS: The sample was 28 CFS patients and 29 healthy controls aged 11-19 years and the parent of each participant. IQ was assessed using the AH4 group test of general intelligence and a self-rating scale which measured perceived IQ. RESULTS: Parents' perceptions of their children's IQ were significantly higher for individuals with CFS than healthy controls. CONCLUSIONS: High expectations may need to be addressed within the context of treatment.
Goedendorp MM, Knoop H, Schippers GM, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. m.goedendorp@nkcv.umcn.nl	The lifestyle of patients with chronic fatigue syndrome and the effect on fatigue and functional impairments.	J Hum Nutr Diet. 2009 Jun;22(3):226-31. Epub 2009 Feb 17.	BACKGROUND: Little is known about the lifestyle of patients with chronic fatigue syndrome (CFS) and its influence on symptoms of CFS. The present study aimed to investigate the lifestyle of patients with CFS, and to assess whether lifestyle factors are related to fatigue and functional impairments. METHODS: Two hundred and forty-seven patients fulfilling the Center for Disease Control criteria for CFS were included. Validated questionnaires were used to collect data on lifestyle factors, smoking, intake of alcohol, fat, fibres, fruit and vegetables, body mass index (BMI), fatigue severity and functional impairments. RESULTS: Of the CFS patients, 23% smoked, 32% had an unhealthy BMI, and none had an unhealthy alcohol intake. A majority had an unhealthy food intake: 70% had unhealthy fat, fruit and vegetable intake, and 95% had unhealthy fibre intake. Compared with the general Dutch population, significantly fewer CFS patients were overweight. Significantly more female CFS patients abstained from alcohol, and fewer male CFS patients smoked. Unhealthy lifestyle factors were not significantly associated with fatigue severity or functional impairments. CONCLUSIONS: CFS patients tend to lead a healthier lifestyle compared to the general Dutch population. However, no relationship was found between lifestyle factors and fatigue severity and functional impairments in CFS.
Goldenberg DL.	Department of Rheumatology, Newton-Wellesley Hospital, Newton, Massachusetts 02462, USA. dgoldenb@massmed.org	Diagnosis and differential diagnosis of fibromyalgia.	Am J Med. 2009 Dec;122(12 Suppl):S14-21.	Fibromyalgia is a chronic functional illness that presents with widespread musculoskeletal pain as well as a constellation of symptoms including fatigue, cognitive dysfunction, sleep difficulties, stiffness, anxiety, and depressed mood. The diagnosis of fibromyalgia, similar to other functional disorders, requires that organic diseases are not causing the symptoms. Systemic and rheumatic diseases can be ruled out by a patient history, physical examination, and laboratory investigations. Because there are no specific laboratory tests for fibromyalgia, the 1990 American College of Rheumatology (ACR) classification criteria have been used in clinical settings; however, they are not ideal for individual patient diagnosis. Clinicians should be aware of limitations inherent in using tender points in the diagnosis of fibromyalgia. The multiple symptoms of fibromyalgia often overlap with those of related disorders and may further complicate the diagnosis. One of the most challenging diagnostic dilemmas that clinicians face is distinguishing fibromyalgia from other central pain disorders (e.g., irritable bowel syndrome, chronic fatigue syndrome, migraine). Screening questions based on published criteria can be used as a first approach in diagnosing functional illnesses. Numerous studies report a higher prevalence of psychiatric disorders in patients with fibromyalgia. Therefore, a careful history and evaluation should be taken for the presence of primary mood disturbances. To date, there is no

				"gold standard" for diagnosing fibromyalgia. Until a better clinical case definition of fibromyalgia exists, all diagnostic criteria should be interpreted with caution, considered rudimentary, and subject to modification. (c) 2009 Elsevier Inc.
Gordon B, Lubitz L.	Physiotherapy Department, Austin Hospital, Heidelberg, Vic, Australia. brett.gordon@austin.org.au	Promising outcomes of an adolescent chronic fatigue syndrome inpatient programme.	J Paediatr Child Health. 2009 May;45(5):286-90.	INTRODUCTION: Chronic fatigue syndrome (CFS) is a condition of prolonged and disabling fatigue, which is accompanied by characteristic constitutional and neuropsychiatric symptoms. In children and adolescents, this condition occurring at a developmentally vulnerable time adds to the disability affecting self-concept, autonomy, body image, socialisation, sexuality and academic problems. This case series looks at the effects of a graded exercise programme on physical outcomes, fatigue and mental state in an adolescent population. METHODS: Data sets from 16 adolescents who completed combined exercise training as part of the 4-week inpatient intensive CFS programme at the Austin Hospital, Melbourne were analysed. All patients completed an exercise assessment and three questionnaires before beginning any training. A paediatrician (LL) confirmed the diagnosis according to the Fukuda criteria in all patients. Exercise was carefully supervised and prescribed daily by an exercise physiologist (BG) according to each individual's ability and response with the basic aim of increasing exercise tolerance and improving muscle strength and endurance. RESULTS: There was an 18% improvement in volitional time to fatigue (P= 0.02) and 17% improvement in peak oxygen uptake (VO(2peak)) (P= 0.01). Upper body strength and function improved with a remarkable 70% increase in the number of push-ups. Fatigue severity was reported to improve by 13% (P= 0.01) and depression index improved significantly by 42% (P= 0.02). CONCLUSIONS: The significance of these improvements cannot be underestimated as an improvement in physical capacity through increased time to fatigue and less severe fatigue allows adolescents to resume school, social and family activities.
Gottfries CG, Matousek M, Zachrisson O.	Institutionen för neurovetenskap och fysiologi, Sahlgrenska akademin, Göteborgs universitet. cgg@gottfries.se	[Immunologic disturbances can explain chronic fatigue syndrome. Biological findings point towards somatogenesis] [Article in Swedish]	Lakartidningen. 2009 Sep 2-8;106(36):2209-10, 2212-5.	
Goudsmit EM, Ho-Yen DO, Dancey CP.	School of Psychology, University of East London, London, UK. ellengoudsmit@hotmail.com	Learning to cope with chronic illness. Efficacy of a multi-component treatment for people with chronic fatigue syndrome.	Patient Educ Couns. 2009 Nov;77(2):231-6. Epub 2009 Jul 2. Comment in: Patient Educ Couns. 2009 Nov;77(2):153-4.	OBJECTIVE: The aim of this study was to determine the efficacy of an out-patient, multi-component programme developed for patients with chronic fatigue syndrome (CFS). METHODS: Twenty-two patients were assessed before and after six months of treatment. Findings were compared with 22 individuals on the waiting list. The programme offered medical care as well as information and counselling to help patients to understand, accept and cope with their illness. RESULTS: At six months, there were significant differences between the groups for fatigue, self-efficacy and anxiety. Overall, 82% of the treated patients reported feeling better and 23% had improved to such a degree that they were discharged from the clinic. The gains were maintained at twelve months. CONCLUSION: This programme was found to be both helpful and acceptable and may provide a useful first-line intervention for many patients with CFS. PRACTICE IMPLICATIONS: Short, pragmatic programmes may be as effective as cognitive-behaviour therapy.

Goudsmit EM, Stouten B, Howes S.	University of East London, UK. ellengoudsmit@hotmail.com	Illness intrusiveness in myalgic encephalomyelitis: an exploratory study.	J Health Psychol. 2009 Mar;14(2):215-21.	This study assessed the relationship between illness intrusiveness, symptoms, disability and depression in patients with myalgic encephalomyelitis (ME). Participants were 16 patients with ME and eight patients with ME plus co-morbid disorders. The patients with co-morbid disorders reported greater illness intrusiveness than the patients with ME alone, but there were no differences between the groups on the other variables. Significant correlations were found between illness intrusiveness on the one hand, and fatigue, cognitive dysfunction, disability and depression, on the other. We conclude that ME is a disabling illness, which has a major impact on various life domains.
Gow JW, Hagan S, Herzyk P, Cannon C, Behan PO, Chaudhuri A.	Essex Centre for Neurological Sciences, Oldchurch Hospital, Romford, RM7 0BE, UK. chaudhuria@gmail.com.	A gene signature for post-infectious chronic fatigue syndrome.	BMC Med Genomics. 2009 Jun 25;2:38.	ABSTRACT: BACKGROUND: At present, there are no clinically reliable disease markers for chronic fatigue syndrome. DNA chip microarray technology provides a method for examining the differential expression of mRNA from a large number of genes. Our hypothesis was that a gene expression signature, generated by microarray assays, could help identify genes which are dysregulated in patients with post-infectious CFS and so help identify biomarkers for the condition. METHODS: Human genome-wide Affymetrix GeneChip arrays (39,000 transcripts derived from 33,000 gene sequences) were used to compare the levels of gene expression in the peripheral blood mononuclear cells of male patients with post-infectious chronic fatigue (n = 8) and male healthy control subjects (n = 7). RESULTS: Patients and healthy subjects differed significantly in the level of expression of 366 genes. Analysis of the differentially expressed genes indicated functional implications in immune modulation, oxidative stress and apoptosis. Prototype biomarkers were identified on the basis of differential levels of gene expression and possible biological significance CONCLUSION: Differential expression of key genes identified in this study offer an insight into the possible mechanism of chronic fatigue following infection. The representative biomarkers identified in this research appear promising as potential biomarkers for diagnosis and treatment.
Gupta A, Vij G, Sharma S, Tirkey N, Rishi P, Chopra K.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India.	Curcumin, a polyphenolic antioxidant, attenuates chronic fatigue syndrome in murine water immersion stress model.	Immunobiology. 2009;214(1):33-9. Epub 2008 Jun 17.	Chronic fatigue syndrome, infection and oxidative stress are interrelated in epidemiological case studies. However, data demonstrating scientific validation of epidemiological claims regarding effectiveness of nutritional supplements for chronic fatigue syndrome are lacking. This study is designed to evaluate the effect of natural polyphenol, curcumin, in a mouse model of immunologically induced fatigue, where purified lipopolysaccharide (LPS) and Brucella abortus (BA) antigens were used as immunogens. The assessment of chronic fatigue syndrome was based on chronic water-immersion stress test for 10 min daily for 19 days and the immobility time was taken as the marker of fatigue. Mice challenged with LPS or BA for 19 days showed significant increase in the immobility time and hyperalgesia on day 19, as well as marked increase in serum tumor necrosis factor-alpha (TNF-alpha) levels. Concurrent treatment with curcumin resulted in significantly decreased immobility time as well as hyperalgesia. There was significant attenuation of oxidative stress as well as TNF-alpha levels. These findings strongly suggest that during immunological activation, there is significant increase in oxidative stress and curcumin can be a valuable option in the treatment of chronic fatigue syndrome.
Hadlandsmyth K, Vowles KE.	Bath and Wiltshire Adult Chronic Fatigue Syndrome Service, Royal National Hospital	Does depression mediate the relation between fatigue severity and disability in	J Psychosom Res. 2009 Jan;66(1):31-5. Epub 2008 Nov 22.	OBJECTIVE: Chronic fatigue syndrome (CFS) is often associated with significant levels of disability. Although fatigue and depression have been found to be independently related to severity of disability, it is not clear how these three factors are mutually related. The present study sought to address this issue by specifically testing a model of mediation whereby depression was hypothesized to influence relations between fatigue and disability. METHODS: Participants included 90 individuals seeking

	for Rheumatic Diseases, Bath, UK. kehb8c@umsl.edu	chronic fatigue syndrome sufferers?		treatment for CFS at a tertiary care facility. Each provided demographic information and completed standardized measures of depression and fatigue severity, as well as a measure of disability, which assessed difficulties in physical, psychosocial, and independence domains. RESULTS: Analyses indicated that depression and fatigue were positively correlated with one another, as well as all three disability domains. Analyses of mediation indicated that depression completely mediated the relation between fatigue and psychosocial disability and partially mediated the relation between fatigue and the other two disability domains. Indirect effects tests indicated that the inclusion of depression in the statistical models was statistically meaningful. CONCLUSIONS: These results replicate previous findings that fatigue and depression are independently related to disability in those with CFS. A more complex statistical model, however, suggested that depression severity substantially influenced the strength of the relation between fatigue and disability levels across a range of domains, including complete mediation in areas involving psychosocial functioning. These results may aid in clarifying contemporary conceptualizations of CFS and provide guidance in the identification of appropriate treatment targets.
Haig-Ferguson A, Tucker P, Eaton N, Hunt L, Crawley E.	Centre for Child and Adolescent Health, University of Bristol, Bristol, UK. andrew.haig-ferguson@bristol.ac.uk	Memory and attention problems in children with chronic fatigue syndrome or myalgic encephalopathy.	Arch Dis Child. 2009 Oct;94(10):757-62. Epub 2008 Nov 11.	OBJECTIVE: To understand more about the problems children with chronic fatigue syndrome (CFS) or myalgic encephalopathy (ME) experience with memory and attention, and to test the feasibility of quantitative measurement of both memory and attention. DESIGN: Four-item semistructured questionnaire and neuropsychological test battery with 10 psychometric subtests. SETTING: Family home of the child taking part. PATIENTS: 20 children with a diagnosis of CFS/ME experiencing memory and/or concentration problems were recruited between April and October 2007 from a regional CFS/ME clinical service (female 13; average age 13.5 years; range 8-16). METHODS: Each child, parent and teacher was asked to describe the child's memory and attention problems. Responses were subject to thematic analysis by two independent researchers. In addition, each child completed a battery of 10 tests to measure: processing speed; attention; immediate and delayed memory; working memory; executive function. Raw scores were converted into age-scaled scores and the children's psychometric scores on the 10 tests taken were compared with normative data using t tests. RESULTS: Children with CFS/ME, their parents and teachers described problems with focussed attention, sustained attention, recall and stress. Scores for sustained attention (mean 8.1, 95% CI 6.3 to 9.9), switching attention (7.5, 5.5 to 9.4), divided attention (6.9, 5.5 to 8.2), auditory learning (8.2, 6.8 to 9.6) and immediate recall (8.7, 7.3 to 10.0) appeared lower than the normative mean of 10. CONCLUSIONS: Children with CFS/ME appear to experience problems with attention, which may have adverse implications for verbal memory. These cognitive problems may explain some of the educational difficulties associated with CFS.
Hamilton WT, Gallagher AM, Thomas JM, White PD.	Academic Unit of Primary Health Care, University of Bristol, Bristol, UK.	Risk markers for both chronic fatigue and irritable bowel syndromes: a prospective case-control study in	Psychol Med. 2009 Nov;39(11):1913-21. Epub 2009 Apr 15.	BACKGROUND: Fatigue syndromes and irritable bowel syndrome (IBS) often occur together. Explanations include being different manifestations of the same condition and simply sharing some symptoms. METHOD: A matched case-control study in UK primary care, using data collected prospectively in the General Practice Research Database (GPRD). The main outcome measures were: health-care utilization, specific symptoms and diagnoses. Risk markers were divided into distant (from 3 years to 1 year before diagnosis) and recent (1 year before diagnosis). RESULTS: A total of 4388 patients with any fatigue syndrome were matched to two groups of patients: those attending for IBS

		primary care.		and those attending for another reason. Infections were specific risk markers for both syndromes, with viral infections being a risk marker for a fatigue syndrome [odds ratios (ORs) 2.3-6.3], with a higher risk closer to onset, and gastroenteritis a risk for IBS (OR 1.47, compared to a fatigue syndrome). Chronic fatigue syndrome (CFS) shared more distant risk markers with IBS than other fatigue syndromes, particularly other symptom-based disorders (OR 3.8) and depressive disorders (OR 2.3), but depressive disorders were a greater risk for CFS than IBS (OR 2.4). Viral infections were more of a recent risk marker for CFS compared to IBS (OR 2.8), with gastroenteritis a greater risk for IBS (OR 2.4). CONCLUSIONS: Both fatigue and irritable bowel syndromes share predisposing risk markers, but triggering risk markers differ. Fatigue syndromes are heterogeneous, with CFS sharing predisposing risks with IBS, suggesting a common predisposing pathophysiology.
Hannonen P.	Keski-Suomen keskussairaala, sisätautien vastuualue, Keskussairaalantie 19, 40620 Jyväskylä.	[Is diagnosing fibromyalgia necessary?][Article in Finnish]	Duodecim. 2009;125(5):521-6.	Fibromyalgia is a controversial pain syndrome with chronic widespread pain (occurring on both sides of the body as well as axially below and above the waist) and unexplained fatigue as the predominating features. Fibromyalgia involves lots of symptoms focusing on different organ systems. In sensory examination the most significant finding is general allodynia. The widespread chronic pain and tender points at certain locations as reported by the patient differentiate fibromyalgia patients from those suffering from other diseases of the musculoskeletal system.
Hardy SE.	Division of Geriatric Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania 15213, USA. hardysdom.pitt.edu	Methylphenidate for the treatment of depressive symptoms, including fatigue and apathy, in medically ill older adults and terminally ill adults.	Am J Geriatr Pharmacother. 2009 Feb;7(1):34-59.	BACKGROUND: Depressive symptoms, fatigue, and apathy are common symptoms among medically ill older adults and patients with advanced disease, and have been associated with morbidity and mortality. Methylphenidate has been used to treat these symptoms because of its rapid effect. Despite the long history of methylphenidate use for the treatment of depressive symptoms, fatigue, and apathy, there is little definitive evidence to support its use. OBJECTIVE: The aim of this paper was to review the efficacy and tolerability of methylphenidate in the treatment of depressive symptoms, fatigue, and apathy in medically ill older adults and adults receiving palliative care. METHODS: English-language articles presenting systematic reviews, clinical trials, or case series describing the use of methylphenidate for the treatment of depressive symptoms, fatigue, or apathy in medically ill older adults or adults receiving palliative care were identified. The key words methylphenidate and either depressive, depression, fatigue, or apathy were used to search the Cochrane Database, MEDLINE, PsycINFO, and International Pharmaceutical Abstracts. Included articles addressed depressive symptoms, fatigue, or apathy in (1) older adults (generally, age > or =65 years), particularly those with comorbid medical illness; (2) adults receiving palliative care; and (3) adults with other chronic illnesses. I excluded articles regarding treatment of depression in healthy young adults; bipolar disorder and attention-deficit/hyperactivity disorder; and narcolepsy, chronic fatigue syndrome, and related disorders. RESULTS: A total of 19 controlled trials of methylphenidate in medically ill older adults or patients in palliative care were identified. Unfortunately, their conflicting results, small sample sizes, and poor methodologic quality limited the ability to draw inferences regarding the efficacy of methylphenidate, although evidence of tolerability was stronger. The available evidence suggests possible effectiveness of methylphenidate for depressive symptoms, fatigue, and apathy in various medically ill populations. CONCLUSION: In the absence of definitive evidence of effectiveness, trials of low-dose methylphenidate in medically ill adults with depression, fatigue, or apathy, with

				monitoring for response and adverse effects, are appropriate.
Harvey SB, Wessely S, Kuh D, Hotopf M.	Institute of Psychiatry, King's College London, London, UK. s.harvey@iop.kcl.ac.uk	The relationship between fatigue and psychiatric disorders: evidence for the concept of neurasthenia.	J Psychosom Res. 2009 May;66(5):445-54. Epub 2009 Mar 3.	OBJECTIVE: Fatigue and psychiatric disorders frequently occur comorbidly and share similar phenomenological features. There has been debate as to whether chronic fatigue, or neurasthenia, should be considered an independent syndrome distinct from psychiatric disorders. We aimed to establish whether persistent fatigue can occur independently from psychiatric disorders and to test the hypothesis that fatigue without comorbid psychiatric symptoms has unique premorbid risk factors. We also aimed to investigate the psychological outcome of any individuals with fatigue. METHODS: The MRC National Survey of Health and Development was used to prospectively follow 5362 participants from birth. A sample of nonfatigued individuals without psychiatric disorder was selected at age 36 and followed until age 43 years (n=2714). At age 43, the presence of new onset fatigue and/or psychiatric disorder was assessed. Information on a number of potential premorbid risk factors was collected between ages 0 and 36 years. Individuals with fatigue but no comorbid psychiatric disorder were then followed up at age 53 years. RESULTS: At age 43 years, 201 (7.4%) participants reported significant levels of new onset fatigue in the absence of comorbid psychiatric disorder. Despite the absence of case level psychiatric disorder, these individuals did report increased levels of some psychological symptoms. Excessive childhood energy (adjusted OR 2.63, 95% CI 1.55-4.48, P<.001) and being overweight at age 36 (adjusted OR 1.62, 95% CI 1.05-2.49, P=.03) were specific risk factors for fatigue without psychiatric disorder but not fatigue with comorbid psychiatric illness. Neuroticism was a risk factor for fatigue both with and without comorbid psychiatric disorder. Negative life events and a family history of psychiatric illness were only risk factors for fatigue when it occurred comorbidly with psychiatric illness. CONCLUSIONS: A significant proportion of the adult population will suffer from fatigue without comorbid psychiatric disorder. While fatigue and psychiatric disorders share some risk factors, excessive energy in childhood and being overweight as an adult appear to be specific risk factors for fatigue. Our results confirm the significant overlap between fatigue and psychiatric disorders, while also providing evidence for neurasthenia as a separate diagnosis.
Harvey SB, Wessely S.		Tired all the time: can new research on fatigue help clinicians?Comment on: Br J Gen Pract. 2009 Apr;59(561):e93-100.	Br J Gen Pract. 2009 Apr;59(561):237-9.	
Harvey SB, Wessely S.	Institute of Psychiatry, King's College London, London, UK. samuel.b.harvey@kcl.ac.uk	Chronic fatigue syndrome: identifying zebras amongst the horses.	BMC Med. 2009 Oct 12;7:58. Comment on: BMC Med. 2009;7:57.	There are currently no investigative tools or physical signs that can confirm or refute the presence of chronic fatigue syndrome (CFS). As a result, clinicians must decide how long to keep looking for alternative explanations for fatigue before settling on a diagnosis of CFS. Too little investigation risks serious or easily treatable causes of fatigue being overlooked, whilst too many increases the risk of iatrogenic harm and reduces the opportunity for early focused treatment. A paper by Jones et al published this month in BMC Medicine may help clinicians in deciding how to undertake such

				investigations. Their results suggest that if clinicians look for common psychiatric and medical conditions in those complaining of prolonged fatigue, the rate of detection will be higher than previously estimated. The most common co-morbid condition identified was depression, suggesting a simple mental state examination remains the most productive single investigation in any new person presenting with unexplained fatigue. Currently, most diagnostic criteria advice CFS should not be diagnosed when an active medical or psychiatric condition which may explain the fatigue is identified. We discuss a number of recent prospective studies that have provided valuable insights into the aetiology of chronic fatigue and describe a model for understanding chronic fatigue which may be equally relevant regardless of whether or not an apparent medical cause for fatigue can be identified. See the associated research paper by Jones et al: http://www.biomedcentral.com/1741-7015/7/57.
Häuser W, Bernardy K, Uçeyler N, Sommer C.	Department of Internal Medicine, Klinikum Saarbrücken, Winterberg 1, D-66119 Saarbrücken, Germany. whaeuser@klinikum-saarbruecken.de	Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis.	JAMA. 2009 Jan 14;301(2):198-209.	CONTEXT: Fibromyalgia syndrome (FMS) is a chronic pain disorder associated with multiple debilitating symptoms and high disease-related costs. Effective treatment options are needed. OBJECTIVES: To determine the efficacy of antidepressants in the treatment of FMS by performing a meta-analysis of randomized controlled clinical trials. DATA SOURCES: MEDLINE, PsycINFO, Scopus, and the Cochrane Library databases were searched through August 2008. Reference sections of original studies, meta-analyses, and reviews on antidepressants in FMS were reviewed. STUDY SELECTION: Randomized placebo-controlled trials with tricyclic and tetracyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs) were analyzed. DATA EXTRACTION AND DATA SYNTHESIS: Two authors independently extracted data. Effects were summarized using standardized mean differences (SMDs) by a random-effects model. RESULTS: Eighteen randomized controlled trials (median duration, 8 weeks; range, 4-28 weeks) involving 1427 participants were included. Overall, there was strong evidence for an association of antidepressants with reduction in pain (SMD, -0.43; 95% confidence interval [CI], -0.55 to -0.30), fatigue (SMD, -0.13; 95% CI, -0.26 to -0.01), depressed mood (SMD, -0.26; 95% CI, -0.39 to -0.12), and sleep disturbances (SMD, -0.32; 95% CI, -0.46 to -0.18). There was strong evidence for an association of antidepressants with improved health-related quality of life (SMD, -0.31; 95% CI, -0.42 to -0.20). Effect sizes for pain reduction were large for TCAs (SMD, -1.64; 95% CI, -2.57 to -0.71), medium for MAOIs (SMD, -0.54; 95% CI, -1.02 to -0.07), and small for SSRIs (SMD, -0.39; 95% CI, -0.77 to -0.01) and SNRIs (SMD, -0.36; 95% CI, -0.46 to -0.25). CONCLUSION: Antidepressant medications are associated with improvements in pain, depression, fatigue, sleep disturbances, and health-related quality of life in patients with FMS.
Häuser W, Grulke N, Michalski D, Hoffmann A, Akritidou I, Klauenberg S, Maier C, Hinz A.	Zentrum für interdisziplinäre Schmerztherapie/Innere Medizin I, Klinikum Saarbrücken gGmbH, Saarbrücken, Deutschland.	[Intensity of limb pain and fatigue in fibromyalgia syndrome, depressive disorders and chronic back pain. A criterion for differentiation][Art	Schmerz. 2009 Jun;23(3):267-74.	BACKGROUND: A symptom-based diagnosis of fibromyalgia syndrome (FMS) without tender point examination is needed for primary care. We tested if a symptom-based diagnosis of FMS can be founded on the intensity of the symptoms musculoskeletal pain and fatigue. METHODS: FMS patients from 4 different settings (n=464 members of the German Fibromyalgia Association DFV, n=33 from a private practice of rheumatology, n=36 from a tertiary care pain department, n=162 from medical expertise), patients with depressive disorders from 2 different settings (n=24 from a university department of psychiatry, n=311 from an out-patient university psychosomatic department), patients with chronic back pain from an out-patient training center (n=691) and persons from a representative German population sample (n=1977) were compared using the subscales of the Giessen subjective

	whaeuser@klinikum-saarbruecken.de	icle in German]		complaints list GBB 24. RESULTS: The greatest mean differences between FMS patients and the other samples were found within the subscales "limb pains" and "fatigue". FMS patients scored higher in the subscales "heart problems" and "dyspepsia", but both subscales did not contribute to a differentiation of the samples. The rates of reclassification of the subsamples based on the subscales "limb pains" and "fatigue" ranged between 80 and 93%. CONCLUSION: High levels of the intensity of chronic widespread musculoskeletal pain and chronic fatigue may form the basis of a symptom-based diagnosis of FMS.
Heim C, Nater UM, Maloney E, Boneva R, Jones JF, Reeves WC.	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Woodruff Memorial Research Bldg, Ste 4311, Atlanta, GA 30322, USA. cmheim@emory.edu	Childhood trauma and risk for chronic fatigue syndrome: association with neuroendocrine dysfunction.	Arch Gen Psychiatry. 2009 Jan;66(1):72-80.	CONTEXT: Childhood trauma appears to be a potent risk factor for chronic fatigue syndrome (CFS). Evidence from developmental neuroscience suggests that early experience programs the development of regulatory systems that are implicated in the pathophysiology of CFS, including the hypothalamic-pituitary-adrenal axis. However, the contribution of childhood trauma to neuroendocrine dysfunction in CFS remains obscure. OBJECTIVES: To replicate findings on the relationship between childhood trauma and risk for CFS and to evaluate the association between childhood trauma and neuroendocrine dysfunction in CFS. Design, Setting, and PARTICIPANTS: A case-control study of 113 persons with CFS and 124 well control subjects identified from a general population sample of 19 381 adult residents of Georgia. MAIN OUTCOME MEASURES: Self-reported childhood trauma (sexual, physical, and emotional abuse; emotional and physical neglect), psychopathology (depression, anxiety, and posttraumatic stress disorder), and salivary cortisol response to awakening. RESULTS: Individuals with CFS reported significantly higher levels of childhood trauma and psychopathological symptoms than control subjects. Exposure to childhood trauma was associated with a 6-fold increased risk of CFS. Sexual abuse, emotional abuse, and emotional neglect were most effective in discriminating CFS cases from controls. There was a graded relationship between exposure level and CFS risk. The risk of CFS conveyed by childhood trauma further increased with the presence of posttraumatic stress disorder symptoms. Only individuals with CFS and with childhood trauma exposure, but not individuals with CFS without exposure, exhibited decreased salivary cortisol concentrations after awakening compared with control subjects. CONCLUSIONS: Our results confirm childhood trauma as an important risk factor of CFS. In addition, neuroendocrine dysfunction, a hallmark feature of CFS, appears to be associated with childhood trauma. This possibly reflects a biological correlate of vulnerability due to early developmental insults. Our findings are critical to inform pathophysiological research and to devise targets for the prevention of CFS.
Hickie I, Davenport T, Vernon SD, Nisenbaum R, Reeves WC, Hadzi-Pavlovic D, Lloyd A; International Chronic Fatigue Syndrome Study Group.	Brain and Mind Research Institute, Camperdown, NSW, Australia. ianh@med.usyd.edu.au	Are chronic fatigue and chronic fatigue syndrome valid clinical entities across countries and health-care settings?	Aust N Z J Psychiatry. 2009 Jan;43(1):25-35.	OBJECTIVE: The validity of the diagnosis of chronic fatigue syndrome and related chronic fatigue states remains controversial, particularly in psychiatry. This project utilized international epidemiological and clinical research data to test construct validity across diagnostic categories, health-care settings and countries. Relevant demographic, symptom and diagnostic data were obtained from 33 studies in 21 countries. The subjects had fatigue lasting 1-6 months (prolonged fatigue), or >6 months (chronic fatigue), or met diagnostic criteria for chronic fatigue syndrome. METHOD: Common symptom domains were derived by factor analytic techniques. Mean scores on each symptom factor were compared across diagnostic categories, health-care settings and countries. RESULTS: Data were obtained on 37,724 subjects (n = 20,845 female, 57%), including from population-based studies (n = 15,749, 42%), studies in primary care (n = 19 472, 52%), and secondary or specialist

				tertiary referral clinics (n = 2503, 7%). The sample included 2013 subjects with chronic fatigue, and 1958 with chronic fatigue syndrome. A five-factor model of the key symptom domains was preferred ('musculoskeletal pain/fatigue', 'neurocognitive difficulties', 'inflammation', 'sleep disturbance/fatigue' and 'mood disturbance') and was comparable across subject groups and settings. Although the core symptom profiles were similar, some differences in symptoms were observed across diagnostic categories, health-care settings and between countries. CONCLUSIONS: The construct validity of chronic fatigue and chronic fatigue syndrome is supported by an empirically derived factor structure from existing international datasets.
Hokama Y, Campora CE, Hara C, Kuribayashi T, Le Huynh D, Yabusaki K.	Department of Pathology, John A. Burns School of Medicine, University of Hawaii at Mânoa, Honolulu, Hawaii 96822, USA.	Anticardiolipin antibodies in the sera of patients with diagnosed chronic fatigue syndrome.	J Clin Lab Anal. 2009;23(4):210-2.	Examination of anticardiolipin antibodies (ACAs) in the sera of patients clinically diagnosed with chronic fatigue syndrome (CFS) using an enzyme-linked immunoassay procedure demonstrated the presence of immunoglobulin M isotypes in 95% of CFS serum samples tested. The presence of immunoglobulin G and immunoglobulin A isotypes were also detected in a subset of the samples. Future studies will focus on elucidating whether alterations to mitochondrial inner membranes and/or metabolic functions play a possible role in the expression of ACAs.
Huang LC, Hsu SY, Lin E.	Department of Psychiatry, National Taiwan University Hospital Yun-Lin Branch, Taiwan. psychidr@gmail.com	A comparison of classification methods for predicting Chronic Fatigue Syndrome based on genetic data.	J Transl Med. 2009 Sep 22;7:81.	BACKGROUND: In the studies of genomics, it is essential to select a small number of genes that are more significant than the others for the association studies of disease susceptibility. In this work, our goal was to compare computational tools with and without feature selection for predicting chronic fatigue syndrome (CFS) using genetic factors such as single nucleotide polymorphisms (SNPs). METHODS: We employed the dataset that was original to the previous study by the CDC Chronic Fatigue Syndrome Research Group. To uncover relationships between CFS and SNPs, we applied three classification algorithms including naive Bayes, the support vector machine algorithm, and the C4.5 decision tree algorithm. Furthermore, we utilized feature selection methods to identify a subset of influential SNPs. One was the hybrid feature selection approach combining the chi-squared and information-gain methods. The other was the wrapper-based feature selection method. RESULTS: The naive Bayes model with the wrapper-based approach performed maximally among predictive models to infer the disease susceptibility dealing with the complex relationship between CFS and SNPs. CONCLUSION: We demonstrated that our approach is a promising method to assess the associations between CFS and SNPs.
Hui JS.	Institute of Acupuncture and Moxibustion, China Academy of Chinese Medical Sciences, Beijing 100700, China.	Acupuncture treatment of chronic fatigue syndrome.	J Tradit Chin Med. 2009 Sep;29(3):234-6.	
Hurwitz BE, Coryell VT, Parker M, Martin P,	Behavioral Medicine Research Center, University	Chronic fatigue syndrome: illness severity, sedentary	Clin Sci (Lond). 2009 Oct 19;118(2):125-35.	The study examined whether deficits in cardiac output and blood volume in a CFS (chronic fatigue syndrome) cohort were present and linked to illness severity and sedentary lifestyle. Follow-up analyses assessed whether differences in cardiac output levels between CFS and control groups were

Laperriere A, Klimas NG, Sfakianakis GN, Bilsker MS.	of Miami, Miami, FL 33136, USA. bhurwitz@miami.edu	lifestyle, blood volume and evidence of diminished cardiac function.	Comment in: Clin Sci (Lond). 2010 Jan;118(2):121-3.	corrected by controlling for cardiac contractility and TBV (total blood volume). The 146 participants were subdivided into two CFS groups based on symptom severity data, severe (n=30) and non-severe (n=26), and two healthy non-CFS control groups based on physical activity, sedentary (n=58) and non-sedentary (n=32). Controls were matched to CFS participants using age, gender, ethnicity and body mass. Echocardiographic measures indicated that the severe CFS participants had 10.2% lower cardiac volume (i.e. stroke index and end-diastolic volume) and 25.1% lower contractility (velocity of circumferential shortening corrected by heart rate) than the control groups. Dual tag blood volume assessments indicated that the CFS groups had lower TBV, PV (plasma volume) and RBCV (red blood cell volume) than control groups. Of the CFS subjects with a TBV deficit (i.e. > or = 8% below ideal levels), the mean+/-S.D. percentage deficit in TBV, PV and RBCV were -15.4+/-4.0, -13.2+/-5.0 and -19.1+/-6.3% respectively. Lower cardiac volume levels in CFS were substantially corrected by controlling for prevailing TBV deficits, but were not affected by controlling for cardiac contractility levels. Analyses indicated that the TBV deficit explained 91-94% of the group differences in cardiac volume indices. Group differences in cardiac structure were offsetting and, hence, no differences emerged for left ventricular mass index. Therefore the findings indicate that lower cardiac volume levels, displayed primarily by subjects with severe CFS, were not linked to diminished cardiac contractility levels, but were probably a consequence of a co-morbid hypovolaemic condition. Further study is needed to address the extent to which the cardiac and blood volume alterations in CFS have physiological and clinical significance.
Inamitsu T.	Section of Psychosomatic Medicine, Fukuoka Dental College.	[Functional somatic syndrome in dental practice] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1749-54.	Functional somatic syndromes (FSSs) are common in dental as well as medical practice. Many patients with unexplained symptoms in oro-maxillo-facial areas visit dentists, but they are not diagnosed and treated properly. Temporomandibular disorder, atypical facial pain, and glossodynia (burning mouth syndrome) are included in dental FSSs. These diseases overlap with each other and with FSSs in other organs, such as myofacial pain syndrome, tension-type headache, fibromyalgia, and chronic fatigue syndrome. They coexist with mental disorders, such as anxiety disorder, mood disorder, and somatoform disorder. Multidisciplinary and holistic approaches should be applied to dental FSSs; pharmacological therapy (antidepressants), physical therapy, and cognitive-behavioral therapy. Clinicians have to support a patient in"enjoying his/her life with symptoms". Dental specialists in "oral medicine" with psychosomatic viewpoints are now required.
Jammes Y, Steinberg JG, Delliaux S, Brégeon F.	UMR MD2 (P2COE), Faculté de Médecine, Université de la Méditerranée, North Hospital, Assistance Publique - Hôpitaux de Marseille, France. yves.jammes@univ	Chronic fatigue syndrome combines increased exercise-induced oxidative stress and reduced cytokine and Hsp responses.	J Intern Med. 2009 Aug;266(2):196-206. Epub 2009 May 19.	OBJECTIVES: As heat shock proteins (Hsp) protect the cells against the deleterious effects of oxidative stress, we hypothesized that Hsp expression might be reduced in patients suffering from chronic fatigue syndrome (CFS) who present an accentuated exercise-induced oxidative stress. DESIGN: This case-control study compared nine CFS patients to a gender-, age- and weight-matched control group of nine healthy sedentary subjects. INTERVENTIONS: All subjects performed an incremental cycling exercise continued until exhaustion. We measured ventilation and respiratory gas exchange and evoked compound muscle potential (M-wave) recorded from vastus lateralis. Repetitive venous blood sampling allowed measurements of two markers of oxidative stress [thiobarbituric acid reactive substances (TBARS) and reduced ascorbic acid (RAA)], two cytokines (IL-6 and TNF-alpha) and two Hsp (Hsp27 and Hsp70) at rest, during maximal exercise and the 60-min recovery period. RESULTS: Compared with controls, resting CFS patients had low baseline levels of RAA and Hsp70. Their

	med.fr			response to maximal exercise associated (i) M-wave alterations indicating reduced muscle membrane excitability, (ii) early and accentuated TBARS increase accompanying reduced changes in RAA level, (iii) absence of significant increase in IL-6 and TNF-alpha, and (iv) delayed and marked reduction of Hsp27 and Hsp70 variations. The post-exercise increase in TBARS was accentuated in individuals having the lowest variations of Hsp27 and Hsp70. CONCLUSIONS: The response of CFS patients to incremental exercise associates a lengthened and accentuated oxidative stress, which might result from delayed and insufficient Hsp production.
Jason L, Benton M, Torres-Harding S, Muldowney K.	DePaul University, Center for Community Research, Chicago, IL 60614, USA. Ljason@depaul.edu	The impact of energy modulation on physical functioning and fatigue severity among patients with ME/CFS.	Patient Educ Couns. 2009 Nov;77(2):237-41. Epub 2009 Apr 8. Comment in: Patient Educ Couns. 2009 Nov;77(2):153-4.	OBJECTIVE: The energy envelope postulates that patients with Myalgic Encephalomyelitis/chronic fatigue syndrome (ME/CFS) will improve functioning when maintaining expended energy levels at the same level as available energy level. METHODS: Estimated weekly Energy Quotients were established by dividing expended energy level by perceived energy level and multiplying by 100. Two groups of patients were identified following participation in a non-pharmacologic intervention trial. Some were able to keep expended energy close to available energy and others were not successful at this task. RESULTS: Those who were able to stay within their energy envelope had significant improvements in physical functioning and fatigue severity. CONCLUSION: Findings suggest that helping patients with ME/CFS maintain appropriate energy expenditures in coordination with available energy reserves can help improve functioning over time. PRACTICE IMPLICATIONS: Health care professionals that treat patients with ME/CFS might incorporate strategies that help patients self-monitor and self-regulate energy expenditures.
Jason L, Porter N, Shelleby E, Till L, Bell DS, Lapp CW, Rowe K, De Meirleir K.	Center for Community Research, DePaul University, Chicago, IL 60614, USA. Ljason@depaul.edu	Severe versus Moderate criteria for the new pediatric case definition for ME/CFS.	Child Psychiatry Hum Dev. 2009 Dec;40(4):609-20. Epub 2009 Jun 10.	The new diagnostic criteria for pediatric ME/CFS are structurally based on the Canadian Clinical Adult case definition, and have more required specific symptoms than the (Fukuda et al. Ann Intern Med 121:953-959, 1994) adult case definition. Physicians specializing in pediatric ME/CFS referred thirty-three pediatric patients with ME/CFS and 21 youth without the illness. Those who met ME/CFS criteria were separated into Severe and Moderate categories. Significant differences were found for symptoms within each of the six major categories: fatigue, post-exertional malaise, sleep, pain, neurocognitive difficulties, and autonomic/neuroendocrine/immune manifestations. In general, the results showed participants who met the Severe ME/CFS criteria reported the highest scores, the Moderate ME/CFS group show scores that were a little lower, and the control group evidenced the lowest scores. Findings indicate that the Pediatric Case Definition for ME/CFS can distinguish between those with this illness and controls, and between those with Severe versus Moderate manifestations of the illness.
Jason LA, Roesner N, Porter N, Parenti B, Mortensen J, Till L.	DePaul University.	Provision of social support to individuals with chronic fatigue syndrome.	J Clin Psychol. 2009 Nov 9. [Epub ahead of print]	The present study evaluated a buddy program designed to provide support for individuals with chronic fatigue syndrome (CFS). The intervention involved weekly visits by a student paraprofessional, who helped out with tasks that needed to be done in an effort to reduce some of the taxing demands and responsibilities that participants regularly encountered. This model of rehabilitation focused on avoiding overexertion in persons with CFS, aiming to avoid setbacks and relapses while increasing their tolerance for activity. Participants with CFS were randomly assigned to either a 4-month buddy intervention or a control condition. Posttest results showed that individuals who received a student buddy intervention had significantly greater reductions in fatigue severity and increases in vitality than individuals in the control condition. There were no significant changes between groups for

				physical functioning and stress. Buddy interventions that help patients with CFS reduce overexertion and possibly remain within their energy envelopes can be thought of as representing a different paradigm than nonpharmacologic interventions that focus only on increasing levels of activity through graded exercise. (c) 2009 Wiley Periodicals, Inc. J Clin Psychol 66:1-10, 2010.
Jones JF, Lin JM, Maloney EM, Boneva RS, Nater UM, Unger ER, Reeves WC.	Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MS A15, Atlanta, GA 30333, USA. jaj9@cdc.gov	An evaluation of exclusionary medical/psychiatric conditions in the definition of chronic fatigue syndrome.	BMC Med. 2009 Oct 12;7:57. Comment in: BMC Med. 2009;7:58.	BACKGROUND: The diagnosis of chronic fatigue syndrome (CFS) in research studies requires the exclusion of subjects with medical and psychiatric conditions that could confound the analysis and interpretation of results. This study compares illness parameters between individuals with CFS who have and those who do not have exclusionary conditions. METHODS: We used a population-based telephone survey of randomly selected individuals, followed by a clinical evaluation in the study metropolitan, urban, and rural counties of Georgia, USA. The medical and psychiatric histories of the subjects were examined and they underwent physical and psychiatric examinations and laboratory screening. We also employed the multidimensional fatigue inventory (MFI), the medical outcomes survey short form-36 (SF-36) and the US Centres for Disease Control and Prevention symptom inventory (SI). RESULTS: Twenty-nine percent (1,609) of the 5623 subjects who completed the detailed telephone interview reported exclusionary diagnoses and we diagnosed an exclusionary condition in 36% of 781 clinically evaluated subjects. Both medical and psychiatric exclusionary conditions were more common in women, blacks and participants from rural areas. Subjects with and without exclusions had similar levels of fatigue and impairment as measured by the MFI and SF-36; those with CFS-like illness (not meeting the formal CFS definition) were more likely to have an exclusionary diagnosis. After adjusting for demographics, body mass index, fatigue subscales, SF-36 subscales and CFS symptoms, CFS-like illness did not remain significantly associated with having an exclusionary diagnosis. CONCLUSION: Medical and psychiatric illnesses associated with fatigue are common among the unwell. Those who fulfill CFS-like criteria need to be evaluated for potentially treatable conditions. Those with exclusionary conditions are equally impaired as those without exclusions.
Jørstad RG, Nøjd MM.		[Compensation claims following meningococcal vaccine B trial] [Article in Norwegian]Comment on: Tidsskr Nor Laegeforen. 2009 Mar 26;129(7):642-3.	Tidsskr Nor Laegeforen. 2009 Jun 25;129(13):1352.	
Kaabia N, Letaief A.	Service de médecine interne et maladies infectieuses, CHU Farhat-Hached, rue	[Q Fever in Tunisia] [Article in French]	Pathol Biol (Paris). 2009 Jul;57(5):439-43. Epub 2008 Jun 12.	Q fever is a common zoonosis with almost a worldwide distribution caused by Coxiella burnetii. Farm animals and pets are the main reservoirs of infection and transmission to humans is usually via inhalation of contaminated aerosols. Infection in humans is often asymptomatic, but it can manifest as an acute disease (usually a self-limited flu-like illness, pneumonia or hepatitis) or as a chronic form (mainly endocarditis, but also hepatitis and chronic-fatigue syndrome). In Tunisia, although

	Mohamed-Karoui, 4000 Sousse, Tunisie. naoufelkaabia2001@yahoo.fr			prevalence of anti-Coxiella burnetii was high among blood donors, Q fever was rarely reported and frequently miss diagnosed by physicians. This study is a review of epidemiological and clinical particularities of Q fever in Tunisia.
Kane JM, Correll CU, Goff DC, Kirkpatrick B, Marder SR, Vester-Blokland E, Sun W, Carson WH, Pikalov A, Assunção-Talbott S.	Department of Psychiatry, The Zucker Hillside Hospital, Glen Oaks, NY 11004-1150, USA. psychiatry@lij.edu	A multicenter, randomized, double-blind, placebo-controlled, 16-week study of adjunctive aripiprazole for schizophrenia or schizoaffective disorder inadequately treated with quetiapine or risperidone monotherapy.	J Clin Psychiatry. 2009 Oct;70(10):1348-57.	OBJECTIVE: Combining antipsychotics is common practice in the treatment of schizophrenia. This study investigated aripiprazole adjunctive to risperidone or quetiapine for treating schizophrenia and schizoaffective disorder. METHOD: In this multicenter, double-blind, 16-week, placebo-controlled study conducted at 43 American sites from July 2006 to October 2007, patients with chronic, stable schizophrenia or schizoaffective disorder diagnosed with DSM-IV-TR were randomly assigned to receive aripiprazole (2-15 mg/d) or placebo in addition to a stable regimen of quetiapine (400-800 mg/d) or risperidone (4-8 mg/d). The primary outcome measure was the mean change from baseline to endpoint (week 16, last observation carried forward) in the Positive and Negative Syndrome Scale (PANSS) total score. RESULTS: 323 subjects being treated with either risperidone (n = 177) or quetiapine (n = 146) were randomly assigned to receive adjunctive aripiprazole (n = 168) or placebo (n = 155). Baseline characteristics were similar (mean PANSS total score: aripiprazole, 74.5; placebo, 75.9) except for history of suicide attempts (aripiprazole, 27%; placebo, 40%). Nearly 70% of subjects in each arm completed the trial. Adjunctive aripiprazole and placebo groups were similar in the mean change from baseline to endpoint in the PANSS total score (aripiprazole, -8.8; placebo, -8.9; P = .942). The incidence of treatment-emergent adverse events was similar between groups. Mean changes in Simpson-Angus Scale, Abnormal Involuntary Movement Scale, and Barnes Akathisia Rating Scale scores were not statistically significantly different. Adjunctive aripiprazole was associated with statistically significantly greater decreases in mean serum prolactin levels from baseline than was adjunctive placebo (-12.6 ng/mL for aripiprazole vs -2.2 ng/mL for placebo; P < .001), an effect that was seen in the risperidone subgroup (-18.7 ng/mL vs -1.9 ng/mL; P < .001) but not in the quetiapine subgroup (-3.01 ng/mL vs +0.15 ng/mL; P = .104). CONCLUSIONS: The addition of aripiprazole to risperidone or quetiapine was not associated with improvement in psychiatric symptoms but was generally safe and well tolerated. Further research is warranted to explore whether antipsychotic combination therapy offers benefits to particular patient populations-for example, in cases of hyperprolactinemia. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00325689. Copyright 2009 Physicians Postgraduate Press, Inc.
Kang HK, Li B, Mahan CM, Eisen SA, Engel CC.	Department of Veterans Affairs, Environmental Epidemiology Service, Washington DC 20420, USA. han.kang@va.gov	Health of US veterans of 1991 Gulf War: a follow-up survey in 10 years.	J Occup Environ Med. 2009 Apr;51(4):401-10.	OBJECTIVE: To assess periodically the health status of a cohort of 1991 Gulf War veterans by comparing various health outcomes with those of their military peers who were not deployed to the Gulf. METHODS: We conducted a follow-up health survey to collect health information among population-based samples of 30,000 veterans (15,000 Gulf War veterans and 15,000 Gulf Era veterans) using a structured questionnaire. RESULTS: Gulf veterans reported significantly higher rates of unexplained multi-symptom illness, chronic fatigue syndrome-like illness, posttraumatic stress disorder, functional impairment, health care utilization, a majority of selected physical conditions and all mental disorders queried during the survey than did Gulf Era veteran controls. CONCLUSIONS: Fourteen years after deployment, 1991 Gulf War veterans continue to report a higher prevalence of

				many adverse health outcomes, compared with Gulf Era veterans.
Karlsson I		[Fatigue syndromes do not belong among depressive and anxiety disorders][Article in Swedish]Comment on: Lakartidningen. 2008 Nov 19-25;105(47):3393-4.	Lakartidningen. 2009 Jan 14-20;106(3):132; author reply 132.	.
Kato K, Sullivan PF, Evengård B, Pedersen NL.	School of Nursing and Rehabilitation, International University of Health and Welfare at Odawara, Kanagawa, Japan. kenji-kato@umin.ac.jp	A population-based twin study of functional somatic syndromes.	Psychol Med. 2009 Mar;39(3):497-505. Epub 2008 Jun 26.	BACKGROUND: The mechanisms underlying the co-occurrence of the functional somatic syndromes are largely unknown. No empirical study has explicitly examined how genetic and environmental factors influence the co-morbidity of these syndromes. We aimed to examine how the co-morbidity of functional somatic syndromes is influenced by genetic and environmental factors that are in common to the syndromes. METHOD: A total of 31318 twins in the Swedish Twin Registry aged 41-64 years underwent screening interviews via a computer-assisted telephone system from 1998 to 2002. Four functional somatic syndromes (chronic widespread pain, chronic fatigue, irritable bowel syndrome, and recurrent headache) and two psychiatric disorders (major depression and generalized anxiety disorder) were assessed using structured questions based on standard criteria for each illness in a blinded manner. RESULTS: Multivariate twin analyses revealed that a common pathway model with two latent traits that were shared by the six illnesses fit best to the women's data. One of the two latent traits loaded heavily on the psychiatric disorders, whereas the other trait loaded on all four of the functional somatic syndromes, particularly chronic widespread pain, but not on the psychiatric disorders. All illnesses except the psychiatric disorders were also affected by genetic influences that were specific to each. CONCLUSIONS: The co-occurrence of functional somatic syndromes in women can be best explained by affective and sensory components in common to all these syndromes, as well as by unique influences specific to each of them. The findings clearly suggest a complex view of the multifactorial pathogenesis of these illnesses.
Kato YH, Yamate M, Tsujikawa M, Nishigaki H, Tanaka Y, Yunoki M, Kuratsune H, Watanabe Y, Ikuta K.		No apparent difference in the prevalence of parvovirus B19 infection between chronic fatigue syndrome patients and healthy controls in Japan.	J Clin Virol. 2009 Mar;44(3):246-7. Epub 2009 Feb 5.	

Katz BZ, Shiraishi Y, Mears CJ, Binns HJ, Taylor R.	Department of Pediatrics, Division of Infectious Diseases, Northwestern University Feinberg School of Medicine and Children's Memorial Hospital, Chicago, Illinois 60614, USA. bkatz@northwestern.edu	Chronic fatigue syndrome after infectious mononucleosis in adolescents.	Pediatrics. 2009 Jul;124(1):189-93.	OBJECTIVE: The goal was to characterize prospectively the course and outcome of chronic fatigue syndrome in adolescents during a 2-year period after infectious mononucleosis. METHODS: A total of 301 adolescents (12-18 years of age) with infectious mononucleosis were identified and screened for nonrecovery 6 months after infectious mononucleosis by using a telephone screening interview. Nonrecovered adolescents underwent a medical evaluation, with follow-up screening 12 and 24 months after infectious mononucleosis. After blind review, final diagnoses of chronic fatigue syndrome at 6, 12, and 24 months were made by using established pediatric criteria. RESULTS: Six, 12, and 24 months after infectious mononucleosis, 13%, 7%, and 4% of adolescents, respectively, met the criteria for chronic fatigue syndrome. Most individuals recovered with time; only 2 adolescents with chronic fatigue syndrome at 24 months seemed to have recovered or had an explanation for chronic fatigue at 12 months but then were reclassified as having chronic fatigue syndrome at 24 months. All 13 adolescents with chronic fatigue syndrome 24 months after infectious mononucleosis were female and, on average, they reported greater fatigue severity at 12 months. Reported use of steroid therapy during the acute phase of infectious mononucleosis did not increase the risk of developing chronic fatigue syndrome. CONCLUSIONS: Infectious mononucleosis may be a risk factor for chronic fatigue syndrome in adolescents. Female gender and greater fatigue severity, but not reported steroid use during the acute illness, were associated with the development of chronic fatigue syndrome in adolescents. Additional research is needed to determine other predictors of persistent fatigue after infectious mononucleosis.
Kean S.		Virology. Chronic fatigue and prostate cancer: a retroviral connection?	Science. 2009 Oct 9;326(5950):215.	
Kelsall HL, McKenzie DP, Sim MR, Leder K, Forbes AB, Dwyer T.	Monash Centre for Occupational and Environmental Health, Department of Epidemiology and Preventive Medicine, Monash University, Alfred Hospital, Melbourne, Australia. helen.kelsall@med.monash.edu.au	Physical, psychological, and functional comorbidities of multisymptom illness in Australian male veterans of the 1991 Gulf War.	Am J Epidemiol. 2009 Oct 15;170(8):1048-56. Epub 2009 Sep 17.	Multisymptom illness is more prevalent in 1991 Gulf War veterans than in military comparison groups; less is known about comorbidities. The authors compared physical, psychological, and functional comorbidities in Australian male Gulf War I veterans with those in actively (non-Gulf) deployed and nondeployed military personnel by using a questionnaire and medical assessment in 2000-2002. Multisymptom illness was more common in male Gulf War veterans than in the comparison group (odds ratio (OR) = 1.80, 95% confidence interval (CI): 1.48, 2.19). Stratifying by deployment status in the comparison group made little difference in this association. Gulf War veterans with multisymptom illness had increased psychiatric disorders, including major depression (OR = 6.31, 95% CI: 4.19, 9.52) and posttraumatic stress disorder (OR = 9.77, 95% CI: 5.39, 18.59); increased unexplained chronic fatigue (OR = 13.32, 95% CI: 7.70, 23.05); and more reported functional impairment and poorer quality of life, but objective physical and laboratory outcomes were similar to those for veterans without multisymptom illness. Similar patterns were found in the comparison groups; differences across the 3 groups were statistically significant for only hospitalization, obstructive liver disease, and Epstein-Barr virus exposure. Multisymptom illness is more prevalent in Gulf War I veterans, but the pattern of comorbidities is similar for actively deployed and nondeployed military personnel.
Kerr JR, Gough J,	St George's	Antibody to	J Gen Virol.. [Epub	Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME) is a neuro-immune disease of

Richards SC, Main J, Enlander D, McCreary M, Komaroff AL, Chia JK.	University of London;	parvovirus B19 nonstructural protein is associated with chronic arthralgia in patients with Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME).	ahead of print]	uncertain pathogenesis. Human parvovirus B19 infection has been shown to occur just prior to development of the onset of CFS/ME in several cases, although B19 seroprevalence studies do not shown any significant differences between CFS/ME and controls. In this study, we analysed parvovirus B19 markers in CFS/ME patients (n=200), diagnosed according to Fukuda CDC criteria, and normal blood donors (n=200). Serum from each subject was tested for anti-B19 VP2 IgM and IgG (by Biotrin ELISA), anti-B19 NS1 IgM and IgG (by immunoflourescence), and B19 DNA by real-time PCR. CFS/ME patients and normal blood donors had a similar B19 seroprevalence (75% versus 78%, respectively). Eighty-three CFS patients (41.5%) as compared with fourteen (7%) of normal blood donors tested positive for anti-B19 NS1 IgG (chi(2)= 64.8; P<0.0001; Odds ratio = 9.42, CI 5.11 - 17.38). Of these 83 patients, 61 complained of chronic joint pain, while 22 did not. Parvovirus B19 DNA was detected in serum of 11 CFS patients and none of the controls by Taqman real-time PCR (chi(2) = 9.35, P<0.002. Positivity for anti-B19 NS1 IgG was associated with higher expression levels of the human CFS-associated genes NHLH1 and GABPA. As NS1 antibodies are thought to indicate chronic or severe courses of B19 infection, these findings suggest that although the seroprevalence of B19 in CFS patients is similar to controls, the immune control of the virus may not be efficient.
Kindlon T.		Response to: exercise performance and chronic pain in chronic fatigue syndrome: the role of pain catastrophizing.	Pain Med. 2009 Sep;10(6):1144; author reply 1145-6. Epub 2009 Sep 9. Comment on: Pain Med. 2008 Nov;9(8):1164-72.	
Kindlon T.		Change in grey matter volume cannot be assumed to be due to cognitive behavioural therapy.	Brain. 2009 Jul;132(Pt 7):e119; author reply e120. Epub 2009 Jan 29. Comment on: Brain. 2009 Jun;132(Pt 6):e110; author reply e111.	
Kindlon TP.		Chronic fatigue syndrome. Many questions remain about treatments for CFS.	BMJ. 2009 Apr 7;338:b1371. doi: 10.1136/bmj.b1371.	
Knoop H, van der Meer JW, Bleijenberg G.		Chronic fatigue in Gulf War veterans: should it be	Psychol Med. 2009 Aug;39(8):1401-2. Epub 2009 Apr 23.	

		treated as chronic fatigue syndrome?	Comment on: Psychol Med. 2008 Jul;38(7):953-61.	
Kuitwaard K, Bos-Eyssen ME, Blomkwist-Markens PH, van Doorn PA.	Department of Neurology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands. k.kuitwaard@erasmusmc.nl	Recurrences, vaccinations and long-term symptoms in GBS and CIDP.	J Peripher Nerv Syst. 2009 Dec;14(4):310-5.	We determined the frequency of recurrent Guillain-Barré syndrome (GBS), whether vaccinations led to recurrences of GBS or an increase of disability in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and we assessed the prevalence of pain, fatigue and the impact on quality of life after GBS and CIDP. Additionally, we assessed the presence of common auto-immune disorders. Four hundred and sixty-one members of the Dutch society of neuromuscular disorders received a questionnaire. Two hundred and forty-five GBS and seventy-six CIDP patients were included (response rate 70%). Nine patients had a confirmed recurrent GBS, and two patients had experienced both GBS and CIDP. Common auto-immune diseases were reported in 9% of GBS and 5% of CIDP patients. None of the 106 GBS patients who received a flu vaccination (range 1-37 times, total 775 vaccinations) reported a recurrence thereafter. Five out of twenty-four CIDP patients who received a flu vaccination (range 1-17 times) reported an increase in symptoms. Pain or severe fatigue was reported in about 70% of patients after the diagnosis of GBS (median 10 years) or after onset of CIDP (median 6 years), and quality of life was significantly reduced. Flu vaccinations seem relatively safe. GBS and CIDP patients often experience pain, fatigue and a reduced quality of life for many years after the diagnosis.
Kumar A, Garg R.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India. kumaruips@yahoo.com	Protective effects of antidepressants against chronic fatigue syndrome-induced behavioral changes and biochemical alterations.	Fundam Clin Pharmacol. 2009 Feb;23(1):89-95. Epub 2009 Jan 10.	Chronic fatigue syndrome (CFS) is characterized by profound fatigue, which substantially interferes with daily activities. The aim of this study was to explore the protective effects of antidepressants in an animal model of CFS in mice. Male albino mice were forced to swim individually for a period of 6-min session each for 7 days. Imipramine (10 and 20 mg/kg), desipramine (10 and 20 mg/kg) and citalopram (5 and 10 mg/kg) were administered 30 min before forced swimming test on each day. Various behavior tests (immobility time, locomotor activity, anxiety-like behavior by plus maze and mirror chamber) followed by biochemical parameters (lipid peroxidation, reduced glutathione, catalase and nitrite level) were assessed in chronic stressed mice. Chronic forced swimming for 7 days significantly caused increase in immobility period, impairment in locomotor activity, anxiety-like behavior, and oxidative stress (raised lipid peroxidation, nitrite activity and reduced glutathione and catalase activity) as compared with naïve mice ($P < 0.05$). Seven days of pretreatment with imipramine (10 and 20 mg/kg), desipramine (10 and 20 mg/kg), and citalopram (5 and 10 mg/kg) significantly reduced immobility time, improved locomotor activity and anti-anxiety effect (in both plus maze and mirror chamber test), and attenuated oxidative stress in chronic stressed mice as compared with control (chronic fatigues) ($P < 0.05$). These results suggested that these drugs have protective effect and could be used in the management of chronic fatigue like conditions.
Kuo YH, Tsai WJ, Loke SH, Wu TS, Chiou WF.	National Research Institute of Chinese Medicine, Taipei, Taiwan, ROC.	Astragalus membranaceus flavonoids (AMF) ameliorate chronic fatigue syndrome induced by food	J Ethnopharmacol. 2009 Feb 25;122(1):28-34. Epub 2008 Dec 6.	AIM OF THE STUDY: Alteration of immune function may be associated with chronic fatigue syndrome (CFS) and this study reveals the immunoregulatory effect of Astragalus membranaceus flavonoids (AMF). MATERIALS AND METHODS: CF rats were induced by food intake restriction plus forced swimming for 6 weeks. RESULTS: An atrophied spleen associated with a significantly decreased spleen/body weight ratio and a reduced spleen cells proliferation was found in CF rats when compared with home cage controls. AMF given orally at 20, 50 and 100 mg/kg body weight once a day

		intake restriction plus forced swimming.		consecutively for 6 weeks could recover the reduced cell proliferation. A switch to Th1-dominated immune regulation was observed in CF rats as the cultured splenocytes produced more interleukin-2 (IL-2) but less IL-4 when compared with controls. Supplementation with AMF could significantly counteract the aberrant cytokine production and rats received AMF exhibited higher endurance capacity to swim when compared with those without AMF administration. Checking the spectrum signals confirmed that the three major isoflavones contained in AMF were ononin, formononetin, and demethylhomopterocarpin. CONCLUSION: Alterations of immune function may be associated with CFS and the tonic effects of AMF against CF may be attributable to balance the abnormal cytokine level by isoflavones.
Kuwabara N, Itoh Y, Igarshi T, Fukunaga Y.	Department of Pediatrics, Nippon Medical School, Bunkyo City, Tokyo, Japan.	Autoantibodies to lens epithelium-derived growth factor/transcription co-activator P75 (LEDGF/P75) in children with chronic nonspecific complaints and with positive antinuclear antibodies.	Autoimmunity. 2009 Sep;42(6):492-6.	Autoimmune fatigue syndrome (AIFS) is characterized by chronic nonspecific complaints, consistently positive antinuclear antibodies (ANA), and lack of alternate medical explanations. A newly recognized antibody, named anti-Sa, was detected in approximately 40% of the patients by Western blot (WB) using HeLa extract. Some patients with AIFS later develop chronic fatigue syndrome (CFS), and most of them are positive for anti-Sa. On the other hand, Muro et al. reported anti-DFS70 in patients with CFS. Anti-Sa and anti-DFS70 were turned out to be same specificities by exchanging studies of blind sera. The target antigen of anti-DFS70 was identified as lens epithelium derived growth factor/transcription co-activator p75 (LEDGF/p75). The objectives of this study are to confirm whether the target antigen of anti-Sa is also LEDGF/p75, and to develop ELISA system by using recombinant protein. Recombinant protein of LEDGF/p75 was purchased from Protein One (Bethesda, MD, USA). We developed an ELISA system to detect anti-LEDGF/p75 by coating this recombinant protein. 226 sera of AIFS patients (including 36 CFS patients) were applied to this ELISA assay and Western immunoblot, and it was revealed that anti-Sa-positive sera defined by WB and sera positive for anti-LEDGF/p75 on ELISA were identical. Moreover, reactivities of anti-Sa on WB were inhibited by pre-incubating with recombinant LEDGF/p75, and eluted antibodies from the nitrocellulose membrane could react on the ELISA. These results confirm that the Sa antigen is LEDGF/p75. The ELISA assay using recombinant LEDGF/p75 could be a promising tool for measuring anti-Sa and consequently for diagnosing CFS.
Lam MH, Wing YK, Yu MW, Leung CM, Ma RC, Kong AP, So WY, Fong SY, Lam SP.	Department of Psychiatry, The Chinese University of Hong Kong, China.	Mental morbidities and chronic fatigue in severe acute respiratory syndrome survivors: long-term follow-up.	Arch Intern Med. 2009 Dec 14;169(22):2142-7.	BACKGROUND: Short-term follow-up studies of severe acute respiratory syndrome (SARS) survivors suggested that their physical conditions continuously improved in the first year but that their mental health did not. We investigated long-term psychiatric morbidities and chronic fatigue among SARS survivors. METHODS: All SARS survivors from the hospitals of a local region in Hong Kong were assessed by a constellation of psychometric questionnaires and a semistructured clinical interview for the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) to determine the presence of psychiatric disorders and chronic fatigue problems. RESULTS: Of 369 SARS survivors, 233 (63.1%) participated in the study (mean period of time after SARS, 41.3 months). Over 40% of the respondents had active psychiatric illnesses, 40.3% reported a chronic fatigue problem, and 27.1% met the modified 1994 Centers for Disease Control and Prevention criteria for chronic fatigue syndrome. Logistic regression analysis suggested that being a health care worker at the time of SARS infection (odds ratio [OR], 3.24; 95% confidence interval [CI], 1.12- 9.39; P = .03), being unemployed at follow-up (OR, 4.71; 95% CI, 1.50-14.78; P = .008), having a perception of social stigmatization (OR, 3.03; 95% CI, 1.20-7.60; P = .02), and having applied to the SARS survivors' fund (OR, 2.92; 95% CI, 1.18-7.22; P =

				.02) were associated with an increased risk of psychiatric morbidities at follow-up, whereas application to the SARS survivors' fund (OR, 2.64; 95% CI, 1.07-6.51; P = .04) was associated with increased risk of chronic fatigue problems. CONCLUSIONS: Psychiatric morbidities and chronic fatigue persisted and continued to be clinically significant among the survivors at the 4-year follow-up. Optimization of the treatment of mental health morbidities by a multidisciplinary approach with a view for long-term rehabilitation, especially targeting psychiatric and fatigue problems and functional and occupational rehabilitation, would be needed.
Land ST.	Loddon, Norwich, UK. derek.land@electramail.co.uk	20 years ago: The British Homoeopathic Journal, January 1989.	Homeopathy. 2009 Jan;98(1):65-7; discussion 71-2.	
Lansang MC, Farmer T, Kennedy L.	Department of Medicine, Division of Endocrinology, University of Florida, Gainesville, Florida 32610, USA. lansamc@medicine.ufl.edu	Diagnosing the unrecognized systemic absorption of intra-articular and epidural steroid injections.	Endocr Pract. 2009 May-Jun;15(3):225-8.	OBJECTIVE: To present a case series of patients who were misdiagnosed with endocrine disorders because of failure to recognize the systemic absorption of intra-articular and epidural steroids and to discuss the utility of performing a urine screen to detect synthetic glucocorticoids. METHODS: In this case series, we describe the clinical, laboratory, and imaging findings of 3 patients referred to our clinic, each with a presumed endocrine disorder. RESULTS: Patient 1 was a 54-year-old woman with weakness, loss of appetite, and a hormonal profile suggestive of hypopituitarism. Patient 2 was a 49-year-old woman with chronic fatigue and history of physical abuse, whose history and test results were compatible with growth hormone deficiency secondary to head trauma. Patient 3 was a 46-year-old woman who was diagnosed with endogenous Cushing syndrome despite normal 24-hour urinary cortisol excretion. In each case, we subsequently elicited a history of intra-articular or epidural glucocorticoid injections, and a urine screen documented the presence of synthetic glucocorticoids. Systemic absorption of the injected steroids was thus determined to be the cause of the symptoms and abnormal laboratory findings in each case. CONCLUSIONS: The potential for harm from intra-articular and epidural glucocorticoid administration is underrecognized by physicians, leading to expensive investigation, false diagnoses, and unnecessary treatment. A urine screen for synthetic glucocorticoids is a valuable adjunct towards appropriate diagnosis.
Lee E, Cho S, Kim K, Park T.	Interdisciplinary Program in Bioinformatics, Seoul National University, Seoul, Republic of Korea. eunjee01@gmail.com	An integrated approach to infer causal associations among gene expression, genotype variation, and disease.	Genomics. 2009 Oct;94(4):269-77. Epub 2009 Jun 18.	Gene expression data and genotype variation data are now capable of providing genome-wide patterns across many different clinical conditions. However, the separate analysis of these data has limitations in elucidating the complex network of gene interactions underlying complex traits, such as common human diseases. More information about the identity of key driver genes of common diseases comes from integrating these two heterogeneous types of data. We developed a two-step procedure to characterize complex diseases by integrating genotype variation data and gene expression data. The first step elucidates the causal relationship among genetic variation, gene expression level, and disease. Based on the causal relationship determined at the first step, the second step identifies significant gene expression traits whose effects on disease status or whose responses to disease status are modified by the specific genotype variation. For the selected significant genes, a pathway enrichment analysis can be performed to identify the genetic mechanism of a complex disease. The proposed two-step procedure was shown to be an effective method for

				integrating three different levels of data, i.e., genotype variation, gene expression and disease status. By applying the proposed procedure to a chronic fatigue syndrome (CFS) dataset, we identified a list of potential causal genes for CFS, and found an evidence for difference in genetic mechanisms of the etiology between CFS without 'a major depressive disorder with melancholic features' (CFS) and CFS with 'a major depressive disorder with melancholic features' (CFS-MDD/m). Especially, the SNPs within NR3C1 gene were shown to differently influence the susceptibility of developing CFS and CFS-MDD/m through integrative action with gene expression levels.
Lee P, Greenfield JR, Campbell LV.		Vitamin D insufficiency--a novel mechanism of statin-induced myalgia?	Clin Endocrinol (Oxf). 2009 Jul;71(1):154-5. Epub 2008 Oct 16.	
Lemle MD.		Hypothesis: chronic fatigue syndrome is caused by dysregulation of hydrogen sulfide metabolism.	Med Hypotheses. 2009 Jan;72(1):108-9. Epub 2008 Sep 16.	
Li H, Meng S, Levine SM, Stratton CW, Tang YW.	Department of Pathology, Vanderbilt University School of Medicine, Nashville, TN 37232, United States.	Sensitive, qualitative detection of human herpesvirus-6 and simultaneous differentiation of variants A and B.	J Clin Virol. 2009 Sep;46(1):20-3. Epub 2009 Jun 21.	BACKGROUND: The current limitations of laboratory testing for the detection of human herpesvirus virus 6 (HHV-6) in clinical specimens with low HHV-6 viral loads make this area a priority for further research and development. OBJECTIVES: To develop and validate a sensitive qualitative assay for simultaneous HHV-6 detection and variant differentiation. METHODS: We developed a diagnostic procedure, which combines a magnetic bead-based nucleic acid extraction, PCR amplification, and colorimetric microtiter plate identification (MAG-PCR-EIA), for the sensitive detection of HHV-6 and the simultaneous differentiation of HHV-6A and HHV-6B. RESULTS: Analytic sensitivities of the MAG-PCR-EIA assay were 10 copies per reaction for both HHV-6A and HHV-6B variants, which is equivalent to 20 copies/ml when 1ml of clinical specimen was processed. A proficiency panel containing 11 blinded specimens covering HHV-6A viral loads from 0 to 100,000 copies was tested, and the MAG-PCR-EIA was able to detect the lowest concentration at one copy in 200microl. A panel of 27 urine specimens, which were collected from patients with and without chronic fatigue syndrome, was tested by the MAG-PCR-EIA. HHV-6 was detected in two (HHV-6A) patients who have chromosomally integrated HHV-6A and in one (HHV-6B) patient who was a healthy control and diagnosed as cervical cancer later on. The HHV-6 results did not correlate with results previously determined by HHV-6 antigenemia in urine. CONCLUSION: With large specimen volumes processed and an additional signal amplification incorporated, the MAG-PCR-EIA provides a sensitive and qualitative system for HHV-6 detection and simultaneous variant differentiation. Clinical relevance of the assay awaits further investigation.
Li ZC, Zhao Y, Dou ZH, Yu L, Wu H,	Department of Infectious	[Clinical features of 66 children with	Zhongguo Dang Dai Er Ke Za Zhi.	OBJECTIVE: To study the clinical features of pediatric acquired immunodeficiency syndrome(AIDS). METHODS: The epidemiological, clinical and laboratory data of 66 children with AIDS were

Zhang FJ.	Diseases, Beijing Youan Hospital, Capital Medical University, Beijing 100069, China.	acquired immunodeficiency syndrome][Article in Chinese]	2009 Feb;11(2):93-5.	retrospectively studied. RESULTS: Of the 66 patients, 46 (69.7%) were male and 20 (30.3%) were female, with a mean age of 8.7 years (ranged 2-16 years). The mean age at diagnosis was 7.7 years (ranged 2-15 years). Vertical transmission as the route of infection was documented in 48 cases (72.7%). Fourteen children (21.2%) were infected through blood or blood products. The route of infection could not be identified in 4 cases (6.1%). Body weight loss was noted in 43 cases (65.2%), anemia in 42 cases (63.7%), fever in 40 cases (60.6%), fatigue in 38 cases (57.6%), rash in 31 cases (47.0%), chronic cough in 28 cases (12.1%), chronic diarrhea in 24 cases (36.4%), CNS involvement in 16 cases (24.2%), oral thrush in 13 cases (19.7%), and hepatosplenomegaly in 12 cases (18.2%). Body height of 30 cases (45.4%) and body weight of 26 cases (39.4%) ranked the lower level. The immune system was severely suppressed in 59 cases (89.4%) and moderately suppressed in 7 cases (10.6%). CONCLUSIONS: Vertical transmission remained the most common route of pediatric HIV infection. There were various clinical manifestations in children with AIDS. The immune systems of the majority of children with this disorder were severely suppressed.
Liang CZ, Li HJ, Wang ZP, Xing JP, Hu WL, Zhang TF, Ge WW, Hao ZY, Zhang XS, Zhou J, Li Y, Zhou ZX, Tang ZG, Tai S.	Department of Urology, The First Affiliated Hospital of Anhui Medical University, Hefei, China.	The prevalence of prostatitis-like symptoms in China.	J Urol. 2009 Aug;182(2):558-63. Epub 2009 Jun 13. Comment in: J Urol. 2009 Aug;182(2):427-8.	PURPOSE: We studied the prevalence of prostatitis-like symptoms and identified their associated risk factors in a population based Chinese sample. MATERIALS AND METHODS: A volunteer group of 15,000 eligible men residing in Beijing, Anhui, Xi'an, Guangzhou and Gansu cities or provinces were invited randomly to take part in the survey to complete a questionnaire that elicited information regarding sociodemographics, Eysenck personality questionnaire, current stress and health ratings, lifestyle, medical history, expressed prostatic secretion evaluation, score of the National Institutes of Health Chronic Prostatitis Symptom Index and International Index of Erectile Function-5. RESULTS: Information on 12,743 (84.95%) men was collected. Of these men 1,071 (8.4%) reported prostatitis-like symptoms (mean National Institutes of Health Chronic Prostatitis Symptom Index pain score 7.55 +/- 3.22). The percent of chronic prostatitis was 4.5% (571) among the symptoms group according to past urological history and expressed prostatic secretion evaluation. Subjects with prostatitis-like symptoms (mean age 34.56 +/- 13.48 years) had higher mean pain and urinary symptoms scores (7.53 +/- 3.22 and 2.84 +/- 2.72, respectively) compared with subjects without prostatitis-like symptoms (1.18 +/- 2.32 and 0.72 +/- 1.66 for pain and urinary symptoms scores, respectively, mean age 30.7 +/- 10.17) (pain and symptoms scores, p <0.05). The quality of life score was 6.03 +/- 2.88 and 3.83 +/- 2.55 in groups with symptoms or nonsymptoms, respectively (p <0.05). CONCLUSIONS: Prostatitis-like symptoms are a multifactorial problem affecting men of all ages (15 to 60 years) and demographics, and the prevalence is high in China. The syndrome is closely related to alcohol consumption, cigarette smoking, frequent intercourse, as well as fatigue, pressure and too little sleep. These findings suggest that risk factors for this condition are largely modifiable and highlight potential targets for future prevention.
Libman E, Creti L, Baltzan M, Rizzo D, Fichten CS, Bailes S.	Department of Psychiatry, SMBD-Jewish General Hospital, Concordia University,	Sleep apnea and psychological functioning in chronic fatigue syndrome.	J Health Psychol. 2009 Nov;14(8):1251-67.	Objectives were to explore: (1) whether sleep apnea/hypopnea syndrome (SAHS) should be considered a chronic fatigue syndrome (CFS) comorbidity, rather than a diagnostic exclusion criterion; and (2) to compare sleep/wake/ psychopathology in individuals with CFS, controls and another illness. Participants (CFS, SAHS, controls) completed questionnaires and were evaluated for SAHS; 68 percent were subsequently diagnosed with SAHS. CFS participants with and without SAHS did not differ. Both clinical groups were less well adjusted than controls. We conclude that SAHS should not be an

	Montreal, Quebec, Canada. eva.libman@mcgill.ca			exclusion criterion for CFS and that psychological problems in CFS seem a consequence of coping with illness.
Light AR, White AT, Hughen RW, Light KC.	Department of Anesthesiology, University of Utah, Salt Lake City, Utah 84132-2304, USA. alan.light@hsc.utah.edu	Moderate exercise increases expression for sensory, adrenergic, and immune genes in chronic fatigue syndrome patients but not in normal subjects.	J Pain. 2009 Oct;10(10):1099-112. Epub 2009 Jul 31.	Chronic fatigue syndrome (CFS) is characterized by debilitating fatigue, often accompanied by widespread muscle pain that meets criteria for fibromyalgia syndrome (FMS). Symptoms become markedly worse after exercise. Previous studies implicated dysregulation of the sympathetic nervous system (SNS), and immune system (IS) in CFS and FMS. We recently demonstrated that acid sensing ion channel (probably ASIC3), purinergic type 2X receptors (probably P2X4 and P2X5) and the transient receptor potential vanilloid type 1 (TRPV1) are molecular receptors in mouse sensory neurons detecting metabolites that cause acute muscle pain and possibly muscle fatigue. These molecular receptors are found on human leukocytes along with SNS and IS genes. Real-time, quantitative PCR showed that 19 CFS patients had lower expression of beta-2 adrenergic receptors but otherwise did not differ from 16 control subjects before exercise. After a sustained moderate exercise test, CFS patients showed greater increases than control subjects in gene expression for metabolite detecting receptors ASIC3, P2X4, and P2X5, for SNS receptors alpha-2A, beta-1, beta-2, and COMT and IS genes for IL10 and TLR4 lasting from 0.5 to 48 hours ($P < .05$). These increases were also seen in the CFS subgroup with comorbid FMS and were highly correlated with symptoms of physical fatigue, mental fatigue, and pain. These new findings suggest dysregulation of metabolite detecting receptors as well as SNS and IS in CFS and CFS-FMS. PERSPECTIVE: Muscle fatigue and pain are major symptoms of CFS. After moderate exercise, CFS and CFS-FMS patients show enhanced gene expression for receptors detecting muscle metabolites and for SNS and IS, which correlate with these symptoms. These findings suggest possible new causes, points for intervention, and objective biomarkers for these disorders.
Lim JY, Kim KE, Choe G.	Department of Rehabilitation, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea.	Myotonic dystrophy mimicking postpolio syndrome in a polio survivor.	Am J Phys Med Rehabil. 2009 Feb;88(2):161-4.	We describe a 38-yr-old polio survivor with newly developed weakness from myotonic dystrophy. He suffered muscle atrophy and weakness in his legs as a result of poliomyelitis at the age of 3 yrs. After a stable interval of about 30 yrs, he felt new weakness and fatigue in his legs. Electromyography revealed generalized myotonic discharges, early recruitment, and findings of chronic denervation in his left leg. Genetic testing was consistent with myotonic dystrophy type 1. A biopsy from the right gastrocnemius revealed findings of both myotonic dystrophy and chronic denervation. This case report shows the importance of considering other uncommon conditions in the differential diagnoses of postpolio syndrome.
Lin E, Hsu SY.	Vita Genomics, Inc., Jung-Shing Road, Wugu Shiang, Taipei, Taiwan. eugene.lin@vitagenomics.com	A Bayesian approach to gene-gene and gene-environment interactions in chronic fatigue syndrome.	Pharmacogenomics. 2009 Jan;10(1):35-42.	INTRODUCTION: In the study of genomics, it is essential to address gene-gene and gene-environment interactions for describing the complex traits that involves disease-related mechanisms. In this work, our goal is to detect gene-gene and gene-environment interactions resulting from the analysis of chronic fatigue syndrome patients' genetic and demographic factors including SNPs, age, gender and BMI. MATERIALS & METHODS: We employed the dataset that was original to the previous study by the Centers for Disease Control and Prevention Chronic Fatigue Syndrome Research Group. To investigate gene-gene and gene-environment interactions, we implemented a Bayesian based method for identifying significant interactions between factors. Here, we employed a two-stage Bayesian

				variable selection methodology based on Markov Chain Monte Carlo approaches. RESULTS: By applying our Bayesian based approach, NR3C1 was found in the significant two-locus gene-gene effect model, as well as in the significant two-factor gene-environment effect model. Furthermore, a significant gene-environment interaction was identified between NR3C1 and gender. These results support the hypothesis that NR3C1 and gender may play a role in biological mechanisms associated with chronic fatigue syndrome. CONCLUSION: We demonstrated that our Bayesian based approach is a promising method to assess the gene-gene and gene-environment interactions in chronic fatigue syndrome patients by using genetic factors, such as SNPs, and demographic factors such as age, gender and BMI.
Lin JM, Brimmer DJ, Boneva RS, Jones JF, Reeves WC.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. dwe3@cdc.gov	Barriers to healthcare utilization in fatiguing illness: a population-based study in Georgia.	BMC Health Serv Res. 2009 Jan 20;9:13.	BACKGROUND: The purpose of this study was to determine the prevalence of barriers to healthcare utilization in persons with fatiguing illness and describe its association with socio-demographics, the number of health conditions, and frequency of healthcare utilization. Furthermore, we sought to identify what types of barriers interfered with healthcare utilization and why they occurred. METHODS: In a cross-sectional population-based survey, 780 subjects, 112 of them with chronic fatigue syndrome (CFS), completed a healthcare utilization questionnaire. Text analysis was used to create the emerging themes from verbatim responses regarding barriers to healthcare utilization. Multiple logistic regression was performed to examine the association between barriers to healthcare utilization and other factors. RESULTS: Forty percent of subjects reported at least one barrier to healthcare utilization. Of 112 subjects with CFS, 55% reported at least one barrier to healthcare utilization. Fatiguing status, reported duration of fatigue, insurance, and BMI were significant risk factors for barriers to healthcare utilization. After adjusting for socio-demographics, medication use, the number of health problems, and frequency of healthcare utilization, fatiguing status remained significantly associated with barriers to healthcare utilization. Subjects with CFS were nearly 4 times more likely to forego needed healthcare during the preceding year than non-fatigued subjects while those with insufficient fatigue (ISF) were nearly 3 times more likely.Three domains emerged from text analysis on barriers to healthcare utilization: 1) accessibility; 2) knowledge-attitudes-beliefs (KABs); and, 3) healthcare system. CFS and reported duration of fatigue were significantly associated with each of these domains. Persons with CFS reported high levels of healthcare utilization barriers for each domain: accessibility (34%), healthcare system (25%), and KABs (19%). In further examination of barrier domains to healthcare utilization, compared to non-fatigued persons adjusted ORs for CFS having "accessibility", "KAB" and "Healthcare System" barrier domains decreased by 40%, 30%, and 19%, respectively. CONCLUSION: Barriers to healthcare utilization pose a significant problem in persons with fatiguing illnesses. Study results suggested two-fold implications: a symptom-targeted model focusing on symptoms associated with fatigue; and an interactive model requiring efforts from patients and providers to improve interactions between them by reducing barriers in accessibility, KABs, and healthcare system.
Lin JM, Brimmer DJ, Maloney EM, Nyarko E, Belue R, Reeves WC.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-	Further validation of the Multidimensional Fatigue Inventory	Popul Health Metr. 2009 Dec 15;7:18.	ABSTRACT: BACKGROUND: The Multidimensional Fatigue Inventory (MFI-20) was developed in 1995. Since then, it has been widely used in cancer research and cancer-related illnesses but has never been validated in fatiguing illnesses or in a large US population-selected sample. In this study, we sought to examine the reliability and validity of the MFI-20 in the population of the state of Georgia, USA.

	borne and Enteric Diseases, Centers for Disease Control and Prevention, Mail Stop A-15, 1600 Clifton Rd, NE, Atlanta, GA, USA. dwe3@cdc.gov.	in a US adult population sample.		Further, we assessed whether the MFI-20 could serve as a complementary diagnostic tool in chronically fatigued and unwell populations. METHODS: The data derive from a cross-sectional population-based study investigating the prevalence of chronic fatigue syndrome (CFS) in Georgia. The study sample was comprised of three diagnostic groups: CFS-like (292), chronically unwell (269), and well (222). Participants completed the MFI-20 along with several other measures of psychosocial functioning, including the Medical Outcomes Survey Short Form-36 (SF-36), the Zung Self-Rating Depression Scale (SDS), and the Spielberger State-Trait Anxiety Inventory (STAI). We assessed the five MFI-20 subscales using several criteria: inter-item correlations, corrected item-total correlations, internal consistency reliability (Cronbach's alpha coefficients), construct validity, discriminant (known-group) validity, floor/ceiling effects, and convergent validity through correlations with the SF-36, SDS, and STAI instruments. RESULTS: Averaged inter-item correlations ranged from 0.38 to 0.61, indicating no item redundancy. Corrected item-total correlations for all MFI-20 subscales were greater than 0.30, and Cronbach's alpha coefficients achieved an acceptable level of 0.70. No significant floor/ceiling effect was observed. Factor analysis demonstrated factorial complexity. The MFI-20 also distinguished clearly between three diagnostic groups on all subscales. Furthermore, correlations with depression (SDS), anxiety (STAI), and functional impairment (SF-36) demonstrated strong convergent validity. CONCLUSIONS: This study provides support for the MFI-20 as a valuable tool when used in chronically unwell and well populations. It also suggests that the MFI-20 could serve as a complementary diagnostic tool in fatiguing illnesses, such as CFS.
Lombardi VC, Ruscetti FW, Das Gupta J, Pfost MA, Hagen KS, Peterson DL, Ruscetti SK, Bagni RK, Petrow-Sadowski C, Gold B, Dean M, Silverman RH, Mikovits JA.	Whittemore Peterson Institute, Reno, NV 89557, USA.	Detection of an infectious retrovirus, XMRV, in blood cells of patients with chronic fatigue syndrome.	Science. 2009 Oct 23;326(5952):585-9. Epub 2009 Oct 8. Comment in: Science. 2009 Oct 23;326(5952):530-1.	Chronic fatigue syndrome (CFS) is a debilitating disease of unknown etiology that is estimated to affect 17 million people worldwide. Studying peripheral blood mononuclear cells (PBMCs) from CFS patients, we identified DNA from a human gammaretrovirus, xenotropic murine leukemia virus-related virus (XMRV), in 68 of 101 patients (67%) as compared to 8 of 218 (3.7%) healthy controls. Cell culture experiments revealed that patient-derived XMRV is infectious and that both cell-associated and cell-free transmission of the virus are possible. Secondary viral infections were established in uninfected primary lymphocytes and indicator cell lines after their exposure to activated PBMCs, B cells, T cells, or plasma derived from CFS patients. These findings raise the possibility that XMRV may be a contributing factor in the pathogenesis of CFS.
Lorusso L, Mikhaylova SV, Capelli E, Ferrari D, Ngonga GK, Ricevuti G.	Department of Neurology, Mellino Mellini Hospital, Chiari, Brescia, Italy.	Immunological aspects of chronic fatigue syndrome.	Autoimmun Rev. 2009 Feb;8(4):287-91. Epub 2008 Sep 16.	Chronic fatigue syndrome (CFS) is a specific clinical condition that characterises unexplained disabling fatigue and a combination of non-specific accompanying symptoms for at least 6 months, in the absence of a medical diagnosis that would otherwise explain the clinical presentation. Other common symptoms include headaches, myalgia, arthralgia, and post-exertional malaise; cognitive difficulties, with impaired memory and concentration; unrefreshing sleep; and mood changes. Similar disorders have been described for at least two centuries and have been differently named neurasthenia, post-viral fatigue, myalgic encephalomyelitis and chronic mononucleosis. Recent longitudinal studies suggest that some people affected by chronic fatigue syndrome improve with time but that most remain functionally impaired for several years. The estimated worldwide prevalence of CFS is 0.4-1% and it affects over 800,000 people in the United States and approximately 240,000 patients in the UK.

				No physical examination signs are specific to CFS and no diagnostic tests identify this syndrome. The pathophysiological mechanism of CFS is unclear. The main hypotheses include altered central nervous system functioning resulting from an abnormal immune response against a common antigen; a neuroendocrine disturbance; cognitive impairment caused by response to infection or other stimuli in sentient people. The current concept is that CFS pathogenesis is a multifactorial condition. Various studies have sought evidence for a disturbance in immunity in people with CFS. An alteration in cytokine profile, a decreased function of natural killer (NK) cells, a presence of autoantibodies and a reduced responses of T cells to mitogens and other specific antigens have been reported. The observed high level of pro-inflammatory cytokines may explain some of the manifestations such as fatigue and flu-like symptoms and influence NK activity. Abnormal activation of the T lymphocyte subsets and a decrease in antibody-dependent cell-mediated cytotoxicity have been described. An increased number of CD8+ cytotoxic T lymphocytes and CD38 and HLA-DR activation markers have been reported, and a decrease in CD11b expression associated with an increased expression of CD28+ T subsets has been observed. This review discusses the immunological aspects of CFS and offers an immunological hypothesis for the disease processes.
Lundin A.	FoUU-sektionen, Psykiatri Nordöst, Danderyds sjukhus, Stockholm. anders.w.lundin@sll.se	[Chronic fatigue syndrome--a useful diagnosis?] [Article in Swedish]	Lakartidningen. 2009 Sep 2-8;106(36):2194, 2196.	
Lyle N, Gomes A, Sur T, Munshi S, Paul S, Chatterjee S, Bhattacharyya D.	Department of Pharmacology, Institute of Post Graduate Medical Education & Research, 244-B, A. J. C. Bose Road, Kolkata 700020, India. lyle.nazmun@gmail.com	The role of antioxidant properties of Nardostachys jatamansi in alleviation of the symptoms of the chronic fatigue syndrome.	Behav Brain Res. 2009 Sep 14;202(2):285-90. Epub 2009 Apr 16.	An experimental model of chronic fatigue syndrome (CFS) is utilized for evaluation of antidepressant, anti-stress effects, wherein the rat is forced to swim in water for 15 min/day on 21 consecutive days. Rats were divided into stressed control, stressed plus standard drug (Panax ginseng) and stressed plus 200 and 500 mg/kg of test drug, i.e., Nardostachys jatamansi extract (NJE) given orally. The immobility during each 5 min periods of 0-5, 5-10 and 10-15 min of stress were noted. Similarly the climbing (struggling) behaviour was noted in the above four groups of rats in intervals of 5 min. The locomotor activity and also the anxiety state in animals were evaluated in an elevated plus maze after CFS in all the four groups. There was a significant increase in despair behaviour and anxiety in stressed control animals on successive days of CFS. Locomotor activity gradually decreased in stressed control group. Treatment with NJE (200 and 500 mg/kg) significantly reversed both paradigms. Biochemical analysis showed that CFS significantly increased lipid peroxidation, nitrite and superoxide dismutase levels and decreased catalase level in rat brain. Administration of NJE (200 and 500 mg/kg) tended to normalize both augmented lipid peroxidation, nitrite, superoxide dismutase activities and catalase level significantly. NJE per se has an antioxidant effect. The results indicate that CFS may lead to oxidative stress, which is mitigated by NJE and so its antioxidant property may be responsible for anti-stress effect of NJE.
Maes M, Mihaylova I, Kubera M,	Maes Clinics, Antwerp, Belgium. crc.mh@telenet.be	Increased 8-hydroxy-deoxyguanosine, a	Neuro Endocrinol Lett. 2009 Dec 30;30(6). [Epub	There is now evidence that major depression and myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS) are accompanied by partially overlapping pathophysiological mechanisms, i.e. activation of various inflammatory and oxidative & nitrosative (IO&NS) pathways. The aim of the

Uytterhoeven M, Vrydags N, Bosmans E.	.	marker of oxidative damage to DNA, in major depression and myalgic encephalomyelitis / chronic fatigue syndrome.	ahead of print]	present study was to examine the urinary excretion of 8-hydroxy-deoxyguanosine (8-OhdG), a marker of oxidative damage to DNA, in depression; ME/CFS; and depression and ME/CFS. Toward this end, morning urine was sampled for the assays of 8-OHdG and creatinine, in 44 patients with ME/CFS; 25 with major depression; 23 with depression and ME/CFS; and 17 normal controls. Severity of fatigue and somatic symptoms was measured by means of the Fibromyalgia and CFS Rating (FF) scale. We found that 49.0% of the variance in the urinary excretion of 8-OHdG was predicted by the regression on creatinine. Consequently, the urinary 8-OHdG excretion should be expressed as the residualized 8-OHdG values after partialling out the effects of creatinine and not by computing the 8-OHdG / creatinine ratio. We found that the residualized urinary excretion of 8-OHdG (adjusted for creatinine) was significantly higher in patients with depression and ME/CFS than in normal controls and all other patients. In the patient group, there were significant correlations between the urinary 8-OHdG and the total score on the FF scale and sadness and flu-like malaise. The findings show increased oxidatively generated DNA damage in patients with major depression and ME/CFS and, therefore, further extent the role played by IO&NS pathways in the pathophysiology of both disorders. Since oxidatively damage to DNA is a risk factor for atherosclerosis and neurodegeneration, our results also explain previous findings on increased cardiovascular morbidity in depression and ME/CFS, and neurodegenerative processes in depression.
Maes M, Twisk FN.	Maes Clinics, Antwerp, Belgium. crc.mh@telenet.be .	Why myalgic encephalomyelitis/ chronic fatigue syndrome (ME/CFS) may kill you: disorders in the inflammatory and oxidative and nitrosative stress (IO&NS) pathways may explain cardiovascular disorders in ME/CFS.	Neuro Endocrinol Lett. 2009 Dec 30;30(6). [Epub ahead of print]	There is evidence that disorders in inflammatory and oxidative and nitrosative (IO&NS) pathways and a lowered antioxidant status are important pathophysiological mechanisms underpinning myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS). Important precipitating and perpetuating factors for ME/CFS are (amongst others) bacterial and viral infections; bacterial translocation due to an increased gut permeability; and psychological stress. Recently, Jason et al (2006) reported that the mean age of patients with myalgic encephalomyelitis/chronic fatigue syndrome dying from heart failure, i.e. 58.7 years, is significantly lower than the age of those dying from heart failure in the general US population, i.e. 83.1 years. These findings implicate that ME/CFS is a risk factor to cardio-vascular disorder. This review demonstrates that disorders in various IO&NS pathways provide explanations for the earlier mortality due to cardiovascular disorders in ME/CFS. These pathways are: a) chronic low grade inflammation with extended production of nuclear factor kappa B and COX-2 and increased levels of tumour necrosis factor alpha; b) increased O&NS with increased peroxide levels, and phospholipid oxidation including oxidative damage to phosphatidylinositol; c) decreased levels of specific antioxidants, i.e. coenzyme Q10, zinc and dehydroepiandrosterone-sulphate; d) bacterial translocation as a result of leaky gut; e) decreased omega-3 polyunsatutared fatty acids (PUFAs), and increased omega-6 PUFA and saturated fatty acid levels; and f) the presence of viral and bacterial infections and psychological stressors. The mechanisms whereby each of these factors may contribute towards cardio-vascular disorder in ME/CFS are discussed. ME/CFS is a multisystemic metabolic-inflammatory disorder. The aberrations in IO&NS pathways may increase the risk for cardiovascular disorders.
Maes M, Twisk FN.	Maes Clinics, Antwerp, Belgium. crc.mh@telenet.be	Chronic fatigue syndrome: la bête noire of the	Neuro Endocrinol Lett. 2009;30(3):300-11.	The World Health Organization acknowledges Myalgic Encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS) to be a medical illness. ME/CFS is characterized by disorders in the inflammatory and oxidative and nitrosative stress (IO&NS) pathways. In 2002, the Belgian government started with the

		Belgian health care system.		development of CFS "Reference Centers", which implement a "psychosocial" model. The medical practices of these CFS Centers are defined by the Superior Health Council, e.g. treatment should be based upon Cognitive Behavioral Therapy (CBT) and Graded Exercise Therapy (GET); and biological assessments and treatments of ME/CFS should not be employed. Recently, the Belgian government has evaluated the outcome of the treatments at the CFS Centers. They concluded that a "rehabilitation therapy" with CBT/GET yielded no significant efficacy in the treatment of ME/CFS and that CBT/GET cannot be considered to be curative therapies. In case reports, we have shown that patients who were "treated" at those CFS centers with CBT/GET in fact suffered from IO&NS disorders, including intracellular inflammation, an increased translocation of gram-negative enterobacteria (leaky gut), autoimmune reactions and damage by O&NS. Considering the fact that these findings are exemplary for ME/CFS patients and that GET may even be harmful, it means that many patients are maltreated by the Belgian CFS Centers. Notwithstanding the above, the government and the CFS Centers not only continue this unethical and immoral policy, but also reinforce their use of CBT/GET in patients with ME/CFS treated at those Centers.
Maes M.	Clinical Research Centre of Mental Health (CRC-MH), Antwerp, Belgium. crc.mh@telenet.be	Inflammatory and oxidative and nitrosative stress pathways underpinning chronic fatigue, somatization and psychosomatic symptoms.	Curr Opin Psychiatry. 2009 Jan;22(1):75-83.	PURPOSE OF REVIEW: The aim of this paper is to review recent findings on inflammatory and oxidative and nitrosative stress (IO&NS) pathways in chronic fatigue and somatization disorder. RECENT FINDINGS: Activation of IO&NS pathways is the key phenomenon underpinning chronic fatigue syndrome (CFS): intracellular inflammation, with an increased production of nuclear factor kappa beta (NFkappabeta), cyclo-oxygenase-2 (COX-2) and inducible NO synthase (iNOS); and damage caused by O&NS to membrane fatty acids and functional proteins. These IO&NS pathways are induced by a number of trigger factors, for example psychological stress, strenuous exercise, viral infections and an increased translocation of LPS from gram-bacteria (leaky gut). The 'psychosomatic' symptoms experienced by CFS patients are caused by intracellular inflammation (aches and pain, muscular tension, fatigue, irritability, sadness, and the subjective feeling of infection); damage caused by O&NS (aches and pain, muscular tension and fatigue); and gut-derived inflammation (complaints of irritable bowel). Inflammatory pathways (monocytic activation) are also detected in somatizing disorder. SUMMARY: 'Functional' symptoms, as occurring in CFS and somatization, have a genuine organic cause, that is activation of peripheral and central IO&NS pathways and gut-derived inflammation. The development of new drugs, aimed at treating those disorders, should target these IO&NS pathways.
Maes M.	Maes Clinics, Antwerp, Belgium. crc.mh@telenet.be .	"Functional" or "psychosomatic" symptoms, e.g. a flu-like malaise, aches and pain and fatigue, are major features of major and in particular of melancholic depression: time to amend the	Neuro Endocrinol Lett. 2009 Nov 29;30(5). [Epub ahead of print]	FULL TITLE: "Functional" or "psychosomatic" symptoms, e.g. a flu-like malaise, aches and pain and fatigue, are major features of major and in particular of melancholic depression: time to amend the diagnostic criteria for major depression and the rating scales that measure severity of illness. BACKGROUND: Major depression is characterized by multifarious symptoms and symptoms clusters, such as the melancholic and anxiety symptom clusters. There is a strong comorbidity and a biological similarity between major depression and myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS). AIM: The aim of the present study was to examine "psychosomatic" symptoms reminiscent of ME/CFS in major depression. Toward this end, we examined the 12-item Fibromyalgia and Chronic Fatigue Syndrome Rating (FF) Scale and the Hamilton Depression Rating Scale (HDRS) in 103 major depressed patients by means of multivariate pattern recognition methods. RESULTS: Our findings support the existence of two factors, i.e. a fatigue and somatic (F&S) factor, i.e aches and pain,

		diagnostic criteria for major depression and.		muscular tension, fatigue, concentration difficulties, failing memory, irritability, irritable bowel, headache, and a subjective experience of infection; and a depression factor, i.e. sadness, irritability, sleep disorders, autonomic symptoms, and a subjective experience of infection. Cluster analysis performed on the 12 FF items found two different clusters, which were separated by highly significant differences in the F&S items, the most significant being a subjective experience of infection, aches and pain, muscular tension, fatigue, concentration difficulties and failing memory. Multivariate analyses showed that the differences between both clusters were quantitatively, and not qualitatively, and reflected the severity of the F&S dimension. There was a strong association between the F&S symptoms and melancholia and chronic depression. Treatment resistant depression was characterized by higher scores on the depression factor score. There was a strong correlation between the HDRS score and the FF items, fatigue, a subjective experience of infection, and sadness. CONCLUSIONS: Our findings show that F&S symptoms are a major feature of depression and largely predict severity of illness, and chronic and melancholic depression. It is concluded that the diagnostic criteria of depression and melancholia and rating scales to measure severity of illness should be modified to include the F&S symptom profile.
Magnus P, Brubakk O, Nyland H, Wold BH, Gjessing HK, Brandt I, Eidem T, Nøkleby H, Stene-Larsen G.	Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway. per.magnus@fhi.no	Vaccination as teenagers against meningococcal disease and the risk of the chronic fatigue syndrome.	Vaccine. 2009 Jan 1;27(1):23-7. Epub 2008 Nov 5.	The etiology of chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) is unknown. In Norway, a vaccine against Neisseria meningitides group B was administered to teenagers in 1988--1989 in a protection trial. In order to estimate the relative risk of CFS/ME according to vaccine history, we conducted a case-control study in 2007, with 201 cases diagnosed at one of two hospitals and 389 controls. The adjusted odds ratio for CFS/ME was 1.06 (95% CI: 0.67-1.66) for subjects who received the active vaccine contrasted to subjects who did not. Using this design, no statistically significant association between vaccination against meningococcal disease in teenagers and occurrence of CFS/ME could be observed.
Maloney EM, Boneva R, Nater UM, Reeves WC.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne and Enteric Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MS A-15, Atlanta, GA 30333, USA. evm3@cdc.gov	Chronic fatigue syndrome and high allostatic load: results from a population-based case-control study in Georgia.	Psychosom Med. 2009 Jun;71(5):549-56. Epub 2009 May 4.	OBJECTIVE: To confirm the association of chronic fatigue syndrome (CFS) with high allostatic load (AL) level, examine the association of subsyndromal CFS with AL level, and investigate the effect of depression on these relationships and the association of AL with functional impairment, fatigue, symptom severity, fatigue duration, and type of CFS onset. AL represents the cumulative physiologic effect of demands to adapt to stress. METHODS: Population-based case-control study of 83 persons with CFS, 202 persons with insufficient symptoms or fatigue for CFS (ISF), and 109 well controls living in Georgia. Unconditional logistic regression was used to generate odds ratios (ORs) as measures of the association of AL with CFS. RESULTS: Relative to well controls, each 1-point increase in allostatic load index (ALI) was associated with a 26% increase in likelihood of having CFS (OR(adjusted) = 1.26, 95% Confidence Interval (CI) = 1.00, 1.59). This association remained in the presence and absence of depression (OR(adjusted) = 1.35, CI = 1.07, 1.72; OR(adjusted) = 1.35, CI = 1.10, 1.65). Compared with the ISF group, each 1-point increase in ALI was associated with a 10% increase in likelihood of having CFS (OR(adjusted) = 1.10, CI = 0.93, 1.31). Among persons with CFS, the duration of fatigue was inversely correlated with ALI (r = -.26, p = .047). CONCLUSIONS: Compared with well controls, persons with CFS were significantly more likely to have a high AL. AL increased in a gradient across well, ISF, and CFS groups.
Mantovani G,	Department of	Phase II	J Mol Med. 2009	Chronic inflammation is one of the main features of cancer cachexia. Experimental and clinical studies

Macciò A, Madeddu C, Serpe R, Antoni G, Massa E, Dessì M, Panzone F.	Medical Oncology, University of Cagliari, Cagliari, Italy, mantovan@medicina.unica.it.	nonrandomized study of the efficacy and safety of COX-2 inhibitor celecoxib on patients with cancer cachexia.	Oct 3. [Epub ahead of print]	showed that cyclooxygenase-2 inhibitors, such as celecoxib, may be beneficial in counteracting major symptoms of this devastating syndrome. We carried out a prospective phase II clinical trial to test the safety and effectiveness of an intervention with the COX-2 inhibitor celecoxib (300 mg/day for 4 months) on key variables of cachexia (lean body mass, resting energy expenditure, serum levels of proinflammatory cytokines, and fatigue) in patients with advanced cancer at different sites. A sample of 24 patients was enrolled from January to December 2008 and all were deemed assessable. A significant increase of lean body mass and a significant decrease of TNF-alpha were observed. Moreover, an improvement of grip strength, quality of life, performance status, and Glasgow prognostic score was shown. There were no grade 3/4 toxicities. Patient compliance was very good; no patient had to reduce the celecoxib dosage nor interrupt treatment. Our results showed that the COX-2 selective inhibitor celecoxib is an effective single agent for the treatment of cancer cachexia. Although the treatment of cancer cachexia, a multifactorial syndrome, is more likely to yield success with a multitargeted approach; in the present study, we were able to show that a treatment, such as celecoxib, addressing a single target, albeit very important as chronic inflammation, could have positive effects. Therefore, phase III clinical trials are warranted to test the efficacy and safety of celecoxib.
Marchesini G, Bianchi G.		Nonalcoholic fatty liver disease: Disease and comorbidity--effects on quality of life.	Nat Rev Gastroenterol Hepatol. 2009 Sep;6(9):504-6.	Nonalcoholic fatty liver disease has long been neglected by health-care professionals unless affected patients develop cirrhosis; however, new research shows this disease impairs health-related quality of life. The association of nonalcoholic fatty liver disease with chronic metabolic diseases and cardiovascular complications restricts our ability to define a specific role for liver damage in the poor perceived health status of these patients.
Marmion BP, Sukocheva O, Storm PA, Lockhart M, Turra M, Kok T, Ayres J, Routledge H, Graves S.	Q fever Research Group, SA Pathology/Hanson Institute, Adelaide, Australia. bpmarmion@iprimus.com.au	Q fever: persistence of antigenic non-viable cell residues of Coxiella burnetii in the host--implications for post Q fever infection fatigue syndrome and other chronic sequelae.	QJM. 2009 Oct;102(10):673-84. Epub 2009 Jun 25. Comment in: QJM. 2009 Oct;102(10):671-2.	BACKGROUND: Our previous studies of persistence of Coxiella burnetii in humans after an initial acute Q fever infection revealed raised, maintained antibody levels and low levels of coxiella genomic DNA at the age of 5 years from onset in Australian patients and at 12 years in patients in the 1989 Birmingham UK Q fever outbreak. Attempts to isolate the coxiella in standard cell culture and susceptible mice by serial passage of PCR positive PBMC and bone marrow were negative. AIM: To retest PCR positive patient samples by more sensitive methods for viable coxiellas and for the coxiella cell components of antigen and specific lipopolysaccharide (LPS). To re-interpret the previous results in the light of the new information. To review the pertinent literature for a concept of an immuno-modulatory complex generated by the current studies. DESIGN: Laboratory case study. METHODS: Stored patient samples were inoculated into SCID mice that were followed for 60 days. Mouse spleen and liver samples were then examined by PCR assay for targets in the COM1 and IS1111a sequences and for antigens by IFA with a polyclonal rabbit antiserum to C. burnetii Phase 1 and a monoclonal antiserum to Phase 1 LPS (details; O. Sukocheva et al., unpublished data). RESULTS: All specimens, including a recently excised heart valve from a Birmingham patient with late developing endocarditis, were infection negative in SCID mice. Dilutions of SCID mouse spleen and liver homogenates titrated in PCR assays were negative at dilutions attained by control mice inoculated with an endpoint dilution of a viable prototype strain of C. burnetii. Sections of the spleens from all specimens showed a complex of coxiella antigen-LPS by IFA. DISCUSSION/REVIEW: We advance a concept of long-term

				persistence of a non-infective, non-biodegraded complex of coxiella cell components with its antigens and specific LPS [so called Immunomodulatory complex (IMC)] associated with traces of genomic DNA that signalled its presence in our earlier studies. The IMC's survival in patients for at least 12 years, and in one patient for 70 years implies a capacity for serial passage in macrophages with effective down-regulation of their biodegrading functions. The review assesses the compatibility of the IMC concept in relation to cogent literature on C. burnetii interactions with macrophage and cell-mediated immunity. Some remaining gaps in our knowledge of the organ sites and duration of carriage of viable coxiellas after initial infection are also identified.
Martinez D, Cassol CM, Rahmeier L.		How much sleep apnea is too much?	Arthritis Res Ther. 2009;11(4):409; author reply 410-1. Epub 2009 Jul 15. Comment on: Arthritis Res Ther. 2008;10(3):R56.	
Mathew SJ, Mao X, Keegan KA, Levine SM, Smith EL, Heier LA, Otcheretko V, Coplan JD, Shungu DC.	Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, USA.	Ventricular cerebrospinal fluid lactate is increased in chronic fatigue syndrome compared with generalized anxiety disorder: an in vivo 3.0 T (1)H MRS imaging study.	NMR Biomed. 2009 Apr;22(3):251-8.	Chronic fatigue syndrome (CFS) is a controversial diagnosis because of the lack of biomarkers for the illness and its symptom overlap with neuropsychiatric, infectious, and rheumatological disorders. We compared lateral ventricular volumes derived from tissue-segmented T(1)-weighted volumetric MRI data and cerebrospinal fluid (CSF) lactate concentrations measured by proton MRS imaging ((1)H MRSI) in 16 subjects with CFS (modified US Centers for Disease Control and Prevention criteria) with those in 14 patients with generalized anxiety disorder (GAD) and in 15 healthy volunteers, matched group-wise for age, sex, body mass index, handedness, and IQ. Mean lateral ventricular lactate concentrations measured by (1)H MRSI in CFS were increased by 297% compared with those in GAD ($P < 0.001$) and by 348% compared with those in healthy volunteers ($P < 0.001$), even after controlling for ventricular volume, which did not differ significantly between the groups. Regression analysis revealed that diagnosis accounted for 43% of the variance in ventricular lactate. CFS is associated with significantly raised concentrations of ventricular lactate, potentially consistent with recent evidence of decreased cortical blood flow, secondary mitochondrial dysfunction, and/or oxidative stress abnormalities in the disorder.
Matsuda Y, Matsui T, Kataoka K, Fukada R, Fukuda S, Kuratsune H, Tajima S, Yamaguti K, Kato YH, Kiriike N.	Department of Neuropsychiatry, Osaka City University Graduate School of Medicine, Osaka, Japan. mackham10@yahoo.co.jp	A two-year follow-up study of chronic fatigue syndrome comorbid with psychiatric disorders.	Psychiatry Clin Neurosci. 2009 Jun;63(3):365-73.	AIMS: Chronic fatigue syndrome patients often have comorbid psychiatric disorders such as major depressive disorders and anxiety disorders. However, the outcomes of chronic fatigue syndrome and the comorbid psychiatric disorders and the interactions between them are unknown. Therefore, a two-year prospective follow-up study was carried out on chronic fatigue syndrome patients with comorbid psychiatric disorders. METHODS: A total of 155 patients who met the Japanese case definition of chronic fatigue syndrome were enrolled in this study. Comorbid psychiatric disorders were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders 4th edition criteria. Patients with comorbid psychiatric disorders received psychiatric treatment in addition to medical therapy for chronic fatigue syndrome. Seventy patients participated in a follow-up interview approximately 24 months later. RESULTS: Of the 70 patients with chronic fatigue syndrome, 33 patients were diagnosed as having comorbid psychiatric disorders including 18 major depressive

				disorders. Sixteen patients with psychiatric disorders and eight patients with major depressive disorders did not fulfill the criteria of any psychiatric disorders at the follow up. As for chronic fatigue syndrome, nine out of the 70 patients had recovered at the follow up. There is no significant influence of comorbid psychiatric disorders on the outcome of chronic fatigue syndrome. CONCLUSIONS: Chronic fatigue syndrome patients have a relatively high prevalence of comorbid psychiatric disorders, especially major depressive disorders. The outcomes of chronic fatigue syndrome and psychiatric disorders are independent. Therefore treatment of comorbid psychiatric disorders is necessary in addition to the medical treatment given for chronic fatigue syndrome.
Maurer MS, Cuddihy P, Weisenberg J, Delisle S, Strong BM, Gao Q, Kachnowski S, Howell J.	Cardiology Division, Department of Medicine, Columbia University Medical Center, New York, New York, USA. msm10@columbia.edu	The prevalence and impact of anergia (lack of energy) in subjects with heart failure and its associations with actigraphy.	J Card Fail. 2009 Mar;15(2):145-51. Epub 2008 Dec 6.	BACKGROUND: Anergia (lack of energy) is a newly delineated, criterion-based geriatric syndrome. Because heart failure (HF) is a common chronic condition among older adults and a because a cardinal symptom of HF is reduced energy, we characterized the degree of anergia in subjects with HF and evaluated its relevance to disease severity, functional performance, and quality of life. METHODS AND RESULTS: Prospective 3-month cohort study among a convenience sample of 61 subjects (61 +/- 15 years, 48% women, ejection fraction 41 +/- 16%) with New York Heart Association (NYHA) Class I-III HF were studied. The criterion for anergia was based on the major criterion "sits around for lack of energy" and any 2 of 6 minor criteria. Principal measures in addition to demographic and clinical characteristics included functional performance (NYHA class, 6-minute walk, cardiopulmonary exercise testing), plasma B-type natriuretic peptide, and quality of life (SF-12 and Minnesota Living with Heart Failure Questionnaire). To evaluate the relevance of anergia to daily function, each subject wore an Actigraph, a watch-like wrist device that continuously and automatically monitors patient activity levels and energy expenditure, for 3 months. Anergia was prevalent in 39% of this population. Anergia was associated with decrements in functional capacity (higher NYHA Class and lower 6-minute walk distance) as well as reduction in quality of life, but was not associated with ejection fraction. Actigraphy data demonstrated that HF subjects with anergia spent significantly less time performing moderate physical activity and the peak activity counts per day were significantly lower than HF subjects without anergia. Additionally, the amplitude of circadian rhythm was lower, suggesting altered sleep and activity patterns in HF subjects with anergia compared with those without anergia. Over the 3 months of follow-up, there was a significant association between anergia and intercurrent hospitalization. CONCLUSIONS: Anergia is significantly associated with several of the cardinal domains of HF. Its presence is associated with demonstrable differences in both physical activity and circadian rhythm as measured by actigraphy and an increased risk of hospitalizations. Accordingly, anergia may be a target for intervention among HF subjects.
May M, Emond A, Crawley E.	Bristol University, United Kingdom.	Phenotypes of Chronic Fatigue Syndrome in Children and Young People.	Arch Dis Child. 2009 Oct 19. [Epub ahead of print]	OBJECTIVE: To investigate the heterogeneity of chronic fatigue syndrome (CFS/ME) in children and young people. SETTING: Regional specialist CFS/ME service. Patients: Children and young people aged < 19 years old. METHODS: Exploratory factor analysis was performed on symptoms present at assessment in 333 children and young people with CFS/ME. Linear and logistic regression analysis of data from self completed assessment forms was used to explore the associations between the retained factors and sex, age, length of illness, depression, anxiety and markers of severity (fatigue, physical function, pain and school attendance). RESULTS: Three phenotypes were identified using factor analysis: Musculoskeletal (Factor 1) had loadings on muscle and joint pain and hypersensitivity

				to touch, and was associated with worse fatigue (regression coefficient 0.47, 95% CI 0.25, 0.68, p <0.001), physical function (regression coefficient -0.52, 95% CI -0.83, -0.22, p= 0.001) and pain. . Factor 2 (Migraine) loaded on noise and light hypersensitivity, headaches, nausea, abdominal pain and dizziness and was most strongly associated with physical function and pain. Sore throat phenotype, (Factor 3) had loadings on sore throat and tender lymph nodes and was not associated with fatigue or pain. There was no evidence that phenotypes were associated with age, length of illness or symptoms of depression (regression coefficient for association of depression with Musculoskeletal pain -0.02, 95% CI -0.27, 0.23, p= 0.87). The Migraine phenotype was associated with anxiety (0.40, 95% CI 0.06, 0.74, p=0.02). Implications: CFS/ME is heterogeneous in children with 3 phenotypes at presentation that are differentially associated with severity and are unlikely to be due to age or length of illness.
McKay PG, Duffy T, Martin CR.	School of Health, Nursing and Midwifery, University of West of Scotland, Ayr, UK.	Are chronic fatigue syndrome and fibromyalgia the same? Implications for the provision of appropriate mental health intervention.	J Psychiatr Ment Health Nurs. 2009 Dec;16(10):884-94.	Chronic fatigue syndrome and fibromyalgia represent distinct diagnostic entities within both the clinical and research literature. A common feature of both presentations is that they are often accompanied by a significant mental health burden. A further salient feature of both conditions is that there is no consistent consensus on aetiology. Evaluation of the features of each disorder seems to present a convincing case that both disorders may indeed have a common aetiology and further, the possibility exists that chronic fatigue syndrome and fibromyalgia represent the same underlying disorder. Paradoxically, given this possibility it is remarkable that both patient groups are treated clinically with considerably different approaches to care and management. Mental health practitioners will come into contact with both groups of patients when support for the psychological consequences of diagnosis are necessary; however, many practitioners will be unaware of the debate regarding the aetiological ambiguities surrounding these presentations. The purpose of this review is to highlight the above issues in order to both facilitate awareness of the current aetiological/diagnostic impasse and facilitate provision of optimum mental health support.
Mease PJ, Clauw DJ, Gendreau RM, Rao SG, Kranzler J, Chen W, Palmer RH.	Seattle Rheumatology Associates, 1101 Madison Street, Suite 1000, Seattle, WA 98104, USA. pmease@philipmease.com	The efficacy and safety of milnacipran for treatment of fibromyalgia. a randomized, double-blind, placebo-controlled trial.Erratum in: J Rheumatol. 2009 Mar;36(3):661.	J Rheumatol. 2009 Feb;36(2):398-409.	OBJECTIVE: To evaluate the safety and efficacy of milnacipran, a dual norepinephrine and serotonin reuptake inhibitor, in the treatment of fibromyalgia (FM). METHODS: A 27-week, randomized, double-blind, multicenter study compared milnacipran 100 and 200 mg/day with placebo in the treatment of 888 patients with FM. Two composite responder definitions were used to classify each patient's individual response to therapy. "FM responders" concurrently satisfied response criteria for improvements in pain (visual analog scale 24-h morning recall), patient global impression of change (PGIC), and physical functioning (SF-36 Physical Component Summary); while "FM pain responders" concurrently satisfied response criteria for improvements in pain and PGIC. RESULTS: At the primary endpoint, after 3-month stable dose treatment, a significantly higher percentage of milnacipran-treated patients met criteria as FM responders versus placebo (milnacipran 200 mg/day, p = 0.017; milnacipran 100 mg/day, p = 0.028). A significantly higher percentage of patients treated with milnacipran 200 mg/day also met criteria as FM pain responders versus placebo (p = 0.032). Significant pain reductions were observed after Week 1 with both milnacipran doses. At 15 weeks, milnacipran 200 mg/day led to significant improvements over placebo in pain (realtime, daily and weekly recall; all measures, p < 0.05), PGIC (p < 0.001), fatigue (p = 0.016), cognition (p = 0.025), and multiple SF-36 domains. Milnacipran was safe and well tolerated by the majority of patients during 27 weeks of treatment; nausea and headache were the most common adverse events. CONCLUSION:

				Milnacipran is safe and effective for the treatment of multiple symptoms of FM.
Mease PJ.	Seattle Rheumatology Associates, Swedish Medical Center, Seattle, Washington, USA. pmease@nwlink.com	Further strategies for treating fibromyalgia: the role of serotonin and norepinephrine reuptake inhibitors.	Am J Med. 2009 Dec;122(12 Suppl):S44-55.	Fibromyalgia and associated conditions such as irritable bowel syndrome and temporomandibular disorder involve dysfunctions in central sensitization and pain modulation. Central nervous system dysfunction may also contribute to other symptoms characteristic of fibromyalgia, such as fatigue and sleep disturbance. Two key neurotransmitters in the pain modulation pathway are serotonin and norepinephrine. Preclinical studies using animal models of chronic pain have shown that pharmacologic agents that combine serotonergic and noradrenergic reuptake inhibition, thus augmenting the function of these neurotransmitters, have stronger analgesic effects than agents that inhibit reuptake of either neurotransmitter alone. Although tricyclic antidepressants (TCAs) inhibit reuptake of both serotonin and norepinephrine and have shown efficacy for the treatment of fibromyalgia, long-term use of these drugs is limited owing to poor tolerability. Unlike TCAs, the newer dual reuptake inhibitors of serotonin and norepinephrine, such as the drugs approved by the US Food and Drug Administration (FDA) for fibromyalgia, milnacipran and duloxetine, do not possess significant affinity for other neurotransmitter systems, resulting in diminished side effects and enhanced tolerability. Both duloxetine and milnacipran have shown efficacy in clinical trials by improving pain and other symptoms associated with fibromyalgia. Both compounds inhibit the serotonin and norepinephrine transporters; however, there is a difference in their affinities and selectivity for these transporters. Although duloxetine has affinity for both receptors, it is somewhat more selective for the serotonin transporter. In contrast, milnacipran is somewhat more selective for norepinephrine than serotonin reuptake inhibition. Pharmacologic agents that specifically target serotonin and norepinephrine reuptake may prove to be valuable tools in the treatment of fibromyalgia. (c) 2009 Elsevier Inc.
Meeus M, Mistiaen W, Lambrecht L, Nijs J.	Department of Health Sciences, Van Aertselaerstraat 31, 2170 Merksem, Belgium.	Immunological similarities between cancer and chronic fatigue syndrome: the common link to fatigue?	Anticancer Res. 2009 Nov;29(11):4717-26.	Cancer and chronic fatigue syndrome (CFS) are both characterised by fatigue and severe disability. Besides fatigue, certain aspects of immune dysfunctions appear to be present in both illnesses. In this regard, a literature review of overlapping immune dysfunctions in CFS and cancer is provided. Special emphasis is given to the relationship between immune dysfunctions and fatigue. Abnormalities in ribonuclease (RNase) L and hyperactivation of nuclear factor kappa beta (NF-kappaB) are present in CFS and in prostate cancer. Malfunctioning of natural killer (NK) cells has long been recognised as an important factor in the development and reoccurrence of cancer, and has been documented repeatedly in CFS patients. The dysregulation of the RNase L pathway, hyperactive NF-kappaB leading to disturbed apoptotic mechanisms and oxidative stress or excessive nitric oxide, and low NK activity may play a role in the two diseases and in the physiopathology of the common symptom fatigue. However, in cancer the relation between the immune dysfunctions and fatigue has been poorly studied. Immunological abnormalities to such as a dysregulated RNase L pathway, hyperactive NF-kappaB, increased oxidative stress and reduced NK cytotoxicity, among others, are present in both diseases. These anomalies may be part of the physiopathology of some of the common complaints, such as fatigue. Further studies to confirm the hypotheses given here are warranted.
Menzies V, Lyon DE.		Integrated Review of the Association of Cytokines With	Biol Res Nurs. 2009 Nov 22. [Epub ahead of print]	Fibromyalgia (FMS) is a chronic widespread pain (CWP) and fatigue syndrome that affects three to six million adults in the United States. Core symptoms of FMS include pain, fatigue, and mood and sleep disturbances. To date, consensus has not been reached among researchers regarding the

		Fibromyalgia and Fibromyalgia Core Symptoms.		pathogenesis of FMS nor the specific role of cytokine activation on the neuroendocrine-immune response patterns in persons with FMS. The purpose of this article is to describe and synthesize the results of research studies focused on the relationship between cytokines and FMS and among cytokines and core symptoms of FMS. There is some support in the literature for relationships among FMS symptoms and cytokines; however, there are discrepant findings related to whether proinflammatory and anti-inflammatory cytokines are elevated or reduced in persons with FMS and whether their levels correlate with the core symptoms of this disorder. Although the use of cytokine biomarkers must be considered exploratory at this time due to the lack of consistent empirical findings, biobehavioral research focused on understanding the relationship of FMS with cytokines may lead to a better understanding of this complex syndrome. This knowledge may ultimately contribute to the development of interventions for symptom management that address not only the symptom manifestation but also a biological mediator of symptoms.
Million M, Lepidi H, Raoult D.	CNRS, UMR 6236, IRD 198, unité de recherche sur les maladies infectieuses et tropicales émergentes, faculté de médecine, université de la Méditerranée, 27, boulevard Jean-Moulin, 13385 Marseille cedex 05, France. matthieumillion@gmail.com	[Q fever: current diagnosis and treatment options][Article in French]	Med Mal Infect. 2009 Feb;39(2):82-94. Epub 2008 Nov 14.	Q fever is a zoonotic disease caused by the ubiquitous pathogen Coxiella burnetii responsible for acute and chronic clinical manifestations. Its geographically heterogeneous prevalence seems mainly related to the clinician interest and the availability of a reference center. Its polymorphic clinical expression imposes reference to diagnosis in presence of pneumonia, hepatitis, prolonged fever or endocarditis with no proof of its etiology. The diagnosis is mainly serological. If acute Q fever is most often benign, endocarditis is constantly fatal without treatment. The treatment is effective and well tolerated, but must be adapted to the acute or chronic pattern, the presence of a heart valve disease, an aneurysm or a vascular prosthesis, an immunodeficiency and the specific problem of pregnancy.
Miwa K, Fujita M.		Increased oxidative stress suggested by low serum vitamin E concentrations in patients with chronic fatigue syndrome.	Int J Cardiol. 2009 Aug 14;136(2):238-9. Epub 2008 Aug 6.	Serum alpha-tocopherol concentrations were determined in 50 patients with chronic fatigue syndrome (CFS) and 40 control subjects (Control). Prevalence of each or any coronary risk factor was not significantly different between CFS and Control. CFS had significantly lower alpha-tocopherol concentrations than Control. The concentrations were significantly lower in the subjects with any coronary risk factors than those without in CFS as well as Control. Even among the subjects with any coronary risk factors and also among those without, CFS had significantly lower alpha-tocopherol concentrations than Control. In conclusion, CFS had significantly lower alpha-tocopherol concentrations irrespective of coronary risk factors than Control, suggesting the presence of increased oxidative stress in CFS.
Miwa K, Fujita M.	Department of Internal Medicine,	Cardiac function fluctuates during	J Cardiol. 2009 Aug;54(1):29-35.	BACKGROUND: "Small heart syndrome", previously referred to as so-called "neurocirculatory asthenia" associated with a small heart shadow on the chest roentgenogram, is characterized by

	Nanto Family and Community Medical Center, 577 Matsubara, Nanto, Toyama 939-1518, Japan.	exacerbation and remission in young adults with chronic fatigue syndrome and "small heart".	Epub 2009 Mar 28.	weakness or fatigue even after mild exertion, palpitation, dyspnea, and fainting, many of which resemble symptoms in patients with chronic fatigue syndrome (CFS). METHODS AND RESULTS: The study population comprised 42 patients with CFS younger than 40 years of age. Cardiothoracic ratio was determined on the chest roentgenogram and echocardiographic examination was performed to evaluate both the cardiac chamber size and function. "Small heart" (cardiothoracic ratio </=42%) on the chest X-ray photograph was noted in 26 (62%) of the study CFS patients. Echocardiographic examination demonstrated significantly smaller mean values of both the left ventricular (LV) end-diastolic and end-systolic dimensions, stroke volume indexes and cardiac indexes in CFS patients with "small heart" than in those without it and also in 20 control subjects. Thus, CFS patients with "small heart" had an actually small LV chamber and poor cardiac performance. During a long follow-up period of 10 CFS patients with "small heart", all echocardiographic parameters mentioned above improved and cardiothoracic ratios increased significantly during the remission phase as compared with exacerbation phase. CONCLUSIONS: "Small heart" on the chest X-ray photograph was prevalently noted in CFS patients. Echocardiographic examination revealed that CFS patients with "small heart" had an actually small LV chamber and poor cardiac performance. Cardiac functional changes evaluated by repeated examinations appeared to be directly associated with the severity of their symptoms. Small heart syndrome with impaired cardiac function may contribute to the development of CFS through low cardiac output as a constitutional factor.
Miwa K, Fujita M.	Department of Internal Medicine, Nanto Family and Community Medical Center, Nanto, Toyama, Japan. miwa.kunihisa@city.nanto.lg.jp	Cardiovascular dysfunction with low cardiac output due to a small heart in patients with chronic fatigue syndrome.	Intern Med. 2009;48(21):1849-54. Epub 2009 Nov 2.	OBJECTIVE: Little attention has been paid to possible cardiovascular involvement in patients with chronic fatigue syndrome (CFS), although many of their symptoms and signs suggest cardiovascular dysfunction. Possible cardiovascular symptoms and cardiac function were investigated in CFS patients. METHODS: Cardiovascular symptoms were intensively investigated and cardiac function was evaluated echocardiographically. PATIENTS: Fifty-three patients (23 men and 30 women, mean age: 31+/-7 years) with CFS under 50 years were studied. RESULTS: Slender build (body mass index <20 kg/m(2)) was common (47%). Possible cardiovascular symptoms including shortness of breath (32%), dyspnea on effort (28%), rapid heartbeat (38%), chest pain (43%), fainting (43%), orthostatic dizziness (45%) and coldness of feet (42%), were all frequent complaints. Hypotension (28%) was occasionally noted. Electrocardiograms frequently revealed right axis deviation (21%) and severe sinus arrhythmia (34%) suggesting accentuated parasympathetic nervous activity. Small heart shadow (cardiothoracic ratio <or=42%) was noted on the chest roentgenogram in 32 patients (60%). Echocardiographic examination demonstrated low cardiac indexes (<2 L/min/m(2)) with low stroke volume indexes (<30 mL/m(2)) due to a small left ventricular chamber in 19 (36%, p<0.05 vs. 8% in 36 controls). None had reduced left ventricular ejection fraction. CONCLUSION: Cardiovascular symptoms are common in CFS patients. Cardiac dysfunction with low cardiac output due to small left ventricular chamber may contribute to the development of chronic fatigue as a constitutional factor in a considerable number of CFS patients.
Miyaoka H, Miyachi H, Oishi S.	Department of Psychiatry, Kitasato University, School of	[Is "functional somatic syndrome" clinically useful?] [Article in	Nippon Rinsho. 2009 Sep;67(9):1726-30.	The functional somatic syndrome is applied to several syndromes characterized by medically unexplained physical symptoms, such as irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, etc. Both physical and psychiatric treatments are usually necessary for these syndromes and the term functional somatic syndrome was advocated to inform clinicians in America of this fact.

	Medicine.	Japanese]		However, We believe this term will not be useful in Japan, because most Japanese clinicians are already aware of this fact and treatment is different in each syndrome included in FSS.
Moniuszko A, Czupryna P, Zajkowska J, Pancewicz SA, Grygorczuk S, Kondrusik M.	Department of Infectious Diseases and Neuroinfections, Medical University of Bialystok, Poland. annamoniuszko@op.pl	[Post Lyme syndrome as a clinical problem][Article in Polish]	Pol Merkur Lekarski. 2009 Mar;26(153):227-30.	Lyme disease is a chronic tick borne disease, caused by spirochetes B. burgdorferi. The condition influences mostly on skin, nervous system, skeletal system and circulatory system. Recently more and more reports of so called "Post Lyme syndrome (PLS)" have appeared. PLS is a new clinical, diagnostic and therapeutic problem connected with patients with a history of Lyme disease (with proper antibiotic treatment). The symptoms of Post Lyme Syndrome may be present throughout months or even years. These are: fatigue, widespread musculoskeletal pain, dysmnesia, concentration difficulties. Pathogenesis of PLS is unknown. It is suspected that main factors responsible for PLS are: slow regression of infection, its turning into chronic process and permanent destruction of tissues or induction of immunological response against B. burgdorferi. Diagnostic of PLS is difficult. Mostly results of serological examination are negative. In some cases antibodies titer is positive as a sign of past disease. So far there is no causative treatment of PLS. Antidepressants, painkillers and anti-inflammatory medicines are recommended.
Murakami M.	Department of Psychosomatic Internal Medicine, Nihon University Itabashi Hospital.	[Treatment of myalgia] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1759-65.	Fibromyalgia (FM) conceptualized by the American College of Rheumatology is characterized by long-lasting chronic widespread pain and stiffness of the fibro-muscular system associated with various unidentified symptoms. Since most of the patients are female and the onset and clinical course of FM involves various kinds of bio-psychosocial stress factors, it is very important to consider the psychosomatic background of the patient. The symptom of FM is not readily improved with conventional analgesic drugs, antirheumatic agents or various kinds of physiotherapy, however current guidelines recommend tricyclic antidepressants, SSRIs and SNRIs as first-line therapies to treat the multiple symptom of the FM. It is considered that antidepressants may operate the functional impairment of descending (efferent) analgesic system, in which serotonin and noradrenaline take an important role. Among 199 certified physicians of the Japanese Society of Psychosomatic Medicine, the largest number of respondents selected SSRI, SNRI and other antidepressants as first-line drugs. Because the psychological and physical exhaustion due to an irregular life style, physical strain, and accumulated fatigue may be the key stress factors for the organization of symptoms, psychosomatic approach and guidance should be conducted to enable patients to reduce stress in daily life. For the problems of personality and psychological stress, counseling and advanced psychotherapy such as cognitive behavioral therapy (CBT) should be also conducted.
Mutsuura H, Kanbara K, Fukunaga M, Yamamoto K, Ban I, Kitamura K, Nakai Y.	Department of Psychosomatic Medicine, Kansai Medical University, Moriguchi-shi, Osaka 570-8507, Japan. mutsuurh@takii.kmu.ac.jp	Depression and anxiety correlate differently with salivary free cortisol in the morning in patients with functional somatic syndrome.	Appl Psychophysiol Biofeedback. 2009 Dec;34(4):291-8. Epub 2009 Aug 7.	Patients presenting with functional somatic syndrome (FSS) are common, and the symptoms are persistent and difficult to treat for doctors and costly for society. The aim of this study was to clarify the common pathophysiology of FSS, especially the relationship between hypothalamic-pituitary-adrenal (HPA) axis function and psychological characteristics of patients with FSS. The subjects were 45 patients with FSS and 29 healthy controls. Salivary free cortisol was measured in the morning, and psychological tests examining depression, anxiety and quality of life (QOL) were performed on the same day. In patients with FSS, depressive scores showed a significant negative correlation with salivary free cortisol in the morning, although in healthy controls, cortisol showed a significant positive correlation with depressive scores. In addition, the correlation between other psychological test scores and cortisol secretion in patients with FSS contrasted with that of controls. The

				relationship between cortisol and depression, anxiety or QOL, suggests that the HPA axis of patients with FSS is dysfunctional and does not function properly when patients with FSS are under stress. This dysfunction may explain the pathology of medically unexplained persistent symptoms of patients with FSS.
Myhill S, Booth NE, McLaren-Howard J.		Chronic fatigue syndrome and mitochondrial dysfunction.	Int J Clin Exp Med. 2009;2(1):1-16. Epub 2009 Jan 15.	This study aims to improve the health of patients suffering from chronic fatigue syndrome (CFS) by interventions based on the biochemistry of the illness, specifically the function of mitochondria in producing ATP (adenosine triphosphate), the energy currency for all body functions, and recycling ADP (adenosine diphosphate) to replenish the ATP supply as needed. Patients attending a private medical practice specializing in CFS were diagnosed using the Centers for Disease Control criteria. In consultation with each patient, an integer on the Bell Ability Scale was assigned, and a blood sample was taken for the "ATP profile" test, designed for CFS and other fatigue conditions. Each test produced 5 numerical factors which describe the availability of ATP in neutrophils, the fraction complexed with magnesium, the efficiency of oxidative phosphorylation, and the transfer efficiencies of ADP into the mitochondria and ATP into the cytosol where the energy is used. With the consent of each of 71 patients and 53 normal, healthy controls the 5 factors have been collated and compared with the Bell Ability Scale. The individual numerical factors show that patients have different combinations of biochemical lesions. When the factors are combined, a remarkable correlation is observed between the degree of mitochondrial dysfunction and the severity of illness ($P<0.001$). Only 1 of the 71 patients overlaps the normal region. The "ATP profile" test is a powerful diagnostic tool and can differentiate patients who have fatigue and other symptoms as a result of energy wastage by stress and psychological factors from those who have insufficient energy due to cellular respiration dysfunction. The individual factors indicate which remedial actions, in the form of dietary supplements, drugs and detoxification, are most likely to be of benefit, and what further tests should be carried out.
Nakagami A, Tsujiuchi T.	Graduate School of Human Sciences, Waseda University.	[Functional somatic syndromes from the view of cultural anthropology] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1683-8.	The functional somatic syndromes have acquired major socio-cultural and political dimensions. Socio-cultural factors clearly affect symptoms, suffering, and disability perception and reporting. And knowledge of explanatory models of bodily distress for patients from different cultural backgrounds is useful in the establishment of a stable doctor -patient relationship. FSS may be an operational category to bridge between medical explanatory model and patient's model. According to medical anthropology, sickness has two faces; illness and disease. "Disease" is the problem from the practitioner's perspective, and "illness" is the human experience of symptoms and suffering. In this paper, the anthropological research on chronic fatigue syndrome as "not real" illness experience was described.
Nakao M.	Department of Hygiene and Public Health & Division of Psychosomatic Medicine, Teikyo University School of Medicine.	[Etiology of functional somatic syndromes] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1661-8.	Functional somatic syndromes are defined as several related syndromes that are characterized more by symptoms, suffering, and disability than by structural or functional abnormality. These syndromes include irritable bowel syndrome, tension-type headache, chronic fatigue syndrome, and fibromyalgia. Such syndromes have similarities in terms of definition, diagnosis, etiology, and treatment. To elucidate the pathogenesis of functional somatic syndromes, it is important to focus on gender-related factors, comorbidities of depression and anxiety, physiological responses like autonomic nervous function and hypothalamic-pituitary-adrenal axis, and patient-doctor relationship. Based on

				recent literatures, mood state and somatosensory amplification are suggested to play an important role in the psychopathological mechanism of functional somatic syndromes, and genetic and environmental factors need to be considered as well.
Nater UM, Lin JM, Maloney EM, Jones JF, Tian H, Boneva RS, Raison CL, Reeves WC, Heim C.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.	Psychiatric comorbidity in persons with chronic fatigue syndrome identified from the Georgia population.	Psychosom Med. 2009 Jun;71(5):557-65. Epub 2009 May 4.	OBJECTIVE: To compare the prevalence of psychiatric disorders in persons with chronic fatigue syndrome (CFS) identified from the general population and a chronically ill group of people presenting with subsyndromic CFS-like illness ("insufficient symptoms or fatigue" (ISF)). Previous studies in CFS patients from primary and tertiary care clinics have found high rates of psychiatric disturbance, but this may reflect referral bias rather than true patterns of comorbidity with CFS. METHODS: We used random digit dialing to identify unwell individuals. A detailed telephone interview identified those with CFS-like illness. These individuals participated in a 1-day clinical evaluation to confirm CFS or ISF status. We identified 113 cases of CFS and 264 persons with ISF. To identify current and lifetime psychiatric disorders, participants completed the Structured Clinical Interview for DSM-IV. RESULTS: Sixty-four persons (57%) with CFS had at least one current psychiatric diagnosis, in contrast to 118 persons (45%) with ISF. One hundred one persons (89%) with CFS had at least one lifetime psychiatric diagnosis compared with 208 persons (79%) with ISF. Of note, only 11 persons (9.8%) with CFS and 25 persons (9.5%) with ISF reported having seen a mental healthcare specialist during the past 6 months. CONCLUSIONS: Our findings indicate that current and lifetime psychiatric disorders commonly accompany CFS in the general population. Most CFS cases with comorbid psychiatric conditions had not sought appropriate help during the past 6 months. These results demonstrate an urgent need to address psychiatric disorders in the clinical care of CFS cases.
Neu D, Cappeliez B, Hoffmann G, Verbanck P, Linkowski P, Le Bon O.	Brugmann University Hospital, Sleep Laboratory, and Unit for Chronobiology U78, Université Libre de Bruxelles (U.L.B), Brussels, Belgium. daniel.neu@chu-brugmann.be	High slow-wave sleep and low-light sleep: chronic fatigue syndrome is not likely to be a primary sleep disorder.	J Clin Neurophysiol. 2009 Jun;26(3):207-12.	The status of chronic fatigue syndrome (CFS) is still under debate. Mainstream views still often consider it as an undetected primary sleep disorder or as the psychosomatic expression of a related anxiety or depression syndrome. Both primary sleep disorder and CFS are often related to unrefreshing sleep and affective daytime symptoms. The present study compares nonrapid eye movement sleep distribution between patients with a primary sleep disorder and "pure" CFS patients without sleep or mood disorders. Intensity measures of affective symptoms are also analyzed. Sleep variables of 32 pure CFS (mean age, 41.9 +/- 8.7 years; 25 women), 30 Sleep Apnea Hypopnea Syndrome patients (mean age, 43.7 +/- 6.7 years; 13 women), and 14 healthy controls (mean age, 40.2 +/- 7.6 years; 9 women) were compared. Related affective symptoms were assessed using the self-reported Zung anxiety and depression scales. The study confirms previous reports on increased slow-wave sleep in CFS patients. Both patient groups showed similar sleep duration and efficiency. Sleep efficiency was lower in both patient groups compared with controls. CFS patients showed a higher microarousal index than controls. Anxiety, but not depression symptoms were more intense in the CFS group. The distribution of nonrapid eye movement sleep in CFS differs sizeably from what can be observed in a primary sleep disorder.
Newton JL, Sheth A, Shin J, Pairman J, Wilton K, Burt JA, Jones DE.	Cardiovascular Investigation Unit, Institute of Cellular Medicine, Newcastle	Lower ambulatory blood pressure in chronic fatigue syndrome.	Psychosom Med. 2009 Apr;71(3):361-5. Epub 2009 Mar 17.	OBJECTIVE: To examine blood pressure circadian rhythm in subjects with chronic fatigue syndrome (CFS) and appropriate normal and fatigued controls to correlate parameters of blood pressure regulation with perception of fatigue in an observational cohort study. The cause of CFS remains unknown and there are no effective treatments. METHODS: To address whether inactivity was a confounder, we performed a 24-hour ambulatory blood pressure monitoring in the following three

	University, Newcastle NE2 4HH, UK. julia.newton@nuth.northy.nhs.uk			subject groups: 1) CFS patients (Fukuda Diagnostic criteria) (n = 38); 2) normal controls (n = 120); and 3) a fatigue comparison group (n = 47) with the autoimmune liver disease primary biliary cirrhosis (PBC). All patients completed a measure of fatigue severity (Fatigue Impact Scale). In view of the different demographics between the patient groups, patients were age- and sex-matched on a case-by-case basis to normal controls and blood pressure parameters were compared. RESULTS: Compared with the control population, the CFS group had significantly lower systolic blood pressure ($p < .0001$) and mean arterial blood pressure ($p = .0002$) and exaggerated diurnal variation ($p = .009$). There was a significant inverse relationship between increasing fatigue and diurnal variation of blood pressure in both the CFS and PBC groups ($p < .05$). CONCLUSION: Lower blood pressure and abnormal diurnal blood pressure regulation occur in patients with CFS. We would suggest the need for a randomized, placebo-controlled trial of agents to increase blood pressure such as midodrine in CFS patients with an autonomic phenotype.
Ocon AJ, Medow MS, Taneja I, Clarke D, Stewart JM.	Department of Physiology, The Center for Hypotension, New York Medical College, Valhalla, New York 10532, USA.	Decreased upright cerebral blood flow and cerebral autoregulation in normocapnic postural tachycardia syndrome.	Am J Physiol Heart Circ Physiol. 2009 Aug;297(2):H664-73. Epub 2009 Jun 5.	Postural tachycardia syndrome (POTS), a chronic form of orthostatic intolerance, has signs and symptoms of lightheadedness, loss of vision, headache, fatigue, and neurocognitive deficits consistent with reductions in cerebrovascular perfusion. We hypothesized that young, normocapnic POTS patients exhibit abnormal cerebral autoregulation (CA) that results in decreased static and dynamic cerebral blood flow (CBF) autoregulation. All subjects had continuous recordings of mean arterial pressure (MAP) and CBF velocity (CBFV) using transcranial Doppler sonography in both the supine supine position and during a 70 degrees head-up tilt. During tilt, POTS patients (n = 9) demonstrated a higher heart rate than controls (n = 7) (109 +/- 6 vs. 80 +/- 2 beats/min, $P < 0.05$), whereas controls demonstrated a higher MAP than POTS (87 +/- 2 vs. 77 +/- 3 mmHg, $P < 0.05$). Also during tilt, mean CBFV decreased 19.5 +/- 2.6% in POTS patients versus 10.3 +/- 2.0% in controls ($P < 0.05$). We then used a transfer function analysis of MAP and CFBV in the frequency domain to quantify these changes. The low-frequency (LF; 0.04-0.15 Hz) component of CBFV variability increased during tilt in POTS patients (supine: 3 +/- 0.9 vs. tilt: 9 +/- 2, $P < 0.02$). In POTS patients, there was an increase in LF and high-frequency coherence between MAP and CBFV, an increase in LF gain, and a lack of significant change in phase. Static CA may be less effective in POTS patients compared with controls, since immediately after tilt CBFV decreased more in POTS patients and was highly oscillatory and autoregulation did not restore CBFV to baseline values until the subjects became supine. Dynamic CA may be less effective in POTS patients because MAP and CBFV during tilt became almost perfectly synchronous. We conclude that dynamic and static autoregulation of CBF are less effective in POTS patients compared with control subjects during orthostatic challenge.
Ogawa H, Hida W.	Health Administration Center, Tohoku University.	[Chronic obstructive pulmonary disease (COPD)] [Article in Japanese]	Nippon Rinsho. 2009 Aug;67(8):1518-24.	Insomnia is common in many patients with chronic obstructive pulmonary disease (COPD). The causes of insomnia are sleep induced pathophysiological effect of COPD itself, COPD comorbidities and the presence of coexisted obstructive sleep apnea. Sleep has profound adverse effects on respiration and gas exchange in patients with COPD. There are several mechanisms underlying oxygen desaturation during sleep. They include decreased functional residual capacity, decreased ventilatory responses to hypoxia and hypercapnia, impaired respiratory mechanical effectiveness, respiratory muscle fatigue, decreased respiratory drive, and increased upper airway resistance. COPD comorbidities include DM, cardiovascular diseases, osteoporosis, depression, and GERD. The coexistence of COPD and sleep

				apnea-hypopnea syndrome has been denominated "overlap syndrome".
Oka T, Kanemitsu Y.	Department of Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University.	[Biomedical and psychosocial treatment of fatigue in functional somatic syndrome] [Article in Japanese]	Nippon Rinsho. 2009 Sep;67(9):1778-82.	Fatigue is one of the most common complaints of patients with functional somatic syndrome (FSS), which includes chronic fatigue syndrome (CFS). Although the etiology of fatigue related to FSS remains unclear, accumulating evidence has shown that cognitive behavioral therapy and graded exercise therapy are effective for treating fatigue in patients with CFS. This suggests that psychosocial intervention and physical rehabilitation, as well as biomedical treatment, play an important role in treating fatigue in FSS patients. Here we provide an overview of the biomedical and psychosocial treatments for fatigue in cases of FSS.
Oliveira WR, Ferreira GN, Rady PL, Festa C, Tyring SK.	Department of Dermatology, University of São Paulo, São Paulo, Brazil. walmarroncalli@uol.com.br	Epidermodysplasia verruciformis associated with myelodysplastic syndrome: an intriguing association.	J Cutan Med Surg. 2009 Nov-Dec;13(6):317-20.	BACKGROUND: Epidermodysplasia verruciformis (EV) is a rare genodermatosis characterized by massive infection with human papillomaviruses (HPVs) and development of skin cancer. Myelodysplastic syndromes (MDSs) are a group of chronic conditions that involve dysplastic hematopoiesis, peripheral blood cytopenias, and a high incidence of progression into leukemia. METHODS: We describe the intriguing association of these two premalignant conditions (EV and MDS) in one patient. These diagnoses were confirmed by histopathologic examination and cytogenetic abnormalities of bone marrow cells. RESULTS: The patient presented initially with clinical features typical of EV and impairment of cell-mediated immunity. In the skin lesions, HPVs 23 and 25 were identified by nested polymerase chain reaction. Six years later, he had recurrent episodes of mucosal bleeding with fever, weakness, and fatigue. At this time, severe refractory anemia and neutropenia were observed, and bone marrow smears showed hypercellularity with abnormal dysplastic megakaryocytes. The cytogenetic pattern showed abnormalities involving trisomy of chromosomes 8 and 21. The patient received a diagnosis of the indolent subtype of MDS. CONCLUSIONS: Through the observation of our patient and review of the literature, we hypothesized that the pathomechanisms, including the role of oncogenes and cytokines, are connected to the progression to malignancy in these settings.
Ortega-Hernandez OD, Cuccia M, Bozzini S, Bassi N, Moscavitch S, Diaz-Gallo LM, Blank M, Agmon-Levin N, Shoenfeld Y.	Department of Medicine B and Center for Autoimmune Diseases, Sheba Medical Center, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.	Autoantibodies, polymorphisms in the serotonin pathway, and human leukocyte antigen class II alleles in chronic fatigue syndrome: are they associated with age at onset and specific symptoms?	Ann N Y Acad Sci. 2009 Sep;1173:589-99.	This study aimed to determine the influence of autoantibodies, polymorphisms in the serotonin pathway, and human leukocyte antigen (HLA) class II genes on age at chronic fatigue syndrome (CFS) onset and symptoms. Eighty-one CFS patients were enrolled, and clinical data were recorded. Autoantibodies to different components of the central nervous system were tested. Polymorphisms in the promoter of the serotonin transporter gene (I/s) and a single nucleotide polymorphism in the serotonin receptor-2A gene (A/G) as well as HLA class II alleles were determined. Multivariate logistic-regression analyses were carried out. The mean age at CFS onset +/- SD was 33.5 +/- 12.5 years. An age at CFS onset (ACFSO) during the third decade of life was associated with the serotonin receptor AA genotype and the HLA-DRB1*03 allele. An ACFSO during the fourth decade of life was associated with the HLA-DRB1*07 allele, whereas an ACFSO > or = 43 years was associated with having at least one copy of the serotonin G allele. Concerning CFS symptoms, the serotonin AG genotype was protective against depressive symptoms. Although having at least one copy of the serotonin A allele and being female were associated with risk for arthralgia, the presence of antineuronal cell antibodies was protective against this. Episodes of unexplained fever were associated with the HLA-DRB1*11 allele. None of the genetic or serological features was associated with myalgia. None of the antibodies determined correlated with any ACFSO or other symptoms. Our results reveal that in CFS, like other

				autoimmune diseases, different genetic features are related to age at CFS onset and symptoms.
Ortega-Hernandez OD, Shoenfeld Y.	Department of Internal Medicine B and Research for Autoimmune Diseases, Sheba Medical Center, Tel Hashomer, Israel.	Infection, vaccination, and autoantibodies in chronic fatigue syndrome, cause or coincidence?	Ann N Y Acad Sci. 2009 Sep;1173:600-9.	Chronic fatigue syndrome (CFS) is a heterogeneous syndrome of unknown etiology and physiopathology. CFS patients complain about disabling fatigue, depression, difficulty with memory, and concomitant skeletal and muscular pain. Interestingly enough, there is certain overlap between CFS symptoms, autoimmune rheumatic disease, and infectious diseases. Certain neuroendocrine-immune abnormalities have also been described, and autoantibodies commonly described in some autoimmune diseases have been found in CFS patients as well. An increasing number of autoantibodies, mainly directed against other nuclear cell components, have been illustrated. Likewise, an association between some infectious agents, antibody production, and later CFS onset has been reported. Similarly, vaccination is depicted as playing an important role in CFS onset. Recently, a case report pointed toward a causal association between silicone breast linkage, hepatitis B virus vaccination, and CFS onset in a previous healthy woman. Such findings suggest that there is a likely deregulation of the immune system influenced by specific agents (infections, vaccination, and products, such as silicone). Evidence suggests that CFS is a complex disease in which several risk factors might interact to cause its full expression. Thus, although different alterations have been found in CFS patients, undoubtedly the main feature is central nervous system involvement with immunological alterations. Therefore, a new term neuro-psycho-immunology must be quoted. New studies based on this concept are needed in order to investigate syndromes, such as CFS, in which immunological alterations are thought to be associated with concomitant psychological and health disturbances.
Øyane N, van den Hoven AM, Fetveit A, Pallesen S, Bjorvatn B.	Institutt for samfunnsmedisinske fag, Universitetet i Bergen og Nasjonalt kompetansesenter for søvnsykdommer, Haukeland universitetssykehus, 5021 Bergen og Bergen Søvnsenter, Norway. nicolas.oyane@isf.uib.no	[Symptom patterns in chronic sleep disorders] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2009 Oct 8;129(19):2011-4.	BACKGROUND: Sleep disorders are classified into six main categories: insomnias, circadian rhythm disorders, sleep-related movement disorders, sleep-related breathing disorders, hypersomnias and parasomnias. The aim of this article is to shed light on differences between these categories with respect to symptom patterns. MATERIAL AND METHODS: The main sources of information are the diagnosis manual published by the American Academy of Sleep Medicine in 2005 and papers identified through non-systematic searches in Pubmed. RESULTS: Long sleep onset latency is most common in patients with insomnia, delayed sleep phase syndrome and restless legs while nightly awakenings are most common in patients with insomnia, restless legs and the sleep apnoea syndrome. Excessive daytime sleepiness is most pronounced in patients with hypersomnia, sleep apnoea syndrome and delayed sleep phase syndrome, whereas patients with insomnia rarely have this problem. Fatigue is a common feature of all sleep disorders, especially insomnia. The diagnosis of insomnia, circadian rhythm disturbances, restless legs and most parasomnias is mainly based on anamnestic data. Objective sleep recordings are necessary to diagnose sleep apnoea syndrome, hypersomnia and periodic leg movement during sleep. INTERPRETATION: The six sleep disorder categories differ substantially with respect to symptom patterns. Sleep disorders can often be distinguished from each other by use of anamnestic data without resorting to further assessment, but objective sleep recordings are needed for accurate diagnosis of some patients.
Pae CU, Marks DM, Patkar AA, Masand PS, Luyten	Holy Family Hospital, The Catholic University	Pharmacological treatment of chronic fatigue	Expert Opin Pharmacother. 2009	Chronic fatigue syndrome (CFS) is characterized by chronic, medically unexplained fatigue associated with effort- and stress-intolerance, widespread pain, and impairment in sleep and concentration. Although this constellation of symptoms is highly prevalent in clinical practice, the pathophysiological

P, Serretti A.	of Korea College of Medicine, Department of Psychiatry, Bucheon 420717, Kyeonggi-Do, South Korea. pae@catholic.ac.kr	syndrome: focusing on the role of antidepressants.	Jul;10(10):1561-70.	mechanisms underlying CFS are poorly understood. Current evidence indicates similarities in symptomatology, and possibly etiology and pathogenesis, between CFS and depression. Additionally, there is significant overlap between CFS and the syndrome of fibromyalgia for which antidepressants have shown consistent efficacy. Data regarding antidepressant treatment of CFS is less copious and less uniformly positive, such that antidepressant use in CFS remains controversial. The current review aims to summarize available data related to antidepressants and other psychotropic agents in CFS to provide a platform for clinicians to make decisions in their treatment of this challenging syndrome. We identified relevant studies through a PubMed literature search with a combination of the following search terms: 'fatigue,' 'depression,' 'antidepressant,' 'etiology' (e.g., 'neurobiology,' 'neurotransmitter,' 'genetic'), 'diagnosis,' and 'treatment' (e.g., 'antidepressant' plus the specific name). In addition, studies were also identified via the reference sections of retrieved articles. The authors thoroughly reviewed major findings from the scanned literatures and eventually synthesized them, providing summary, interpretation, and future directions.
Pall ML.	The Tenth Paradigm Research Group and School of Molecular Biosciences (WSU), 638 NE 41st Ave., Portland, OR 97232-3312, USA. martin_pall@wsu.edu	Do sauna therapy and exercise act by raising the availability of tetrahydrobiopterin?	Med Hypotheses. 2009 Oct;73(4):610-3. Epub 2009 Jul 5.	Sauna therapy has been used to treat a number of different diseases known or thought to have a tetrahydrobiopterin (BH4) deficiency. It has been interpreted to act in multiple chemical sensitivity by increasing chemical detoxification and excretion but there is no evidence that this is its main mode of action. Sauna therapy may act to increase BH4 availability via two distinct pathways. Increased blood flow in heated surface tissues leads to increased vascular shear stress, inducing increased activity of GTP cyclohydrolase I (GTPCH-I) in those vascular tissues which will lead to increasing BH4 synthesis. A second mechanism involves the heat shock protein Hsp90, which is induced by even modest heating of mammalian tissues. Sauna heating of these surface tissues may act via Hsp90, which interacts with the GTPCH-I complex and is reported to produce increased GTPCH-I activity by lowering its degradation. The increased consequent availability of BH4 may lead to lowered nitric oxide synthase uncoupling, such as has been reported for the eNOS enzyme. Increased BH4 synthesis in surface tissues of the body will produce increased circulating BH4 which will feed BH4 to other body tissues that may have been BH4 deficient. Similar mechanisms may act in vigorous exercise due to the increased blood shear stresses and possibly also heating of the exercising tissues and heart. There is a large and rapidly increasing number of diseases that are associated with BH4 depletion and these may be candidates for sauna therapy. Such diseases as hypertension, vascular endothelial dysfunction, multiple chemical sensitivity and heart failure are thought to be helped by sauna therapy and chronic fatigue syndrome and fibromyalgia may also be helped and there are others that may be good candidates for sauna therapy.
Panossian A, Wikman G.	Swedish Herbal Institute Research and Development, Spårvägen 2, SE-43296 Askloster, Sweden. alexander.panossian@shi.se	Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective	Curr Clin Pharmacol. 2009 Sep;4(3):198-219. Epub 2009 Sep 1.	The aim of this review article is to assess the level of scientific evidence presented by clinical trials of adaptogens in fatigue, and to provide a rationale at the molecular level for verified effects. Strong scientific evidence is available for Rhodiola rosea SHR-5 extract, which improved attention, cognitive function and mental performance in fatigue and in chronic fatigue syndrome. Good scientific evidence has been documented in trails in which Schisandra chinensis and Eleutherococcus senticosus increased endurance and mental performance in patients with mild fatigue and weakness. Based on their efficacy in clinical studies, adaptogens can be defined as a pharmacological group of herbal preparations that increase tolerance to mental exhaustion and enhance attention and mental

		activity.		endurance in situations of decreased performance. The beneficial stress-protective effect of adaptogens is related to regulation of homeostasis via several mechanisms of action associated with the hypothalamic-pituitary-adrenal axis and the control of key mediators of stress response such as molecular chaperons (e.g. Hsp70), stress-activated c-Jun N-terminal protein kinase (JNK1), Forkhead Box O transcription factor DAF-16, cortisol and nitric oxide (NO). The key point of action of phytoadaptogens appears to be their up-regulating and stress-mimetic effects on the "stress-sensor" protein Hsp70, which plays an important role in cell survival and apoptosis. Hsp70 inhibits the expression of NO synthase II gene and interacts with glucocorticoid receptors directly and via the JNK pathway, thus affecting the levels of circulating cortisol and NO. Prevention of stress-induced increase in NO, and the associated decrease in ATP production, results in increased performance and endurance. Adaptogen-induced up-regulation of Hsp70 triggers stress-induced JNK-1 and DAF-16-mediated pathways regulating the resistance to stress and resulting in enhanced mental and physical performance and, possibly, increased longevity.
Papadopoulos A, Ebrecht M, Roberts AD, Poon L, Rohleder N, Cleare AJ.	King's College London, Institute of Psychiatry, Section of Neurobiology of Mood Disorders, Division of Psychological Medicine, London SE5 8AF, United Kingdom.	Glucocorticoid receptor mediated negative feedback in chronic fatigue syndrome using the low dose (0.5 mg) dexamethasone suppression test.	J Affect Disord. 2009 Jan;112(1-3):289-94. Epub 2008 Jun 24.	BACKGROUND: Chronic fatigue syndrome (CFS) is associated with hypocortisolism, but it is not yet clear the extent to which enhanced negative feedback may underlie this finding. METHODS: We undertook a low-dose dexamethasone (0.5 mg) suppression test in 18 CFS patients and 20 matched, healthy controls. We measured salivary cortisol levels at 0800 h, 1200 h, 1600 h and 2000 h before and after the administration of 0.5 mg of dexamethasone. RESULTS: Basal cortisol output was raised in this group of CFS patients compared to controls. Overall, the percentage suppression following dexamethasone administration was no different between CFS (mean+/-sem: 80.4+/-4.4%) and controls (76.2+/-4.9 %). However, the sub-group of patients with CFS and comorbid depression (n=9) showed a significant hypersuppression of salivary cortisol in response to dexamethasone (89.0+/-1.9%; $p<0.05$ v controls). LIMITATIONS: The sub-group analysis was on small numbers and should be considered preliminary. Dexamethasone probes only glucocorticoid medicated negative feedback but does not probe mineralocorticoid feedback, the other main physiological feedback mechanism. CONCLUSION: We found partial support for the hypothesis of enhanced negative feedback in CFS but only in patients with comorbid depression and also in the context of a sample of patients with elevated basal cortisol levels, which is an atypical finding in the literature.
Paralikar VP, Weiss MG, Agashe M, Sarmukaddam S.		Diagnosing chronic fatigue syndrome.	Br J Psychiatry. 2009 Oct;195(4):369; author reply 369-370. Comment on: Br J Psychiatry. 2009 Feb;194(2):117-22.	
Pariante CM.	Sections of Perinatal Psychiatry & Stress, Psychiatry	Chronic fatigue syndrome and the immune system: "findings in search	Brain Behav Immun. 2009 Mar;23(3):325-6. Comment on:	

	and Immunology (SPI-Lab), Institute of Psychiatry, King's College London, 125 Coldharbour Lane, London SE5 9NU, UK. c.pariante@iop.kcl.ac.uk	of meanings".	Brain Behav Immun. 2009 Mar;23(3):327-37.	
Peng H, Chen Q, Tan Y.	Laboratory Animal Center, Chongqing Medical University, No. 1, Yi Xue Yuan Road, Chongqing 400016, China.	Frequent ejaculation associated free radical and lactic acid accumulation cause noninfectious inflammation and muscle dysfunction: a potential mechanism for symptoms in Chronic Prostatitis/Chronic Pelvic Pain Syndrome.	Med Hypotheses. 2009 Sep;73(3):372-3. Epub 2009 May 10.	BACKGROUND: The prevalence of prostatitis is extremely high, with vast majority belongs to National Institutes of Health Category III: Chronic Prostatitis (CP)/Chronic Pelvic Pain Syndromes (CPPS). The etiology of CP/CPPS is noninfectious, with no precise mechanisms has been elucidated to date. HYPOTHESIS: During male ejaculation, the pelvic muscles undergo coordinated intense contraction to expel the semen out of the male genital tract, a process associated with locally increased levels of lactic acid and free radicals as byproducts. In this regards, repetitive sexual activities with frequent ejaculation would impede the drainage and cause accumulation of these byproducts in the pelvic region, triggering consequent local pathophysiological changes such as edema, venous dilation and muscular malfunction, which further leads to common complaints in CP/CPPS patients such as lower urinary tract symptoms, pelvic discomfort and pain. RATIONALE: Large cohort studies have revealed that frequent ejaculation is associated with higher risk of prostatitis, especially in young men. Also, clear evidences from sports medical research has shown that intense muscular contraction will lead to locally increased production of free radicals and lactic acid. Therefore, the pelvic muscles during ejaculation would induce substantial increase of these byproducts, which if not cleared effectively, could trigger series of local cellular/tissue damages resulting in inflammation, muscular fatigue and dysfunction. If our hypothesis were validated, it could be suggested that at least in some patients, the treatment of CP/CPPS could be tuned as dealing with post-sports recovery, such as hot bath to promote local blood circulation and free radical scavenger drugs such as vitamin C and E to neutralize free radicals.
Pietrangelo T, Mancinelli R, Toniolo L, Montanari G, Vecchiet J, Fanò G, Fulle S.	Department of Basic and Applied Medical Sciences (BAMS), Center for Excellence on Aging (CeSI), University G. d'Annunzio Chieti-Pescara, Chieti, Italy. tiziana@unich.it	Transcription profile analysis of vastus lateralis muscle from patients with chronic fatigue syndrome.	Int J Immunopathol Pharmacol. 2009 Jul-Sep;22(3):795-807.	Chronic fatigue syndrome (CFS) is a disabling condition characterized by unexplained chronic fatigue that impairs normal activities. Many body systems are affected and etiology has not yet been identified. In addition to immunological and psychological aspects, skeletal muscle symptoms are prominent in CFS patients. In an effort to establish which pathways might be involved in the onset and development of muscle symptoms, we used global transcriptome analysis to identify genes that were differentially expressed in the vastus lateralis muscle of female and male CFS patients. We found that the expression of genes that play key roles in mitochondrial function and oxidative balance, including superoxide dismutase 2, were altered, as were genes involved in energy production, muscular trophism and fiber phenotype determination. Importantly, the expression of a gene encoding a component of the nicotinic cholinergic receptor binding site was reduced, suggesting impaired neuromuscular transmission. We argue that these major biological processes could be involved in

				and/or responsible for the muscle symptoms of CFS.
Pietrangelo T, Toniolo L, Paoli A, Fulle S, Puglielli C, Fanò G, Reggiani C.	Dept. Basic and Applied Medical Sciences (BAMS), Center for Excellence on Ageing (CeSI), University - G. dAnnunzio- Chieti-Pescara, Chieti, Italy. tiziana@unich.it	Functional characterization of muscle fibres from patients with chronic fatigue syndrome: case-control study.	Int J Immunopathol Pharmacol. 2009 Apr-Jun;22(2):427-36.	Chronic fatigue syndrome (CFS) is a disabling condition characterized by unexplained chronic fatigue that impairs normal activities. Although immunological and psychological aspects are present, symptoms related to skeletal muscles, such as muscle soreness, fatigability and increased lactate accumulation, are prominent in CFS patients. In this case-control study, the phenotype of the same biopsy samples was analyzed by determining i) fibre-type proportion using myosin isoforms as fibre type molecular marker and gel electrophoresis as a tool to separate and quantify myosin isoforms, and ii) contractile properties of manually dissected, chemically made permeable and calcium-activated single muscle fibres. The results showed that fibre-type proportion was significantly altered in CSF samples, which showed a shift from the slow- to the fast-twitch phenotype. Cross sectional area, force, maximum shortening velocity and calcium sensitivity were not significantly changed in single muscle fibres from CSF samples. Thus, the contractile properties of muscle fibres were preserved but their proportion was changed, with an increase in the more fatigue-prone, energetically expensive fast fibre type. Taken together, these results support the view that muscle tissue is directly involved in the pathogenesis of CSF and it might contribute to the early onset of fatigue typical of the skeletal muscles of CFS patients.
Plastiras S, Kampessi O.	Department of Pathophysiology, University of Athens School of Medicine Laiko University Hospital, 11527 Athens Greece.	Acute lymphocytic crisis following herpes simplex type 1 virus hepatitis in a nonimmunocompromised man: a case report.	J Med Case Reports. 2009 Aug 3;3:7492.	INTRODUCTION: An increase in circulating lymphocytes can be seen following infections such as infectious mononucleosis and pertussis, or in lymphoproliferative disorders such as acute and chronic lymphocytic leukemia. Acute lymphocytic crisis following herpes simplex virus hepatitis has not been described in the literature. CASE PRESENTATION: A 52-year-old man was admitted to our hospital reporting low-grade fever for the previous seven days, and fatigue. During the fifth day of hospitalization, the patient developed a lymphocytic crisis and, after further tests the patient was diagnosed as having herpes simplex virus hepatitis. CONCLUSION: This case report shows that herpes simplex virus type 1 is a possible cause of an acute lymphocytic crisis similar to other well known infectious agents such as Epstein-Barr virus, cytomegalovirus, human immunodeficiency virus, human herpes virus type 6, adenovirus, toxoplasma and human T-cell lymphotropic virus. Furthermore, this case report expands the clinical spectrum of herpes simplex virus hepatitis, since it is reported in a nonimmunocompromised patient presenting with atypical acute lymphocytic syndrome.
Podolecki T, Podolecki A, Hrycek A.	Independent Public Central Clinical Hospital, Katowice, Poland. tomekpod@interia.pl	Fibromyalgia: pathogenetic, diagnostic and therapeutic concerns.	Pol Arch Med Wewn. 2009 Mar;119(3):157-61.	Musculoskeletal pains are one of the most common complaints reported by patients. In 1972, Smythe described the generalized pain and tenderness on palpation at specific points and, 4 years later, the term fibromyalgia was introduced for determining the disease syndrome. The etiology and pathogenesis of fibromyalgia are still unknown. This disease appears probably multi-factorial. It is considered that the changes in the neuronal activity in the central nervous system, abnormal metabolism of biogenic amines and immunological disorders may among other things, contribute to the development of the disease. The complaints are non characteristic and highly sujective, which makes it substantially difficult to differentiate between fibromialgia and both chronic fatigue syndrome and psychosomatic diseases. The treatment of fibromyalgia is complex and long-term. The antidepressants and psychotherapy is of vital importance. The effectiveness of locally used agents is also being emphasized. Fibromyalgia has become a serious social problem in the well developed countries in the recent years. Therefore, of importance are efforts to appropriately diagnose

				fibromyalgia and to implement its appropriate treatment that resolves disease symptoms in a possibly maximum degree.
Puri BK, Agour M, Gunatilake KD, Fernando KA, Gurusinghe AI, Treasaden IH.	MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College School of Medicine, Hammersmith Hospital, Du Cane Road, London W12 0HS, England, UK. basant.puri@imperial.ac.uk	An in vivo proton neurospectroscopy study of cerebral oxidative stress in myalgic encephalomyelitis (chronic fatigue syndrome).	Prostaglandins Leukot Essent Fatty Acids. 2009 Nov-Dec;81(5-6):303-5. Epub 2009 Nov 10.	A particularly important family of antioxidant defence enzymes in the body are the glutathione peroxidases, which remove H(2)O(2) by coupling its reduction to H(2)O with oxidation of reduced glutathione (GSH) to oxidised glutathione (GSSG). There are suggestions that GSH in the peripheral blood may be reduced in myalgic encephalomyelitis, which is a highly disabling neurological disease of unknown aetiology. Since many of the symptoms relate to cerebral functioning, it would seem probable that peripheral blood GSH findings would be reflected in lower cerebral GSH levels. The aim of this study was to carry out the first direct assessment of cerebral GSH levels in myalgic encephalomyelitis; the hypothesis being tested was that cerebral GSH levels would be reduced in myalgic encephalomyelitis. Cerebral proton neurospectroscopy was carried out at a magnetic field strength of 3T in 26 subjects; spectra were obtained from 20x20x20mm(3) voxels using a point-resolved spectroscopy pulse sequence. The mean cerebral GSH level in the myalgic encephalomyelitis patients was 2.703 (SD 2.311) which did not differ significantly from that in age- and gender-matched normal controls who did not have any history of neurological or other major medical disorder (5.191, SD 8.984; NS). Therefore our study does not suggest that GSH is reduced in the brain in myalgic encephalomyelitis. At the present time, based on the results of this study, there is no evidence to support the suggestion that, by taking glutathione supplements, an improvement in the brain-related symptomatology of myalgic encephalomyelitis may occur.
Puri BK, Tsaluchidu S, Treasaden IH.	MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College London, Hammersmith Hospital, London, UK. basant.puri@csc.mrc.ac.uk	Serial structural MRI analysis and proton and 31PMR spectroscopy in the investigation of cerebral fatty acids in major depressive disorder, Huntington's disease, myalgic encephalomyelitis and in forensic schizophrenic patients.	World Rev Nutr Diet. 2009;99:31-45. Epub 2009 Jan 9.	
Quillinan N, Mohammad A, Mannion G, O'Keeffe D, Bergin D, Coughlan R, Mc Dermott MF,	1 Department of Rheumatology, Merlin Park Hospital (Galway University Hospital),	Imaging evidence for persistent subclincal fasciitis and arthritis in TNF Receptor-Associated	Ann Rheum Dis. 2009 Nov 12. [Epub ahead of print]	TNF Receptor-Associated Periodic Syndrome (TRAPS) [1], formerly known as familial Hibernian fever (FHF) [2, 3] is an archetypal hereditary periodic fever syndrome and is an autosomal dominant condition characterised by mutations in the TNFRSF1A gene [4, 5]. Periodicity of fevers is typical of TRAPS with peritonitis, arthritis and fasciitis. It is also well recognised that some patients continue to feel unwell between attacks. That subclincal TRAPS is still ongoing in such circumstances is supported by persistent acute phase response [6, 7]. There are no specific features to localise a site for this

McGonagle D.	Renmore, Galway, Ireland;	Periodic Syndrome (TRAPS) between febrile attacks.		persistent inflammatory response and, to date, no studies have been done to investigate this interesting observation. Whole body magnetic resonance imaging (MRI) has recently been introduced for the assessment of various skeletal pathologies including malignancy, myositis and arthritis [8-12]. MRI in inflammatory disorders has the capacity to show both soft tissue inflammatory changes and osteitis. We hypothesised that patients with TRAPS without obvious clinical manifestations and the absence of fevers have subclincal disease affecting the anatomical territories that are prone to inflammation during acute attacks. Herein, we confirm that some cases of TRAPS do indeed have ongoing soft tissue and joint inflammation between attacks. Given that autoinflammatory disorders, like TRAPS, are diseases of the innate immune system, these findings support the concept of persistent innate immune activation between attacks. The Galway (Ireland) TRAPS cohort consists of 15 affected family members, 2 of whom have amyloidosis and all having the T50M mutation in the TNFRSF1A gene [13]. A total of 9 members of this family attend the clinic regularly. Persistently raised inflammatory markers were found in 7 of these patients, 2 members did not give consent for MRI due to claustrophobia. A total of 5 members participated in the study, however during the course of the study; one of these patients had normal inflammatory markers in spite of having persistently raised markers before screening. Interview and clinical examination were performed to document symptoms, frequency of flares, inflammatory markers and medications (Table 1). All cases described classical attacks of fever, sweats, abdominal pain and serositis. They also had symptoms between attacks including prominent myalgia, arthralgia, malaise and fatigue, with persistently elevated inflammatory markers in 4 out of 5 patients confirming ongoing disease activity between attacks. After obtaining informed consent, all 5 cases had whole body scanning on a Siemens 1.5 T MRI (Siemens-AG, Symphony). Images were reviewed on Agfa PACS High resolution workstation by two fellowship trained musculoskeletal radiologists. One patient had a flare during the MRI and was rescanned between flares. MRI results are shown in Table 1. Bilateral knee and hip effusions and bone oedema of left tibia were found in one patient, who was asymptomatic at the time of his scan and did not have osteoarthritis clinically or radiologically in this knee. Repeat MRI of the left knee was done. It is possible that the knee changes could have been contributed to by ligament injury and joint degeneration that was asymptomatic. Only one MRI of 5 was completely normal with corresponding normal inflammatory markers (Figure 1). In conclusion, we provide MRI evidence for persistent subclinical tissue inflammation in an identical pattern to that seen during classical attacks of TRAPS. This suggests that the innate immune driven pathology is actually chronic and most likely represents recurrent acute attacks of subclinical tissue inflammation. Unlike some other conditions of chronic innate immune activation including Blau syndrome, the inflammation in TRAPS does not appear to lead to target organ destruction [14]. The utility of whole body MRI for exploring febrile illness with a TRAPS phenotype without TNFRS1A mutations is also worthy of consideration.
Raison CL, Lin JM, Reeves WC.	Department of Psychiatry and Behavioral Sciences, Emory University School	Association of peripheral inflammatory markers with chronic fatigue in a	Brain Behav Immun. 2009 Mar;23(3):327-37. Epub 2008 Dec 11.	Alterations in the innate immune response may contribute to the pathogenesis of chronic fatigue syndrome (CFS). However, studies have been limited by small sample sizes, use of patients from tertiary care settings, inappropriate selection of controls, and failure to control for confounding demographic, medical and behavioral factors independently associated with immune activity. It is also not known whether specific symptoms account for observed associations between CFS and the

	of Medicine, 1365C Clifton Road, Room 5004, Atlanta, GA 30322, USA. craison@emory.edu	population-based sample.Comment in: Brain Behav Immun. 2009 Mar;23(3):325-6.		innate immune response. To address these limitations, the current study examined plasma concentrations of high-sensitivity c-reactive protein (hs-CRP), white blood cell count (WBC) and a combined inflammation factor in a large population-based sample. Log-transformed mean plasma concentrations of hs-CRP were increased in subjects with CFS (n=102) and in subjects with unwellness symptoms that did not meet diagnostic criteria for CFS (defined as "insufficient fatigue" [ISF]) (n=240) when compared to subjects who were well (n=115). Log transformed WBC was increased in ISF and was increased at a trend level in CFS. The combined inflammation factor was increased in both CFS and ISF. Subjects with CFS and ISF did not differ on any of the inflammation measures. In the entire subject population, the physical component summary score (PCS), but not the mental component summary score (MCS), from the Medical Outcomes Study Short Form-36 (SF-36) was negatively associated with each of the inflammation measures. Depressive symptoms were also associated with increased log hs-CRP. After adjustment for age, sex, race, location of residence, BMI, depressive status and immune-modulating medications, subjects classified as ISF continued to demonstrate increased log hs-CRP, WBC and elevations on the inflammation factor when compared to well controls; however, associations between CFS and log hs-CRP and the inflammation factor were no longer statistically significant. After adjustment, PCS score also remained independently associated with each of the inflammation measures. These findings support a role for innate immune activation in unexplained fatigue and unwellness, but do not suggest that immune activation is specific to CFS.
Ramdharry GM, Day BL, Reilly MM, Marsden JF.	St. George's School of Physiotherapy Kingston University, London, UK.	Hip flexor fatigue limits walking in Charcot-Marie-Tooth disease.	Muscle Nerve. 2009 Jul;40(1):103-11.	Charcot-Marie-Tooth (CMT) disease results in distal lower limb weakness that affects walking. In this study we assess the role of the hip flexors in compensating for distal weakness while walking and the effects of prolonged walking on these putative compensatory strategies. Eighteen subjects with CMT disease were compared with 14 matched controls while they walked on a treadmill to a predetermined point of perceived effort. A significant reduction was observed in peak hip flexor velocity during walking and hip flexor maximal voluntary contraction. In a second session following selective fatigue of the hip flexors, hip flexor velocity decreased immediately on walking, and walking duration was greatly reduced. This study suggests that hip flexors compensate for distal weakness and that fatigue in the hip flexors can limit walking duration. Treatments directed toward improving proximal muscle strength may therefore help to delay onset of hip flexor fatigue and thus prolong walking duration.
Rao AV, Bested AC, Beaulne TM, Katzman MA, Iorio C, Berardi JM, Logan AC.	Integrative Care Centre of Toronto, 3600 Ellesmere Road, Unit 4, Toronto, Ontario M1C 4Y8, Canada. aclnd@cfs-fm.org.	A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome.	Gut Pathog. 2009 Mar 19;1(1):6.	ABSTRACT: Chronic fatigue syndrome (CFS) is complex illness of unknown etiology. Among the broad range of symptoms, many patients report disturbances in the emotional realm, the most frequent of which is anxiety. Research shows that patients with CFS and other so-called functional somatic disorders have alterations in the intestinal microbial flora. Emerging studies have suggested that pathogenic and non-pathogenic gut bacteria might influence mood-related symptoms and even behavior in animals and humans. In this pilot study, 39 CFS patients were randomized to receive either 24 billion colony forming units of Lactobacillus casei strain Shirota (LcS) or a placebo daily for two months. Patients provided stool samples and completed the Beck Depression and Beck Anxiety Inventories before and after the intervention. We found a significant rise in both Lactobacillus and Bifidobacteria in those taking the LcS, and there was also a significant decrease in anxiety symptoms among those taking the probiotic vs controls (p = 0.01). These results lend further support to the

				presence of a gut-brain interface, one that may be mediated by microbes that reside or pass through the intestinal tract.
Revicki DA, Rentz AM, Luo MP, Wong RL, Doward LC, McKenna SP.	Center for Health Outcomes Research, United Biosource Corporation, Bethesda, MD, USA. carrie.bray@jkmed.com	Retraction. Psychometric characteristics of the ankylosing spondylitis quality of life questionnaire, short form 36 health survey, and functional assessment of chronic illness therapy-fatigue subscale.	Health Qual Life Outcomes. 2009 Jan 30;7:6.	
Reynolds NL, Brown MM, Jason LA.	DePaul University.	The relationship of Fennell phases to symptoms among patients with chronic fatigue syndrome.	Eval Health Prof. 2009 Sep;32(3):264-80. Epub 2009 Aug 20.	The Fennell Phase Inventory (FPI) is an instrument designed to measure phases of the illnesses known as Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). The current study explored how the FPI was related to physical and psychological functioning as well as coping style. Based on FPI scores, 111 adults with ME/CFS were placed in one of three groups: crisis, stabilization, or resolution. Results showed that the crisis group demonstrated significantly worse functioning than at least one other group for depression, quality of life, mental functioning, anxiety, and self-efficacy; and utilized less adaptive coping styles. These results indicate that patients with ME/CFS who are in the crisis phase tend to experience more severe psychological and physical symptoms and utilize poorer coping strategies. Those in the resolution phase maintain the most adaptive coping strategies. Implications for these findings are discussed.
Roberts AD, Charler ML, Papadopoulos A, Wessely S, Chalder T, Cleare AJ.	King's College London, Institute of Psychiatry, Department of Psychological Medicine, London, UK.	Does hypocortisolism predict a poor response to cognitive behavioural therapy in chronic fatigue syndrome?	Psychol Med. 2009 Jul 17:1-8. [Epub ahead of print]	BACKGROUND: There is evidence that patients with chronic fatigue syndrome (CFS) have mild hypocortisolism. The clinical significance of this is unclear. We aimed to determine whether hypocortisolism exerted any effect on the response of CFS to cognitive behavioural therapy (CBT).MethodWe measured 24-h urinary free cortisol (UFC) in 84 patients with Centers for Disease Control and Prevention (CDC)-defined CFS (of whom 64 were free from psychotropic medication) who then received CBT in a specialist, tertiary out-patient clinic as part of their usual clinical care. We also measured salivary cortisol output from 0800 to 2000 h in a subsample of 56 psychotropic medication-free patients. RESULTS: Overall, 39% of patients responded to CBT after 6 months of treatment. Lower 24-h UFC output was associated with a poorer response to CBT but only in psychotropic medication-free patients. A flattened diurnal profile of salivary cortisol was also associated with a poor response to CBT. CONCLUSIONS: Low cortisol is of clinical relevance in CFS, as it is associated with a poorer response to CBT. Hypocortisolism could be one of several maintaining factors that interact in the persistence of CFS.
Roberts AD,	King's College	Salivary cortisol	J Affect Disord.	BACKGROUND: There is evidence that patients with chronic fatigue syndrome (CFS) have mild

Papadopoulos AS, Wessely S, Chalder T, Cleare AJ.	London, Institute of Psychiatry, Department of Psychological Medicine, De Crespigny Park, London SE5 8AF, UK.	output before and after cognitive behavioural therapy for chronic fatigue syndrome.	2009 May;115(1-2):280-6. Epub 2008 Oct 19.	hypocortisolism. One theory about the aetiology of this hypocortisolism is that it occurs late in the course of CFS via factors such as inactivity, sleep disturbance, chronic stress and deconditioning. We aimed to determine whether therapy aimed at reversing these factors--cognitive behavioural therapy for CFS--could increase cortisol output in CFS. METHODS: We measured diurnal salivary cortisol output between 0800 and 2000 h before and after 15 sessions (or 6 months) of CBT in 41 patients with CDC-defined CFS attending a specialist, tertiary outpatient clinic. RESULTS: There was a significant clinical response to CBT, and a significant rise in salivary cortisol output after CBT. LIMITATIONS: We were unable to control for the passage of time using a non-treated CFS group. CONCLUSIONS: Hypocortisolism in CFS is potentially reversible by CBT. Given previous suggestions that lowered cortisol may be a maintaining factor in CFS, CBT offers a potential way to address this.
Robinson M, Gray SR, Watson MS, Kennedy G, Hill A, Belch JJ, Nimmo MA.	Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK.	Plasma IL-6, its soluble receptors and F-isoprostanes at rest and during exercise in chronic fatigue syndrome.	Scand J Med Sci Sports. 2009 Apr 13. [Epub ahead of print]	The aim of the current study was to investigate the levels of interleukin-6 (IL-6), its soluble receptors (sIL-6R and sgp130) and F(2)-isoprostanes, at rest and during exercise, in patients with chronic fatigue syndrome (CFS). Six male CFS patients and six healthy controls performed an incremental exercise test to exhaustion and a submaximal exercise bout to exhaustion. Blood samples taken in the submaximal test at rest, immediately post-exercise and 24 h post-exercise were analyzed for IL-6, sIL-6R, sgp130 and F(2)-isoprostanes. A further 33 CFS and 33 healthy control participants gave a resting blood sample for IL-6 and sIL-6R measurement. During the incremental exercise test only power output at the lactate threshold was lower ($P<0.05$) in the CFS group. F(2)-isoprostanes were higher ($P<0.05$) in CFS patients at rest and this difference persisted immediately and 24 h post-exercise. The exercise study found no differences in IL-6, sIL-6R or sgp130 at any time point between groups. In the larger resting group, there were no differences in IL-6 and sIL-6R between CFS and control groups. This investigation has demonstrated that patients with CFS do not have altered plasma levels of IL-6, sIL-6R or sgp130 either at rest or following exercise. F(2)-isoprostanes, however, were consistently higher in CFS patients.
Rodríguez MA, Afari N, Buchwald DS; National Institute of Diabetes and Digestive and Kidney Diseases Working Group on Urological Chronic Pelvic Pain. Collaborators: Afari N, Buchwald DS, Clauw D, Dimitrakov J, Kusek J, Mullins C, Nyberg L, Payne C,	Department of Psychology, University Rey Juan Carlos, Madrid, Spain.	Evidence for overlap between urological and nonurological unexplained clinical conditions.	J Urol. 2009 Nov;182(5):2123-31. Epub 2009 Sep 16.	PURPOSE: Unexplained clinical conditions share common features such as pain, fatigue, disability out of proportion to physical examination findings, inconsistent laboratory abnormalities, and an association with stress and psychosocial factors. We examined the extent of the overlap among urological and nonurological unexplained clinical conditions characterized by pain. We describe the limitations of previous research and suggest several possible explanatory models. MATERIALS AND METHODS: Using hallmark symptoms and syndromes as search terms a search of 12 databases identified a total of 1,037 full-length published articles in 8 languages from 1966 to April 2008. The search focused on the overlap of chronic pelvic pain, interstitial cystitis, painful bladder syndrome, chronic prostatitis/chronic pelvic pain syndrome or vulvodynia with fibromyalgia, chronic fatigue syndrome, temporomandibular joint and muscle disorders or irritable bowel syndrome. We abstracted information on authorship, type of case and control groups, eligibility criteria, case definitions, study methods and major findings. RESULTS: The literature suggests considerable comorbidity between urological and nonurological unexplained clinical conditions. The most robust evidence for overlap was for irritable bowel syndrome and urological unexplained syndromes with some estimates of up to 79% comorbidity between chronic pelvic pain and symptoms of irritable bowel syndrome. However, most studies were limited by methodological problems, such as varying

Peñacoba C, Pezzone M, Pontari M, Potts J, Rodríguez MA, Warren J.				case definitions and selection of controls. CONCLUSIONS: The overlap between urological and selected nonurological unexplained clinical conditions is substantial. Future research should focus on using standardized definitions, and rigorously designed, well controlled studies to further assess comorbidity, clarify the magnitude of the association and examine common pathophysiological mechanisms.
Romano JM, Jensen MP, Schmaling KB, Hops H, Buchwald DS.	Department of Psychiatry and Behavioral Sciences, University of Washington, Box 356560, Seattle, WA, 98195, USA, jromano@u.washington.edu.	Illness behaviors in patients with unexplained chronic fatigue are associated with significant other responses.	J Behav Med. 2009 Nov 14. [Epub ahead of print]	Chronic fatigue syndrome (CFS) and unexplained chronic fatigue (CF) are characterized by compromised functional status and physical disability. Prior research on chronic pain has suggested that social factors may contribute to disability. This study examined the relationship between significant other responses and patient outcomes in patients with unexplained CF. Questionnaire data were collected from 117 patients on physical function, fatigue, pain, illness behaviors and responses of significant others to them, and depression. Ninety-four SOs reported their perceptions of patient illness behavior and their responses. Thirty-seven of these dyads also completed a series of household activities while being videotaped. Dyadic interactions were coded and analyzed. Both reported and observed solicitous responses by the significant other were associated with reported and observed patient illness behavior. Negative responses to patient illness behavior by significant others were associated with higher levels of patient depressive symptoms. The findings provide support for the role of operant behavioral factors in the context of chronic fatigue. They also suggest that further research on the relationship between dysfunction and significant other responses in patients with CFS or CF appears warranted and may have implications for treatment development.
Rudolph T, Larsen JP, Farbu E.	Department of Neurology, Stavanger University Hospital, Stavanger, Norway. mokum99@online.no	Is there a need for long-term follow-up in chronic idiopathic polyneuropathy?	Acta Neurol Scand. 2009 Nov;120(5):347-52. Epub 2009 Sep 10.	OBJECTIVE: To evaluate the long-term functional status and well-being in patients with chronic idiopathic polyneuropathy (CIP) in comparison to Guillain-Barré syndrome (GBS) and healthy controls. MATERIALS AND METHODS: Forty-two CIP and 42 GBS-patients were examined at median 5 and 6 years after disease onset and were compared with 50 healthy controls. The Fatigue Severity Scale (FSS), Visual Analogue Scale for pain (VAS), Disability Rating Index (DRI) and Medical Outcome Study 36-item short-form health status scale (SF-36) were used. Variables at onset and symptoms at follow-up were correlated with outcome measurements in GBS. RESULTS: Patients with CIP and GBS had more pain and disability than healthy controls. Additionally, CIP-patients were more fatigued than healthy controls. Patients with CIP were more fatigued [FSS 4.9 (SD 1.6) vs 3.8 (SD 1.8); $P < 0.01$] and disabled [DRI 4.1 (SD 2.3) vs 2.5 (SD 2.1); $P = 0.05$] than those with GBS. Physical functioning on the SF-36 was more impaired in CIP than GBS, compared with healthy controls. CONCLUSIONS: Patients with CIP and GBS seem to develop persistent impairment on long-term functional status and well-being, more clearly in CIP, reflecting the importance of long-term follow-up in further disease management.
Sachdeva AK, Kuhad A, Tiwari V, Chopra K.	Pharmacology Research Laboratory, University Institute of Pharmaceutical Sciences, UGC Centre of Advanced Study,	Epigallocatechin gallate ameliorates chronic fatigue syndrome in mice: behavioral and biochemical evidence.	Behav Brain Res. 2009 Dec 28;205(2):414-20. Epub 2009 Jul 28.	Three decades after the coining of the term chronic fatigue syndrome, the diagnosis of this illness is still symptom based and the aetiology remains elusive. Chronic fatigue syndrome pathogenesis seems to be multifactorial and the possible involvement of immune system is supported. The present study was designed to evaluate the effects of the epigallocatechin gallate in a mouse model of immunologically induced chronic fatigue. On 19th day, after lipopolysaccharide/Brucella abortus administration, the mice showed significant increase in immobility period, post swim fatigue and thermal hyperalgesia. Behavioral deficits were coupled with enhanced oxidative-nitrosative stress as evident by increased lipid peroxidation, nitrite levels and decreased endogenous antioxidant enzymes

	Punjab University, Chandigarh 160 014, India.			(superoxide dismutase, reduced glutathione and catalase) and inflammation (increased levels of tumor necrosis factor-alpha and tissue growth factor-beta). Chronic treatment with epigallocatechin gallate restored these behavioral and biochemical alterations in mice. The present study points out towards the beneficial effect of epigallocatechin gallate in the amelioration of chronic fatigue syndrome and thus may provide a new, effective and powerful strategy to treat chronic fatigue syndrome.
Sakudo A, Kato YH, Tajima S, Kuratsune H, Ikuta K.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University, Yamadaoka, Suita, Osaka 565-0871, Japan. sakudo@biken.osaka-u.ac.jp	Visible and near-infrared spectral changes in the thumb of patients with chronic fatigue syndrome.	Clin Chim Acta. 2009 May;403(1-2):163-6. Epub 2009 Feb 25.	BACKGROUND: Chronic fatigue syndrome (CFS) patients show a persistent fatigue condition with muscle pain and impairment of concentration, memory, and sleep. Presently, the physiological basis of CFS remains unclear. In this study, spectroscopic differences in the thumb were compared between 103 CFS patients and 122 healthy controls to examine possible changes of levels of oxygenated or deoxygenated hemoglobin. METHODS: Visible and near-infrared (Vis-NIR) spectroscopy was used to examine possible changes in the region of 600-1100 nm. RESULTS: Vis-NIR spectra showed sharp peaks at 694, 970 and 1060 nm and broad peaks in the regions of 740-760 and 830-850 nm. As these peaks are possibly related to oxyhemoglobin, cytochrome c oxidase and water, levels of these factors were compared between the two groups. Statistical analysis of the absorbance of Vis-NIR spectra showed a significant decrease in water content, a significant increase in oxyhemoglobin content, and a significant increase in the oxidation of heme a+a(3) and copper in cytochrome c oxidase in CFS patients. CONCLUSIONS: These changes imply accelerated blood flow and energy metabolism in the thumbs of CFS patients.
Sakudo A, Kuratsune H, Kato YH, Ikuta K.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University, Yamadaoka, Suita, Osaka 565-0871, Japan. sakudo@biken.osaka-u.ac.jp	Secondary structural changes of proteins in fingernails of chronic fatigue syndrome patients from Fourier-transform infrared spectra.	Clin Chim Acta. 2009 Apr;402(1-2):75-8. Epub 2008 Dec 30.	BACKGROUND: Generally, nails can be an index of health, with abnormalities sometimes found under diseased conditions. Fatigue is also supposed to affect the condition of nails. Possible differences in infrared (IR) spectra of nail plates of chronic fatigue syndrome (CFS) patients compared to healthy control subjects were investigated in this study. METHODS: Using an attenuated total reflection (ATR)-Fourier-transform infrared (FTIR) spectrophotometer, spectra in the region of 4000-600 cm(-1) were obtained. The amide I region was then separated by Fourier deconvolution and curve fitting based on the Gauss and Lorentz formula and revealed differences in the secondary structural content of proteins compared to healthy donors. RESULTS: The specific secondary structural pattern commonly observed in nails of male and female CFS patients in the absence and presence of medication indicated a decreased alpha-helix content and increased beta-sheet content, suggesting reduced levels of normal elements of the nail plate. CONCLUSIONS: This provides the first evidence of alterations in the fingernails of CFS patients which could be detected by IR spectroscopy. Possible explanations for the alterations will be discussed.
Sampogna F, Frontani M, Baliva G, Lombardo GA, Alvetreti G, Di Pietro C, Tabolli S, Russo G, Abeni D.	Health Services Research Unit, Instituto Dermopatico dell'Immacolata, Rome, Italy.	Quality of life and psychological distress in patients with cutaneous lymphoma.	Br J Dermatol. 2009 Apr;160(4):815-22. Epub 2008 Dec 16.	BACKGROUND: Cutaneous lymphomas may have a profound impact on patients' health-related quality of life (HRQoL) and psychological well-being. OBJECTIVES: To evaluate HRQoL and psychological distress in patients with cutaneous lymphoma, and to evaluate them in relation to personal and clinical characteristics. METHODS: Patients with cutaneous T-cell lymphoma or cutaneous B-cell lymphoma (CBCL) were consecutively recruited in a dermatological hospital. Data on HRQoL were collected using a dermatology-specific questionnaire, the Skindex-29, and an oncology-specific questionnaire, the EORTC QLQ-C30. RESULTS: Of 95 patients, there were 24 with CBCL, 59 with mycosis fungoides (MF) and 12 with Sézary syndrome (SS). The most frequent items reported in

				Skindex-29 were itching and sensitive skin, being annoyed by the disease, worry that it could get worse, affected interactions, and impairment in sexual life. The most frequent problems appearing from the EORTC QLQ-C30 analysis were fatigue, pain and insomnia. A worse HRQoL was observed for all the scales in patients with SS, followed by MF, and CBCL. HRQoL impairment in all histotypes was higher in women than in men, in patients with probable anxiety or depression, and when the disease worsened. The highest prevalence of probable anxiety or depression was observed in patients treated with systemic steroids (60%) and interferon (50%). CONCLUSIONS: The detailed evaluation of HRQoL and psychological problems in patients with cutaneous lymphomas, and their relationship with clinical variables, may give important information on the burden of the disease for patients, and thus improve communication and satisfaction with care.
Santhouse AM.	South London and Maudsley NHS Foundation Trust, London, UK.	Review: CBT reduces fatigue in adults with chronic fatigue syndrome but effects at follow-up unclear.Comment on: Cochrane Database Syst Rev. 2008;(3):CD001027 .	Evid Based Ment Health. 2009 Feb;12(1):16.	
Scheeres K, Knoop H, Meer J, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre (4628), PO Box 9101, 6500 HB Nijmegen, The Netherlands. korinescheeres@gmail.com	Clinical assessment of the physical activity pattern of chronic fatigue syndrome patients: a validation of three methods.	Health Qual Life Outcomes. 2009 Apr 1;7:29.	BACKGROUND: Effective treatment of chronic fatigue syndrome (CFS) with cognitive behavioural therapy (CBT) relies on a correct classification of so called 'fluctuating active' versus 'passive' patients. For successful treatment with CBT is it especially important to recognise the passive patients and give them a tailored treatment protocol. In the present study it was evaluated whether CFS patient's physical activity pattern can be assessed most accurately with the 'Activity Pattern Interview' (API), the International Physical Activity Questionnaire (IPAQ) or the CFS-Activity Questionnaire (CFS-AQ). METHODS: The three instruments were validated compared to actometers. Actometers are until now the best and most objective instrument to measure physical activity, but they are too expensive and time consuming for most clinical practice settings. In total 226 CFS patients enrolled for CBT therapy answered the API at intake and filled in the two questionnaires. Directly after intake they wore the actometer for two weeks. Based on receiver operating characteristic (ROC) curves the validity of the three methods were assessed and compared. RESULTS: Both the API and the two questionnaires had an acceptable validity (0.64 to 0.71). None of the three instruments was significantly better than the others. The proportion of false predictions was rather high for all three instrument. The IPAQ had the highest proportion of correct passive predictions (sensitivity 70.1%). CONCLUSION: The validity of all three instruments appeared to be fair, and all showed rather high proportions of false classifications. Hence in fact none of the tested instruments could really be called satisfactory. Because the IPAQ showed to be the best in correctly predicting 'passive' CFS patients, which is most essentially related to treatment results, it was concluded that the IPAQ is the preferable alternative for an actometer

				when treating CFS patients in clinical practice.
Schrijvers D, Van Den Eede F, Maas Y, Cosyns P, Hulstijn W, Sabbe BG.	Collaborative Antwerp Psychiatric Research Institute, Faculty of Medicine, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium. didier.schrijvers@ua.ac.be	Psychomotor functioning in chronic fatigue syndrome and major depressive disorder: a comparative study.	J Affect Disord. 2009 May;115(1-2):46-53. Epub 2008 Sep 24.	BACKGROUND: Studies comparing chronic fatigue syndrome (CFS) and major depressive disorder (MDD) reported similarities as well as differences between the two disorders. However, whereas psychomotor symptoms have been studied extensively in MDD, such research in CFS is more limited. Moreover, the few studies that compared cognitive and motor performance in MDD and CFS yielded inconsistent results. This study hence directly compares fine psychomotor functioning in both syndromes. METHODS: Thirty-eight patients diagnosed with CFS without a current major depressive episode (MDE), 32 MDD patients with a current MDE and 38 healthy controls performed two computerized copying tasks differing in complexity: a line-copying task that mainly requires motor effort and a figure-copying task requiring additional cognitive efforts. All participants were female. A multivariate general linear model was used to compute group differences. RESULT: Overall, both patient groups performed more slowly than the controls. Compared to CFS patients, patients with MDD needed significantly more time to copy the single lines but no such between-group performance difference was observed for the figure reproductions. In this latter copying task, the increasing complexity of the figures resulted in prolonged reaction times for all three participant groups with the effect being larger and the magnitude similar for the two patient groups. LIMITATIONS: All patients were female and most were on psychotropic medication. CONCLUSIONS: Both the MDD and CFS patients tested demonstrated an overall fine motor slowing, with the motor component being more affected in the MDD patients than in the CFS patients while both patient groups showed similar cognitive impairments.
Shapiro JS.	shapirjs@umich.edu	Does varicella-zoster virus infection of the peripheral ganglia cause Chronic Fatigue Syndrome?	Med Hypotheses. 2009 Nov;73(5):728-34. Epub 2009 Jun 10.	This article posits that infection of the peripheral ganglia causes at least some cases of Chronic Fatigue Syndrome (CFS), with a neurotropic herpesvirus, particularly varicella-zoster virus (VZV), as the most likely cause of the infection. Virtually all CFS symptoms could be produced by an infection of the peripheral ganglia, with infection of the autonomic ganglia causing fatigue, postural hypotension, and sleep disturbances, and infection of the sensory ganglia causing sensory symptoms such as chronic pain. Furthermore, infections of the peripheral ganglia are known to cause long-term nerve dysfunction, which would help explain the chronic course of CFS. Herpesviruses have long been suspected as the cause of CFS; this theory has recently been supported by studies showing that administering antiherpes agents causes substantial improvement in some CFS patients. VZV is known to frequently reactivate in the peripheral ganglia of previously healthy adults and cause sudden, debilitating illness, making it a likely candidate as a cause of CFS. Moreover, many of the symptoms of CFS overlap with those of herpes zoster (shingles), with the exception that painful rash is not one of the symptoms of CFS. A model is therefore proposed in which CFS is one of the many manifestations of zoster sine herpete; that is, herpes zoster without rash. Furthermore, re-exposure to VZV in the form of chickenpox has become less common in the past few decades; without such re-exposure, immunity to VZV drops, which could explain the increased incidence of CFS. Co-infection with multiple herpesviruses is a possibility, as some CFS patients show signs of infection with other herpesviruses including Epstein-Barr, Cytomegalovirus, and HHV6. These three herpesviruses can attack immune cells, and may therefore promote neurotropic herpesvirus reactivation in the ganglia. The possibility of VZV as the causal agent in CFS has previously received almost no attention; the possibility that CFS

				involves infection of the peripheral ganglia has likewise been largely overlooked. This suggests that the search for a viral cause of CFS has been far from exhaustive. Several antiherpes drugs are available, as is a vaccine for VZV; more research into such agents as possible treatments for CFS is urgently needed.
Sheedy JR, Wettenhall RE, Scanlon D, Gooley PR, Lewis DP, McGregor N, Stapleton DI, Butt HL, DE Meirleir KL.	Bio21 Institute of Biotechnology and Molecular Science, Department of Biochemistry and Molecular Biology, Victoria, Australia.	Increased d-lactic Acid intestinal bacteria in patients with chronic fatigue syndrome.	In Vivo. 2009 Jul-Aug;23(4):621-8.	Patients with chronic fatigue syndrome (CFS) are affected by symptoms of cognitive dysfunction and neurological impairment, the cause of which has yet to be elucidated. However, these symptoms are strikingly similar to those of patients presented with D-lactic acidosis. A significant increase of Gram positive facultative anaerobic faecal microorganisms in 108 CFS patients as compared to 177 control subjects ($p<0.01$) is presented in this report. The viable count of D-lactic acid producing Enterococcus and Streptococcus spp. in the faecal samples from the CFS group (3.5 x 10(7) cfu/L and 9.8 x 10(7) cfu/L respectively) were significantly higher than those for the control group (5.0 x 10(6) cfu/L and 8.9 x 10(4) cfu/L respectively). Analysis of exometabolic profiles of Enterococcus faecalis and Streptococcus sanguinis, representatives of Enterococcus and Streptococcus spp. respectively, by NMR and HPLC showed that these organisms produced significantly more lactic acid ($p<0.01$) from (13)C-labeled glucose, than the Gram negative Escherichia coli. Further, both E. faecalis and S. sanguinis secrete more D-lactic acid than E. coli. This study suggests a probable link between intestinal colonization of Gram positive facultative anaerobic D-lactic acid bacteria and symptom expressions in a subgroup of patients with CFS. Given the fact that this might explain not only neurocognitive dysfunction in CFS patients but also mitochondrial dysfunction, these findings may have important clinical implications.
Sheng R, Xu X, Tang Q, Bian D, Li Y, Qian C, He X, Gao X, Pan R, Wang C, Luo Y, Xia Y, Dai Y.	Department of Pharmacology of Chinese Materia Medica, China Pharmaceutical University, 24 Tong Jia Xiang Road, Nanjing 210009, China, yuedaicpu@hotmail.com.	Polysaccharide of Radix Pseudostellariae Improves Chronic Fatigue Syndrome Induced by Poly I:C in Mice.	Evid Based Complement Alternat Med.. [Epub ahead of print]	Radix Pseudostellariae is used as a tonic drug in traditional Chinese medicine with immunomodulating and anti-fatigue activities, and the polysaccharide is considered as the main active component. The purpose of this study is to examine the effect of the polysaccharide isolated from Radix Pseudostellariae (PRP) on mouse chronic fatigue syndrome (CFS) induced by intraperitoneal injection of polyriboinosinic:polyribocytidylic acid (poly I:C), a double-stranded synthetic RNA. It has shown that the fatigue symptom of mice lasted at least 1 week as evaluated by forced swimming time. PRP (100, 200, 400 mg kg(-1)), orally administered 3 days before poly I:C injection, showed dose-dependent anti-fatigue effects. In addition, poly I:C led to evident alternations in neuroendocrine and immune systems of mice, such as reduced spontaneous activity and learning ability, declined serum level of corticosterone, increased weight indexes and T lymphocyte numbers in thymuses and spleens, and increased CD4(+)/CD8(+) ratio but decreased proliferation ability of T lymphocytes in spleens. PRP alleviated the abnormalities caused by poly I:C, and restored the function of hosts to normal conditions. The findings suggest that PRP is beneficial to CFS, and the underlying mechanisms of action involve neuroendocrine and immune systems.
Sigmon SC, Herning RI, Better W, Cadet JL, Griffiths RR.	Department of Psychiatry, University of Vermont College of Medicine, SATC-UHC, Room 1415,	Caffeine withdrawal, acute effects, tolerance, and absence of net beneficial effects of chronic	Psychopharmacology (Berl). 2009 Jul;204(4):573-85. Epub 2009 Feb 25.	RATIONALE: Although the subjective effects of caffeine abstinence, acute and chronic administration, and tolerance are well described, the corresponding neurophysiological effects are not. OBJECTIVES: Caffeine withdrawal, acute caffeine effects, caffeine tolerance, and net beneficial effects of chronic caffeine administration were investigated using cerebral blood flow velocity, quantitative electroencephalography (EEG), and subjective effects. MATERIALS AND METHODS: Sixteen regular caffeine users participated in this double-blind, within-subject study during which they received acute

	Burlington, VT, 05401, USA. stacey.sigmon@uvm.edu	administration: cerebral blood flow velocity, quantitative EEG, and subjective effects.		caffeine and placebo challenges (1) while maintained on 400 mg caffeine daily for > or =14 days and (2) while maintained on placebo for > or =14 days. Blood flow velocity was determined for the middle (MCA) and anterior (ACA) cerebral arteries using pulsed transcranial Doppler sonography. EEG was recorded from 16 scalp sites. Subjective effects were assessed with questionnaires. RESULTS: Acute caffeine abstinence (evaluated 24 h after placebo substitution) increased mean, systolic, and diastolic velocity in the MCA and ACA and decreased pulsatility index in the MCA. Acute caffeine abstinence increased EEG theta and decreased beta 2 power. Acute caffeine abstinence also increased measures of Tired, Fatigue, Sluggish, and Weary and decreased ratings of Energetic, Friendly, Lively, and Vigor. Acute caffeine effects were demonstrated across a wide range of measures, including cerebral blood flow, EEG, and subjective effects. Tolerance and "complete" tolerance were observed on subjective but not physiological measures. Chronic caffeine effects were demonstrated only on the measure of EEG beta 2 power. CONCLUSION: Acute caffeine abstinence and administration produced changes in cerebral blood flow velocity, EEG, and subjective effects. Tolerance to subjective but not physiological measures was demonstrated. There was almost no evidence for net effects of chronic caffeine administration on these measures. Overall, these findings provide the most rigorous demonstration to date of physiological effects of caffeine withdrawal.
Silva-Tinoco R, Castillo-Martínez L, Orea-Tejeda A, Orozco-Gutiérrez JJ, Vázquez-Díaz O, Montaño-Hernández P, Flores-Rebollar A, Reza-Albarrán A.	Heart Failure Clinic, Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City, Mexico.	Developing thyroid disorders is associated with poor prognosis factors in patient with stable chronic heart failure.	Int J Cardiol. 2009 Feb 8. [Epub ahead of print]	We sought to assess the developing of thyroid disorders in forty eight patients with chronic stable heart failure and without thyroid abnormalities during six months follow-up. Thyroid function disorders were observed in 27.1% of the subjects: sick euthyroid syndrome (12.5%), subclinical hypothyroidism (10.4%) and overt hypothyroidism (6.2%). Subjects with higher thyroid stimulating hormone (TSH) levels at the end of the study had more hospitalizations. The developing of altered thyroid profile was related to lower hemoglobin levels, smaller phase angle with bioelectrical impedance method and more fatigue perception by the patients. This abnormal thyroid function behavior on stable chronic heart failure and was observed as part of the disease progress and was associated to worse prognosis factors as lower phase angle and anemia.
Smith AK, Maloney EM, Falkenberg VR, Dimulescu I, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vector-Borne and Enteric Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MSG41, Atlanta, GA 30333, USA.	An angiotensin-1 converting enzyme polymorphism is associated with allostatic load mediated by C-reactive protein, interleukin-6 and cortisol.	Psychoneuroendocrinology. 2009 May;34(4):597-606. Epub 2008 Dec 10.	Allostatic load (AL) is a theoretical framework that describes the cumulative physiologic effects of adaptation to change or stress throughout the lifespan. AL is operationalized by a composite index of multiple biomarkers. Accordingly, genes, behavior and environment contribute to AL. To determine if individual differences in AL may be influenced by inherent genetic variation, we calculated an allostatic load index (ALI) for 182 Caucasian subjects derived from a population-based study of chronic fatigue syndrome. Nearly 65% of the subjects in this study sample reported fatiguing illness. ALI was calculated based on 11 measures representing metabolic, cardiovascular, inflammatory, hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS) activities. Subjects were dichotomized into high (ALI > or = 3) or low (ALI < 3) AL groups, and the association between high AL and 129 polymorphisms in 32 genes related to the HPA axis, neurotransmission, inflammation, cardiovascular and metabolic functions were evaluated. Polymorphisms in angiotensin-1 converting enzyme (ACE), corticotropin-releasing hormone receptor 1 (CRHR1), and serotonin receptors (HTR3A and HTR4) were associated with AL (p=0.0007-0.0486), but only one polymorphism, rs4968591, in ACE remained significant after correction for multiple comparisons. The T allele of ACE rs4968591 was more common in subjects with high AL (67.5%) than in subjects with low AL (49.3%)

				(p=0.0007), and this effect appeared independent of age, sex, body mass index and fatigue status. Additionally, high interleukin-6 (IL-6; p(trend)=0.04), and C-reactive protein (CRP; p(trend)=0.01) levels, as well as low urinary cortisol levels in females (p=0.03) were associated with the T allele, which may result in allele-specific binding of the transcription factor, E2F1. Our results suggest a role for ACE in the bidirectional communication between the central nervous and immune systems in response to stress. Further studies will be needed (a) to replicate the association between AL and ACE polymorphisms in population studies designed to differentiate the effects of sex, age and racial/ethnic background, (b) to evaluate the effect of allele-specific binding of E2F1 at rs4968591, and (c) to examine the role of ACE in the co-regulation of CRP, IL-6 and cortisol.
Smith WR, Strachan ED, Buchwald D.	Department of Psychiatry and Behavioral Sciences, School of Medicine, University of Washington, Seattle, WA 98195, USA. wrsmith@u.washington.edu	Coping, self-efficacy and psychiatric history in patients with both chronic widespread pain and chronic fatigue.	Gen Hosp Psychiatry. 2009 Jul-Aug;31(4):347-52. Epub 2009 May 2.	OBJECTIVE: To investigate the relationship of coping style and self-efficacy to functional impairment in a group of patients with both chronic widespread pain (CWP) and chronic fatigue, as well as the possible mediating role of psychiatric diagnosis. METHODS: We identified 138 consecutive clinic patients who met criteria for CWP and chronic fatigue. We collected demographic and clinical characteristics, as well as measures of emotion-focused and problem-focused coping styles, fatigue-related self-efficacy and self-reported general health. Psychiatric diagnoses were determined with a structured interview. Short Form-36 subscales of pain-related and fatigue-related functioning were the dependent variables in ordinal multiple regression analyses to identify the best-fit model for each. RESULTS: In the final model for pain, increased functional impairment was associated with increased emotion-focused coping as well as less education, lower general health scores and higher body mass index. Conversely, in the final model for fatigue, increased functional impairment was significantly associated with less emotion-focused coping, lower general health scores and lower self-efficacy. CONCLUSIONS: The unexpected finding that emotion-focused coping was associated differently with chronic pain and fatigue among patients who experience both symptoms is discussed in the context of the research on the effects of self-efficacy and possible treatment approaches.
Sorensen B, Jones JF, Vernon SD, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vector-Borne, and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, United States of America.	Transcriptional control of complement activation in an exercise model of chronic fatigue syndrome.	Mol Med. 2009 Jan-Feb;15(1-2):34-42. Epub 2008 Nov 10.	Complement activation resulting in significant increases of C4a split product may be a marker of postexertional malaise in individuals with chronic fatigue syndrome (CFS). This study focused on identification of the transcriptional control that may contribute to the increased C4a in CFS subjects after exercise. We used quantitative reverse-transcription polymerase chain reaction to evaluate differential expression of genes in the classical and lectin pathways in peripheral blood mononuclear cells (PBMCs). Calibrated expression values were normalized to the internal reference gene peptidylpropyl isomerase B (PPIB), the external reference gene ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit (rbcL), or the geometric mean (GM) of the genes ribosomal protein, large, P0 (RPLP0) and phosphoglycerate kinase 1 (PGK1). All nine genes tested, except mannose-binding lectin 2 (MBL2), were expressed in PBMCs. At 1 hour postexercise, C4, mannan-binding lectin serine protease 2 (MASP2) and ficolin 1 (FCN1) transcripts were detected at higher levels (> or = 2-fold) in at least 50% (4 of 8) of CFS subjects and were detected in 88% (7 of 8) CFS subjects when subjects with overexpression of either C4 or MASP2 were combined. Only an increase in the MASP2 transcript was statistically significant (PPIB, P = 0.001; GM, P = 0.047; rbcL, P = 0.045). This result may be due to the significant but transient downregulation of MASP2 in control subjects (PPIB, P = 0.023; rbcL, P = 0.027). By 6 hours postexercise, MASP2 expression was similar in both

				groups. In conclusion, lectin pathway responded to exercise differentially in CFS than in control subjects. MASP2 down-regulation may act as an antiinflammatory acute-phase response in healthy subjects, whereas its elevated level may account for increased C4a and inflammation-mediated postexertional malaise in CFS subjects.
Stahl SM.	Department of Psychiatry, University of California, San Diego, CA, USA. smstahl@neiglobal.com	Fibromyalgia--pathways and neurotransmitters.	Hum Psychopharmacol. 2009 Jun;24 Suppl 1:S11-7.	Fibromyalgia is a syndrome of widespread chronic pain associated with sleep disorders, depressed mood, cognitive impairment and fatigue. Its etiology and pharmacopathology are poorly understood but it is thought to result from a dysfunction of central pain processing mechanisms leading to generalised pain sensitisation. Pain perception is the result of a bidirectional process of ascending and descending pathways. Nociceptive input from peripheral afferent neurons is sent via the dorsal horn of the spinal cord to the higher brain centres involved in pain perception. Some descending inhibitory projections to the spinal cord attenuate the nociceptive effects. Numerous neurotransmitters including serotonin, dopamine, noradrenaline and substance P are involved in these processes. In other neuronal pathways in the brain, the same neurotransmitters are involved in mood control, sleep regulation and cognitive function providing a neurochemical substrate for the wide range of symptoms seen in fibromyalgia. Attenuation of neuronal hyperactivity through ligands acting at the alpha2-delta subunits of voltage-dependent calcium channels and increased inhibitory activity of the descending pathways by inhibition of serotonin and noradrenaline reuptake are two mechanisms that are currently exploited by new medication for the treatment of fibromyalgia. Copyright (c) 2009 John Wiley & Sons, Ltd.
Staines DR, Brenu EW, Marshall-Gradisnik S.	Queensland Health, Gold Coast Population Health Unit, Southport, Gold Coast, Queensland, Australia;	Postulated vasoactive neuropeptide immunopathology affecting the blood-brain/blood-spinal barrier in certain neuropsychiatric fatigue-related conditions: A role for phosphodiesterase inhibitors in treatment?	Neuropsychiatr Dis Treat. 2009;5:81-9. Epub 2009 Apr 8.	Neuropsychiatric symptoms occur in a number of neurological fatigue-related conditions including multiple sclerosis (MS), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and chronic fatigue syndrome (CFS). These conditions have been attributed variably to neuroinflammatory and neurodegenerative processes. While autoimmune pathology, at least in part, has long been suspected in these conditions proof has been elusive. Autoimmune pathomechanisms affecting the blood-brain barrier (BBB) or blood-spinal barrier (BSB) may predispose the BBB/BSB to 'leakiness' and be a precursor to additional autoimmune events resulting in neuroinflammatory or neurodegenerative processes. The aim of the paper is to postulate immunopathology of the cerebrospinal perivascular compartment involving certain vasoactive neuropeptides, specifically pituitary adenylate cyclase-activating polypeptide (PACAP) and vasoactive intestinal peptide (VIP), in the etiology of certain neuropsychiatric fatigue-related conditions such as MS, ALS, PD, and CFS. Vasoactive neuropeptides (VNs) such as PACAP and VIP have critical roles as neurotransmitters, vasodilators including perfusion and hypoxia regulators, and immune and nociception modulators. PACAP and VIP are widely distributed in the central nervous system (CNS) and have key roles in CNS blood vessels including maintaining functional integrity of the BBB and BSB. Autoimmunity affecting these VNs would likely have a detrimental effect on BBB and BSB functioning arguably predisposing to further pathological processes. Virchow-Robin spaces (VRS) are perivascular compartments surrounding small vessels within the CNS which contribute to the BBB and BSB integrity and contain PACAP and VIP receptors. Autoimmunity of these receptors would likely affect BBB and VRS function and therefore may contribute to the etiology of these conditions by affecting CNS and immunological homeostasis, including promoting neuropsychological symptomatology. PACAP and VIP, as potent activators of

				adenylate cyclase (AC), have a key role in cyclic adenosine monophosphate (cAMP) production affecting regulatory T cell (Treg) and other immune functions. Phosphodiesterase enzymes (PDEs) catalyze cAMP and PDE inhibitors (PDEIs) maintain cAMP levels and have proven and well known therapeutic benefit in animal models such as experimental allergic encephalomyelitis (EAE). Therefore PDEIs may have a role in therapy for certain neuropsychiatric fatigue-related conditions.
Stewart JM.	Department of Pediatrics and Physiology, New York Medical College, Hawthorne, NY 10532, USA. stewart@nymc.edu	Chronic fatigue syndrome: comments on deconditioning, blood volume and resulting cardiac function.	Clin Sci (Lond). 2009 Oct 19;118(2):121-3. Comment on: Clin Sci (Lond). 2010 Jan;118(2):125-35.	Cardiovascular and autonomic dysfunction have been suggested to underlie the symptoms accompanying CFS (chronic fatigue syndrome). In the present issue of Clinical Science, Hurwitz and co-workers have investigated whether deficits were present in cardiac output and blood volume in a cohort of patients with CFS and if these were linked to illness severity and sedentary lifestyle. The results clearly demonstrate reduced cardiac stroke volume and cardiac output in more severely afflicted patients with CFS, which is primarily attributable to a measurable reduction in blood volume. Similar findings are observed in microgravity and bed rest deconditioning, in forms of orthostatic intolerance and, to a lesser extent, in sedentary people. The circulatory consequences of reduced cardiac output may help to account for many of the findings of the syndrome.
Stubhaug B.		[Treatment of chronic fatigue syndrome][Article in Norwegian]	Tidsskr Nor Laegeforen. 2009 Jun 11;129(12):1209.	
Sullivan A, Nord CE, Evengård B.	Division of Clinical Microbiology, F82, Department of Laboratory Medicine, Karolinska University Hospital Huddinge, Karolinska Institutet, SE-14186 Stockholm, Sweden. asa.sullivan@ki.se	Effect of supplement with lactic-acid producing bacteria on fatigue and physical activity in patients with chronic fatigue syndrome.	Nutr J. 2009 Jan 26;8:4.	Disturbances in intestinal microbial ecology and in the immune system of the host have been implicated as a part of the pathogenesis in chronic fatigue syndrome. Probiotic lactic acid producing bacteria have been shown to prevent and alleviate gastrointestinal disturbances and to normalize the cytokine profile which might be of an advantage for patients suffering from chronic fatigue syndrome. The aim of the study was to evaluate the effect of Lactobacillus paracasei ssp. paracasei F19, Lactobacillus acidophilus NCFB 1748 and Bifidobacterium lactis Bb12 on fatigue and physical activity in CFS patients. Fifteen patients fulfilling the criteria set by international researchers in the field at the US Centre for Disease Control and Prevention in 1994 for chronic fatigue syndrome, were included in the study. The patients had high fatigue severity scores and high disability scores. During the first two weeks baseline observations without treatment were assessed, succeeded by four weeks of intake of a probiotic product and a four-week follow-up period. The fatigue, health and physical activity was assessed by the use of the Visual Analogue Scales and the SF-12 Health Survey. Faecal samples were collected and the normal microflora was analysed. Neurocognitive functions improved during the study period while there were no significant changes in fatigue and physical activity scores. No major changes occurred in the gastrointestinal microflora. At the end of the study 6 of 15 patients reported that they had improved according to the assessment described. The findings in this study that improvement of health is possible to achieve should encourage further studies with interventions with probiotics in patients with CFS.
Sun JF, Wu RR, Norris C, Noone AM, Amankwa-Sakyi M, Slack R,	Lombardi Comprehensive Cancer Center, Georgetown	Safety of chronic low-dose capecitabine as maintenance	Gastrointest Cancer Res. 2009 Jul;3(4):134-40.	BACKGROUND: Maintenance chemotherapy is not routinely used in gastrointestinal (GI) cancers. Capecitabine is an oral formulation that is enzymatically converted to 5-fluorouracil preferentially in tumor tissue. We hypothesize that capecitabine could be used as a long-term maintenance therapy to improve outcomes in patients with high-risk GI cancers following standard chemotherapy regimens.

Marshall JL.	University Medical Center, Washington, DC.	therapy in gastrointestinal cancers.		METHODS: We conducted a retrospective study to assess the toxicity of maintenance capecitabine in 28 patients with a variety of advanced GI malignancies. Capecitabine 1,000 mg twice daily without interruption was used for the first 11 patients. The dose was reduced to 1,000 mg twice daily 5 days per week in 8 patients who developed hand-foot syndrome. The remaining patients began treatment on the same abbreviated schedule. All documented clinical adverse events were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (v3.0, 2003). RESULTS: Main toxicities were grade 1/2 fatigue and hand-foot syndrome. Only one grade 3 toxicity was observed and no grade 4 toxicities were seen. We also observed a significant increase in red blood cell mean corpuscular volume in participants, which may have potential use as a biomarker to monitor therapeutic response. CONCLUSIONS: Fixed therapeutic doses of oral capecitabine 1,000 mg twice daily, 5 days on, 2 days off, can be administered chronically with a high level of safety and should be explored in larger prospective studies to demonstrate efficacy in GI malignancies, especially pancreatic and metastatic colorectal cancers.
Sutcliffe K, Gray J, Tan MP, Pairman J, Wilton K, Parry SW, Newton JL.	UK NIHR Biomedical Research Centre in Ageing - Cardiovascular Theme, Newcastle, UK.	Home orthostatic training in chronic fatigue syndrome--a randomized, placebo-controlled feasibility study.	Eur J Clin Invest. 2010 Jan;40(1):18-24. Epub 2009 Nov 12.	BACKGROUND: Orthostatic (Tilt)-training is an effective treatment for neurally mediated hypotension (NMH). NMH is a frequent finding in chronic fatigue syndrome (CFS). We evaluated home orthostatic training (HOT) in CFS in a randomized placebo-controlled feasibility study. METHODS: Thirty-eight patients with CFS (Fukuda Criteria) were randomly allocated to daily tilt training (n = 19) or sham training (n = 19) for 6 months. Haemodynamic responses to standing were performed in all subjects using continuous technology (Taskforce) at enrolment, week 1, 4 and 24. Symptom response and compliance were assessed using diaries. RESULTS: Two patients (one from each arm) withdrew from the study. Fourteen patients in each group complied completely or partially, and patients found the training manageable and achievable. Compared to the sham group, blood pressure while standing dropped to 8.0 mmHg less in the HOT group at 4 weeks (95% CI: 1.0 to 15.0, P = 0.03). At 4 weeks, the HOT group had higher total peripheral resistance compared to the sham group; mean difference 70.2, 95% CI: -371.4 to 511.8. Changes were maintained at 6 months. There was no significant difference in fatigue between groups at 4 weeks (mean difference 1.4, 95% CI: -13.5 to 16.2), but there was a trend towards improvement in fatigue at 6 months. Compliers had lower fatigue compared to non-compliers. CONCLUSIONS: A placebo-controlled study of HOT in CFS is feasible. HOT is well tolerated and generally complied with. A likely physiological rationale for HOT in CFS is related to reductions in orthostatic intolerance. An adequately powered study including strategies to enhance compliance is warranted.
Tak LM, Riese H, de Bock GH, Manoharan A, Kok IC, Rosmalen JG.	Interdisciplinary Center for Psychiatric Epidemiology, University Medical Center Groningen, University of Groningen, Hanzeplein 1, 9700	As good as it gets? A meta-analysis and systematic review of methodological quality of heart rate variability studies in functional somatic	Biol Psychol. 2009 Oct;82(2):101-10. Epub 2009 May 20.	Autonomic nervous system (ANS) dysfunction is a potential mechanism connecting psychosocial stress to functional somatic disorders (FSD), such as chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome. We present the first meta-analysis and systematic review of methodological study quality on the association between cardiac ANS dysfunction, measured as parasympathetic nervous system (PNS) activity using heart rate variability (HRV), and FSD. Literature search revealed 23 available studies including data on 533 FSD patients. Meta-analysis on a subgroup of 14 studies with suitable outcome measures indicated lower PNS activity in FSD patients compared to controls (weighted standardized mean difference (SMD)=-0.32, 95% CI -0.63 to -0.01, p=0.04). The reliability of this summary estimate was, however, significantly limited by unexplained heterogeneity in the effect

	RB, Groningen, The Netherlands.	disorders.		sizes and potential publication bias (weighted SMD after correction for funnel plot asymmetry=0.01, 95% CI -0.34 to 0.36, p=0.95). The systematic review of overall methodological quality of HRV studies in FSD demonstrates that there is substantial room for improvement, especially in selection of healthy control subjects, blinding of researchers performing HRV measurements, report of adequate HRV outcomes, and assessment of and adjustment for potential confounders. Methodological study quality was, however, not a significant predictor of study findings. We conclude that current available evidence is not adequate to firmly reject or accept a role of ANS dysfunction in FSD. Quality criteria and recommendations to improve future research on HRV in FSD are provided.
Tan PJ, Xu M, Sessler DI, Bashour CA.	Anesthesiology Institute, Department of Quantitative Health Sciences, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195, USA.	Operation timing does not affect outcome after coronary artery bypass graft surgery.	Anesthesiology. 2009 Oct;111(4):785-9.	BACKGROUND: Human factors such as fatigue, circadian rhythms, scheduling, and staffing may have an impact on patient care over the course of a day across all medical specialties. Research by the transportation industry concludes that human performance is degraded by shift work, circadian rhythm disturbances, and prolonged duty. This study investigated whether the timing of coronary artery bypass graft surgery affects outcomes. METHODS: The outcomes of coronary artery bypass graft surgery patients were analyzed according to the hour of the day, day of the workweek, month, and moon phase in which the surgery started. All patients who underwent isolated coronary artery bypass graft surgery between January 1, 1993 and July 1, 2006 were considered for the study.The primary outcome measurement was a compound morbidity outcome of six variables defined by the Society of Thoracic Surgeons. These outcomes included (1) in-hospital death, (2) acute postoperative myocardial infarction, (3) neurologic morbidity, including focal or global neurologic deficits or death without awakening, (4) serious infection morbidity consisting of sepsis syndrome or septic shock, (5) new-onset renal failure requiring dialysis, and (6) postoperative ventilatory support exceeding 72 h. RESULTS: The composite morbidity and in-hospital mortality rates were 4.8% and 1.4%, respectively. The number of cases each weekday, each month of the year, and during each phase of the moon were consistent. None of the time factors significantly affected the composite morbidity outcome. CONCLUSIONS: Elective coronary artery bypass graft surgery can be scheduled throughout the workday, any day of the work week and in any month of the year without compromising outcome.
Taylor A, Glover V, Marks M, Kammerer M.	Imperial College London, Institute of Reproductive and Developmental Biology, Hammersmith Campus, Du Cane Road, London W12 0NN, UK. alyx.taylor@imperial.ac.uk	Diurnal pattern of cortisol output in postnatal depression.	Psychoneuroendocrinology. 2009 Sep;34(8):1184-8. Epub 2009 Apr 29.	This study investigated the diurnal output of saliva cortisol in women with symptoms of depression postnatally. Twenty-one depressed and 30 non-depressed women at 7.5 weeks postpartum, and 21 non-perinatal controls, collected saliva at waking, 30 min, and 3 and 12h postwaking. Women who were not depressed postnatally showed a pattern of cortisol secretion over the day similar to non-perinatal controls. There was a significant difference in diurnal pattern between postnatally depressed and postnatally non-depressed women, due to a difference in the first two time points (waking and +30 min): compared to the other two groups who each had a significant increase in cortisol levels from waking to +30 min, the depressed women had significantly higher cortisol levels at waking and no increase at +30 min. The lack of a morning rise in the depressed women is similar to that reported for posttraumatic stress disorder and chronic fatigue syndrome and may reflect a response, in vulnerable women, to the marked cortisol withdrawal that occurs after delivery.
Thomas M, Smith A.	Centre for Occupational and	An investigation into the cognitive	Open Neurol J. 2009 Feb 27;3:13-	This study addresses, among other things, the debate as to whether cognitive deficits do occur with a diagnosis of Chronic Fatigue Syndrome (CFS). Previous studies have indicated a potential mismatch

	Health Psychology, School of Psychology, Cardiff University, UK.	deficits associated with chronic fatigue syndrome.	23.	between subjective patient ratings of impairment and clinical assessment. In an attempt to tackle some of the methodological problems faced by previous research in this field, this study recruited a large sample of CFS patients where adequate diagnosis had been made and administered an extensive battery of measures. In doing so this study was able to replicate previous published evidence of clear cognitive impairment in this group and demonstrate also that these deficits occurred independent of psychopathology. The conclusion drawn is that cognitive impairments can be identified if appropriate measures are used. Furthermore, the authors have shown that performance changes in these measures have been used to assess both efficacy of a treatment regime and rates of recovery.
Tian H, Brimmer DJ, Lin JM, Tumpey AJ, Reeves WC.	Centers for Diseases Control and Prevention, Chronic Viral Disease Branch, Division of Viral and Rickettsial Diseases, Atlanta, GA 30333, USA. ejq7@cdc.gov	Web usage data as a means of evaluating public health messaging and outreach.	J Med Internet Res. 2009 Dec 21;11(4):e52.	BACKGROUND: The Internet is increasingly utilized by researchers, health care providers, and the public to seek medical information. The Internet also provides a powerful tool for public health messaging. Understanding the needs of the intended audience and how they use websites is critical for website developers to provide better services to the intended users. OBJECTIVE: The aim of the study was to examine the utilization of the chronic fatigue syndrome (CFS) website at the Centers for Disease Control and Prevention (CDC). We evaluated (1) CFS website utilization, (2) outcomes of a CDC CFS public awareness campaign, and (3) user behavior related to public awareness campaign materials and CFS continuing medical education courses. METHODS: To describe and evaluate Web utilization, we collected Web usage data over an 18-month period and extracted page views, visits, referring domains, and geographic locations. We used page views as the primary measure for the CFS awareness outreach effort. We utilized market basket analysis and Markov chain model techniques to describe user behavior related to utilization of campaign materials and continuing medical education courses. RESULTS: The CDC CFS website received 3,647,736 views from more than 50 countries over the 18-month period and was the 33rd most popular CDC website. States with formal CFS programs had higher visiting density, such as Washington, DC; Georgia; and New Jersey. Most visits (71%) were from Web search engines, with 16% from non-search-engine sites and 12% from visitors who had bookmarked the site. The public awareness campaign was associated with a sharp increase and subsequent quick drop in Web traffic. Following the campaign, user interest shifted from information targeting consumer basic knowledge to information for health care professionals. The market basket analysis showed that visitors preferred the 60-second radio clip public service announcement over the 30-second one. Markov chain model results revealed that most visitors took the online continuing education courses in sequential order and were less likely to drop out after they reached the Introduction pages of the courses. CONCLUSIONS: The utilization of the CFS website reflects a high level of interest in the illness by visitors to the site. The high utilization shows the website to be an important online resource for people seeking basic information about CFS and for those looking for professional health care and research information. Public health programs should consider analytic methods to further public health by understanding the characteristics of those seeking information and by evaluating the outcomes of public health campaigns. The website was an effective means to provide health information about CFS and serves as an important public health tool for community outreach.
Tietjen GE, Brandes JL,	University of Toledo College of	Childhood Maltreatment and	Headache. 2009 Oct 21. [Epub	(Headache 2009;**:**-**) Objective.- To evaluate in a headache clinic population the relationship of childhood maltreatment on the prevalence of pain conditions comorbid with migraine. Background.-

Peterlin BL, Eloff A, Dafer RM, Stein MR, Drexler E, Martin VT, Hutchinson S, Aurora SK, Recober A, Herial NA, Utley C, White L, Khuder SA.	Medicine, Toledo, OH, USA (G.E. Tietjen, N.A. Herial, C. Utley, L. White, and S.A. Khuder); Nashville Neuroscience Group, Nashville, TN, USA (J.L. Brandes); Drexel University College of Medicine, Philadelphia, PA, USA (B.L. Peterlin); University of Calgary, Calgary, AB, Canada (A. Eloff); Loyola University Medical Center, Maywood, IL, USA (R.M. Dafer); John Muir Medical Center, Walnut Creek, CA, USA (M.R. Stein); Maimonides Medical Center, Brooklyn, NY, USA (E. Drexler); University of Cincinnati, Cincinnati, OH, USA (V.T. Martin); Orange County Migraine & Headache Center, Irvine, CA, USA (S. Hutchinson); Swedish Headache Center, Seattle,	Migraine (Part III). Association With Comorbid Pain Conditions.	ahead of print]	Childhood maltreatment is highly prevalent and has been frequently associated with recurrent headache. The relationship of maltreatment and pain has, however, been a subject of some debate. Methods.- Cross-sectional data on self-reported physician-diagnosed pain conditions were electronically collected from persons with migraine (diagnosed according to International Classification of Headache Disorders-2), seeking treatment in headache clinics at 11 centers across the US and Canada. These included irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), fibromyalgia (FM), interstitial cystitis (IC), arthritis, endometriosis, and uterine fibroids. Other information included demographics, migraine characteristics (frequency, headache-related disability), remote and current depression (The Patient Health Questionnaire-9), and remote and current anxiety (The Beck Anxiety Inventory). Patients also completed the Childhood Trauma Questionnaire regarding sexual, emotional, and physical abuse, and emotional and physical neglect under the age of 18 years old. Statistical analyses accounted for the survey design and appropriate procedures in SAS such as surveymeans, surveyfreq, and surveylogistic were applied to the weighted data. Results.- A total of 1348 migraineurs (88% women) were included in this study (mean age 41 years). Based on physician diagnosis or validated criteria, 31% had IBS, 16% had CFS, and 10% had FM. Diagnosis of IC was reported by 6.5%, arthritis by 25%, and in women, endometriosis was reported by 15% and uterine fibroids by 14%. At least 1 comorbid pain condition was reported by 61%, 2 conditions by 18%, and 3 or more by 13%. Childhood maltreatment was reported by 58% of the patients. Emotional abuse was associated with increased prevalence of IBS, CFS, arthritis, and physical neglect with arthritis. In women, physical abuse was associated with endometriosis and physical neglect with uterine fibroids. Emotional abuse, and physical abuse and neglect ($P < .0001$ for all) were also associated with increased total number of comorbid conditions. In ordinal logistic regression models, adjusted for sociodemographics and current depression (prevalence 28%) and anxiety (prevalence 56%), emotional abuse (odds ratios [OR] = 1.69, 95% confidence intervals [CI]: 1.224-2.33) and physical neglect (OR = 1.73, 95% CI: 1.22-2.46) were independently associated with an increased number of pain conditions. The cohort of women, similarly, had associations of emotional abuse (OR = 1.94, 95% CI: 1.40-2.72) and physical neglect (OR = 1.90, 95% CI: 1.34-2.68) with an increased number of pain comorbidities. Conclusion.- The association of childhood maltreatment and pain was stronger in those reporting multiple pain conditions and multiple maltreatment types. This finding suggests that in migraineurs childhood maltreatment may be a risk factor for development of comorbid pain disorders.

	WA, USA (S.K. Aurora); University of Iowa, Iowa City, IA, USA (A. Recober).			
Tietjen GE, Brandes JL, Peterlin BL, Eloff A, Dafer RM, Stein MR, Drexler E, Martin VT, Hutchinson S, Aurora SK, Recober A, Herial NA, Utley C, White L, Khuder SA.	The University of Toledo College of Medicine, Toledo, OH, USA.	Allodynia in migraine: association with comorbid pain conditions.	Headache. 2009 Oct;49(9):1333-44.	BACKGROUND: Cutaneous allodynia (CA) in migraine is a clinical manifestation of central nervous system sensitization. Several chronic pain syndromes and mood disorders are comorbid with migraine. In this study we examine the relationship of migraine-associated CA with these comorbid conditions. We also evaluate the association of CA with factors such as demographic profiles, migraine characteristics, and smoking status that may have an influence on the relationships of CA to pain and mood. METHODS: Data are from a cross-sectional multicenter study of comorbid conditions in persons seeking treatment in headache clinics. Diagnosis of migraine was determined by a physician based on the International Classification of Headache Disorders-II criteria. Participants completed a self-administered questionnaire ascertaining sociodemographics, migraine-associated allodynia, physician-diagnosed comorbid medical and psychiatric disorders, headache-related disability, current depression, and anxiety. RESULTS: A total of 1413 migraineurs (mean age = 42 years, 89% women) from 11 different headache treatment centers completed a survey on the prevalence of comorbid conditions. Aura was reported by 38% and chronic headache by 35% of the participants. Sixty percent of the study population reported at least one migraine-related allodynic symptom, 10% reported > or =4 symptoms. Symptoms of CA were associated with female gender, body mass index, current smoking, presence of aura, chronic headaches, transformed headaches, severe headache-related disability, and duration of migraine illness from onset. The prevalence of self-reported physician diagnosis of comorbid pain conditions (irritable bowel syndrome, chronic fatigue syndrome, fibromyalgia) and psychiatric conditions (current depression and anxiety) was also associated with symptoms of CA. Adjusted ordinal regression indicated a significant association between number of pain conditions and severity of CA (based on symptom count). Adjusting for sociodemographics, migraine characteristics, and current depression and anxiety, the likelihood of reporting symptoms of severe allodynia was much higher in those with 3 or more pain conditions (odds ratio = 3.03, 95% confidence interval: 1.78-5.17), and 2 pain conditions (odds ratio = 2.67, 95% confidence interval: 1.78-4.01) when compared with those with no comorbid pain condition. CONCLUSION: Symptoms of CA in migraine were associated with current anxiety, depression, and several chronic pain conditions. A graded relationship was observed between number of allodynic symptoms and the number of pain conditions, even after adjusting for confounding factors. This study also presents the novel association of CA symptoms with younger age of migraine onset, and with cigarette smoking, in addition to confirming several previously reported findings.
Trock D	.	Tired, achy, and overweight, the inflammatory nature of obesity.Comment	J Clin Rheumatol. 2009 Feb;15(1):50.	

		on: J Clin Rheumatol. 2007 Feb;13(1):12-5.		
Turan T, Izgi HB, Ozsoy S, Tanrıverdi F, Basturk M, Asdemir A, Beşirli A, Esel E, Sofuoglu S.	Department of Psychiatry, Erciyes University Medical School, Kayseri, Turkey.	The Effects of Galantamine Hydrobromide Treatment on Dehydroepiandrosterone Sulfate and Cortisol Levels in Patients with Chronic Fatigue Syndrome.	Psychiatry Investig. 2009 Sep;6(3):204-210. Epub 2009 Jun 23.	OBJECTIVE: Mental fatigue, cognitive disorders, and sleep disturbances seen in chronic fatigue syndrome (CFS) may be attributed to cholinergic deficit. A functional deficiency of cholinergic neurotransmission may cause the hypothalamic-pituitary-adrenal axis hypoactivity seen in CFS. Therefore, we investigated the alterations in stress hormones such as cortisol and dehydroepiandrosterone sulfate (DHEAS) in CFS patients before and after 4-week administration of galantamine hydrobromide, a selective acetylcholinesterase inhibitor, and aimed to investigate whether there are any relationships between the probable hormonal changes and cholinergic treatment. METHODS: Basal levels of cortisol and DHEAS were measured in 29 untreated CFS patients who were diagnosed according to Centers for Disease Control (CDC) criteria and in 20 healthy controls. In the patient group, four weeks after 8 mg/d galantamine hydrobromide treatment, cortisol and DHEAS levels were measured again. After the treatment 22 patients who stayed in study were divided into two subgroups as responders and nonresponders according to the reduction in their Newcastle Research Group ME/CFS Score Card (NRG) scores. RESULTS: Important findings of this study are lower pre-and post-treatment cortisol levels and in all CFS patients compared to controls (F=4.129, p=0.049; F=4.803, p=0.035, respectively); higher basal DHEAS values and higher DHEAS/cortisol molar ratios which were normalized following four weeks' treatment with 8 mg/d galantamine hydrobromide in the treatment-respondent group (F=5.382, p=0.029; F=5.722, p=0.025, respectively). CONCLUSION: The findings of the decrease in basal DHEAS levels and DHEAS/cortisol molar ratios normalizing with galantamine treatment may give some support to the cholinergic deficit hypothesis in CFS.
Twisk FNM, Maes M.	ME-de-patiënten Foundation, Limmen, the Netherlands, the Netherlands	A review on cognitive behavorial therapy (CBT) and graded exercise therapy (GET) in myalgic encephalomyelitis (ME) / chronic fatigue syndrome (CFS): CBT/GET is not only ineffective and not evidence-based, but also potentially harm	Neuroendocrinol Lett. 2009;30(3):275-420.	Benign Myalgic Encephalomyelitis (ME) / Chronic Fatigue Syndrome (CFS) is a debilitating disease which, despite numerous biological abnormalities has remained highly controversial. Notwithstanding the medical pathogenesis of ME/CFS, the (bio)psychosocial model is adopted by many governmental organizations and medical profes-sio-nals to legitimize the combination of Cognitive Behavioral Therapy (CBT) and Graded Exercise Therapy (GET) for ME/CFS. Justified by this model CBT and GET aim at eliminating presumed psychogenic and socially induced maintaining factors and reversing deconditioning, respectively. In this review we invalidate the (bio)psychosocial model for ME/CFS and demonstrate that the success claim for CBT/GET to treat ME/CFS is unjust. CBT/GET is not only hardly more effective than non-interventions or standard medical care, but many patients report that the therapy had affected them adversely, the majority of them even reporting substantial deterioration. Moreover, this review shows that exertion and thus GET most likely have a negative impact on many ME/CFS patients. Exertion induces post-exertional malaise with a decreased physical performan-ce/aerobic capacity, increased muscoskeletal pain, neurocognitive impairment, “fatigue”, and weakness, and a long lasting “recovery” time. This can be explained by findings that exertion may amplify pre-existing pa-thophysiological abnormalities underpinning ME/CFS, such as inflammation, immune dysfunction, oxidative and nitrosative stress, channelopathy, defec-tive stress response mechanisms and a hypoactive hypothalamic-pituitary-adrenal axis. We conclude that it is unethical to

				treat patients with ME/CFS with ineffective, non-evidence-based and potentially harmful "rehabilitation therapies", such as CBT/GET.
Ulvestad E.	Avdeling for mikrobiologi og immunologi Haukeland universitetssjukehus og Gades Institutt Universitetet i Bergen 5021 Bergen. elling.ulvestad@helse-bergen.no	[Expert--but on what?][Article in NorwegianComment in: Tidsskr Nor Laegeforen. 2009 Jun 25;129(13):1352.	Tidsskr Nor Laegeforen. 2009 Mar 26;129(7):642-3.	Chronic fatigue syndrome has received much attention owing to its debilitating character. The question as to whether the vaccine against meningococcus group B can provoke chronic fatigue syndrome has recently been addressed. Consensus in Norway seems to be that the vaccine does not provoke the syndrome. The article presents my reasons for questioning this conclusion.
Vallings R.	Howick Health and Medical Clinic, New Zealand.	A case of Chronic Fatigue Syndrome following H1N1 influenza (swine influenza).	J Clin Pathol. 2009 Oct 26. [Epub ahead of print]	Case report of an adolescent boy who was diagnosed as suffering from Chronic Fatigue Syndrome 5 months after infection with H1N1 influenza.
van Alfen N, van der Werf SP, van Engelen BG.	Department of Neurology, Neuromuscular Centre Nijmegen, Donders Center for Neuroscience, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. n.vanalfen@neuro.umcn.nl	Long-term pain, fatigue, and impairment in neuralgic amyotrophy.	Arch Phys Med Rehabil. 2009 Mar;90(3):435-9.	OBJECTIVES: Recently, it has become clear that neuralgic amyotrophy (NA; idiopathic and hereditary brachial plexus neuropathy) has a less optimistic prognosis than usually assumed. To optimize treatment and management of these patients, one needs to know the residual symptoms and impairments they suffer. Therefore, the objective of this study was to describe the prevalence of pain, psychologic symptoms, fatigue, functional status, and quality of life in patients with NA. SETTING: Neurology outpatient department of an academic teaching hospital. PARTICIPANTS: NA patients (N=89) were studied, and clinical details were recorded. Self-report data were on average collected 2 years after the onset of the last NA episode. MAIN OUTCOME MEASURES: Pain was assessed with the McGill Pain Questionnaire, fatigue with the Checklist Individual Strength, and psychologic distress with the Symptom Checklist 90. Functional status and handicap were assessed with the modified Rankin Scale and Medical Outcomes Study 36-Item Short-Form Health Survey. RESULTS: Pain was usually localized in the right shoulder and upper arm, matching the clinical predilection site for paresis in NA. About a quarter to a third of the patients reported significant long-term pain and fatigue, and half to two thirds still experienced impairments in daily life. Over one third of the individual patients suffered from severe fatigue. The group did not fulfill the criteria of chronic fatigue or major psychologic distress. There was no correlation of pain or fatigue with the level of residual paresis on a Medical Research Council scale, but patients with a comorbid condition fared worse than patients without. CONCLUSIONS: A significant number of NA patients suffer from persistent pain and fatigue, leading to impairment. Symptoms were not correlated with psychologic distress. This makes it likely that they are caused by residual shoulder or arm dysfunction but not as part of a chronic pain or fatigue syndrome in these patients.

Van Campen E, Van Den Eede F, Moorkens G, Schotte C, Schacht R, Sabbe BG, Cosyns P, Claes SJ.	Dept. of Psychiatry, Antwerp University Hospital, Antwerp, Belgium.	Use of the Temperament and Character Inventory (TCI) for assessment of personality in chronic fatigue syndrome.	Psychosomatics. 2009 Mar-Apr;50(2):147-54.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by severe and prolonged fatigue, along with a set of nonspecific symptoms and signs, such as sore throat, muscle pain, headaches, and difficulties with concentration or memory. OBJECTIVE: The study examined whether CFS is associated with specific dimensions of Cloninger's psychobiological model of personality. METHOD: Personality profiles were compared between 38 CFS patients and 42 control subjects by means of the Temperament and Character Inventory (TCI). RESULTS: The CFS group showed significantly higher scores on Harm-Avoidance and Persistence. CONCLUSION: The current study shows a significant association between specific personality characteristics and CFS. These personality traits may be implicated in the onset and/or perpetuation of CFS and may be a productive focus for psychotherapy.
Van Houdenhove B, Luyten P.	Department of Psychiatry, University of Leuven, Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Treatment of chronic fatigue syndrome: how to find a 'new equilibrium'?	Patient Educ Couns. 2009 Nov;77(2):153-4. Epub 2009 Sep 20. Comment on: Patient Educ Couns. 2009 Nov;77(2):237-41. Patient Educ Couns. 2009 Nov;77(2):231-6.	
Van Houdenhove B, Van Den Eede F, Luyten P.	Department of Liaison Psychiatry, University Hospitals K.U. Leuven, Herestraat 49, B-3000 Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Does hypothalamic-pituitary-adrenal axis hypofunction in chronic fatigue syndrome reflect a 'crash' in the stress system?	Med Hypotheses. 2009 Jun;72(6):701-5. Epub 2009 Feb 23.	The etiopathogenesis of chronic fatigue syndrome (CFS) remains poorly understood. Although neuroendocrine disturbances - and hypothalamic-pituitary-adrenal (HPA) axis hypofunction in particular - have been found in a large proportion of CFS patients, it is not clear whether these disturbances are cause or consequence of the illness. After a review of the available evidence we hypothesize that that HPA axis hypofunction in CFS, conceptualized within a system-biological perspective, primarily reflects a fundamental and persistent dysregulation of the neurobiological stress system. As a result, a disturbed balance between glucocorticoid and inflammatory signaling pathways may give rise to a pathological cytokine-induced sickness response that may be the final common pathway underlying central CFS symptoms, i.e. effort/stress intolerance and pain hypersensitivity. This comprehensive hypothesis on HPA axis hypofunction in CFS may stimulate diagnostic refinement of the illness, inform treatment approaches and suggest directions for future research, particularly focusing on the neuroendocrine-immune interface and possible links between CFS, early and recent life stress, and depression.
Van Houdenhove B, Van Hoof E, Becq K, Kempke S, Luyten P, De Meirleir K.	Department of Liaison Psychiatry, University Hospital Gasthuisberg, Herestraat 49, Leuven B-3000, Belgium.	A comparison of patients with chronic fatigue syndrome in two "ideologically" contrasting clinics.	J Nerv Ment Dis. 2009 May;197(5):348-53.	Aim of the present study was to compare chronic fatigue syndrome (CFS) patients, attending 2 "ideologically" contrasting clinics for CFS, on various patient and illness characteristics. Fifty-nine CFS patients of each clinic, located in Leuven and Brussels (Belgium), participated. Patients did not differ with regard to age, levels of fatigue, psychopathology, and self-efficacy. However, patients from the psychosocially-oriented clinic had a lower level of education, reported more progressive illness onset, and attributed their illness more to psychological causes. Patients in the biologically-oriented clinic reported more pain, and showed higher levels of social functioning, motivation and vitality, as well as

	boudewijn.vanhoudenhove@uz.kuleuven.ac.be			fewer limitations related to emotional problems. It is concluded that CFS patients attending the 2 clinics could not be distinguished along dualistic biological/psychosocial lines, but those reporting sudden illness onset and making somatic attributions were more likely to be represented in the biologically-oriented clinic.
van Ittersum MW, van Wilgen CP, Hilberdink WK, Groothoff JW, van der Schans CP.	Hanze University Groningen, University of Applied Sciences, Center for Research and Development in Health Care and in Nursing, Groningen, The Netherlands. m.w.van.ittersum@pl.hanze.nl	Illness perceptions in patients with fibromyalgia.	Patient Educ Couns. 2009 Jan;74(1):53-60. Epub 2008 Sep 23.	OBJECTIVE: Former studies in chronic diseases showed the importance of patients' beliefs and perceptions. The Revised Illness Perception Questionnaire was developed to assess these illness perceptions. Our goal was to investigate psychometric properties of the IPQ-R for Fibromyalgia Dutch language version (IPQ-R FM-Dlv) and to describe illness perceptions of participants with FM. METHODS: 196 patients completed the IPQ-R FM-Dlv. Internal consistency, domain structure and inter domain correlations were calculated and compared to the IPQ-R English language version. Scores were compared with chronic fatigue syndrome (CFS), rheumatoid arthritis (RA), and coronary heart disease (CHD). RESULTS: Most psychometric properties were comparable to those of the original IPQ-R. Participants showed a lack of understanding of their illness, expected their FM to be chronic and to have a lot of negative consequences on functioning. In 17 out of 24 domains significant differences were found between FM and CFS, RA, and CHD patients. CONCLUSION: The IPQ-R FM-Dlv showed acceptable psychometric properties, although some aspects need closer examination. Illness perceptions of FM patients on the Dutch questionnaire were non-comparable to CFS, RA, and CHD patients on the English questionnaire. PRACTICE IMPLICATIONS: The IPQ-R FM-Dlv can be used to assess illness perceptions of Dutch FM patients.
van Nes SI, Vanhoutte EK, Faber CG, Garssen M, van Doorn PA, Merkies IS; PeriNomS Study Group. Collaborators: Bennett D, van den Berg LH, Van den Bergh PY, Cornblath DR, Dalakas M, Devigili G, van Doorn PA, Faber CG, Gorson KC, Hadden RD, Hahn AF, Hartung HP, Hughes RA, Lauria G, Léger JM, Lewis RA, Lunn MP, Merkies IS,	Department of Neurology, Erasmus Medical Centre Rotterdam, Rotterdam, The Netherlands. s.vannes@erasmusmc.nl	Improving fatigue assessment in immune-mediated neuropathies: the modified Rasch-built fatigue severity scale.	J Peripher Nerv Syst. 2009 Dec;14(4):268-78.	Fatigue is a major disabling complaint in patients with immune-mediated neuropathies (IN). The 9-item fatigue severity scale (FSS) has been used to assess fatigue in these conditions, despite having limitations due to its classic ordinal construct. The aim was to improve fatigue assessment in IN through evaluation of the FSS using a modern clinimetric approach [Rasch unidimensional measurement model (RUMM2020)]. Included were 192 stable patients with Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) or polyneuropathy associated with monoclonal gammopathy of undetermined significance (MGUSP). The obtained FSS data were exposed to RUMM2020 model to investigate whether this scale would meet its expectations. Also, reliability and validity studies were performed. The original FSS did not meet the Rasch model expectations, primarily based on two misfitting items, one of these also showing bias towards the factor 'walking independent.' After removing these two items and collapsing the original 7-point Likert options to 4-point response categories for the remaining items, we succeeded in constructing a 7-item Rasch-built scale that fulfilled all requirements of unidimensionality, linearity, and rating scale model. Good reliability and validity were also obtained for the modified FSS scale. In conclusion, a 7-item linearly weighted Rasch-built modified FSS is presented for more proper assessment of fatigue in future studies in patients with immune-mediated neuropathies.

Nobile-Orazio E, Notermans NC, Padua L, Reilly MM, Smith B.				
van Wilgen CP, Dijkstra PU, Versteegen GJ, Fleuren MJ, Stewart R, van Wijhe M.	Pain Centre, Department of Anesthesiology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands. c.p.van.wilgen@sport.umcg.nl	Chronic pain and severe disuse syndrome: long-term outcome of an inpatient multidisciplinary cognitive behavioural programme.	J Rehabil Med. 2009 Feb;41(3):122-8.	OBJECTIVE: Patients with chronic pain and severe disuse syndrome have pain with physiological, psychological and social adaptations. The duration and severity of complaints, combined with previously failed treatments, makes them unsuitable for treatment in primary care. DESIGN: A prospective waiting list controlled study. PATIENTS: A total of 32 patients with chronic pain for at least one year and severe disuse syndrome were included in an inpatient multidisciplinary cognitive behavioural treatment. METHODS: Patients were assessed before the waiting list period, before the clinical phase, after the clinical phase and after follow-ups of 6 months and one year. The visual analogue scale for pain and fatigue were assessed. Muscle strength of the arms and legs, arm endurance and a 6-minute walking test were used to assess physical outcome. The Symptom Checklist-90, RAND-36, pain cognition list and the Tampa scale for kinesiophobia were used to assess psychological outcome. RESULTS: Long-term significant ($p < 0.001$) improvements were found for pain, fatigue, walking distance, muscle strength, anxiety, depression, somatization, negative self-efficacy, and catastrophizing in the intervention period. CONCLUSION: An inpatient multidisciplinary cognitive behavioural programme is beneficial for patients with chronic pain and a severe disuse syndrome.
Vandenbergen J, Vanheule S, Rosseel Y, Desmet M, Verhaeghe P.	Department of Psychoanalysis and Clinical Consulting, Ghent University, Ghent, Belgium. jan.vandenbergen@telenet.be	Unexplained chronic fatigue and core conflictual relationship themes: A study in a chronically fatigued population.	Psychol Psychother. 2009 Mar;82(Pt 1):31-40. Epub 2008 Aug 25.	OBJECTIVE: Unexplained fatigue syndromes are multidimensional phenomena that involve a constellation of symptoms. This paper explores whether typical relationship patterns are associated with self-reported and clinically rated fatigue symptoms in chronically fatigued patients. METHOD: Relationship patterns were assessed by means of the core conflictual relationship theme (CCRT) method. This method examines transference patterns, and was applied to interview data collected from chronically fatigued patients (N=30). Chronic fatigue was assessed by means of a self-report questionnaire and was also rated clinically. RESULTS: Both self-reported and clinically rated fatigue correlated with relationship themes. The intensity of fatigue related to the perception of others as not respecting and as negatively interfering. The typical reaction of the self to relationships consists of feeling disrespected, anger, passivity, and reduced feelings of self-consistency. CONCLUSION: Patients' perception of interpersonal relationships as distressing may be pivotal in understanding these results. Implications for clinical intervention and future research are indicated.
Van't Leven M, Zielhuis GA, van der Meer JW, Verbeek AL, Bleijenberg G.	1 Department of Epidemiology, Biostatistics and HTA, Radboud University Nijmegen Medical Centre, the Netherlands.	Fatigue and chronic fatigue syndrome-like complaints in the general population.	Eur J Public Health. 2009 Aug 18. [Epub ahead of print]	BACKGROUND: Most knowledge on chronic fatigue (CF) and chronic fatigue syndrome (CFS) is based on clinical studies, not representative of the general population. This study aimed to assess the prevalence of fatigue in an adult general population and to identify associations with lifestyle factors. METHODS: Total 22 500 residents of Nijmegen were selected at random and interviewed by questionnaire. Data on 9062 respondents (43% response) were analysed, taken into account age, gender and concomitant disease. Subjects were classified into four groups: not fatigued (NF, reference group), short-term fatigue (SF, <6 months), chronic fatigue (CF, >/=6 months) and CFS-like fatigue (in accordance with the Center for Disease Control criteria for CFS, without clinical confirmation). RESULTS: Our study population showed the following breakdown: NF 64.4% (95% CI 63.6-65.6%), SF

				4.9% (95% CI 4.5-5.4%), CF 30.5% (95% CI 29.5-31.4%) and CFS-like fatigue 1.0% (95% CI 0.8-1.2%). Compared with the NF group, more of the CFS respondents were female [odds ratio (OR) = 1.9], obese (OR = 4.1), using analgesics (OR = 7.8), had a low alcohol intake (OR = 0.4), were eating less healthy food (OR = 0.5) and were physically less active (OR = 0.1). These associations largely applied to the SF and CF group. The fatigue could have been due to a concomitant disease in 34 and 55.5% of the SF and CF cases, respectively. CONCLUSION: The prevalence of CF in the general population appears to be much higher than previously indicated. Even with strict criteria for CFS, it is estimated that approximately 1% of the adult population experiences this condition. Interestingly, a large part of this group remains unrecognized by the general practitioner. A striking similarity in lifestyle pattern between SF, CF and CFS calls for further research.
Veldman J, Van Houdenhove B, Verguts J.	Department of Obstetrics and Gynaecology, University Hospital Gasthuisberg, Catholic University Leuven, Louvain, Belgium.	Chronic fatigue syndrome: a hormonal origin? A rare case of dysmenorrhea membranacea.	Arch Gynecol Obstet. 2009 May;279(5):717-20. Epub 2008 Sep 12.	BACKGROUND: Membranous dysmenorrhea is a rare entity involving expulsion of fragments of endometrium retaining the shape of the uterus. The condition is often linked to high progesterone levels. An association with a chronic fatigue syndrome was never described. CASE: A 44-year-old woman with a chronic fatigue syndrome (CFS), presented with membranous dysmenorrhea after taking an oral contraceptive pill containing ethinylestradiol 0.02 mg and desogestrel 0.15 mg for 3 months in a continuous regimen as treatment for dysfunctional bleeding. Oral contraception was discontinued and she resumed normal menstruations. Remarkably, she mentioned complete disappearance of the CFS since expulsion of the tissue and started working again. CONCLUSION: The occurrence of membranous dysmenorrhea with a dissolving chronic fatigue syndrome is very rare and was never described before. This case suggests a hormonal dysfunction as a possible cause of chronic fatigue syndrome. A review of the literature on membranous dysmenorrhea is presented.
Viaene M, Vermeir G, Godderis L.	Department of Occupational, Environmental and Insurance Medicine, Catholic University of Leuven, UZ St. Rafaël, Leuven, Belgium. m.k.viaene@opzgeel.be	Sleep disturbances and occupational exposure to solvents.	Sleep Med Rev. 2009 Jun;13(3):235-43. Epub 2009 Feb 7.	A solvent can be defined as "a liquid that has the ability to dissolve, suspend or extract other materials, without chemical change to the material or solvent". Numerous chemical or technical processes rely on these specific properties of organic solvents in industry. Occupational exposure to solvents is not rare and some activities may cause substantial exposure to these substances in the workforce. Short-term or acute exposures cause a prenarcotic syndrome, and long lasting exposure conditions have been associated with various neurological and neuropsychiatric disorders, e.g., anosmia, hearing loss, colour vision dysfunctions, peripheral polyneuropathy and depression, but most significantly with the gradual development of an irreversible toxic encephalopathy. For the last 3 decades reports and epidemiological studies have been published reporting sleep disturbances among other complaints, related to long-term exposure to these compounds. In addition, the question has been posed if solvents can be the cause of a sleep apnoea syndrome in exposed workers, or on the contrary, if these workers are misdiagnosed and 'common' sleep apnoea syndromes are the cause of their chronic symptoms of fatigue and memory and attentional disturbances.
Vij G, Gupta A, Chopra K.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Punjab	Modulation of antigen-induced chronic fatigue in mouse model of water immersion	Fundam Clin Pharmacol. 2009 Jun;23(3):331-7. Epub 2009 Mar 11.	It is believed that physical stress, infection and oxidative stress are involved in the development of chronic fatigue syndrome. There is little evidence stating the beneficial role of nutritional supplements in chronic fatigue syndrome. Based on this, this study was designed to evaluate the effect of naringin, a natural polyphenol, in a mouse model of immunologically-induced fatigue, wherein purified lipopolysaccharide (LPS) as well as Brucella abortus (BA) antigen was used as

	University, Chandigarh-160014, India.	stress by naringin, a polyphenolic antioxidant.		immunogens. The assessment of chronic fatigue syndrome was based on chronic water-immersion stress test for 10 mins as well as measurement of hyperalgesia for 19 days. Immobility time and tail withdrawal latency as well as oxidative stress were taken as the markers of fatigue. Mice challenged with LPS or BA for 19 days showed significant increase in the immobility time, hyperalgesia and oxidative stress on 19th day. Serum tumor necrosis factor-alpha (TNF-alpha) levels markedly increased with LPS or BA challenge. Concurrent treatment with naringin resulted in the significant decrease in the immobility time as well as hyperalgesia. There was significant attenuation of oxidative stress as well as in TNF-alpha levels. Present findings strongly suggest the role of oxidative stress and immunological activation in the pathophysiology of chronic fatigue syndrome, and treatment with naringin can be a valuable option in chronic fatigue syndrome.
Walker K, Lindner H, Noonan M.	School of Psychology, Australian Catholic University, Melbourne, Victoria, Australia. mskarenwalker.@gmail.com	The role of coping in the relationship between depression and illness severity in chronic fatigue syndrome.	J Allied Health. 2009 Summer;38(2):91-9.	The self-regulatory model (SRM) proposes that both cognitive and emotional illness representations influence the coping processes adopted in response to an illness. AIM: This study used the SRM to explore the role of coping in the relationship between depression and self-appraisals of illness severity in a population of patients with chronic fatigue syndrome (CFS). METHODS: The sample comprised 156 participants, 34 men and 121 women, aged between 18 and 78 yrs, who had been medically diagnosed with CFS. Participants were asked to complete three questionnaires: the Cardiac Depression Scale, Ways of Coping Questionnaire, and Severity Subscale of the Illness Perceptions Questionnaire-Revised. RESULTS: Analyses revealed that almost 70% of the participants were moderately or severely depressed. Additionally, two particular subscales, social support seeking and positive reappraisals, emerged as positively contributing to self-appraisals of illness severity (beta = 0.20 [$p < 0.05$] and beta = 0.21 [$p < 0.05$], respectively), thereby supporting the SRM. Furthermore, results indicated that a combination of depression and coping was a better predictor of illness severity than depression alone, accounting for 22% of the variance compared with 8%, respectively. CONCLUSIONS: The findings suggest that focusing on depression, and particularly coping styles, during treatment interventions could have important implications for therapeutic interventions. This could lead to better treatment strategies for health professionals who work with patients with CFS.
Wang JH, Chai TQ, Lin GH, Luo L.	The First Hospital Affiliated to Guangzhou TCM University, Guangzhou 510405, China.	Effects of the intelligent-turtle massage on the physical symptoms and immune functions in patients with chronic fatigue syndrome.	J Tradit Chin Med. 2009 Mar;29(1):24-8.	OBJECTIVE: To evaluate the effects of the intelligent-turtle massage on the physical symptoms and immune functions in patients with chronic fatigue syndrome (CFS). METHODS: 182 cases of CFS were randomly divided into an experimental group of 91 cases treated by the intelligent-turtle massage, and a control group of 91 cases treated with the conventional massage method. After 2 courses of treatment, the therapeutic effects were statistically analyzed with the accumulated score for the improved clinical symptoms; and the changes of IgA, IgM and IgG were compared in 96 cases. RESULTS: There was a significant difference between the two groups in the accumulated scores for improvement of the symptoms ($P<0.05$). A remarkable difference was found in the therapeutic effect. And there was a significant difference in the IgA, IgM and IgG levels between the two groups ($P<0.05$). CONCLUSION: The intelligent-turtle massage is an effective therapy for relieving the physical symptoms of CFS, and it may show certain effects on the immune functions.
Wang JJ, Song YJ, Wu ZC, Chu XO, Wang QM, Wei	Hospital of Acupuncture and Moxibustion, China	[Randomized controlled study on influence of	Zhongguo Zhen Jiu. 2009 Oct;29(10):780-4.	OBJECTIVE: To observe effects of acupuncture on quality of life of patients with chronic fatigue syndrome (CFS). METHODS: Randomized, controlled and single-blinded study method was used, 70 cases were divided into an observation group and a control group, 35 cases in each group. The

LN, Wang XJ, Meng H.	Academy of Chinese Medical Sciences, Beijing 100700, China. wjj751@sina.com	acupuncture for life quality of patients with chronic fatigue syndrome] [Article in Chinese]		observation group was treated with acupuncture at Baihui (GV 20), Danzhong (CV 17), Zhongwan (CV 12), Qihai (CV 6), Guanyuan (CV 4), Hegu (LI 4), Zusanli (ST 36), etc.; the control group was treated with acupuncture at non-meridian points (2 cm to the acupoints), thrice a week. The treatment was given for 14 times. The World Health Organization Quality of Life (WHOQOL-BREF) scale was used to evaluate the patients' quality of life before and after treatment. RESULTS: The physiological field, individuals own perception of his health condition and total score were significantly improved after treatment in the observation group (all P<0.05); there were no obvious changes in the psychology, social relationships, environment and subjective feelings about the quality of life (all P>0.05). The score of the environmental field in the control group was significantly decreased compared to that before treatment (P<0.05), and there were no significant changes in the other scores. There were no adverse effects in patients. CONCLUSION: Acupuncture can improve the quality of life of CFS patients, especially in physiological field and the individual perception to his well being. Acupuncture has high safety, and the acupoints has high specific degree than non-meridian points.
Warren JW, Howard FM, Cross RK, Good JL, Weissman MM, Wesselmann U, Langenberg P, Greenberg P, Clauw DJ.	Department of Medicine, Epidemiology and Preventive Medicine, and Neurology, University of Maryland School of Medicine, Baltimore, Maryland, USA.	Antecedent nonbladder syndromes in case-control study of interstitial cystitis/painful bladder syndrome.	Urology. 2009 Jan;73(1):52-7. Epub 2008 Nov 8.	OBJECTIVES: Probing for clues to the pathogenesis of interstitial cystitis/painful bladder syndrome (IC/PBS), we sought antecedent nonbladder syndromes that distinguished incident IC/PBS cases from matched controls. METHODS: Female incident IC/PBS cases were recruited nationally, and their IC/PBS onset date (index date) was established. The controls were recruited by national random digit dialing and matched to the cases by sex, age, region, and interval between the (assigned) index date and interview. The prevalence of 24 nonbladder syndromes before the index date was assessed, 7 by multiple methods. RESULTS: The cases with IC/PBS had greater antecedent prevalence of 11 syndromes, and 243 of 313 cases (78%) vs 145 of 313 controls (45%) had multiple syndromes (P < .001). Fibromyalgia-chronic widespread pain (FM-CWP), chronic fatigue syndrome, sicca syndrome, and irritable bowel syndrome were associated with each other by pairwise and factor analyses using numerous assumptions. Cases with FM-CWP, chronic fatigue syndrome, sicca syndrome, and/or irritable bowel syndrome (n = 141, 45%) were more likely to have other syndromes (ie, migraine, chronic pelvic pain, depression, and allergy). Three other syndrome clusters were identified; each was associated with this FM-CWP cluster. CONCLUSIONS: Eleven antecedent syndromes were more often diagnosed in those with IC/PBS, and most syndromes appeared in clusters. The most prominent cluster comprised FM-CWP, chronic fatigue syndrome, sicca syndrome, and irritable bowel syndrome; most of the other syndromes and identified clusters were associated with it. Among the hypotheses generated was that some patients with IC/PBS have a systemic syndrome and not one confined to the bladder.
Watanabe K.	Department of Neuropsychiatry, Watanabe Hospital.	[Paroxysmal perceptual alteration in comparison with hallucination--a review of its clinical reports and discussion of its	Seishin Shinkeigaku Zasshi. 2009;111(2):127-36.	The syndrome of paroxysmal perceptual alteration (PPA) was first described by Yamaguchi in 1985. Since then, many PPA cases have been reported, and its pathophysiological mechanism has been proposed: a suppressed (blocked) mesolimbic and mesocortical dopaminergic system and sequential compensatory increase of noradrenergic neuronal activity are crucial for the occurrence of PPA. PPA is characterized by hypersensitivity of perception, psychedelic experience (brightening of colors, sharpening of contrast, visual distortion, etc.), and somatic schema disorder (one feels that one is floating, one's extremities are being pulled and elongated, etc.). PPA in chronic schizophrenic patients occurs abruptly like an attack mainly in the evening, often precipitated by fatigue. During the attack,

		pathophysiological mechanism in the present day, when second generation antipsychotics are widely used][Article in Japanese		patients also suffer from mood and thought alteration (anxiety, agitation, depressive mood, and inability to distract their thoughts from one thing), but they are aware that symptoms of PPA are not real and apprehensive about them. The attack ceases gradually and spontaneously while the patient rests or sleeps. These clinical features are clearly different from those of schizophrenic hallucinations. It is believed that PPA is closely related to neuroleptic treatment by conventional antipsychotics. I reported the prevalence of PPA as 4.0% in 1991 when high potential D2 blocking agents were prevailing. The occurrence of PPA has been significantly reduced to the present, when second generation (atypical) antipsychotics are prevailing. However, in my inquiry in 2004, the prevalence of PPA was 3.6% in cases treated with risperidone (RIS), while the rates were 0 in cases treated with olanzapine (OLZ), quetiapine (QTP), and perospirone (PRS). Several cases of PPA have been reported in patients who were treated with OLZ and PRS. Until now, no cases of PPA have been reported who were treated with QTP and aripiprazole (APZ). The prevalence of PPA among cases treated with these second generation antipsychotics might be related to the differences in these agents regarding their affinity for the D2 receptor: RIS has a sustained and close binding affinity, which might be similar to those of conventional antipsychotics, OLZ shows a sustained and loose binding affinity, PRS exhibits a transient and close binding affinity, whereas QTP has a transient and loose binding affinity. APZ is a partial agonist of the D2 receptor; APZ acts as an agonist under the condition of intrinsic dopaminergic dysfunction, which might prevent the occurrence of PPA.
Weinstein AA, Drinkard BM, Diao G, Furst G, Dale JK, Straus SE, Gerber LH.	Center for Study of Chronic Illness and Disability, George Mason University, Fairfax, VA 22030, USA. aweinst2@gmu.edu	Exploratory analysis of the relationships between aerobic capacity and self-reported fatigue in patients with rheumatoid arthritis, polymyositis, and chronic fatigue syndrome.	PM R. 2009 Jul;1(7):620-8.	OBJECTIVE: To determine if self-reported levels of physical activity and fatigue are related to peak oxygen uptake (VO(2peak)) and whether these relationships differ among the patient groups (rheumatoid arthritis [RA], polymyositis [PM], and chronic fatigue syndrome [CFS]). DESIGN: Correlational investigation. SETTING: Two ambulatory research clinics at the National Institutes of Health, Clinical Center, Bethesda, MD. PARTICIPANTS: There were 9 patients with PM, 10 with RA, and 10 with CFS. All patients met case criteria for their respective diagnoses. METHODS/MAIN OUTCOME MEASUREMENTS: VO(2peak) during bicycle ergometry and self-reported fatigability, fatigue, and physical activity. VO(2peak) was used as the criterion measurement of physiological fatigue with which the self-reported variables were compared. RESULTS: The Pearson r revealed that self-reported physical activity correlated with VO(2peak) (r = 61, P = .01). However, fatigability and fatigue did not correlate with VO(2peak). Linear regression analysis was performed to assess the effects of diagnosis group, self-reported activity level or fatigue, and their interaction. A trend in the data showed a distinctive relationship between fatigue/fatigability within the 3 groups. In addition, when controlling for group status, self-reported activity predicted aerobic capacity as measured by VO(2peak). CONCLUSIONS: This study confirms that patients with chronic, but stable RA, PM, or CFS are fatigued and have significantly decreased aerobic capacity. Self-reports of physical activity predicted VO(2peak), and may be used as an indicator of activity-based aerobic capacity. Self-reports of fatigue, however, did not correlate with VO(2peak) and hence are assessing something other than an index of aerobic capacity, and provide additional information about patients' perceptions, which will require further investigation.
Wells DL.	School of Psychology,	Associations between pet	J Altern Complement Med.	OBJECTIVE: This study explored the association between pet ownership and self-reported health in people suffering from chronic fatigue syndrome (CFS). METHODS: One hundred and ninety-three

	Queen's University Belfast, Northern Ireland, United Kingdom. d.wells@qub.ac.uk	ownership and self-reported health status in people suffering from chronic fatigue syndrome.	2009 Apr;15(4):407-13.	(193) people with medically diagnosed CFS completed a postal survey designed to collect information on illness severity, physical and psychologic health, and pet ownership practices. RESULTS: Most of the participants were female (72.0%), over 45 years of age (57.1%) and married (41.1%) with no children (63.1%). Pets were owned by 58.3% of the sample, with dogs and cats being the most commonly kept types of companion animal. The general health of the participants was discovered to be poor, as assessed by scores on the Chalder Fatigue Questionnaire (CFQ), General Health Questionnaire-12 (GHQ-12), and Short-Form-36 (SF-36) health survey. Pet ownership was not significantly associated with scores on the CFQ, GHQ-12, or SF-36 scales, although pet owners considered their animals to offer them a range of health benefits, notably those associated with mental well-being. CONCLUSIONS: Overall, findings suggest no statistically significant association between pet ownership and self-reported health in people with CFS. Nonetheless, people suffering from this condition believe that their pets have the potential to enhance quality of life. Although animals should not be regarded as a panacea for people with long-term conditions such as CFS, they may, nonetheless, serve a valuable, and currently underutilized, role in promoting well-being, whether in their own right, or in conjunction with more traditional forms of therapy.
Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, London SE5 9RJ, UK. s.wessely@iop.kcl.ac.uk	Surgery for the treatment of psychiatric illness: the need to test untested theories.	J R Soc Med. 2009 Oct;102(10):445-51.	
Weston S, Townsend S.	Shropshire Enablement Team.	Using a DVD to help people with chronic fatigue syndrome learn the technique of pacing.	Nurs Times. 2009 Nov 17-23;105(45):26-7.	The Shropshire Enablement Team, a specialist community rehabilitation team, has produced a DVD and booklet on pacing for people with chronic fatigue syndrome/ME. Pacing is a technique for managing fatigue, and involves achieving the correct balance between rest and activity. This article explains the benefits of pacing, and how the DVD and booklet have enabled the team to better support clients.
Wormser GP, Schwartz I.	Division of Infectious Diseases, Department of Medicine, York Medical College, Munger Pavilion Room 245, Valhalla, NY 10595, USA.	Antibiotic treatment of animals infected with Borrelia burgdorferi.	Clin Microbiol Rev. 2009 Jul;22(3):387-95.	Despite resolution of the objective manifestations of Lyme disease after antibiotic treatment, a minority of patients have fatigue, musculoskeletal pain, and/or difficulties with concentration or short-term memory of uncertain etiology; these are called post-Lyme disease symptoms or, in more severe cases, post-Lyme disease syndrome or "chronic Lyme disease." Several recent studies in which Borrelia burgdorferi-infected animals were treated with antibiotic therapy have demonstrated the presence of PCR positivity for B. burgdorferi DNA in the absence of culture positivity. In mice that were treated with antibiotic therapy, residual spirochetes could be taken up by ticks during a blood meal and could be transmitted to SCID mice. These spirochetes are attenuated; their presence is not associated with either inflammation or disease. In this review the methodology and findings of these studies are critically analyzed, and the significance of the results with regard to human Lyme disease is

	gary_wormser@nymc.edu			evaluated, with special emphasis on whether these studies provide useful insights into post-Lyme disease syndrome. A serious methodological concern is the failure to consider the pharmacokinetic-pharmacodynamic properties of the antibiotic in choosing the dosage regimen used. We conclude that there is no scientific evidence to support the hypothesis that such spirochetes, should they exist in humans, are the cause of post-Lyme disease syndrome.
Wormser GP, Shapiro ED.	Division of Infectious Diseases, Department of Medicine, New York Medical College, Munger Pavilion Room 245, Valhalla, NY 10595, USA. gary_wormser@nymc.edu	Implications of gender in chronic Lyme disease.	J Womens Health (Larchmt). 2009 Jun;18(6):831-4.	BACKGROUND: "Post-Lyme disease syndrome" refers to prolonged subjective symptoms after antibiotic treatment and resolution of an objective manifestation of Borrelia burgdorferi infection (Lyme disease). "Chronic Lyme disease" is a vaguely defined term that has been applied to patients with unexplained prolonged subjective symptoms, whether or not there was or is evidence of B. burgdorferi infection. OBJECTIVE: To determine if the population of patients with chronic Lyme disease differs from the populations of patients with either Lyme disease or post-Lyme disease syndrome by examining the gender of patients with these diagnoses. Methods: Data on gender were compiled in this cross-sectional study based on a systematic review of published studies of antibiotic treatment in United States patients with post-Lyme disease syndrome (n = 184) or chronic Lyme disease (n = 490), and on cases of adults with Lyme disease reported to the Centers for Disease Control and Prevention from 2003 to 2005 (n = 43,282). RESULTS: Patients with chronic Lyme disease were significantly more likely to be female than were patients diagnosed with either Lyme disease (odds ratio [OR] 2.42, 95% confidence interval [CI] 1.98-2.94, $p < 0.0001$) or with post-Lyme disease syndrome (OR 2.32, 95% CI 1.62-3.34, $p < 0.0001$). CONCLUSIONS: Patients with chronic Lyme disease differ with regard to gender from those with either B. burgdorferi infection or post-Lyme disease syndrome. This finding suggests that illnesses with a female preponderance, such as fibromyalgia, chronic fatigue syndrome, or depression, may be misdiagnosed as chronic Lyme disease.
Wu J, Ding HS, Ye DT.	Graduate School at Shenzhen, Tsinghua University, Shenzhen 518055, China. wuj@sz.tsinghua.edu.cn	[Evaluating fatigue resistance effect of health food by near-infrared tissue oximeter] [Article in Chinese]	Guang Pu Xue Yu Guang Pu Fen Xi. 2009 Sep;29(9):2357-60.	Currently, chronic fatigue syndrome (CFS) seriously affects people's normal living and work. In the present paper, the physiological parameters, such as tissue oxygenation saturation and heart rate, were used to evaluate the subjects' fatigue degree, and the fatigue resistance capsule and coffee were taken as a measure to adjust the fatigue. Human tissue oxygen saturation (rSO2) can be monitored noninvasively and in real time by near infrared spectroscopy (NIRS) based on spatially-resolved spectroscopy. Aiming at those brainworkers who need to work in an office for a long time; two static experiments were designed to evaluate the fatigue degree of the subjects who either take the fatigue resistance capsules/coffee or not. The rSO2 and heart rate (HR) of the subjects in the experiment group and contrast group were measured respectively for fatigue evaluation. This work particularly analyzed the changes in rSO2 in these two groups. The results show that the rSO2 of subjects in the experiment group evidently increased compared to that in the contrast group when the subjects took the fatigue resistance capsule or coffee, thereby show that the health food can reduce the fatigue to a certain extent.
Wyller VB, Eriksen HR, Malterud K.	Division of Paediatrics, Rikshospitalet University Hospital, Oslo,	Can sustained arousal explain the Chronic Fatigue Syndrome?	Behav Brain Funct. 2009 Feb 23;5:10.	ABSTRACT: We present an integrative model of disease mechanisms in the Chronic Fatigue Syndrome (CFS), unifying empirical findings from different research traditions. Based upon the Cognitive activation theory of stress (CATS), we argue that new data on cardiovascular and thermoregulatory regulation indicate a state of permanent arousal responses - sustained arousal - in this condition. We suggest that sustained arousal can originate from different precipitating factors (infections,

	Norway. brwylle@online.no.			psychosocial challenges) interacting with predisposing factors (genetic traits, personality) and learned expectancies (classical and operant conditioning). Furthermore, sustained arousal may explain documented alterations by establishing vicious circles within immunology (Th2 (humoral) vs Th1 (cellular) predominance), endocrinology (attenuated HPA axis), skeletal muscle function (attenuated cortical activation, increased oxidative stress) and cognition (impaired memory and information processing). Finally, we propose a causal link between sustained arousal and the experience of fatigue. The model of sustained arousal embraces all main findings concerning CFS disease mechanisms within one theoretical framework.
Yan S, Li HZ, Zhang XY, Li HJ.	Department of Urology, Peking Union Medical College Hospital, Peking Union Medical College, Chinese Academy of Medical Science, Beijing 100730, China.	[Retrospective analysis of the combined therapy of terazosin with chlormezanone for chronic prostatitis/chronic pelvic pain syndrome] [Article in Chinese]	Zhonghua Nan Ke Xue. 2009 Aug;15(8):717-20.	OBJECTIVE: To investigate the efficacy and safety of the alpha1-receptor inhibitor terazosin combined with chlormezanone in the treatment of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS). METHODS: A total of 168 CPPS patients, aged 20 -50 (mean 32.9) years and with the disease course of 3 months to 7 years (mean 17 months), were equally randomized into a terazosin group (n = 58), a chlormezanone group (n = 38) and a terazosin + chlormezanone (T + C) group (n = 72), and treated accordingly for 4 weeks. All the patients were scored on NIH-CPSI (National Institute of Health-Chronic Prostatitis Symptom Index) after the treatment and the therapeutic effects were compared among the three groups. RESULTS: Of the total number of patients, 159 completed the treatment and were evaluated, including 55 of the terazosin group, 35 of the chlormezanone group and 69 of the T + C group. After the treatment, the NIH-CPSI scores of the three groups decreased from 24.05 +/- 3.02 to 16.15 +/- 3.25 (mean 7.90), from 23.43 +/- 3.58 to 17.51 +/- 3.08 (mean 5.92), and from 23.93 +/- 3.30 to 15.01 +/- 3.08 (mean 8.92), respectively, with statistically significant differences from pretreatment ($P < 0.05$) as well as between the combined therapy group and the other two ($P < 0.05$). The adverse events included postural hypotension (17.1% in the terazosin group and 15.4% in the T + C group), dysspermatism (3.4% in the terazosin group only), lassitude, fatigue and anorexia (18.5% in the chlormezanone group and 12.6% in the T + C group). Nine of the patients failed to accomplish the treatment because of adverse events, 3 (5.2%) in the terazosin group, 3 (7.9%) in the chlormezanone group and 3 (12.6%) in the T + C group. CONCLUSION: Both terazosin and chlormezanone can relieve the symptoms in CP/CPPS patients and improve their life quality, but their combined use may produce a better efficacy than either terazosin or chlormezanone used alone.
Zhang L, Goudh J, Christmas D, Mattey D, Richards S, Main J, Enlander D, Honeybourne D, Ayres J, Nutt DJ, Kerr J.	St George's University of London, United Kingdom;	Microbial infections in eight genomic subtypes of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME).	J Clin Pathol. 2009 Dec 2. [Epub ahead of print]	We have previously reported genomic subtypes of CFS/ME based on expression of 88 human genes. In this study we attempted to reproduce these findings, determine specificity of this signature to CFS/ME, and test for associations between CFS/ME subtype and infection. We determined expression levels of 88 human genes in blood of 61 new patients with idiopathic CFS/ME (according to Fukuda criteria), 6 patients with Q-fever associated CFS/ME form the Birmingham Q-fever outbreak (according to Fukuda criteria), 14 patients with endogenous depression (according to DSM-IV criteria) and 18 normal blood donors. In patients with CFS/ME differential expression was confirmed for all 88 genes. Q-CFS/ME patients had similar patterns of gene expression to idiopathic CFS/ME. Gene expression in endogenous depression patients was similar to that in the normal controls, except for upregulation of five genes (APP, CREBBP, GNAS, PDCD2, PDCD6). Clustering of combined gene data in CFS/ME patients for this and our previous study (n=117 CFS/ME patients) revealed genomic subtypes with distinct differences in SF-36 scores, clinical phenotypes, severity and geographical distribution. Antibody

				testing for Epstein-Barr virus (EBV), enterovirus, Coxiella burnetii and parvovirus B19 revealed subtype-specific relationships for EBV and enterovirus, the two most common infectious triggers of CFS/ME.
Ziemssen T.	MS Center, Neurological University Clinic, Dresden, Germany. Tjalf.Ziemssen@uniklinikum-dresden.de	Multiple sclerosis beyond EDSS: depression and fatigue.	J Neurol Sci. 2009 Feb 1;277 Suppl 1:S37-41.	Depression and fatigue are common symptoms of multiple sclerosis and are the primary determinants of impaired quality of life in this demyelinating neurological disease. The twelve-month prevalence of major depression in patients with multiple sclerosis is around 15%. Untreated depression is associated with suicidal ideation, impaired cognitive function and poor adherence to immunomodulatory treatment. For these reasons, systematic screening and management of depressive symptoms is recommended for all patients with multiple sclerosis. There is some evidence that interferon-beta treatment may exacerbate depressive symptoms and a switch to glatiramer acetate can be envisaged in patients treated with an interferon-beta in whom depressive symptoms become an issue. Fatigue is present in over three-quarters of patients with multiple sclerosis. It is considered the most debilitating symptom of the disease and is a major reason for work absenteeism. There is growing evidence that immunomodulatory treatments, in particular glatiramer acetate, improve fatigue symptoms in patients with multiple sclerosis.

2008				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No authors listed]		Drug-induced interstitial pneumonia.	Prescrire Int. 2008 Apr;17(94):61-3.	(1) Interstitial pneumonia usually develops gradually. The signs and symptoms are non-specific, and generally include dyspnea, cough, fatigue, and weight loss. In other cases onset is acute, sometimes beginning with a flu-like syndrome. Interstitial pneumonia can lead to acute respiratory failure, sometimes gradual deterioration of respiratory function, and pulmonary fibrosis progressing to respiratory failure. The fibrosis does not regress when the causal factor is withdrawn. (2) There are numerous causes of interstitial pneumonia, including medicinal drugs. (3) Amiodarone generally induces slow and insidious lung disease. (4) Methotrexate induces lung disease. Most cytotoxic drugs cause chronic dose-dependent lung disease and fibrosis, in some cases long after treatment cessation. (5) The many other implicated drugs include nitrofurantoin, Nonsteroidal antiandrogens, drugs that induce connective tissue diseases, laxatives based on mineral oil, and many other drugs, some of which are known to cause hypersensitivity reactions. (6) In practice, a drug-related cause should be kept in mind in cases of interstitial pneumonia, as symptoms generally improve after drug withdrawal, unless fibrosis has already started to develop.
[No authors listed]		Cognitive behavioral therapy for chronic fatigue syndrome.	Harv Ment Health Lett. 2008 Oct;25(4):7.	
[No authors listed]		Drug-induced interstitial pneumonia.	Prescrire Int. 2008 Apr;17(94):61-3.	(1) Interstitial pneumonia usually develops gradually. The signs and symptoms are non-specific, and generally include dyspnea, cough, fatigue, and weight loss. In other cases onset is acute, sometimes beginning with a flu-like syndrome. Interstitial pneumonia can lead to acute respiratory failure, sometimes gradual deterioration of respiratory function, and pulmonary fibrosis progressing to respiratory failure. The fibrosis does not regress when the causal factor is withdrawn. (2) There are numerous causes of interstitial pneumonia, including medicinal drugs. (3) Amiodarone generally induces slow and insidious lung disease. (4) Methotrexate induces lung disease. Most cytotoxic drugs cause chronic dose-dependent lung disease and fibrosis, in some cases long after treatment cessation. (5) The many other implicated drugs include nitrofurantoin, Nonsteroidal antiandrogens, drugs that induce connective tissue diseases, laxatives based on mineral oil, and many other drugs, some of which are known to cause hypersensitivity reactions. (6) In practice, a drug-related cause should be kept in mind in cases of interstitial pneumonia, as symptoms generally improve after drug withdrawal, unless fibrosis has already started to develop.
Abeles M, Solitar BM, Pillinger MH, Abeles AM.	Division of Rheumatology, Department of Medicine, The University of Connecticut School of Medicine, Farmington, USA.	Update on fibromyalgia therapy.	Am J Med. 2008 Jul;121(7):555-61.	Primary fibromyalgia, a poorly-understood chronic pain syndrome, is characterized by widespread musculoskeletal pain, nonrestorative sleep, fatigue, psychological distress, and specific regions of localized tenderness, all in the absence of otherwise apparent organic disease. While the etiology of fibromyalgia is unclear, accumulating data suggest that disordered central pain processing likely plays a role in the pathogenesis of symptoms. Although various pharmacological treatments have been studied and espoused for treating fibromyalgia, no single drug or group of drugs has proved to be particularly useful in treating fibromyalgia patients as a whole, and only one drug to date has earned U.S. Food and Drug Administration approval for treating the syndrome in the United States. This

	aabeles@uchc.edu			review critically and systematically evaluates clinical investigations of medicinal and nonmedicinal treatments for fibromyalgia dating from 1970 to 2007.
Ablin JN, Buskila D.	Tel Aviv Sourasky Medical Center, Rheumatology Institute, Tel Aviv, Israel.	Emerging therapies for fibromyalgia.	Expert Opin Emerg Drugs. 2008 Mar;13(1):53-62.	BACKGROUND: Fibromyalgia syndrome (FMS) is a disorder characterized by widespread pain, tenderness, and fatigue. High prevalence marks the syndrome which is considered to reflect altered central pain processing. Fibromyalgia syndrome runs a chronic, non-progressive course, extracting high price owing to impaired quality of life, restricted vocational capacity, and increased health care utilization. OBJECTIVE: To review current and emerging trends in the treatment of FMS. Methods: A rigorous search of published literature, abstract presentations, and industry provided data was performed. RESULTS/CONCLUSION: The recent FDA approval of pregabalin as a first specific medication for FMS may herald a new era for the development of medications with higher specificity and efficacy for this hitherto frustrating condition.
Abzug MJ.	Department of Pediatrics, (Pediatric Infectious Diseases), University of Colorado School of Medicine, The Children's Hospital, Denver, CO 80218, USA. abzug.mark@tchden.org	The enteroviruses: an emerging infectious disease? The real, the speculative and the really speculative.	Adv Exp Med Biol. 2008;609:1-15.	
Aggarwal VR, McBeth J, Zakrzewska JM, Macfarlane GJ.	Primary Care Dentistry, Arthritis Research Campaign Epidemiology Unit, Division of Epidemiology and Health Sciences, The Medical School, University of Manchester, Oxford Road, Manchester, M13 9PT. vishal.r.aggarwal@manchester.ac.uk	Unexplained orofacial pain - is an early diagnosis possible?	Br Dent J. 2008 Aug 9;205(3):E6; discussion 140-1. Epub 2008 Jul 4. Comment in: Br Dent J. 2008 Oct 25;205(8):414; author reply 414.	Aim To identify distinct characteristics of unexplained orofacial pain that could be used by dental practitioners in making an early diagnosis.Methods Subjects reporting orofacial pain in a postal questionnaire-based cross-sectional survey were invited for clinical examination. The interviewer was blinded to the questionnaire responses of the subjects. A diagnosis was made following the examination and subjects were assigned into two groups: unexplained pain and dental pain. The questionnaire responses of subjects who had consulted a healthcare professional within these two groups were then compared with particular attention to demographics, orofacial pain characteristics, consultation behaviour and relationship with other unexplained syndromes.Results Subjects who had consulted for their pain and were assigned to the unexplained orofacial pain group were significantly ($p < 0.05$) more likely to report the following characteristics: pain descriptors (nagging, aching, tingling), pain pattern (worse with stress), site (poorly localised), duration (persistent/chronic), high disability, multiple consultations and co-morbidities (teeth grinding, reporting of other unexplained syndromes).Conclusion This study has shown that unexplained orofacial pain has distinct characteristics that differentiate it from other common dental conditions. This provides a good evidence base which can reduce uncertainty among dental practitioners, allowing them to make an early diagnosis.

Ahboucha S, Butterworth RF, Pomier-Layrargues G, Vincent C, Hassoun Z, Baker GB.	Neuroscience Research Unit, University de Montreal, Montreal, QC, Canada. samir.ahboucha@ualberta.ca	Neuroactive steroids and fatigue severity in patients with primary biliary cirrhosis and hepatitis C.	Neurogastroenterol Motil. 2008 Jun;20(6):671-9. Epub 2008 Feb 13.	Fatigue is one of the most common non-specific symptoms associated with several disease states including liver diseases. Recently, it was reported that levels of progesterone metabolites such as allopregnanolone (3alpha,5alpha-tetrahydroprogesterone; 3alpha,5alpha-THP) and isopregnanolone (3beta,5alpha-THP) were increased in plasma of patients with chronic fatigue syndrome. We hypothesize that THP metabolites might be associated with fatigue commonly observed in chronic liver diseases. We evaluated fatigue scores and plasma levels of five progesterone metabolites in 16 patients with primary biliary cirrhosis (PBC), 12 patients with chronic hepatitis C (CHC) and 11 age-matched controls. The fatigue impact scale (FIS) ratio was significantly increased ($P < 0.01$) in patients with PBC and CHC compared to controls. Plasma levels of 3alpha,5alpha-THP and pregnanolone (3alpha,5beta-THP) were significantly increased in PBC and CHC patients. The other progesterone metabolites, i.e. 3beta,5alpha-THP, 3beta,5beta-THP and 3alpha,5alpha-tetrahydrodeoxycorticosterone were either undetectable or detected only in some patients. Plasma levels of 3alpha,5alpha-THP and 3alpha,5beta-THP were found to be significantly higher in patients with fatigue ($P < 0.05$), while those of patients without fatigue were not significantly different from controls. Both 3alpha,5alpha-THP and 3alpha,5beta-THP are positive allosteric modulators of the gamma-aminobutyric acid type A (GABA-A) receptor and readily cross the blood-brain barrier. The present preliminary findings suggest that increased inhibition through GABA-A receptors due to the accumulation of neuroinhibitory steroids may represent an important pathophysiological mechanism of fatigue in chronic liver diseases.
Ahboucha S, Pomier-Layrargues G, Vincent C, Hassoun Z, Tamaz R, Baker G, Butterworth RF.	Neuroscience Research Unit, CHUM-Hôpital Saint-Luc, 1058 St.-Denis, Montreal, Quebec 2X 3J4, Canada.	Reduced plasma dehydroepiandrosterone sulfate levels are significantly correlated with fatigue severity in patients with primary biliary cirrhosis.	Neurochem Int. 2008 Mar-Apr;52(4-5):569-74. Epub 2007 Jun 19.	Fatigue is a common debilitating complication of primary biliary cirrhosis (PBC), the pathophysiologic mechanism of which is poorly understood. Recently, the neuroactive steroid dehydroepinadrosterone sulfate (DHEAS) was reported to be implicated in Chronic Fatigue Syndrome in the absence of liver disease. The present study was undertaken to analyse fatigue scores and their relationship with disease severity and circulating levels of DHEAS as well as its precursors DHEA and pregnenolone in PBC patients with (n=15) or without fatigue (n=10) compared to control subjects (n=11). Fatigue was assessed using the fatigue impact scale (FIS) including cognitive, physical and psychosocial subclasses. Steroids were measured by radioimmunoassay or gas chromatography/mass spectrometry. Plasma concentrations of DHEAS were significantly reduced in PBC patients with fatigue as compared to controls, while those of its precursors DHEA and pregnenolone remained within the control range. Plasma levels of DHEAS in PBC patients were significantly correlated with fatigue severity as reflected by total FIS scores including total ($rp=-0.42$; $p=0.018$), as well as the cognitive ($rp=-0.37$; $p=0.03$), physical ($rp=-0.48$; $p=0.006$) and psychosocial ($rp=-0.35$; $p=0.04$) subclasses of fatigue scores. No correlation of fatigue scores was observed with indices of liver function. These findings suggest that reduced levels of the neurosteroid DHEAS may contribute to fatigue in patients with PBC; substitutive therapy using DHEAS or its precursor DHEA could be beneficial in the management of fatigue in patients with low levels of DHEAS.
Ahlborg G Jr, Glise K, Jonsdortir IH, Wiegner L.	Institutet för stressmedicin, Västra Frölunda. gunnar.ahlborg@st	[Bad basis for statements about burnout syndrome] [Article	Lakartidningen. 2008 Apr 9-15;105(15):1118-9.	

	ressmedicin.com	in Swedish]		
Allen PR.	University of Utah College of Nursing, 10 South 2000 East, Salt Lake City, UT 84112-5880, USA. Peggy.Allen@hsc.utah.edu	Chronic fatigue syndrome: implications for women and their health care providers during the childbearing years.	J Midwifery Womens Health. 2008 Jul-Aug;53(4):289-301; quiz 399.	Chronic fatigue syndrome is a complex debilitating medical disorder that affects approximately 4 million persons in the United States, predominantly women. There has been little scientific exploration about the experience of pregnancy, childbirth, and the postpartum period for women with this disorder. A review of the literature and current research findings addressing the epidemiology, diagnosis, symptoms, and treatment of chronic fatigue syndrome are presented, as well as the currently available data regarding the experience of women with chronic fatigue syndrome anticipating or experiencing pregnancy and the postpartum period. Expert opinion is presented along with current evidence to provide guidelines for the care of women with chronic fatigue syndrome during pregnancy, labor and birth, lactation, and the postpartum period.
Amsterdam JD, Shults J, Rutherford N.	Depression Research Unit, Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA, United States. jamsterd@mail.med.upenn.edu	Open-label study of s-citalopram therapy of chronic fatigue syndrome and co-morbid major depressive disorder.	Prog Neuropsychopharmacol Biol Psychiatry. 2008 Jan 1;32(1):100-6. Epub 2007 Aug 3.	OBJECTIVE: Chronic fatigue syndrome (CFS) is a debilitating disorder with prominent symptoms of malaise, fatigue, myalgia, arthralgia, and impaired concentration. The symptoms of CFS may often overlap those of Major Depressive Disorder (MDD). Treatment of CFS has generally been disappointing. We hypothesized that s-citalopram therapy may improve the symptoms of both disorders in CFS patients with co-morbid depression. METHODS: 16 patients received s-citalopram 10 mg to 20 mg daily for up to 12 weeks. Outcome measures of CFS included the Chalder Fatigue Questionnaire (CFQ), the multi-dimensional Fatigue Impact Scale (FIS), the CFS symptom rating (CFS-SR) 100 mm visual analogue scale, and the clinical global impressions severity (CGI/S) and change (CGI/C) ratings. Secondary outcomes of MDD included the Hamilton Depression Rating (HAM-D), Beck Depression Inventory (BDI), and the CGI/S and CGI/C ratings of MDD. RESULTS: We observed reductions in the mean CFQ score ($p<0.0005$), FIS score ($p<0.0005$), and CGI/S ($p<0.0005$) and CGI/C ($p<0.0005$) ratings over time. There was a significant improvement in 5 of the 8 CFS-SR symptoms: post-exertion malaise ($p=0.001$), headaches ($p<0.0005$), un-refreshing sleep ($p<0.0005$), and impaired memory and concentration ($p<0.0005$). There was also a reduction in mean HAM-D ($p<0.0005$), BDI ($p<0.0005$), CGI/S ($p=0.001$) and CGI/C ($p<0.0005$) ratings of MDD. LIMITATIONS: The sample size was limited and the study design was not double-blind or placebo controlled. CONCLUSION: We observed a significant reduction in both CFS and co-morbid MDD symptom severity ratings, and improvement in 5 of 8 core somatic symptoms of CFS during s-citalopram therapy.
Annoni JM, Staub F, Bogousslavsky J, Brioschi A.	Neurological Department, Lausanne University Hospital and Medical School, 1011, Lausanne, Switzerland. Jean-Marie.Annoni@hcuge.ch	Frequency, characterisation and therapies of fatigue after stroke.	Neurol Sci. 2008 Sep;29 Suppl 2:S244-6.	Post-stroke objective or subjective fatigue occurs in around 50% of patients and is frequent (30%) even after minor strokes. It can last more than one year after the event, and is characterised by a different quality from usual fatigue and good response to rest. Associated risk factors include age, single patients, female, disability, depression, attentional impairment and sometimes posterior strokes, but also inactivity, overweight, alcohol and sleep apnoea syndrome. There are few therapy studies, but treatment may include low-intensity training, cognitive therapy, treatment of associated depression, wakefulness-promoting agents like modafinil, correction of risk factors and adaptation of activities.
Anthenelli RM, Blom TJ, McElroy	Tri-State Tobacco and Alcohol	Preliminary evidence for	Addiction. 2008 Apr;103(4):687-94.	AIMS: Study aims were threefold: (i) to determine the feasibility, potential efficacy and safety of topiramate as an aid to smoking cessation; (ii) to examine potential predictors of abstinence including

SL, Keck PE Jr.	Research Center, Cincinnati Veterans Affairs Medical Center, Cincinnati, OH 45220, USA. robert.anthenelli@va.gov	gender-specific effects of topiramate as a potential aid to smoking cessation.		gender; and (iii) to explore topiramate's effects on tobacco withdrawal and post-cessation weight gain. DESIGN: Randomized, double-blind, placebo-controlled, 11-week clinical trial with a 6-week dosage titration period and 5 weeks of maintenance treatment. SETTING: Single-site, out-patient, randomized clinical trial. PARTICIPANTS: Thirty-eight adult male and 49 female chronic smokers who smoked an average of > 10 cigarettes per day and who were motivated to try to quit smoking. INTERVENTION: Random assignment to receive either topiramate (n = 43) up to 200 mg daily in divided doses or placebo (n = 44) orally combined with brief counseling over an 11-week period. MEASUREMENTS: Carbon monoxide (CO)-confirmed 4-week prolonged abstinence rate during weeks 8-11. Changes in tobacco withdrawal, body weight and safety parameters were also assessed. FINDINGS: Overall, no significant increase in the prolonged abstinence rate was detected, but logistic regression analysis indicated significant gender-specific differences. Men treated with topiramate were nearly 16 times more likely to quit smoking than women on topiramate [37.5% versus 3.7%; odds ratio (OR) = 15.6; P = 0.016] and were roughly four times more likely to quit smoking than placebo-treated men (37.5% versus 13.6%; OR = 3.8; P = 0.098). Topiramate-treated men reported significantly lower tobacco withdrawal scores than both women taking topiramate and men on placebo. On average, male cessators on placebo gained 3.30 kg, whereas topiramate led to a 0.72 kg weight loss (P = 0.03). Study discontinuation rates due to adverse events (AEs) were significantly higher in the topiramate group (topiramate 23% versus placebo 2%). The most commonly reported AEs in the topiramate arm were paraesthesia, fatigue, difficulty with concentration/attention and nervousness. CONCLUSIONS: Topiramate produced gender-specific effects on smoking cessation. Male smokers had markedly greater quit rates than female smokers and men were roughly four times more likely to quit smoking when treated with topiramate as compared to placebo. Topiramate was fairly well tolerated, although higher discontinuation rates were seen. Topiramate's triple effects aiding smoking abstinence, attenuating nicotine withdrawal and preventing post-cessation weight gain might make it a promising agent for treating tobacco addiction, at least in men.
Armitage R, Landis C, Hoffmann R, Lentz M, Watson N, Goldberg J, Buchwald D.	Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA. rosearmi@umich.edu	Power spectral analysis of sleep EEG in twins discordant for chronic fatigue syndrome.	J Psychosom Res. 2009 Jan;66(1):51-7. Epub 2008 Nov 25.	OBJECTIVE: The purpose of the study was to evaluate quantitative sleep electroencephalogram (EEG) frequencies in monozygotic twins discordant for chronic fatigue syndrome. METHODS: Thirteen pairs of female twins underwent polysomnography. During the first night, they adapted to the sleep laboratory, and during the second night, their baseline sleep was assessed. Visual stage scoring was conducted on sleep electroencephalographic records according to standard criteria, and power spectral analysis was used to quantify delta through beta frequency bands, processed in 6-s blocks. Data were averaged across sleep stage within each twin and coded for sleep stage and the presence or absence of chronic fatigue syndrome (CFS). A completely within-subjects repeated measure multivariate analysis of variance evaluated twin pairs by frequency band by sleep stage interactions and simple effects. The relationship between alpha and delta EEG was also assessed across twin pairs. RESULTS: No significant differences in spectral power in any frequency band were found between those with CFS and their nonfatigued cotwins. Phasic alpha activity, coupled with delta was noted in five subjects with CFS but was also present in 4/5 healthy twins, indicating this finding likely reflects genetic influences on the sleep electroencephalogram rather than disease-specific sleep pathology. CONCLUSIONS: The genetic influences on sleep polysomnography and microarchitecture appear to be

				stronger than the disease influence of chronic fatigue syndrome, despite greater subjective sleep complaint among the CFS twins. EEG techniques that focus on short duration events or paradigms that probe sleep regulation may provide a better description of sleep abnormalities in CFS.
Aspler AL, Bolshin C, Vernon SD, Broderick G.	Department of Medicine, Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, T6G 2H7, Canada. gordon.broderick @ualberta.ca.	Evidence of inflammatory immune signaling in chronic fatigue syndrome: A pilot study of gene expression in peripheral blood.	Behav Brain Funct. 2008 Sep 26;4:44.	ABSTRACT: BACKGROUND: Genomic profiling of peripheral blood reveals altered immunity in chronic fatigue syndrome (CFS) however interpretation remains challenging without immune demographic context. The object of this work is to identify modulation of specific immune functional components and restructuring of co-expression networks characteristic of CFS using the quantitative genomics of peripheral blood. METHODS: Gene sets were constructed a priori for CD4+ T cells, CD8+ T cells, CD19+ B cells, CD14+ monocytes and CD16+ neutrophils from published data. A group of 111 women were classified using empiric case definition (U.S. Centers for Disease Control and Prevention) and unsupervised latent cluster analysis (LCA). Microarray profiles of peripheral blood were analyzed for expression of leukocyte-specific gene sets and characteristic changes in co-expression identified from topological evaluation of linear correlation networks. RESULTS: Median expression for a set of 6 genes preferentially up-regulated in CD19+ B cells was significantly lower in CFS ($p = 0.01$) due mainly to PTPRK and TSPAN3 expression. Although no other gene set was differentially expressed at $p < 0.05$, patterns of co-expression in each group differed markedly. Significant co-expression of CD14+ monocyte with CD16+ neutrophil ($p = 0.01$) and CD19+ B cell sets ($p = 0.00$) characterized CFS and fatigue phenotype groups. Also in CFS was a significant negative correlation between CD8+ and both CD19+ up-regulated ($p = 0.02$) and NK gene sets ($p = 0.08$). These patterns were absent in controls. CONCLUSION: Dissection of blood microarray profiles points to B cell dysfunction with coordinated immune activation supporting persistent inflammation and antibody-mediated NK cell modulation of T cell activity. This has clinical implications as the CD19+ genes identified could provide robust and biologically meaningful basis for the early detection and unambiguous phenotyping of CFS.
Axe EK, Paul Satz, Fawzy I. Fawzy		Cognitive Function and Major Depression in Chronic Fatigue: The Apathy Construct	Journal of Chronic Fatigue Syndrome 2008; 14 (4): 19-38	Objective: The current study examined cognitive function, major depressive disorder (MDD), and apathy construct symptoms in a large multi-site surveillance study of chronic fatigue syndrome conducted by the Centers for Disease Control and Prevention. Method: Subjects underwent neuropsychological testing and were administered the Diagnostic Interview Schedule to establish psychiatric diagnoses. Questions in the Beck Depression Inventory relating to motivation were used to develop an apathy construct. Results: Neuropsychological test results showed impairment in multiple cognitive domains in over 25% of the cohort, and raised proportions of outliers in motor and executive function. Memory complaints were not associated with tests of memory function. The apathy construct rather than MDD was associated with impaired cognition. Conclusions: Impaired cognition in chronic fatigue does not appear to be associated with MDD but rather with endorsement of construct symptoms. Similar associations were reported in medical conditions with known etiologies. These results suggest a potential biological basis for apathy construct symptoms.
Baars EW, Gans S, Ellis EL.	Healthcare & Nutrition Department, Louis Bolk Instituut, Driebergen, The	The effect of hepar magnesium on seasonal fatigue symptoms: a pilot study.	J Altern Complement Med. 2008 May;14(4):395-402.	OBJECTIVES: To evaluate the effect of the anthroposophic drug hepar magnesium D10 intravenously administered on seasonal fatigue symptoms. DESIGN: Time series with two measurements per week, starting before onset of treatment until three measurements after finishing treatment in a regular way. SETTINGS: Six anthroposophic general practitioner practices in the Netherlands. SUBJECTS: Twenty-three (23) patients with seasonal fatigue symptoms. INTERVENTIONS: Hepar magnesium D10

	Netherlands. e.baars@louisbolk.nl			intravenously administered every week. OUTCOME MEASURES: Mean division of 24 hours in categories: sleep, rest, everyday activities, and activities that require a large effort; fatigue-related single questions: unusual emotional response to events, problems with short-term memory, the degree to which fatigue after effort continues for longer than 2 hours, the degree to which people at the end of the day have a complete lack of energy; and the degree to which people are still fit after the evening meal; Multidimensional Fatigue Index: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue; subjective experiences with regard to the effect of the treatment. RESULTS: (1) No changes in division in 24-hour categories were found; (2) pretreatment versus post-treatment analyses (after 1 and 2.5 weeks, at the end of treatment, and 1.5 weeks after the end of treatment) demonstrated overall large statistically significant differences. Eighteen (18) of 22 patients (82%) who completed the final questionnaire judged that treatment overall had been effective for their fatigue symptoms. Nine (9) patients (41%) judged a strong improvement and 9 patients (41%) a light improvement as a result of the treatment. Four (4) patients reported no change. On average, patients received treatment 4.5 times. CONCLUSIONS: There are clear indications that hepar magnesium D10 intravenously administered can have a positive effect on subsyndromal seasonal affective disorder symptoms of fatigue. A more controlled trial is indicated to study the (long-term) effects of hepar magnesium.
Baetz M, Bowen R.	University of Saskatchewan, Saskatoon, Saskatchewan, Canada. m.baetz@usak.ca	Chronic pain and fatigue: Associations with religion and spirituality.	Pain Res Manag. 2008 Sep-Oct;13(5):383-8.	BACKGROUND: Conditions with chronic, non-life-threatening pain and fatigue remain a challenge to treat, and are associated with high health care use. Understanding psychological and psychosocial contributing and coping factors, and working with patients to modify them, is one goal of management. An individual's spirituality and/or religion may be one such factor that can influence the experience of chronic pain or fatigue. METHODS: The Canadian Community Health Survey (2002) obtained data from 37,000 individuals 15 years of age or older. From these data, four conditions with chronic pain and fatigue were analyzed together -- fibromyalgia, back pain, migraine headaches and chronic fatigue syndrome. Additional data from the survey were used to determine how religion and spirituality affect psychological well-being, as well as the use of various coping methods. RESULTS: Religious persons were less likely to have chronic pain and fatigue, while those who were spiritual but not affiliated with regular worship attendance were more likely to have those conditions. Individuals with chronic pain and fatigue were more likely to use prayer and seek spiritual support as a coping method than the general population. Furthermore, chronic pain and fatigue sufferers who were both religious and spiritual were more likely to have better psychological well-being and use positive coping strategies. INTERPRETATION: Consideration of an individual's spirituality and/or religion, and how it may be used in coping may be an additional component to the overall management of chronic pain and fatigue.
Bains W.	Delta G Ltd, 37 The Moor, Melbourn, Royston, Herts SG8 6ED, UK. william@delta-g.com	Treating Chronic Fatigue states as a disease of the regulation of energy metabolism.	Med Hypotheses. 2008 Oct;71(4):481-8. Epub 2008 Aug 5.	Chronic Fatigue Syndrome is a physiological state in which the patient feels high levels of fatigue without an obvious organic cause, which affects around 1 in 400 people in the developed world. A wide range of causes have been suggested, including immune or hormonal dysfunction, viral or bacterial infection, and psychological somatization. It is likely that several causes are needed to trigger the disease, and that the triggers are different from the mechanisms that maintain fatigue over months or years. Many treatments have been tested for CFS, with very limited success - a programme

				of combined CBT and graded exercise shows the most effect. I suggest that patients with CFS have a reduced ability to increase mitochondrial energy production when exertion requires it, with fewer mitochondria that are each more efficient, and hence nearer to their maximum energy output, than normal. A range of indirect evidence suggests that the renin-angiotensin system stimulates mitochondrial responsiveness and reduces mitochondrial efficiency: chronic under-stimulation of this system could contribute to CFS aetiology. If correct, this means that CFS can be successfully treated with RAS agonists (eg angiotensin mimetics), or adrenergic agonists. It also suggests that there will be a positive link between the use of adrenergic- and RAS-blocking drugs and CFS incidence, and a negative link between adrenergic agonist use and CFS.
Bassi N, Amital D, Amital H, Doria A, Shoenfeld Y.	Department of Rheumatology, University of Padova, Padova, Italy.	Chronic fatigue syndrome: characteristics and possible causes for its pathogenesis.	Isr Med Assoc J. 2008 Jan;10(1):79-82.	Chronic fatigue syndrome is a heterogeneous disorder with unknown pathogenesis and etiology, characterized by disabling fatigue, difficulty in concentration and memory, and concomitant skeletal and muscular pain. Several mechanisms have been suggested to play a role in CFS, such as excessive oxidative stress following exertion, immune imbalance characterized by decreased natural killer cell and macrophage activity, immunoglobulin G subclass deficiencies (IgG1, IgG3) and decreased serum concentrations of complement component. Autoantibodies were also suggested as a possible factor in the pathogenesis of CFS. Recent studies indicate that anti-serotonin, anti-microtubule-associated protein 2 and anti-muscarinic cholinergic receptor 1 may play a role in the pathogenesis of CFS. It has been demonstrated that impairment in vasoactive neuropeptide metabolism may explain the symptoms of CFS.
Bellmann-Weiler R, Schroecksnadel K, Holzer C, Larcher C, Fuchs D, Weiss G.	Department of General Internal Medicine, Clinical Immunology and Infectious Diseases, Innsbruck Medical University, Innsbruck, Austria.	IFN-gamma mediated pathways in patients with fatigue and chronic active Epstein Barr virus-infection.	J Affect Disord. 2008 May;108(1-2):171-6. Epub 2007 Oct 22.	BACKGROUND: Chronic active Epstein Barr virus (EBV)-infection is characterized by mononucleosis like symptoms including fatigue, lymphadenopathy and/or hepatosplenomegaly and serologic evidence for ongoing EBV replication. Interferon-gamma (IFN-gamma) triggers several antiviral mechanisms in target cells including the induction of indoleamine-2,3-dioxygenase (IDO), which degrades the essential amino acid tryptophan to kynurenine. Because tryptophan is a precursor of the neurotransmitter 5-hydroxytryptamine (serotonin), tryptophan depletion by IDO can cause mood disturbances in patients with chronic immune activation. METHODS: This study investigated the tryptophan metabolism in 20 patients with chronic active EBV-infection, who were followed up for 4 to 8 months and in 10 healthy age-matched controls. The clinical suspicion of chronic active EBV infection was verified by the presence of circulating antibodies against EBV early antigen (EA) and virus capsid antigen (VCA). RESULTS: Patients with detectable EBV-DNA had higher serum neopterin ($p<0.01$) and lower tryptophan concentrations ($p=0.01$) than EBV-DNA negative patients. Serum concentrations of neopterin, indicating Th-1 mediated immune activation via IFN-gamma, were positively correlated to enhanced tryptophan degradation ($rs=0.650$, $p<0.001$) in patients, but not in healthy individuals. Patients suffering from more severe symptoms (as assessed by questionnaires) tended to have aggravated tryptophan degradation. CONCLUSION: Our data show that EBV viremia is associated with cell-mediated immune activation and increased tryptophan degradation, which may partly account for the symptoms found in this disorder.
Belotti L, Bigoni F, Pezzoli F, Mosconi G.	USC Medicina del Lavoro, USS Servizio Sanitario	[Chronic fatigue syndrome: from misunderstood	G Ital Med Lav Ergon. 2007 Jul-Sep;29(3	The aim of this paper is to report the case of a Physiotherapist working in a big hospital, affected by Chronic Fatigue Syndrome (CFS). After the diagnosis, made in an High Specialized Center, the Occupational Health Physician, with the cooperation of the Nursing Managing Direction, the Chief of

	Aziendale, Ospedali Riuniti di Bergamo. lbelotti@ospedaliriuniti.bergamo.it	illness to cause of job fitness management problem and of work total disability in a physiotherapist. Case report] [Article in Italian]	Suppl):819-20.	the Department of Rehabilitation and the Physiotherapists Coordinator, had to cope with the job fitness management. Afterwards the patient, in accordance with the Physician of a Trade Union Medical Office and the Occupational Health Physician, tried to obtain the disability pension, that at the end was given by the Medical Commission of the ASL.
Ben-Zvi A, Vernon SD, Broderick G.	Department of Chemical and Materials Engineering, University of Alberta, Edmonton, Alberta, Canada.	Model-based therapeutic correction of hypothalamic-pituitary-adrenal axis dysfunction.	PLoS Comput Biol. 2009 Jan;5(1):e1000273. Epub 2009 Jan 23.	The hypothalamic-pituitary-adrenal (HPA) axis is a major system maintaining body homeostasis by regulating the neuroendocrine and sympathetic nervous systems as well modulating immune function. Recent work has shown that the complex dynamics of this system accommodate several stable steady states, one of which corresponds to the hypocortisol state observed in patients with chronic fatigue syndrome (CFS). At present these dynamics are not formally considered in the development of treatment strategies. Here we use model-based predictive control (MPC) methodology to estimate robust treatment courses for displacing the HPA axis from an abnormal hypocortisol steady state back to a healthy cortisol level. This approach was applied to a recent model of HPA axis dynamics incorporating glucocorticoid receptor kinetics. A candidate treatment that displays robust properties in the face of significant biological variability and measurement uncertainty requires that cortisol be further suppressed for a short period until adrenocorticotropic hormone levels exceed 30% of baseline. Treatment may then be discontinued, and the HPA axis will naturally progress to a stable attractor defined by normal hormone levels. Suppression of biologically available cortisol may be achieved through the use of binding proteins such as CBG and certain metabolizing enzymes, thus offering possible avenues for deployment in a clinical setting. Treatment strategies can therefore be designed that maximally exploit system dynamics to provide a robust response to treatment and ensure a positive outcome over a wide range of conditions. Perhaps most importantly, a treatment course involving further reduction in cortisol, even transient, is quite counterintuitive and challenges the conventional strategy of supplementing cortisol levels, an approach based on steady-state reasoning.
Beqaj SH, Lerner AM, Fitzgerald JT.	Pathgroup Labs, Nashville, TN, USA.	Immunoassay with cytomegalovirus early antigens from gene products p52 and CM2 (UL44 and UL57) detects active infection in patients with chronic fatigue syndrome.	J Clin Pathol. 2008 May;61(5):623-6. Epub 2007 Nov 23.	AIMS: To investigate whether the use of recombinant early antigens for detection of antibodies to human cytomegalovirus (HCMV) gene products CM(2) (UL44, UL57) and p52 (UL44) is specific in the diagnosis and differentiation of active HCMV infection in a subset of patients with chronic fatigue syndrome (CFS), a diagnosis which is often missed by the current ELISA assay that uses crude viral lysate antigen. METHODS: At a single clinic from 1999 to 2001, a total of 4774 serological tests were performed in 1135 patients with patients using two immunoassays, Copalis and ELISA. The Copalis immunoassay utilised HCMV early gene products of UL44 and UL57 recombinant antigens for detection of HCMV IgM antibody, and viral capsid antigen for detection of HCMV IgG antibody. The ELISA immunoassay utilised viral crude lysate as antigen for detection of both HCMV IgG and IgM. RESULTS: 517 patients (45.6%) were positive for HCMV IgG by both assays. Of these, 12 (2.2%) were positive for HCMV(V) IgM serum antibody by HCMV ELISA assay, and 61 (11.8%) were positive for IgM

				HCMV serum antibody by Copalis assay. The Copalis assay that uses HCMV early recombinant gene products CM(2) (UL44, UL57) and p52 (UL44) in comparison with ELISA was 98% specific. CONCLUSIONS: Immunoassays that use early antigen recombinant HCMV CM(2) and p52 are five times more sensitive than HCMV ELISA assay using viral lysate, and are specific in the detection and differentiation of active HCMV infection in a subset of patients with CFS.
Bezerra Fontenele J, Leal LK, Félix FH.		All that shine is not gold: modelling the true relation between orthostatic intolerance, fibromyalgia and chronic fatigue syndromes. Comment on: Clin Auton Res. 2008 Dec;18(6):300-7.	Clin Auton Res. 2008 Dec;18(6):298; author reply 299.	
Bhattacharjee M, Botting CH, Sillanpää MJ.	School of Mathematics and Statistics, University of St Andrews, St Andrews, Fife KY16 9ST, Scotland.	Bayesian biomarker identification based on marker-expression proteomics data.	Genomics. 2008 Dec;92(6):384-92. Epub 2008 Aug 15.	We are studying variable selection in multiple regression models in which molecular markers and/or gene-expression measurements as well as intensity measurements from protein spectra serve as predictors for the outcome variable (i.e., trait or disease state). Finding genetic biomarkers and searching genetic-epidemiological factors can be formulated as a statistical problem of variable selection, in which, from a large set of candidates, a small number of trait-associated predictors are identified. We illustrate our approach by analyzing the data available for chronic fatigue syndrome (CFS). CFS is a complex disease from several aspects, e.g., it is difficult to diagnose and difficult to quantify. To identify biomarkers we used microarray data and SELDI-TOF-based proteomics data. We also analyzed genetic marker information for a large number of SNPs for an overlapping set of individuals. The objectives of the analyses were to identify markers specific to fatigue that are also possibly exclusive to CFS. The use of such models can be motivated, for example, by the search for new biomarkers for the diagnosis and prognosis of cancer and measures of response to therapy. Generally, for this we use Bayesian hierarchical modeling and Markov Chain Monte Carlo computation.
Blazquez A, Ruiz E, Vazquez A, de Sevilla TF, Garcia-Quintana A, Garcia-Quintana J, Alegre J.	Department of Chronic Fatigue Syndrome, Vall Hebron Hospital and Delfos Medical Center, Spain. asikien@yahoo.es	Sexual dysfunction as related to severity of fatigue in women with CFS.	J Sex Marital Ther. 2008 May-Jun;34(3):240-7.	To assess sexual function in women with chronic fatigue syndrome. The study included 27 women, aged 20 to 45 years, with chronic fatigue syndrome (CFS) and 15 healthy female controls. Sexual function was measured with the Golombok Rust Inventory of Sexual Satisfaction (GRISS) questionnaire and five clinical questions. In the patient group, total fatigue impact scale (FIS) score correlated with the GRISS satisfaction (r:-0.471, P < .005), avoidance (r: 0.632, P < .001) and sensuality (r: -0.445, P = .008) subscales. The GRISS satisfaction, avoidance, and sensuality subscale results and the fact of seeing the sexual act as a negative experience correlated with the intensity of fatigue in women with CFS.
Boneva RS, Decker	Chronic Viral	Higher heart rate	Auton Neurosci.	Autonomic nervous system (ANS) dysfunction has been suggested in patients with chronic fatigue

MJ, Maloney EM, Lin JM, Jones JF, Helgason HG, Heim CM, Rye DB, Reeves WC.	Diseases Branch, National Center for Zoonotic, Vector-borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30329, USA. rboneva@cdc.gov	and reduced heart rate variability persist during sleep in chronic fatigue syndrome: a population-based study.	2007 Dec 30;137(1-2):94-101. Epub 2007 Sep 12.	syndrome (CFS). In this study, we sought to determine whether increased heart rate (HR) and reduced heart rate variability (HRV) parameters observed in CFS patients during wakefulness persist during sleep. To this end, we compared heart rate (HR) and HRV as indicators of ANS function in CFS subjects and non-fatigued (NF) controls in a population-based, case-control study. Thirty subjects with CFS and 38 NF controls, matched for age-, sex- and body mass index, were eligible for analysis. Main outcome measures included mean RR interval (RRI), HR, and HRV parameters derived from overnight ECG. Plasma aldosterone and norepinephrine levels, medicines with cardiovascular effect, and reported physical activity were examined as covariates. General Linear Models were used to assess significance of associations and adjust for potential confounders. Compared to controls, CFS cases had significantly higher mean HR (71.4 vs 64.8 bpm), with a shorter mean RRI [840.4 (85.3) vs 925.4(97.8) ms] ($p<0.0004$, each), and reduced low frequency (LF), very low frequency (VLF), and total power (TP) of HRV ($p<0.02$, all). CFS cases had significantly lower plasma aldosterone ($p<0.05$), and tended to have higher plasma norepinephrine levels. HR correlated weakly with plasma norepinephrine ($r=0.23$, $p=0.05$) and moderately with vitality and fatigue scores ($r=-0.49$ and 0.46, respectively, $p<0.0001$). Limitation in moderate physical activity was strongly associated with increased HR and decreased HRV. Nevertheless, among 42 subjects with similar physical activity limitations, CFS cases still had higher HR (71.8 bpm) than respective controls (64.9 bpm), $p=0.023$, suggesting that reduced physical activity could not fully explain CFS-associated differences in HR and HRV. After adjusting for potential confounders case-control differences in HR and TP remained significant ($p<0.05$). Conclusion: the presence of increased HR and reduced HRV in CFS during sleep coupled with higher norepinephrine levels and lower plasma aldosterone suggest a state of sympathetic ANS predominance and neuroendocrine alterations. Future research on the underlying pathophysiologic mechanisms of the association is needed.
Boone KB.	Center for Forensic Sciences, Alliant University, and Los Angeles Biomedical Institute, Los Angles, CA, USA.	Fixed Belief in Cognitive Dysfunction Despite Normal Neuropsychological Scores: Neurocognitive Hypochondriasis?	Clin Neuropsychol. 2008 Oct 16:1-21. [Epub ahead of print]	A subset of patients who present for neuropsychological testing report dysfunction in daily life activities secondary to cognitive deficits, but are found on formal testing to have no objective abnormalities, raising the possibility of "neurocognitive hypochondriasis." Such a case is presented, and the factors that appear to give rise to this presentation are explored. Cases of hypochondriacal overconcern regarding cognitive function are likely not rare, particularly given research showing there is little correlation between objective report of cognitive dysfunction and actual test scores in such conditions as mild traumatic brain injury, chronic fatigue syndrome, fibromyalgia, toxic mold exposure, and post-polio syndrome.
Boorom KF, Smith H, Nimri L, Viscogliosi E, Spanakos G, Parkar U, Li LH, Zhou XN, Ok UZ, Leelayoova S, Jones MS.	Blastocystis Research Foundation, 5060 SW Philomath Blvd, #202, Corvallis, OR 97333, USA. director@bhomcenter.org.	Oh my aching gut: irritable bowel syndrome, Blastocystis, and asymptomatic infection.	Parasit Vectors. 2008 Oct 21;1(1):40.	ABSTRACT: Blastocystis is a prevalent enteric protozoan that infects a variety of vertebrates. Infection with Blastocystis in humans has been associated with abdominal pain, diarrhea, constipation, fatigue, skin rash, and other symptoms. Researchers using different methods and examining different patient groups have reported asymptomatic infection, acute symptomatic infection, and chronic symptomatic infection. The variation in accounts has lead to disagreements concerning the role of Blastocystis in human disease, and the importance of treating it. A better understanding of the number of species of Blastocystis that can infect humans, along with realization of the limitations of the existing clinical laboratory diagnostic techniques may account for much of the disagreement. The possibility that disagreement was caused by the emergence of particular pathogenic variants of Blastocystis is

				discussed, along with the potential role of Blastocystis infection in irritable bowel syndrome (IBS). Findings are discussed concerning the role of protease-activated receptor-2 in enteric disease which may account for the presence of abdominal pain and diffuse symptoms in Blastocystis infection, even in the absence of fever and endoscopic findings. The availability of better diagnostic techniques and treatments for Blastocystis infection may be of value in understanding chronic gastrointestinal illness of unknown etiology.
Bourrillon A.	Service de pédiatrie générale, hôpital Robert-Debré, 75019 Paris. antoine.bourrillon @rdb.aphp.fr	[Tired children and school] [Article in French]	Rev Prat. 2008 Apr 15;58(7):731-6.	Fatigue is a commonly observed symptom in school environments. Its clinical diagnosis is established based on symptomatology, which varies depending on the age. At school, daily rhythm disorders followed by breakdowns are common causes of school fatigue, requiring adequate corrective measures. Organic causes of school fatigue are uncommon in school environments. They are mostly infectious and suggest in rare occasions a severe condition. Detecting fatigue requires a thorough anamnestic investigation, which most of the time enables to identify the factors responsible for asthenia and suggest correctives measures. Chronic fatigue syndrome affects first and foremost teenagers and its pathophysiological assessment can lead to a better understanding of lasting fatigue in children.
Bramsen I.	Centre of Expertise Participation, Occupation and Health, Rotterdam University, Rotterdam, The Netherlands.	Can CBT substantially change grey matter volume in chronic fatigue syndrome?	Brain. 2008 Aug 29. [Epub ahead of print]	
Brimmer DJ, McCleary KK, Lupton TA, Faryna KM, Hynes K, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. dyv4@cdc.gov	A train-the-trainer education and promotion program: chronic fatigue syndrome--a diagnostic and management challenge.	BMC Med Educ. 2008 Oct 15;8:49.	BACKGROUND: Chronic fatigue syndrome (CFS) is a complicated illness for providers and patients. Fewer than 20% of persons with CFS have been diagnosed and treated. For providers, compounding the issue are the challenges in making a diagnosis due to the lack of a biomedical marker. METHODS: The objective of the CFS diagnosis and management curriculum was to instruct core trainers as to the evaluation, diagnosis, and management of CFS. Over a two year period, 79 primary care physicians, physician assistants, and nurse practitioners from diverse regions in the U.S. participated as core trainers in a two day Train-the-Trainer (TTT) workshop. As core trainers, the workshop participants were expected to show increases in knowledge, self-efficacy, and management skills with the primary goal of conducting secondary presentations. RESULTS: The optimal goal for each core trainer to present secondary training to 50 persons in the health care field was not reached. However, the combined core trainer group successfully reached 2064 primary care providers. Eighty-two percent of core trainers responded "Very good" or "Excellent" in a post-tessurvey of self-efficacy expectation and CFS diagnosis. Data from the Chicago workshops showed significant improvement on the Primary Care Opinion Survey ($p < 0.01$) and on the Relevance and Responsibility Factors of the CAT survey ($p = 0.03$ and $p = 0.04$, respectively). Dallas workshop data show a significant change from pre- to post-test scores on the CFS Knowledge test ($p = 0.001$). Qualitative and process evaluation data revealed that target audience and administrative barriers impacted secondary training feasibility. CONCLUSION: Data show the workshop was successful in meeting the objectives of increasing CFS knowledge and

				raising perceived self-efficacy towards making a diagnosis. The CFS TTT program informed an educational provider project by shifting the format for physicians to grand rounds and continuing medical education design while retaining TTT aspects for nurse practitioners and physicians assistants. Evaluations also indicate that secondary trainings may be more readily employed and accepted if administrative barriers are addressed early in the planning phases.
Buitenhuis J, de Jong PJ, Jaspers JP, Groothoff JW.	Medical Department, Univé Insurance and Department of Social Medicine, University Medical Center Groningen, University of Groningen, the Netherlands. j.buitenhuis@unive.nl	Catastrophizing and causal beliefs in whiplash.	Spine. 2008 Oct 15;33(22):2427-33; discussion 2434.	STUDY DESIGN: Prospective cohort study. OBJECTIVE: This study investigates the role of pain catastrophizing and causal beliefs with regard to severity and persistence of neck complaints after motor vehicle accidents. SUMMARY OF BACKGROUND DATA.: In previous research on low back pain, somatoform disorders and chronic fatigue syndrome, pain catastrophizing and causal beliefs were found to be related to perceived disability and prognosis. Furthermore, it has been argued with respect to whiplash that culturally dependent symptom expectations are responsible for a chronic course. METHODS: Individuals involved in traffic accidents who initiated compensation claim procedures with a Dutch insurance company were sent questionnaires (Q1) containing the Neck Disability Index, the Pain Catastrophizing Scale, and the Causal Beliefs Questionnaire-Whiplash. Of 1252 questionnaires dispatched, 747 (59.7%) were returned. Only car occupants with neck complaints were included in this study (n = 140). Complaints were monitored using additional questionnaires administered 6 (Q2) and 12 months (Q3) after the accident. RESULTS: Pain catastrophizing and causal beliefs were related to the severity of concurrent whiplash disability. The severity of initial complaints was related to the severity and persistence of whiplash complaints. Attributing initial neck complaints to whiplash was found to predict the persistence of disability at 6 and 12 months follow-up, over and above the severity of the initial complaints. CONCLUSION: The results suggest that causal beliefs may play a major role in the perceived disability and course of neck complaints after motor vehicle accidents, whereas pain catastrophizing is predominantly related to concurrent disability.The current findings are consistent with the view that an early conviction that neck complaints are caused by the medico-cultural entity whiplash has a detrimental effect on the course of symptoms.
Bullinger M.	Institut für Medizinische Psychologie, Universitätskliniku m Hamburg-Eppendorf, 20246 Hamburg. bullinger@uke.uni-hamburg.de	[Environmental health conditions] [Article in German]	Psychother Psychosom Med Psychol. 2008 Nov;58(11):430-8; quiz 439-40. Epub 2008 Oct 31.	
Busconi BB, DeAngelis N, Guerrero PE.	Department of Orthopedics, U-Mass Medical School, Worcester, MA, USA. BusconiB@ummhc	The proximal biceps tendon: tricks and pearls.	Sports Med Arthrosc. 2008 Sep;16(3):187-94.	The diagnosis and treatment of proximal biceps tendon injuries continue to be a challenge. The difficulty lies on determining if there is isolated biceps pathology versus concomitant rotator cuff tears or instability. Imaging modalities, such as magnetic resonance imaging, continue to provide us with the extra tool to help us confirm our suspicion of additional pathology. Symptomatic biceps tendon tears can undergo debridement, tenotomy, or tenodesis if nonoperative measures fail to provide relief. Reports from performing a biceps tenotomy often give similar functional outcomes compared

	.org			with tenodesis. Cosmetic deformity on the lateral arm may be noted with tenodesis and initial fatigue. Tenodesis may subject the patient to a longer rehabilitation process and increased pain. The decision of which one should be performed lies between the physician and the patient's expectations.
Carlsson B.	Västrums läkarmottagning, Gusum. bjorna99@telia.com	[Fatigue syndrome--a disease to be taken seriously by the Swedish Social Insurance Agency] [Article in Swedish]	Lakartidningen. 2008 Apr 23-May 6;105(17-18):1314-5.	
Caro XJ, Winter EF, Dumas AJ.	Division of Rheumatology, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. xjcaro@earthlink.net	A subset of fibromyalgia patients have findings suggestive of chronic inflammatory demyelinating polyneuropathy and appear to respond to IVIg.	Rheumatology (Oxford). 2008 Feb;47(2):208-11.	OBJECTIVES: The aetiopathogenesis of the fibromyalgia syndrome (FMS) remains unknown. Recent reports, however, suggest that a subgroup of FMS subjects has an immune-mediated disease. Therefore, our primary objective was to study FMS subjects for evidence of an immune-mediated demyelinating polyneuropathy. Our secondary objective was to determine the effects of treating these FMS subjects with the immune modulator, intravenous immunoglobulin (IVIg). METHODS: Fifty-eight FMS subjects, 26 rheumatic non-FMS subjects and 52 non-rheumatic non-FMS subjects were studied. Subjective measures of paraesthesias, weakness, stocking hypaesthesia, pain, fatigue and stiffness were made. Objective measures of tenderness, proximal muscle strength and electrodiagnostic (EDX) evidence of polyneuropathy and demyelination were also made. Eleven other FMS subjects underwent sural nerve biopsy. RESULTS: Paraesthesias, subjective weakness and stocking hypaesthesia were more common in FMS than in rheumatic non-FMS (P < or = 0.0001). Proximal muscle strength was less in FMS than in rheumatic non-FMS (P < or = 0.0001). EDX demonstrated a distal demyelinating polyneuropathy, suggestive of chronic inflammatory demyelinating polyneuropathy (CIDP), in 33% of FMS subjects. No rheumatic non-FMS subject had polyneuropathy (P = 0.005), or demyelination (P = 0.05). Fifteen FMS/CIDP subjects were subsequently treated with IVIg (400 mg/kg each day for 5 days). Pain (P = 0.01), tenderness (P = 0.001) and strength (P = 0.04) improved significantly. Fatigue and stiffness trended towards improvement. CONCLUSIONS: A significant subset of FMS subjects have clinical and EDX findings suggestive of CIDP. IVIg treatment shows promise in treating this subset. These observations have implications for better understanding and treating some FMS patients.
Carville SF, Arendt-Nielsen S, Bliddal H, Blotman F, Branco JC, Buskila D, Da Silva JA, Danneskiold-SamsÃ¸e B, Dincer F, Henriksson C, Henriksson KG, Kosek E, Longley K,	Academic Rheumatology Unit, King's College London, Weston Education Centre, Cutcombe Road, London SE5 9RJ, UK. serena.carville@kcl.ac.uk	EULAR evidence-based recommendations for the management of fibromyalgia syndrome.	Ann Rheum Dis. 2008 Apr;67(4):536-41. Epub 2007 Jul 20.	OBJECTIVE: To develop evidence-based recommendations for the management of fibromyalgia syndrome. METHODS: A multidisciplinary task force was formed representing 11 European countries. The design of the study, including search strategy, participants, interventions, outcome measures, data collection and analytical method, was defined at the outset. A systematic review was undertaken with the keywords "fibromyalgia", "treatment or management" and "trial". Studies were excluded if they did not utilise the American College of Rheumatology classification criteria, were not clinical trials, or included patients with chronic fatigue syndrome or myalgic encephalomyelitis. Primary outcome measures were change in pain assessed by visual analogue scale and fibromyalgia impact questionnaire. The quality of the studies was categorised based on randomisation, blinding and allocation concealment. Only the highest quality studies were used to base recommendations on.

McCarthy GM, Perrot S, Puszczewicz M, Sarzi-Puttini P, Silman A, SpÃ¤th M, Choy EH; EULAR.				When there was insufficient evidence from the literature, a Delphi process was used to provide basis for recommendation. RESULTS: 146 studies were eligible for the review. 39 pharmacological intervention studies and 59 non-pharmacological were included in the final recommendation summary tables once those of a lower quality or with insufficient data were separated. The categories of treatment identified were antidepressants, analgesics, and "other pharmacological" and exercise, cognitive behavioural therapy, education, dietary interventions and "other non-pharmacological". In many studies sample size was small and the quality of the study was insufficient for strong recommendations to be made. CONCLUSIONS: Nine recommendations for the management of fibromyalgia syndrome were developed using a systematic review and expert consensus.
Caseras X, Mataix-Cols D, Rimes KA, Giampietro V, Brammer M, Zelaya F, Chalder T, Godfrey E.	Division of Psychological Medicine and Psychiatry, King's College London, Institute of Psychiatry, London, UK.	The neural correlates of fatigue: an exploratory imaginal fatigue provocation study in chronic fatigue syndrome.	Psychol Med. 2008 Jul;38(7):941-51. Epub 2008 Apr 30.	BACKGROUND: Fatigue is the central symptom in chronic fatigue syndrome (CFS) and yet very little is known about its neural correlates. The aim of this study was to explore the functional brain response, using functional magnetic resonance imaging (fMRI), to the imaginal experience of fatigue in CFS patients and controls.MethodWe compared the blood oxygen level dependent (BOLD) responses of 12 CFS patients and 11 healthy controls to a novel fatigue provocation procedure designed to mimic real-life situations. A non-fatiguing anxiety-provoking condition was also included to control for the non-specific effects of negative affect. RESULTS: During the provocation of fatigue, CFS patients reported feelings of both fatigue and anxiety and, compared to controls, they showed increased activation in the occipito-parietal cortex, posterior cingulate gyrus and parahippocampal gyrus, and decreased activation in dorsolateral and dorsomedial prefrontal cortices. The reverse pattern of findings was observed during the anxiety-provoking scenarios. CONCLUSIONS: The results may suggest that, in CFS patients, the provocation of fatigue is associated with exaggerated emotional responses that patients may have difficulty suppressing. These findings are discussed in relation to the cognitive-behavioural model of CFS.
Cathébras P, Lauwers A.	Service de médecine interne, hôpital Nord, CHU de Saint-Etienne, 42055 Saint-Etienne Cedex 2, France. pascal.cathebras@chu-st-etienne.fr	[Should we make the diagnosis of fibromyalgia?] [Article in French]	Rev Prat. 2009 Jan 20;59(1):25-31.	Fibromyalgia is a functional somatic syndrome characterized by widespread musculoskeletal pain, fatigue, poor sleep, and exercise intolerance, frequently (but inconstantly) associated with psychological distress. Fibromyalgia is a common condition, affecting predominantly middle-aged women, with a chronic course. Fibromaylgia should be differentiated from, and may be associated with, a number of metabolic, rheumatic, neurological or psychiatric conditions. The most plausible pathophysiologic mechanism involves an alteration of pain modulation at the peripheral and central levels of the nervous system ("sensitization"). Psychosocial factors play an important role in precipitating and maintaining symptoms, health care utilization, and disablement. Treatments of fibromyalgia rely mainly on the acknowledgement of pain and distress, patient education, analgesics, balneotherapy and physiotherapy, physical reconditioning (aerobic exercise), and certain antidepressants.
Check JH, Katsoff D, Kaplan H, Liss J, Boimel P.	The University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School at	A disorder of sympathomimetic amines leading to increased vascular permeability may be the etiologic	108: Med Hypotheses. 2008;70(3):671-7. Epub 2007 Aug 31.	There is an evidence that increased capillary permeability in the standing position is related to a deficit in the sympathetic nervous system. The leakage of this fluid leads to various clinical conditions which frequently puzzle the consulting physician because despite the frequency of this condition intelligent physicians and patients are unaware of the cause of their condition. One of the most common manifestations is the inability to lose weight despite proper dieting. A randomized study comparing the efficacy of a diuretic, a converting enzyme inhibitor, spironolactone and a sympathomimetic

	Camden, Cooper Hospital/University Medical Center, Department of Obstetrics and Gynecology, Camden, NJ, United States. laurie@ccivf.com	factor in various treatment refractory health problems in women.		amine on weight loss in diet refractory women found that only the latter in the form of dextroamphetamine sulfate demonstrated significant weight reduction over a six month time span. In fact, the dextroamphetamine sulfate proved effective when given in the next 6 months to the three groups failing to respond for the first 6 months. The diagnosis of a deficit in sympathomimetic amines is established by demonstrating an abnormal clearance of a water load in the erect position and exclusion of other conditions that are associated with an abnormal free water clearance, e.g., hypothyroidism, renal or liver disease or congestive heart failure. The original definition of an abnormal water load test was excretion of <55% of a 1500 ml water load in 6h but we found that <75% defines a greater population who suffer from this problem. There are several conditions that have proven refractory to conventional theory that respond quickly and effectively to sympathomimetic amines. There have been many anecdotal reports of relieving interactable pain syndromes quickly and efficiently with sympathomimetic amine theory, despite failure with a multitude of other therapies. These include interstitial cystitis and pelvic pain that was attributed to endometriosis, gastrointestinal pain including esophagitis and gastroparesis, headaches, joint pain, fibromyalgia, and carpal tunnel syndrome. It is not clear if the improvement in pain is related to a decrease in fluid retention or a direct effect of the sympathomimetic amines on the sympathetic nervous system. Sympathomimetic amine theory has helped other conditions besides pain, e.g., chronic fatigue, vasomotor symptoms in young women not associated with decreased ovarian egg reserve, and chronic urticaria resistant to all other therapies. Thus, these studies strongly suggest that physicians be aware of this condition involving a deficit in the sympathetic nervous system when faced with various enigmatic complaints especially if standard therapy has not proven effective.
Chen GL, Xiao GM, Zheng XL.	Rehabilitation Treatment Center, Gansu Provincial Hospital of TCM, Lanzhou 730050, China. chenguolian1234@163.com	[Observation on therapeutic effect of multiple cupping at back-shu points on chronic fatigue syndrome] [Article in Chinese]	Zhongguo Zhen Jiu. 2008 Jun;28(6):405-7.	OBJECTIVE: To observe therapeutic effect of multiple cupping at back-shu points of zang-and fu-organs on chronic fatigue syndrome. METHODS: One hundred and ninety-one cases were randomly divided into 2 groups. The multiple cupping group (n = 142) were treated with multiple cupping along both sides of the spinal cord, and the acupuncture group (n = 49) were treated with acupuncture at acupoints selected according to TCM syndrome differentiation. Their therapeutic effects were assessed by clinical symptoms and Fatigue Assessment Indexes (FAI). RESULTS: The total effective rate was 97.9% in the multiple cupping group and 79.6% in the acupuncture group with a very significant difference between the two groups (P < 0.01), and after treatment, there was a very significant difference between the two groups in FAI score (P < 0.01). CONCLUSION: Multiple cupping at back-shu points of zang-and fu-organs is an effective method for chronic fatigue syndrome.
Chen R, Liang FX, Moriya J, Yamakawa J, Sumino H, Kanda T, Takahashi T.	Department of General Medicine, Kanazawa Medical University, Ishikawa, Japan.	Chronic fatigue syndrome and the central nervous system.	J Int Med Res. 2008 Sep-Oct;36(5):867-74.	An increasing amount of neuroimaging evidence supports the hypothesis that chronic fatigue syndrome patients have structural or functional abnormalities within the brain. Moreover, some neurotrophic factors, neurotransmitters and cytokines have also been evaluated in order to elucidate the mechanism of abnormal neuropsychic findings in chronic fatigue syndrome. In this review, we suggest that the focal point of chronic fatigue syndrome research should be transferred to the central nervous system.
Chen R, Moriya J, Luo X, Yamakawa JI, Takahashi T,	Department of General Medicine, Kanazawa Medical	Hochu-Ekki-to Combined with Interferon-Gamma	Immunopharmacol Immunotoxicol. 2008 Sep 12:1-15.	The purpose of this study was to evaluate the beneficial effect of Hochu-ekki-to (TJ-41) combined with interferon-gamma (IFNgamma) on daily activity, immunological and neurological alternation in a mouse model of chronic fatigue syndrome (CFS). CFS was induced by 6 times of repeated injection of

Sasaki K, Yoshizaki F.	University, Ishikawa, Japan.	Moderately Enhances Daily Activity of Chronic Fatigue Syndrome Mice by Increasing NK Cell Activity, but not Neuroprotection.	[Epub ahead of print]	Brucella abortus antigen every 2 weeks. Both single TJ-41 and TJ-41 combined with IFNgamma increased running activity and thymus weight of CFS mice, while thicker thymic cortex together with elevation of natural killer cell activity was only found in the combined treatment group. No significant improvement was observed in the atrophic brain and decreased expression level of brain-derived neurotrophic factor and Bcl-2 mRNA in hippocampus in both treatment groups. Our results suggest that TJ-41 combined with IFNgamma might have a protective effect on the marked reduction in the activity in a model of CFS via normalization of host immune responses, but not neuroprotection.
Chen R, Moriya J, Yamakawa JI, Takahashi T, Kanda T.	Department of General Medicine, Kanazawa Medical University, 1-1 Daigaku, Uchinada-machi, Kahoku-gun, Ishikawa 920-0293, Japan. kandat@kanazawa-med.ac.jp.	Traditional Chinese Medicine for Chronic Fatigue Syndrome.	Evid Based Complement Alternat Med. 2008 Feb 27. [Epub ahead of print]	More and more patients have been diagnosed as having chronic fatigue syndrome (CFS) in recent years. Western drug use for this syndrome is often associated with many side-effects and little clinical benefit. As an alternative medicine, traditional Chinese medicine (TCM) has provided some evidences based upon ancient texts and recent studies, not only to offer clinical benefit but also offer insights into their mechanisms of action. It has perceived advantages such as being natural, effective and safe to ameliorate symptoms of CFS such as fatigue, disordered sleep, cognitive handicaps and other complex complaints, although there are some limitations regarding the diagnostic standards and methodology in related clinical or experimental studies. Modern mechanisms of TCM on CFS mainly focus on adjusting immune dysfunction, regulating abnormal activity in the hypothalamic-pituitary-adrenal (HPA) axis and serving as an antioxidant. It is vitally important for the further development to establish standards for 'zheng' of CFS, i.e. the different types of CFS pathogenesis in TCM, to perform randomized and controlled trials of TCM on CFS and to make full use of the latest biological, biochemical, molecular and immunological approaches in the experimental design.
Chen R, Moriya J, Yamakawa JI, Takahashi T, Li Q, Morimoto S, Iwai K, Sumino H, Yamaguchi N, Kanda T.	Department of General Medicine, Kanazawa Medical University, 1-1 Daigaku, Uchinada-machi, Kahoku-gun, Ishikawa, 920-0293, Japan.	Brain Atrophy in a Murine Model of Chronic Fatigue Syndrome and Beneficial Effect of Hochu-ekki-to (TJ-41).	Neurochem Res. 2008 Mar 4. [Epub ahead of print]	Brain-derived neurotrophic factor (BDNF) is associated with the main symptoms of chronic fatigue sydrome (CFS) and neuron apoptosis. Nevertheless, no study has been performed directly to explore the relationship between CFS, BDNF and neuron apoptosis. We induced a CFS model by six injections of killed Brucella abortus antigen in BALB/c mice and treated them with Hochu-ekki-to (TJ-41). Daily running activity, body weight (BW), ratio of cerebral weight to BW (CW/BW) and expression levels of BDNF and Bcl-2 mRNA in the hippocampus were determined. The daily activity and CW/BW decreased significantly in the CFS model. BDNF and Bcl-2 mRNA expression levels in the hippocampus were suppressed in the CFS model and TJ-41 treated mice, while no significant difference was found between them. We improved a murine model to investigate the relationship between CFS and brain dysfunction. In this model, reduced daily activity might have been associated with decreased hippocampal BDNF mRNA expression, hippocampal apoptosis and brain atrophy. TJ-41 increased the daily running activity of the model, which was independent of brain recovery.
Chester AC.		Chronic rhinosinusitis-related fatigue: does the Internet provide a clue? Comment on: Ear Nose Throat J.	Ear Nose Throat J. 2008 Jun;87(6):310; author reply 310.	

		2007 Aug;86(8):482, 484-6.		
Chew-Graham C, Dixon R, Shaw JW, Smyth N, Lovell K, Peters S.	School of Community-Based Medicine, University of Manchester, Manchester, M13 9PL, UK. cchew@manchester.ac.uk.	Practice Nurses' views of their role in the management of Chronic Fatigue Syndrome/Myalagic Encephalitis: a qualitative study.	BMC Nurs. 2009 Jan 22;8:2.	ABSTRACT: BACKGROUND: NICE guidelines suggest that patients with Chronic Fatigue Syndrome/Myalgic Encephalitis (CFS/ME) should be managed in Primary Care. Practice Nurses are increasingly being involved in the management of long-term conditions, so are likely to also have a growing role in managing CFS/ME. However their attitudes to, and experiences of patients with CFS/ME and its management must be explored to understand what barriers may exist in developing their role for this group of patients. The aim of this study was to explore Practice Nurses' understanding and beliefs about CFS/ME and its management. METHODS: Semi-structured interviews with 29 Practice Nurses. Interviews were transcribed verbatim and an iterative approach used to develop themes from the dataset. RESULTS: Practice nurses had limited understanding about CFS/ME which had been largely gained through contact with patients, friends, personal experiences and the media rather than formal training. They had difficulty seeing CFS/ME as a long term condition. They did identify a potential role they could have in management of CFS/ME but devalued their own skills in psychological intervention, and suggested counselling would be an appropriate therapeutic option. They recognised a need for further training and on going supervision from both medical and psychological colleagues. Some viewed the condition as contentious and held pejorative views about CFS/ME. Such scepticism and negative attitudes will be a significant barrier to the management of patients with CFS/ME in primary care. CONCLUSION: The current role of Practice Nurses in the ongoing management of patients with CFS/ME is limited. Practice Nurses have little understanding of the evidence-base for treatment of CFS/ME, particularly psychological therapies, describing management options in terms of advice giving, self-help or counselling. Practice Nurses largely welcomed the potential development of their role in this area, but identified barriers and training needs which must be addressed to enable them to feel confident managing of patients with this condition. Training must begin by addressing negative attitudes to patients with CFS/ME.
Chew-Graham CA, Cahill G, Dowrick C, Wearden A, Peters S.	School of Community-Based Medicine, University of Manchester, Manchester, UK. carolyn.chew-graham@manchester.ac.uk	Using multiple sources of knowledge to reach clinical understanding of chronic fatigue syndrome.	Ann Fam Med. 2008 Jul-Aug;6(4):340-8.	PURPOSE: Chronic fatigue syndrome (CFS), or myalgic encephalitis (ME), is a contentious condition and often a diagnosis of exclusion. Current policy in the United Kingdom recommends management in primary care. We explored how patients with CFS/ME and family physicians understand this condition and how their understanding might affect the primary care consultation. METHODS: We undertook a qualitative study with patients and family physicians from North West England participating in a primary care-based randomized controlled trial (FINE Trial). Data were collected through purposive sampling and in-depth semistructured interviews with 24 patients and 14 family physicians. We analyzed interview transcripts using constant comparison methods. RESULTS: Family physicians access social and cultural knowledge to reach a clinical understanding of CFS/ME and its management. Patients recognize the difficulties family physicians encounter in understanding their symptoms and access similar nonclinical sources of information. We suggest that both patients and physicians use biomedical discourse within the consultation: the physician to maintain the position as an expert, the patient to engage the physician. CONCLUSIONS: Family physicians obtain information about CFS/ME from their nonprofessional world, which they incorporate into their professional realm. Patients and

				physicians describe the use of the discourse of science within consultations about CFS/ME. This form of shared understanding could lead to a positive collaborative interaction. Family physicians need a biomedical, evidence-based knowledge about CFS/ME. There is potential to use the rich knowledge base that patients can bring to consultations in training initiatives directed at family physicians.
Chia JK, Chia AY.	EV Med Research, Lomita, California 90717, USA. evmed@sbcglobal.net	Chronic fatigue syndrome is associated with chronic enterovirus infection of the stomach. Comment in: J Clin Pathol. 2008 Jan;61(1):1-2.	J Clin Pathol. 2008 Jan;61(1):43-8. Epub 2007 Sep 13.	BACKGROUND AND AIMS: The aetiology for chronic fatigue syndrome (CFS) remains elusive although enteroviruses have been implicated as one of the causes by a number of studies. Since most CFS patients have persistent or intermittent gastrointestinal (GI) symptoms, the presence of viral capsid protein 1 (VP1), enterovirus (EV) RNA and culturable virus in the stomach biopsy specimens of patients with CFS was evaluated. METHODS: 165 consecutive patients with CFS underwent upper GI endoscopies and antrum biopsies. Immunoperoxidase staining was performed using EV-specific monoclonal antibody (mAb) or a control mAb specific for cytomegalovirus (CMV). RT-PCR ELISA was performed on RNA extracted from paraffin sections or samples preserved in RNA later. Biopsies from normal stomach and other gastric diseases served as controls. 75 samples were cultured for EV. RESULTS: 135/165 (82%) biopsies stained positive for VP1 within parietal cells, whereas 7/34 (20%) of the controls stained positive (p< or =0.001). CMV mAb failed to stain any of the biopsy specimens. Biopsies taken from six patients at the onset of the CFS/abdominal symptoms, and 2-8 years later showed positive staining in the paired specimens. EV RNA was detected in 9/24 (37%) paraffin-embedded biopsy samples; 1/21 controls had detectable EV RNA (p<0.01); 1/3 patients had detectable EV RNA from two samples taken 4 years apart; 5 patient samples showed transient growth of non-cytopathic enteroviruses. CONCLUSION: Enterovirus VP1, RNA and non-cytopathic viruses were detected in the stomach biopsy specimens of CFS patients with chronic abdominal complaints. A significant subset of CFS patients may have a chronic, disseminated, non-cytolytic form of enteroviral infection, which could be diagnosed by stomach biopsy.
Cho HJ, Bhugra D, Wessely S.	Department of Psychiatry, Federal University of São Paulo, São Paulo, Brazil. h.cho@iop.kcl.ac.uk	'Physical or psychological?'- a comparative study of causal attribution for chronic fatigue in Brazilian and British primary care patients.	Acta Psychiatr Scand. 2008 Jul;118(1):34-41. Epub 2008 May 22.	OBJECTIVE: Causal attribution influences symptom experience, help-seeking behaviour and prognosis in chronic fatigue syndrome. We compared causal attribution of patients with unexplained chronic fatigue (UCF) in Brazil and Britain. METHOD: Primary care attenders in SÃ£o Paulo (n = 3914) and London (n = 2459) were screened for the presence of UCF. Those with UCF (SÃ£o Paulo n = 452; London n = 178) were assessed for causal attribution (physical vs. psychosocial), perceived chronicity (i.e. reported duration of fatigue) and disability. RESULTS: British UCF patients were more likely to attribute their fatigue to physical causes (adjusted odds ratio 1.70, P = 0.037) and perceived their fatigue to be more chronic (adjusted beta 0.15, P = 0.002). There was no significant difference in current disability (adjusted beta -0.01, P = 0.81). CONCLUSION: Despite similar disability levels, UCF patients in different cultural settings presented different attributions and perceptions about their illness. Sociocultural factors may have an important role in shaping illness attribution and perception around chronic fatigue.
Cho HJ, Menezes PR, Bhugra D, Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, King's College	The awareness of chronic fatigue syndrome: a comparative study in Brazil and the	J Psychosom Res. 2008 Apr;64(4):351-5.	OBJECTIVE: While in many Western affluent countries there is widespread awareness of chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME), little is known about the awareness of CFS/ME in low- and middle-income countries. We compared the awareness of CFS in Brazil and the United Kingdom. METHODS: Recognition and knowledge of CFS were assessed among 120 Brazilian specialist doctors in two major university hospitals using a typical case vignette of CFS.

	London, United Kingdom. h.cho@iop.kcl.ac.uk	United Kingdom.		We also surveyed 3914 and 2435 consecutive attenders in Brazilian and British primary care clinics, respectively, concerning their awareness of CFS. RESULTS: When given a typical case vignette of CFS, only 30.8% [95% confidence interval (CI), 22.7-39.9%] of Brazilian specialist doctors mentioned chronic fatigue or CFS as a possible diagnosis, a proportion substantially lower than that observed in Western affluent countries. Similarly, only 16.2% (95% CI, 15.1-17.4%) of Brazilian primary care attenders were aware of CFS, in contrast to 55.1% (95% CI, 53.1-57.1%) of their British counterparts (P<.001). This difference remained highly significant after controlling for patients' sociodemographic and socioeconomic characteristics (P<.001). CONCLUSIONS: The awareness of CFS was substantially lower in Brazil than the United Kingdom. The observed difference may influence patients' help-seeking behavior and both doctors' and patients' beliefs and attitudes in relation to fatigue-related syndromes. Attempts to promote the awareness of CFS should be considered in Brazil, but careful plans are required to ensure the delivery of sound evidence-based information.
Cho HJ, Menezes PR, Hotopf M, Bhugra D, Wessely S.	Department of Preventive Medicine, University of São Paulo Medical School, University Hospital, University of São Paulo, Brazil. h.cho@iop.kcl.ac.uk	Comparative epidemiology of chronic fatigue syndrome in Brazilian and British primary care: prevalence and recognition.	Br J Psychiatry. 2009 Feb;194(2):117-22.	BACKGROUND: Although fatigue is a ubiquitous symptom across countries, clinical descriptions of chronic fatigue syndrome have arisen from a limited number of high-income countries. This might reflect differences in true prevalence or clinical recognition influenced by sociocultural factors. AIMS: To compare the prevalence, physician recognition and diagnosis of chronic fatigue syndrome in London and São Paulo. METHOD: Primary care patients in London (n=2459) and São Paulo (n=3914) were surveyed for the prevalence of chronic fatigue syndrome. Medical records were reviewed for the physician recognition and diagnosis. RESULTS: The prevalence of chronic fatigue syndrome according to Centers for Disease Control 1994 criteria was comparable in Britain and Brazil: 2.1% v. 1.6% (P=0.20). Medical records review identified 11 diagnosed cases of chronic fatigue syndrome in Britain, but none in Brazil (P<0.001). CONCLUSIONS: The primary care prevalence of chronic fatigue syndrome was similar in two culturally and economically distinct nations. However, doctors are unlikely to recognise and label chronic fatigue syndrome as a discrete disorder in Brazil. The recognition of this illness rather than the illness itself may be culturally induced.
Ciccone DS, Weissman L, Natelson BH.	UMDNJ-New Jersey Medical School, USA. donald.ciccone@va.gov	Chronic fatigue syndrome in male gulf war veterans and civilians: a further test of the single syndrome hypothesis.	J Health Psychol. 2008 May;13(4):529-36.	Different modes of fatigue onset in male Gulf War veterans versus male civilians raise the possibility that chronic fatigue syndrome (CFS) may not be a single disease entity. We addressed this issue by comparing 45 male veterans with CFS to 84 male civilians who satisfied identical case criteria. All were evaluated for fibromyalgia (FM), multiple chemical sensitivity and psychiatric comorbidity. CFS was more likely to present in a sudden flu-like manner in civilians than veterans ($p < .01$) and comorbid FM was more prevalent in civilians ($p < .01$). These findings question the assumption that all patients with CFS suffer from the same underlying disorder.
Clark LV, White PD.		Chronic fatigue syndrome. Comment on: J Rehabil Med. 2008 Apr;40(4):241-7	J Rehabil Med. 2008 Nov;40(10):882-3; author reply 883-5.	
Coaccioli S, Varrassi G, Sabatini C,	Department of Internal Medicine and Rheumatology	Fibromyalgia: nosography and therapeutic	Pain Pract. 2008 May-Jun;8(3):190-201. Epub 2008	Fibromyalgia (FM) is an important cause of morbidity and health expenditure. Severe widespread extra-articular chronic pain, along with nonrestorative sleep, dominates the clinical syndrome. The pathogenesis of FM remains unclear. While dysfunction in serotoninergic neurotransmission is

Marinangeli F, Giuliani M, Puxeddu A.	Unit, Perugia University School of Medicine, Terni, Italy. scoaccioli@tin.it	perspectives.	Mar 27. Comment in: Pain Pract. 2008 May-Jun;8(3):155.	believed to play an important role, several neurologic and immuno-endocrine mechanisms may also be relevant. A theory is advanced based on an inherited imbalance in neuro-vegetative systems resulting from increased sympathetic tone because of a metabolic deficiency in the serotoninergic system that, when exposed to a precipitating event, leads to the development of the clinical manifestations of FM. The importance of both nonpharmacological treatments and multimodal medication management is stressed.
Courjaret J, Schotte CK, Wijnants H, Moorkens G, Cosyns P.	Department of Psychiatry, University Hospital Antwerp, Edegem, Belgium. kim.courjaret@uza.be	Chronic fatigue syndrome and DSM-IV personality disorders.	J Psychosom Res. 2009 Jan;66(1):13-20. Epub 2008 Nov 22.	OBJECTIVE: Personality is an important factor in the research of the chronic fatigue syndrome (CFS). Although some studies report a high rate of personality disorders--around the 40% level--in samples of patients with CFS, the generalizability of these findings can be questioned. The present study evaluates the prevalence of Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) personality disorders in a sample of female CFS patients and in two control groups. METHOD: The ADP-IV questionnaire (Assessment of DSM Personality Disorders IV) was used to assess the DSM-IV-TR personality disorders at a dimensional and categorical level in a sample of 50 female CFS patients and in two matched control samples of Flemish civilians (n=50) and psychiatric patients (n=50). RESULTS: The results indicate a striking lack of statistical significant differences between the CFS sample and the Flemish control group at the level of dimensional Trait scores, number of criteria, and prevalence rates of personality disorder diagnoses. Unsurprisingly, higher scores at these levels were obtained within the psychiatric sample. The prevalence of an Axis II disorder was 12% in the Flemish and CFS samples, whereas the psychiatric sample obtained a prevalence of 54%. CONCLUSION: The prominent absence of any significant difference in personality disorder characteristics between the female Flemish general population and the CFS samples seems to suggest only a minor etiological role for personality pathology, as defined by the DSM-IV Axis II, within CFS.
Crawley E, Sterne J.	Bristol University, United Kingdom.	Association between school absence and physical function in paediatric CFS/ME.	Arch Dis Child. 2008 Nov 11. [Epub ahead of print]	OBJECTIVE: To investigate factors associated with school attendance and physical function in paediatric Chronic Fatigue Syndrome/Myalgic Encephalopathy (CFS/ME). DESIGN: Cross sectional study. SETTING: Regional specialist CFS/ME service. Patients: Children and young people aged <18. OUTCOME MEASURES: Self reported school attendance and physical function measured using the physical function subscale of the SF36. METHODS: Linear and logistic regression analysis of data from self completed assessment forms on children attending a regional specialist service between 2004 and 2007. Analyses were done in two groups of children: (1) with a completed Spence Children's Anxiety Scale (SCAS) and (2) with a completed Hospital Anxiety and Depression Scale (HADS). RESULTS: Of 211 children with CFS/ME, 62% attended 40% of school or less. In children with completed SCAS, those with better physical function were more likely to attend school (adjusted OR 1.70, 95% CI 1.36 to 2.13). This was also true for those with completed HADS (adjusted OR 2.05 95% CI 1.4, 3.01). Increasing fatigue and pain and low mood were associated with worse physical function. There was no evidence that anxiety, gender, age at assessment, family history of CFS/ME or time from onset of symptoms to assessment in clinic were associated with school attendance or physical function. Implications: Paediatricians should recognise that reduced school attendance is associated with reduced physical function rather than anxiety. Improving school attendance in children with CFS/ME should focus on evidence-based interventions to improve physical function, particularly concentrating

				on interventions that are likely to reduce pain and fatigue.
Daley M, Morin CM, Leblanc M, Grégoire JP, Savard J, Baillargeon L.	Ecole de Psychologie, Université Laval, Pavillon F.A.S., Quebec, Canada G1K 0A6; Centre d'étude des troubles du sommeil, Centre de recherche Université Laval-Robert Giffard, Quebec, Canada.	Insomnia and its relationship to health-care utilization, work absenteeism, productivity and accidents.	Sleep Med. 2008 Aug 25. [Epub ahead of print]	BACKGROUND AND PURPOSE: To document and provide a micro analysis of the relationship between insomnia and health problems, health-care use, absenteeism, productivity and accidents. PARTICIPANTS AND METHODS: A population-based sample of 953 French-speaking adults from Québec, Canada. Participants were categorized as having insomnia syndrome (SYND) or insomnia symptoms (SYMPT) or as good sleepers (GS). They completed questionnaires on sleep, health, use of health-care services and products, accidents, work absences and reduced work productivity. Data were also obtained from the Québec-government-administered health insurance board on selected variables (e.g., consultations with health-care professionals, diagnoses). RESULTS: There were significantly more individuals in the SYND group relative to the GS group reporting at least one chronic health problem (83% vs. 53%; OR: 2.78) and who had consulted a health-care professional in the past year (81% vs. 60%; OR: 2.8). There were also higher proportions of individuals in the SYND group than in the GS group who had used prescription medications (57% vs. 30.7%; OR: 2.8), most notably to treat insomnia, mood and anxiety disorders, or who had used over-the-counter products (75.6% vs. 62.0%; OR: 1.8) and alcohol as a sleep aid (17.8% vs. 3.9%; OR: 4.6). In terms of daytime function, 25.0% of the SYND had been absent from work relative to 17.1% of GS (OR: 1.7), 40.6% reported having experienced reduced productivity compared to 12.3% of GS (OR: 4.8) and non-motor-vehicle accidents occurred at higher rates in the SYND group (12.5% vs. 6.4% for GS; OR: 2.4). No differences were found for hospitalisations or motor-vehicle accidents. Most of the associations remained significant even after controlling for psychiatric comorbidity. Rates for the SYMPT group were situated between SYND and GS on all major dependent variables. Furthermore, insomnia and fatigue were perceived as contributing significantly to accidents, absences and decreased work productivity, regardless of insomnia status. CONCLUSIONS: This study indicates that insomnia is associated with significant morbidity in terms of health problems and health-care utilization, work absenteeism and reduced productivity, and risk of non-motor-vehicle accidents. Future studies should evaluate whether treating insomnia can reverse this morbidity.
Dalla Libera L, Vescovo G, Volterrani M.	CNR Institute of Neurosciences, Padova, Italy.	Physiological basis for contractile dysfunction in heart failure.	Curr Pharm Des. 2008;14(25):2572-81.	The purpose of this review is to enlighten the mechanisms of skeletal muscle dysfunction in heart failure. The muscle hypothesis suggests that chronic heart failure (CHF) symptoms, dyspnoea and fatigue are due to skeletal muscle alterations. Hyperventilation due to altered ergoreflex seems to be the cause of shortness of breath. Qualitative and quantitative changes occurring in the skeletal muscle, such as muscle wastage and shift from slow to fast fibers type, are likely to be responsible for fatigue. Mechanisms leading to muscle wastage in chronic heart failure, include cytokine-triggered skeletal muscle apoptosis, but also ubiquitin/proteasome and non-ubiquitin-dependent pathways. The regulation of fibre type involves the growth hormone/insulin-like growth factor 1/calcineurin/ transcriptional coactivator PGC1 cascade. The imbalance between protein synthesis and degradation plays an important role. Protein degradation can occur through ubiquitin-dependent and non-ubiquit-independent pathways. Systems controlling ubiquitin/ proteasome activation have been described. These are triggered by tumour necrosis factor and growth hormone/ insulin-like growth factor 1. However, an important role is played by apoptosis. In humans, and experimental models of heart failure, programmed cell death has been found in skeletal muscle and interstitial cells. Apoptosis is

				triggered by tumour necrosis factor and in vitro experiments have shown that it can be induced by its second messenger sphingosine. Apoptosis correlates with the severity of the heart failure syndrome. It involves activation of caspases 3 and 9 and mitochondrial cytochrome c release. Sarcomeric protein oxidation and its consequent contractile impairment can form another cause of skeletal muscle dysfunction in CHF.
Davies S, Crawley E.	Department of Women and Children's Health, Southmead Hospital, Bristol, UK.	Chronic fatigue syndrome in children aged 11 years old and younger.	Arch Dis Child. 2008 May;93(5):419-21. Epub 2008 Jan 11.	Children in primary school can be very disabled by chronic fatigue syndrome or ME (CFS/ME). The clinical presentation in this age group (under 12 years old) is almost identical to that in older children. AIM: To describe children who presented to the Bath paediatric CFS/ME service under the age of 12 years. METHOD: Inventories measuring fatigue, pain, functional disability, anxiety, family history and symptoms were collected prospectively for all children presenting to the Bath CFS/ME service between September 2004 and April 2007. Data from children who presented to the service under the age of 12 are described and compared to those who presented at age 12 or older. RESULTS: 178 children (under the age of 18) were diagnosed as having CFS/ME using the RCPCH criteria out of 216 children assessed. The mean age at assessment for children with CFS/ME was 14.5 years old (SD 2.9). Thirty-two (16%) children were under 12 years at the time of assessment, four children were under 5 years and the youngest child was 2 years old. Children under 12 were very disabled with mean school attendance of just over 40% (average 2 days a week), Chalder fatigue score of 8.29 (CI 7.14 to 9.43 maximum possible score = 11) and pain visual analogue score of 39.7 (possible range 0-100). Comparison with children aged 12 or older showed that both groups were remarkably similar at assessment. Twenty-four out of the 26 children with complete symptom lists would have been diagnosed as having CFS/ME using the stricter adult Centers of Disease Control and prevention (CDC) criteria. CONCLUSION: Disability in the under-12 age group was high, with low levels of school attendance, high levels of fatigue, anxiety, functional disability and pain. The clinical pattern seen is almost identical to that seen in older children, and the majority of children would also be diagnosed as having CFS/ME using the stricter adult definition.
de Lange FP, Koers A, Kalkman JS, Bleijenberg G, Hagoort P, Meer JW, Toni I.	F. C. Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, The Netherlands, Expert Center Chronic Fatigue, Radboud University Nijmegen Medical Center, The Netherlands,	Reply to: can CBT substantially change grey matter volume in chronic fatigue syndrome?	Brain. 2008 Aug 30. [Epub ahead of print]	

	Nijmegen Institute for Cognition and Information, Radboud University Nijmegen, The Netherlands and Department of General Internal Medicine, Radboud University Nijmegen Medical Center, The Netherlands.			
de Lange FP, Koers A, Kalkman JS, Bleijenberg G, Hagoort P, van der Meer JW, Toni I.	F.C. Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, Kapittelweg 29, 6500 HB Nijmegen, The Netherlands. florisdelange@gmail.com	Increase in prefrontal cortical volume following cognitive behavioural therapy in patients with chronic fatigue syndrome.	Brain. 2008 Aug;131(Pt 8):2172-80. Epub 2008 Jun 28.	Chronic fatigue syndrome (CFS) is a disabling disorder, characterized by persistent or relapsing fatigue. Recent studies have detected a decrease in cortical grey matter volume in patients with CFS, but it is unclear whether this cerebral atrophy constitutes a cause or a consequence of the disease. Cognitive behavioural therapy (CBT) is an effective behavioural intervention for CFS, which combines a rehabilitative approach of a graded increase in physical activity with a psychological approach that addresses thoughts and beliefs about CFS which may impair recovery. Here, we test the hypothesis that cerebral atrophy may be a reversible state that can ameliorate with successful CBT. We have quantified cerebral structural changes in 22 CFS patients that underwent CBT and 22 healthy control participants. At baseline, CFS patients had significantly lower grey matter volume than healthy control participants. CBT intervention led to a significant improvement in health status, physical activity and cognitive performance. Crucially, CFS patients showed a significant increase in grey matter volume, localized in the lateral prefrontal cortex. This change in cerebral volume was related to improvements in cognitive speed in the CFS patients. Our findings indicate that the cerebral atrophy associated with CFS is partially reversed after effective CBT. This result provides an example of macroscopic cortical plasticity in the adult human brain, demonstrating a surprisingly dynamic relation between behavioural state and cerebral anatomy. Furthermore, our results reveal a possible neurobiological substrate of psychotherapeutic treatment.
De Meirleir K, Neil McGregor		Editorial. Lyme Disease in US ME/CFS Patients: A Psychiatric Data Analysis Related to the Apathy Construct	Journal of Chronic Fatigue Syndrome 2008; 14 (4): 1-4	

de Tommaso M, Sardaro M, Serpino C, Costantini F, Vecchio E, Pia Prudenzano M, Lamberti P, Livrea P.	Neurological and Psychiatric Sciences Department, Neurophysiopathology of Pain Unit, University of Bari, Bari, Italy.	Fibromyalgia comorbidity in primary headaches.	Cephalalgia. 2008 Dec 15. [Epub ahead of print]	de Tommaso M, Sardaro M, Serpino C, Costantini F, Vecchio E, Pia Prudenzano M, Lamberti P & Livrea P. Fibromyalgia comorbidity in primary headaches. Cephalalgia 2008. London. ISSN 0333-1024Fibromyalgia syndrome (FMS) is a chronic pain condition of unknown aetiology characterized by diffuse pain and tenderness at tender points. The aim of the study was to assess the prevalence and clinical features of FMS in the different forms of primary headaches, in a tertiary headache centre. Primary headache patients (n = 217) were selected and submitted to the Total Tenderness Score, anxiety and depression scales, Migraine Disability Assessment, allodynia questionnaire, Short Form 36 Health Survey and the Medical Outcomes Study-Sleep Scale. In patients with FMS, the Multidimensional Assessment of Fatigue, the Pain Visual Analog Scale, the Manual Tender Point Survey and the Fibromyalgia Impact Questionnaire were employed. FMS was present in 36.4% of patients and prevailed significantly in tension-type headache and in patients with higher headache frequency. Headache frequency, pericranial muscle tenderness, anxiety and sleep inadequacy were especially associated with FMS comorbidity. In the FMS patients, fatigue and pain at tender points were significantly correlated with headache frequency. FMS seems increasingly prevalent with increased headache frequency, for the facilitation of central sensitization phenomena favoured by anxiety and sleep disturbances.
Deary V.	Institute of Health and Society, Newcastle University, Newcastle Upon Tyne, UK. vincent.deary@ncl.ac.uk	A precarious balance: using a self-regulation model to conceptualize and treat chronic fatigue syndrome.	Br J Health Psychol. 2008 May;13(Pt 2):231-6. Epub 2008 Feb 8.	The problem posed by chronic fatigue syndrome (CFS) to the affected individual can be conceptualized, using Leventhal's common sense model, as a health threat to be encoded and coped with accordingly. The current paper adopts an alternative use of self-regulation theory. It is hypothesized that in CFS the health threat is no longer the illness, but anything that threatens to disrupt a precarious accommodation to it. It is argued that attempts at threat regulation may become inadvertently self-defeating, promoting the threats they attempt to diminish. Evidence is presented for homeostatic mechanisms in physiological, neurocognitive and affective domains, and for their potential to become locked in vicious circles. It is further argued that illness attributions, rather than being independent cognitive processes, may be intimately linked with emotional and somatic processes. Damasio's somatic marker hypothesis is used to suggest ways in which the self-regulation of highly interconnected somatic, affective, and cognitive states may be substantially implicated in the maintenance of CFS. This perspective is used to reconsider effective treatment and to suggest new interventions. The self-regulation model is a potentially powerful explanatory framework for the consideration and treatment of CFS and medically unexplained symptoms in general.
Dhir A, Kulkarni SK.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh-160014, India.	Venlafaxine reverses chronic fatigue-induced behavioral, biochemical and neurochemical alterations in mice.	Pharmacol Biochem Behav. 2008 Jun;89(4):563-71. Epub 2008 Feb 12.	A state of chronic fatigue was produced in mice by subjecting them to forced swim inside a rectangular jar of specific dimensions everyday for a 6 min session for 15 days. Immobility period was recorded on alternate days. The effect of venlafaxine, a dual reuptake inhibitor of serotonin and norepinephrine was evaluated in this murine model of chronic fatigue. Venlafaxine was administered daily and on the days of testing, it was injected 30 min before forced swim session. On the 16th day i.e. 24 h after the last dose of venlafaxine, various behavioral, biochemical and neurotransmitter estimations in the brain were carried out. There was a significant increase in immobility period in vehicle treated mice on successive days, the maximum immobility score reaching on the 7th day and sustained till 15th day. Behavioral parameters revealed hyperlocomotion, anxiety response, muscle incoordination, hyperalgesia and memory deficit. Biochemical analysis showed a significant increase in

				lipid peroxidation, nitrite and myeloperoxidase levels and a decrease in the reduced glutathione (GSH) levels in brain homogenates. Further, there was a decrease in adrenal ascorbic acid following chronic forced swim. The neurotransmitter estimations in the brain samples revealed a decrease in norepinephrine, serotonin and dopamine levels on chronic exposure to forced swim for 15 days. Daily treatment with venlafaxine (8 and 16 mg/kg, i.p.) for 15 days produced a significant reduction in immobility period and reversed various behavioral, biochemical and neurotransmitter alterations induced by chronic fatigue. Venlafaxine could be of therapeutic potential in the treatment of chronic fatigue.
Dickson A, Toft A, O'Carroll RE.	School of Health and Social Sciences, Napier University, Edinburgh, UK.	Neuropsychological functioning, illness perception, mood and quality of life in chronic fatigue syndrome, autoimmune thyroid disease and healthy participants.	Psychol Med. 2009 Jan 15:1-10. [Epub ahead of print]	BACKGROUND: This study attempted to longitudinally investigate neuropsychological function, illness representations, self-esteem, mood and quality of life (QoL) in individuals with chronic fatigue syndrome (CFS) and compared them with both healthy participants and a clinical comparison group of individuals with autoimmune thyroid disease (AITD).MethodNeuropsychological evaluation was administered at two time points, five weeks apart. Twenty-one individuals with CFS, 20 individuals with AITD and 21 healthy participants were matched for age, pre-morbid intelligence, education level and socio-economic status (SES). All groups also completed measures of illness perceptions, mood, self-esteem and QoL at both time points. RESULTS: The CFS group showed significantly greater impairment on measures of immediate and delayed memory, attention and visuo-constructional ability, and reported significantly higher levels of anxiety and depression. After controlling for the effects of mood, the CFS group still demonstrated significant impairment in attention. The CFS group also reported significantly lower self-reported QoL than the AITD and healthy participants. In terms of illness perceptions, the AITD group believed that their condition would last longer, that they had more treatment control over their condition, and reported less concern than the CFS group. CONCLUSIONS: These results suggest that the primary cognitive impairment in CFS is attention and that this is not secondary to affective status. The lower treatment control perceptions and greater illness concerns that CFS patients report may be causally related to their affective status.
Dietert RR, Dietert JM.	Department of Microbiology and Immunology, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853, USA. rrd1@cornell.edu	Possible role for early-life immune insult including developmental immunotoxicity in chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME).	Toxicology. 2008 May 2;247(1):61-72. Epub 2008 Feb 8.	Chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis (ME) in some countries, is a debilitating disease with a constellation of multi-system dysfunctions primarily involving the neurological, endocrine and immune systems. While substantial information is available concerning the complex dysfunction-associated symptoms of CFS, environmental origins of the disease have yet to be determined. Part of the dilemma in identifying the cause(s) has been the focus on biomarkers (hormones, neurotransmitters, cytokines, infectious agents) that are contemporary with later-life CFS episodes. Yet, recent investigations on the origins of environmental diseases of the neurological, endocrine, reproductive, respiratory and immune systems suggest that early life toxicologic and other insults are pivotal in producing later-life onset of symptoms. As with autism and childhood asthma, CFS can also occur in children where the causes are certainly early-life events. Immune dysfunction is recognized as part of the CFS phenotype but has received comparatively less attention than aberrant neurological or endocrine function. However, recent research results suggest that early life immune insults (ELII) including developmental immunotoxicity (DIT), which is induced by xenobiotics, may offer an important clue to the origin(s) of CFS. The developing immune system is a sensitive and novel target for environmental insult (xenobiotic, infectious agents, stress) with major ramifications for

				postnatal health risks. Additionally, many prenatal and early postnatal neurological lesions associated with postnatal neurobehavioral diseases are now recognized as linked to prenatal immune insult and inflammatory dysregulation. This review considers the potential role of ELII including DIT as an early-life component of later-life CFS.
Dobkin BH.	Department of Neurology, University of California Los Angeles, Los Angeles, CA 90095, USA. bdobkin@mednet.ucla.edu	Fatigue versus activity-dependent fatigability in patients with central or peripheral motor impairments.	Neurorehabil Neural Repair. 2008 Mar-Apr;22(2):105-10.	In the rehabilitation literature, fatigue is a common symptom of patients with any neurological impairment when defined as a subjective lack of physical and mental energy that interferes with usual activities. Some complaints may, however, arise from fatigability , an objective decline in strength as routine use of muscle groups proceeds. By this refined definition of fatigue, exercise or sustained use reduces the ability of muscles to produce force or power, regardless of whether the task can be sustained. Fatigability may be masked clinically because (1) the degree of weakening is not profound, (2) activity-induced weakness rapidly lessens with cessation of exertion, and (3) clinicians rarely test for changes in strength after repetitive movements to objectively entertain the diagnosis. The repetitive movements that induce fatigability during daily activities are an iterative physiological process that depends on changing states induced by activation of spared central and peripheral neurons and axons and compromised muscle. Fatigability may be especially difficult to localize in patients undergoing neurorehabilitation, in part because no finite boundary exists between the central and peripheral components of motor reserve and endurance. At the bedside, however, manual muscle testing before and after repetitive movements could at least put some focus on the presence of fatigability in any patient with motor impairments and related disabilities. Reliable measures of fatigability beyond a careful clinical examination, such as physiological changes monitored by cerebral functional neuroimaging techniques and more standardized central and peripheral electrical and magnetic stimulation paradigms, may help determine the mechanisms of activity-dependent weakening and lead to specific therapies. Testable interventions to increase motor reserve include muscle strengthening and endurance exercises, varying the biomechanical requirements of repetitive muscle contractions, and training-induced neural plasticity or pharmacologic manipulations to enhance synaptic efficacy.
Dorko E, Kalinova Z, Weissova T, Pilipcinec E.	Department of Epidemiology, Faculty of Medicine, Srobarova 2, 041 80 Kosice, Slovak Republic. erikdorco@pobox.sk	Seroprevalence of antibodies to Coxiella burnetii among employees of the Veterinary University in Kosice, eastern Slovakia.	Ann Agric Environ Med. 2008 Jun;15(1):119-24.	Coxiella burnetii is an obligate intracellular pathogen known to be the causative agent of Q fever, a zoonosis with worldwide occurrence. The organism has been found in many wild and domestic animals. Infected animals shed highly stable bacteria in urine, faeces, milk, and through placental and birth fluids. Humans acquire the infection mainly by inhaling infected aerosols, or by ingesting contaminated raw milk or fresh dairy products; tick transmission has been proven but is probably rare. The aim of the present study was to determine the titres of immunoglobulin IgG against phase I and II of C. burnetii, and to evaluate the risk factors that might be associated with exposure to C. burnetii among employees of the Veterinary University. Venous blood was obtained from 92 employees. IgG antibodies were determined by ELISA method modified in our laboratory using whole cells of the Nine Mile C. burnetii strain. The questionnaire was filled out by every subject to obtain epidemiological and clinical date. Phase I antibodies were detected in 35 subjects, i.e. in 38%, and phase II antibodies in 58 subjects, i.e. in 63%. When using the titre > or = 1:800 as a cut-off level, 2 samples were positive for phase I antibodies (2.1%) and 12 for phase II antibodies (13%). Factors predisposing to infection or exposure to C. burnetii included professional orientation and regular contact with farm animals and

				pets. Clinical history of some seropositive subjects revealed substantial problems, such as fever of unknown origin, rheumatic disease, disease of heart, liver, respiratory tract (particularly atypical pneumonia), chronic fatigue syndrome and spontaneous abortion in females. Q fever is a profession-related disease and prevention of its spreading within the risk population groups requires observation of basic safety rules.
Dunleavy M, Bradford A, O'Halloran KD.	Royal College of Surgeons in Ireland, Department of Physiology and Medical Physics. mdunleavy@rcsi.ie	Oxidative stress impairs upper airway muscle endurance in an animal model of sleep-disordered breathing.	Adv Exp Med Biol. 2008;605:458-62.	Obstructive sleep apnoea is characterised by intermittent hypoxia due to recurrent obstructions of the pharyngeal airway during sleep. We have shown that chronic intermittent hypoxia impairs respiratory muscle function and CNS control of upper airway patency. In this study, we tested the hypothesis that disruption of an endogenous antioxidant defence system exacerbates the effects of intermittent hypoxia on upper airway muscle contractile function. Thirty-two male Wistar rats were placed in restrainers with their heads in hoods in which the ambient oxygen concentration could be modified by controlling the gas supply to the hoods. Sixteen rats were exposed to alternating equal periods of hypoxia and normoxia, twice per minute, 8 hours per day for 1 week. The remaining 16 animals were exposed to normoxia continuously under identical experimental conditions. In both groups, half the animals received daily injections of buthionine sulfoxamine (BSO), an inhibitor of the rate-limiting enzyme in glutathione synthesis. The other half received daily vehicle injections. At the end of the 1-week treatment period, the sternohyoid muscles were removed and fatigue characteristics were determined in vitro. Intermittent hypoxia was associated with a decrease in sternohyoid muscle endurance, an effect that was exacerbated by treatment with BSO. In separate experiments, daily treatment with the antioxidant N-acetyl cysteine blocked the deleterious effects of intermittent hypoxia on respiratory muscle function. We suggest that oxidative stress contributes to impaired upper airway muscle endurance in our animal model and that endogenous glutathione may be especially important in limiting free radical-induced muscle dysfunction. Our results may have particular relevance to respiratory disorders associated with recurrent hypoxia, such as the sleep apnoea/hypopnoea syndrome.
Emami MH, Haghdani S, Tavakkoli H, Mahzouni P.	Department of Gastroenterology, Alzahra University Hospital, Isfahan University of Medical Sciences, Isfahan, Iran. mh_emami@med.mui.ac.ir	Endoscopic polypectomy resection of blue rubber bleb nevus lesions in small bowel.	Indian J Gastroenterol. 2008 Jul-Aug;27(4):165-6.	Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder characterized by cutaneous and gastrointestinal (GI) venous malformations. The treatment of BRBNS is primarily supportive and ablative. Ablative therapy involves endoscopic or surgical treatment of GI venous malformations. We describe a 20-year-old woman who had multiple venous malformations all over the GI tract as well as cutaneous lesions. She had suffered from several episodes of melena, chronic anemia and fatigue for 10 years, which were treated temporarily by iron supplementation and blood transfusion. The endoscopic examination of the GI tract and total colonoscopy revealed multiple bluish sessile and polypoid venous malformations 2-3 cm in size throughout the GI tract. Argon plasma coagulation (APC) and polypectomy was done for all gastric and colonic lesions, respectively. Ileoscopy showed a large wide base vascular polypoid lesion at about 70 cm from the ileocecal valve with active bleeding; this was removed by snare polypectomy. One week later, she was discharged in good condition. At about 6 months' follow up she did not report any bleeding attack. Endoscopic polypectomy can be useful in patients with large and polypoid lesions of BRBNs which are not controlled with supportive therapy. Further experience is needed to evaluate the risks versus benefits of this approach.
Erdman KM.	Baylor College of	How biological	JAAPA. 2008	

	Medicine PA Program, Houston, Texas, USA.	abnormalities separate CFS from depression.	Mar;21(3):19-23.	
Exley C, Swarbrick L, Gherardi RK, Authier FJ.	Birchall Centre for Inorganic Chemistry and Materials Science, Keele University, Staffordshire ST5 5BG, UK. c.exley@chem.keele.ac.uk	A role for the body burden of aluminium in vaccine-associated macrophagic myofasciitis and chronic fatigue syndrome.	Med Hypotheses. 2009 Feb;72(2):135-9. Epub 2008 Nov 11.	Macrophagic myofasciitis and chronic fatigue syndrome are severely disabling conditions which may be caused by adverse reactions to aluminium-containing adjuvants in vaccines. While a little is known of disease aetiology both conditions are characterised by an aberrant immune response, have a number of prominent symptoms in common and are coincident in many individuals. Herein, we have described a case of vaccine-associated chronic fatigue syndrome and macrophagic myofasciitis in an individual demonstrating aluminium overload. This is the first report linking the latter with either of these two conditions and the possibility is considered that the coincident aluminium overload contributed significantly to the severity of these conditions in this individual. This case has highlighted potential dangers associated with aluminium-containing adjuvants and we have elucidated a possible mechanism whereby vaccination involving aluminium-containing adjuvants could trigger the cascade of immunological events which are associated with autoimmune conditions including chronic fatigue syndrome and macrophagic myofasciitis.
Eyigor S, Ozdedeli S, Durmaz B.	Ege University Medical Faculty, Department of Physical and Rehabilitation Medicine, Bornova, Izmir, Turkey. eyigor@hotmail.com	The prevalence of generalized soft tissue rheumatic conditions in Turkish medical students.	J Clin Rheumatol. 2008 Apr;14(2):65-8.	OBJECTIVE: To assess the prevalence of generalized soft tissue rheumatism (GSTR) in medical students in Izmir, Turkey. METHODS: Medical students from each grade of Medical School of Ege University, Izmir, Turkey, were evaluated by a survey and physical examination for GSTR including fibromyalgia (FM) syndrome, myofascial pain syndrome (MPS), benign joint hypermobility syndrome (BJHS), and chronic fatigue syndrome. FM Impact Questionnaire was assessed in FM diagnosed students. Short Form-36 (SF-36) was obtained from each student to determine the quality of life. RESULTS: Among the participants (n = 306), 191 were women (62.4%) and 115 were men (37.6%) and mean age was 20.23 +/- 1.56. Fifty-eight students (19%) were diagnosed with a GSTR. The distributions of the diagnoses were: 6 (2%) FM, 21 (6.9%) MPS, 28 (9.2%) BJHS, 1 (0.3%) chronic fatigue syndrome, and 2 students (0.7%) had both BJHS and MPS. Fifty-three (27.7%) women and 5 (4.3%) men were diagnosed with a GSTR ($P < 0.01$). Mean FM Impact Questionnaire score was 50.8 in FM diagnosed students. Physical role, vitality, and mental subscores of SF-36 were significantly lower in the students having a GSTR ($P < 0.05$). CONCLUSION: This is the first study performed in medical students to find out the prevalence of generalized soft tissue rheumatic conditions. Although medical students are under high stress due to hard training, the prevalence of GSTR in medical students was found similar to previous reports in the general population.
Fairhall N, Aggar C, Kurrle SE, Sherrington C, Lord S, Lockwood K, Monaghan N, Cameron ID.	Rehabilitation Studies Unit, Faculty of Medicine, The University of Sydney, Sydney Australia. nfairhall@george.org.au	Frailty Intervention Trial (FIT).	BMC Geriatr. 2008 Oct 13;8:27.	BACKGROUND: Frailty is a term commonly used to describe the condition of an older person who has chronic health problems, has lost functional abilities and is likely to deteriorate further. However, despite its common use, only a small number of studies have attempted to define the syndrome of frailty and measure its prevalence. The criteria Fried and colleagues used to define the frailty syndrome will be used in this study (i.e. weight loss, fatigue, decreased grip strength, slow gait speed, and low physical activity). Previous studies have shown that clinical outcomes for frail older people can be improved using multi-factorial interventions such as comprehensive geriatric assessment, and single interventions such as exercise programs or nutritional supplementation, but no interventions have been developed to specifically reverse the syndrome of frailty.We have developed a

				multidisciplinary intervention that specifically targets frailty as defined by Fried et al. We aim to establish the effects of this intervention on frailty, mobility, hospitalisation and institutionalisation in frail older people. METHODS AND DESIGN: A single centre randomised controlled trial comparing a multidisciplinary intervention with usual care. The intervention will target identified characteristics of frailty, functional limitations, nutritional status, falls risk, psychological issues and management of chronic health conditions. Two hundred and thirty people aged 70 and over who meet the Fried definition of frailty will be recruited from clients of the aged care service of a metropolitan hospital. Participants will be followed for a 12-month period. DISCUSSION: This research is an important step in the examination of specifically targeted frailty interventions. This project will assess whether an intervention specifically targeting frailty can be implemented, and whether it is effective when compared to usual care. If successful, the study will establish a new approach to the treatment of older people at risk of further functional decline and institutionalisation. The strategies to be examined are readily transferable to routine clinical practice and are applicable broadly in the setting of aged care health services. TRIAL REGISTRATION: Australian New Zealand Clinical Trails Registry: ACTRN12608000250336.
Faulkner S, Smith A.	University of Glamorgan, UK. sfaulkne@glam.ac.uk	A longitudinal study of the relationship between psychological distress and recurrence of upper respiratory tract infections in chronic fatigue syndrome.	Br J Health Psychol. 2008 Feb;13(Pt 1):177-86.	OBJECTIVES: Previous research has found that chronic fatigue syndrome (CFS) patients report increased susceptibility to upper respiratory tract illnesses (URTIs) when compared with healthy volunteers. This study aimed to replicate and extend this research by investigating the role of psychological distress (stress and negative mood) in the recurrence of URTIs in CFS patients as well as its role in the recurrence of CFS symptoms. DESIGN: A 15-week diary study. METHODS: Measures of psychological stress, negative mood, recurrence of URTIs and symptoms were recorded each week for a 15-week period. CFS patients (N=21), who had been assessed and diagnosed according to the Oxford criteria, were recruited from the Cardiff Chronic Fatigue Clinic and compared with a matched group of healthy controls (N=18). Frequency of occurrence of infectious illness and the relationship between psychological stress/negative mood and occurrence of illness were assessed. RESULTS: CFS patients reported more URTIs than the controls. Stress scores (and negative mood) were significantly higher in the week prior to the occurrence of URTIs than in weeks when no subsequent illness occurred. High levels of psychological stress also preceded the severity of reported symptoms of fatigue in the CFS group. CONCLUSIONS: CFS patients reported more frequent URTIs than healthy controls and these recurrences were preceded by high levels of psychological stress. High levels of stress were also associated with greater subsequent fatigue. Possible explanations of these results are discussed.
Fawkes-Kirby TM, Wheeler MA, Anton HA, Miller WC, Townson AF, Weeks CA.	School of Rehabilitation Sciences, University of British Columbia, Vancouver, British Columbia, Canada.	Clinical correlates of fatigue in spinal cord injury.	Spinal Cord. 2008 Jan;46(1):21-5. Epub 2007 Apr 3.	STUDY DESIGN: Retrospective chart review. OBJECTIVES: To determine the prevalence of fatigue in an outpatient spinal cord injury population and to examine the clinical variables contributing to that fatigue. SETTING: GF Strong Rehabilitation Centre, Vancouver, British Columbia, Canada. METHODS: Medical charts of 76 individuals admitted to the GF Strong Outpatient SCI Program between December 2004 and December 2005 were reviewed. Data collected included information on clinical characteristics, demographics and Fatigue Severity Scale (FSS) scores. Multivariable analysis was completed to determine the independent association between these variables and fatigue severity. RESULTS: A total of 57% (95% confidence interval (CI)=45-67%) of the sample were found to have fatigue severe enough to interfere with function. People that were admitted for medical reasons; had

				pain, spasticity, incomplete injuries, and/or were on more that one medication with a known side effect of fatigue had significantly higher FSS scores. Multivariable analysis indicated incomplete injury was the only statistically significant predictor of a higher FSS scores; pain approached significance (P=0.07, CI=-0.09, 2.06). Together these variables account for 18% of the variance in FSS scores in this sample. CONCLUSION: Fatigue among individuals with spinal cord injury who are seeking outpatient rehabilitation is very common. The severity of fatigue was greater for individuals with incomplete lesions. Pain was also a potentially important covariate of fatigue. Further research is required to determine what else contributes to fatigue severity beyond these clinical variables as only minimal variance was accounted for in our model.
Findlay SM.	Adolescent Medicine, Department of Pediatrics, McMaster University, Hamilton, Ontario.	The tired teen: A review of the assessment and management of the adolescent with sleepiness and fatigue.	Paediatr Child Health. 2008 Jan;13(1):37-42.	The symptoms of sleepiness and fatigue are frequently encountered when caring for adolescents. Up to 40% of healthy teens experience regular sleepiness, defined as an increased tendency to fall asleep. Fatigue is the perception of low energy following normal activity and is reported by up to 30% of well teens. Chronic fatigue syndrome is an unusual syndrome with severe fatigue accompanied by other physical and neurological symptoms. A thorough assessment is required for all teens with sleepiness and fatigue; however, a treatable underlying medical condition is rarely found. Most fatigue and sleepiness in teens is attributable to lifestyle issues, notably too little time spent sleeping. Physicians are in a position to screen for, assess and manage these common conditions in teens.
Finn AJ, Flynn MK, White WL.		Cutaneous complication of chronic fatigue: an answer from the horse's mouth.	Arch Dermatol. 2008 Sep;144(9):1238-40.	
Fischer PR, Johnson JN, Brands CK.	Mayo Clinic, USA.	Fatigue, exercise intolerance, and weakness: lessons on herding zebras.	Minn Med. 2008 Nov;91(11):38-40.	
Fisher MM, Rose M.	Royal North Shore Hospital of Sydney, St Leonards, NSW 2065, Australia. mfisher@med.usyd.edu.au	Anaesthesia for patients with idiopathic environmental intolerance and chronic fatigue syndrome.	Br J Anaesth. 2008 Oct;101(4):486-91.	BACKGROUND: Idiopathic environmental intolerance syndrome (IEI), formerly known as multiple chemical sensitivity syndrome (MCSS), and chronic fatigue syndrome (CFS) are controversial diseases and there is little information in the literature regarding the appropriate conduct of anaesthesia in such patients. METHODS: We studied 27 patients referred to our anaesthetic allergy clinic with IEI and CFS and performed literature and web searches on anaesthesia in these disorders. RESULTS: The patients had a significant incidence of adverse events related to anaesthesia which were not allergic in nature. The adverse effects usually occurred postoperatively and were self limiting. Patients with IEI and CFS are not at risk of anaphylaxis and there is no scientific evidence that any drug or technique is excessively hazardous. Neither our patients nor the review of the scientific literature supported available web-based recommendations for the anaesthetic management of patients with IEL and CFS. CONCLUSIONS: We suggest that the anaesthetist may be best to use the technique they would use if the patient did not have CFS or IEI but avoid drugs to which there is a history of adverse response. Anaesthesia is likely to be associated with adverse effects in these patients but the effects are not likely to be severe. A series of recommendations for the safe and harmonious conduct of anaesthesia

				in patients with CFS and IEI are provided.
Friedberg F, Sohl S.	Stony Brook University.	Cognitive-behavior therapy in chronic fatigue syndrome: is improvement related to increased physical activity?	J Clin Psychol. 2009 Feb 11;65(4):423-442. [Epub ahead of print]	This multiple case study of cognitive-behavioral treatment (CBT) for chronic fatigue syndrome (CFS) compared self-report and behavioral outcomes. Eleven relatively high-functioning participants with CFS received 6-32 sessions of outpatient graded-activity oriented CBT. Self-report outcomes included measures of fatigue impact, physical function, depression, anxiety, and global change. Behavioral outcomes included actigraphy and the 6-minute walking test. Global change ratings were very much improved (n=2), much improved (n=2), improved (n=5), and no change (n=2). Of those reporting improvement, clinically significant actigraphy increases (n=3) and decreases (n=4) were found, as well as no significant change (n=2). The nature of clinical improvement in CBT trials for high-functioning CFS patients may be more ambiguous than that postulated by the cognitive-behavioral model. (c) 2009 Wiley Periodicals, Inc. J Clin Psychol, 65:1-20, 2009.
Friedberg F, Sohl SJ, Halperin PJ.	Department of Psychiatry and Behavioral Science, Stony Brook University, New York 11794-8790, USA. Fred.Friedberg@stonybrook.edu	Teaching medical students about medically unexplained illnesses: a preliminary study.	Med Teach. 2008;30(6):618-21.	BACKGROUND: This study examined how an interactive seminar focusing on two medically unexplained illnesses, chronic fatigue syndrome (CFS) and fibromyalgia, influenced medical student attitudes toward CFS, a more strongly stigmatized illness. METHODS: Forty-five fourth year medical students attended a 90 minute interactive seminar on the management of medically unexplained illnesses that was exemplified with CFS and fibromyalgia. A modified version of the CFS attitudes test was administered immediately before and after the seminar. RESULTS: Pre-seminar assessment revealed neutral to slightly favorable toward CFS. At the end of the seminar, significantly more favorable attitudes were found toward CFS in general ($t(42) = 2.77$; $P < 0.01$) and for specific items that focused on (1) supporting more CFS research funding ($t(42) = 4.32$; $P < 0.001$; (2) employers providing flexible hours for people with CFS ($t(42) = 3.52$, $P < 0.01$); and (3) viewing CFS as not primarily a psychological disorder ($t(42) = 2.87$, $P < 0.01$). Thus, a relatively brief exposure to factual information on specific medically unexplained illnesses was associated with more favorable attitudes toward CFS in fourth year medical students. CONCLUSION: This type of instruction may lead to potentially more receptive professional attitudes toward providing care to these underserved patients.
Friedberg F, Sohl SJ.	Department of Psychiatry and Behavioral Science, Stony Brook University, Stony Brook, NY 11794-8790, USA. fred.friedberg@stonybrook.edu	Memory for fatigue in chronic fatigue syndrome: the relation between weekly recall and momentary ratings.	Int J Behav Med. 2008 Jan-Mar;15(1):29-33.	BACKGROUND: Understanding how patients with chronic fatigue syndrome (CFS) recall their fatigue is important because fatigue is a core clinical dimension of this poorly understood illness. PURPOSE: This study assessed the associations between momentary fatigue ratings and weekly recall of fatigue in 71 participants with CFS. METHOD: During the three-week data collection period, fatigue intensity was recorded six times a day in electronic diaries. At the end of each week, participants were asked to recall their fatigue intensity for that week. Statistical analyses were done with t-tests and Pearson's and intraclass correlations. RESULTS: Average weekly recall of fatigue intensity was significantly higher than average momentary ratings. Furthermore, moderate to high Pearson's correlations and intraclass correlations (consistency and absolute agreement) between recall and momentary fatigue ratings were found. CONCLUSION: Individuals with CFS recalled consistently higher levels of fatigue in comparison to real-time momentary ratings, yet the level of agreement between the two measures was moderate to high. These findings may have implications for the conduct of office examinations for CFS.
Friedberg F, Sohl	Department of	Longitudinal	J Behav Med. 2008	The purpose of this 2-year prospective study was to compare standard self-report and ecologically-

SJ.	Psychiatry and Behavioral Science Putnam Hall, South Campus, Stony Brook University, Stony Brook, NY, 11794-8790, USA, fred.friedberg@stonybrook.edu.	change in chronic fatigue syndrome: what home-based assessments reveal.	Dec 20. [Epub ahead of print]	based outcome measures in patients with chronic fatigue syndrome (CFS). Standard measures assessed physical function, fatigue impact, psychological variables, and global impression of change ratings. Ecological measures included actigraphy, a structured activity record, and an electronic fatigue/energy diary. Results for this high functioning sample (N = 75) revealed that self-report global improvement was significantly associated with lower momentary fatigue and fatigue impact, and a higher frequency of standing up (at home), but not with actigraphy or psychological variables. However, actigraphy change was significantly correlated with change in self-report physical function. At follow-up, only a small minority (<20%) scored in the healthy adult range for fatigue impact and physical function. The findings suggest that home-based measures of symptom severity and physical functioning may provide evidence of change (or lack of change) that is important for interpreting standard self-report outcomes in CFS.
Fuite J, Vernon SD, Broderick G.	Department of Medicine, Division of Pulmonary Faculty of Medicine and Dentistry, University of Alberta, 2E4.41 Walter Mackenzie Health Sciences Centre, 8440-112 Street, Edmonton, AB, Canada.	Neuroendocrine and immune network re-modeling in chronic fatigue syndrome: an exploratory analysis.	Genomics. 2008 Dec;92(6):393-9. Epub 2008 Oct 1.	This work investigates the significance of changes in association patterns linking indicators of neuroendocrine and immune activity in patients with chronic fatigue syndrome (CFS). Gene sets preferentially expressed in specific immune cell isolates were integrated with neuroendocrine data from a large population-based study. Co-expression patterns linking immune cell activity with hypothalamic-pituitary-adrenal (HPA), thyroidal (HPT) and gonadal (HPG) axis status were computed using mutual information criteria. Networks in control and CFS subjects were compared globally in terms of a weighted graph edit distance. Local re-modeling of node connectivity was quantified by node degree and eigenvector centrality measures. Results indicate statistically significant differences between CFS and control networks determined mainly by re-modeling around pituitary and thyroid nodes as well as an emergent immune sub-network. Findings align with known mechanisms of chronic inflammation and support possible immune-mediated loss of thyroid function in CFS exacerbated by blunted HPA axis responsiveness.
Fulle S, Pietrangelo T, Mancinelli R, Saggini R, Fano G.	Ce.S.I.-Center for Research on Ageing, Università "G. d'Annunzio", Chieti-Pescara, Italy.	Specific correlations between muscle oxidative stress and chronic fatigue syndrome: a working hypothesis.	J Muscle Res Cell Motil. 2007;28(6):355-62. Epub 2008 Feb 15.	Chronic fatigue syndrome (CFS) is a relatively common disorder defined as a status of severe persistent disabling fatigue and subjective unwellness. While the biological basis of the pathology of this disease has recently been confirmed, its pathophysiology remains to be elucidated. Moreover, since the causes of CFS have not been identified, treatment programs are directed at symptom relief, with the ultimate goal of the patient regaining some level of pre-existing function and well-being. Several studies have examined whether CFS is associated with: (i) a range of infectious agents and or immune disturbance; (ii) specific changes of activity in the central or peripheral nervous systems; and (iii) elevated stress periods, which may be associated with the pathology via genetic mechanisms. The role of oxidative stress in CFS is an emerging focus of research due to evidence of its association with some pathological features of this syndrome. New data collectively support the presence of specific critical points in the muscle that are affected by free radicals and in view of these considerations, the possible role of skeletal muscle oxidative imbalance in the genesis of CFS is discussed.
Fuller-Thomson E, Nimigon J.	Department of Family and Community Medicine,	Factors associated with depression among individuals with chronic	Fam Pract. 2008 Dec;25(6):414-22. Epub 2008 Oct 3.	OBJECTIVES: Most previous research regarding chronic fatigue syndrome (CFS) and depression has relied on clinical samples. The current research determined the prevalence and correlates of depression among individuals with CFS in a community sample. METHODS: The nationally representative Canadian Community Health Survey, conducted in 2000/2001, included an unweighted

	University of Toronto, Toronto, Ontario M5S 1A1, Canada. esme.fuller.thomson@utoronto.ca	fatigue syndrome: findings from a nationally representative survey.		sample size of 1045 individuals who reported a diagnosis of CFS and had complete data on depression. Respondents with CFS who were depressed (n = 369) were compared to those who were not depressed (n = 676). Chi-square analyses, t-tests and a logistic regression were conducted. RESULTS: Thirty-six per cent of individuals with CFS were depressed. Among individuals with CFS, depression was associated with lower levels of mastery and self-esteem. In the logistic regression analyses, the odds of depression among individuals with CFS were higher for females, younger respondents, those with lower incomes and food insecurity and those whose activities were limited by pain. Two in five depressed individuals had not consulted with any mental health professional in the preceding year. Twenty-two per cent of depressed respondents had seriously considered suicide in the past year. Individuals with CFS who were depressed were particularly heavy users of family physicians, with an average of 11.1 visits annually (95% confidence interval = 10.7, 11.6). CONCLUSION: It is important for clinicians to assess depression and suicidal ideation among their patients with CFS, particularly among females, those reporting moderate to severe pain, low incomes and inadequate social support.
Gadalla T.	Faculty of Social Work at the University of Toronto.	Association of comorbid mood disorders and chronic illness with disability and quality of life in Ontario, Canada.	Chronic Dis Can. 2008;28(4):148-54.	Mood disorders are more prevalent in individuals with chronic physical illness compared to individuals with no such illness. These disorders amplify the disability associated with the physical condition and adversely affect its course, thus contributing to occupational impairment, disruption in interpersonal and family relationships, poor health and suicide. This study used data collected in the Canadian Community Health Survey, cycle 3.1 (2005) to examine factors associated with comorbid mood disorders and to assess their association with the quality of life of individuals living in Ontario. Results indicate that individuals with chronic fatigue syndrome, fibromyalgia, bowel disorder or stomach or intestinal ulcers had the highest rates of mood disorders. The odds of having a comorbid mood disorder were higher among women, the single, those living in poverty, the Canadian born and those between 30 and 69 years of age. The presence of comorbid mood disorders was significantly associated with short-term disability, requiring help with instrumental daily activities and suicidal ideation. Health care providers are urged to proactively screen chronically ill patients for mood disorders, particularly among the subgroups found to have elevated risk for these disorders.
Gadalla TM.	Faculty of Social Work, University of Toronto, Toronto, Ontario, Canada. tahany.gadalla@utoronto.ca	Disability associated with comorbid anxiety disorders in women with chronic physical illness in Ontario, Canada.	Women Health. 2008;48(1):1-20.	Anxiety disorders are more prevalent in individuals with chronic physical illness compared to individuals with no such illness, and about twice as prevalent in women as in men. This study used data collected in the 2005 Canadian Community Health Survey (21,198 women and 20,478 men) to examine factors associated with comorbid anxiety disorders and to assess the relation of these disorders on short-term disability and suicidal ideation. Comorbid anxiety disorders were more prevalent among women who were young, single, poor, and Canadian-born, and among women with chronic fatigue syndrome; fibromyalgia, bowel disorder or stomach or intestinal ulcers, or bronchitis had the highest rates of anxiety disorders. The presence of comorbid anxiety disorders was significantly associated with short-term disability, requiring help with instrumental daily activities, and suicidal ideation. Our findings underscore the importance of early detection and treatment of anxiety disorders in the physically ill, especially those who also suffer from mood disorders.
Galland BC, Jackson PM, Sayers RM, Taylor	Department of Women's & Children's Health,	A matched case control study of orthostatic	Pediatr Res. 2008 Feb;63(2):196-202.	This study aimed to define cardiovascular and heart rate variability (HRV) changes following head-up tilt (HUT) in children/adolescents with chronic fatigue syndrome (CFS) in comparison to age- and gender-matched controls. Twenty-six children/adolescents with CFS (11-19 y) and controls underwent

BJ.	University of Otago, Dunedin 9015, New Zealand. barbara.galland@otago.ac.nz	intolerance in children/adolescents with chronic fatigue syndrome.		70-degree HUT for a maximum of 30 min, but returned to horizontal earlier at the participant's request with symptoms of orthostatic intolerance (OI) that included lightheadedness. Using electrocardiography and beat-beat finger blood pressure, a positive tilt was defined as OI with 1) neurally mediated hypotension (NMH); bradycardia (HR <75% of baseline), and hypotension [systolic pressure (SysP) drops >25 mm Hg)] or 2) postural orthostatic tachycardia syndrome (POTS); HR increase >30 bpm, or HR >120 bpm (with/without hypotension). Thirteen CFS and five controls exhibited OI generating a sensitivity and specificity for HUT of 50.0% and 80.8%, respectively. POTS without hypotension occurred in seven CFS subjects but no controls. POTS with hypotension and NMH occurred in both. Predominant sympathetic components to HRV on HUT were measured in CFS tilt-positive subjects. In conclusion, CFS subjects were more susceptible to OI than controls, the cardiovascular response predominantly manifest as POTS without hypotension, a response unique to CFS suggesting further investigation is warranted with respect to the pathophysiologic mechanisms involved.
Geisser ME, Strader Donnell C, Petzke F, Gracely RH, Clauw DJ, Williams DA.	Chronic Pain and Fatigue Research Center, Dept. of Internal Medicine, Div. of Rheumatology, Univ. of Michigan, Ann Arbor, MI 48108, USA. mgeisser@med.umich.edu	Comorbid somatic symptoms and functional status in patients with fibromyalgia and chronic fatigue syndrome: sensory amplification as a common mechanism.	Psychosomatics. 2008 May-Jun;49(3):235-42.	BACKGROUND: Somatic symptoms are common in conditions such as fibromyalgia (FM) and chronic fatigue syndrome (CFS). OBJECTIVE: Authors investigated a potential shared pathologic mechanism: a generalized perceptual abnormality where there is heightened responsiveness to varied sensory stimulation, including pain. METHOD: A composite measure of sensory sensitivity was created and compared with measures of somatic symptoms, comorbid psychological disturbances, and self-reported physical functioning in 38 patients with FM and/or CFS. RESULTS: Sensory amplification influenced physical functioning indirectly through pain intensity, and physical symptoms and fatigue also independently contributed to physical functioning. CONCLUSION: Sensory amplification may be an underlying pathophysiologic mechanism in these disorders that is relatively independent of depression and depressive symptoms.
Gilje AM, Söderlund A, Malterud K.	Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway.	Obstructions for quality care experienced by patients with chronic fatigue syndrome (CFS)--a case study.	Patient Educ Couns. 2008 Oct;73(1):36-41. Epub 2008 May 16. Comment in: Patient Educ Couns. 2008 Oct;73(1):1-2.	OBJECTIVE: To explore obstructions for quality care from experiences by patients suffering from chronic fatigue syndrome (CFS). METHODS: Qualitative case study with data drawn from a group meeting, written answers to a questionnaire and a follow-up meeting. Purposeful sample of 10 women and 2 men of various ages, recruited from a local patient organization, assumed to have a special awareness for quality care. RESULTS: CFS patients said that lack of acknowledgement could be even worse than the symptoms. They wanted their doctors to ask questions, listen to them and take them seriously, instead of behaving degrading. Many participants felt that the doctors psychologized too much, or trivialized the symptoms. Participants described how doctors' lack of knowledge about the condition would lead to long-term uncertainty or maltreatment. Even with doctors who were supportive, it would usually take months and sometimes years until a medical conclusion would be reached, or other disorders were ruled out. Increased physical activity had been recommend, but most of the informants experienced that this made them worse. CONCLUSION: Current medical scepticism and ignorance regarding CFS shapes the context of medical care and the illness experiences of CFS patients, who may feel they neither get a proper assessment nor management. PRACTICE IMPLICATIONS: CFS patients' reports about patronizing attitudes and ignorance among doctors call for development of evidence based strategies and empowerment of patients, acknowledging the patients'

				understanding of symptoms and the complex nature of the disease. The NICE guidelines emphasize the need of patient participation and shared decision-making.
Gimsing P, Hansen M, Knudsen LM, Knoblauch P, Christensen IJ, Ooi CE, Buhl-Jensen P.	Department of Hematology, Finsen Center, University Hospital Rigshospitalet, Copenhagen, Denmark. peter.gimsing@rh.regionh.dk	A phase I clinical trial of the histone deacetylase inhibitor belinostat in patients with advanced hematological neoplasia.	Eur J Haematol. 2008 Sep;81(3):170-6. Epub 2008 May 27.	PURPOSE: To determine the safety, dose-limiting toxicity and maximum tolerated dose (MTD) of the novel hydroxamate histone deacetylase inhibitor belinostat (PXD101) in patients with advanced hematological neoplasms. PATIENTS AND METHODS: Sequential dose-escalating cohorts of three to six patients with hematological malignancies received belinostat administered as a 30-min i.v. infusion on days 1-5 of a 21-d cycle. Experience from a parallel dose-finding study in patients with solid tumors influenced the selection of the final dose. RESULTS: Sixteen patients received belinostat at one of three dose levels: 600 mg/m(2)/d (three patients), 900 mg/m(2)/d (three patients) and 1000 mg/m(2)/d (10 patients), the dose determined to be the MTD in a phase I solid tumor study [Steele et al. (2008) Clin Cancer Res, 14, 804-10]. The most common treatment-related adverse events (all grades) were nausea (50%), vomiting (31%), fatigue (31%) and flushing (31%). No grade 3 or 4 hematological toxicity compared with baseline occurred except one case of grade 3 lymphopenia. There were two related grade 4 adverse events of renal failure observed. Both events occurred in patients with multiple myeloma and had similar characteristics, i.e. an acute episode of decrease in renal function (pre-existing nephropathy in one patient), with a metabolic profile and decrease in tumor burden consistent with tumor lysis syndrome. No other related grade 4 events were noted. The only related grade 3 events noticed in more than one patient were fatigue and neurological symptoms (one patient had status epilepticus in association with uremia and one patient had paresthesia), all other related grade 3 events occurred in single patients. No cardiac events were noted. No complete or partial remissions were noted in these heavily pre-treated (median of four prior regimens) patients. However, five patients, including two patients with diffuse large-cell lymphoma [including one patient with transformed chronic myelocytic leukaemia (CLL)], two patients with CLL and one patient with multiple myeloma, achieved disease stabilization in of two to nine treatment cycles. CONCLUSIONS: Intravenous belinostat at 600, 900 and 1000 mg/m(2)/d is well tolerated by patients with hematological malignancies. The study was carried out in parallel to a similar dose-finding study in patients with solid tumors, in which the MTD was determined to be 1000 mg/m(2)/d days 1-5 in a 21-d cycle. This dose can also be recommended for phase II studies in patients with hematological neoplasms.
Goedendorp MM, Knoop H, Schippers GM, Bleijenberg G.	Expert Centre for Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.	The lifestyle of patients with chronic fatigue syndrome and the effect on fatigue and functional impairments.	J Hum Nutr Diet. 2009 Feb 13. [Epub ahead of print]	Abstract Background: Little is known about the lifestyle of patients with chronic fatigue syndrome (CFS) and its influence on symptoms of CFS. The present study aimed to investigate the lifestyle of patients with CFS, and to assess whether lifestyle factors are related to fatigue and functional impairments. Methods: Two hundred and forty-seven patients fulfilling the Center for Disease Control criteria for CFS were included. Validated questionnaires were used to collect data on lifestyle factors, smoking, intake of alcohol, fat, fibres, fruit and vegetables, body mass index (BMI), fatigue severity and functional impairments. Results: Of the CFS patients, 23% smoked, 32% had an unhealthy BMI, and none had an unhealthy alcohol intake. A majority had an unhealthy food intake: 70% had unhealthy fat, fruit and vegetable intake, and 95% had unhealthy fibre intake. Compared with the general Dutch population, significantly fewer CFS patients were overweight. Significantly more female CFS patients abstained from alcohol, and fewer male CFS patients smoked. Unhealthy lifestyle factors

				were not significantly associated with fatigue severity or functional impairments. Conclusions: CFS patients tend to lead a healthier lifestyle compared to the general Dutch population. However, no relationship was found between lifestyle factors and fatigue severity and functional impairments in CFS.
Griffith JP, Zarrouf FA.	Internal Medicine/Psychiatry Residency Program, West Virginia University, Charleston.	A Systematic Review of Chronic Fatigue Syndrome: Don't Assume It's Depression.	Prim Care Companion J Clin Psychiatry. 2008;10(2):120-8.	Objective: Chronic fatigue syndrome (CFS) is characterized by profound, debilitating fatigue and a combination of several other symptoms resulting in substantial reduction in occupational, personal, social, and educational status. CFS is often misdiagnosed as depression. The objective of this study was to evaluate and discuss different etiologies, approaches, and management strategies of CFS and to present ways to differentiate it from the fatigue symptom of depression.Data Sources: A MEDLINE search was conducted to identify existing information about CFS and depression using the headings chronic fatigue syndrome AND depression. The alternative terms major depressive disorder and mood disorder were also searched in conjunction with the term chronic fatigue syndrome. Additionally, MEDLINE was searched using the term chronic fatigue. All searches were limited to articles published within the last 10 years, in English. A total of 302 articles were identified by these searches. Also, the term chronic fatigue syndrome was searched by itself. This search was limited to articles published within the last 5 years, in English, and resulted in an additional 460 articles. Additional publications were identified by manually searching the reference lists of the articles from both searches.Study Selection and Data Extraction: CFS definitions, etiologies, differential diagnoses (especially depression) and management strategies were extracted, reviewed, and summarized to meet the objectives of this article.Data Synthesis: CFS is underdiagnosed in more than 80% of the people who have it; at the same time, it is often misdiagnosed as depression. Genetic, immunologic, infectious, metabolic, and neurologic etiologies were suggested to explain CFS. A biopsychosocial model was suggested for evaluating, managing, and differentiating CFS from depression.Conclusions: Evaluating and managing chronic fatigue is a challenging situation for physicians, as it is a challenging and difficult condition for patients. A biopsychosocial approach in the evaluation and management is recommended. More studies about CFS manifestations, evaluation, and management are needed.
Grinde B.	National Institute of Public Health, P.O. Box 4404, Nydalen, 0403 Oslo, Norway.	Is chronic fatigue syndrome caused by a rare brain infection of a common, normally benign virus?	Med Hypotheses. 2008;71(2):270-4. Epub 2008 Apr 25.	Chronic fatigue syndrome (CFS) is a disabling disease of unknown aetiology. A variety of factors have been suggested as possible causes. Although the symptoms and clinical findings are heterogeneous, the syndrome is sufficiently distinct, at least in relation to the more obvious cases, that a common explanation seems likely. In this paper, it is proposed that the disease is caused by a ubiquitous, but normally benign virus, e.g., one of the circoviruses. Circoviruses are chronically present in a majority of people, but are rarely tested for diagnostically. Normally these viruses do not penetrate the blood-brain barrier, but exceptions have been reported, and related viruses cause disease in the central nervous system of animals. The flu-like illness that often precedes the onset of CFS may either suppress immune function, causing an increased viremia, and/or lower the blood-brain barrier. In both cases the result may be that a virus already present in the blood enters the brain. It is well known that zoonotic viruses typically are more malignant than viruses with a long history of host-virus evolution. Similarly, a virus reaching an unfamiliar organ may cause particular problems.
Grossi ML, Goldberg MB,	Faculty of Dentistry, Catholic	Irritable bowel syndrome patients	Int J Prosthodont. 2008 May-	PURPOSE: This study aimed to assess the use of neuropsychologic tests as a tool to differentiate, or not, between a nonresponding chronic pain condition of nonmuscular origin, irritable bowel syndrome

Locker D, Tenenbaum HC.	University of Rio Grande do Sul, Brazil. mlgrossi@pucrs.br	versus responding and nonresponding temporomandibular disorder patients: a neuropsychologic profile comparative study.	Jun;21(3):201-9.	(IBS) (n = 20), versus 2 pain conditions of muscular origin, responding (n = 36) and nonresponding (n = 24) temporomandibular disorders. MATERIALS AND METHODS: The neuropsychologic tests used were the simple and multiple-choice reaction-time tests, California Verbal Learning Tests, the Brown-Peterson Consonant Trigram Auditory Memory Test, Sleep Assessment Questionnaire, and Beck Depression Inventory, as well as fatigue and energy level assessments (100-mm visual analog scale). RESULTS: Most of the tests used were capable of significantly differentiating between responding TMD versus IBS patients. Conversely, no statistically significant difference was found between nonresponding TMD versus IBS patients. Overall, the nonresponding TMD and IBS groups did worse in the neuropsychologic assessment than the responding TMD group, with higher memory deficits, levels of depression and fatigue, more sleep disturbances, and lower energy levels. CONCLUSIONS: These data suggested that 2 nonresponding chronic pain conditions of different origins may share similar neuropsychologic test results compared to a responding condition. These findings are consistent with the hypothesis that nonresponding chronic pain disorders, irrespective of peripheral location, may be regulated centrally and have similar neuropsychologic impacts.
Gupta A, Vij G, Sharma S, Tirkey N, Rishi P, Chopra K.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India.	Curcumin, a polyphenolic antioxidant, attenuates chronic fatigue syndrome in murine water immersion stress model.	Immunobiology. 2009;214(1):33-9. Epub 2008 Jun 17.	Chronic fatigue syndrome, infection and oxidative stress are interrelated in epidemiological case studies. However, data demonstrating scientific validation of epidemiological claims regarding effectiveness of nutritional supplements for chronic fatigue syndrome are lacking. This study is designed to evaluate the effect of natural polyphenol, curcumin, in a mouse model of immunologically induced fatigue, where purified lipopolysaccharide (LPS) and Brucella abortus (BA) antigens were used as immunogens. The assessment of chronic fatigue syndrome was based on chronic water-immersion stress test for 10 min daily for 19 days and the immobility time was taken as the marker of fatigue. Mice challenged with LPS or BA for 19 days showed significant increase in the immobility time and hyperalgesia on day 19, as well as marked increase in serum tumor necrosis factor-alpha (TNF-alpha) levels. Concurrent treatment with curcumin resulted in significantly decreased immobility time as well as hyperalgesia. There was significant attenuation of oxidative stress as well as TNF-alpha levels. These findings strongly suggest that during immunological activation, there is significant increase in oxidative stress and curcumin can be a valuable option in the treatment of chronic fatigue syndrome.
Gur A, Oktayoglu P.	Department of Physical Medicine and Rehabilitation, Medical Faculty, Dicle University, 21280 Diyarbakir, Turkey. alig@dicle.edu.tr	Central nervous system abnormalities in fibromyalgia and chronic fatigue syndrome: new concepts in treatment.	Curr Pharm Des. 2008;14(13):1274-94.	Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are poorly understood disorders that share similar demographic and clinical characteristics. The etiology and pathophysiology of these diseases remain unclear. Because of the similarities between both disorders it was suggested that they share a common pathophysiological mechanisms, namely, central nervous system (CNS) dysfunction. Current hypotheses center on atypical sensory processing in the CNS and dysfunction of skeletal muscle nociception and the hypothalamic-pituitary-adrenal (HPA) axis. Researches suggest that the (CNS) is primarily involved in both disorders in regard to the pain, fatigue and sleep disturbances. Many patients experience difficulty with concentration and memory and many others have mood disturbance, including depression and anxiety. Although fibromyalgia is common and associated with substantial morbidity and disability, there are no US Food and Drug Administration (FDA)-approved treatments except pregabalin. Recent pharmacological treatment studies about fibromyalgia have focused on selective serotonin and norepinephrine (NE) reuptake inhibitors, which enhance serotonin and NE neurotransmission in the descending pain pathways and lack many of the adverse side effects

				associated with tricyclic medications. CFS is a descriptive term used to define a recognisable pattern of symptoms that cannot be attributed to any alternative condition. The symptoms are currently believed to be the result of disturbed brain function. To date, no pharmacological agent has been reliably shown to be effective treatment for CFS. Management strategies are therefore primarily directed at relief of symptoms and minimising impediments to recovery. This chapter presents data demonstrating CFS, abnormal pain processing and autonomic nervous system (ANS) dysfunction in FM and CFS and concludes by reviewing the new concepts in treatments in CFS and FM.
Hadlandsmyth K, Vowles KE.	Bath and Wiltshire Adult Chronic Fatigue Syndrome Service, Royal National Hospital for Rheumatic Diseases, Bath, UK. kehb8c@umsl.edu	Does depression mediate the relation between fatigue severity and disability in chronic fatigue syndrome sufferers?	J Psychosom Res. 2009 Jan;66(1):31-5. Epub 2008 Nov 22.	OBJECTIVE: Chronic fatigue syndrome (CFS) is often associated with significant levels of disability. Although fatigue and depression have been found to be independently related to severity of disability, it is not clear how these three factors are mutually related. The present study sought to address this issue by specifically testing a model of mediation whereby depression was hypothesized to influence relations between fatigue and disability. METHODS: Participants included 90 individuals seeking treatment for CFS at a tertiary care facility. Each provided demographic information and completed standardized measures of depression and fatigue severity, as well as a measure of disability, which assessed difficulties in physical, psychosocial, and independence domains. RESULTS: Analyses indicated that depression and fatigue were positively correlated with one another, as well as all three disability domains. Analyses of mediation indicated that depression completely mediated the relation between fatigue and psychosocial disability and partially mediated the relation between fatigue and the other two disability domains. Indirect effects tests indicated that the inclusion of depression in the statistical models was statistically meaningful. CONCLUSIONS: These results replicate previous findings that fatigue and depression are independently related to disability in those with CFS. A more complex statistical model, however, suggested that depression severity substantially influenced the strength of the relation between fatigue and disability levels across a range of domains, including complete mediation in areas involving psychosocial functioning. These results may aid in clarifying contemporary conceptualizations of CFS and provide guidance in the identification of appropriate treatment targets.
Haig-Ferguson A, Tucker P, Eaton N, Hunt L, Crawley E.	University of Bristol, United Kingdom.	Memory and attention problems in children with CFS/ME.	Arch Dis Child. 2008 Nov 11. [Epub ahead of print]	OBJECTIVE: To understand more about the problems children with CFS/ME experience with their memory and attention, and to test the feasibility of quantitative measurement of both memory and attention. DESIGN: 4 item semi-structured questionnaire and Neuropsychological test battery with 10 psychometric subtests. SETTING: Family home of the child taking part. Patients: 20 children with a diagnosis of CFS/ME and experiencing memory and/or concentration problems were recruited between April and October 2007 from a regional CFS/ME clinical service (Female=13; Average age 13.5yrs; Range 8 - 16 yrs). METHODS: Each child, parent and teacher was asked to describe the child's memory and attention problems. Responses were subject to thematic analysis by two independent researchers. In addition each child completed a battery of 10 tests to measure: Processing speed; Attention; Immediate and Delayed Memory; Working Memory; Executive Function. Raw scores were converted into age-scaled scores and the children's psychometric scores on the 10 tests taken were compared with normative data using t-tests. RESULTS: Children with CFS/ME, their parents and teachers described problems with focussed attention, sustained attention, recall and stress. Children's scores were compared to normative data. Scores for sustained attention (mean 8.1, 95% CI 6.3-9.9),

				switching attention (7.5, 5.5-9.4), divided attention (6.9, 5.5-8.2), auditory learning (8.2, 6.8-9.6) and immediate recall (8.7, 7.3-10.0) appeared lower than the normative mean of 10. CONCLUSIONS: Children with CFS/ME appear to experience problems with attention, which may have adverse implications for verbal memory. These cognitive problems may explain some of the educational difficulties associated with Chronic Fatigue Syndrome.
Hamilton NA, Affleck G, Tennen H, Karlson C, Luxton D, Preacher KJ, Templin JL.	Department of Psychology, University of Kansas, USA. nancyh@ku.edu	Fibromyalgia: the role of sleep in affect and in negative event reactivity and recovery.	Health Psychol. 2008 Jul;27(4):490-7.	OBJECTIVE: Fibromyalgia (FM) syndrome is a chronic pain condition characterized by diffuse muscle pain, increased negative mood, and sleep disturbance. Until recently, sleep disturbance in persons with FM has been modeled as the result of the disease process or its associated pain. The current study examined sleep disturbance (i.e., sleep duration and sleep quality) as a predictor of daily affect, stress reactivity, and stress recovery. DESIGN AND MEASURES: A hybrid of daily diary and ecological momentary assessment methodology was used to evaluate the psychosocial functioning of 89 women with FM. Participants recorded numeric ratings of pain, fatigue, and positive and negative affect 3 times throughout the day for 30 consecutive days. At the end of each day, participants completed daily diary records of positive and negative life events. In addition, participants reported on their sleep duration and sleep quality each morning. RESULTS: After accounting for the effects of positive events, negative events, and pain on daily affect scores, it was found that sleep duration and quality were prospectively related to affect and fatigue. Furthermore, the effects of inadequate sleep on negative affect were cumulative. In addition, an inadequate amount of sleep prevented affective recovery from days with a high number of negative events. CONCLUSIONS: These results lend support to the hypothesis that sleep is a component of allostatic load and has an upstream role in daily functioning. PsycINFO Database Record (c) 2008 APA, all rights reserved.
Harrell-Sanders D.		But you look so normal.	J Pain Palliat Care Pharmacother. 2008;22(1):1.	
Harvey SB, Wadsworth M, Wessely S, Hotopf M.	Institute of Psychiatry, King's College London, London, UK. s.harvey@iop.kcl.ac.uk	Etiology of chronic fatigue syndrome: testing popular hypotheses using a national birth cohort study.	Psychosom Med. 2008 May;70(4):488-95. Epub 2008 Mar 31.	OBJECTIVE: To review the etiology of chronic fatigue syndrome (CFS) and test hypotheses relating to immune system dysfunction, physical deconditioning, exercise avoidance, and childhood illness experiences, using a large prospective birth cohort. METHODS: A total of 4779 participants from the Medical Research Council's National Survey of Health and Development were prospectively followed for the first 53 years of their life with >20 separate data collections. Information was collected on childhood and parental health, atopic illness, levels of physical activity, fatigue, and participant's weight and height at multiple time points. CFS was identified through self-report during a semistructured interview at age 53 years with additional case notes review. RESULTS: Of 2983 participants assessed at age 53 years, 34 (1.1%, 95% Confidence Interval 0.8-1.5) reported a diagnosis of CFS. Those who reported CFS were no more likely to have suffered from childhood illness or atopy. Increased levels of exercise throughout childhood and early adult life and a lower body mass index were associated with an increased risk of later CFS. Participants who later reported CFS continued to exercise more frequently even after they began to experience early symptoms of fatigue. CONCLUSIONS: Individuals who exercise frequently are more likely to report a diagnosis of CFS in later life. This may be due to the direct effects of this behavior or associated personality factors. Continuing to be active despite increasing fatigue may be a crucial step in the development of CFS.

Häuser W, Akritidou I, Felde E, Klauenberg S, Maier C, Hoffmann A, Köllner V, Hinz A.	Zentrum für Schmerztherapie/Innere Medizin I (Gastroenterologie, Hepatologie, Stoffwechsel- und Infektionskrankheiten, Psychosomatik), Klinikum Saarbrücken gGmbH, Winterberg 1, 66119, Saarbrücken. whaeuser@klinikum-saarbruecken.de	[Steps towards a symptom-based diagnosis of fibromyalgia syndrome. Symptom profiles of patients from different clinical settings] [Article in German]	Z Rheumatol. 2008 Oct;67(6):511-5.	BACKGROUND: A symptom-based diagnosis of fibromyalgia syndrome (FMS) without tender point examination is helpful for primary medical care. We tested whether a symptom-based diagnosis of FMS can be based on the symptoms of musculoskeletal pain and fatigue. METHODS: The most frequent and severe symptoms in FMS patients from four different settings (n= 464 from a self-help organization, n=162 from medical expertise, n= 33 from a private rheumatology practice, n=36 from a tertiary-care pain department) were assessed using the Giessen Subjective Complaints List GBB 24. The most frequent and severe symptoms were assessed and compared to those of a representative German population sample. A k-means cluster analysis was performed to identify sub-groups with and without additional vegetative symptoms within the total sample of FMS patients. RESULTS: The most frequent and severe symptoms in all four sub-samples were low back pain, limb pain and fatigue. The greatest mean differences between FMS patients and the general population were found in the subscales "limb pain" and "fatigue". Cluster analysis identified three sub-groups of patients which were all characterized by severe limb pain and fatigue, as well as varying degrees of vegetative symptoms. SUMMARY: Following the exclusion of inflammatory rheumatoid, endocrinological and neurological diseases, a symptom-based clinical diagnosis of FMS can be based on of the key symptoms of chronic widespread musculoskeletal pain, as well as chronic fatigue.
Häuser W, Bernardy K, Uçeyler N, Sommer C.	Department of Internal Medicine, Klinikum Saarbrücken, Winterberg 1, D-66119 Saarbrücken, Germany. whaeuser@klinikum-saarbruecken.de	Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis.	JAMA. 2009 Jan 14;301(2):198-209.	CONTEXT: Fibromyalgia syndrome (FMS) is a chronic pain disorder associated with multiple debilitating symptoms and high disease-related costs. Effective treatment options are needed. OBJECTIVES: To determine the efficacy of antidepressants in the treatment of FMS by performing a meta-analysis of randomized controlled clinical trials. DATA SOURCES: MEDLINE, PsycINFO, Scopus, and the Cochrane Library databases were searched through August 2008. Reference sections of original studies, meta-analyses, and reviews on antidepressants in FMS were reviewed. STUDY SELECTION: Randomized placebo-controlled trials with tricyclic and tetracyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs) were analyzed. DATA EXTRACTION AND DATA SYNTHESIS: Two authors independently extracted data. Effects were summarized using standardized mean differences (SMDs) by a random-effects model. RESULTS: Eighteen randomized controlled trials (median duration, 8 weeks; range, 4-28 weeks) involving 1427 participants were included. Overall, there was strong evidence for an association of antidepressants with reduction in pain (SMD, -0.43; 95% confidence interval [CI], -0.55 to -0.30), fatigue (SMD, -0.13; 95% CI, -0.26 to -0.01), depressed mood (SMD, -0.26; 95% CI, -0.39 to -0.12), and sleep disturbances (SMD, -0.32; 95% CI, -0.46 to -0.18). There was strong evidence for an association of antidepressants with improved health-related quality of life (SMD, -0.31; 95% CI, -0.42 to -0.20). Effect sizes for pain reduction were large for TCAs (SMD, -1.64; 95% CI, -2.57 to -0.71), medium for MAOIs (SMD, -0.54; 95% CI, -1.02 to -0.07), and small for SSRIs (SMD, -0.39; 95% CI, -0.77 to -0.01) and SNRIs (SMD, -0.36; 95% CI, -0.46 to -0.25). CONCLUSION: Antidepressant medications are associated with improvements in pain, depression, fatigue, sleep disturbances, and health-related quality of life in patients with FMS.
Häuser W, Zimmer C, Felde E, Köllner	Zentrum für Schmerztherapie/I	[What are the key symptoms of	Schmerz. 2008 Apr;22(2):176-83.	INTRODUCTION: A new definition of fibromyalgia syndrome (FMS) based on symptoms and without tender points is discussed from a rheumatological viewpoint. METHODS: The German Fibromyalgia

V.	nnere Medizin I (Gastroenterologie, Hepatologie, Stoffwechsel- und Infektionskrankheiten, Psychosomatik), Klinikum Saarbrücken gGmbH, Winterberg 1, 66119, Saarbrücken, Germany. whaeuser@klinikum-saarbruecken.de	fibromyalgia? Results of a survey of the German Fibromyalgia Association] [Article in German]		Association (DFV) developed a questionnaire on potential symptoms in FM based on a list of symptoms established by members of the DFV. The questionnaire was sent to all 3,996 members of the DFV. RESULTS: Of the 753 questionnaires 699 were returned (95% women, most frequent age between 50-60 years) and evaluated. The rank order of the most frequent symptoms (>or=97% of the respondents) was muscle pain with varying locations, low back pain, fatigue, morning stiffness, non-restorative sleep, concentration problems, lack of energy, low productivity and forgetfulness. CONCLUSION: The key symptoms of FM are chronic widespread pain, non-restorative sleep and subjective disabilities. The frequency of general and extra-musculoskeletal symptoms underlines that FMS is more than just a "pain disorder".
Heim C, Nater UM, Maloney E, Boneva R, Jones JF, Reeves WC.	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Woodruff Memorial Research Bldg, Ste 4311, Atlanta, GA 30322, USA. cmheim@emory.edu	Childhood trauma and risk for chronic fatigue syndrome: association with neuroendocrine dysfunction.	Arch Gen Psychiatry. 2009 Jan;66(1):72-80.	CONTEXT: Childhood trauma appears to be a potent risk factor for chronic fatigue syndrome (CFS). Evidence from developmental neuroscience suggests that early experience programs the development of regulatory systems that are implicated in the pathophysiology of CFS, including the hypothalamic-pituitary-adrenal axis. However, the contribution of childhood trauma to neuroendocrine dysfunction in CFS remains obscure. OBJECTIVES: To replicate findings on the relationship between childhood trauma and risk for CFS and to evaluate the association between childhood trauma and neuroendocrine dysfunction in CFS. Design, Setting, and PARTICIPANTS: A case-control study of 113 persons with CFS and 124 well control subjects identified from a general population sample of 19 381 adult residents of Georgia. MAIN OUTCOME MEASURES: Self-reported childhood trauma (sexual, physical, and emotional abuse; emotional and physical neglect), psychopathology (depression, anxiety, and posttraumatic stress disorder), and salivary cortisol response to awakening. RESULTS: Individuals with CFS reported significantly higher levels of childhood trauma and psychopathological symptoms than control subjects. Exposure to childhood trauma was associated with a 6-fold increased risk of CFS. Sexual abuse, emotional abuse, and emotional neglect were most effective in discriminating CFS cases from controls. There was a graded relationship between exposure level and CFS risk. The risk of CFS conveyed by childhood trauma further increased with the presence of posttraumatic stress disorder symptoms. Only individuals with CFS and with childhood trauma exposure, but not individuals with CFS without exposure, exhibited decreased salivary cortisol concentrations after awakening compared with control subjects. CONCLUSIONS: Our results confirm childhood trauma as an important risk factor of CFS. In addition, neuroendocrine dysfunction, a hallmark feature of CFS, appears to be associated with childhood trauma. This possibly reflects a biological correlate of vulnerability due to early developmental insults. Our findings are critical to inform pathophysiological research and to devise targets for the prevention of CFS.
Hickie I,	Brain and Mind	Are chronic fatigue	Aust N Z J	OBJECTIVE: The validity of the diagnosis of chronic fatigue syndrome and related chronic fatigue states

Davenport T, Vernon SD, Nisenbaum R, Reeves WC, Hadzi-Pavlovic D, Lloyd A; International Chronic Fatigue Syndrome Study Group. Collaborators: Bleijenberg G, van der Werf SP, Prins JB, Blenkiron PM, Buchwald D, Smith WR, Edwards R, Lynch S, Kirmayer LJ, Taillefer SS, Lee S, Martin NG, Gillespie NA, McIlvenny S, Sartorius N, Ustun TB, Skapinakis P, Wessely S, Chalder T, Hotopf M, Nimnuan C, Candy B, Darbishire L, Ridsdale L, White PD, Thomas JM, Wilhelm K, Wilson A.	Research Institute, Camperdown, NSW, Australia. ianh@med.usyd.edu.au	and chronic fatigue syndrome valid clinical entities across countries and health-care settings?	Psychiatry. 2009 Jan;43(1):25-35.	remains controversial, particularly in psychiatry. This project utilized international epidemiological and clinical research data to test construct validity across diagnostic categories, health-care settings and countries. Relevant demographic, symptom and diagnostic data were obtained from 33 studies in 21 countries. The subjects had fatigue lasting 1-6 months (prolonged fatigue), or >6 months (chronic fatigue), or met diagnostic criteria for chronic fatigue syndrome. METHOD: Common symptom domains were derived by factor analytic techniques. Mean scores on each symptom factor were compared across diagnostic categories, health-care settings and countries. RESULTS: Data were obtained on 37,724 subjects (n = 20,845 female, 57%), including from population-based studies (n = 15,749, 42%), studies in primary care (n = 19 472, 52%), and secondary or specialist tertiary referral clinics (n = 2503, 7%). The sample included 2013 subjects with chronic fatigue, and 1958 with chronic fatigue syndrome. A five-factor model of the key symptom domains was preferred ('musculoskeletal pain/fatigue', 'neurocognitive difficulties', 'inflammation', 'sleep disturbance/fatigue' and 'mood disturbance') and was comparable across subject groups and settings. Although the core symptom profiles were similar, some differences in symptoms were observed across diagnostic categories, health-care settings and between countries. CONCLUSIONS: The construct validity of chronic fatigue and chronic fatigue syndrome is supported by an empirically derived factor structure from existing international datasets.
Higashimoto T, Baldwin EE, Gold JI, Boles RG.	Division of Medical Genetics and the Saban Research Institute, Childrens Hospital Los Angeles, Los Angeles, California, USA.	Reflex sympathetic dystrophy: complex regional pain syndrome type I in children with mitochondrial disease and maternal inheritance.	Arch Dis Child. 2008 May;93(5):390-7. Epub 2008 Jan 11.	OBJECTIVE: Complex regional pain syndrome type I (CRPS-I), previously known as reflex sympathetic dystrophy (RSD), is an idiopathic condition characterised by localised, abnormally intense and prolonged pain, allodynia and autonomic nervous system changes (ie, swelling, skin colour and temperature changes and altered perspiration) that usually appear following a "noxious" trigger such as trauma or surgery. The objective of this report is to demonstrate that children with CRPS-I can have additional dysautonomic conditions secondary to an underlying maternally inherited mitochondrial disease, an association not previously published. METHODS: Medical records of about 500 patients seen by one paediatric metabolic geneticist were reviewed to identify children meeting established CRPS diagnostic criteria. RESULTS: CRPS-I was present in eight children in seven families, each of which also had additional functional/dysautonomic conditions, the most common (> or = 4 cases per

				condition) being gastrointestinal dysmotility, migraine, cyclic vomiting and chronic fatigue. All seven probands studied met Nijmegen (2002) diagnostic criteria for definite mitochondrial disease on the basis of the clinical signs and symptoms and biochemical analyses. Six of the seven families met our pedigree-based criteria for probable maternal inheritance. CONCLUSION: In one tertiary-care paediatric genetics practice, children meeting the CRPS-I diagnostic criteria frequently had additional autonomic-related conditions secondary to maternally inherited mitochondrial disease, suggesting that mitochondrial DNA sequence variants can predispose children towards the development of CRPS-I and other dysautonomias. CRPS-I should be considered in patients with mitochondrial disease who complain of idiopathic pain. Maternally inherited mitochondrial disease may not be a rare cause of CRPS-I, especially in children who present with other manifestations of dysautonomia.
Hoad A, Spickett G, Elliott J, Newton J.	Northern CFS/ME Clinical Network, Equinox House, Silver Fox Way, Cobalt Business Park, Newcastle upon Tyne.	Postural orthostatic tachycardia syndrome is an under-recognized condition in chronic fatigue syndrome.	QJM. 2008 Dec;101(12):961-5. Epub 2008 Sep 19.	BACKGROUND: It has been suggested that postural orthostatic tachycardia syndrome (POTS) be considered in the differential diagnosis of those with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). Currently, measurement of haemodynamic response to standing is not recommended in the UK NICE CFS/ME guidelines. OBJECTIVES: To determine prevalence of POTS in patients with CFS/ME. DESIGN: Observational cohort study. METHODS: Fifty-nine patients with CFS/ME (Fukuda criteria) and 52 age- and sex-matched controls underwent formal autonomic assessment in the cardiovascular laboratory with continuous heart rate and beat-to-beat blood pressure measurement (Task Force, CNSystems, Graz Austria). Haemodynamic responses to standing over 2 min were measured. POTS was defined as symptoms of orthostatic intolerance associated with an increase in heart rate from the supine to upright position of >30 beats per minute or to a heart rate of >120 beats per minute on standing. RESULTS: Maximum heart rate on standing was significantly higher in the CFS/ME group compared with controls (106 +/- 20 vs. 98 +/- 13; P = 0.02). Of the CFS/ME group, 27% (16/59) had POTS compared with 9% (5) in the control population (P = 0.006). This difference was predominantly related to the increased proportion of those in the CFS/ME group whose heart rate increased to >120 beats per minute on standing (P = 0.0002). Increasing fatigue was associated with increase in heart rate (P = 0.04; r(2) = 0.1). CONCLUSION: POTS is a frequent finding in patients with CFS/ME. We suggest that clinical evaluation of patients with CFS/ME should include response to standing. Studies are needed to determine the optimum intervention strategy to manage POTS in those with CFS/ME.
Hobday RA, Thomas S, O'Donovan A, Murphy M, Pinching AJ.	Infection and Immunity Speciality Group, St Bartholomew's Hospital, West Smithfield, London, UK. rhonahobday@yahoo.co.uk	Dietary intervention in chronic fatigue syndrome.	J Hum Nutr Diet. 2008 Apr;21(2):141-9.	BACKGROUND: Anecdotal reports and books have been published linking an over growth of Candida Albicans with chronic fatigue syndrome (CFS), suggesting dietary change as a treatment option. Little scientific data has been published to validate this controversial theory. This study aims to determine the efficacy of dietary intervention on level of fatigue and quality of life (QoL) in individuals with CFS. METHODS: A 24-week randomized intervention study was conducted with 52 individuals diagnosed with CFS. Patients were randomized to either a low sugar low yeast (LSLY) or healthy eating (HE) dietary interventions. Primary outcome measures were fatigue as measured by the Chalder Fatigue Score and QoL measured by Medical Outcomes Survey Short Form-36. RESULTS: A high drop out rate occurred with 13 participants not completing the final evaluation (7HE/6LSLY). Intention to treat analysis showed no statistically significant differences on primary outcome measurements. CONCLUSION: In this randomized control trial, a LSLY diet appeared to be no more efficacious on

				levels of fatigue or QoL compared to HE. Given the difficulty with dietary compliance experienced by participants, especially in the LSLY group, it would appear HE guidance is a more pragmatic approach than advocating a complicated dietary regime.
Hokama Y, Empey-Campora C, Hara C, Higa N, Siu N, Lau R, Kuribayashi T, Yabusaki K.	Department of Pathology, University of Hawaii-Manoa, Honolulu, HI 96822, USA. yoshitsu@hawaii.edu	Acute phase phospholipids related to the cardiolipin of mitochondria in the sera of patients with chronic fatigue syndrome (CFS), chronic Ciguatera fish poisoning (CCFP), and other diseases attributed to chemicals, Gulf War, and marine toxins.	J Clin Lab Anal. 2008;22(2):99-105.	This study examined 328 CFS sera in a study with 17 CCFP, 8 Gulf War Veterans (GWV), 24 Prostate Cancer (PC), and 52 normal sera in the modified Membrane Immunobead Assay (MIA) procedure for CTX. Three hundred and twenty-eight CFS patients' sera were examined by the modified MIA with purified MAb-CTX and 91.2% gave a titre > or =1:40. 76% of the 17 CCFP sera samples and 100% of the 8 GWV sera samples also had a titre > or =1:40. 92.3% of 52 normal sera showed titres of 1:20 or less, while 4 gave titres of > or =1:40. In addition, 41 sera were examined for Anti-Cardiolipin (aCL) by a commercial ELISA procedure with 87.8% demonstrating IgM, IgM+IgA, or IgM+IgG aCL antibodies. These results showed mostly the IgM aCL antibody alone in the sera samples. In addition, 41 serum samples were examined for aCL, with 37 showing positive for aCL, representing 90.2% positive for the three disease categories examined: CFS, CCFP and GWV. Examination for antiMitochondrial-M2 autoantibody (aM-M2) in 28 patients (CFS (18), CCFP (5), and GWV (5)) was negative for aM-M2. Inhibition analysis with antigens, CTX, CFS "Acute Phase Lipids", commercial Cardiolipin (CL) and 1,2-Dipalmitoyl-sn-Glycero-3-[Phospho-L-Serine] (PS) and antibodies, MAb-CTX and aCL from patients' serum show that the phospholipids in CL and CTX are antigenically indistinguishable with antibodies MAb-CTX and CFS-aCL. Preliminary chemical analyses have shown the lipids to be phospholipids associated with CL of the mitochondria. We designate this "Acute Phase Lipid" comparable to "Acute Phase Proteins" (C-reactive protein (CRP) and Serum Amyloid A (SAA)) in inflammatory conditions. (Copyright) 2008 Wiley-Liss, Inc.
Hollingsworth KG, Newton JL, Taylor R, McDonald C, Palmer JM, Blamire AM, Jones DE.	Newcastle Magnetic Resonance Centre, Newcastle University, Newcastle-upon-Tyne, United Kingdom.	Pilot study of peripheral muscle function in primary biliary cirrhosis: potential implications for fatigue pathogenesis.	Clin Gastroenterol Hepatol. 2008 Sep;6(9):1041-8. Epub 2008 Aug 8.	BACKGROUND & AIMS: Primary biliary cirrhosis (PBC) is characterized in 95% of patients by autoantibody responses directed against the mitochondrial antigen pyruvate dehydrogenase complex (PDC). Although anti-PDC inhibits PDC function in vitro, mitochondrial function in vivo in PBC has not been examined. METHODS:(31)P magnetic resonance spectroscopy was performed in PBC patients (n = 15) and fatigued (chronic fatigue syndrome/myalgic encephalomyelitis, n = 8), cholestatic (primary sclerosing cholangitis [PSC], n = 4), and normal (n = 8) controls to define mitochondrial function and pH regulation in peripheral muscle during exercise at 25% and 35% of maximum voluntary contraction. RESULTS: Normal, chronic fatigue syndrome/myalgic encephalomyelitis, and PSC subjects all showed close correlation between kinetics of adenosine diphosphate (ADP) and phosphocreatine (PCr) recovery after low-impact exercise, reflecting the normal tight regulation of PCr "response" by mitochondria to ADP "drive." This relationship was lost in PBC patients, indicating mitochondrial dysfunction (normal r(2) = 0.78, P < .005; PBC r(2) = 0.007, P = ns). Ratio between PCr and ADP recovery half-times (constant in controls, indicating normal mitochondrial responsivity) was significantly elevated in PBC patients (but not PSC) and was associated with anti-PDC levels. At higher levels of exercise PBC (but not PSC) patients showed excess muscle acidosis, with pH correlating with elevation of PCr/ADP recovery ratio, indicating a link to mitochondrial dysfunction. PBC patients alone also showed significant prolongation of muscle pH recovery time after exercise (unrelated to mitochondrial function), which correlated with clinical fatigue. CONCLUSIONS: PBC patients exhibit a variable degree of muscle mitochondrial dysfunction that manifests as excess acidosis after exercise.

				The extent to which patients can recover rapidly from acidosis appears to determine whether they are clinically fatigued.
Hou R, Moss-Morris R, Bradley BP, Peveler R, Mogg K.	School of Medicine, University of Southampton, Southampton, United Kingdom.	Attentional bias towards health-threat information in chronic fatigue syndrome.	J Psychosom Res. 2008 Jul;65(1):47-50.	OBJECTIVE: To investigate whether individuals with chronic fatigue syndrome (CFS) show an attentional bias towards health-threat information. METHODS: Attentional bias (AB) was assessed in individuals with CFS and healthy controls using a visual probe task which presented health-threat and neutral words and pictures for 500 ms. Self-report questionnaires were used to assess CFS symptoms, depression, anxiety, and social desirability. RESULTS: Compared to a healthy control group, the CFS group showed an enhanced AB towards heath-threat stimuli relative to neutral stimuli. The AB was not influenced by the type of stimulus (pictures vs. words). CONCLUSION: The finding of an AB towards health-threat information in individuals with CFS is supportive of models of CFS which underlie cognitive behavior therapy.
Houdenhove BV, Eede FV, Luyten P.	Department of Liaison Psychiatry, University Hospitals K.U. Leuven, Herestraat 49, B-3000 Leuven, Belgium.	Does hypothalamic-pituitary-adrenal axis hypofunction in chronic fatigue syndrome reflect a 'crash' in the stress system?	Med Hypotheses. 2009 Feb 21. [Epub ahead of print]	The etiopathogenesis of chronic fatigue syndrome (CFS) remains poorly understood. Although neuroendocrine disturbances - and hypothalamic-pituitary-adrenal (HPA) axis hypofunction in particular - have been found in a large proportion of CFS patients, it is not clear whether these disturbances are cause or consequence of the illness. After a review of the available evidence we hypothesize that that HPA axis hypofunction in CFS, conceptualized within a system-biological perspective, primarily reflects a fundamental and persistent dysregulation of the neurobiological stress system. As a result, a disturbed balance between glucocorticoid and inflammatory signaling pathways may give rise to a pathological cytokine-induced sickness response that may be the final common pathway underlying central CFS symptoms, i.e. effort/stress intolerance and pain hypersensitivity. This comprehensive hypothesis on HPA axis hypofunction in CFS may stimulate diagnostic refinement of the illness, inform treatment approaches and suggest directions for future research, particularly focusing on the neuroendocrine-immune interface and possible links between CFS, early and recent life stress, and depression.
Huang Y, Liao XM, Li XX, Song YB.	Southern Medical University, Guangzhou 510515, China.	Clinical observation on the effects of Bo's abdominal acupuncture in 40 cases of chronic fatigue syndrome.	J Tradit Chin Med. 2008 Dec;28(4):264-6.	OBJECTIVE: To observe the curative effect of Bo's abdominal acupuncture on chronic fatigue syndrome (CFS). METHODS: Forty cases with CFS were treated by Bo's abdominal acupuncture at the points for conducting qi back to its origin and 4 points on the abdomen once a day for 2 weeks. Scores for symptoms and scores for fatigue questionnaires were compared before and after treatment. RESULTS: After treatment, the clinical symptoms of patients were differently alleviated, and scores for symptoms, mental condition and neural feeling in questionnaires on fatigue were obviously reduced ($P<0.01$-0.05). CONCLUSION: Bo's abdominal acupuncture has a good curative effect on general disease with complex symptoms, especially on lassitude, anorexia, insomnia, amnesia, diarrhea, and general pain.
Jasiukeviciene L, Vasiliauskas D, Kavoliūniene A, Marcinkeviciene J, Grybauskiene R, Grizas V, Tumyniene V..	Institute of Cardiology, Kaunas University of Medicine, Lithuania. lina.jas@med.kmu.lt	[Evaluation of a chronic fatigue in patients with moderate-to-severe chronic heart failure] [Article in	Medicina (Kaunas). 2008;44(5):366-72.	THE AIM OF THE STUDY: To evaluate the chronic fatigue and its relation to the function of hypothalamus-pituitary-adrenal axis in patients with New York Heart Association (NYHA) functional class III-IV chronic heart failure. MATERIAL AND METHODS: A total of 170 patients with NYHA functional class III-IV chronic heart failure completed MFI-20L, DUFS, and DEFS questionnaires assessing chronic fatigue and underwent echocardiography. Blood cortisol concentration was assessed at 8:00 am and 3:00 pm, and plasma N-terminal brain natriuretic pro-peptide (NT-proBNP) concentration was measured at 8:00 am. Neurohumoral investigations were repeated before

		Lithuanian]		cardiopulmonary exercise test and after it. RESULTS: The results of all questionnaires showed that 100% of patients with NYHA functional class III-IV heart failure complained of chronic fatigue. The level of overall fatigue was 54.5+/-31.5 points; physical fatigue - 56.8+/-24.6 points. Blood cortisol concentration at 8:00 am was normal (410.1+/-175.1 mmol/L) in majority of patients. Decreased concentration was only in four patients (122.4+/-15.5 mmol/L); one of these patients underwent heart transplantation. In the afternoon, blood cortisol concentration was insufficiently decreased (355.6+/-160.3 mmol/L); reaction to a physical stress was attenuated (Delta 92.9 mmol/L). Plasma NT-proBNP concentration was 2188.9+/-1852.2 pg/L; reaction to a physical stress was diminished (Delta 490.3 pg/L). CONCLUSION: All patients with NYHA class III-IV heart failure complained of daily chronic fatigue. Insufficiently decreased blood cortisol concentration in the afternoon showed that in the presence of chronic fatigue in long-term cardiovascular organic disease, disorder of a hypothalamus-pituitary-adrenal axis is involved.
Jason L, Muldowney K, Torres-Harding S.	DePaul University, Chicago, IL, USA.	The Energy Envelope Theory and myalgic encephalomyelitis/ chronic fatigue syndrome.	AAOHN J. 2008 May;56(5):189-95. Erratum in: AAOHN J. 2008 Jul;56(7):288. Muldowney, Kathleen [added]; Torres-Harding, Susan [added].	Individuals with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) have little stamina and endurance, and pose a challenge for nursing professionals. The Energy Envelope Theory, which posits that maintaining expended energy levels consistent with available energy levels may reduce the frequency and severity of symptoms, is particularly useful when working with clients with ME/CFS. Anecdotal support from the client community for this theory supports its use as a management tool for ME/CFS, but little formal research has been done in this area. In this study, a daily energy quotient was established by dividing the expended energy level by the perceived energy level and multiplying by 100. It was predicted that those participants who expended energy beyond their level of perceived energy would have more severe fatigue and symptoms and lower levels of physical and mental functioning. Findings are congruent with the Energy Envelope Theory as they indicated that the daily energy quotient was related to several indices of functioning including depression, anxiety, fatigue, pain, quality of life, and disability. The overall results provide support for a strategy health care professionals can use when working with clients with ME/CFS.
Jason LA, Judith A. Richman		How Science Can Stigmatize: The Case of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2008; 14 (4): 85-103	Objective: This article reviews issues involving the name of an illness, chronic fatigue syndrome (CFS), along with flawed epidemiologic approaches, which may have further contributed to the diagnostic skepticism and stigma that those with CFS encounter. Methods: Patient groups around the world are currently engaged in a major effort to rename this syndrome as either myalgic encephalomyelitis or myalgic encephalopathy, to undo the negative effects of the name previously given to this illness by scientists. Moreover, during the last 15 years, estimated rates of CFS have dramatically increased in both Great Britain and the United States. Results: We suggest that the increases in both the United States and Great Britain are due to a broadening of the case definition to additionally include cases with primary psychiatric conditions. Conclusion: Using a broad or narrow definition of CFS will have crucial influences on CFS epidemiologic findings, on rates of psychiatric comorbidity, and ultimately on the likelihood of finding a biological marker and identified etiology
Jason LA, Susan Torres-Harding Kevin Maher Nadia Reynolds		Baseline Cortisol Levels Predict Treatment Outcomes in	Journal of Chronic Fatigue Syndrome 2008; 14 (4): 39-59	Objective: Understanding how nonpharmacologic interventions differentially affect the subgroups of patients with chronic fatigue syndrome (CFS) might provide insights into the pathophysiology of this illness. In this exploratory study, baseline measures of normal versus abnormal cortisol were compared on a variety of immune markers and other self-report measures. Normal versus abnormal

Molly Brown, Matthew Sorenson, Julie Donalek, Karina Corradi, Mary Fletcher, Tony Lu		Chronic Fatigue Syndrome Nonpharmacologic Clinical Trial		cortisol ratings were used as predictors in a nurse-delivered nonpharmacologic intervention. Methods: Participants diagnosed with CFS were assigned to 6-month nonpharmacologic interventions. Individuals were classified as having abnormal or normal cortisol levels on the basis of scores over the five testing times. Cortisol levels were considered abnormal if they continued to rise, were flat, or were at abnormally low over time. Results: Across interventions, those with abnormal cortisol at the baseline appeared not to improve over time, whereas those with normal baseline cortisol evidenced improvements on a number of immunologic and self-report measures. Conclusion: It appears that, in subgroups of individuals with CFS, baseline cortisol markers are associated with outcome trajectories for nonpharmacologic treatment trials. The implications of these findings are discussed.
Javaras KN, Pope HG, Lalonde JK, Roberts JL, Nillni YI, Laird NM, Bulik CM, Crow SJ, McElroy SL, Walsh BT, Tsuang MT, Rosenthal NR, Hudson JI	Department of Biostatistics, Harvard School of Public Health, Boston, Mass., USA. javaras@wisc.edu	Co-occurrence of binge eating disorder with psychiatric and medical disorders.	J Clin Psychiatry. 2008 Feb;69(2):266-73.	BACKGROUND: Prior studies suggest that certain psychiatric and medical disorders co-occur with binge eating disorder (BED). However, there has been no large, community-based study with diagnoses made by clinician interviewers. We used data from that type of study to assess the co-occurrence of various psychiatric and medical disorders with DSM-IV BED and with subthreshold BED. METHOD: From October 2002 to July 2004, we interviewed 150 probands with BED, 150 probands without BED, and 888 of their first-degree relatives (135 of whom had BED, and 54 of whom met specific partial criteria for BED that we defined as subthreshold BED). Study participants were interviewed using the Structured Clinical Interview for DSM-IV to assess BED and other psychiatric disorders and a supplemental structured interview to assess certain medical disorders; participants also completed a self-report questionnaire, the Bad Things Scale. For each psychiatric and medical disorder, we calculated the age- and sex-adjusted co-occurrence odds ratio: the odds of having that disorder in one's lifetime among individuals with (full or subthreshold) lifetime BED compared to individuals without lifetime BED. We also used subjects' responses to the Bad Things Scale to adjust for adversity over-reporting, a type of response bias that could result in spurious findings of co-occurrence. RESULTS: Full BED co-occurred significantly with bipolar disorder, major depressive disorder, bulimia nervosa but not anorexia nervosa, most anxiety disorders, substance use disorders, body dysmorphic disorder, kleptomania, irritable bowel syndrome, and fibromyalgia. These results changed little after correcting for adversity over-reporting. Subthreshold BED co-occurred significantly with many, but not all, of the significantly co-occurring disorders for full BED. CONCLUSION: BED and, to a lesser degree, subthreshold BED exhibit substantial lifetime co-occurrence with psychiatric and medical disorders.
Jellinger KA.	Vienna, Austria.	Chronic Fatigue Syndrome (CFS/ME), 2nd edn.	Eur J Neurol. 2009 Feb 7. [Epub ahead of print]	PMID: 19220428 [PubMed - as supplied by publisher]
Jhanji V, Beltz J, Vajpayee RB.	Centre for Eye Research Australia, University of Melbourne, Royal Victorian Eye and Ear Hospital,	Contact lens-related acanthamoeba keratitis in a patient with chronic fatigue	Eye Contact Lens. 2008 Nov;34(6):335-6.	PURPOSE: To report a case of contact lens-related Acanthamoeba keratitis associated with improper lens hygiene in a patient with chronic fatigue syndrome (CFS). METHODS: Contact lens-related Acanthamoeba keratitis was diagnosed in a 58-year-old man with a history of CFS. After medical management failed to prevail, a penetrating keratoplasty was performed in the affected eye. RESULTS: There was no recurrence of Acanthamoeba keratitis after surgery. Complete re-epithelialization of the graft was observed with a best-corrected visual acuity of 20/80 in the operated eye at the last follow-

	Melbourne, Australia.	syndrome.		up (3 months). CONCLUSIONS: Our case report highlights the fact that concurrent incapacitating illnesses like CFS may not allow proper care of contact lenses thereby making patients prone to contact lens-related corneal infections.
Jones JF.	Chronic Viral Diseases Branch, Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vectorborne, and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. jaj9@cdc.gov	An extended concept of altered self: chronic fatigue and post-infection syndromes.	Psychoneuroendocrinology. 2008 Feb;33(2):119-29. Epub 2007 Dec 26.	Sickness behavior in active infectious diseases is defined here as the responses to cytokines and other mediators of inflammation as well as the adaptability of a pre-existing integrated immunological, psychological, neurological, and philosophical self. These complex behaviors are biologically advantageous to the afflicted individual, but they also impact surrounding individuals. If chronic conditions, such as chronic fatigue syndrome or post-infection fatigue, exhibiting these behaviors follow infection in the absence of ongoing changes in immunological self associated with an active infection or subsequent injury, they are currently considered illness states rather than true diseases. Self-referential recognition (interoception) of bodily processes by the brain and subsequent unconscious and conscious adaptive responses arising in the brain, i.e., in the endocrine system and immune systems, which are initiated during the infection and would normally lead to positive maintenance, may become maladaptive and lead to an "extended altered self state." Exploratory measurements of such alterations using a "top-down" approach such as monitoring responses to appropriate challenges can be obtained using functional brain imaging techniques. Once identified, processes remediable to biological/pharmacologic and/or psychological intervention can be targeted in directed trials.
Jonsson K, Hedelin H.	Research and Development Centre and Department of Urology, Karnsjukhuset, Skovde, Sweden.	Chronic abacterial prostatitis: Living with a troublesome disease affecting many aspects of life.	Scand J Urol Nephrol. 2008;42(6):545-50.	OBJECTIVE: Chronic abacterial prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a disease of yet not clarified aetiology where the symptoms, voiding dysfunction and pelvic pain are difficult to alleviate. The aim of this study is to arrive at an understanding of how it influences the individual afflicted. MATERIALS AND METHODS: Ten men with CP/CPPS were interviewed about their situation. The interviews were transcribed and analysed using a phenomenological perspective. RESULTS: The often severe symptoms influence well-being and a life in more or less constant fear of a relapse is described. A majority manages, despite the problems, to endure and conceal the problems. The situation can, however, become unbearable and force the man to seek solitude or lose his temper. Social isolation and restrictions at work and during recreational activities were thus reported by those more severely afflicted. Confirmation from the healthcare system that the disease is not life threatening and affirmation that they are not unwanted and neglected are essential. CONCLUSIONS: Men with CP/CPPS are mostly able to live a normal life, although it is often difficult and the people around them are rarely given an insight into their world, where their existence is focused on attempts to obtain confirmation, control abrupt mood fluctuations and develop coping strategies. They have much in common with other patient groups afflicted by chronic pain, such as difficulties in performing at work and severe fatigue. More specific for CP/CPPS is the presence of additional symptoms, which individually can severely impair quality of life. Accepting the situation and developing coping strategies are consequently challenges for a man with CP/CPPS.
Jorgensen R.	Mayo Clinic College of Medicine, Rochester,	Chronic fatigue: an evolutionary concept analysis.	J Adv Nurs. 2008 Jul;63(2):199-207.	AIM: This paper is a report of a concept analysis of chronic fatigue. BACKGROUND: Fatigue is a prevalent symptom encompassing both acute and chronic manifestations. It is chronic fatigue that is most problematic because of its duration and impact on life quality. The rise in prevalence of chronic conditions will result in a need to address coexistent symptoms, clarification of which is needed.

	Minnesota, USA. jorgensen.roberta@mayo.edu			Chronic fatigue is one of the most common symptoms in chronic illness. Clarification of the concept and an understanding of its use by discipline are needed. DATA SOURCES: The evolutionary method of concept analysis was used to ascertain the attributes, antecedents, consequences and surrogate terms for chronic fatigue. A review of the literature published between 1966 and 2007 was carried out to determine the contextual use of the concept of chronic fatigue among disciplines. Sources used for this analysis included CINAHL, Medline, PsychINFO and Social Work Abstracts and the search yielded 66 papers. RESULTS: The chronic fatigue experience is associated with a multitude of physical, psychological and social factors. The defining attributes of chronic fatigue are constancy, abnormality, whole-body experience, inexplicability and disabling. The antecedents of chronic fatigue are physical disease, psychopathology, female gender and a history of abuse. Consequences found include social isolation and stigmatization, physical inactivity, psychological disturbances and a reduced quality of life. CONCLUSION: Further research is needed to identify the aetiology of chronic fatigue and to address the social context of living with this disabling symptom.
Joyner MJ, Masuki S.	Dept. of Anesthesiology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA, joyner.michael@mayo.edu	POTS versus deconditioning: the same or different?	Clin Auton Res. 2008 Dec;18(6):300-7. Epub 2008 Aug 12. Comment in: Clin Auton Res. 2008 Dec;18(6):298; author reply 299.	The 2007 Streeten Lecture focused on the idea that physical deconditioning plays a key role in the symptomology and pathophysiology of POTS. Parallels were drawn between the physiological responses to orthostatic stress seen in POTS patients and the physiological responses seen in "normal" humans after prolonged periods of bedrest, deconditioning, or space flight. Additionally, the idea that endurance exercise training might ameliorate some of these symptoms was also advanced. Finally, potential parallels between POTS, chronic fatigue syndrome, and fibromyalgia were also drawn and the potential role of exercise training as a "therapeutic intervention" in all three conditions was raised. The conceptual model for the lecture was that after some "initiating event" chronic deconditioning plays a significant role in the pathophysiology of these conditions, and these physiological changes in conjunction with "somatic hypervigilence" explain many of the complaints that this diverse group of patients have. Additionally, the idea that systematic endurance exercise training might be helpful was advanced, and data supportive of this idea was reviewed. The main conclusion is that the medical community must retain their empathy for patients with unusual conditions but at the same time send a firm but empowering message about physical activity. As always, we must also ask what do the ideas about physical activity and inactivity and the conditions mentioned above not explain?
Kaabia N, Letaief A.	Service de médecine interne et maladies infectieuses, CHU Farhat-Hached, rue Mohamed-Karoui, 4000 Sousse, Tunisie..	[Q fever in Tunisia.] [Article in French]	Pathol Biol (Paris). 2008 Jun 11. [Epub ahead of print]	Q fever is a common zoonosis with almost a worldwide distribution caused by Coxiella burnetii. Farm animals and pets are the main reservoirs of infection and transmission to humans is usually via inhalation of contaminated aerosols. Infection in humans is often asymptomatic, but it can manifest as an acute disease (usually a self-limited flu-like illness, pneumonia or hepatitis) or as a chronic form (mainly endocarditis, but also hepatitis and chronic-fatigue syndrome). In Tunisia, although prevalence of anti-Coxiella burnetii was high among blood donors, Q fever was rarely reported and frequently miss diagnosed by physicians. This study is a review of epidemiological and clinical particularities of Q fever in Tunisia.
Kalaitzakis E, Carlsson E, Josefsson A, Bosaeus I.	Department of Internal Medicine, Sahlgrenska University	Quality of life in short-bowel syndrome: impact of fatigue and	Scand J Gastroenterol. 2008;43(9):1057-65.	OBJECTIVE: Patients with short-bowel syndrome (SBS) have impaired health-related quality of life (QoL). However, comparisons of QoL data with the data on other chronic gastrointestinal diseases are not available. The aim of this study was to assess QoL in SBS patients compared with that in the general population and with patients with inflammatory bowel disease (IBD). The potential relation

	Hospital, Gothenburg, Sweden.	gastrointestinal symptoms.		between fatigue and gastrointestinal symptoms and impaired QoL in these patients was also investigated. MATERIAL AND METHODS: Four validated questionnaires were used to measure aspects of QoL (SF-36), psychological distress (hospital anxiety and depression scale, HAD), fatigue (fatigue impact scale, FIS), and gastrointestinal symptoms (gastrointestinal symptom rating scale, GSRS) in 26/28 patients (93%) attending a SBS clinic (median age 62 years, 15 F/11 M) at a tertiary referral center. Persons from the general population (n=286) as well as patients with IBD (n=41) of similar age and gender distribution as the SBS group acted as controls. RESULTS: SBS patients had significantly lower SF-36 physical and mental component summaries than those in the general population as well as significantly lower SF-36 physical ($p<0.05$) but not mental ($p>0.05$) component summaries compared with those of IBD patients. Fatigue and gastrointestinal symptoms were more severe in SBS patients than in IBD patients ($p>0.05$). The SF-36 physical component summary was independently related to the physical FIS dimension (beta=-0.4, p=0.004), the GSRS eating dysfunction dimension (beta=-0.31, p=0.025), and opiate use (beta=-0.28, p=0.031), regardless of diagnosis (SBS or IBD). CONCLUSIONS: Patients with SBS show poor QoL compared with that in the general population and also impairment of mainly physical health compared with that in patients with IBD. Fatigue and gastrointestinal symptoms are more severe in patients with SBS, which has an impact on QoL.
Kalkman JS, Zwarts MJ, Schillings ML, van Engelen BG, Bleijenberg G.	Department of Medical Psychology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.	Different types of fatigue in patients with facioscapulohumeral dystrophy, myotonic dystrophy and HMSN-I. Experienced fatigue and physiological fatigue.	Neurol Sci. 2008 Sep;29 Suppl 2:S238-40.	Although fatigue is a common symptom in neuromuscular disorders, little is known about different types of fatigue. Sixty-five FSHD, 79 adult-onset MD and 73 HMSN type I patients were studied. Experienced fatigue was assessed with the CIS-fatigue subscale. Physiological fatigue was measured during a 2-min sustained maximal voluntary contraction of the biceps brachii muscle using the twitch interpolation technique to assess central activation failure (CAF) and peripheral fatigue. Experienced fatigue, CAF and peripheral fatigue appeared to be predominantly separate types of fatigue.
Karlsson I.		[Fatigue syndromes do not belong among depressive and anxiety disorders] [Article in Swedish]	Lakartidningen. 2009 Jan 14-20;106(3):132; author reply 132. Comment on: Lakartidningen. 2008 Nov 19-25;105(47):3393-4.	
Kato K, Sullivan PF, Evengård B, Pedersen NL.	School of Nursing and Rehabilitation, International University of	A population-based twin study of functional somatic	Psychol Med. 2009 Mar;39(3):497-505. Epub 2008 Jun 26.	BACKGROUND: The mechanisms underlying the co-occurrence of the functional somatic syndromes are largely unknown. No empirical study has explicitly examined how genetic and environmental factors influence the co-morbidity of these syndromes. We aimed to examine how the co-morbidity of functional somatic syndromes is influenced by genetic and environmental factors that are in common

	Health and Welfare at Odawara, Kanagawa, Japan.	syndromes.		to the syndromes.MethodA total of 31318 twins in the Swedish Twin Registry aged 41-64 years underwent screening interviews via a computer-assisted telephone system from 1998 to 2002. Four functional somatic syndromes (chronic widespread pain, chronic fatigue, irritable bowel syndrome, and recurrent headache) and two psychiatric disorders (major depression and generalized anxiety disorder) were assessed using structured questions based on standard criteria for each illness in a blinded manner. RESULTS: Multivariate twin analyses revealed that a common pathway model with two latent traits that were shared by the six illnesses fit best to the women's data. One of the two latent traits loaded heavily on the psychiatric disorders, whereas the other trait loaded on all four of the functional somatic syndromes, particularly chronic widespread pain, but not on the psychiatric disorders. All illnesses except the psychiatric disorders were also affected by genetic influences that were specific to each. CONCLUSIONS: The co-occurrence of functional somatic syndromes in women can be best explained by affective and sensory components in common to all these syndromes, as well as by unique influences specific to each of them. The findings clearly suggest a complex view of the multifactorial pathogenesis of these illnesses.
Kato YH, Yamate M, Tsujikawa M, Nishigaki H, Tanaka Y, Yunoki M, Kuratsune H, Watanabe Y, Ikuta K.	Department of Virology, Research Institute for Microbial Diseases, Osaka University, 3-1, Yamadaoka, Suita, Osaka 565-0871, Japan.	No apparent difference in the prevalence of parvovirus B19 infection between chronic fatigue syndrome patients and healthy controls in Japan.	J Clin Virol. 2009 Mar;44(3):246-7. Epub 2009 Feb 5.	Publication Types: Letter
Kawasaki H, Yahata K, Okamoto C, Imamaki H, Seta K, Sugawara A.	Department of Nephrology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan.	[Myasthenia-like syndrome induced by cibenzoline overdose in a patient with chronic kidney disease] [Article in Japanese]	Nippon Jinzo Gakkai Shi. 2008;50(7):942-7.	A female in her late 60s with chronic kidney disease was admitted to the emergency department with complaints of dizziness four days prior to hospitalization. Cibenzoline (300 mg/day) was administered for atrial fibrillation, which was detected in an electrocardiogram. After three days, she experienced blepharoptosis and was admitted for suspected myasthenia gravis. However, the anti-acetylcholine receptor antibody and edrophonium tests were negative. On day four after hospitalization, she suffered from pneumonia with pleural effusion and she was put on a respirator for four days. From day 16 after hospitalization, she had diarrhea and her renal function worsened. At the same time, a gradual aggravation of right blepharoptosis, dull headache, weakness and difficulty in chewing were noted. She experienced dyspnea on day 31 after hospitalization. Chest X-ray film did not show a pneumonia shadow or pleural effusion, and arterial blood gases revealed hypercapnia; she was diagnosed as having CO2 narcosis due to respiratory muscle fatigue and was put on a respirator again. Myasthenia-like syndrome was suspected because of a probable overdose of cibenzoline and administration of cibenzoline was withdrawn. Her condition improved and she was taken off the respirator on day 35 after hospitalization. Repetitive stimulation of 5 Hz was applied to her right facial nerve along with evoked electromyogram(EMG) on days 2 and 11 after discontinuing cibenzoline. On day 2, the EMG showed a waning phenomenon, whereas no such phenomenon was seen on day 11. The blood concentration of cibenzoline immediately after withdrawal was extremely high (2448

				ng/mL). When this drug is administered to a patient with chronic kidney disease, attention must be paid to the indication, dose, and manifestation of the possible side effects.
Kelly M, Gagne R, Newman JD, Olney C, Gualtieri C, Trail D.		Assessment of fibromyalgia & chronic fatigue syndrome: a new protocol designed to determine work capability--chronic pain abilities determination (CPAD).	Ir Med J. 2008 Oct;101(9):277-8.	The objective was to design a protocol to assess work ability in people suffering ill-defined painful and disabling disorders, the outstanding prototype of which is fibromyalgia/chronic fatigue syndrome (FM/CSF).Following an extensive literature search, the mos appropriate components of current methods of assessment of physical and cognitive abilities were incorporated into the protocol, occasionally with appropriate modification to suit the specific requirements of the individual. The initial part of the assessment consists of a standard history taking, principally focusing on the patient's self-reported physical and cognitive abilities and disabilities, as well as the completion of established pain and fatigue scales, and relevant disability questionnaires. Following this, physical and cognitive abilities are objectively assessed on two separate occasions, utilizing computerized hand-held dynamometers, inclinometers, algometers, and force dynamometers. Specific work simulation tests using the industrial standards Methods-Time-Measurement testing are availed of, as is aerobic testing using the Canadian Aerobic Fitness Test (CAFT). Objective computerised neuro-cognitive testing are also utilised as an integral component of the assessment. All results are then subject to specific computerized analysis and compared to normative and standardised work-based databases. The designed system produces reliable, consistent and reproducible results. It also proves capable of detecting any inconsistencies in patient input and results, in addition to being independent of any possible assessor bias. A new protocol has been designed to determine the working capability of individuals who suffer from various chronic disabling conditions, and represents a significant step forward in a difficult but rapidly expanding area of medical practice.
Kerr JR, Burke B, Petty R, Gough J, Fear D, Mattey DL, Axford JS, Dalgleish AG, Nutt DJ.	Department of Cellular and Molecular Medicine, St George's University of London, London, UK. jkerr@sgul.ac.uk	Seven genomic subtypes of chronic fatigue syndrome/myalgic encephalomyelitis: a detailed analysis of gene networks and clinical phenotypes.	J Clin Pathol. 2008 Jun;61(6):730-9. Epub 2007 Dec 5.	AIM: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a multisystem disease, the pathogenesis of which remains undetermined. The authors have recently reported a study of gene expression that identified differential expression of 88 human genes in patients with CFS/ME. Clustering of quantitative PCR (qPCR) data from patients with CFS/ME revealed seven distinct subtypes with distinct differences in Medical Outcomes Survey Short Form-36 scores, clinical phenotypes and severity. METHODS: In this study, for each CFS/ME subtype, those genes whose expression differed significantly from that of normal blood donors were identified, and then gene interactions, disease associations and molecular and cellular functions of those gene sets were determined. Genomic analysis was then related to clinical data for each CFS/ME subtype. RESULTS: Genomic analysis revealed some common (neurological, haematological, cancer) and some distinct (metabolic, endocrine, cardiovascular, immunological, inflammatory) disease associations among the subtypes. Subtypes 1, 2 and 7 were the most severe, and subtype 3 was the mildest. Clinical features of each subtype were as follows: subtype 1 (cognitive, musculoskeletal, sleep, anxiety/depression); subtype 2 (musculoskeletal, pain, anxiety/depression); subtype 3 (mild); subtype 4 (cognitive); subtype 5 (musculoskeletal, gastrointestinal); subtype 6 (postexertional); subtype 7 (pain, infectious, musculoskeletal, sleep, neurological, gastrointestinal, neurocognitive, anxiety/depression). CONCLUSION: It was particularly interesting that in the seven genomically derived subtypes there were distinct clinical syndromes, and that those which were most severe were also those with anxiety/depression, as would be expected in a disease with a biological basis.

Kerr JR, Mattey DL.	Department of Cellular and Molecular Medicine, St. George's University of London, United Kingdom. jkerr@sgul.ac.uk	Preexisting psychological stress predicts acute and chronic fatigue and arthritis following symptomatic parvovirus B19 infection.	Clin Infect Dis. 2008 May 1;46(9):e83-7.	BACKGROUND: Psychological stress is thought to be an important factor in the pathogenesis of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). Therefore, we sought to examine this relationship in the context of parvovirus B19 infection.METHODS: Thirty-nine patients with laboratory-documented acute parvovirus B19 infection were asked to complete questionnaires on negative life events, perceived stress, and negative affect relevant to the time of onset of parvovirus infection and during the preceding 12 months. These scores were combined into an overall stress index, which was then examined for associations with particular parvovirus-associated symptoms at acute infection and during the ensuing 1-3 years. Additional characteristics monitored included presence of parvovirus antibodies and nucleic acid, cortisol level, dehydroepiandrosterone level, autoantibodies, levels of a range of serum cytokines, and human leukocyte antigen class I and II alleles. RESULTS: Stress index was significantly associated with development of fatigue during the acute phase of parvovirus B19 infection and also with chronic fatigue and arthritis occurring 1-3 years following acute parvovirus B19 infection. Logistic regression that included all clinical variables indicated that a high stress index at the time of onset of infection was the primary predictor of CFS/ME 1-3 years following acute parvovirus B19 infection (odds ratio, 25.7; 95% confidence interval, 1.7-121.9; P=.005).CONCLUSIONS: We report a highly significant association between psychological stress and development of acute and chronic fatigue and arthritis several years following laboratory-documented acute parvovirus B19 infection.
Kerr JR, Petty R, Burke B, Gough J, Fear D, Sinclair LI, Mattey DL, Richards SC, Montgomery J, Baldwin DA, Kellam P, Harrison TJ, Griffin GE, Main J, Enlander D, Nutt DJ, Holgate ST.	Department of Cellular & Molecular Medicine, St. George's University of London, London. jkerr@sgul.ac.uk	Gene expression subtypes in patients with chronic fatigue syndrome/myalgic encephalomyelitis.	J Infect Dis. 2008 Apr 15;197(8):1171-84.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a multisystem disease, the pathogenesis of which remains undetermined. We set out to determine the precise abnormalities of gene expression in the blood of patients with CFS/ME. We analyzed gene expression in peripheral blood from 25 patients with CFS/ME diagnosed according to the Centers for Disease Control and Prevention diagnostic criteria and 50 healthy blood donors, using a microarray with a cutoff fold difference of expression of >or=2.5. Genes showing differential expression were further analyzed in 55 patients with CFS/ME and 75 healthy blood donors, using quantitative polymerase chain reaction. Differential expression was confirmed for 88 genes; 85 were upregulated, and 3 were downregulated. Highly represented functions were hematological disease and function, immunological disease and function, cancer, cell death, immune response, and infection. Clustering of quantitative polymerase chain reaction data from patients with CFS/ME revealed 7 subtypes with distinct differences in Medical Outcomes Survey Short Form-36 scores, clinical phenotypes, and severity.
Kerr JR, Taylor-Robinson D.	Department of Cellular and Molecular Medicine, St. George's University of London, London.	David Arthur John Tyrrell CBE: 19 June 1925 - 2 May 2005.	Biogr Mem Fellows R Soc. 2007;53:349-63.	David Tyrrell is remembered by physicians and scientists principally for his discovery of the common cold viruses and elucidation of their pathogenesis, but also for his work in various other areas, including influenza, bovine spongiform encephalopathy (BSE) and chronic fatigue syndrome (CFS). David possessed a deep humanity, honesty, perseverance and a vision of collaboration as a means of making discoveries that would contribute meaningfully to the alleviation of human suffering. He also had a warmth and a mischievous sense of humour that was frequently directed at bureaucracy, which he thoroughly disliked.
Kerr JR.		Enterovirus infection of the stomach in chronic fatigue	J Clin Pathol. 2008 Jan;61(1):1-2. Epub 2007 Sep 14.	

		syndrome/myalgic encephalomyelitis Comment on: J Clin Pathol. 2008 Jan;61(1):43-8.		
Kerr JR.	St. George's University of London, Cranmer Terrace, London SW17 0RE, United Kingdom. jkerr@sgul.ac.uk	Gene profiling of patients with chronic fatigue syndrome/myalgic encephalomyelitis.	Curr Rheumatol Rep. 2008 Dec;10(6):482-91.	Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a multisystem disease, the pathogenesis of which remains undetermined. Following two microarray studies, we reported the differential expression of 88 human genes in patients with CFS; 85 of these genes were upregulated and 3 were downregulated. The top functional categories of these 88 genes were hematologic disease and function, immunologic disease and function, cancer, cell death, immune response, and infection. Clustering of quantitative polymerase chain reaction data from CFS/ME patients revealed seven subtypes with distinct differences in Short Form (SF)-36 scores, clinical phenotypes, and severity. Gene signatures in each subtype implicate five human genes as possible targets for specific therapy. Development of a diagnostic test for subtype status is now a priority. The possibility that these subtypes represent individual host responses to particular microbial infections is being investigated and may provide another route to specific therapies for CFS patients.
Kilshaw S.	Department of Anthropology, University College London, 14 Taviton Street, London, UK. s.kilshaw@ucl.ac.uk	Gulf war syndrome: a reaction to psychiatry's invasion of the military?	Cult Med Psychiatry. 2008 Jun;32(2):219-37.	Following the 1991 Gulf War, a number of soldiers who fought there began to complain of various symptoms and disorders, the collection of which came to be known as Gulf War syndrome (GWS). A debate has raged about the nature and cause of this illness, with many suggesting that it is a psychiatric condition. GWS continues to be a contested illness, yet there is no disputing that many Gulf veterans are ill. This article considers the way in which GWS sufferers understand their illness to be physical in nature and the way in which they negotiate and resist psychological theories of their illness. Based on 14 months of ethnographic fieldwork in the United Kingdom, data for this article were collected mainly by in-depth, semistructured interviews with GWS sufferers, their family members, doctors, and scientists, as well as healthy Gulf veterans. A total of 93 informants were interviewed, including 67 UK Gulf veterans, most of whom were ill. The paper argues that despite the increasing presence of psychiatry in military discourse, GWS reveals the way that people are able to transform, negotiate and even negate its power and assumptions.
Kim SH, Lee K, Lim HS.	Department of Internal Medicine, Dongguk University College of Medicine, Republic of Korea.	Prevalence of chronic widespread pain and chronic fatigue syndrome in Korean livestock raisers.	J Occup Health. 2008;50(6):525-8. Epub 2008 Oct 23.	PMID: 18946188 [PubMed - indexed for MEDLINE]
Kishi A, Struzik ZR, Natelson BH, Togo F, Yamamoto Y.	Graduate School of Education, The University of Tokyo, 7-3-1 Hongo, Bunkyo-	Dynamics of sleep stage transitions in healthy humans and patients with chronic fatigue	Am J Physiol Regul Integr Comp Physiol. 2008 Jun;294(6):R1980-7. Epub 2008 Apr	Physiological and/or pathological implications of the dynamics of sleep stage transitions have not, to date, been investigated. We report detailed duration and transition statistics between sleep stages in healthy subjects and in others with chronic fatigue syndrome (CFS); in addition, we also compare our data with previously published results for rats. Twenty-two healthy females and 22 female patients with CFS, characterized by complaints of unrefreshing sleep, underwent one night of

	ku, Tokyo, Japan.	syndrome.	16.	polysomnographic recording. We find that duration of deep sleep (stages III and IV) follows a power-law probability distribution function; in contrast, stage II sleep durations follow a stretched exponential and stage I, and REM sleep durations follow an exponential function. These stage duration distributions show a gradually increasing departure from the exponential form with increasing depth of sleep toward a power-law type distribution for deep sleep, suggesting increasing complexity of regulation of deeper sleep stages. We also find a substantial number of REM to non-REM sleep transitions in humans, while this transition is reported to be virtually nonexistent in rats. The relative frequency of this REM to non-REM sleep transition is significantly lower in CFS patients than in controls, resulting in a significantly greater relative transition frequency of moving from both REM and stage I sleep to awake. Such an alteration in the transition pattern suggests that the normal continuation of sleep in light or REM sleep is disrupted in CFS. We conclude that dynamic transition analysis of sleep stages is useful for elucidating yet-to-be-determined human sleep regulation mechanisms with pathophysiological implications.
Knoop H, Stulemeijer M, de Jong LW, Fiselier TJ, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University, Nijmegen Medical Centre, Postbox 9011, 6525 EC Nijmegen, The Netherlands. j.knoop@nkcv.umcn.nl	Efficacy of cognitive behavioral therapy for adolescents with chronic fatigue syndrome: long-term follow-up of a randomized, controlled trial.	Pediatrics. 2008 Mar;121(3):e619-25.	OBJECTIVES: The purpose of this work was to assess the long-term outcome of adolescents with chronic fatigue syndrome who received cognitive behavioral therapy and to determine the predictive value of fatigue severity and physical impairments of the adolescent and the fatigue severity of the mother at baseline for the outcome of the treatment at follow-up. PATIENTS AND METHODS: Sixty-six adolescent patients with chronic fatigue syndrome who previously participated in a randomized, controlled trial that showed that cognitive behavioral therapy was more effective than a waiting-list condition in reducing fatigue and improving physical functioning were contacted for a follow-up assessment. Fifty participants of the follow-up study had received cognitive behavioral therapy for chronic fatigue syndrome (32 formed the cognitive behavioral therapy group in the original trial, and 18 patients received cognitive behavioral therapy after the waiting period). The remaining 16 patients had refused cognitive behavioral therapy after the waiting period. The main outcome measures were fatigue severity (Checklist Individual Strength), physical functioning (Short-Form General Health Survey), and school attendance. RESULTS: Data were complete for 61 patients at follow-up (cognitive behavioral therapy group: 47 patients; no-treatment group: 14 patients). The mean follow-up time was 2.1 years. There was no significant change in fatigue severity between posttreatment and follow-up in the cognitive behavioral therapy group. There was a significant further increase in physical functioning and school attendance (10% increase). The adolescents in the cognitive behavioral therapy group were significantly less fatigued and significantly less functionally impaired and had higher school attendance at follow-up than those in the no-treatment group. Fatigue severity of the mother was a significant predictor of treatment outcome. CONCLUSIONS: The positive effects of cognitive behavioral therapy in adolescents with chronic fatigue syndrome are sustained after cognitive behavioral therapy. Higher fatigue severity of the mother predicts lower treatment outcome in adolescent patients.
Knoop H, van der Meer JW, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University	Guided self-instructions for people with chronic fatigue	Br J Psychiatry. 2008 Oct;193(4):340-1.	A minimal intervention, based on cognitive-behavioural therapy for chronic fatigue syndrome and consisting of self-instructions combined with email contact, was tested in a randomised controlled trial (ISRCTN27293439). A total of 171 patients participated in the trial: 85 were allocated to the intervention condition and 86 to the waiting-list condition. All patients met the Centers for Disease

	Nijmegen Medical Centre, Nijmegen, The Netherlands. j.knoop@nkcv.umcn.nl	syndrome: randomised controlled trial.		Control and Prevention criteria for chronic fatigue syndrome. An intention-to-treat analysis showed a significant decrease in fatigue and disability after self-instruction. The level of disability was negatively correlated with treatment outcome. Guided self-instructions are an effective treatment for patients with relatively less severe chronic fatigue syndrome.
Kong MH, Lee EJ, Lee SY, Cho SJ, Hong YS, Park SB.	Department of Family Practice, Ajou University, Suwon, Korea. MHKong@paran.com	Effect of human placental extract on menopausal symptoms, fatigue, and risk factors for cardiovascular disease in middle-aged Korean women.	Menopause. 2008 Mar-Apr;15(2):296-303.	OBJECTIVE: In Korea, human placental extract (HPE) has recently been used to treat various diseases (chronic liver diseases, menopause syndrome, chronic fatigue, skin pigment diseases, etc.), but evidence-based studies are not yet sufficient. The aim of this study was to examine the effects of HPE on menopausal symptoms, fatigue, and risk factors for cardiovascular disease in middle-aged Korean women in a randomized controlled trial. DESIGN: Korean women, aged 40 to 64 years, with menopausal symptoms and fatigue were recruited as participants. The women were randomly assigned to a placebo group or an HPE group. The HPE group received subcutaneous injections of HPE in the abdomen for 8 weeks, whereas the placebo group received normal saline. Then, the Menopause Rating Scale, and Fatigue Severity Scale, and Visual Analog Scale were administered, and risk factors for cardiovascular disease were assessed. RESULTS: The Menopause Rating Scale total baseline score was not different between the two groups; however, the score of the HPE group decreased significantly at 8 weeks compared with that of the placebo group (P = 0.033). Fatigue Severity Scale and Visual Analog Scale scores of the placebo group did not change, whereas the scores of the HPE group decreased significantly during the study period (Fatigue Severity Scale, P = 0.002; Visual Analog Scale, P = 0.001). The baseline 17beta-estradiol level was not significantly different between the two groups, but the 17beta-estradiol level of the HPE group was significantly increased at 8 weeks compared with that of the placebo group (P = 0.031). No changes in risk factors for cardiovascular disease were observed in either group. CONCLUSIONS: Menopausal symptoms and fatigue in middle-aged Korean women improved after 8 weeks of HPE treatment, whereas risk factors for cardiovascular disease did not change during the study period.
Kornreich C, Szombat M, Vandriette YM, Dan B.	Brugmann Hospital Brussels, Belgium.	Association of chronic fatigue syndrome and acute psychotic episode: is it coincidental?	Prim Care Companion J Clin Psychiatry. 2008;10(5):412.	PMID: 19158983 [PubMed - in process]
Kos D, Kerckhofs E, Nagels G, D'hooghe MB, Ilsbroukx S.	Vrije Universiteit Brussel, Department of Rehabilitation Research, Brussels, Belgium. Daphne.Kos@vub.ac.be	Origin of fatigue in multiple sclerosis: review of the literature.	Neurorehabil Neural Repair. 2008 Jan-Feb;22(1):91-100. Epub 2007 Apr 4.	Fatigue is one of the most common and most disabling symptoms of multiple sclerosis (MS). Although numerous studies have tried to reveal it, no definite pathogenesis factor behind this fatigue has been identified. Fatigue may be directly related to the disease mechanisms (primary fatigue) or may be secondary to non-disease-specific factors. Primary fatigue may be the result of inflammation, demyelination, or axonal loss. A suggested functional cortical reorganization may result in a higher energy demand in certain brain areas, culminating in an increase of fatigue perception. Higher levels of some immune markers were found in patients with MS-related fatigue, whereas other studies rejected this hypothesis. There may be a disturbance in the neuroendocrine system related to fatigue, but it is not clear whether this is either the result of the interaction with immune activation or the

				trigger of this process. Fatigue may be secondary to sleep problems, which are frequently present in MS and in their turn result from urinary problems, spasms, pain, or anxiety. Pharmacologic treatment of MS (symptoms) may also provoke fatigue. The evidence for reduced activity as a cause of secondary fatigue in MS is inconsistent. Psychological functioning may at least play a role in the persistence of fatigue. Research did not reach consensus about the association of fatigue with clinical or demographic variables, such as age, gender, disability, type of MS, education level, and disease duration. In conclusion, it is more likely to explain fatigue from a multifactor perspective than to ascribe it to one mechanism. The current evidence on the pathogenesis of primary and secondary fatigue in MS is limited by inconsistency in defining specific aspects of the concept fatigue, by the lack of appropriate assessment tools, and by the use of heterogeneous samples. Future research should overcome these limitations and also include longitudinal designs.
Kowalski A, Rebas E, Zylińska L.	Department of Molecular Neurochemistry, Medical University of Lodz, 6/8 Mazowiecka St., 92-215 Lodz, Poland. antek3000@tlen.pl	[Gamma-aminobutyric acid--metabolism and its disorders] [Article in Polish]	Postepy Biochem. 2007;53(4):356-60.	Gamma-aminobutyric acid is a major inhibitory neurotransmitter in the central nervous system. GABA metabolism is dependent on the activity of three enzymes: glutamic acid decarboxylase, GABA-transaminase and succinic semialdehyde dehydrogenase. Decreased activity of these enzymes may cause many neurological syndromes, such as stiff-person syndrome, chronic fatigue syndrome, anxiety disorders and seizures. This article is a review of most important problems related to an impairment of GABA metabolism.
Kumagi T, Heathcote EJ.	Department of Medicine, Toronto Western Hospital (University Health Network/University of Toronto), Toronto, Ontario, Canada. masato_teru@yahoo.co.jp	Primary biliary cirrhosis.	Orphanet J Rare Dis. 2008 Jan 23;3:1.	Primary biliary cirrhosis (PBC) is a chronic and slowly progressive cholestatic liver disease of autoimmune etiology characterized by injury of the intrahepatic bile ducts that may eventually lead to liver failure. Affected individuals are usually in their fifth to seventh decades of life at time of diagnosis, and 90% are women. Annual incidence is estimated between 0.7 and 49 cases per million-population and prevalence between 6.7 and 940 cases per million-population (depending on age and sex). The majority of patients are asymptomatic at diagnosis, however, some patients present with symptoms of fatigue and/or pruritus. Patients may even present with ascites, hepatic encephalopathy and/or esophageal variceal hemorrhage. PBC is associated with other autoimmune diseases such as Sjogren's syndrome, scleroderma, Raynaud's phenomenon and CREST syndrome and is regarded as an organ specific autoimmune disease. Genetic susceptibility as a predisposing factor for PBC has been suggested. Environmental factors may have potential causative role (infection, chemicals, smoking). Diagnosis is based on a combination of clinical features, abnormal liver biochemical pattern in a cholestatic picture persisting for more than six months and presence of detectable antimitochondrial antibodies (AMA) in serum. All AMA negative patients with cholestatic liver disease should be carefully evaluated with cholangiography and liver biopsy. Ursodeoxycholic acid (UDCA) is the only currently known medication that can slow the disease progression. Patients, particularly those who start UDCA treatment at early-stage disease and who respond in terms of improvement of the liver biochemistry, have a good prognosis. Liver transplantation is usually an option for patients with liver failure and the outcome is 70% survival at 7 years. Recently, animal models have been discovered that may provide a new insight into the pathogenesis of this disease and facilitate appreciation for novel treatment in

				PBC.
Kumar A, Garg R, Kumar P.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, 160014, India. kumaruips@yahoo.com	Nitric oxide modulation mediates the protective effect of trazodone in a mouse model of chronic fatigue syndrome.	Pharmacol Rep. 2008 Sep-Oct;60(5):664-72.	The present study was conducted with the aim of elucidating the possible role of nitric oxide (NO) in the neuroprotective effects of trazodone used to treat chronic fatigue syndrome (CFS) in mice. Male albino mice were forced to swim for a six minute session each day for 7 days and the immobility period was recorded every other day. Trazodone (5 mg/kg and 10 mg/kg) was administered each day 30 min before the forced swim test. In addition, L-arginine (100 mg/kg) and L-NAME (5 mg/kg) were administered 15 min before administration of trazodone (5 mg/kg). Various behavioral tests, including locomotor (actophotometer) and anxiety (mirror chamber and plus maze) tests, as well as biochemical parameters (lipid peroxidation, reduced glutathione, catalase, and nitrites) were evaluated on the 8th day. Forced swimming for 7 days caused a chronic fatigue-like condition, anxiety-like behavior, impairments in locomotor activity, and oxidative damage (increased lipid peroxidation and nitrite levels, and depletions in the reduced forms of glutathione and catalase activity) in animals. Pretreatment with L-NAME (5 mg/kg) potentiated the antioxidant effect of trazodone (5 mg/kg). However, L-arginine (100 mg/kg) pretreatment reversed the protective effect of trazodone (5 mg/kg) ($p<0.05$). The present study suggests the possible involvement of NO signaling in the protective effect of trazodone.
Kumar A, Garg R.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160014, India.	Protective effects of antidepressants against chronic fatigue syndrome - induced behavioral changes and biochemical alterations.	Fundam Clin Pharmacol. 2009 Jan 10. [Epub ahead of print]	Abstract Chronic fatigue syndrome (CFS) is characterized by profound fatigue, which substantially interferes with daily activities. The aim of this study was to explore the protective effects of antidepressants in an animal model of CFS in mice. Male albino mice were forced to swim individually for a period of 6-min session each for 7 days. Imipramine (10 and 20 mg/kg), desipramine (10 and 20 mg/kg) and citalopram (5 and 10 mg/kg) were administered 30 min before forced swimming test on each day. Various behavior tests (immobility time, locomotor activity, anxiety-like behavior by plus maze and mirror chamber) followed by biochemical parameters (lipid peroxidation, reduced glutathione, catalase and nitrite level) were assessed in chronic stressed mice. Chronic forced swimming for 7 days significantly caused increase in immobility period, impairment in locomotor activity, anxiety-like behavior, and oxidative stress (raised lipid peroxidation, nitrite activity and reduced glutathione and catalase activity) as compared with naïve mice ($P < 0.05$). Seven days of pretreatment with imipramine (10 and 20 mg/kg), desipramine (10 and 20 mg/kg), and citalopram (5 and 10 mg/kg) significantly reduced immobility time, improved locomotor activity and anti-anxiety effect (in both plus maze and mirror chamber test), and attenuated oxidative stress in chronic stressed mice as compared with control (chronic fatigues) ($P < 0.05$). These results suggested that these drugs have protective effect and could be used in the management of chronic fatigue like conditions.
Kumar R.	Department of Family Medicine, University of Chicago, Chicago, Illinois 60637, USA. rkumar@medicine.bsd.uchicago.edu	Approved and investigational uses of modafinil : an evidence-based review.	Drugs. 2008;68(13):1803-39.	Modafinil is a wake-promoting agent that is pharmacologically different from other stimulants. It has been investigated in healthy volunteers, and in individuals with clinical disorders associated with excessive sleepiness, fatigue, impaired cognition and other symptoms. This review examines the use of modafinil in clinical practice based on the results of randomized, double-blind, placebo-controlled clinical trials available in the English language in the MEDLINE database. In sleep-deprived individuals, modafinil improves mood, fatigue, sleepiness and cognition to a similar extent as caffeine but has a longer duration of action. Evidence for improved cognition in non-sleep-deprived healthy volunteers is controversial.Modafinil improves excessive sleepiness and illness severity in all three disorders for

				which it has been approved by the US FDA, i.e. narcolepsy, shift-work sleep disorder and obstructive sleep apnoea with residual excessive sleepiness despite optimal use of continuous positive airway pressure (CPAP). However, its effects on safety on the job and on morbidities associated with these disorders have not been ascertained. Continued use of CPAP in obstructive sleep apnoea is essential. Modafinil does not benefit cataplexy.In very small, short-term trials, modafinil improved excessive sleepiness in patients with myotonic dystrophy. It was efficacious in fairly large studies of attention deficit hyperactivity disorder (ADHD) in children and adolescents, and was as efficacious as methylphenidate in a small trial, but has not been approved by the FDA, in part because of its serious dermatological toxicity. In a trial of 21 non-concurrent subjects, with 2-week treatment periods, modafinil was as effective as dexamfetamine in adult ADHD. Modafinil was helpful for depressive symptoms in bipolar disorder in a trial that excluded patients with stimulant-induced mania. A single dose of modafinil may hasten recovery from general anaesthesia after day surgery. A single dose of modafinil improved the ability of emergency room physicians to attend didactic lectures after a night shift, but did not improve their ability to drive home and caused sleep disturbances subsequently.Modafinil had a substantial placebo effect on outcomes such as fatigue, excessive sleepiness and depression in patients with traumatic brain injury, major depressive disorder, schizophrenia, post-polio fatigue and multiple sclerosis; however, it did not provide any benefit greater than placebo.Trials of modafinil for excessive sleepiness in Parkinson's disease, cocaine addiction and cognition in chronic fatigue syndrome provided inconsistent results; all studies had extremely small sample sizes. Modafinil cannot be recommended for these conditions until definitive data become available.Modafinil induces and inhibits several cytochrome P450 isoenzymes and has the potential for interacting with drugs from all classes. The modafinil dose should be reduced in the elderly and in patients with hepatic disease. Caution is needed in patients with severe renal insufficiency because of substantial increases in levels of modafinil acid. Common adverse events with modafinil include insomnia, headache, nausea, nervousness and hypertension. Decreased appetite, weight loss and serious dermatological have been reported with greater frequency in children and adolescents, probably due to the higher doses (based on bodyweight) used. Modafinil may have some abuse/addictive potential although no cases have been reported to date.
Kung WW, Lu PC.	Graduate School of Social Service, Fordham University, New York, New York 10023-7484, USA. kung@fordham.edu	How symptom manifestations affect help seeking for mental health problems among Chinese Americans.	J Nerv Ment Dis. 2008 Jan;196(1):46-54.	This study aims to examine how help-seeking behaviors of Chinese Americans are associated with the types of mental disorder, the tendency to somatize symptoms, social disruptiveness of symptoms, and comorbidity. Based on data from the Chinese American Psychiatric Epidemiological Study, we examined 246 Chinese Americans with a diagnosable major depressive disorder, anxiety disorder, or somatoform disorder, using hierarchical logistic regression analyses. Compared with respondents with somatoform disorder, those with anxiety or depressive disorder were 94% and 87% less likely to seek professional help. The tendency to somatize distress is positively related to soliciting help, especially medical help. Social disruptiveness had a very potent positive association with help seeking whereas comorbidity is nonsignificant when the symptom severity is controlled. The overall picture indicates that somatic expression of distress is a major impetus to help seeking, which happens to concur with the cultural conceptualization and subjective embodied experience of mental disorders among Chinese.

Kuo YH, Tsai WJ, Loke SH, Wu TS, Chiou WF.	National Research Institute of Chinese Medicine, Taipei, Taiwan, ROC.	Astragalus membranaceus flavonoids (AMF) ameliorate chronic fatigue syndrome induced by food intake restriction plus forced swimming.	J Ethnopharmacol. 2009 Feb 25;122(1):28-34. Epub 2008 Dec 6.	AIM OF THE STUDY: Alteration of immune function may be associated with chronic fatigue syndrome (CFS) and this study reveals the immunoregulatory effect of Astragalus membranaceus flavonoids (AMF). MATERIALS AND METHODS: CF rats were induced by food intake restriction plus forced swimming for 6 weeks. RESULTS: An atrophied spleen associated with a significantly decreased spleen/body weight ratio and a reduced spleen cells proliferation was found in CF rats when compared with home cage controls. AMF given orally at 20, 50 and 100mg/kg body weight once a day consecutively for 6 weeks could recover the reduced cell proliferation. A switch to Th1-dominated immune regulation was observed in CF rats as the cultured splenocytes produced more interleukin-2 (IL-2) but less IL-4 when compared with controls. Supplementation with AMF could significantly counteract the aberrant cytokine production and rats received AMF exhibited higher endurance capacity to swim when compared with those without AMF administration. Checking the spectrum signals confirmed that the three major isoflavones contained in AMF were ononin, formononetin, and demethylhomopterocarpin. CONCLUSION: Alterations of immune function may be associated with CFS and the tonic effects of AMF against CF may be attributable to balance the abnormal cytokine level by isoflavones.
Lemle MD.		Hypothesis: chronic fatigue syndrome is caused by dysregulation of hydrogen sulfide metabolism.	Med Hypotheses. 2009 Jan;72(1):108-9. Epub 2008 Sep 16.	
Leocani L, Colombo B, Comi G.	Institute of Experimental Neurology Dept. of Neurology, Clinical Neurophysiology, Neurorehabilitation, Univ. Vita-Salute and Scientific Institute San Raffaele, Via Olgettina 60, 20132, Milan, Italy. letizia.leocani@hsr.it	Physiopathology of fatigue in multiple sclerosis.	Neurol Sci. 2008 Sep;29 Suppl 2:S241-3.	Fatigue is an overwhelming sense of tiredness or lack of energy, affecting both mental and physical domains. Fatigue is reported by about 50% of patients with multiple sclerosis (MS), and may be independent from depressed mood or weakness. Recently, the importance of distinguishing between subjective complaint and objective signs of fatigue has been emphasized, since the self-reported increase of subjective cognitive fatigue may not be related to a decline of cognitive performances. There is a general consensus that fatigue in MS is a central phenomenon, related to several factors. Neurophysiological studies revealed an impairment of volitional drive to the descending motor pathways and functional imaging studies indicated a selective involvement of frontal cortex and basal ganglia. Thus, the physiopathology of fatigue may rely on dysfunction of circuits involving thalamus, basal ganglia, and frontal cortex, which, affected by the MS lesions or disturbed in their function by the products of inflammation, could be the substrate of fatigue. The abnormal subjective fatigue observed in MS and perhaps in other neurological disorders could be due to a higher brain working load required to perform a given mental or physical activity, or to an internal overestimation of such load.
Lerner AM, Beqaj SH, Fitzgerald JT.	Department of Medicine, Wayne State University School of Medicine	Validation of the energy index point score to serially measure the	In Vivo. 2008 Nov-Dec;22(6):799-801.	BACKGROUND: A simple quantitative accurate method for assessing the degree of fatigue in patients with chronic fatigue syndrome (CFS) is necessary for physicians and patients. Severity of the disease and recovery can, thus, be assayed. PATIENT AND METHODS: From February 1-27, 2007, fifty-six consecutive CFS patients at a single treatment center were simultaneously evaluated by the patient

	and William Beaumont Hospital, Royal Oak, MI, USA. amartinlerner@yahoo.com	degree of disability in patients with chronic fatigue syndrome.		with the fatigue severity score (FSS), and by consensus of both patient and physician by the energy index (EI) point score. RESULTS: The FSS and EI correlated well, 0.67, p<0.001. CONCLUSION: The El point score is a validated reliable method to assess fatigue in CFS patients.
Li ZC, Zhao Y, Dou ZH, Yu L, Wu H, Zhang FJ.	Department of Infectious Diseases, Beijing Youan Hospital, Capital Medical University, Beijing 100069, China. treatment@chinaaids.cn.	[Clinical features of 66 children with acquired immunodeficienecy syndrome.] [Article in Chinese]	Zhongguo Dang Dai Er Ke Za Zhi. 2009 Feb;11(2):93-5.	OBJECTIVE: To study the clinical features of pediatric acquired immunodeficienecy syndrome(AIDS). METHODS: The epidemiological, clinical and laboratory data of 66 children with AIDS were retrospectively studied. RESULTS: Of the 66 patients, 46 (69.7%) were male and 20 (30.3%) were female, with a mean age of 8.7 years (ranged 2-16 years). The mean age at diagnosis was 7.7 years (ranged 2-15 years). Vertical transmission as the route of infection was documented in 48 cases (72.7%). Fourteen children (21.2%) were infected through blood or blood products. The route of infection could not be identified in 4 cases (6.1%). Body weight loss was noted in 43 cases (65.2%), anemia in 42 cases (63.7%), fever in 40 cases (60.6%), fatigue in 38 cases (57.6%), rash in 31 cases (47.0%), chronic cough in 28 cases (12.1%), chronic diarrhea in 24 cases (36.4%), CNS involvement in 16 cases (24.2%), oral thrush in 13 cases (19.7%), and hepatosplenomegaly in 12 cases (18.2%). Body height of 30 cases (45.4%) and body weight of 26 cases (39.4%) ranked the lower level. The immune system was severely suppressed in 59 cases (89.4%) and moderately suppressed in 7 cases (10.6%). CONCLUSIONS: Vertical transmission remained the most common route of pediatric HIV infection. There were various clinical manifestations in children with AIDS. The immune systems of the majority of children with this disorder were severely suppressed.
Lim JY, Kim KE, Choe G.	Department of Rehabilitation, Seoul National University College of Medicine, Seoul National University Bundang Hospital, Korea.	Myotonic dystrophy mimicking postpolio syndrome in a polio survivor.	Am J Phys Med Rehabil. 2009 Feb;88(2):161-4.	We describe a 38-yr-old polio survivor with newly developed weakness from myotonic dystrophy. He suffered muscle atrophy and weakness in his legs as a result of poliomyelitis at the age of 3 yrs. After a stable interval of about 30 yrs, he felt new weakness and fatigue in his legs. Electromyography revealed generalized myotonic discharges, early recruitment, and findings of chronic denervation in his left leg. Genetic testing was consistent with myotonic dystrophy type 1. A biopsy from the right gastrocnemius revealed findings of both myotonic dystrophy and chronic denervation. This case report shows the importance of considering other uncommon conditions in the differential diagnoses of postpolio syndrome.
Lin E, Hsu SY.	Vita Genomics, Inc., Jung-Shing Road, Wugu Shiang, Taipei, Taiwan. eugene.lin@vitagenomics.com	A Bayesian approach to gene-gene and gene-environment interactions in chronic fatigue syndrome.	Pharmacogenomics. 2009 Jan;10(1):35-42.	INTRODUCTION: In the study of genomics, it is essential to address gene-gene and gene-environment interactions for describing the complex traits that involves disease-related mechanisms. In this work, our goal is to detect gene-gene and gene-environment interactions resulting from the analysis of chronic fatigue syndrome patients' genetic and demographic factors including SNPs, age, gender and BMI. MATERIALS & METHODS: We employed the dataset that was original to the previous study by the Centers for Disease Control and Prevention Chronic Fatigue Syndrome Research Group. To investigate gene-gene and gene-environment interactions, we implemented a Bayesian based method for identifying significant interactions between factors. Here, we employed a two-stage Bayesian variable selection methodology based on Markov Chain Monte Carlo approaches. RESULTS: By applying our Bayesian based approach, NR3C1 was found in the significant two-locus gene-gene effect model, as well as in the significant two-factor gene-environment effect model. Furthermore, a

				significant gene-environment interaction was identified between NR3C1 and gender. These results support the hypothesis that NR3C1 and gender may play a role in biological mechanisms associated with chronic fatigue syndrome. CONCLUSION: We demonstrated that our Bayesian based approach is a promising method to assess the gene-gene and gene-environment interactions in chronic fatigue syndrome patients by using genetic factors, such as SNPs, and demographic factors such as age, gender and BMI.
Lin JM, Brimmer DJ, Boneva RS, Jones JF, Reeves WC.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne and Enteric Diseases, Centers for Disease Control and Prevention, Mail Stop A-15, 1600 Clifton Rd, NE, Atlanta, GA 30333, USA. dwe3@cdc.gov.	Barriers to healthcare utilization in fatiguing illness: a population-based study in Georgia.	BMC Health Serv Res. 2009 Jan 20;9:13.	ABSTRACT: BACKGROUND: The purpose of this study was to determine the prevalence of barriers to healthcare utilization in persons with fatiguing illness and describe its association with socio-demographics, the number of health conditions, and frequency of healthcare utilization. Furthermore, we sought to identify what types of barriers interfered with healthcare utilization and why they occurred. METHODS: In a cross-sectional population-based survey, 780 subjects, 112 of them with chronic fatigue syndrome (CFS), completed a healthcare utilization questionnaire. Text analysis was used to create the emerging themes from verbatim responses regarding barriers to healthcare utilization. Multiple logistic regression was performed to examine the association between barriers to healthcare utilization and other factors. RESULTS: Forty percent of subjects reported at least one barrier to healthcare utilization. Of 112 subjects with CFS, 55% reported at least one barrier to healthcare utilization. Fatiguing status, reported duration of fatigue, insurance, and BMI were significant risk factors for barriers to healthcare utilization. After adjusting for socio-demographics, medication use, the number of health problems, and frequency of healthcare utilization, fatiguing status remained significantly associated with barriers to healthcare utilization. Subjects with CFS were nearly 4 times more likely to forego needed healthcare during the preceding year than non-fatigued subjects while those with insufficient fatigue (ISF) were nearly 3 times more likely.Three domains emerged from text analysis on barriers to healthcare utilization: 1) accessibility; 2) knowledge-attitudes-beliefs (KABs); and, 3) healthcare system. CFS and reported duration of fatigue were significantly associated with each of these domains. Persons with CFS reported high levels of healthcare utilization barriers for each domain: accessibility (34%), healthcare system (25%), and KABs (19%). In further examination of barrier domains to healthcare utilization, compared to non-fatigued persons adjusted ORs for CFS having "accessibility", "KAB" and "Healthcare System" barrier domains decreased by 40%, 30%, and 19%, respectively. CONCLUSION: Barriers to healthcare utilization pose a significant problem in persons with fatiguing illnesses. Study results suggested two-fold implications: a symptom-targeted model focusing on symptoms associated with fatigue; and an interactive model requiring efforts from patients and providers to improve interactions between them by reducing barriers in accessibility, KABs, and healthcare system.
Lipowsky C, Schorl-Schweikardt BA, Kehl O, Brändle M.	Fachbereich für Endokrinologie und Diabetologie, Departement für Innere Medizin, Kantonsspital St. Gallen.	[19-year-old patient with adrenal cortex insufficiency--only the tip of the iceberg. Polyendocrine	Praxis (Bern 1994). 2008 Jan 23;97(2):77-81.	We report on a 19-year-old woman with polyglandular autoimmune syndrome type II (APS II). She was diagnosed with addison's disease and hypothyroidism due to chronic autoimmune thyroiditis. Her mother had celiac disease and her brohter had diabetes mellitus typ 1. Chronic autoimmune thyroiditis was diagnosed in her mother, subsequently. In patients and their relatives, who have autoimmune disorders, a search for autoimmune polyglandular syndrome is crucial. Consequently, it would be appropriate that the patient and all family members are asked for clinical signs and symptoms of autoimmune disorders. Annual measurement of morning cortisol, TSH and fasting

	christof.lipowsky@kssg.ch	autoimmune syndrome type II (Schmidt syndrome)] [Article in German]		plasma glucose may useful. Screening of affected individuals as well as their first-degree relatives for celiac disease is recommended. Therapy of APS II consists of hormone replacement therapy, but thyroxin replacement may induce life-threatening adrenal failure in a patient with untreated Addison's disease. Thus, in case of doubt hydrocortisone should be given before the thyroxine administration is started.
Lorusso L, Mikhaylova SV, Capelli E, Ferrari D, Ngonga GK, Ricevuti G.	Department of Neurology, Mellino Mellini Hospital, Chiari, Brescia, Italy.	Immunological aspects of chronic fatigue syndrome.	Autoimmun Rev. 2009 Feb;8(4):287-91. Epub 2008 Sep 16.	Chronic fatigue syndrome (CFS) is a specific clinical condition that characterises unexplained disabling fatigue and a combination of non-specific accompanying symptoms for at least 6 months, in the absence of a medical diagnosis that would otherwise explain the clinical presentation. Other common symptoms include headaches, myalgia, arthralgia, and post-exertional malaise; cognitive difficulties, with impaired memory and concentration; unrefreshing sleep; and mood changes. Similar disorders have been described for at least two centuries and have been differently named neurasthenia, post-viral fatigue, myalgic encephalomyelitis and chronic mononucleosis. Recent longitudinal studies suggest that some people affected by chronic fatigue syndrome improve with time but that most remain functionally impaired for several years. The estimated worldwide prevalence of CFS is 0.4-1% and it affects over 800,000 people in the United States and approximately 240,000 patients in the UK. No physical examination signs are specific to CFS and no diagnostic tests identify this syndrome. The pathophysiological mechanism of CFS is unclear. The main hypotheses include altered central nervous system functioning resulting from an abnormal immune response against a common antigen; a neuroendocrine disturbance; cognitive impairment caused by response to infection or other stimuli in sentient people. The current concept is that CFS pathogenesis is a multifactorial condition. Various studies have sought evidence for a disturbance in immunity in people with CFS. An alteration in cytokine profile, a decreased function of natural killer (NK) cells, a presence of autoantibodies and a reduced responses of T cells to mitogens and other specific antigens have been reported. The observed high level of pro-inflammatory cytokines may explain some of the manifestations such as fatigue and flu-like symptoms and influence NK activity. Abnormal activation of the T lymphocyte subsets and a decrease in antibody-dependent cell-mediated cytotoxicity have been described. An increased number of CD8+ cytotoxic T lymphocytes and CD38 and HLA-DR activation markers have been reported, and a decrease in CD11b expression associated with an increased expression of CD28+ T subsets has been observed. This review discusses the immunological aspects of CFS and offers an immunological hypothesis for the disease processes.
Lowry TJ, Pakenham KI.	School of Psychology, University of Queensland, Brisbane, Queensland, Australia.	Health-related quality of life in chronic fatigue syndrome: predictors of physical functioning and psychological distress.	Psychol Health Med. 2008 Mar;13(2):222-38.	This study investigated health-related quality of life (HRQoL; physical functioning and psychological distress) in an Australian chronic fatigue syndrome (CFS) population. The aims of the study were to compare HRQoL in those with CFS to the normal population, and to investigate the extent to which sociodemographic (age, gender, partner status, education), illness-related (illness duration, symptom frequency), and fatigue severity (physical, mental) variables predicted HRQoL. A total of 139 people meeting CFS criteria completed questionnaires. HRQoL was assessed using standardised measures of distress and physical functioning. Compared with norms, those with CFS obtained significantly lower scores on all physical functioning areas, whereas 63% of participants reported clinically significant psychological distress. Hierarchical regression analyses indicated that physical fatigue severity and symptom frequency were the strongest predictors of deficits in physical domain HRQoL. Physical

				HRQoL outcomes were also predicted by mental fatigue severity, older age, and female gender. All predictors were unrelated to psychological distress apart from weak positive associations with physical fatigue and symptom frequency. Results identify a potent set of predictors of HRQoL and show that CFS has a pervasive negative impact on quality of life, particularly physical and psychological functioning.
Lundberg I, Allebeck P, Westerholm P, Agren H.	Institutionen för medicinska vetenskaper, Uppsala universitet. ingvar.lundberg@medsci.uu.se	[Fatigue and its causes--who governs the connection?] [Article in Swedish]	Lakartidningen. 2008 Nov 19-25;105(47):3393-4. Comment in: Lakartidningen. 2009 Jan 14-20;106(3):132; author reply 132.	
Lytsy P, Westin M.	Centrum för miljö-relaterad ohälsa och stress. Per.lytsy@pubcare.uu.se	[Fatigue syndrome--a diagnosis with scientific shortages] [Article in Swedish]	Lakartidningen. 2008 May 21-27;105(21):1592-3.	
Maes M, Leunis JC.	MCare4U Outpatient Clinics, Belgium.	Normalization of leaky gut in chronic fatigue syndrome (CFS) is accompanied by a clinical improvement: effects of age, duration of illness and the translocation of LPS from gram-negative bacteria.	Neuro Endocrinol Lett. 2008 Dec;29(6):902-10.	BACKGROUND: There is now evidence that an increased translocation of LPS from gram negative bacteria with subsequent gut-derived inflammation, i.e. induction of systemic inflammation and oxidative & nitrosative stress (IO&NS), is a new pathway in chronic fatigue syndrome (CFS). METHODS: The present study examines the serum concentrations of IgA and IgM to LPS of gram-negative enterobacteria, i.e. Hafnia Alvei; Pseudomonas Aeruginosa, Morganella Morganii, Pseudomonas Putida, Citrobacter Koseri, and Klebsielle Pneumoniae in CFS patients both before and after intake of natural anti-inflammatory and anti-oxidative substances (NAIOSs), such as glutamine, N-acetyl cysteine and zinc, in conjunction with a leaky gut diet during 10-14 months. We measured the above immune variables as well as the Fibromyalgia and Chronic Fatigue Syndrome Rating Scale in 41 patients with CFS before and 10-14 months after intake of NAIOSs. RESULTS: Subchronic intake of those NAIOSs significantly attenuates the initially increased IgA and IgM responses to LPS of gram negative bacteria. Up to 24 patients showed a significant clinical improvement or remission 10-14 months after intake of NAIOSs. A good clinical response is significantly predicted by attenuated IgA and IgM responses to LPS, the younger age of the patients, and a shorter duration of illness (< 5 years). DISCUSSION: The results show that normalization of the IgA and IgM responses to translocated LPS may predict clinical outcome in CFS. The results support the view that a weakened tight junction barrier with subsequent gut-derived inflammation is a novel pathway in CFS and that it is a new target for drug development in CFS. Meanwhile, CFS patients with leaky gut can be treated with specific NAIOSs and a leaky gut diet.
Maes M, Mihaylova I,	MCare4U Outpatient Clinics,	An IgM-mediated immune response	Neuro Endocrinol Lett. 2008	BACKGROUND: It has been shown that chronic fatigue syndrome (CFS) and major depression (MDD) are accompanied by signs of oxidative stress and by a decreased antioxidant status. The aim of the

Kubera M, Leunis JC.	Antwerp, Belgium. crc.mh@telenet.be	directed against nitro-bovine serum albumin (nitro-BSA) in chronic fatigue syndrome (CFS) and major depression: evidence that nitrosative stress is another factor underpinning the comorbidity between major depression and CFS.	Jun;29(3):313-9.	present study was to examine whether CFS and MDD are accompanied by an IgM-mediated immune response directed against nitro-serum bovine albumin (BSA), which is a neoepitope of BSA formed by damage caused by nitrosative stress. AIMS: Toward this end, we examined serum IgM antibodies to nitro-BSA in 13 patients with CFS, 14 subjects with partial CFS, 16 patients with MDD and 11 normal controls. RESULTS: We found that the prevalence and mean values for the serum IgM levels directed against nitro-BSA were significantly greater in patients with partial CFS, CFS and MDD than in normal controls, and significantly greater in CFS than in those with partial CFS and MDD. We found significant and positive correlations between serum IgM levels directed against nitro-BSA and symptoms of the FibroFatigue scale, i.e. aches and pain and muscular tension. There was also a strong positive correlation between serum IgM titers directed against nitro-BSA and an index of increased gut permeability ("leaky gut"), i.e. serum IgM and IgA directed against LPS of different gram-negative enterobacteria. DISCUSSION: The abovementioned results indicate that both CFS and MDD are accompanied by a) an increased gut permeability which has allowed an exaggerated passage of BSA through a compromised epithelial barrier; b) increased nitrosative stress which has induced damage to BSA; and c) an IgM-mediated immune response which is directed against the nitro-BSA neoepitopes. Nitrosative stress is one of the factors underpinning the comorbidity and clinical overlap between CFS and MDD.
Maes M.	Clinical Research Centre of Mental Health (CRC-MH), Antwerp, Belgium. crc.mh@telenet.be	Inflammatory and oxidative and nitrosative stress pathways underpinning chronic fatigue, somatization and psychosomatic symptoms.	Curr Opin Psychiatry. 2009 Jan;22(1):75-83.	PURPOSE OF REVIEW: The aim of this paper is to review recent findings on inflammatory and oxidative and nitrosative stress (IO&NS) pathways in chronic fatigue and somatization disorder. RECENT FINDINGS: Activation of IO&NS pathways is the key phenomenon underpinning chronic fatigue syndrome (CFS): intracellular inflammation, with an increased production of nuclear factor kappa beta (NFkappabeta), cyclo-oxygenase-2 (COX-2) and inducible NO synthase (iNOS); and damage caused by O&NS to membrane fatty acids and functional proteins. These IO&NS pathways are induced by a number of trigger factors, for example psychological stress, strenuous exercise, viral infections and an increased translocation of LPS from gram-bacteria (leaky gut). The 'psychosomatic' symptoms experienced by CFS patients are caused by intracellular inflammation (aches and pain, muscular tension, fatigue, irritability, sadness, and the subjective feeling of infection); damage caused by O&NS (aches and pain, muscular tension and fatigue); and gut-derived inflammation (complaints of irritable bowel). Inflammatory pathways (monocytic activation) are also detected in somatizing disorder. SUMMARY: 'Functional' symptoms, as occurring in CFS and somatization, have a genuine organic cause, that is activation of peripheral and central IO&NS pathways and gut-derived inflammation. The development of new drugs, aimed at treating those disorders, should target these IO&NS pathways.
Magnus P, Brubakk O, Nyland H, Wold BH, Gjessing HK, Brandt I, Eidem T, Nøkleby H, Stene-Larsen G.	Division of Epidemiology, Norwegian Institute of Public Health, Oslo, Norway. per.magnus@fhi.no	Vaccination as teenagers against meningococcal disease and the risk of the chronic fatigue syndrome.	Vaccine. 2009 Jan 1;27(1):23-7. Epub 2008 Nov 5.	The etiology of chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) is unknown. In Norway, a vaccine against Neisseria meningitides group B was administered to teenagers in 1988--1989 in a protection trial. In order to estimate the relative risk of CFS/ME according to vaccine history, we conducted a case-control study in 2007, with 201 cases diagnosed at one of two hospitals and 389 controls. The adjusted odds ratio for CFS/ME was 1.06 (95% CI: 0.67-1.66) for subjects who received the active vaccine contrasted to subjects who did not. Using this design, no statistically significant association between vaccination against meningococcal disease in teenagers and occurrence of CFS/ME could be observed.

Majer M, Welberg LA, Capuron L, Miller AH, Pagnoni G, Reeves WC.	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia, USA.	Neuropsychological performance in persons with chronic fatigue syndrome: results from a population-based study.	Psychosom Med. 2008 Sep;70(7):829-36. Epub 2008 Jul 7.	OBJECTIVE: To examine the neuropsychological function characterized in subjects with chronic fatigue syndrome (CFS) at the same time controlling for relevant confounding factors. CFS is associated with symptoms of neuropsychological dysfunction. Objective measures of neuropsychological performance have yielded inconsistent results possibly due to sample selection bias, diagnostic heterogeneity, comorbid psychiatric disorders, and medication usage. METHOD: CFS subjects (n = 58) and well controls (n = 104) from a population-based sample were evaluated, using standardized symptom severity criteria. Subjects who had major psychiatric disorders or took medications known to influence cognition were excluded. Neuropsychological function was measured using the Cambridge Neuropsychological Test Automated Battery (CANTAB). RESULTS: Compared with controls, CFS subjects exhibited significant decreases in motor speed as measured in the simple and five-choice movement segments of the CANTAB reaction time task. CFS subjects also exhibited alterations in working memory as manifested by a less efficient search strategy on the spatial working memory task, fewer % correct responses on the spatial recognition task, and prolonged latency to a correct response on the pattern recognition task. A significantly higher percentage of CFS subjects versus controls exhibited evidence of neuropsychological impairment (defined by performance 1 standard deviation below the CANTAB normative mean) in tasks of motor speed and spatial working memory. Impairment in CFS subjects versus control subjects ranged from 20% versus 4.8% in five-choice movement time ($p = .002$) to 27.8% versus 10.6% in search strategy on the spatial working memory task ($p = .006$). CONCLUSIONS: These results confirm and quantify alterations in motor speed and working memory in CFS subjects independent of comorbid psychiatric disease and medication usage.
Malaguarnera M, Gargante MP, Cristaldi E, Colonna V, Messano M, Koverech A, Neri S, Vacante M, Cammalleri L, Motta M.	Centro di Ricerca La Grande Senescenza, Università degli Studi di Catania, Via Messina 829, I-95126 Catania, Italy.	Acetyl L-carnitine (ALC) treatment in elderly patients with fatigue.	Arch Gerontol Geriatr. 2008 Mar-Apr;46(2):181-90. Epub 2007 Jul 20.	Fatigue is one of the conditions most frequently complained by the elderly. There are few effective treatment options for patients with chronic fatigue syndrome. To determine the efficacy, tolerability and impact on the fatigue, as well as on cognitive and functional status of elderly subjects with acetyl L-carnitine (ALC), 96 aged subjects (>70 years, range 71-88) were investigated (50 females and 46 males; mean age 76.2+/-7.6 and 78.4+/-6.4 years, respectively). They met four or more of the Holmes major criteria or at least six of Fukuda minor criteria. Fatigue was measured with the Wessely and Powell [Wessely, S., Powell, R., 1989. Fatigue syndromes: a comparison of chronic postviral fatigue with neuromuscular and affective disorders. J. Neurol. Neurosurg. Psychiatry 52, 940-948] scores, with the fatigue severity scale. At the end of the treatment, we observed a decrease of physical fatigue: 6.2 ($p<0.001$), of mental fatigue: 2.8 ($p<0.001$), of severity fatigue: 21.0 ($p<0.001$) and improvements in functional status: 16.1 ($p<0.001$) and cognitive functions: 2.7 ($p<0.001$). By the end of the treatment, significant differences between the two groups were found for the following parameters: muscle pain -27% versus -3% ($p<0.05$); prolonged fatigue after exercise: 51% versus -4% ($p<0.0001$); sleep disorders: 28% versus 4% ($p<0.05$); physical fatigue: 7 versus -0.5 ($p<0.0001$); mental fatigue: -3.3 versus 0.6 ($p<0.0001$); fatigue severity scale: -22.5 versus 1.2 ($p<0.0001$); functional status 17.1 versus 0.6 ($p<0.0001$); mini mental state examination (MMSE) improvements: 3.4 versus 0.5 ($p<0.0001$). Our data show that administering ALC may reduce both physical and mental fatigue in elderly and improves both the cognitive status and physical functions.
Malouff JM, Thorsteinsson EB,	University of New England, Armidale,	Efficacy of cognitive	Clin Psychol Rev. 2008	A meta-analysis of the efficacy of cognitive behavioral therapy (CBT) in treating chronic fatigue included 15 effect sizes for between-group outcome comparisons. Across analyses, which included a

Rooke SE, Bhullar N, Schutte NS.	Australia. jmalouff@une.edu.au	behavioral therapy for chronic fatigue syndrome: a meta-analysis.	Jun;28(5):736-45. Epub 2007 Nov 1.	total of 1371 participants, there was a significant difference, d=0.48, in post-treatment fatigue between participants receiving CBT and those in control conditions. Results indicate that CBT for chronic fatigue syndrome tends to be moderately efficacious. Dropout rates in CBT varied from 0-42%, with a mean of 16%. In the five studies that reported the number of CBT clients who were no longer in the clinical range with regard to fatigue at the latest follow-up, the percentage varied from 33% to 73% of those assigned to CBT, with a mean of 50%. Moderator results suggest directions for future investigations.
Marques A.	Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD 20892, USA. amarques@niaid.nih.gov	Chronic Lyme disease: a review.	Infect Dis Clin North Am. 2008 Jun;22(2):341-60, vii-viii.	Studies have shown that most patients diagnosed with chronic Lyme disease either have no objective evidence of previous or current infection with Borrelia burgdorferi or are patients who should be classified as having post-Lyme disease syndrome, which is defined as continuing or relapsing nonspecific symptoms (such as fatigue, musculoskeletal pain, and cognitive complaints) in a patient previously treated for Lyme disease. Despite extensive study, there is currently no clear evidence that post-Lyme disease syndrome is caused by persistent infection with B burgdorferi. Four randomized placebo-controlled studies have shown that antibiotic therapy offers no sustained benefit to patients who have post-Lyme disease syndrome. These studies also showed a substantial placebo effect and a significant risk of treatment-related adverse events. Further research to elucidate the mechanisms underlying persistent symptoms after Lyme disease and controlled trials of new approaches to the treatment and management of these patients are needed.
Martinez-Lavin M, Infante O, Lerma C.	National Institute of Cardiology, Mexico City, Mexico. mmlavin@infosel.net.mx	Hypothesis: the chaos and complexity theory may help our understanding of fibromyalgia and similar maladies.	Semin Arthritis Rheum. 2008 Feb;37(4):260-4. Epub 2007 Jun 14.	BACKGROUND: Modern clinicians are often frustrated by their inability to understand fibromyalgia and similar maladies since these illnesses cannot be explained by the prevailing linear-reductionist medical paradigm. OBJECTIVE: This article proposes that new concepts derived from the Complexity Theory may help understand the pathogenesis of fibromyalgia, chronic fatigue syndrome, and Gulf War syndrome. METHODS: This hypothesis is based on the recent recognition of chaos fractals and complex systems in human physiology. RESULTS: These nonlinear dynamics concepts offer a different perspective to the notion of homeostasis and disease. They propose that the essence of disease is dysfunction and not structural damage. Studies using novel nonlinear instruments have shown that fibromyalgia and similar maladies may be caused by the degraded performance of our main complex adaptive system. This dysfunction explains the multifaceted manifestations of these entities. CONCLUSIONS: To understand and alleviate the suffering associated with these complex illnesses, a paradigm shift from reductionism to holism based on the Complexity Theory is suggested. This shift perceives health as resilient adaptation and some chronic illnesses as rigid dysfunction.
Mathew SJ, Mao X, Keegan KA, Levine SM, Smith EL, Heier LA, Otcheretko V, Coplan JD, Shungu DC.	Department of Psychiatry, Mount Sinai School of Medicine, New York, NY, USA.	Ventricular cerebrospinal fluid lactate is increased in chronic fatigue syndrome compared with generalized anxiety disorder: an in vivo 3.0 T (1)H MRS	NMR Biomed. 2008 Oct 21;22(3):251-258. [Epub ahead of print]	Chronic fatigue syndrome (CFS) is a controversial diagnosis because of the lack of biomarkers for the illness and its symptom overlap with neuropsychiatric, infectious, and rheumatological disorders. We compared lateral ventricular volumes derived from tissue-segmented T(1)-weighted volumetric MRI data and cerebrospinal fluid (CSF) lactate concentrations measured by proton MRS imaging ((1)H MRSI) in 16 subjects with CFS (modified US Centers for Disease Control and Prevention criteria) with those in 14 patients with generalized anxiety disorder (GAD) and in 15 healthy volunteers, matched group-wise for age, sex, body mass index, handedness, and IQ. Mean lateral ventricular lactate concentrations measured by (1)H MRSI in CFS were increased by 297% compared with those in GAD ($P < 0.001$) and by 348% compared with those in healthy volunteers ($P < 0.001$), even after controlling for

		imaging study.		ventricular volume, which did not differ significantly between the groups. Regression analysis revealed that diagnosis accounted for 43% of the variance in ventricular lactate. CFS is associated with significantly raised concentrations of ventricular lactate, potentially consistent with recent evidence of decreased cortical blood flow, secondary mitochondrial dysfunction, and/or oxidative stress abnormalities in the disorder. Copyright (c) 2008 John Wiley & Sons, Ltd.
Meeus M, Nijs J, McGregor N, Meeusen R, De Schutter G, Truijen S, FrÃ©mont M, Van Hoof E, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Belgium.	Unravelling intracellular immune dysfunctions in chronic fatigue syndrome: interactions between protein kinase R activity, RNase L cleavage and elastase activity, and their clinical relevance.	In Vivo. 2008 Jan-Feb;22(1):115-21.	This study examined possible interactions between immunological abnormalities and symptoms in CFS. Sixteen CFS patients filled in a battery of questionnaires, evaluating daily functioning, and underwent venous blood sampling, in order to analyse immunological abnormalities. Ribonuclease (RNase) L cleavage was associated with RNase L activity (rs=0.570; p=0.021), protein kinase R (PKR) (rs=0.716; p=0.002) and elastase activity (rs=0.500; p=0.049). RNase L activity was related to elastase (rs=0.547; p=0.028) and PKR activity (rs=0.625; p=0.010). RNase L activity (rs=0.535; p=0.033), elastase activity (rs=0.585; p=0.017) and RNase L cleavage (rs=0.521; p=0.038) correlated with daily functioning. This study suggests that in CFS patients an increase in elastase activity and subsequent RNase L cleavage is accompanied by increased activity of both the PKR and RNase L enzymes. RNase L and elastase activity are related to daily functioning, thus evidence supporting the clinical importance of these immune dysfunctions in CFS patients was provided.
Meeus M, Nijs J, Van de Wauwer N, Toeback L, Truijen S.	Division of Musculoskeletal Physiotherapy, Department of Health Sciences, University College Antwerp HA, Belgium.	Diffuse noxious inhibitory control is delayed in chronic fatigue syndrome: an experimental study.	Pain. 2008 Oct 15;139(2):439-48. Epub 2008 Jul 9.	Deficient endogenous pain inhibition, e.g. Diffuse noxious inhibitory controls (DNIC), or hormonal abnormalities like hypocortisolism, could be responsible for chronic widespread pain in Chronic Fatigue Syndrome (CFS). Thirty-one CFS-patients with chronic pain and 31 healthy controls were subjected to spatial summation of thermal noxious stimuli by gradual immersion (ascending or descending) of the arm in warm water (46 degrees C). They rated pain intensity every 15s. Every immersion took 2 min, alternated with 5 min rest. Before and after immersion, salivary cortisol was assessed. Overall pain ratings were higher in CFS-patients, but the evolution was not different between patients and controls, during both ascending and descending immersion. Pain intensity and immersed surface were only correlated during the descending session in both patients (r=.334) and controls (r=.346). When comparing the first and the last 15s of every emersion, it was found that pain inhibition starts slower for CFS-patients in comparison to healthy subjects. Both pre- or post-values and cortisol response did not differ between controls and patients. The drop in cortisol was significantly correlated to pain intensity in CFS (r between .357 and .402). In addition to the hyperalgesia in CFS, DNIC react slower to spatial summation of thermal noxious stimuli. We found no evidence for hypocortisolism in CFS, and the cortisol response to nociception was not different in CFS compared to healthy subjects. In conclusion, delayed pain inhibition may play a role in chronic widespread pain in CFS but further research is required.
Metzger K, Frémont M, Roelant C, De Meirleir K.	Protea Biopharma, Z.1-Researchpark 100, 1731 Zellik, Belgium.	Lower frequency of IL-17F sequence variant (His161Arg) in chronic fatigue syndrome patients.	Biochem Biophys Res Commun. 2008 Nov 7;376(1):231-3. Epub 2008 Sep 5.	Chronic fatigue syndrome (CFS) is characterized by immune dysfunctions including chronic immune activation, inflammation, and alteration of cytokine profiles. T helper 17 (Th17) cells belong to a recently identified subset of T helper cells, with crucial regulatory function in inflammatory and autoimmune processes. Th17 cells are implicated in allergic inflammation, intestinal diseases, central nervous system inflammation, disorders that may all contribute to the pathophysiology of CFS. IL-17F

				is one of the pro-inflammatory cytokines secreted by Th17 cells. We investigated the association between CFS and the frequency of rs763780, a C/T genetic polymorphism leading to His161Arg substitution in the IL-17F protein. The His161Arg variant (C allele) antagonizes the pro-inflammatory effects of the wild-type IL-17F. A significantly lower frequency of the C allele was observed in the CFS population, suggesting that the His161Arg variant may confer protection against the disease. These results suggest a role of Th17 cells in the pathogenesis of CFS.
Mini L, Wang-Weigand S, Zhang J.	Takeda Pharmaceuticals North America, Inc., Deerfield, Illinois 60015, USA. lmini@tpna.com	Ramelteon 8 mg/d versus placebo in patients with chronic insomnia: post hoc analysis of a 5-week trial using 50% or greater reduction in latency to persistent sleep as a measure of treatment effect.	Clin Ther. 2008 Jul;30(7):1316-23.	BACKGROUND: Ramelteon is a selective MT1/MT2 melatonin receptor agonist approved by the US Food and Drug Administration for insomnia treatment. OBJECTIVE: The aim of this post hoc analysis was to compare the efficacy and tolerability of ramelteon 8 mg/d versus placebo in adults with chronic insomnia. METHODS: This study analyzed data from a previously published 5-week, randomized, double-blind, placebo-controlled study. Patients aged 18 to 64 years with chronic insomnia were randomly assigned to receive ramelteon 8 or 16 mg/d or placebo QD for 5 weeks. Sleep parameters were evaluated using polysomnography at weeks 1, 3, 5, and 6 (placebo runout). In this post hoc analysis, patients who received ramelteon 8 mg (approved dose) or placebo in the original study were evaluated using a primary end point of a=50% reduction from baseline in latency to persistent sleep (LPS). RESULTS: A total of 270 adults (ramelteon 8 mg, 139 patients, mean age, 38.0 years; placebo, 131 patients, mean age, 39.7 years) met the criteria for inclusion in this analysis. One patient from the original study (ramelteon 8-mg/d group) was excluded from the post hoc analysis based on a lack of evaluable LPS data. Ramelteon was associated with significantly greater proportions of patients who achieved a > or = 50% reduction in LPS compared with placebo at weeks 1 (63.0% vs 39.7%; P < 0.001), 3 (63.0% vs 41.2%; P < 0.001), and 5 (65.9% vs 48.9%; P < 0.005). No rebound insomnia or withdrawal effects were observed. Headache (19.4% and 18.3%), fatigue (9.4% and 2.3%), and somnolence (7.9% and 1.5%) were the most common adverse events. CONCLUSIONS: In this post hoc analysis of data from patients with chronic insomnia, a significantly greater percentage experienced a > or = 50% reduction in LPS with ramelteon 8 mg/d versus placebo. This improvement was evident at week 1 and was sustained through 5 weeks of treatment. Ramelteon 8 mg was well tolerated in this study, with no evidence of withdrawal or rebound insomnia.
Miwa K, Fujita M.	Department of Internal Medicine, Nanto Home and Regional Medical Center, 577 Matsubara, Nanto, Toyama 939-1518, Japan.	Increased oxidative stress suggested by low serum vitamin E concentrations in patients with chronic fatigue syndrome.	Int J Cardiol. 2008 Aug 4. [Epub ahead of print]	Serum alpha-tocopherol concentrations were determined in 50 patients with chronic fatigue syndrome (CFS) and 40 control subjects (Control). Prevalence of each or any coronary risk factor was not significantly different between CFS and Control. CFS had significantly lower alpha-tocopherol concentrations than Control. The concentrations were significantly lower in the subjects with any coronary risk factors than those without in CFS as well as Control. Even among the subjects with any coronary risk factors and also among those without, CFS had significantly lower alpha-tocopherol concentrations than Control. In conclusion, CFS had significantly lower alpha-tocopherol concentrations irrespective of coronary risk factors than Control, suggesting the presence of increased oxidative stress in CFS.
Miwa K, Fujita M.	Division of Internal Medicine, Fukuda General Hospital, Osaka.	Small heart syndrome in patients with chronic fatigue	Clin Cardiol. 2008 Jul;31(7):328-33.	BACKGROUND: Small heart syndrome has previously been reported as neurocirculatory asthenia, associated with a small heart shadow on a chest roentgenogram. This is characterized as weakness or fatigue even after ordinary exertion, palpitation, dyspnea, and fainting, resembling patients with chronic fatigue syndrome (CFS). HYPOTHESIS: Small heart syndrome may be prevalent in patients with

	kmiwa@fukuda-hsp.jp	syndrome.		CFS. METHODS: The study population consisted of 56 patients (<50 y of age) with CFS, and 38 control subjects. Chest roentgenographic, echocardiographic, and physical examinations were performed. RESULTS: Small heart syndrome (cardiothoracic ratio <or= 42%) was significantly more prevalent in the CFS group (61%) than in the control group (24%) (p < 0.01). In CFS patients with a small heart (n = 34), narrow chest (88%), orthostatic dizziness (44%), foot coldness (41%), pretibial pitting edema (32%), r-kidney palpability (47%), and mitral valve prolapse (29%), were all significantly more prevalent than in the control group, and also in the CFS patients without small heart syndrome. Echocardiographic examination demonstrated significantly smaller values of both the left ventricular (LV) end-diastolic dimensions and end-systolic, and stroke volume and cardiac indexes in CFS with a small heart, as compared with control subjects with a normal heart size (42% < cardiothoracic ratio < 50%). CONCLUSIONS: A considerable number of CFS patients have a small heart. Small heart syndrome may contribute to the development of CFS as a constitutional factor predisposing to fatigue, and may be included in the genesis of CFS. Copyright (c) 2008 Wiley Periodicals, Inc.
Moldofsky H.	Faculty of Medicine, University of Toronto, Sleep Disorders Clinic of the Centre for Sleep and Chronobiology, 340 College Street, Suite 580, Toronto, ON MST 3A9, Canada. h.moldofsky@utoronto.ca	The significance of the sleeping-waking brain for the understanding of widespread musculoskeletal pain and fatigue in fibromyalgia syndrome and allied syndromes.	Joint Bone Spine. 2008 Jul;75(4):397-402. Epub 2008 May 5.	The clinical focus of rheumatologists on the widespread pain and numerous tender points in specific anatomic regions in their patients who show no evidence for disease pathology has lead to the characterization of such peripheral symptoms as a specific disorder of the musculoskeletal system, now commonly known as fibromyalgia. This rheumatologic diagnostic entity has resulted in relative inattention to an understanding of their patients' common complaints of unrefreshing sleep, chronic fatigue and psychological distress. Experimental evidence from humans and animal studies indicate that there is an inter-relationship of disturbances in the physiology of the sleeping-waking brain with the widespread musculoskeletal pain, chronic fatigue, and psychological distress in patients with hitherto unexplained pain/fatigue illnesses, e.g., fibromyalgia and chronic fatigue syndromes. The emerging knowledge of the dysfunction of the nervous system in such patients has lead to the study of novel medications that affect neurotransmitter functions, e.g., pregabalin, serotonin/noradrenaline compounds and sodium oxybate that are shown to improve many of the symptoms of such patients.
Molnár G.	BMSZKI Orvosi Krízis Szolgálat, Budapest. mogab@citromail.hu	[Depressive type of drawing test without melancholy] [Article in Hungarian]	Neuropsychopharmacol Hung. 2008 Jun;10(3):159-64.	Depressed patients draw small figures in the left upper corner of sheet in House-Tree-Person (H-T-P) Test. This type of drawing rarely was drawn by patients without melancholic complains. In the Crisis Intervention Department at the Budapest Social Center (Hungary), 5 homeless male patients between 42-67 years of ages were found with depressive type of drawing in the H-T-P Test, but without melancholy. One had alcoholic encephalopathy with mild cognitive disorder, four had alcoholic or vascular types of dementia. Three had severe apathy. One was euphoric, undiscriminating with logorhea, but reported depression without sadness in Beck Depression Inventory. One had retarded thinking. Psycho-organic signs were well demonstrated in demented patients' drawings. Four patients represented human figures without hands, which symbolized helplessness. Apathy frequently was reported to be the only syndrome in psycho-organic, chronic fatigue, burn out syndromes, or even in exhaustive depression and sickness-behaviour, but it could not be classified in ICD-10 or DSM-IV-TR. Apathy, like depression, responded to antidepressive treatments, therefore, this similarity of syndromes could be responsible for our lethargic patients' depressive type of drawings. Furthermore,

				clinically abortive depressions perhaps could be demonstrated only by nonverbal drawing test. Psycho-organic and depressive signs of drawings were reported to be independent of each other, therefore, dementia could not cause our patients' depressive type of drawings. So, H-T-P Drawing Test was a useful nonverbal method of psycho-organic patients' investigation, which demonstrated depression in patients without verbally manifest melancholic illness.
Nancy AL, Shoenfeld Y.	Center for Autoimmune Diseases, Department of Medicine B, Sheba Medical Center, Tel-Hashomer, Israel.	Chronic fatigue syndrome with autoantibodies--the result of an augmented adjuvant effect of hepatitis-B vaccine and silicone implant.	Autoimmun Rev. 2008 Oct;8(1):52-5. Epub 2008 Aug 24.	BACKGROUND: Chronic fatigue syndrome (CFS) that defines by prolonged fatigue and other manifestations, was recently integrated into a spectrum of central sensitivity syndromes including several diseases as fibromylagia. CFS etiology is multi-factorial commonly triggered by infectious agents. Vaccines, induce an immune response similarly to infections, and may trigger just like infections autoimmune diseases, CFS and fibromyalgia. Furthermore vaccines contain an adjuvant which enhances their immune stimulation. CASE PRESENTATION: A 56-year-old woman was diagnosed with CFS accompanied by fibromyalgia, demyelination and autoantibodies. Her illness begun following the 2nd dose of hepatitis-B vaccine, and was aggravated by the 3rd vaccination. She underwent silicone breast implantation 6 years before vaccination with no adverse events. However, between the 2nd and 3rd vaccination she suffered a breast injury with local inflammation. Upon explanation of her breast implants silicone leak was observed. DISCUSSION: Vaccines have been reported to precede CFS mainly following exposure to multiple vaccinations (e.g. the Gulf war syndrome), or as an adverse response to the vaccine adjuvant (e.g. the macrophagic myofasciitis syndrome). Silicone is considered an adjuvant to the immune system, and may induce "the adjuvant disease". Silicone implant, especially silicone leak relationship with autoimmunity and CFS has been the focus of considerable debates. CONCLUSION: Our patient illness started following hepatitis-B vaccine, suggesting that it was caused or accelerated by vaccination. In parallel to vaccination our patient suffered from breast injury, which might represent the time of silicone leak. The exposure to the adjuvant, silicone, might have augmented her immune response to the vaccine. To the best of our knowledge this is the first case of combined adverse effect to vaccine and silicone. Vaccine safety in individuals with silicone implants requires further studies.
Nao S, Adachi Y, Sato S.	Department of Anesthesiology, Intensive Care Unit of University Hospital, Hamamatsu University School of Medicine, Hamamatsu.	[Anesthesia for a patient with Cushing's disease and hepatitis B] [Article in Japanese]	Masui. 2008 Jun;57(6):745-7.	A 34-year-old female patient complaining of general fatigue and liver dysfunction was diagnosed as acute aggravation of chronic hepatitis B. She showed a complication of Cushing's disease and hepatitis was initially treated with lamivudine administration as well as inhibition and supplementation of cortisol, because hypercortisolemia could induce massive liver necrosis with hepatitis. After inducing remission phase, Hardy's operation for pituitary microadenoma was scheduled. Induction and maintenance of anesthesia were achieved by administration of propofol and analgesia was attained by intermittent administration of fentanyl. Liver function was well maintained during perioperative period and no complication concerning anesthesia was observed.
Naschitz JE, Slobodin G, Sharif D, Fields M, Isseroff H, Sabo E, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center and Rappaport	Electrocardiographic QT interval and cardiovascular reactivity in fibromyalgia differ	Eur J Intern Med. 2008 May;19(3):187-91. Epub 2007 Nov 19.	BACKGROUND: Fibromyalgia (FM) and chronic fatigue syndrome (CFS) frequently overlap clinically and have been considered variants of one common disorder. We have recently shown that CFS is associated with a short corrected electrocardiographic QT interval (QTc). In the present study, we evaluated whether FM and CFS can be distinguished by QTc. METHODS: The study groups were comprised of women with FM (n=30) and with CFS (n=28). The patients were evaluated with a 10 min

	Family Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. Naschitz@tx.technion.ac.il	from chronic fatigue syndrome.		supine-30 min head-up tilt test. The electrocardiographic QT interval was corrected for heart rate (HR) according to Fridericia's equation (QTc). In addition, cardiovascular reactivity was assessed based on blood pressure and HR changes and was expressed as the 'hemodynamic instability score' (HIS). RESULTS: The average supine QTc in FM was 417 ms (SD 25) versus 372 ms (SD 22) in CFS (p<0.0001); the supine QTc cut-off <385.7 ms was 79% sensitive and 87% specific for CFS vs. FM. The average QTc at the 10th minute of tilt was 409 ms (SD 18) in FM versus 367 ms (SD 21) in CFS (p<0.0001); the tilt QTc cut-off <383.3 ms was 71% sensitive and 91% specific for CFS vs. FM. The average HIS in FM patients was -3.52 (SD 1.96) versus +3.21 (SD 2.43) in CFS (p<0.0001). CONCLUSION: A relatively short QTc and positive HIS characterize CFS patients and distinguish them from FM patients. These data may support the contention that FM and CFS are separate disorders.
Nater UM, Maloney E, Boneva RS, Gurbaxani BM, Lin JM, Jones JF, Reeves WC, Heim C.	Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, Mail Stop A-15, Atlanta, Georgia 30333, USA.	Attenuated morning salivary cortisol concentrations in a population-based study of persons with chronic fatigue syndrome and well controls.	J Clin Endocrinol Metab. 2008 Mar;93(3):703-9. Epub 2007 Dec 26.	CONTEXT: A substantial body of research on the pathophysiology of chronic fatigue syndrome (CFS) has focused on hypothalamic-pituitary-adrenal axis dysregulation. The cortisol awakening response has received particular attention as a marker of hypothalamic-pituitary-adrenal axis dysregulation. OBJECTIVE: The objective of the current study was to evaluate morning salivary cortisol profiles in persons with CFS and well controls identified from the general population. DESIGN AND SETTING: We conducted a case-control study at an outpatient research clinic. CASES AND OTHER PARTICIPANTS: We screened a sample of 19,381 residents of Georgia and identified those with CFS and a matched sample of well controls. Seventy-five medication-free CFS cases and 110 medication-free well controls provided complete sets of saliva samples. MAIN OUTCOME MEASURES: We assessed free cortisol concentrations in saliva collected on a regular workday immediately upon awakening and 30 and 60 min after awakening. RESULTS: There was a significant interaction effect, indicating different profiles of cortisol concentrations over time between groups, with the CFS group showing an attenuated morning cortisol profile. Notably, we observed a sex difference in this effect. Women with CFS exhibited significantly attenuated morning cortisol profiles compared with well women. In contrast, cortisol profiles were similar in men with CFS and male controls. CONCLUSIONS: CFS was associated with an attenuated morning cortisol response, but the effect was limited to women. Our results suggest that a sex difference in hypocortisolism may contribute to increased risk of CFS in women.
Nater UM, Youngblood LS, Jones JF, Unger ER, Miller AH, Reeves WC, Heim C.	Chronic Viral Diseases Branch, Centers for Disease Control and Prevention, Mail Stop A-15, Atlanta, GA 30333, USA.	Alterations in diurnal salivary cortisol rhythm in a population-based sample of cases with chronic fatigue syndrome.	Psychosom Med. 2008 Apr;70(3):298-305. Epub 2008 Mar 31.	OBJECTIVE: To examine diurnal salivary cortisol rhythms and plasma IL-6 concentrations in persons with chronic fatigue syndrome (CFS), persons not fulfilling a diagnosis of CFS (we term them cases with insufficient symptoms or fatigue, ISF) and nonfatigued controls (NF). Previous studies of CFS patients have implicated the hypothalamic-pituitary-adrenal axis and the immune system in the pathophysiology of CFS, although results have been equivocal. METHODS: Twenty-eight people with CFS, 35 persons with ISF, and 39 NF identified from the general population of Wichita, Kansas, were admitted to a research ward for 2 days. Saliva was collected immediately on awakening (6:30 AM), at 08:00 AM, 12 noon, 4:00 PM, 8:00 PM and at bedtime (10:00 PM) and plasma was obtained at 7:30 AM. Salivary cortisol concentrations were assessed using radioimmunoassay, and plasma IL-6 was measured using sandwich enzyme-linked immunosorbent assay. RESULTS: People with CFS demonstrated lower salivary cortisol concentrations in the morning and higher salivary cortisol concentrations in the evening compared with both ISF and NF groups indicating a flattening of the diurnal cortisol profile. Mean plasma IL-6 concentrations were highest in CFS compared with the other

				groups, although these differences were no longer significant after controlling for BMI. Attenuated decline of salivary cortisol concentrations across the day and IL-6 concentration were associated with fatigue symptoms in CFS. CONCLUSIONS: These results suggest an altered diurnal cortisol rhythm and IL-6 concentrations in CFS cases identified from a population-based sample.
Neu D, Hoffmann G, Moutrier R, Verbanck P, Linkowski P, Le Bon O.	University Hospital Brugmann, Sleep Laboratory, Université Libre de Bruxelles (ULB), Brussels, Belgium. daniel.neu@chu-brugmann.be	Are patients with chronic fatigue syndrome just 'tired' or also 'sleepy'?	J Sleep Res. 2008 Dec;17(4):427-31. Epub 2008 Oct 17.	It is presently unclear whether chronic fatigue syndrome (CFS) patients exhibit daytime sleepiness in addition to fatigue. Both, fatigue, such as that seen in CFS patients, and excessive daytime sleepiness, such as in sleep apnea-hypopnea syndrome (SAHS), remain poorly understood. Both daytime conditions are generally related to unrefreshing sleep and show affective symptoms. This study's objective was to contribute to the understanding of the relationship between fatigue and sleepiness in CFS patients not co-morbid for primary sleep or psychiatric disorders. We compared 16 untreated CFS patients (mean age 32.8, all females) with 13 untreated SAHS (mean age 47.7, all females) patients and 12 healthy controls (mean age 32.2, all females). Objective sleepiness was measured using multiple sleep latency tests (MSLT). Subjective sleepiness and fatigue were assessed with the Epworth Sleepiness Scale and the Fatigue Severity Scale, respectively. Mean Sleep Latency (SL) on the MSLT was significantly shorter in SAHS patients than in CFS patients and CFS patients showed significantly shorter mean SL than matched controls but within normal range. Subjective sleepiness was greatest in SAHS patients and subjective fatigue was highest in CFS patients. Affective symptoms showed highest intensities in CFS patients. While higher than the control group on all measures, compared to SAHS, the CFS group had higher subjective fatigue and lower subjective and objective sleepiness. Despite possible overlap in symptoms and signs of both daytime conditions, our data indirectly support the clinical distinction between fatigue and sleepiness.
Neustadt J, Pieczenik SR.	Montana Integrative Medicine, Bozeman, MT 59718, USA. drneustadt@gmail.com	Medication-induced mitochondrial damage and disease.	Mol Nutr Food Res. 2008 Jul;52(7):780-8.	Since the first mitochondrial dysfunction was described in the 1960s, the medicine has advanced in its understanding the role mitochondria play in health and disease. Damage to mitochondria is now understood to play a role in the pathogenesis of a wide range of seemingly unrelated disorders such as schizophrenia, bipolar disease, dementia, Alzheimer's disease, epilepsy, migraine headaches, strokes, neuropathic pain, Parkinson's disease, ataxia, transient ischemic attack, cardiomyopathy, coronary artery disease, chronic fatigue syndrome, fibromyalgia, retinitis pigmentosa, diabetes, hepatitis C, and primary biliary cirrhosis. Medications have now emerged as a major cause of mitochondrial damage, which may explain many adverse effects. All classes of psychotropic drugs have been documented to damage mitochondria, as have stain medications, analgesics such as acetaminophen, and many others. While targeted nutrient therapies using antioxidants or their precursors (e. g., N-acetylcysteine) hold promise for improving mitochondrial function, there are large gaps in our knowledge. The most rational approach is to understand the mechanisms underlying mitochondrial damage for specific medications and attempt to counteract their deleterious effects with nutritional therapies. This article reviews our basic understanding of how mitochondria function and how medications damage mitochondria to create their occasionally fatal adverse effects.
Nicolson GL, Nancy L. Nicolson, Joerg Haier		Chronic Fatigue Syndrome Patients Subsequently Diagnosed with	Journal of Chronic Fatigue Syndrome 2008; 14 (4): 5-17	Objective: We examined the blood of 48 North American chronic fatigue syndrome (CFS) patients subsequently diagnosed with Lyme disease (Borrelia burgdorferi infection) and compared these with 50 North American CFS patients without evidence of Borrelia burgdorferi infections for presence of Mycoplasma species coinfections using forensic polymerase chain reaction. Results: We found that

		Lyme Disease Borrelia burgdorferi: Evidence for Mycoplasma Species Coinfections		68.75% of CFS/Lyme patients show evidence of mycoplasma coinfections (odds ratio [OR] = 41.8; confidence limits [CL] = 11.3–155; and p < .001) compared with controls, whereas 50% of CFS patients without a diagnosis of Lyme disease show Mycoplasma coinfections (OR = 19.0; CL = 5.3–69; and p < .001) compared with controls. Because CFS patients without a diagnosis of Lyme disease have a high prevalence of one of four Mycoplasma species and a majority show evidence of multiple infections, we examined CFS/Lyme patients' blood for various Mycoplasma species. We found that CFS patients with Lyme disease mostly had single species Mycoplasma infections (OR = 31.7; CL = 8.6–116; and p < .001) with a preponderance of Mycoplasma fermentans infections (50% of patients; OR = 59.0; CL = 7.6–460; and p < .001), whereas the most commonly found Mycoplasma species in CFS patients without Lyme disease was Mycoplasma pneumoniae(34% of patients; OR = 14.94; CL = 3.3–69; and p < .001). Conclusions: The results indicate that a subset of CFS patients show evidence of infection with Borrelia burgdorferi, and a large fraction of these patients were also infected with Mycoplasma fermentans and to a lesser degree with other Mycoplasma species.
Nijrolder I, van der Horst H, van der Windt D.	Department of General Practice, EMGO Institute, VU University Medical Centre, Amsterdam, The Netherlands. i.nijrolder@vumc.nl	Prognosis of fatigue. A systematic review.	J Psychosom Res. 2008 Apr;64(4):335-49.	OBJECTIVE: The objective of the study was to summarize evidence on the course and prognostic factors of fatigue in primary care patients and in the community. METHODS: Two reviewers independently screened identified citations, discussed eligible studies, and assessed methodological quality of selected studies. Data concerning study population, duration of follow-up, measurement of fatigue, outcome, and prognostic factors were extracted. Studies with populations selected by a specific disease or postpartum condition were excluded. RESULTS: We selected 21 articles reporting on 11 (partly) primary care cohorts and six community cohorts. Follow-up was up to 1 year in primary care and up to 4 years in the community, and in most studies that presented duration of fatigue, participants were chronically fatigued. Because of wide heterogeneity of studies, a qualitative analysis was performed. Recovery of fatigue varied widely, but no differences were found between settings. Sufficient evidence for an association with recovery was found for lower severity of fatigue, and limited evidence was found for good self-reported health, mental health, and psychological attributions. A major deficit in methodological quality of most studies was a potential bias due to low or selective response or loss to follow-up. CONCLUSION: Most studies on fatigue included patients with long symptom duration at baseline, making it difficult to study prognosis early in the course of fatigue. To provide clear evidence on prognosis in fatigued persons, prognostic studies should use an optimal design including selection of an inception cohort with limited duration of fatigue at baseline, a sufficient sample size, and information on rates and selectivity of response and loss to follow-up.
Nijrolder I, van der Windt DA, van der Horst HE.	Department of General Practice, EMGO Institute, VU University Medical Centre, Amsterdam, The Netherlands. i.nijrolder@vumc.nl	Prognosis of fatigue and functioning in primary care: a 1-year follow-up study.	Ann Fam Med. 2008 Nov-Dec;6(6):519-27.	PURPOSE: Although fatigue is a common presenting symptom in primary care and its course and outcomes often remain unclear, cohort studies among patients seeking care for fatigue are scarce. We therefore aimed to investigate patterns in the course of fatigue and relevant secondary outcomes in a large cohort of patients who sought care for a main symptom of fatigue. METHODS: We performed an observational cohort study in 147 primary care practices. Patients consulting their general practitioner for a new episode of fatigue were sent questionnaires at 1, 4, 8, and 12 months after baseline. We collected measures of fatigue, perceived health and functioning, absenteeism, psychological symptoms, and sleep using the Checklist Individual Strength, the 36-Item Short Form Health Survey, the Four-Dimensional Symptoms Questionnaire, and the Pittsburgh Sleep Questionnaire Inventory.

				Patients were classified into 4 subgroups based on fatigue severity scores over time. We assessed patterns in the course of all outcomes in these subgroups and in the total population, and tested changes over time and differences between subgroups. RESULTS: A total of 642 patients were enrolled in the study. Response rates during follow-up ranged between 82% and 88%. For 75% of the patients, 4 distinct groups could be discerned: 26% of patients had continuously high scores for fatigue, 17% had a fast recovery, 25% had a slow recovery, and 32% initially improved but then had a recurrence of fatigue. Patterns for the secondary outcomes of symptoms and functioning were all similar to the pattern for fatigue within each of the subgroups. CONCLUSIONS: The findings of this study suggest a longitudinal relationship between the severity of fatigue, impaired functioning, psychological symptoms, and poor sleep. Physicians should be aware that a substantial proportion of patients seeking care for fatigue have these additional health and psychosocial problems.
Nijs J, Adriaens J, Schuermans D, Buyl R, Vincken W.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit, Brussel, Belgium. Jo.Nijs@vub.ac.be	Breathing retraining in patients with chronic fatigue syndrome: a pilot study.	Physiother Theory Pract. 2008 Mar-Apr;24(2):83-94.	The study aimed to 1) examine the point prevalence of asynchronous breathing in chronic fatigue syndrome (CFS) patients; 2) examine whether CFS patients with an asynchronous breathing pattern present with diminished lung function in comparison with CFS patients with a synchronous breathing pattern; and 3) examine whether one session of breathing retraining in CFS patients with an asynchronous breathing pattern is able to improve lung function. Twenty patients fulfilling the diagnostic criteria for CFS were recruited for participation in a pilot controlled clinical trial with repeated measures. Patients presenting with an asynchronous breathing pattern were given 20-30 minutes of breathing retraining. Patients presenting with a synchronous breathing pattern entered the control group and received no intervention. Of the 20 enrolled patients with CFS, 15 presented with a synchronous breathing pattern and the remaining 5 patients (25%) with an asynchronous breathing pattern. Baseline comparison revealed no group differences in demographic features, symptom severity, respiratory muscle strength, or pulmonary function testing data (spirometry). In comparison to no treatment, the session of breathing retraining resulted in an acute (immediately postintervention) decrease in respiratory rate ($p < 0.001$) and an increase in tidal volume ($p < 0.001$). No other respiratory variables responded to the session of breathing retraining. In conclusion, the present study provides preliminary evidence supportive of an asynchronous breathing pattern in a subgroup of CFS patients, and breathing retraining might be useful for improving tidal volume and respiratory rate in CFS patients presenting with an asynchronous breathing motion.
Nijs J, Almond F, De Becker P, Truijen S, Paul L.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Belgium. j.nijs@ha.be	Can exercise limits prevent post-exertional malaise in chronic fatigue syndrome? An uncontrolled clinical trial.	Clin Rehabil. 2008 May;22(5):426-35.	OBJECTIVE: It was hypothesized that the use of exercise limits prevents symptom increases and worsening of their health status following a walking exercise in people with chronic fatigue syndrome. DESIGN: An uncontrolled clinical trial (semi-experimental design). SETTING: Outpatient clinic of a university department. SUBJECTS: Twenty-four patients with chronic fatigue syndrome. INTERVENTIONS: Subjects undertook a walking test with the two concurrent exercise limits. Each subject walked at an intensity where the maximum heart rate was determined by heart rate corresponding to the respiratory exchange ratio = 1.0 derived from a previous submaximal exercise test and for a duration calculated from how long each patient felt they were able to walk. MAIN OUTCOME MEASURES: The Short Form 36 Health Survey or SF-36, the Chronic Fatigue Syndrome Symptom List, and the Chronic Fatigue Syndrome -Activities and Participation Questionnaire were filled in prior to, immediately after and 24 hours after exercise. RESULTS: The fatigue increase

				observed immediately post-exercise (P= 0.006) returned to pre-exercise levels 24 hours post-exercise. The increase in pain observed immediately post-exercise was retained at 24 hours post-exercise (P=0.03). Fourteen of the 24 subjects experienced a clinically meaningful change in bodily pain (change of SF-36 bodily pain score > or =10); 6 indicated that the exercise bout had slightly worsened their health status, and 2 had a clinically meaningful decrease in vitality (change of SF-36 vitality score > or =20). There was no change in activity limitations/participation restrictions. CONCLUSION: It was shown that the use of exercise limits (limiting both the intensity and duration of exercise) prevents important health status changes following a walking exercise in people with chronic fatigue syndrome, but was unable to prevent short-term symptom increases.
Nijs J, Fremont M.	Vrije Universiteit Brussel, Faculty of Physical Education & Physiotherapy, Department of Human Physiology, Building L, Pleinlaan 2, 1050 Brussels, Belgium. Jo.Nijs@vub.ac.be <Jo.Nijs@vub.ac.be>	Intracellular immune dysfunction in myalgic encephalomyelitis/ chronic fatigue syndrome: state of the art and therapeutic implications.	Expert Opin Ther Targets. 2008 Mar;12(3):281-9.	BACKGROUND: Evidence in support of intracellular immune dysfunctions in people with myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS) is accumulating, but few studies have addressed intracellular immunity as a potential therapeutic target. OBJECTIVE: To provide an overview of our present understanding of intracellular immunity in ME/CFS, to relate the intracellular immune dysfunctions to other aspects of the illness like decreased natural killer cell function, the presence of infections and poor exercise performance, and to point to potential therapeutic targets. METHODS: An in-depth review of the scientific literature of intracellular immunity in people with ME/CFS was performed. RESULTS/CONCLUSION: From the scientific literature it is concluded that proteolytic cleavage of the native RNase L enzyme is characteristic of the dysregulation of intracellular immunity in people with ME/CFS, but the origin of the dysregulation is speculative. There is increasing evidence for immune cell apoptosis and upregulation of various aspects of the 2'-5' oligoadenylate (2-5A) synthetase/RNase L pathway in ME/CFS. This review provides the theoretical rationale for conducting studies examining the effectiveness of direct or indirect drug targeting of the 2-5A synthetase/RNase L pathway in ME/CFS patients.
Nijs J, Paul L, Wallman K.	Division of Musculoskeletal Physiotherapy, Department of Health Care Sciences, University College Antwerp, Vrije Universiteit Brussel, Belgium. j.nijs@ha.be	Chronic fatigue syndrome: an approach combining self-management with graded exercise to avoid exacerbations.	J Rehabil Med. 2008 Apr;40(4):241-7. Comment in: J Rehabil Med. 2008 Nov;40(10):882-3; author reply 883-5.	Controversy regarding the aetiology and treatment of patients with chronic fatigue syndrome continues among the medical professions. The Cochrane Collaboration advises practitioners to implement graded exercise therapy for patients with chronic fatigue syndrome using cognitive behavioural principles. Conversely, there is evidence that exercise can exacerbate symptoms in chronic fatigue syndrome, if too-vigorous exercise/activity promotes immune dysfunction, which in turn increases symptoms. When designing and implementing an exercise programme for chronic fatigue syndrome it is important to be aware of both of these seemingly opposing viewpoints in order to deliver a programme with no detrimental effects on the pathophysiology of the condition. Using evidence from both the biological and clinical sciences, this paper explains that graded exercise therapy for people with chronic fatigue syndrome can be undertaken safely with no detrimental effects on the immune system. Exercise programmes should be designed to cater for individual physical capabilities and should take into account the fluctuating nature of symptoms. In line with cognitive behaviourally and graded exercise-based strategies, self-management for people with chronic fatigue syndrome involves encouraging patients to pace their activities and respect their physical and mental limitations, with the ultimate aim of improving their everyday functioning.
Nijs J, Thielemans A.	Department of Human Physiology,	Kinesiophobia and symptomatology in	Psychol Psychother. 2008	OBJECTIVES: The aims of the study were to examine the reliability of the Dutch and French versions of the Tampa scale kinesiophobia (TSK) version chronic fatigue syndrome (CFS), and to examine the

	Vrije Universiteit Brussel, Brussel, Belgium. Jo.Nijs@vub.ac.be	chronic fatigue syndrome: a psychometric study of two questionnaires.	Sep;81(Pt 3):273-83.	reliability and validity of the Dutch and French versions of the CFS symptom list. DESIGN: Repeated-measures design. METHODS: Native Dutch speakers (N=100) and native French (N=48) speakers fulfilling the diagnostic criteria for CFS were asked to list the five most important symptoms and to complete the TSK-CFS, the CFS symptom list, and the Short Form 36 Health Status Survey or SF-36. A modified version of the TSK-CFS and the CFS symptom list was filled in within 24 hours of the first assessment. RESULTS: The French and Dutch version of the TSK-CFS and CFS symptom lists displayed good reliability (ICC>or=.83). The CFS symptom list was internally consistent (Cronbach's alpha>or=.93) and concurrently valid with the SF-36. For the native Dutch and French speakers, respectively, 82 and 78% of the self-reported symptoms matched the content of CFS symptom list. CONCLUSIONS: The results are in support of the psychometric properties of the French and Dutch versions of both the TSK-CFS and the CFS symptom list for assessing kinesiophobia and symptom severity, respectively.
Nijs J, Van de Putte K, Louckx F, Truijen S, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit, Brussels, Belgium. jo.nijs@vub.ac.be	Exercise performance and chronic pain in chronic fatigue syndrome: the role of pain catastrophizing.	Pain Med. 2008 Nov;9(8):1164-72. Epub 2007 Oct 3.	OBJECTIVES: This study aimed to examine the associations between bodily pain, pain catastrophizing, depression, activity limitations/participation restrictions, employment status, and exercise performance in female patients with chronic fatigue syndrome (CFS) who experience widespread pain. DESIGN: Cross-sectional observational study. SETTING: A university-based clinic. PATIENTS: Thirty-six female CFS patients who experienced widespread pain. OUTCOME MEASURES: Patients filled in the Medical Outcomes Short-Form 36 Health Status Survey, the Chronic Fatigue Syndrome Activities and Participation Questionnaire, the Beck Depression Inventory, and the Pain Catastrophizing Scale, and underwent a maximal exercise stress test with continuous monitoring of electrocardiographic and ventilatory parameters. RESULTS: Pain catastrophizing was related to bodily pain (r = -0.70), depression (r = 0.55), activity limitations/participation restrictions (r = 0.68), various aspects of quality of life (r varied between -0.51 and -0.64), and exercise capacity (r varied between -0.41 and -0.61). Based on hierarchical multiple regression analysis, pain catastrophizing accounted for 41% of the variance in bodily pain in female CFS patients who experience chronic widespread musculoskeletal pain. Among the three subscale scores of the Pain Catastrophizing Scale, helplessness and rumination rather than magnification were strongly related to bodily pain. Neither pain catastrophizing nor depression was related to employment status. CONCLUSIONS: These data provide evidence favoring a significant association between pain catastrophizing, bodily pain, exercise performance, and self-reported disability in female patients with CFS who experience widespread pain. Further prospective longitudinal studying of these variables is required.
Ohinata J, Suzuki N, Araki A, Takahashi S, Fujieda K, Tanaka H.	Department of Pediatrics, Asahikawa Medical College, Japan. ohina5p@asahikawa-med.ac.jp	Actigraphic assessment of sleep disorders in children with chronic fatigue syndrome.	Brain Dev. 2008 May;30(5):329-33. Epub 2007 Nov 26.	Children with chronic fatigue syndrome (CFS) often suffer from sleep disorders, which cause many physiological and psychological problems. Understanding sleep characteristics in children with CFS is important for establishing a therapeutic strategy. We conducted an actigraphic study to clarify the problems in sleep/wake rhythm and physical activity in children with CFS. METHODS: Actigraphic recordings were performed for 1-2 weeks in 12 CFS children. The obtained data were compared with those of healthy age-matched children used as the control. RESULTS: Sleep patterns were divided into two groups based on subjects' sleep logs: irregular sleep type and delayed sleep phase type. Compared to the control group, total sleep time was longer and physical activity was lower in both groups of CFS. Continuous sleep for more than 10h was not uncommon in CFS. In the irregular sleep type, impaired daily sleep/wake rhythms and disrupted sleep were observed. CONCLUSION: Using

				actigraphy, we could identify several characteristics of the sleep patterns in CFS children. Actigraphic analysis proved to be useful in detecting sleep/wake problems in children with CFS.
Olson K, Turner AR, Courneya KS, Field C, Man G, Cree M, Hanson J.	Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada. Karin.olson@ualberta.ca	Possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion in advanced cancer. Comment in: Support Care Cancer. 2008 Mar;16(3):215-6.	Support Care Cancer. 2008 Mar;16(3):241-9. Epub 2007 Jul 24.	GOALS: In this theoretical paper, we present the Edmonton Fatigue Framework (EFF), a new framework for the study of tiredness, fatigue, and exhaustion in advanced cancer. MATERIALS AND METHODS: The Fatigue Adaptation Model (FAM), the starting point for the EFF, was drawn from a literature review pertaining to fatigue in depression, chronic fatigue syndrome, cancer, shift workers, and athletes published in the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medical Literature Analysis and Retrieval System Online (MEDLINE), PubMed, PsychINFO, SPORTdiscus, and CancerLit between 1995 and 2004, and from seven qualitative studies conducted by our group. The EFF, an elaboration of the FAM, was constructed after an expansion of our literature review to 2006 and team discussion. The EFF provides new insights into possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion as they occur in both ill and non-ill states. In this paper, however, we consider only possible links in advanced cancer. CONCLUSIONS: We propose that stressors associated with advanced cancer and its supportive treatment trigger declines in four systems -- cognitive function, sleep quality, nutrition, and muscle endurance -- and that these declines reduce one's ability to adapt. While these systems each likely has its own effect on adaptation, we propose that the most important and serious effects arise from interactions among declines in cognitive function, sleep quality, nutrition, and muscle endurance. CONCLUSIONS: Interventions for fatigue have been limited by a lack of understanding about its etiology. Hypotheses arising from the EFF; suggest a new direction for further study that focuses on interactions among cognitive function, sleep quality, nutrition, and muscle endurance.
Osoba T, Derek Pheby, Selena Gray, Luis Nacul		The Development of an Epidemiological Definition for Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2008; 14 (4): 61-84	An epidemiological case-definition was developed to distinguish myalgic encephalomyelitis/chronic fatigue syndrome from other chronic fatiguing conditions by evaluating the discriminatory potential of different criteria from previous definitions. A two-part model was derived using consensus and discriminant analytic approaches. The optimal discriminators for the first part were severe debilitating fatigue affecting physical and mental functioning, a reduction in activity to less than 50% of the patient's premorbid activity level, and muscle discomfort (sensitivity 92%, specificity 66%). The variables for the second part included a reduction in activity to less than 50% of the patient's premorbid activity, myalgia, generalized muscle weakness, migratory arthralgia, and swollen lymph nodes (sensitivity 77%, specificity 88%).
Pall ML.	School of Molecular Biosciences, Washington State University, Pullman, WA 99164-4234, USA. martin_pall@wsu.edu	Post-radiation syndrome as a NO/ONOO- cycle, chronic fatigue syndrome-like disease.	Med Hypotheses. 2008 Oct;71(4):537-41. Epub 2008 Jul 29.	Post-radiation syndrome is proposed to be chronic fatigue syndrome (CFS) or a chronic fatigue syndrome-like illness, initiated by exposure to ionizing radiation. This view is supported by the nitric oxide/peroxynitrite (NO/ONOO-) cycle mechanism, the putative etiologic mechanism for CFS and related illnesses. Ionizing radiation may initiate illness by increasing nitric oxide levels via increased activity of the transcription factor NF-kappaB and consequent increased synthesis of the inducible nitric oxide synthase. Two types of components of the nitric oxide/peroxynitrite cycle have been studied in post-radiation syndrome patients and shown to be elevated. The symptoms and signs of post-radiation syndrome and its chronicity are similar or identical to those of chronic fatigue syndrome and can be explained as being a consequence of nitric oxide/peroxynitrite cycle etiology.

				While the data available to test this view are limited, it provides for the first time a comprehensive explanation for post-radiation syndrome.
Papadopoulos A, Ebrecht M, Roberts AD, Poon L, Rohleder N, Cleare AJ.	King's College London, Institute of Psychiatry, Section of Neurobiology of Mood Disorders, Division of Psychological Medicine, London SE5 8AF, United Kingdom.	Glucocorticoid receptor mediated negative feedback in chronic fatigue syndrome using the low dose (0.5 mg) dexamethasone suppression test.	J Affect Disord. 2009 Jan;112(1-3):289-94. Epub 2008 Jun 24.	BACKGROUND: Chronic fatigue syndrome (CFS) is associated with hypocortisolism, but it is not yet clear the extent to which enhanced negative feedback may underlie this finding. METHODS: We undertook a low-dose dexamethasone (0.5 mg) suppression test in 18 CFS patients and 20 matched, healthy controls. We measured salivary cortisol levels at 0800 h, 1200 h, 1600 h and 2000 h before and after the administration of 0.5 mg of dexamethasone. RESULTS: Basal cortisol output was raised in this group of CFS patients compared to controls. Overall, the percentage suppression following dexamethasone administration was no different between CFS (mean+/-sem: 80.4+/-4.4%) and controls (76.2+/-4.9 %). However, the sub-group of patients with CFS and comorbid depression (n=9) showed a significant hypersuppression of salivary cortisol in response to dexamethasone (89.0+/-1.9%; $p<0.05$ v controls). LIMITATIONS: The sub-group analysis was on small numbers and should be considered preliminary. Dexamethasone probes only glucocorticoid medicated negative feedback but does not probe mineralocorticoid feedback, the other main physiological feedback mechanism. CONCLUSION: We found partial support for the hypothesis of enhanced negative feedback in CFS but only in patients with comorbid depression and also in the context of a sample of patients with elevated basal cortisol levels, which is an atypical finding in the literature.
Pariante CM.	Sections of Perinatal Psychiatry & Stress, Psychiatry and Immunology (SPI-Lab), Institute of Psychiatry, King's College London, 125 Coldharbour Lane, London SE5 9NU, UK. c.pariante@iop.kcl.ac.uk	Chronic fatigue syndrome and the immune system: "findings in search of meanings". Comment on: Brain Behav Immun. 2009 Mar;23(3):327-37.	Brain Behav Immun. 2009 Mar;23(3):325-6.	
Parrish BP, Zautra AJ, Davis MC.	Department of Psychology, Arizona State University. bparrish@udel.edu	The role of positive and negative interpersonal events on daily fatigue in women with fibromyalgia, rheumatoid arthritis, and osteoarthritis.	Health Psychol. 2008 Nov;27(6):694-702.	OBJECTIVE: The current study tested whether daily interpersonal events predicted fatigue from one day to the next among female chronic pain patients. DESIGN: Self-reported fatigue, daily events, pain, sleep quality, depressive symptoms, and functional health across 30 days were assessed in women with rheumatoid arthritis (RA: n = 89), Osteoarthritis (OA: n = 76), and Fibromyalgia syndrome (FM: n = 90). MAIN OUTCOME MEASURES: Self-report fatigue measured on a 0 to 100 scale and fatigue affect from PANAS-X (Watson & Clark, 1994). RESULTS: Multilevel analyses showed that both higher average levels of and daily increases in negative events predicted more fatigue, whereas daily increases in positive events predicted less fatigue. Across all pain conditions, increases in negative events continued to predict higher fatigue on the following day. Moreover, for participants with FM or RA,

				increases in positive events also predicted increased fatigue the following day. Daily increases in fatigue, in turn, predicted poorer functional health on both the same day and the next day. CONCLUSION: These results indicate that both on average and on a daily basis, interpersonal events influence levels of fatigue beyond common physical and psychological correlates of chronic pain and highlight differences between chronic pain groups.
Patrick Neary J, Roberts AD, Leavins N, Harrison MF, Croll JC, Sexsmith JR.	Faculty of Kinesiology & Health Studies, University of Regina, Regina, SK, Canada. patrick.neary@uregina.ca	Prefrontal cortex oxygenation during incremental exercise in chronic fatigue syndrome.	Clin Physiol Funct Imaging. 2008 Nov;28(6):364-72. Epub 2008 Jul 29.	This study examined the effects of maximal incremental exercise on cerebral oxygenation in chronic fatigue syndrome (CFS) subjects. Furthermore, we tested the hypothesis that CFS subjects have a reduced oxygen delivery to the brain during exercise. Six female CFS and eight control (CON) subjects (similar in height, weight, body mass index and physical activity level) performed an incremental cycle ergometer test to exhaustion, while changes in cerebral oxy-haemoglobin (HbO2), deoxy-haemoglobin (HHb), total blood volume (tHb = HbO2 + HHb) and O2 saturation [tissue oxygenation index (TOI), %)] was monitored in the left prefrontal lobe using a near-infrared spectrophotometer. Heart rate (HR) and rating of perceived exertion (RPE) were recorded at each workload throughout the test. Predicted VO2peak in CFS (1331 +/- 377 ml) subjects was significantly (P < or = 0.05) lower than the CON group (1990 +/- 332 ml), and CFS subjects achieved volitional exhaustion significantly faster (CFS: 351 +/- 224 s; CON: 715 +/- 176 s) at a lower power output (CFS: 100 +/- 39 W; CON: 163 +/- 34 W). CFS subjects also exhibited a significantly lower maximum HR (CFS: 154 +/- 13 bpm; CON: 186 +/- 11 bpm) and consistently reported a higher RPE at the same absolute workload when compared with CON subjects. Prefrontal cortex HbO2, HHb and tHb were significantly lower at maximal exercise in CFS versus CON, as was TOI during exercise and recovery. The CFS subjects exhibited significant exercise intolerance and reduced prefrontal oxygenation and tHb response when compared with CON subjects. These data suggest that the altered cerebral oxygenation and blood volume may contribute to the reduced exercise load in CFS, and supports the contention that CFS, in part, is mediated centrally.
Paul L, Rafferty D, Wood L, Maclaren W.	School of Health & Social Care, Glasgow Caledonian University, Glasgow, UK. L.Paul@clinmed.gla.ac.uk	Gait characteristics of subjects with chronic fatigue syndrome and controls at self-selected and matched velocities.	J Neuroeng Rehabil. 2008 May 27;5:16.	BACKGROUND: Gait abnormalities have been reported in individuals with Chronic Fatigue Syndrome (CFS) however no studies exist to date investigating the kinematics of individuals with CFS in over-ground gait. The aim of this study was to compare the over-ground gait pattern (sagittal kinematics and temporal and spatial) of individuals with CFS and control subjects at their self-selected and at matched velocities. METHODS: Twelve individuals with CFS and 12 matched controls participated in the study. Each subject walked along a 7.2 m walkway three times at each of three velocities: self-selected, relatively slow (0.45 ms-1) and a relatively fast (1.34 ms-1). A motion analysis system was used to investigate the sagittal plane joint kinematics and temporal spatial parameters of gait. RESULTS: At self-selected velocity there were significant differences between the two groups for all the temporal and spatial parameters measured, including gait velocity (P = 0.002). For the kinematic variables the significant differences were related to both ankles during swing and the right ankle during stance. At the relatively slower velocity the kinematic differences were replicated. However, the step distances decreased in the CFS population for the temporal and spatial parameters. When the gait pattern of the individuals with CFS at the relatively fast walking velocity (1.30 +/- 0.24 ms-1) was compared to the control subjects at their self-selected velocity (1.32 +/- 0.15 ms-1) the gait pattern of the two groups was very similar, with the exception of both ankles during swing. CONCLUSION: The self-selected gait velocity and/or pattern of individuals with CFS may be used to monitor the disease

				process or evaluate therapeutic intervention. These differences may be a reflection of the relatively low self-selected gait velocity of individuals with CFS rather than a manifestation of the condition itself.
Perrot S, Dickenson AH, Bennett RM.	Center de la Douleur et Service de Médecine Interne, Hôtel-Dieu, University Paris 5 Descartes, Paris, France. serge.perrot@htd.aphp.fr	Fibromyalgia: harmonizing science with clinical practice considerations.	Pain Pract. 2008 May-Jun;8(3):177-89. Epub 2008 Mar 18. Comment in: Pain Pract. 2008 May-Jun;8(3):155.	This review summarizes the present and emerging knowledge base on the pathophysiology, diagnosis, and management of fibromyalgia. EPIDEMIOLOGY: Fibromyalgia is the most common chronic pain syndrome encountered in general medicine and rheumatology. Historically, contemporary concepts of fibromyalgia have evolved in terms of its clinical description and parallel advances in the understanding of its pathophysiology. PATHOPHYSIOLOGY: A generally accepted paradigm postulates that fibromyalgia is the clinical expression of a rheumatologic disorder in which the associated pain is driven primarily by central sensitization and possibly through changes in several neuronal systems but not necessarily reliant on peripheral processes. MANAGEMENT: Several agents, including serotonin-norepinephrine reuptake inhibitors (ie, duloxetine and milnacipran), opioids (ie, tramadol), and the alpha2-delta ligand pregabalin, which recently received U.S. regulatory approval for the treatment of fibromyalgia, have been evaluated in clinical trials, demonstrating benefit in terms of pain reduction and improvement in core symptoms (ie, fatigue and sleep disturbance). The European League Against Rheumatism has developed updated guidelines for the management of fibromyalgia.
Perrot S.	Service de Médecine Interne et Centre de la Douleur, Hôtel-Dieu, Paris, France. serge.perrot@htd.aphp.fr	Fibromyalgia syndrome: a relevant recent construction of an ancient condition?	Curr Opin Support Palliat Care. 2008 Jun;2(2):122-7.	PURPOSE OF REVIEW: Fibromyalgia is considered the most common chronic pain syndrome. This syndrome is poorly understood and not widely accepted as a distinct clinical entity but an increasing number of pharmacological and nonpharmacological treatments are being developed for its management. RECENT FINDINGS: The clinical description of fibromyalgia is now well established, but controversies on diagnostic criteria are increasing. Pathophysiological studies suggest that fibromyalgia is a painful rheumatic disorder in which pain primarily stems from central sensitization and from other neuronal changes, including alterations in peripheral neuronal systems. Central sensitization may also underlie associated symptoms, including anxiety, sleep disorders, fatigue, and other dysfunctions such as irritable bowel syndrome and bladder instability.Several agents, including serotonin-norepinephrine reuptake inhibitors (duloxetine and milnacipran), weak opioids (tramadol), and anticonvulsants (pregabalin), as well as nonpharmacological approaches, have been recently evaluated in clinical trials, demonstrating benefit in terms of pain reduction and improvement of core symptoms (i.e., fatigue and sleep disturbance). SUMMARY: Despite the fact that pathophysiology and diagnostic criteria remain unclear, the level of scientific data collected on this recently described condition should convince clinicians of the existence of this syndrome, allowing improved management of the many patients suffering from chronic pain.
Pouchain D.	1 ter rue du Midi, 94300 Vincennes.	[Fatigued or depressed?] [Article in French]	Encephale. 2008 Jun;34 Spec No 2:S17-20.	
Presson AP, Sobel EM, Papp JC, Suarez CJ, Whistler T, Rajeevan MS, Vernon SD,	Biostatistics, University of California, Los Angeles, CA, USA. apresson@ucla.ed	Integrated weighted gene co-expression network analysis with an application	BMC Syst Biol. 2008 Nov 6;2:95.	BACKGROUND: Systems biologic approaches such as Weighted Gene Co-expression Network Analysis (WGCNA) can effectively integrate gene expression and trait data to identify pathways and candidate biomarkers. Here we show that the additional inclusion of genetic marker data allows one to characterize network relationships as causal or reactive in a chronic fatigue syndrome (CFS) data set. RESULTS: We combine WGCNA with genetic marker data to identify a disease-related pathway and its

Horvath S.	u	to chronic fatigue syndrome.		causal drivers, an analysis which we refer to as "Integrated WGCNA" or IWGCNA. Specifically, we present the following IWGCNA approach: 1) construct a co-expression network, 2) identify trait-related modules within the network, 3) use a trait-related genetic marker to prioritize genes within the module, 4) apply an integrated gene screening strategy to identify candidate genes and 5) carry out causality testing to verify and/or prioritize results. By applying this strategy to a CFS data set consisting of microarray, SNP and clinical trait data, we identify a module of 299 highly correlated genes that is associated with CFS severity. Our integrated gene screening strategy results in 20 candidate genes. We show that our approach yields biologically interesting genes that function in the same pathway and are causal drivers for their parent module. We use a separate data set to replicate findings and use Ingenuity Pathways Analysis software to functionally annotate the candidate gene pathways. CONCLUSION: We show how WGCNA can be combined with genetic marker data to identify disease-related pathways and the causal drivers within them. The systems genetics approach described here can easily be used to generate testable genetic hypotheses in other complex disease studies.
Price JR, Mitchell E, Tidy E, Hunot V.	Department of Psychiatry, University of Oxford, Warneford Hospital, Headington, Oxford, UK, OX3 7JX. jonathan.price@psych.ox.ac.uk	Cognitive behaviour therapy for chronic fatigue syndrome in adults. Update of: Cochrane Database Syst Rev. 2000;(2):CD001027.	Cochrane Database Syst Rev. 2008 Jul 16;(3):CD001027. Comment in: Evid Based Ment Health. 2009 Feb;12(1):16.	BACKGROUND: Chronic fatigue syndrome (CFS) is a common, debilitating and serious health problem. Cognitive behaviour therapy (CBT) may help to alleviate the symptoms of CFS. OBJECTIVES: To examine the effectiveness and acceptability of CBT for CFS, alone and in combination with other interventions, compared with usual care and other interventions. SEARCH STRATEGY: CCDANCTR-Studies and CCDANCTR-References were searched on 28/3/2008. We conducted supplementary searches of other bibliographic databases. We searched reference lists of retrieved articles and contacted trial authors and experts in the field for information on ongoing/completed trials. SELECTION CRITERIA: Randomised controlled trials involving adults with a primary diagnosis of CFS, assigned to a CBT condition compared with usual care or another intervention, alone or in combination. DATA COLLECTION AND ANALYSIS: Data on patients, interventions and outcomes were extracted by two review authors independently, and risk of bias was assessed for each study. The primary outcome was reduction in fatigue severity, based on a continuous measure of symptom reduction, using the standardised mean difference (SMD), or a dichotomous measure of clinical response, using odds ratios (OR), with 95% confidence intervals (CI). MAIN RESULTS: Fifteen studies (1043 CFS participants) were included in the review. When comparing CBT with usual care (six studies, 373 participants), the difference in fatigue mean scores at post-treatment was highly significant in favour of CBT (SMD -0.39, 95% CI -0.60 to -0.19), with 40% of CBT participants (four studies, 371 participants) showing clinical response in contrast with 26% in usual care (OR 0.47, 95% CI 0.29 to 0.76). Findings at follow-up were inconsistent. For CBT versus other psychological therapies, comprising relaxation, counselling and education/support (four studies, 313 participants), the difference in fatigue mean scores at post-treatment favoured CBT (SMD -0.43, 95% CI -0.65 to -0.20). Findings at follow-up were heterogeneous and inconsistent. Only two studies compared CBT against other interventions and one study compared CBT in combination with other interventions against usual care. AUTHORS' CONCLUSIONS: CBT is effective in reducing the symptoms of fatigue at post-treatment compared with usual care, and may be more effective in reducing fatigue symptoms compared with other psychological therapies. The evidence base at follow-up is limited to a small

				group of studies with inconsistent findings. There is a lack of evidence on the comparative effectiveness of CBT alone or in combination with other treatments, and further studies are required to inform the development of effective treatment programmes for people with CFS.
Priebe S, Fakhoury WK, Henningsen P.	Unit for Social and Community Psychiatry, Barts' and the London School of Medicine, Queen Mary University of London, London, UK. s.priebe@qmul.ac.uk	Functional incapacity and physical and psychological symptoms: how they interconnect in chronic fatigue syndrome.	Psychopathology. 2008;41(6):339-45. Epub 2008 Sep 3.	BACKGROUND: It has been argued that perceived functional incapacity might be a primary characteristic of chronic fatigue syndrome (CFS) and could be explained by physical symptoms. If so, it could be expected to be closely associated with physical, but not psychological symptoms. The study tests this hypothesis. SAMPLING AND METHODS: The sample consisted of 73 patients, with a diagnosis of CFS according to the Oxford criteria, randomly selected from clinics in the Departments of Immunology and Psychiatry at St. Bartholomew's Hospital, London. The degree of fatigue experienced by patients was assessed using the Chalder Fatigue Questionnaire and a visual analogue scale. Self-rated instruments were used to measure physical and social functioning, quality of life, and physical and psychological symptoms. RESULTS: Principal-component analysis of all scale scores revealed 2 distinct components, explaining 53% of the total variance. One component was characterized by psychological symptoms and generic quality of life indicators, whilst the other component was made up of physical symptoms, social and physical functioning and indicators of fatigue. CONCLUSIONS: The findings suggest that perceived functional incapacity is a primary characteristic of CFS, which is manifested and/or explained by physical symptoms. (c) 2008 S. Karger AG, Basel.
Przybyłowski T, Bielicki P, Kumor M, Hildebrand K, Maskey-Warzechowska M, Korczyński P, Chazan R.	Department of Pneumology and Allergology, Warsaw Medical University, Warsaw, Poland. przyb@amwaw.edu.pl	Exercise capacity in patients with obstructive sleep apnea syndrome.	J Physiol Pharmacol. 2007 Nov;58 Suppl 5(Pt 2):563-74.	Obstructive sleep apnea syndrome (OSAS) is a common disease characterized by repetitive partial or complete closure of the upper airway during sleep. Cardiovascular disturbances are the most important complications responsible for increased morbidity and mortality. It is suggested that daytime somnolence, chronic fatigue, and nocturnal hypoxemia may further impair muscle function and decrease exercise fitness. The aim of this study was to evaluate cardiopulmonary response to exercise in OSAS patients. One hundred and eleven middle aged (50.2+/-10 yr), obese (BMI 31.0+/-4.6 kg/m2) patients (109 M, 2F) with severe OSAS (AHI 47.2+/-23.1 h(-1)) were enrolled into the study. OSAS was diagnosed with overnight polysomnography and a symptom-limited cardiopulmonary exercise test was performed on a treadmill using Bruce protocol. The results showed that the most frequent reason for exercise termination were: muscle fatigue and/or dyspnea (66+/-), increase in systolic blood pressure>220 mmHg (20%), ECG abnormalities, and chest pain (6%). Although the mean VO2 peak was within the reference value (29.6+/-6 mlO2/kg/min), in 52 patients (46%) VO2 peak was <84% of predicted. Hypertensive response to exercise was diagnosed in 39 of patients (35%). Patients with severe sleep apnea (AHI40>or=h(-1)) were characterized by higher mean blood pressure at rest, at 25%, 50% of maximal work load, at peak exercise and at post-exercise recovery. Several significant correlations between hemodynamic responses to exercise and sleep apnea severity were also noted. We conclude that exercise tolerance can be limited due to hypertensive response in about 20% of patients. Patients with severe OSAS have exaggerated hemodynamic response to exercise and delayed post-exercise blood pressure recovery. Cardiopulmonary response to exercise seems to be related to sleep apnea severity.
Puetz TW, Flowers SS, O'Connor PJ.	Department of Kinesiology, University of	A randomized controlled trial of the effect of	Psychother Psychosom. 2008;77(3):167-74.	BACKGROUND: There is growing evidence that chronic exercise is a promising intervention for combating feelings of low energy and fatigue. Although groups with well-defined medical conditions (for example cancer and heart disease) or unexplained fatigue syndromes consistently have reported

	Georgia, Athens, GA, USA.	aerobic exercise training on feelings of energy and fatigue in sedentary young adults with persistent fatigue.	Epub 2008 Feb 14.	improved feelings of energy and fatigue after chronic exercise, relatively few exercise training studies have been conducted with people who report persistent fatigue yet neither have a medical condition nor reach diagnostic criteria for an unexplained fatigue syndrome. The purpose of this investigation was to use a randomized controlled design to examine the effects of 6 weeks of chronic exercise training on feelings of energy and fatigue in sedentary, healthy young adults reporting persistent fatigue. METHODS: Thirty-six healthy, young adults who reported persistent feelings of fatigue were randomly assigned to a moderate-intensity exercise, low-intensity exercise or no treatment control group. Participants in each condition then visited the exercise laboratory on 18 occasions over a 6-week period. Exercise laboratory visits occurred 3 days per week. Vigor and fatigue mood state scores were obtained at the beginning of the third exercise session each week for 6 weeks. Aerobic fitness was measured before and after intervention. RESULTS: The effect of 6 weeks of exercise training on feelings of fatigue was dependent on exercise intensity; however, the effect on feelings of energy was similar for both the low- and moderate-intensity conditions. The changes in feelings of energy and fatigue were independent of changes in aerobic fitness. CONCLUSIONS: Six weeks of low and moderate exercise training performed by sedentary adults without a well-defined medical condition or an unexplained fatigue syndrome but reporting persistent feelings of fatigue resulted in similarly beneficial effects on feelings of energy. The effects for symptoms of fatigue were moderated by exercise intensity, and the more favorable outcome was realized with low-intensity exercise. Changes in feelings of energy and fatigue following exercise training were unrelated to changes in aerobic fitness. Copyright (c) 2008 S. Karger AG, Basel.
Raison CL, Lin JM, Reeves WC.	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, 1365C Clifton Road, Room 5004, Atlanta, GA 30322, USA. craison@emory.edu	Association of peripheral inflammatory markers with chronic fatigue in a population-based sample.	Brain Behav Immun. 2009 Mar;23(3):327-37. Epub 2008 Dec 11. Comment in: Brain Behav Immun. 2009 Mar;23(3):325-6.	Alterations in the innate immune response may contribute to the pathogenesis of chronic fatigue syndrome (CFS). However, studies have been limited by small sample sizes, use of patients from tertiary care settings, inappropriate selection of controls, and failure to control for confounding demographic, medical and behavioral factors independently associated with immune activity. It is also not known whether specific symptoms account for observed associations between CFS and the innate immune response. To address these limitations, the current study examined plasma concentrations of high-sensitivity c-reactive protein (hs-CRP), white blood cell count (WBC) and a combined inflammation factor in a large population-based sample. Log-transformed mean plasma concentrations of hs-CRP were increased in subjects with CFS (n=102) and in subjects with unwellness symptoms that did not meet diagnostic criteria for CFS (defined as "insufficient fatigue" [ISF]) (n=240) when compared to subjects who were well (n=115). Log transformed WBC was increased in ISF and was increased at a trend level in CFS. The combined inflammation factor was increased in both CFS and ISF. Subjects with CFS and ISF did not differ on any of the inflammation measures. In the entire subject population, the physical component summary score (PCS), but not the mental component summary score (MCS), from the Medical Outcomes Study Short Form-36 (SF-36) was negatively associated with each of the inflammation measures. Depressive symptoms were also associated with increased log hs-CRP. After adjustment for age, sex, race, location of residence, BMI, depressive status and immune-modulating medications, subjects classified as ISF continued to demonstrate increased log hs-CRP, WBC and elevations on the inflammation factor when compared to well controls; however, associations between CFS and log hs-CRP and the inflammation factor were no longer statistically

				significant. After adjustment, PCS score also remained independently associated with each of the inflammation measures. These findings support a role for innate immune activation in unexplained fatigue and unwellness, but do not suggest that immune activation is specific to CFS.
Raszeja-Wyszomirska J, Lawniczak M, Marlicz W, Miezyńska-Kurtycz J, Milkiewicz P.	Pomorska Akademia Medyczna, Samodzielna Pracownia Hepatologii Katedry Gastroenterologii. jorasz@sci.pam.szczecin.pl	[Non-alcoholic fatty liver disease--new view] [Article in Polish]	Pol Merkur Lekarski. 2008 Jun;24(144):568-71.	Non-alcoholic fatty liver disease (NAFLD) covers a wide spectrum of liver pathology--from steatosis alone, through the necroinflammatory disorder of non-alcoholic steatohepatitis (NASH) to cirrhosis and liver cancer. NAFLD/NASH is mostly related with visceral adiposity, obesity, type 2 diabetes melitus (DM t.2) and metabolic syndrome. Pathogenetic concepts of NAFLD include overnutrition and underactivity, insulin resistance (IR) and genetic factor. The prevalence of NAFLD has been estimated to be 17-33% in some countries, NASH may be present in about 1/3 of such cases, while 20-25% of NASH cases could progress to cirrhosis. NAFLD is now recognized as one of the most frequent reason of liver tests elevation without clinical symptoms. Insulin resistance is considering as having a central role in NAFLD pathogenesis. In hepatocytes, IR is related to hyperglycaemia and hyperinsulinaemia, formation of advanced glycation end-products, increased free fatty acids and their metabolites, oxidative stress and altered profiles of adipocytokines. Early stages of fatty liver are clinically silent and include elevation of ALT and GGTP, hyperechogenic liver in USG and/or hepatomegaly. Among clinical symptoms, abdominal discomfort is relatively common as well as chronic fatigue. NAFLD/NASH is not a benign disease, progressive liver biopsy have shown histological progression of fibrosis in 32%, the estimated rate of cirrhosis development is 20% and a liver--related death is 12% over 10 years. No treatment has scientifically proved to ameliorate NAFLD or to avoid its progression. The various therapeutic alternatives are aimed at interfering with the risk factors involved in the pathogenesis of the disorder in order to prevent the progression to end-stage liver disease. The most important therapeutic measure is increasing insulin sensitivity by an attempt to change a lifestyle mostly by dieting and physical activity in order to loose weight. The most used agent is metformin, the others are under controlled trials or their effectiveness is low. NASH is not a common indication for liver transplantation because of the older age distribution of patients and high prevalence of comorbidity, related to metabolic syndrome. Recurence of NASH in the grafted liver is also a relatively frequent complication.
Ravoet C, Mineur P, Robin V, Debusscher L, Bosly A, André M, El Housni H, Soree A, Bron D, Martiat P.	Jules Bordet Institute, Rue Héger-Bordet, 1, 1000 Brussels, Belgium. christophe.ravoet@bordet.be	Farnesyl transferase inhibitor (lonafarnib) in patients with myelodysplastic syndrome or secondary acute myeloid leukaemia: a phase II study.	Ann Hematol. 2008 Nov;87(11):881-5. Epub 2008 Jul 19.	Although an activating mutation of Ras is commonly observed in myelodysplastic syndrome (MDS), the role of Ras in the natural history of MDS remains largely unknown. We prospectively studied efficiency and tolerance of lonafarnib, a compound able to inhibit Ras signalling pathway through an inhibition of farnesyl transferase, in patients with MDS or secondary acute myeloid leukaemia (sAML). Lonafarnib was administered orally at a dose of 200 mg twice daily for three courses of 4 weeks (separated by 1 to 4 weeks without treatment). Sixteen patients were included: FAB/RAEB (n = 10), RAEB-T (n = 2), sAML (n = 2) and chronic myelomonocytic leukaemia (CMML; n = 2); WHO/RAEB-1 (n = 4), RAEB-2 (n = 5), AML (n = 5), CMML (n = 2). Median age was 70 (53-77) years. The karyotype was complex or intermediate in 11 patients, and the International Prognostic Scoring Systems (IPSS) risk groups were low in two patients, INT-1 in one patient, INT-2 in four patients and high in six patients (unknown or not applicable in three patients). Among the 14 patients tested, five had Ras mutations in codons 12, 13 or 61 of N-Ras, K-Ras or H-Ras. One patient was excluded of the analysis for protocol violation, and 15 patients were assessable for tolerance. Gastrointestinal toxicities (diarrhoea, nausea

				and anorexia) and myelosuppression were the major side effects. Other toxicities included infections, fatigue, increase of liver enzymes, arrhythmia and skin rash. One patient died of infection, and the treatment was stopped in one other who developed atrial fibrillation. Doses were reduced in all but one patient treated with more than one course of farnesyl transferase inhibitor. Responses were assessable in 12 patients. A partial response in one sAML patient and a very transient decrease of blast cell count with normalisation of karyotype in one MDS patient were observed. No relation between improvement of marrow parameters and detected Ras mutations was observed. Lonafarnib alone, administered following our schedule, has shown limited activity in patients with MDS or secondary AML. Gastrointestinal and haematological toxicities appear the limiting toxicity in this population of patients.
Regenauer A.	Kompetenzzentrum Medical Research & Underwriting, Münchener Rückversicherungs-Gesellschaft.	[Contentious diseases--a medico-social phenomenon from an insurance medicine perspective] [Article in German]	Versicherungsmedizin. 2008 Mar 1;60(1):3-7.	A group of illnesses that are difficult to assess objectively, comprising such conditions as fibromyalgia, chronic fatigue syndrome, attention-deficit hyperactivity disorder, whiplash injury, and last but not least a multitude of somatoform disorders, has become a growing concern to Western health care systems and insurance industries. Thus far, the medical literature has failed to provide informative overviews of this group, which at first glance admittedly seems to be rather heterogeneous. If at all, the disorders have been grouped together under the term ,,controversial illnesses" to differentiate them from other diseases. The insurance industry - and claims departments, in particular - are increasingly having to deal with this rapidly growing phenomenon, which affects not only life business, but also health, worker's compensation and motor third-party liability. When paying compensation and settling claims, insurers are often left with a feeling that the illness may have been ,,imaginary" or aggravated. Is there a common basis for this new disorder mega-trend - independent of the recognition of the conditions by medical associations? This article aims at providing an overview of the common characteristics of the group of disorders, including a description of the key physical, psychological and social aspects. In particular, it is intended to deepen insurers' understanding of the risks arising from social change. The article also examines the disorder prevalence in Western societies and the possible causes of the significant increase.
Reynolds F, Vivat B, Prior S.	School of Health Sciences and Social Care, Brunel University, Middlesex, UK. frances.reynolds@brunel.ac.uk	Women's experiences of increasing subjective well-being in CFS/ME through leisure-based arts and crafts activities: a qualitative study.	Disabil Rehabil. 2008;30(17):1279-88.	PURPOSE: To understand the meanings of art-making among a group of women living with the occupational constraints and stigma of CFS/ME. The study explored their initial motives for art-making, and then examined how art-making had subsequently influenced their subjective well-being. METHOD: Ten women with CFS/ME were interviewed; three provided lengthy written accounts to the interview questions. FINDINGS: Illness had resulted in devastating occupational and role loss. Participants took many years to make positive lifestyle changes. Art-making was typically discovered once participants had accepted the long-term nature of CFS/ME, accommodated to illness, and reprioritized occupations. Several factors then attracted participants specifically to art-making. It was perceived as manageable within the constraints of ill-health. Participants also tended to be familiar with craft skills; had family members interested in arts and crafts, and some desired a means to express grief and loss. Once established as a leisure activity, art-making increased subjective well-being mainly through providing increased satisfaction in daily life, positive self-image, hope, and contact with the outside world. Participants recommended provision of occupational/recreational counselling earlier in the illness trajectory. CONCLUSIONS: Creative art-making occurred as part of a

				broader acceptance and adjustment process to CFS/ME, and allowed some psychological escape from a circumscribed lifeworld.
Riedl A, Schmidtmann M, Stengel A, Goebel M, Wisser AS, Klapp BF, Mönnikes H.	Division of Hepatology, Gastroenterology, and Endocrinology, Department of Medicine, Charité-University Medical Center, Campus Virchow, Berlin, Germany.	Somatic comorbidities of irritable bowel syndrome: a systematic analysis.	J Psychosom Res. 2008 Jun;64(6):573-82. Epub 2008 Apr 28.	OBJECTIVE: A large number of irritable bowel syndrome (IBS) patients are additionally afflicted with other somatic intestinal and/or extraintestinal comorbidities. The occurrence of one or more comorbidities is correlated with enhanced medical help seeking, worse prognosis, and higher rates of anxiety and depression-all resulting in a reduced quality of life. The aims of this study were, firstly, to review the literature on comorbidities of IBS and to assess gastrointestinal and extraintestinal comorbidities, and, secondly, to evaluate explanatory hypotheses and possible common pathophysiological mechanisms. METHODS: We systematically reviewed the scientific literature in the past 25 years, as cited in MEDLINE. RESULTS: IBS patients present with a twofold increase in somatic comorbidities compared to controls, possibly caused by common pathophysiological mechanisms. Nevertheless, to date, there has been no convincing evidence for a consolidated underlying pathophysiology or somatization. Gastrointestinal disorders, such as functional dyspepsia, gastroesophageal reflux disease, functional constipation, and anal incontinence, occur in almost half of the patients. In a broad variety of extraintestinal comorbidities, fibromyalgia, chronic fatigue syndrome, and chronic pelvic pain are best documented and appear in up to 65%. CONCLUSION: The knowledge and structured assessment of comorbid somatic symptoms might allow to identify subgroups of IBS patients with special characteristics and lead to adaptation of the therapeutic concept.
Rimlinger B.	3 rue Urban V, 34000 Montpellier.	[Fatigue, depressed, depression: concepts and realities] Article in French	Encephale. 2008 Jun;34 Spec No 2:S33-4.	
Rizzieri DA, Feldman E, Dipersio JF, Gabrail N, Stock W, Strair R, Rivera VM, Albitar M, Bedrosian CL, Giles FJ.	Duke University Medical Center, Durham, North Carolina 27710, USA. rizzi003@mc.duke.edu	A phase 2 clinical trial of deforolimus (AP23573, MK-8669), a novel mammalian target of rapamycin inhibitor, in patients with relapsed or refractory hematologic malignancies.	Clin Cancer Res. 2008 May 1;14(9):2756-62.	PURPOSE: Deforolimus (AP23573), a novel non-prodrug rapamycin analogue, inhibits the mammalian target of rapamycin, a downstream effector of the phosphatidylinositol 3-kinase/Akt and nutrient-sensing pathways. A phase 2 trial was conducted to determine the efficacy and safety of single-agent deforolimus in patients with relapsed or refractory hematologic malignancies. EXPERIMENTAL DESIGN: Eligible patients were assigned to one of five disease-specific, parallel cohorts and given 12.5 mg deforolimus as a 30-minute infusion once daily for 5 days every 2 weeks. A Simon two-stage design was used for each cohort. Safety, pharmacokinetics, pharmacodynamics, and antitumor response were assessed. RESULTS: Fifty-five patients received deforolimus as follows: cohort 1 23 acute myelogenous leukemia, two myelodysplastic syndrome and one chronic myelogenous leukemia in nonlymphoid blast phase; cohort 2, one acute lymphocytic leukemia; cohort 3, nine agnogenic myeloid metaplasia; cohort 4, eight chronic lymphocytic leukemia; cohort 5, nine mantle cell lymphoma and two T-cell leukemia/lymphoma. Most patients were heavily pretreated. Of the 52 evaluable patients, partial responses were noted in five (10%), two of seven agnogenic myeloid metaplasia and three of nine mantle cell lymphoma. Hematologic improvement/stable disease was observed in 21 (40%). Common treatment-related adverse events, which were generally mild and

				reversible, were mouth sores, fatigue, nausea, and thrombocytopenia. Decreased levels of phosphorylated 4E-BP1 in 9 of 11 acute myelogenous leukemia/myelodysplastic syndrome patients after therapy showed mammalian target of rapamycin inhibition by deforolimus. CONCLUSIONS: Deforolimus was well-tolerated in patients with heavily pretreated hematologic malignancies, and antitumor activity was observed. Further investigation of deforolimus alone and in combination with other therapeutic agents is warranted in patients with selected hematologic malignancies.
Roberts AD, Papadopoulos AS, Wessely S, Chalder T, Cleare AJ.	King's College London, Institute of Psychiatry, Department of Psychological Medicine, De Crespigny Park, London SE5 8AF, UK; Chronic Fatigue Syndrome Research and Treatment Unit, Maudsley Hospital, Denmark Hill, London, UK.	Salivary cortisol output before and after cognitive behavioural therapy for chronic fatigue syndrome.	J Affect Disord. 2008 Oct 18. [Epub ahead of print]	BACKGROUND: There is evidence that patients with chronic fatigue syndrome (CFS) have mild hypocortisolism. One theory about the aetiology of this hypocortisolism is that it occurs late in the course of CFS via factors such as inactivity, sleep disturbance, chronic stress and deconditioning. We aimed to determine whether therapy aimed at reversing these factors - cognitive behavioural therapy for CFS - could increase cortisol output in CFS. METHODS: We measured diurnal salivary cortisol output between 0800 and 2000h before and after 15 sessions (or 6 months) of CBT in 41 patients with CDC-defined CFS attending a specialist, tertiary outpatient clinic. RESULTS: There was a significant clinical response to CBT, and a significant rise in salivary cortisol output after CBT. LIMITATIONS: We were unable to control for the passage of time using a non-treated CFS group. CONCLUSIONS: Hypocortisolism in CFS is potentially reversible by CBT. Given previous suggestions that lowered cortisol may be a maintaining factor in CFS, CBT offers a potential way to address this.
Romani A.	Laboratorio Potenziali Evocati, Istituto Neurologico C. Mondino, Via Mondino 2, 27100, Pavia, Italy. alfredo.romani@mondino.it	The treatment of fatigue.	Neurol Sci. 2008 Sep;29 Suppl 2:S247-9.	Fatigue is a psychophysiological state that acts on the subject's motivation to engage in and/or to continue strenuous physical or cognitive activities. In various pathological conditions fatigue seems to lose this homeostatic function and presents itself as a symptom. The pathophysiology of fatigue is complex and includes neurological (central and peripheral) dysfunction, and altered neurotransmitter, cytokine, and hormonal settings. Treatment interventions are generally based on a sequential approach including treatment of comorbid factors, nonpharmacological treatments, and drugs.
Romans S, Cohen M.	Women's College Research Institute, Women's College Hospital, Toronto, Canada. sarah.romans@wchospital.ca	Unexplained and underpowered: the relationship between psychosomatic disorders and interpersonal abuse -- a critical review.	Harv Rev Psychiatry. 2008 Jan-Feb;16(1):35-54.	Although it is commonly accepted that interpersonal violence (IntPV) leads to adverse health consequences, the available data are far from decisive. To test the hypothesized link, the authors devised an evidence-based strategy to determine the data quality in studies purporting to link IntPV and some medically unexplained disorders in women (irritable bowel syndrome, chronic pelvic pain, fibromyalgia/chronic fatigue, and other chronic pain syndromes). English language studies with control groups of unaffected women were assessed for the quality of their methodologies. The number of studies, together with the consistency of their findings in each domain, was collated to determine the overall weight of evidence regarding the link for each condition. The quantity and quality of research in each clinical area proved to be sparse. In general, most research was limited to small, convenience samples, with insufficient attention to the design of control groups and to sample size. The evidence

				currently available regarding irritable bowel syndrome, fibromyalgia/chronic fatigue, chronic pelvic pain, and other chronic pain syndromes does not allow for any firm conclusion regarding their link to IntPV. More research - paying particular regard to the methodological concerns identified here - is required in order to generate any definitive conclusions.
Rosenhagen MC, Schmidt U, Ebinger M, Nickel T, Uhr M.		Successful treatment of chronic fatigue syndrome with duloxetine and trijodthyronine--a case study.	J Clin Psychopharmacol. 2008 Feb;28(1):105-7.	
Rudolph T, Larsen JP, Farbu E.	Department of Neurology, Stavanger University Hospital, Stavanger, Norway. mokum99@online.no	The long-term functional status in patients with Guillain-Barré syndrome.	Eur J Neurol. 2008 Dec;15(12):1332-7.	BACKGROUND AND PURPOSE: The purpose of this study was to analyse the long-term impact of Guillain-Barré syndrome (GBS) on quality of life, and the relationship between clinical variables at disease onset and symptoms at follow-up to general health status. METHODS: Forty-two GBS patients were examined at median 6 years after disease onset and were compared with 50 healthy controls. The fatigue severity scale (FSS), visual analogue scale (VAS) for pain, disability rating index (DRI) and medical outcome study 36-item short-form health status scale (SF-36) were applied. Variables at onset and symptoms at follow-up were correlated with outcome measurements in GBS. RESULTS: VAS [2.9 (SD 3.3) vs. 1.5 (SD 1.9); P = 0.01] and DRI [2.5 (SD 2.1) vs. 1.0 (SD 1.5); P < 0.001] were significantly higher in patients with GBS, compared with healthy controls. Decreased physical functioning and general health were found on SF-36. Differences between GBS patients with shorter (<6 years) and longer (> or =6 years) follow-up after onset were not found. CONCLUSIONS: Relatively independent from various variables at onset, patients with GBS seem to have a reduced quality of life and functioning, and the distress seems to have become persistent after the first few years with improvement following the acute disease.
Saiki T, Kawai T, Morita K, Ohta M, Saito T, Rokutan K, Ban N.	Department of General Medicine, Nagoya University Hospital, Nagoya, Japan.	Identification of marker genes for differential diagnosis of chronic fatigue syndrome.	Mol Med. 2008 Sep-Oct;14(9-10):599-607.	Chronic fatigue syndrome (CFS) is a clinically defined condition characterized by long-lasting disabling fatigue. Because of the unknown mechanism underlying this syndrome, there still is no specific biomarker for objective assessment of the pathological fatigue. We have compared gene expression profiles in peripheral blood between 11 drug-free patients with CFS and age- and sex-matched healthy subjects using a custom microarray carrying complementary DNA probes for 1,467 stress-responsive genes. We identified 12 genes whose mRNA levels were changed significantly in CFS patients. Of these 12 genes, quantitative real-time PCR validated the changes in 9 genes encoding granzyme in activated T or natural killer cells (GZMA), energy regulators (ATP5J2, COX5B, and DBI), proteasome subunits (PSMA3 and PSMA4), putative protein kinase c inhibitor (HINT), GTPase (ARHC), and signal transducers and activators of transcription 5A (STAT5A). Next, we performed the same microarray analysis on 3 additional CFS patients and 20 other patients with the chief complaint of long-lasting fatigue related to other disorders (non-CFS patients) and found that the relative mRNA expression of 9 genes classified 79% (11/14) of CFS and 85% (17/20) of the non-CFS patients. Finally, real-time PCR measurements of the levels of the 9 involved mRNAs were done in another group of 18 CFS and 12 non-CFS patients. The expression pattern correctly classified 94% (17/18) of CFS and 92% (11/12) of

				non-CFS patients. Our results suggest that the defined gene cluster (9 genes) may be useful for detecting pathological responses in CFS patients and for differential diagnosis of this syndrome.
Sakudo A, Kato YH, Tajima S, Kuratsune H, Ikuta K.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University, Yamadaoka, Suita, Osaka 565-0871, Japan.	Visible and near-infrared spectral changes in the thumb of patients with chronic fatigue syndrome.	Clin Chim Acta. 2009 Feb 25. [Epub ahead of print]	BACKGROUND: Chronic fatigue syndrome (CFS) patients show a persistent fatigue condition with muscle pain and impairment of concentration, memory, and sleep. Presently, the physiological basis of CFS remains unclear. In this study, spectroscopic differences in the thumb were compared between 103 CFS patients and 122 healthy controls to examine possible changes of levels of oxygenated or deoxygenated hemoglobin. METHODS: Visible and near-infrared (Vis-NIR) spectroscopy was used to examine possible changes in the region of 600-1100 nm. RESULTS: Vis-NIR spectra showed sharp peaks at 694, 970 and 1060 nm and broad peaks in the regions of 740-760 and 830-850 nm. As these peaks are possibly related to oxyhemoglobin, cytochrome c oxidase and water, levels of these factors were compared between the two groups. Statistical analysis of the absorbance of Vis-NIR spectra showed a significant decrease in water content, a significant increase in oxyhemoglobin content, and a significant increase in the oxidation of heme a+a(3) and copper in cytochrome c oxidase in CFS patients. CONCLUSIONS: These changes imply accelerated blood flow and energy metabolism in the thumbs of CFS patients.
Sakudo A, Kuratsune H, Kato YH, Ikuta K.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University, Yamadaoka, Suita, Osaka 565-0871, Japan. sakudo@biken.osaka-u.ac.jp	Secondary structural changes of proteins in fingernails of chronic fatigue syndrome patients from Fourier-transform infrared spectra.	Clin Chim Acta. 2009 Apr;402(1-2):75-8. Epub 2008 Dec 30.	BACKGROUND: Generally, nails can be an index of health, with abnormalities sometimes found under diseased conditions. Fatigue is also supposed to affect the condition of nails. Possible differences in infrared (IR) spectra of nail plates of chronic fatigue syndrome (CFS) patients compared to healthy control subjects were investigated in this study. METHODS: Using an attenuated total reflection (ATR)-Fourier-transform infrared (FTIR) spectrophotometer, spectra in the region of 4000-600 cm(-1) were obtained. The amide I region was then separated by Fourier deconvolution and curve fitting based on the Gauss and Lorentz formula and revealed differences in the secondary structural content of proteins compared to healthy donors. RESULTS: The specific secondary structural pattern commonly observed in nails of male and female CFS patients in the absence and presence of medication indicated a decreased alpha-helix content and increased beta-sheet content, suggesting reduced levels of normal elements of the nail plate. CONCLUSIONS: This provides the first evidence of alterations in the fingernails of CFS patients which could be detected by IR spectroscopy. Possible explanations for the alterations will be discussed.
Sandholzer H, Sobeck C, Sandholzer M, Breivogel B.	Selbst. Abteilung für Allgemeinmedizin, Universität Leipzig. haeb@medizin.uni-leipzig.de	[Presentation, Diagnosis and Management of fatigue in general practice] [Article in German]	MMW Fortschr Med. 2008 Apr 24;150(17):27-30.	
Santell B.	Smedhälsan, Eskilstuna. bosantell@yahoo.se	[Stress patients are able to go back to work after prolonged sick leave] [Article in Swedish]	Lakartidningen. 2008 May 28-Jun 3;105(22):1691.	

Santhouse AM.	South London and Maudsley NHS Foundation Trust, London, UK.	Review: CBT reduces fatigue in adults with chronic fatigue syndrome but effects at follow-up unclear. Comment on: Cochrane Database Syst Rev. 2008;(3):CD001027	Evid Based Ment Health. 2009 Feb;12(1):16.	
Scheeres K, Wensing M, Bleijenberg G, Severens JL.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre (4628), PO Box 9101, 6500 HB, The Netherlands. k.scheeres@nkcv.umcn.nl	Implementing cognitive behavior therapy for chronic fatigue syndrome in mental health care: a costs and outcomes analysis.	BMC Health Serv Res. 2008 Aug 13;8:175.	BACKGROUND: This study investigated the costs and outcomes of implementing cognitive behavior therapy (CBT) for chronic fatigue syndrome (CFS) in a mental health center (MHC). CBT is an evidence-based treatment for CFS that was scarcely available until now. To investigate the possibilities for wider implementation, a pilot implementation project was set up. METHOD: Costs and effects were evaluated in a non-controlled before- and after study with an eight months time-horizon. Both the costs of performing the treatments and the costs of implementing the treatment program were included in the analysis. The implementation interventions included: informing general practitioners (GPs) and CFS patients, training therapists, and instructing the MHC employees. Given the non-controlled design, cost outcome ratios (CORs) and their acceptability curves were analyzed. Analyses were done from a health care perspective and from a societal perspective. Bootstrap analyses were performed to estimate the uncertainty around the cost and outcome results. RESULTS: 125 CFS patients were included in the study. After treatment 37% had recovered from CFS and the mean gained QALY was 0.03. Costs of patients' health care and productivity losses had decreased significantly. From the societal perspective the implementation led to cost savings and to higher health states for patients, indicating dominancy. From the health care perspective the implementation revealed overall costs of 5.320 euros per recovered patient, with an acceptability curve showing a 100% probability for a positive COR at a willingness to pay threshold of 6.500 euros per recovered patient. CONCLUSION: Implementing CBT for CFS in a MHC appeared to have a favorable cost outcome ratio (COR) from a societal perspective. From a health care perspective the COR depended on how much a recovered CFS patient is being valued. The strength of the evidence was limited by the non-controlled design. The outcomes of this study might facilitate health care providers when confronted with the decision whether or not to adopt CBT for CFS in their institution.
Scheeres K, Wensing M, Knoop H, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. k.scheeres@nkcv.u	Implementing cognitive behavioral therapy for chronic fatigue syndrome in a mental health center: a benchmarking	J Consult Clin Psychol. 2008 Feb;76(1):163-71.	OBJECTIVE: This study evaluated the success of implementing cognitive behavioral therapy (CBT) for chronic fatigue syndrome (CFS) in a representative clinical practice setting and compared the patient outcomes with those of previously published randomized controlled trials (RCTs) of CBT for CFS. METHOD: The implementation interventions were the following: spreading information about the new treatment setting to general practitioners and CFS patients; training mental health center (MHC) therapists in CBT for CFS; and organizing changes in the MHC patient workflow. Patient outcomes were documented with validated self-report measures of fatigue and physical functioning before and after treatment. The comparison of the treatment results with RCT results was done following the

	mcn.cl	evaluation.		benchmark strategy. RESULTS: One-hundred forty-three CFS patients were referred to the MHC, of whom 112 started treatment. The implementation was largely successful, but a weak point was the fact that 32% of all referred patients dropped out shortly after or even before starting treatment. Treatment effect sizes were in the range of those found in the benchmark studies. CONCLUSIONS: CBT for CFS can successfully be implemented in an MHC. Treatment results were acceptable, but the relatively large early dropout of patients needs attention.
Scheeres K, Wensing M, Severens H, Adang E, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. k.scheeres@nkcv.umcn.nl	Determinants of health care use in chronic fatigue syndrome patients: a cross-sectional study.	J Psychosom Res. 2008 Jul;65(1):39-46. Epub 2008 May 22.	BACKGROUND: Chronic fatigue syndrome (CFS) is associated with a high use of health care services. To reduce the related costs for patients and society, it will be useful to know which factors determine CFS patients' amount of health care use. Little is known, however, about these factors. METHOD: The present study retrospectively performed a cross-sectional analysis to investigate the possible factors determining CFS patients' health care use. A total of 263 CFS patients, derived from two subgroups (149 from tertiary care and 114 from primary/secondary care), participated. Health care use was measured with a questionnaire asking details on consumption over the past 6 months. Fatigue severity and physical functioning were measured with the subscale Experienced Fatigue of the Checklist Individual Strength (CIS-20) and the subscale Physical Functioning of the SF-36, respectively. Multiple regression analysis, T-tests, and chi(2) tests were performed. RESULTS: The regression analysis revealed that, after controlling for patient characteristics (explaining 13%), fatigue factors added 4% predictive value and certain perpetuating factors of fatigue, including focus on bodily symptoms and attributions of fatigue, added another 5%. The analysis of subgroups revealed that, compared to the tertiary care population, fewer patients from primary/secondary care had visited a medical specialist (50% vs. 71%), used antidepressants (16% vs. 25%) and tranquilizers (3% vs. 18%), and had spent a night in hospital (7% vs. 10%). However, overall costs of health care between these subgroups did not differ. CONCLUSIONS: This study showed that illness duration, physical impairment due to fatigue, and psychological perpetuating factors of fatigue do determine the variance in CFS patients' health care use. These results give clear directions for treating CFS patients and managing health care for CFS.
Schmitt L, Faure K.	CHU de Toulouse, Hôpital Casselardit, 31059 Toulouse Cedex 9.	[Discussion] [Article in French]	Encephale. 2008 Jun;34 Spec No 2:S21-3.	
Schnakers C, Majerus S, Goldman S, Boly M, Van Eeckhout P, Gay S, Pellas F, Bartsch V, Peigneux P, Moonen G, Laureys S.	Cyclotron Research Center, University of Liège, Belgium. C.Schnakers@student.ulg.ac.be	Cognitive function in the locked-in syndrome.	J Neurol. 2008 Mar;255(3):323-30. Epub 2008 Mar 20.	OBJECTIVE : The lockedin syndrome (LIS) originates from a ventro-pontine lesion resulting in a complete quadraplegia and anarthria. Classically, communication remains possible by means of spared vertical eye movements and/or blinking. To allow assessing cognitive functions in LIS patients, we propose here a neuropsychological testing based on eye-coded communication. METHODS : Ten chronic LIS survivors were assessed 1 to 6 years after their brain insult.One patient was evaluated subacutely (at 2 months) and retested at 6 and 16 months.Neuropsychological testing encompassed short- and long-term memory, attention, executive functioning, phonological and semantic processing and verbal intelligence. RESULTS : None of the patients showed alterations in verbal intelligence. Impairments in one or several tests were found in five patients. In three of these patients, neuropsychological deficits could be related to additional cortical or thalamic structural brain lesions.

				In the other 2 patients, weakness or signs of fatigue only were observed in one or two cognitive tasks. Repeated measures in a subacute patient with pure brainstem lesion indicate the recovery of good levels of cognition 6 months after injury. CONCLUSION : Results indicate that LIS patients can recover intact cognitive levels in cases of pure brainstem lesions, and that additional brain injuries are most likely responsible for associated cognitive deficits in the LIS. Furthermore, a systematic neuropsychological assessment in LIS patients would allow detecting their cognitive deficits,which will contribute to improve their quality of life and of communication with family and medical caretakers.
Schrijvers D, Van Den Eede F, Maas Y, Cosyns P, Hulstijn W, Sabbe BG.	Collaborative Antwerp Psychiatric Research Institute (CAPRI), Faculty of Medicine, University of Antwerp (UA), Universiteitsplein 1, 2610 Antwerp, Belgium.	Psychomotor functioning in chronic fatigue syndrome and major depressive disorder: A comparative study.	J Affect Disord. 2008 Sep 23. [Epub ahead of print]	BACKGROUND: Studies comparing chronic fatigue syndrome (CFS) and major depressive disorder (MDD) reported similarities as well as differences between the two disorders. However, whereas psychomotor symptoms have been studied extensively in MDD, such research in CFS is more limited. Moreover, the few studies that compared cognitive and motor performance in MDD and CFS yielded inconsistent results. This study hence directly compares fine psychomotor functioning in both syndromes. METHODS: Thirty-eight patients diagnosed with CFS without a current major depressive episode (MDE), 32 MDD patients with a current MDE and 38 healthy controls performed two computerized copying tasks differing in complexity: a line-copying task that mainly requires motor effort and a figure-copying task requiring additional cognitive efforts. All participants were female. A multivariate general linear model was used to compute group differences. RESULT: Overall, both patient groups performed more slowly than the controls. Compared to CFS patients, patients with MDD needed significantly more time to copy the single lines but no such between-group performance difference was observed for the figure reproductions. In this latter copying task, the increasing complexity of the figures resulted in prolonged reaction times for all three participant groups with the effect being larger and the magnitude similar for the two patient groups. LIMITATIONS: All patients were female and most were on psychotropic medication. CONCLUSIONS: Both the MDD and CFS patients tested demonstrated an overall fine motor slowing, with the motor component being more affected in the MDD patients than in the CFS patients while both patient groups showed similar cognitive impairments.
Schünemann M, Anker SD, Rauchhaus M.	Division of Applied Cachexia Research, Department of Cardiology, Charité Medical School, Berlin, Germany.	Cancer fatigue syndrome reflects clinically non-overt heart failure: an approach towards onco-cardiology.	Nat Clin Pract Oncol. 2008 Nov;5(11):632-3. Epub 2008 Sep 23.	Publication Types: Review
Schutte NS, Malouff JM, Brown RF.	University of New England, Armidale, NSW, Australia. nschutte@une.edu.au	Efficacy of an emotion-focused treatment for prolonged fatigue.	Behav Modif. 2008 Sep;32(5):699-713. Epub 2008 Apr 16.	Previous research findings have suggested a relationship between less adaptive emotional functioning and fatigue. The present study used a research design involving multiple baselines across participants to evaluate the efficacy of a new emotion-focused treatment for prolonged fatigue delivered in a cognitive behavioral therapy framework. The 13 adults participating in the study met the criteria for prolonged fatigue and provided fatigue baselines of 2, 5, or 8 weeks. The results indicated that the treatment was effective, with fatigue severity levels after the initiation of treatment significantly lower than that predicted by baseline patterns, as determined by the split median method of trend estimation. At 3-4 months after treatment, 8 of 11 clients who completed the treatment no longer

				met the criteria for prolonged fatigue.
Schweinhardt P, Sauro KM, Bushnell MC.	Center for Research on Pain, McGill University.	Fibromyalgia: A Disorder of the Brain?	Neuroscientist. 2008 Feb 12. [Epub ahead of print]	This article presents evidence that fibromyalgia patients have alterations in CNS anatomy, physiology, and chemistry that potentially contribute to the symptoms experienced by these patients. There is substantial psychophysical evidence that fibromyalgia patients perceive pain and other noxious stimuli differently than healthy individuals and that normal pain modulatory systems, such as diffuse noxious inhibitory control mechanisms, are compromised in fibromyalgia. Furthermore, functional brain imaging studies revealing enhanced pain-related activations corroborate the patients' reports of increased pain. Neurotransmitter studies show that fibromyalgia patients have abnormalities in dopaminergic, opioidergic, and serotoninergic systems. Finally, studies of brain anatomy show structural differences between the brains of fibromyalgia patients and healthy individuals. The cerebral alterations offer a compelling explanation for the multiple symptoms of fibromyalgia, including widespread pain and affective disturbances. The frequent comorbidity of fibromyalgia with stress-related disorders, such as chronic fatigue, posttraumatic stress disorder, irritable bowel syndrome, and depression, as well as the similarity of many CNS abnormalities, suggests at least a partial common substrate for these disorders. Despite the numerous cerebral alterations, fibromyalgia might not be a primary disorder of the brain but may be a consequence of early life stress or prolonged or severe stress, affecting brain modulatory circuitry of pain and emotions in genetically susceptible individuals.
Seishima M, Mizutani Y, Shibuya Y, Arakawa C.	Department of Dermatology, Ogaki Municipal Hospital, Ogaki City, Japan. marikoseishima@yahoo.co.jp	Chronic fatigue syndrome after human parvovirus B19 infection without persistent viremia.	Dermatology. 2008;216(4):341-6. Epub 2008 Feb 15.	BACKGROUND: It is unclear how often chronic fatigue syndrome (CFS) appears after human parvovirus B19 (B19) infection and whether prolonged B19 viremia or some other factors cause CFS. OBJECTIVES: To determine how often CFS appears after B19 infection and whether prolonged B19 DNA presence, antibody production and persistently reduced complement levels occur in CFS patients after B19 infection. METHODS: Clinical findings were examined in 210 patients after B19 infection, and CH50, C3 and C4 levels were determined. B19 DNA and antibodies to B19 were also tested in 38 patients' sera including 3 with CFS. RESULTS: Serum B19 DNA disappeared after 4-5 months in all 18 patients tested. There are no differences in B19 DNA-positive period between patients with and without persistent symptoms. IgM antibody titers to B19 became reduced after 2 months in all 38 patients. Complement levels persistently decreased in a greater proportion of patients with persistent symptoms. CONCLUSIONS: The present study suggests that we should consider the possibility of CFS after B19 infection and that CFS may be derived from several aspects other than prolonged B19 DNA presence in sera. Copyright 2008 S. Karger AG, Basel.
Silva-Tinoco R, Castillo-Martínez L, Orea-Tejeda A, Orozco-Gutiérrez JJ, Vázquez-Díaz O, Montaño-Hernández P, Flores-Rebollar A, Reza-Albarrán A.	Heart Failure Clinic, Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán", Mexico City, Mexico.	Developing thyroid disorders is associated with poor prognosis factors in patient with stable chronic heart failure.	Int J Cardiol. 2009 Feb 7. [Epub ahead of print]	We sought to assess the developing of thyroid disorders in forty eight patients with chronic stable heart failure and without thyroid abnormalities during six months follow-up. Thyroid function disorders were observed in 27.1% of the subjects: sick euthyroid syndrome (12.5%), subclinical hypothyroidism (10.4%) and overt hypothyroidism (6.2%). Subjects with higher thyroid stimulating hormone (TSH) levels at the end of the study had more hospitalizations. The developing of altered thyroid profile was related to lower hemoglobin levels, smaller phase angle with bioelectrical impedance method and more fatigue perception by the patients. This abnormal thyroid function behavior on stable chronic heart failure and was observed as part of the disease progress and was associated to worse prognosis factors as lower phase angle and anemia.

Singh BB, Khorsan R, Vinjamury SP.	Medicus Research LLC, Midlothian, Virginia, USA.	Influence of comorbidities on improvement of fibromyalgia symptoms when treated with acupuncture: a short report.	Altern Ther Health Med. 2008 Sep-Oct;14(5):24-5.	BACKGROUND: Fibromyalgia syndrome (FMS) is associated with chronic widespread pain, mood alteration, and disability. A definitive treatment plan has not been identified. The genesis of FMS is unclear and generally occurs in women. PURPOSE: To determine whether patient-identified most disruptive comorbidity (MDC) secondary to FMS may have mediated recovery for individual patients. This is a probative analysis of data from an effectiveness study published in the March 2006 issue of Alternative Therapies in Health and Medicine. (2006;12(2):34-41.) METHODS: The American College ofRheumatology (ACR) criteria for FMS was used in participant selection; 21 participants completed the study. RESULTS: The original outcome study indicated significant changes on standardized measures using specific points and numbers of treatment within an 8-week period. The preliminary data on influence ofMDC on improvement were differential related to self-report MDC by patients. CONCLUSIONS: For all MDCs combined, participants experienced significant improvement at 8 weeks of treatment. Participants with irritable bowel syndrome as their MDC generally had a lower percentage of improvement than other MDC cohort groups. This finding has implications for treatment.
Smith AK, Dimulescu I, Falkenberg VR, Narasimhan S, Heim C, Vernon SD, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MSG41, Atlanta, GA 30333, USA.	Genetic evaluation of the serotonergic system in chronic fatigue syndrome.	Psychoneuroendocrinology. 2008 Feb;33(2):188-97.	Chronic fatigue syndrome (CFS) is a debilitating disorder of unknown etiology with no known lesions, diagnostic markers or therapeutic intervention. The pathophysiology of CFS remains elusive, although abnormalities in the central nervous system (CNS) have been implicated, particularly hyperactivity of the serotonergic (5-hydroxytryptamine; 5-HT) system and hypoactivity of the hypothalamic-pituitary-adrenal (HPA) axis. Since alterations in 5-HT signaling can lead to physiologic and behavioral changes, a genetic evaluation of the 5-HT system was undertaken to identify serotonergic markers associated with CFS and potential mechanisms for CNS abnormality. A total of 77 polymorphisms in genes related to serotonin synthesis (TPH2), signaling (HTR1A, HTR1E, HTR2A, HTR2B, HTR2C, HTR3A, HTR3B, HTR4, HTR5A, HTR6, and HTR7), transport (SLC6A4), and catabolism (MAOA) were examined in 137 clinically evaluated subjects (40 CFS, 55 with insufficient fatigue, and 42 non-fatigued, NF, controls) derived from a population-based CFS surveillance study in Wichita, Kansas. Of the polymorphisms examined, three markers (-1438G/A, C102T, and rs1923884) all located in the 5-HT receptor subtype HTR2A were associated with CFS when compared to NF controls. Additionally, consistent associations were observed between HTR2A variants and quantitative measures of disability and fatigue in all subjects. The most compelling of these associations was with the A allele of -1438G/A (rs6311) which is suggested to have increased promoter activity in functional studies. Further, in silico analysis revealed that the -1438 A allele creates a consensus binding site for Th1/E47, a transcription factor implicated in the development of the nervous system. Electrophoretic mobility shift assay supports allele-specific binding of E47 to the A allele but not the G allele at this locus. These data indicate that sequence variation in HTR2A, potentially resulting in its enhanced activity, may be involved in the pathophysiology of CFS.
Smith AK, Maloney EM, Falkenberg VR, Dimulescu I, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vector-	An angiotensin-1 converting enzyme polymorphism is associated with allostatic load	Psychoneuroendocrinology. 2008 Dec 9. [Epub ahead of print]	Allostatic load (AL) is a theoretical framework that describes the cumulative physiologic effects of adaptation to change or stress throughout the lifespan. AL is operationalized by a composite index of multiple biomarkers. Accordingly, genes, behavior and environment contribute to AL. To determine if individual differences in AL may be influenced by inherent genetic variation, we calculated an allostatic load index (ALI) for 182 Caucasian subjects derived from a population-based study of chronic

	Borne and Enteric Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, MSG41, Atlanta, GA 30333, USA; Department of Human Genetics, Emory University School of Medicine, Atlanta, GA, USA.	mediated by C-reactive protein, interleukin-6 and cortisol.		fatigue syndrome. Nearly 65% of the subjects in this study sample reported fatiguing illness. ALI was calculated based on 11 measures representing metabolic, cardiovascular, inflammatory, hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS) activities. Subjects were dichotomized into high (ALI>/=3) or low (ALI<3) AL groups, and the association between high AL and 129 polymorphisms in 32 genes related to the HPA axis, neurotransmission, inflammation, cardiovascular and metabolic functions were evaluated. Polymorphisms in angiotensin-1 converting enzyme (ACE), corticotropin-releasing hormone receptor 1 (CRHR1), and serotonin receptors (HTR3A and HTR4) were associated with AL (p=0.0007-0.0486), but only one polymorphism, rs4968591, in ACE remained significant after correction for multiple comparisons. The T allele of ACE rs4968591 was more common in subjects with high AL (67.5%) than in subjects with low AL (49.3%) (p=0.0007), and this effect appeared independent of age, sex, body mass index and fatigue status. Additionally, high interleukin-6 (IL-6; p(trend)=0.04), and C-reactive protein (CRP; p(trend)=0.01) levels, as well as low urinary cortisol levels in females (p=0.03) were associated with the T allele, which may result in allele-specific binding of the transcription factor, E2F1. Our results suggest a role for ACE in the bidirectional communication between the central nervous and immune systems in response to stress. Further studies will be needed (a) to replicate the association between AL and ACE polymorphisms in population studies designed to differentiate the effects of sex, age and racial/ethnic background, (b) to evaluate the effect of allele-specific binding of E2F1 at rs4968591, and (c) to examine the role of ACE in the co-regulation of CRP, IL-6 and cortisol.
Smits BW, Smeitink JA, van Engelen BG.	Universitair Medisch Centrum St Radboud, Postbus 9101, 6500 HB Nijmegen. b.smits@neuro.umcn.nl	[Mitochondrial diseases; thinking beyond organ specialism necessary] [Article in Dutch]	Ned Tijdschr Geneeskd. 2008 Oct 18;152(42):2275-81. Comment on: Ned Tijdschr Geneeskd. 2008 Oct 18;152(42):2298-301.	Mitochondrial disorders are caused by a defect in intracellular energy production. In general, these are multi-system disorders, predominantly affecting organs with high energy requirements. Due to the fact that mitochondrial disorders are not as rare as is generally assumed, and due to the diversity of symptoms, many different medical specialists will at some time be confronted with these patients. Early recognition ofa mitochondrial disorder reduces patient anxiety and avoids unnecessary ancillary investigations and potentially hazardous treatments. A mitochondrial disease should be considered in the event of dysfunction of more than 2 organ systems or processes with high energy requirements, certainly if there is a positive maternal family history. If fatigue includes exercise-induced muscle pain or muscle weakness, and if muscle pain predominantly occurs during exertion, a mitochondrial disease should be considered. The combination ofdiabetes mellitus and deafness is also a strong indicator of mitochondrial disease. An extensive family history should always be taken. In adults, the most frequently occurring mitochondrial syndromes are chronic progressive external ophthalmoplegia (CPEO), maternally inherited diabetes and deafness syndrome (MIDDS) and Leber's hereditary optic neuropathy. Since much research effort is currently being invested in the development of causal medical treatments, the importance of an early diagnosis is likely to become of increasing importance in the future.
Sohl SJ, Friedberg F.	Psychology Department, Stony Brook University, New York, USA.	Memory for fatigue in chronic fatigue syndrome: relationships to fatigue variability,	Behav Med. 2008 Spring;34(1):29-38.	Fatigue in chronic fatigue syndrome (CFS) is usually assessed with retrospective measures rather than real-time momentary symptom assessments. In this study, the authors hypothesized that in participants with CFS, discrepancies between recalled and momentary fatigue would be related to catastrophizing, anxiety, and depression and to variability of momentary fatigue. They also expected that catastrophizing, anxiety, and depression would be associated with momentary fatigue. The

		catastrophizing, and negative affect.		authors asked 53 adults with CFS to carry electronic diaries for 3 weeks and record their experiences of momentary fatigue. The authors assessed participants' fatigue recall with weekly ratings and administered questionnaires for catastrophizing, depression, and anxiety. Recall discrepancy was significantly related to the variability of momentary fatigue. In addition, catastrophizing, depression, and momentary fatigue were all significantly related to recall discrepancy. Catastrophizing, depression, anxiety, and momentary negative affect were all significantly associated with momentary fatigue. The findings suggest that momentary fatigue in patients with CFS is related to modifiable psychological factors.
Soleo L, Manghisi MS, Panuzzo L, Meliddo G, Lasorsa G, Pesola G, Drago I, Lovreglio P, Urbano ML, Basso A, Ferrara F, Serra R, Gardi S, Savarese MA, Livrea P.	Dipartimento di Medicina Interna e Medicina Pubblica, Sezione di Medicina del Lavoro E.C. Vigliani, Università di Bari, Italy. l.soleo@medlav.uniba.it	[Sleep disorders in cement workers] [Article in Italian]	G Ital Med Lav Ergon. 2008 Jul-Sep;30(3):283-90.	Obstructive Sleep Apnea Syndrome (OSAS) and Excessive Daytime Sleepiness (EDS) are sleep disorders which can increase cardiovascular risk. An health survey was performed on the cement workers to estimate the prevalence of sleep disorders and to investigate occupational, personal and health risk factors that could influence it. A total of 761 male workers, employed at 10 different cement plants of South Italy and Sicily, were examined. All subjects gave informed consent to take part in the survey. The following questionnaires were administered: Berlin Questionnaire to estimate the high risk of OSAS, Epworth Sleepiness Scale for EDS, a questionnaire posing questions about working conditions, personal characteristic, lifestyle, past history of disease and present illness. Statistical analysis was performed with the statistical package SPSS. The prevalence of high risk of OSAS and of EDS resulted respectively in 24.2% and 3.4% of workers. Sleep disorders detected with the two questionnaires were significantly associated. A positive and significant association between OSAS and respectively age, time of employment, BMI, ex-smoker status, neck, waist or hip circumferences, chronic fatigue and arterial hypertension was observed. Subjective variables regarding working conditions (job interest, evaluation oforganization of work and job satisfaction) and alcohol consumption were not associated with the high risk of OSAS. Shift work (2 and 3 shifts) was not associated with the high risk of OSAS. An healthy worker effect was observed for workers who changed from shift work (2 or 3 shifts) to fixed daytime work. For them, this change to fixed daytime work was conditioned by chronic disease like hypertension and obesity. EDS was not dependent, associated or correlated with any of the occupational, personal or pathologic variables investigated in the study. In conclusion the research showed no relationship between working conditions, particularly shift work, and the high risk of OSAS, and the influence of obesity in determining the high risk of OSAS, itself a potential cardiovascular risk factor. The interest of occupational physician has been focused on introducing in health surveillance also measures of health promotion regarding sleep disorders with the aim of preserving health condition in workers.
Sorensen B, Jones JF, Vernon SD, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vector-Borne, and Enteric Diseases, Centers for Disease Control	Transcriptional control of complement activation in an exercise model of chronic fatigue syndrome.	Mol Med. 2009 Jan-Feb;15(1-2):34-42. Epub 2008 Nov 10.	Complement activation resulting in significant increases of C4a split product may be a marker of postexertional malaise in individuals with chronic fatigue syndrome (CFS). This study focused on identification of the transcriptional control that may contribute to the increased C4a in CFS subjects after exercise. We used quantitative reverse-transcription polymerase chain reaction to evaluate differential expression of genes in the classical and lectin pathways in peripheral blood mononuclear cells (PBMCs). Calibrated expression values were normalized to the internal reference gene peptidylpropyl isomerase B (PPIB), the external reference gene ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit (rbcL), or the geometric mean (GM) of the genes ribosomal

	and Prevention, Atlanta, Georgia 30333, United States of America.			protein, large, P0 (RPLP0) and phosphoglycerate kinase 1 (PGK1). All nine genes tested, except mannose-binding lectin 2 (MBL2), were expressed in PBMCs. At 1 hour postexercise, C4, mannan-binding lectin serine protease 2 (MASP2) and ficolin 1 (FCN1) transcripts were detected at higher levels (> or = 2-fold) in at least 50% (4 of 8) of CFS subjects and were detected in 88% (7 of 8) CFS subjects when subjects with overexpression of either C4 or MASP2 were combined. Only an increase in the MASP2 transcript was statistically significant (PPIB, P = 0.001; GM, P = 0.047; rbcL, P = 0.045). This result may be due to the significant but transient downregulation of MASP2 in control subjects (PPIB, P = 0.023; rbcL, P = 0.027). By 6 hours postexercise, MASP2 expression was similar in both groups. In conclusion, lectin pathway responded to exercise differentially in CFS than in control subjects. MASP2 down-regulation may act as an antiinflammatory acute-phase response in healthy subjects, whereas its elevated level may account for increased C4a and inflammation-mediated postexertional malaise in CFS subjects.
Spence VA, Kennedy G, Belch JJ, Hill A, Khan F.	Vascular and Inflammatory Diseases Research Unit, Institute for Cardiovascular Research, Ninewells Hospital and Medical School, University of Dundee, Dundee DD1 9SY, Scotland, UK.	Low-grade inflammation and arterial wave reflection in patients with chronic fatigue syndrome.	Clin Sci (Lond). 2008 Apr;114(8):561-6.	Some of the symptoms reported by people with CFS (chronic fatigue syndrome) are associated with various cardiovascular phenomena. Markers of cardiovascular risk, including inflammation and oxidative stress, have been demonstrated in some patients with CFS, but little is known about the relationship between these and prognostic indicators of cardiovascular risk in this patient group. In the present study, we investigated the relationship between inflammation and oxidative stress and augmentation index, a measure of arterial stiffness, in 41 well-characterized patients with CFS and in 30 healthy subjects. AIx@75 (augmentation index normalized for a heart rate of 75 beats/min) was significantly greater in patients with CFS than in control subjects (22.5+/-1.7 compared with 13.3+/-2.3% respectively; P=0.002). Patients with CFS also had significantly increased levels of CRP (C-reactive protein) (2.58+/-2.91 compared with 1.07+/-2.16 mug/ml respectively; P<0.01) and 8-iso-prostaglandin F(2alpha) isoprostanes (470.7+/-250.9 compared with 331.1+/-97.6 pg/ml respectively; P<0.005). In patients with CFS, AIx@75 correlated significantly with logCRP (r=0.507, P=0.001), isoprostanes (r=0.366, P=0.026), oxidized LDL (low-density lipoprotein) (r=0.333, P=0.039) and systolic blood pressure (r=0.371, P=0.017). In a stepwise multiple regression model, including systolic and diastolic blood pressure, body mass index, CRP, tumour necrosis factor-alpha, interleukin-1, oxidized LDL, high-density lipoprotein-cholesterol levels, isoprostanes, age and gender, AIx@75 was independently associated with logCRP (beta=0.385, P=0.006), age (beta=0.363, P=0.022) and female gender (beta=0.302, P=0.03) in patients with CFS. The combination of increased arterial wave reflection, inflammation and oxidative stress may result in an increased risk of future cardiovascular events. Assessment of arterial wave reflection might be useful for determining cardiovascular risk in this patient group.
Staud R.	Department of Medicine, University of Florida College of Medicine, PO Box 100221, D2-39, Gainesville, FL	Autonomic dysfunction in fibromyalgia syndrome: postural orthostatic tachycardia.	Curr Rheumatol Rep. 2008 Dec;10(6):463-6.	Although fibromyalgia (FM) syndrome is defined by chronic widespread pain and tenderness, additional symptoms, including disabling fatigue and dizziness, are often reported by patients with this chronic illness. Although nonrestorative sleep may play an important role for chronic fatigue in FM, other mechanisms, including dysfunction of the autonomic nervous system (ANS), need to be considered. Many important biological functions, such as heart rate, blood pressure, respirations, and bowel function, are tightly regulated by the ANS. However, dysfunction of the ANS is common in FM and often becomes quite apparent after positional changes from supine to upright. Although such

	32610, USA. staudr@ufl.edu			positional changes sometimes result in syncope, they are more often associated with palpitations and dizziness. Head-up tilt table testing can be used to evaluate autonomic dysfunction and is frequently helpful for the work-up of FM complaints, including fatigue, dizziness, and palpitations. One of the most common events experienced by FM patients during tilt table testing is postural orthostatic tachycardia syndrome, which is defined as a heart rate increase of more than 30 beats per minute after more than 3 minutes of standing upright.
Stubhaug B, Lie SA, Ursin H, Eriksen HR.	Division of Psychiatry, Haukeland University Hospital, N-5021 Bergen, Norway. bjarte.stubhaug@helse-bergen.no	Cognitive-behavioural therapy v. mirtazapine for chronic fatigue and neurasthenia: randomised placebo-controlled trial.	Br J Psychiatry. 2008 Mar;192(3):217-23.	BACKGROUND: Single interventions in chronic fatigue syndrome have shown only limited effectiveness, with few studies of comprehensive treatment programmes. AIMS: To examine the effect of a comprehensive cognitive-behavioural treatment (CCBT) programme compared with placebo-controlled mirtazapine medication in patients with chronic fatigue, and to study the effect of combined medication and CCBT. METHOD: A three-armed randomised clinical trial of mirtazapine, placebo and a CCBT programme was conducted to investigate treatment effect in a patient group (n=72) with chronic fatigue referred to a specialist clinic. The CCBT programme was compared with mirtazapine or placebo therapy for 12 weeks, followed by 12 weeks treatment with a mixed crossover-combination design. Assessments were done at 12 weeks and 24 weeks. RESULTS: By 12 weeks the treatment effect was significantly better in the group initially receiving CCBT, as assessed with the Fatigue Scale (P=0.014) and the Clinical Global Impression Scale (P=0.001). By 24 weeks the treatment group initially receiving CCBT for 12 weeks followed by mirtazapine for 12 weeks showed significant improvement compared with the other treatment groups on the Fatigue Scale (P<0.001) and the Clinical Global Impression Scale (P=0.002). Secondary outcome measures showed overall improvement with no significant difference between treatment groups. CONCLUSIONS: Multimodal interventions may have positive treatment effects in chronic fatigue syndrome. Sequence of interventions seem to be of importance.
Sullivan A, Nord CE, Evengård B.	Division of Clinical Microbiology, F82, Department of Laboratory Medicine, Karolinska University Hospital Huddinge, Karolinska Institutet, SE-14186 Stockholm, Sweden. asa.sullivan@ki.se	Effect of supplement with lactic-acid producing bacteria on fatigue and physical activity in patients with chronic fatigue syndrome.	Nutr J. 2009 Jan 26;8:4.	Disturbances in intestinal microbial ecology and in the immune system of the host have been implicated as a part of the pathogenesis in chronic fatigue syndrome. Probiotic lactic acid producing bacteria have been shown to prevent and alleviate gastrointestinal disturbances and to normalize the cytokine profile which might be of an advantage for patients suffering from chronic fatigue syndrome. The aim of the study was to evaluate the effect of Lactobacillus paracasei ssp. paracasei F19, Lactobacillus acidophilus NCFB 1748 and Bifidobacterium lactis Bb12 on fatigue and physical activity in CFS patients. Fifteen patients fulfilling the criteria set by international researchers in the field at the US Centre for Disease Control and Prevention in 1994 for chronic fatigue syndrome, were included in the study. The patients had high fatigue severity scores and high disability scores. During the first two weeks baseline observations without treatment were assessed, succeeded by four weeks of intake of a probiotic product and a four-week follow-up period. The fatigue, health and physical activity was assessed by the use of the Visual Analogue Scales and the SF-12 Health Survey. Faecal samples were collected and the normal microflora was analysed. Neurocognitive functions improved during the study period while there were no significant changes in fatigue and physical activity scores. No major changes occurred in the gastrointestinal microflora. At the end of the study 6 of 15 patients reported that they had improved according to the assessment described. The findings in this study that improvement of health is possible to achieve should encourage further studies with interventions with

				probiotics in patients with CFS.
Swoboda DA.	City University of New York, USA. dswoboda@york.cuny.edu	Negotiating the diagnostic uncertainty of contested illnesses: physician practices and paradigms.	Health (London). 2008 Oct;12(4):453-78.	In the absence of scientific consensus about contested illnesses such as Chronic Fatigue Syndrome (CFS), Multiple Chemical Sensitivities (MCS), and Gulf War Syndrome (GWS), physicians must make sense of competing accounts and develop practices for patient evaluation. A survey of 800 United States physicians examined physician propensity to diagnose CFS, MCS, and GWS, and the factors shaping clinical decision making. Results indicate that a substantial portion of physicians, including nonexperts, are diagnosing CFS, MCS, and GWS. Diagnosing physicians manage the uncertainty associated with these illnesses by using strategies that enhance bounded rationality and aid in thinking beyond current disease models. Strategies include consulting ancillary information sources, conducting analytically informed testing, and considering physiological explanations of causation. By relying on these practices and paradigms, physicians fit CFS, MCS, and GWS into an explanatory system that makes them credible and understandable to them, their patients, and the medical community. Findings suggest that physicians employ rational decision making for diagnosing contested illnesses, creating a blueprint of how illnesses lacking conclusive pathogenic and etiological explanations can be diagnosed. Findings also suggest that patients with contested illnesses might benefit from working with physicians who use these diagnostic strategies, since they help manage the complexity and ambiguity of the contested illness diagnostic process and aid in diagnosis. In addition, findings provide a window into how emerging illnesses get diagnosed in the absence of medical and scientific consensus, and suggest that diagnosing physicians advance the legitimacy of controversial illnesses by constructing the means for their diagnosis.
Teisan A.	His Wheels International, USA. info@hiswheelsintl.org	My story. God supplies in illness, income, and insurance loss.	J Christ Nurs. 2008 Jan-Mar;25(1):41-3, 45.	PMID: 18846744 [PubMed - indexed for MEDLINE]
ter Wolbeek M, van Doornen LJ, Kavelaars A, Heijnen CJ.	Laboratory of Psychoneuroimmunology, University Medical Center Utrecht, 3508 AB Utrecht, The Netherlands.	Predictors of persistent and new-onset fatigue in adolescent girls.	Pediatrics. 2008 Mar;121(3):e449-57.	OBJECTIVE: The purpose of this study was to investigate the stability of fatigue in adolescents and to explore whether psychological, somatic, and lifestyle factors are involved in the onset and persistence of fatigue during adolescence. METHODS: In this longitudinal study, a total of 653 adolescent girls (aged 14.40 +/- 1.45 years) who previously participated in an epidemiological study filled out questionnaires 6 (T2) and 12 (T3) months after the initial assessment (T1). Fatigue severity, depression, anxiety, and chronic fatigue syndrome-related symptoms were assessed. We determined the prevalence of severely fatigued cases at T2 and T3 and evaluated whether persistently fatigued participants initially differed from nonfatigued participants and participants with transient fatigue. We examined which factors predicted the development of new-onset fatigue and investigated whether changes in fatigue covaried with changes in other complaints and changes in lifestyle. RESULTS: Of all participants who were severely fatigued at T1, 25.7% were persistently fatigued throughout the study. Persistently fatigued participants had higher levels of depression and anxiety at the beginning of the study, were less physically active, and slept shorter. New-onset fatigue was predicted by depression, less physical activity, and more nightlife activities. Interestingly, new onset was not predicted by initial levels of fatigue. Persistently fatigued participants did not differ in initial fatigue severity from short-term fatigued patients. A decrease in fatigue severity was associated with a decrease in depression,

				anxiety, and chronic fatigue syndrome-related symptoms and, to a lesser extent, with an increase in physical activity and sleep duration. CONCLUSIONS: The stability of severe fatigue among adolescents is substantial. The involvement in the onset and persistence of fatigue suggests that both preventive and therapeutic strategies with respect to fatigue treatment in adolescents should concentrate on emotional well-being. Moreover, adolescents at risk should be stimulated to spend more time on physical activities and to sleep longer.
ter Wolbeek M, van Doornen LJ, Schedlowski M, Janssen OE, Kavelaars A, Heijnen CJ.	Laboratory of Psychoneuroimmunology, University Medical Center Utrecht, The Netherlands.	Glucocorticoid sensitivity of immune cells in severely fatigued adolescent girls: a longitudinal study.	Psychoneuroendocrinology. 2008 Apr;33(3):375-85. Epub 2008 Jan 31.	Fatigue during adolescence is associated with somatic and psychological complaints that resemble the pattern of symptoms described for chronic fatigue syndrome (CFS). Studies in CFS and other stress-related syndromes suggested a dysfunction of the interactions between the hypothalamic-pituitary-adrenal axis (HPA-axis) and the immune system, i.e. a changed glucocorticoid (GC) receptor sensitivity of immune cells, to exist. Here we investigated whether severely fatigued girls from a healthy population have altered cortisol production and immune cell sensitivity for the synthetic GC, dexamethasone (DEX). In a longitudinal design, we examined ex vivo DEX sensitivity of monocytes and of T-cell mitogen-induced responses of severely fatigued (N=65) and non-fatigued girls (N=60). Fatigued girls reported more severe comorbid complaints than non-fatigued participants across three measurements during 1 year (T1: spring, T2: autumn, T3: spring) and had higher plasma cortisol levels throughout the study. DEX sensitivity of T-cell mitogen-induced responses showed seasonal variation with increased sensitivity in autumn compared to spring. No systematic variation of monocyte glucocorticoid receptor (GR) sensitivity was observed. Significant rank correlations of DEX sensitivity of T-cell mitogen-induced responses between the three assessments during the year suggest a stable trait of immune function. Groups did not differ in DEX sensitivity on any of the read outs. However, in a persistently fatigued subgroup, sensitivity to DEX was significantly reduced on the level of interferon (IFN)-gamma production. These results show that although fatigued participants had severe (comorbid) complaints, only in the case when symptoms persisted, altered GC sensitivity of immune cells was observed.
Thambirajah AA, Sleigh K, Stiver HG, Chow AW.	Department of Biochemistry and Microbiology,University of Victoria, Victoria, Canada.	Differential heat shock protein responses to strenuous standardized exercise in chronic fatigue syndrome patients and matched healthy controls.	Clin Invest Med. 2008 Dec 1;31(6):E319-27.	PURPOSE: Since physical exertion is known to exacerbate the symptoms of chronic fatigue syndrome (CFS) and metabolic changes and including oxidative stress can modulate heat shock protein (HSP) expression responses, we sought to determine whether HSP expression is altered in CFS patients before and after exercise. Heat shock proteins (HSPs) in peripheral blood mononuclear cells (PBMC) were examined from 6 chronic fatigue syndrome (CFS) patients and 7 controls before and after a standardized treadmill exercise. Basal hsp27 was significantly higher among CFS patients compared to controls, and decreased immediately post-exercise, remaining below basal levels even at 7 days. A similar pattern was observed for HSP60, which gradually decreased in CFS patients but increased in controls post-exercise. These findings suggest an abnormal adaptive response to oxidative stress in CFS, and raise the possibility that HSP profiling may provide a more objective biologic marker for this illness. METHODS: HSP27, HSP60, HSP70 and HSP90 expression from 6 CFS patients and 7 age- and sex-matched controls were examined by western blot analysis of peripheral blood mononuclear cells immediately before, after, and at 1 day and 7 days following a standardized treadmill exercise. RESULTS: Basal HSP27 was higher among CFS patients than in controls (0.54 +/- 0.13 vs. 0.19 +/- 0.06, mean +/- SEM; $P < 0.01$). In addition, these levels in CFS patients decreased immediately post-exercise

				(0.25 +/- 0.09; P < 0.05) and remained below basal levels at day 1 post-exercises (0.18 +/- 0.05; P < 0.05). P < 0.05). This declining expression of HSP27 during the post-exercise period among CFS patients was confirmed by one-way ANOVA analysis with repeated measures (P < 0.05). In contrast, HSP27 levels remained relatively constant following exercise among control subjects. Similar patterns of declining HSP levels in CFS patients were also observed for HSP60 (0.94 +/- 0.40 vs. 1.32 +/- 0.46; P < 0.05), and for HSP90 (0.34 +/- 0.09 vs. 0.49 +/- 0.10; P < 0.05) at day 7 post-exercise compared with basal levels, respectively. In contrast, HSP60 levels in control subjects increased at day 1 (1.09 +/- 0.27) and day 7 (1.24 +/- 0.50) post-exercise compared to corresponding levels immediately post-exercise (0.55 +/- 0.06) (P < 0.05, respectively). CONCLUSION: These preliminary findings suggest an abnormal or defective adaptive response to oxidative stress in CFS, and raise the possibility that HSP profiling may provide a more objective biologic marker for this illness.
Thompson EA, Mathie RT, Baitson ES, Barron SJ, Berkovitz SR, Brands M, Fisher P, Kirby TM, Leckridge RW, Mercer SW, Nielsen HJ, Ratsey DH, Reilly D, Roniger H, Whitmarsh TE.	Bristol Homeopathic Hospital, Bristol, UK. elizabeth.thompson@ubht.nhs.uk	Towards standard setting for patient-reported outcomes in the NHS homeopathic hospitals.	Homeopathy. 2008 Jul;97(3):114-21.	INTRODUCTION: We report findings from a pilot data collection study within a programme of quality assurance, improvement and development across all five homeopathic hospitals in the UK National Health Service (NHS). AIMS: (1) To pilot the collection of clinical data in the homeopathic hospital outpatient setting, recording patient-reported outcome since first appointment; (2) to sample the range of medical complaints that secondary-care doctors treat using homeopathy, and thus identify the nature and complexity of complaints most frequently treated nationally; (3) to present a cross section of outcome scores by appointment number, including that for the most frequently treated medical complaints; (4) to explore approaches to standard setting for homeopathic practice outcome in patients treated at the homeopathic hospitals. METHODS: A total of 51 medical practitioners took part in data collection over a 4-week period. Consecutive patient appointments were recorded under the headings: (1) date of first appointment in the current series; (2) appointment number; (3) age of patient; (4) sex of patient; (5) main medical complaint being treated; (6) whether other main medical complaint(s); (7) patient-reported change in health, using Outcome Related to Impact on Daily Living (ORIDL) and its derivative, the ORIDL Profile Score (ORIDL-PS; range, -4 to +4, where a score <or=-2 or >or=+2 indicates an effect on the quality of a patient's daily life); (8) receipt of other complementary medicine for their main medical complaint. RESULTS: The distribution of patient age was bimodal: main peak, 49 years; secondary peak, 6 years. Male:female ratio was 1:3.5. Data were recorded on a total of 1797 individual patients: 195 first appointments, 1602 follow-ups (FUs). Size of clinical service and proportion of patients who attended more than six visits varied between hospitals. A total of 235 different medical complaints were reported. The 30 most commonly treated complaints were (in decreasing order of frequency): eczema; chronic fatigue syndrome (CFS); menopausal disorder; osteoarthritis; depression; breast cancer; rheumatoid arthritis; asthma; anxiety; irritable bowel syndrome; multiple sclerosis; psoriasis; allergy (unspecified); fibromyalgia; migraine; premenstrual syndrome; chronic rhinitis; headache; vitiligo; seasonal allergic rhinitis; chronic intractable pain; insomnia; ulcerative colitis; acne; psoriatic arthropathy; urticaria; ovarian cancer; attention-deficit hyperactivity disorder (ADHD); epilepsy; sinusitis. The proportion of patients with important co-morbidity was higher in those seen after visit 6 (56.9%) compared with those seen up to and including that point (40.7%; P<0.001). The proportion of FU patients reporting ORIDL-PS>or=+2 (improvement affecting daily living) increased overall with appointment number: 34.5% of patients at visit 2 and

				59.3% of patients at visit 6, for example. Amongst the four most frequently treated complaints, the proportion of patients that reported ORIDL-PS>or=+2 at visit numbers greater than 6 varied between 59.3% (CFS) and 73.3% (menopausal disorder). CONCLUSIONS: We have successfully piloted a process of national clinical data collection using patient-reported outcome in homeopathic hospital outpatients, identifying a wide range and complexity of medical complaints treated in that setting. After a series of homeopathy appointments, a high proportion of patients, often representing "effectiveness gaps" for conventional medical treatment, reported improvement in health affecting their daily living. These pilot findings are informing our developing programme of standard setting for homeopathic care in the hospital outpatient context.
Togo F, Natelson BH, Cherniack NS, FitzGibbons J, Garcon C, Rapoport DM.	Pain and Fatigue Study Center, Department of Neurosciences, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, 30 Bergen Street, Newark, NJ 07103, USA. tougou@p.u-tokyo.ac.jp	Sleep structure and sleepiness in chronic fatigue syndrome with or without coexisting fibromyalgia.	Arthritis Res Ther. 2008;10(3):R56. Epub 2008 May 13.	INTRODUCTION: We evaluated polysomnograms of chronic fatigue syndrome (CFS) patients with and without fibromyalgia to determine whether patients in either group had elevated rates of sleep-disturbed breathing (obstructive sleep apnea or upper airway resistance syndrome) or periodic leg movement disorder. We also determined whether feelings of unrefreshing sleep were associated with differences in sleep architecture from normal. METHODS: We compared sleep structures and subjective scores on visual analog scales for sleepiness and fatigue in CFS patients with or without coexisting fibromyalgia (n = 12 and 14, respectively) with 26 healthy subjects. None had current major depressive disorder, and all were studied at the same menstrual phase. RESULTS: CFS patients had significant differences in polysomnograpic findings from healthy controls and felt sleepier and more fatigued than controls after a night's sleep. CFS patients as a group had less total sleep time, lower sleep efficiency, and less rapid eye movement sleep than controls. A possible explanation for the unrefreshing quality of sleep in CFS patients was revealed by stratification of patients into those who reported more or less sleepiness after a night's sleep (a.m. sleepier or a.m. less sleepy, respectively). Those in the sleepier group reported that sleep did not improve their symptoms and had poorer sleep efficiencies and shorter runs of sleep than both controls and patients in the less sleepy group; patients in the less sleepy group reported reduced fatigue and pain after sleep and had relatively normal sleep structures. This difference in sleep effects was due primarily to a decrease in the length of periods of uninterrupted sleep in the a.m. sleepier group. CONCLUSION: CFS patients had significant differences in polysomnographic findings from healthy controls and felt sleepier and more fatigued than controls after a night's sleep. This difference was due neither to diagnosable sleep disorders nor to coexisting fibromyalgia but primarily to a decrease in the length of periods of uninterrupted sleep in the patients with more sleepiness in the morning than on the night before. This sleep disruption may explain the overwhelming fatigue, report of unrefreshing sleep, and pain in this subgroup of patients.
Travers MK, Lawler J.	Faculty of Nursing & Midwifery, University of Sydney, Australia. mtravers@nursing.usyd.edu.au	Self within a climate of contention: Experiences of chronic fatigue syndrome.	Soc Sci Med. 2008 Jan;66(2):315-26. Epub 2007 Oct 24.	Chronic fatigue syndrome (CFS) is a contested condition associated with scepticism and dispute. This qualitative project examines the illness experiences, and specifically the experiences of self, for people affected with CFS living in Australia. Using grounded theory methods, theory related to the process of self-renewal and adaptation associated with CFS is explicated. Narratives were derived from semi-structured interviews with 19 adults, including 3 people recovered from CFS. Analysis generated the narrative of the struggling self seeking renewal that defined the illness experience of CFS. The struggling self articulated the negative effects to self and personhood associated with CFS, defined as the violation of self, and the consequent efforts of participants to manage symptoms and decrease

				their violation by use of what was termed the Guardian Response and the Reconstructing Response. The Guardian Response provided protection and self-reclamation. The Reconstructing Response fostered self-renewal and meaning. The struggling self occurred within a climate of threats, and it was these threats which provided the catalyst for violation and the responses. Under different conditions the relative strengths of violation, guardianship or reconstruction fluctuated, and it was these fluctuations that presented the participants with the ongoing struggle of CFS.
Turk Charles S, Gatz M, Kato K, Pedersen NL.	Department of Psychology, University of California, Irvine, CA 92697-7085, USA. scharles@uci.edu	Physical health 25 years later: the predictive ability of neuroticism.	Health Psychol. 2008 May;27(3):369-78.	OBJECTIVE: Neuroticism, a personality trait related to distress and emotional stability, is often correlated with physical symptoms and disease presence. Theorists have posited that chronic emotional instability creates physiological changes detrimental to health, yet most findings are based on cross-sectional analyses. The objective of the current study was to examine neuroticism assessed in 1973 and the likelihood of reporting physical conditions 25 years later. DESIGN: Participants included 21676 adult twins (n = 8143 intact twin pairs) ranging from 15 to 47 years old in 1973 who were assessed again between 1998 and 2002. MAIN OUTCOME MEASURES: Thirteen physical conditions, including chronic fatigue syndrome, ulcers, and coronary heart disease, were selected based on their prior theoretical and empirical links to personality traits. RESULTS: Results indicate that the likelihood of having a physical condition is related to higher levels of prior neuroticism, with some associations attenuated when controlling for familial similarity. CONCLUSION: Familial influences are most pronounced for conditions most related to systemic pain, suggesting genetic pathways between neuroticism and these pain experiences.
Uçeyler N, Offenbächer M, Petzke F, Häuser W, Sommer C.	Department of Neurology, University of Würzburg Germany.	New treatment options for fibromyalgia: critical appraisal of duloxetine.	Neuropsychiatr Dis Treat. 2008 Jun;4(3):525-9.	Fibromyalgia syndrome (FMS) is a chronic condition characterized by widespread pain, tender points, fatigue, and sleep disturbance. FMS leads to high disability levels, poor quality of life, and extensive use of medical care. Effective pharmacological treatment options are rare, and treatment effects are often of limited duration. Duloxetine is a new selective serotonin and norepinephrine reuptake inhibitor that is licensed for the treatment of pain in diabetic neuropathy. So far two randomized, placebo-controlled trials have investigated the short-term safety and efficacy of duloxetine 60 mg/day and 120 mg/day in patients suffering from FMS over a period of 12 weeks. Both dosages were superior to placebo in pain relief, and improvement in quality of life and depressive symptoms. The analgesic effect was largely independent of the antidepressant action of duloxetine. The higher dose of 120 mg/day further reduced the tender point count and elevated the tender point pain thresholds. Only mild to moderate adverse effects were reported. Duloxetine 60 mg/day and 120 mg/day has proven to be beneficial in the treatment of FMS symptoms. As true for other antidepressants further studies are needed to assess the long-term efficacy and safety of duloxetine as an additional pharmacological treatment option in FMS.
Ulvestad E.	Department of Microbiology and Immunology, Haukeland University Hospital, and The Gade Institute,	Chronic fatigue syndrome defies the mind-body-schism of medicine : New perspectives on a multiple realisable	Med Health Care Philos. 2008 Feb 21. [Epub ahead of print]	The article maintains that chronic fatigue syndrome can be properly understood only by taking an integrated perspective in which evolutionary, developmental and ecological aspects are considered. The integrative approach, supplemented by a complexity theory and psychoneuroimmunological research, is capable of explaining why there are so few structural aberrations to be found in chronic fatigue syndrome and why specific treatment is so difficult to establish. A major outcome of the investigation, that all individuals with chronic fatigue syndrome are diseased in their own way, emphasises the need to study the development of personalised life histories. It also highlights an

	University of Bergen, Armauer Hansen Building, Bergen, 5021, Norway, elling.ulvestad@helse-bergen.no.	developmental systems disorder.		ethical dimension; personalised disease defies essentialist thinking on patient management. Another major outcome, which follows from the developmental systems perspective, is the dissolution of ontological mind-body dualism. This in turn allows for a methodological complementation of the biological and phenomenological approaches to knowledge. New research strategies that may help to resolve chronic fatigue syndrome, grounded in the revised perspective on individual development, are suggested.
Valdizán Usón JR, Idiazábal Alecha MA..	Servicio de Neurofisiología Clínica, Hospital Universitario Miguel Servet, Paseo Isabel la Católica 1-3, E-50009 Zaragoza, Spain. jrvaldizan@auna.com	Diagnostic and treatment challenges of chronic fatigue syndrome: role of immediate-release methylphenidate.	Expert Rev Neurother. 2008 Jun;8(6):917-27.	Chronic fatigue syndrome (CFS) is a distinct entity belonging to the group of persistent fatigue that can be challenging to diagnose and to treat. It is characterized by a combination of prolonged fatigue, other nonspecific somatic manifestations and neuropsychological symptoms, including difficulties with concentration, short-term memory and thinking, as well as impaired attention and slowed processing speed. Neurostimulants increasing dopamine and norepinephrine activity, such as bupropion, dextroamphetamine and recently immediate-release methylphenidate have been advocated to improve neurocognitive deficits. The use of immediate-release methylphenidate in CFS has been shown in one small study. Using the positive results of this study and the well-known beneficial effects of the drug on a range of similar cognitive symptoms in attention-deficit/hyperactivity disorder, this perspective addresses CFS and other related disorders and provides a discussion on the potential promising role of methylphenidate in the therapeutic armamentarium of CFS.
van Alfen N, van der Werf SP, van Engelen BG.	Department of Neurology, Neuromuscular Centre Nijmegen, Donders Center for Neuroscience, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. n.vanalfen@neuro.umcn.nl	Long-term pain, fatigue, and impairment in neuralgic amyotrophy.	Arch Phys Med Rehabil. 2009 Mar;90(3):435-9.	OBJECTIVES: Recently, it has become clear that neuralgic amyotrophy (NA; idiopathic and hereditary brachial plexus neuropathy) has a less optimistic prognosis than usually assumed. To optimize treatment and management of these patients, one needs to know the residual symptoms and impairments they suffer. Therefore, the objective of this study was to describe the prevalence of pain, psychologic symptoms, fatigue, functional status, and quality of life in patients with NA. SETTING: Neurology outpatient department of an academic teaching hospital. PARTICIPANTS: NA patients (N=89) were studied, and clinical details were recorded. Self-report data were on average collected 2 years after the onset of the last NA episode. MAIN OUTCOME MEASURES: Pain was assessed with the McGill Pain Questionnaire, fatigue with the Checklist Individual Strength, and psychologic distress with the Symptom Checklist 90. Functional status and handicap were assessed with the modified Rankin Scale and Medical Outcomes Study 36-Item Short-Form Health Survey. RESULTS: Pain was usually localized in the right shoulder and upper arm, matching the clinical predilection site for paresis in NA. About a quarter to a third of the patients reported significant long-term pain and fatigue, and half to two thirds still experienced impairments in daily life. Over one third of the individual patients suffered from severe fatigue. The group did not fulfill the criteria of chronic fatigue or major psychologic distress. There was no correlation of pain or fatigue with the level of residual paresis on a Medical Research Council scale, but patients with a comorbid condition fared worse than patients without. CONCLUSIONS: A significant number of NA patients suffer from persistent pain and fatigue, leading to impairment. Symptoms were not correlated with psychologic distress. This makes it likely that they are caused by residual shoulder or arm dysfunction but not as part of a chronic pain or fatigue syndrome in these patients.
van de Putte EM,	University Medical	Deficits of	Arch Pediatr	Publication Types: Comparative Study

Böcker KB, Buitelaar J, Kenemans JL, Engelbert RH, Kuis W, Kimpen JL, Uiterwaal CS.	Center Utrecht, PO Box 85090, 3508 AB Utrecht, the Netherlands. e.vandeputte@umcutrecht.nl	interference control in adolescents with chronic fatigue syndrome.	Adolesc Med. 2008 Dec;162(12):1196-7.	
Van Den Eede F, Moorkens G.		HPA-axis dysfunction in chronic fatigue syndrome: clinical implications.	Psychosomatics. 2008 Sep-Oct;49(5):450.	
Van Houdenhove B, Luyten P.	Dienst Liaisonpsychiatrie, UZ Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Customizing treatment of chronic fatigue syndrome and fibromyalgia: the role of perpetuating factors.	Psychosomatics. 2008 Nov-Dec;49(6):470-7.	BACKGROUND: Syndromes characterized by chronic, medically unexplained fatigue, effort- and stress-intolerance, and widespread pain are highly prevalent in medicine. RESULTS: In chronic fatigue syndrome (CFS) and fibromyalgia (FM), various perpetuating factors may impair patients' quality of life and functioning and impede recovery. Although cognitive-behavioral and graded-exercise therapy are evidence-based treatments, the effectiveness and acceptability of therapeutic interventions in CFS/FM may largely depend on a customized approach taking the heterogeneity of perpetuating factors into account. CONCLUSION: Further research should clarify the aim and outcome of different treatment strategies in CFS/FM, as well as the underlying mechanisms of change, including those facilitating neurobiological recovery.
van Ittersum MW, van Wilgen CP, Hilberdink WK, Groothoff JW, van der Schans CP.	Hanze University Groningen, University of Applied Sciences, Center for Research and Development in Health Care and in Nursing, Groningen, The Netherlands. m.w.van.ittersum@pl.hanze.nl	Illness perceptions in patients with fibromyalgia.	Patient Educ Couns. 2009 Jan;74(1):53-60. Epub 2008 Sep 23.	OBJECTIVE: Former studies in chronic diseases showed the importance of patients' beliefs and perceptions. The Revised Illness Perception Questionnaire was developed to assess these illness perceptions. Our goal was to investigate psychometric properties of the IPQ-R for Fibromyalgia Dutch language version (IPQ-R FM-Dlv) and to describe illness perceptions of participants with FM. METHODS: 196 patients completed the IPQ-R FM-Dlv. Internal consistency, domain structure and inter domain correlations were calculated and compared to the IPQ-R English language version. Scores were compared with chronic fatigue syndrome (CFS), rheumatoid arthritis (RA), and coronary heart disease (CHD). RESULTS: Most psychometric properties were comparable to those of the original IPQ-R. Participants showed a lack of understanding of their illness, expected their FM to be chronic and to have a lot of negative consequences on functioning. In 17 out of 24 domains significant differences were found between FM and CFS, RA, and CHD patients. CONCLUSION: The IPQ-R FM-Dlv showed acceptable psychometric properties, although some aspects need closer examination. Illness perceptions of FM patients on the Dutch questionnaire were non-comparable to CFS, RA, and CHD patients on the English questionnaire. PRACTICE IMPLICATIONS: The IPQ-R FM-Dlv can be used to assess illness perceptions of Dutch FM patients.
Van Oudenhove L, Vandenberghe J, Geeraerts B, Vos R, Persoons P, Fischler B,	Department of Pathophysiology, Gastroenterology Section, University of Leuven &	Determinants of symptoms in functional dyspepsia: gastric sensorimotor	Gut. 2008 Dec;57(12):1666-73. Epub 2008 Jul 14. Comment in: Gut. 2008	BACKGROUND: Gastric sensorimotor dysfunction, psychosocial factors and somatisation are all implicated in symptom generation in functional dyspepsia (FD). AIM: To determine the relative contribution of each of these factors to overall dyspeptic symptom severity and weight loss in FD. METHODS: In 201 consecutive tertiary care patients with FD (mean age 40.1 (SD 12.6) years), gastric sensorimotor function was studied using barostat (sensitivity, compliance and accommodation).

Demyttenaere K, Tack J.	University Hospital Gasthuisberg, Leuven, Belgium.	function, psychosocial factors or somatisation?	Dec;57(12):1642-3.	Psychosocial factors (depression and anxiety disorders, positive and negative affect, perceived stress, alexithymia and history of abuse), somatisation and co-morbid irritable bowel syndrome (IBS) and chronic fatigue symptoms were assessed using self-report questionnaires. Variables were correlated with dyspepsia symptom severity (DSS) and weight loss. Hierarchical multiple linear regression was used to identify determinants of DSS and weight loss. RESULTS: Multiple linear regression identified the following determinants of DSS: gastric sensitivity (beta = 0.77, p = 0.25), depression (beta = 0.12, p = 0.06) and somatisation (beta = 0.48, p<0.0001) (controlling for age and occupation, R(2) = 0.29, p<0.0001). The effect of depression on DSS is partially mediated by somatisation. Gastric sensitivity (beta = 2.87, p = 0.08), history of childhood sexual abuse (beta = 9.37, p = 0.0006), depression (beta = 0.19, p = 0.24) and somatisation (beta = 0.67, p = 0.01) are independent determinants of weight loss (controlling for gender and occupation, R(2) = 0.42, p<0.0001). The effect of depression on weight loss is fully mediated by somatisation. CONCLUSION: Symptom severity and weight loss in FD are determined by psychosocial factors (depression, abuse history) and somatisation, and only to a lesser extent by gastric sensorimotor function. The importance of psychosocial factors and somatisation compared to gastric sensorimotor function is most pronounced in hypersensitive patients.
van Wilgen CP, Dijkstra PU, Versteegen GJ, Fleuren MJ, Stewart R, van Wijhe M.	Pain Centre, Department of Anesthesiology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands. c.p.van.wilgen@sport.umcg.nl	Chronic pain and severe disuse syndrome: long-term outcome of an inpatient multidisciplinary cognitive behavioural programme.	J Rehabil Med. 2009 Feb;41(3):122-8.	OBJECTIVE: Patients with chronic pain and severe disuse syndrome have pain with physiological, psychological and social adaptations. The duration and severity of complaints, combined with previously failed treatments, makes them unsuitable for treatment in primary care. DESIGN: A prospective waiting list controlled study. PATIENTS: A total of 32 patients with chronic pain for at least one year and severe disuse syndrome were included in an inpatient multidisciplinary cognitive behavioural treatment. METHODS: Patients were assessed before the waiting list period, before the clinical phase, after the clinical phase and after follow-ups of 6 months and one year. The visual analogue scale for pain and fatigue were assessed. Muscle strength of the arms and legs, arm endurance and a 6-minute walking test were used to assess physical outcome. The Symptom Checklist-90, RAND-36, pain cognition list and the Tampa scale for kinesiophobia were used to assess psychological outcome. RESULTS: Long-term significant (p < 0.001) improvements were found for pain, fatigue, walking distance, muscle strength, anxiety, depression, somatization, negative self-efficacy, and catastrophizing in the intervention period. CONCLUSION: An inpatient multidisciplinary cognitive behavioural programme is beneficial for patients with chronic pain and a severe disuse syndrome.
Vasiliauskas D, Kavoliūniene A, Jasiukeviciene L, Grizas V, Statkeviciene A, Leimoniene L, Tumyniene V, Kubilius R.	Institute of Cardiology, Kaunas University of Medicine, Sukileliu 17, 50161 Kaunas, Lithuania. donatas@kmu.lt	[Impact of a long-term complex rehabilitation on chronic fatigue and cardiorespiratory parameters in patients with chronic heart failure] [Article in Lithuanian]	Medicina (Kaunas). 2008;44(12):911-21.	The aim of the study was to evaluate the impact of a long-term rehabilitation on chronic fatigue and cardiorespiratory parameters in patients with chronic heart failure. MATERIAL AND METHODS: One hundred seventy patients with class III-IV (NYHA) chronic heart failure were examined. The study population was divided into two groups: long-term rehabilitation group and control group. They underwent cardiopulmonary exercise test and completed questionnaires on chronic fatigue (MFI-20L, DUFS, and DEFS). Measurements were repeated 3 and 6 months after long-term complex rehabilitation. RESULTS: According to the data of MFI-20L, DUFS, and DEFS questionnaires, 170 patients (100%) with class III-IV (NYHA) chronic heart failure complained of fatigue. Overall daily fatigue was 56.8+/-28.5 points on a 100-point scale, and after 6-month rehabilitation, this parameter was statistically significantly reduced on all scales (P<0.05). Physical fatigue and self-care improved in controls. Cardiopulmonary exercise test showed that parameters of hyperventilation, ventilatory

				equivalents, and pCO2 were significantly improved in rehabilitation group after 6 months as compared to baseline data (P<0.05), but not in the control group. CONCLUSION: Patients with class III-IV (NYHA) chronic heart failure experience chronic fatigue, which reduces their motivation and self-care abilities. Long-term complex rehabilitation programs improve all parameters of chronic fatigue, respiratory efficiency, and prognostic indicator of chronic heart failure--ventilatory equivalent for carbon dioxide.
Veldman J, Van Houdenhove B, Verguts J.	Department of Obstetrics and Gynaecology, University Hospital Gasthuisberg, Catholic University Leuven, Herestraat 49, 3000, Louvain, Belgium.	Chronic fatigue syndrome: a hormonal origin? A rare case of dysmenorrhea membranacea.	Arch Gynecol Obstet. 2008 Sep 12. [Epub ahead of print]	BACKGROUND: Membranous dysmenorrhea is a rare entity involving expulsion of fragments of endometrium retaining the shape of the uterus. The condition is often linked to high progesterone levels. An association with a chronic fatigue syndrome was never described. CASE: A 44-year-old woman with a chronic fatigue syndrome (CFS), presented with membranous dysmenorrhea after taking an oral contraceptive pill containing ethinylestradiol 0.02 mg and desogestrel 0.15 mg for 3 months in a continuous regimen as treatment for dysfunctional bleeding. Oral contraception was discontinued and she resumed normal menstruations. Remarkably, she mentioned complete disappearance of the CFS since expulsion of the tissue and started working again. CONCLUSION: The occurrence of membranous dysmenorrhea with a dissolving chronic fatigue syndrome is very rare and was never described before. This case suggests a hormonal dysfunction as a possible cause of chronic fatigue syndrome. A review of the literature on membranous dysmenorrhea is presented.
Viaene M, Vermeir G, Godderis L.	Department of Occupational, Environmental and Insurance Medicine, Catholic University of Leuven, UZ St. Rafaël, Kapucijnenvoer 35-5th floor, 3000 Leuven, Belgium; Expertise Centre of Neurotoxicology and Neuropsychology, Governmental Psychiatric Hospital, Dr. Sanodreef 4, 2440 Geel, Belgium.	Sleep disturbances and occupational exposure to solvents.	Sleep Med Rev. 2009 Feb 5. [Epub ahead of print]	A solvent can be defined as "a liquid that has the ability to dissolve, suspend or extract other materials, without chemical change to the material or solvent". Numerous chemical or technical processes rely on these specific properties of organic solvents in industry. Occupational exposure to solvents is not rare and some activities may cause substantial exposure to these substances in the workforce. Short-term or acute exposures cause a prenarcotic syndrome, and long lasting exposure conditions have been associated with various neurological and neuropsychiatric disorders, e.g., anosmia, hearing loss, colour vision dysfunctions, peripheral polyneuropathy and depression, but most significantly with the gradual development of an irreversible toxic encephalopathy. For the last 3 decades reports and epidemiological studies have been published reporting sleep disturbances among other complaints, related to long-term exposure to these compounds. In addition, the question has been posed if solvents can be the cause of a sleep apnoea syndrome in exposed workers, or on the contrary, if these workers are misdiagnosed and 'common' sleep apnoea syndromes are the cause of their chronic symptoms of fatigue and memory and attentional disturbances.
Viner RM, Clark C, Taylor SJ, Bhui K, Klineberg E, Head J, Booy R,	General and Adolescent Paediatrics Unit, Institute of Child	Longitudinal risk factors for persistent fatigue in adolescents.	Arch Pediatr Adolesc Med. 2008 May;162(5):469-75.	OBJECTIVE: To examine whether sedentary behavior, obesity, smoking, and depression are risk factors for persistent fatigue in adolescents. DESIGN: Longitudinal population-based survey. SETTING: Twenty-eight randomly selected schools in east London, England, in 2001 and 2003. PARTICIPANTS: A total of 1880 adolescents (49% male; 81% nonwhite British) aged 11 to 12 years and 13 to 14 years in 2000.

Stansfeld SA.	Health, University College London, England. r.viner@ich.ucl.ac.uk			INTERVENTION: Confidential questionnaires completed in class. MAIN OUTCOME MEASURES: Persistent fatigue (extreme tiredness twice weekly or more often in the previous month at both surveys), sedentary behavior, physical activity, depressive symptoms, body mass index, and smoking. RESULTS: Severe fatigue was reported in 11% of participants aged 11 to 14 years and 17% of participants aged 13 to 16 years. Eighty-four participants (4%) reported persistent fatigue. Across both surveys, only 3 pupils reported chronic fatigue syndrome. In multivariate logistic regression, risk of persistent fatigue was independently associated with being sedentary for more than 4 hours per day (odds ratio = 1.6; 95% confidence interval, 1.1-2.3; P = .01), being physically active (odds ratio = 1.5; 95% confidence interval, 1.1-2.3; P = .004), and depressive symptoms (odds ratio = 2.0; 95% confidence interval, 1.5-2.7; P < .001) in the first survey, after adjustment for age, sex, and socioeconomic status. Obesity and smoking were not associated with fatigue. CONCLUSIONS: Persistent fatigue is common. Being highly sedentary or highly active independently increased the risk of persistent fatigue, suggesting that divergence in either direction from healthy levels of activity increases the risk for persistent fatigue. Mental health is important in the etiology of persistent fatigue. To help define effective preventive strategies, further work is needed on the mechanisms by which these factors contribute to fatigue.
Walach H, Bosch H, Lewith G, Naumann J, Schwarzer B, Falk S, Kohls N, Haraldsson E, Wiesendanger H, Nordmann A, Tomasson H, Prescott P, Bucher HC.	Samueli Institute, European Office, School of Social Sciences, University of Northampton, Northampton, UK. harald.walach@northampton.ac.uk	Effectiveness of distant healing for patients with chronic fatigue syndrome: a randomised controlled partially blinded trial (EUHEALS).	Psychother Psychosom. 2008;77(3):158-66. Epub 2008 Feb 14.	BACKGROUND: Distant healing, a form of spiritual healing, is widely used for many conditions but little is known about its effectiveness. METHODS: In order to evaluate distant healing in patients with a stable chronic condition, we randomised 409 patients with chronic fatigue syndrome (CFS) from 14 private practices for environmental medicine in Germany and Austria in a two by two factorial design to immediate versus deferred (waiting for 6 months) distant healing. Half the patients were blinded and half knew their treatment allocation. Patients were treated for 6 months and allocated to groups of 3 healers from a pool of 462 healers in 21 European countries with different healing traditions. Change in Mental Health Component Summary (MHCS) score (SF-36) was the primary outcome and Physical Health Component Summary score (PHCS) the secondary outcome. RESULTS: This trial population had very low quality of life and symptom scores at entry. There were no differences over 6 months in post-treatment MHCS scores between the treated and untreated groups. There was a non-significant outcome (p = 0.11) for healing with PHCS (1.11; 95% CI -0.255 to 2.473 at 6 months) and a significant effect (p = 0.027) for blinding; patients who were unblinded became worse during the trial (-1.544; 95% CI -2.913 to -0.176). We found no relevant interaction for blinding among treated patients in MHCS and PHCS. Expectation of treatment and duration of CFS added significantly to the model. CONCLUSIONS: In patients with CFS, distant healing appears to have no statistically significant effect on mental and physical health but the expectation of improvement did improve outcome. Copyright (c) 2008 S. Karger AG, Basel.
Wang T, Zhang Q, Xue X, Yeung A.	Department of TCM Diagnostics, Preclinical College, Beijing University of Chinese Medicine, Beijing,	A systematic review of acupuncture and moxibustion treatment for chronic fatigue	Am J Chin Med. 2008;36(1):1-24.	Studies on the treatment of chronic fatigue syndrome (CFS) with acupuncture and moxibustion in China were reviewed. All studies concluded the treatments were effective, with response rates ranging from 78.95% to 100%. However, the qualities of the studies were generally poor, and none of them used a RCT design. The common acupoints/sites used in the treatment of CFS, which may reflect the collective experience of acupuncturists in China based on Traditional Chinese Medicine theories can be used to evaluate the effectiveness of acupuncture for the treatment of CFS in future studies

	China 100029, China. tianfangwang@hotmail.com	syndrome in China.		using more scientifically rigorous study designs.
Wang TF, Xue XL.	Department of TCM Diagnostics, Beijing University of Chinese Medicine, Beijing. tianfangwang2000@yahoo.com.cn	[Sub-health state and chronic fatigue syndrome] [Article in Chinese]	Zhongguo Zhong Xi Yi Jie He Za Zhi. 2008 Jan;28(1):77-9.	This paper points out that the sub-health state is not equal to chronic fatigue syndrome (CFS) on basis of elaborating the concept and category of sub-health. And the present understanding on concepts of fatigue, chronic fatigue and CFS, as well as the diagnosis criteria and differential diagnosis of CFS are discussed systematically.
Warren JW, Howard FM, Cross RK, Good JL, Weissman MM, Wesselmann U, Langenberg P, Greenberg P, Clauw DJ.	Department of Medicine, Epidemiology and Preventive Medicine, and Neurology, University of Maryland School of Medicine, Baltimore, Maryland, USA.	Antecedent nonbladder syndromes in case-control study of interstitial cystitis/painful bladder syndrome.	Urology. 2009 Jan;73(1):52-7. Epub 2008 Nov 8.	OBJECTIVES: Probing for clues to the pathogenesis of interstitial cystitis/painful bladder syndrome (IC/PBS), we sought antecedent nonbladder syndromes that distinguished incident IC/PBS cases from matched controls. METHODS: Female incident IC/PBS cases were recruited nationally, and their IC/PBS onset date (index date) was established. The controls were recruited by national random digit dialing and matched to the cases by sex, age, region, and interval between the (assigned) index date and interview. The prevalence of 24 nonbladder syndromes before the index date was assessed, 7 by multiple methods. RESULTS: The cases with IC/PBS had greater antecedent prevalence of 11 syndromes, and 243 of 313 cases (78%) vs 145 of 313 controls (45%) had multiple syndromes (P < .001). Fibromyalgia-chronic widespread pain (FM-CWP), chronic fatigue syndrome, sicca syndrome, and irritable bowel syndrome were associated with each other by pairwise and factor analyses using numerous assumptions. Cases with FM-CWP, chronic fatigue syndrome, sicca syndrome, and/or irritable bowel syndrome (n = 141, 45%) were more likely to have other syndromes (ie, migraine, chronic pelvic pain, depression, and allergy). Three other syndrome clusters were identified; each was associated with this FM-CWP cluster. CONCLUSIONS: Eleven antecedent syndromes were more often diagnosed in those with IC/PBS, and most syndromes appeared in clusters. The most prominent cluster comprised FM-CWP, chronic fatigue syndrome, sicca syndrome, and irritable bowel syndrome; most of the other syndromes and identified clusters were associated with it. Among the hypotheses generated was that some patients with IC/PBS have a systemic syndrome and not one confined to the bladder.
Watanabe N, Stewart R, Jenkins R, Bhugra DK, Furukawa TA.	Department of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan. noriow@med.nago	The epidemiology of chronic fatigue, physical illness, and symptoms of common mental disorders: a cross-sectional survey from the second British National Survey of	J Psychosom Res. 2008 Apr;64(4):357-62.	OBJECTIVE: The study aimed to describe the prevalence of chronic fatigue in the general population and to investigate the extent to which its association with physical illness was independent of other symptoms of common mental disorders. METHODS: Data from the second British National Survey of Psychiatric Morbidity (2000) were analyzed. The survey covered people aged 16 to 74 years living in private households. Chronic fatigue (significant reported fatigue lasting 6 months or more) was ascertained using the revised Clinical Interview Schedule. Information on reported physical illness and sociodemographic factors was considered. Psychiatric symptoms were also assessed using the revised Clinical Interview Schedule. RESULTS: The prevalence of chronic fatigue was 15.0%, and this showed a significant association with the number of reported physical illnesses (odds ratio [OR] per reported illness, 1.79; 95% confidence interval, 1.68-1.90). It was higher in midlife, in women, in participants

	ya-cu.ac.jp	Psychiatric Morbidity.		with less skilled occupations, and in those with lower educational attainment. Chronic fatigue was strongly associated with the presence of depressive symptoms (OR, 5.37), anxiety-related symptoms (OR, 4.66), and with sleep complaints (OR, 4.41). After adjustment for all sociodemographic and psychiatric factors, the number of reported physical illnesses was less strongly but still significantly associated with chronic fatigue (OR, 1.51; 1.39-1.63). CONCLUSION: Physical illness is strongly associated with chronic fatigue. Symptoms of common mental disorders are also associated with chronic fatigue, but the association between physical illness and chronic fatigue is evident even after adjusting for psychiatric symptoms. The assessment of physically ill people should include chronic fatigue and psychiatric symptoms.
Whitehouse CR, Boullata J, McCauley LA.	Adult Health/Gerontology Nurse Practitioner Program, School of Nursing, University of Pennsylvania, Philadelphia, PA, USA.	The potential toxicity of artificial sweeteners.	AAOHN J. 2008 Jun;56(6):251-9; quiz 260-1.	Since their discovery, the safety of artificial sweeteners has been controversial. Artificial sweeteners provide the sweetness of sugar without the calories. As public health attention has turned to reversing the obesity epidemic in the United States, more individuals of all ages are choosing to use these products. These choices may be beneficial for those who cannot tolerate sugar in their diets (e.g., diabetics). However, scientists disagree about the relationships between sweeteners and lymphomas, leukemias, cancers of the bladder and brain, chronic fatigue syndrome, Parkinson's disease, Alzheimer's disease, multiple sclerosis, autism, and systemic lupus. Recently these substances have received increased attention due to their effects on glucose regulation. Occupational health nurses need accurate and timely information to counsel individuals regarding the use of these substances. This article provides an overview of types of artificial sweeteners, sweetener history, chemical structure, biological fate, physiological effects, published animal and human studies, and current standards and regulations.
Winceslaus SJ, Pinching AJ, Harris A, Ankrett V, Mark.	Department of GU Medicine, Culverden Suite, Kent & Sussex Hospital, Mount Ephraim, Tunbridge Wells, Kent TN4 8AT, UK. joseph.winceslaus@mtw-tr.nhs.uk	HIV diagnosis: why and how do we miss important clues?	Sex Transm Infect. 2008 Apr;84(2):101-2.	Research has found that a significant proportion of patients diagnosed late with HIV infection had been in contact with healthcare professionals in the preceding year with symptoms attributable to HIV. We report a unique case of late HIV diagnosis missed when seen by a number of specialists and discuss whether with better communication the diagnosis could have been alerted earlier.
Wyller VB, Barbieri R, Thaulow E, Saul JP.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Center, Oslo, Norway. brwylle@online.no	Enhanced vagal withdrawal during mild orthostatic stress in adolescents with chronic fatigue.	Ann Noninvasive Electrocardiol. 2008 Jan;13(1):67-73.	BACKGROUND: Hemodynamic abnormalities have been documented in the chronic fatigue syndrome (CFS), indicating functional disturbances of the autonomic nervous system responsible for cardiovascular regulation. The aim of this study was to investigate autonomic heart rate control during mild orthostatic stress in adolescents with CFS. METHODS: A total of 14 CFS patients and 56 healthy controls having equal distribution of age and gender underwent lower body negative pressure (LBNP) of horizontal line 20 mmHg. The RR interval (RRI) was recorded continuously, and spectral power densities were computed in the low-frequency (LF) band (0.04-0.15 Hz) and the high-frequency (HF) band (0.15-0.50 Hz) from segments of 120-second length, using an autoregressive algorithm. In addition, the time-domain indices SDNN, pNN50, and r-MSSD were computed. RESULTS: At rest, CFS

				had lower RRI than controls (P < 0.05), but indices of variability were similar in the two groups. During LBNP, compared to controls, CFS patients had lower normalized and absolute HF power and r-MSSD (P < 0.05), and higher RRI (P < 0.001), normalized LF power and LF/HF (P < 0.05). CONCLUSIONS: During mild orthostatic stress, adolescents with CFS appear to have enhanced vagal withdrawal, leading to a sympathetic predominance of heart rate control compared to controls. Possible underlying mechanisms include hypovolemia and abnormalities of reflex mechanisms.
Wyller VB, Eriksen HR, Malterud K.		Can sustained arousal explain the Chronic Fatigue Syndrome?	Behav Brain Funct. 2009 Feb 23;5(1):10. [Epub ahead of print]	ABSTRACT: We present an integrative model of disease mechanisms in the Chronic Fatigue Syndrome (CFS), unifying empirical findings from different research traditions. Based upon the Cognitive activation theory of stress (CATS), we argue that new data on cardiovascular and thermoregulatory regulation indicate a state of permanent arousal responses - sustained arousal - in this condition. We suggest that sustained arousal can originate from different precipitating factors (infections, psychosocial challenges) interacting with predisposing factors (genetic traits, personality) and learned expectancies (classical and operant conditioning). Furthermore, sustained arousal may explain documented alterations by establishing vicious circles within immunology (Th2 (humoral) vs Th1 (cellular) predominance), endocrinology (attenuated HPA axis), skeletal muscle function (attenuated cortical activation, increased oxidative stress) and cognition (impaired memory and information processing). Finally, we propose a causal link between sustained arousal and the experience of fatigue. The model of sustained arousal embraces all main findings concerning CFS disease mechanisms within one theoretical framework.
Wyller VB, Saul JP, WallÃ¸e L, Thaulow E.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Center, 0027 Oslo, Norway. brwylle@online.no	Sympathetic cardiovascular control during orthostatic stress and isometric exercise in adolescent chronic fatigue syndrome.	Eur J Appl Physiol. 2008 Apr;102(6):623-32. Epub 2007 Dec 8.	The chronic fatigue syndrome (CFS) has been shown to be associated with orthostatic intolerance and cardiovascular dysregulation. We investigated the cardiovascular responses to combined orthostatic stress and isometric exercise in adolescents with CFS. We included a consecutive sample of 15 adolescents 12-18 years old with CFS diagnosed according to a thorough and standardized set of investigations, and a volunteer sample of 56 healthy control subjects of equal sex and age distribution. Heart rate, systolic, mean and diastolic blood pressure, stroke index, and total peripheral resistance index were non-invasively recorded during lower body negative pressure (LBNP) combined with two consecutive periods of handgrip. In addition, we measured baseline plasma catecholamines, and recorded symptoms. At rest, CFS patients had higher heart rate, diastolic blood pressure, plasma norepinephrine (P < 0.01), mean blood pressure and plasma epinephrine (P < 0.05) than controls. During LBNP, CFS patients had a greater increase in heart rate, diastolic blood pressure, mean blood pressure (P < 0.05) and total peripheral resistance index (n.s.) than controls. During handgrip, CFS patients had a smaller increase in heart rate, diastolic blood pressure (P < 0.05), mean blood pressure and total peripheral resistance index (n.s.) than controls. Our results indicate that adolescents with CFS have increased sympathetic activity at rest with exaggerated cardiovascular response to orthostatic stress, but attenuated cardiovascular response when performing isometric exercise during orthostatic stress. This suggests that CFS might be causally related to sympathetic dysfunction.
Zoppi M, Maresca M.	Dipartimento di Medicina Interna, Sezione di Reumatologia,	Symptoms accompanying fibromyalgia.	Reumatismo. 2008 Jul-Sep;60(3):217-20.	OBJECTIVE: The objective of the study was to investigate the relationship between spontaneous and provoked pain in fibromyalgia and to evaluate the frequency of disturbances associated with muscle pain, including some disturbances which are not usually considered as typical symptoms associated with pain in fibromyalgia. METHODS: In sixty-seven patients with fibromyalgia the severity of

	Università degli Studi di Firenze, Firenze. m.zoppi@dmi.unifi.it			spontaneous pain was assessed by a visual analogue scale and the severity of provoked pain by an original method, which includes the evaluation of the number of tender points and the evaluation of the intensity of provoked pain. The method used to assess the severity of provoked pain is more sensitive than other methods currently used. The occurrence of accompanying symptoms was also evaluated. The investigation included the occurrence of paresthesias of the upper limbs, hemorrhoids and epistaxis, which are not usually considered as typical symptoms associated with fibromyalgia. RESULTS: No significant correlation was observed between the severity of spontaneous and provoked pain. The following disturbances were more frequent in the examined patients than in general population: headache, chronic fatigue, sleep disorders, irritable bowel syndrome, restless legs syndrome, paresthesias in the upper limbs, hemorrhoids and epistaxis. CONCLUSIONS: Spontaneous and provoked pain should be considered two independent clinical features of fibromyalgia. Paresthesias in the upper limbs, hemorrhoids and epistaxis should be considered as typical symptoms associated with fibromyalgia. Hemorrhoids and epistaxis are frequently due to a diathesis characterized by laxity of connective tissues and fibromyalgia could be a consequence of such a diathesis.
Zwarts MJ, Bleijenberg G, van Engelen BG.	University Medical Centre Nijmegen, Institute of Neurology, 920 Department of Clinical Neurophysiology, PO Box 9101, 6500 HB Nijmegen, The Netherlands. M.Zwarts@neuro.umcn.nl	Clinical neurophysiology of fatigue.	Clin Neurophysiol. 2008 Jan;119(1):2-10. Epub 2007 Nov 26.	Fatigue is a multidimensional concept covering both physiological and psychological aspects. Chronic fatigue is a typical symptom of diseases such as cancer, multiple sclerosis (MS), Parkinson's disease (PD) and cerebrovascular disorders but is also presented by people in whom no defined somatic disease has been established. If certain criteria are met, chronic fatigue syndrome can be diagnosed. The 4-item Abbreviated Fatigue Questionnaire allows the extent of the experienced fatigue to be assessed with a high degree of reliability and validity. Physiological fatigue has been well defined and originates in both the peripheral and central nervous system. The condition can be assessed by combining force and surface-EMG measurements (including frequency analyses and muscle-fibre conduction estimations), twitch interpolation, magnetic stimulation of the motor cortex and analysis of changes in the readiness potential. Fatigue is a well-known phenomenon in both central and peripheral neurological disorders. Examples of the former conditions are multiple sclerosis, Parkinson's disease and stroke. Although it seems to be a universal symptom of many brain disorders, the unique characteristics of the concomitant fatigue also point to a specific relationship with several of these syndromes. As regards neuromuscular disorders, fatigue has been reported in patients with post-polio syndrome, myasthenia gravis, Guillain-BarrÃ© syndrome, facioscapulohumeral dystrophy, myotonic dystrophy and hereditary motor and sensory neuropathy type-I. More than 60% of all neuromuscular patients suffer from severe fatigue, a prevalence resembling that of patients with MS. Except for several rare myopathies with specific metabolic derangements leading to exercise-induced muscle fatigue, most studies have not identified a prominent peripheral cause for the fatigue in this population. In contrast, the central activation of the diseased neuromuscular system is generally found to be suboptimal. The reliability of the psychological and clinical neurophysiological assessment techniques available today allows a multidisciplinary approach to fatigue in neurological patients, which may contribute to the elucidation of the pathophysiological mechanisms of chronic fatigue, with the ultimate goal to develop tailored treatments for fatigue in neurological patients. The present report discusses the different manifestations of fatigue and the available tools to assess peripheral

				and central fatigue.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Agarwal AK, Garg R, Ritch A, Sarkar P.	City Hospital, Birmingham, UK. anilabliuk@yahoo.co.uk	Postural orthostatic tachycardia syndrome.	Postgrad Med J. 2007 Jul;83(981):478-80.	Postural orthostatic tachycardia syndrome (POTS) is an autonomic disturbance which has become better understood in recent years. It is now thought to encompass a group of disorders that have similar clinical features, such as orthostatic intolerance, but individual distinguishing parameters--for example, blood pressure and pulse rate. The clinical picture, diagnosis, and management of POTS are discussed.
Ahboucha S, Pomier-Layrargues G, Vincent C, Hassoun Z, Tamaz R, Baker G, Butterworth RF.	Neuroscience Research Unit, CHUM—Hôpital Saint-Luc, 1058 St.-Denis, Montreal, Quebec 2X 3J4, Canada.	Reduced plasma dehydroepiandrosterone sulfate levels are significantly correlated with fatigue severity in patients with primary biliary cirrhosis.	Neurochem Int. 2007 Jun 19 [Epub ahead of print]	Fatigue is a common debilitating complication of primary biliary cirrhosis (PBC), the pathophysiologic mechanism of which is poorly understood. Recently, the neuroactive steroid dehydroepinadrosterone sulfate (DHEAS) was reported to be implicated in Chronic Fatigue Syndrome in the absence of liver disease. The present study was undertaken to analyse fatigue scores and their relationship with disease severity and circulating levels of DHEAS as well as its precursors DHEA and pregnenolone in PBC patients with (n=15) or without fatigue (n=10) compared to control subjects (n=11). Fatigue was assessed using the fatigue impact scale (FIS) including cognitive, physical and psychosocial subclasses. Steroids were measured by radioimmunoassay or gas chromatography/mass spectrometry. Plasma concentrations of DHEAS were significantly reduced in PBC patients with fatigue as compared to controls, while those of its precursors DHEA and pregnenolone remained within the control range. Plasma levels of DHEAS in PBC patients were significantly correlated with fatigue severity as reflected by total FIS scores including total (rp=-0.42; p=0.018), as well as the cognitive (rp=-0.37; p=0.03), physical (rp=-0.48; p=0.006) and psychosocial (rp=-0.35; p=0.04) subclasses of fatigue scores. No correlation of fatigue scores was observed with indices of liver function. These findings suggest that reduced levels of the neurosteroid DHEAS may contribute to fatigue in patients with PBC; substitutive therapy using DHEAS or its precursor DHEA could be beneficial in the management of fatigue in patients with low levels of DHEAS.
Ahmed M. Abdel-Khalek		Chronic Fatigue Syndrome and Its Association with Obsession Compulsion Among a Non-Clinical Sample Using Questionnaires	Journal of Chronic Fatigue Syndrome 2007; 14(3):	The present study investigated the possible association between the Chronic Fatigue Syndrome (CFS) and obsession compulsion (OC). A non-clinical sample of 427 volunteer Kuwaiti male and female college students was recruited. Their ages ranged from 17 to 40 years. They completed the Arabic Scale of CFS (ASCFS) and the Arabic Scale of Obsession Compulsion (ASOC). Both have good reliability and validity. Females had significantly higher mean score on the ASCFS than did their male counterparts. All the intercorrelations between the 20 items as well as the total score of the ASCFS were statistically significant ($p < 0.01$) with the total ASOC score in males and females. It was concluded that there is an obsessive compulsive element in CFS, and both disorders share specific common elements.
Amato MP, De Stefano N.		Longitudinal follow-up of "benign" multiple sclerosis at 20 years.	Neurology. 2007 Aug 28;69(9):938; author reply 938-9. Comment on: Neurology. 2007 Feb 13;68(7):496-500.	

Aminzadeh KK, Etminan M.	Center for Clinical Epidemiology and Evaluation, Vancouver Hospital, Vancouver, Canada.	Dental amalgam and multiple sclerosis: a systematic review and meta-analysis.	J Public Health Dent. 2007 Winter;67(1):64-6.	OBJECTIVES: Amalgam restorations have long been controversial due to their mercury content. Allegations that the mercury may be linked to nervous disorders such as Alzheimer's, chronic fatigue syndrome, and multiple sclerosis (MS) have fueled the calls for the removal of amalgam restorations from dentists' armamentarium. To explore and quantify the association between amalgam restorations and MS we have conducted a systematic review and meta-analysis of the literature. METHODS: A systematic search in Medline (from 1966 to April 2006), EMBASE (2006, Week 16), and the Cochrane library (Issue 2, 2006) for English-language articles meeting specific definitions of MS and amalgam exposure was conducted. Studies were also identified using the references of retrieved articles. Studies were independently reviewed by two authors and disagreements were resolved by consensus. Studies were selected based on an a priori of defined criteria. Odds ratios (ORs) or relative risks were pooled using the random effects model. Heterogeneity was assessed using Q statistics. RESULTS: The pooled OR for the risk of MS among amalgam users was consistent, with a slight, nonstatistically significant increase between amalgam use and risk of MS. CONCLUSION: Future studies that take into consideration the amalgam restoration size and surface area along with the duration of exposure are needed in order to definitively rule out any link between amalgam and MS.
Amsterdam JD, Shults J, Rutherford N.	Depression Research Unit, Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, PA, United States.	Open-label study of s-citalopram therapy of chronic fatigue syndrome and co-morbid major depressive disorder.	Prog Neuropsychopharmacol Biol Psychiatry. 2008 Jan 1;32(1):100-6. Epub 2007 Aug 3.	OBJECTIVE: Chronic fatigue syndrome (CFS) is a debilitating disorder with prominent symptoms of malaise, fatigue, myalgia, arthralgia, and impaired concentration. The symptoms of CFS may often overlap those of Major Depressive Disorder (MDD). Treatment of CFS has generally been disappointing. We hypothesized that s-citalopram therapy may improve the symptoms of both disorders in CFS patients with co-morbid depression. METHODS: 16 patients received s-citalopram 10 mg to 20 mg daily for up to 12 weeks. Outcome measures of CFS included the Chalder Fatigue Questionnaire (CFQ), the multi-dimensional Fatigue Impact Scale (FIS), the CFS symptom rating (CFS-SR) 100 mm visual analogue scale, and the clinical global impressions severity (CGI/S) and change (CGI/C) ratings. Secondary outcomes of MDD included the Hamilton Depression Rating (HAM-D), Beck Depression Inventory (BDI), and the CGI/S and CGI/C ratings of MDD. RESULTS: We observed reductions in the mean CFQ score ($p<0.0005$), FIS score ($p<0.0005$), and CGI/S ($p<0.0005$) and CGI/C ($p<0.0005$) ratings over time. There was a significant improvement in 5 of the 8 CFS-SR symptoms: post-exertion malaise ($p=0.001$), headaches ($p<0.0005$), un-refreshing sleep ($p<0.0005$), and impaired memory and concentration ($p<0.0005$). There was also a reduction in mean HAM-D ($p<0.0005$), BDI ($p<0.0005$), CGI/S ($p=0.001$) and CGI/C ($p<0.0005$) ratings of MDD. LIMITATIONS: The sample size was limited and the study design was not double-blind or placebo controlled. CONCLUSION: We observed a significant reduction in both CFS and co-morbid MDD symptom severity ratings, and improvement in 5 of 8 core somatic symptoms of CFS during s-citalopram therapy.
Andersen Mette Marie, Henrik Permin, Frank Albrecht		Nine-Year Follow-Up of Danish Chronic Fatigue Syndrome (CFS) Patients Impact on Health, Social, Vocational, and	Journal of Chronic Fatigue Syndrome 2007; 14(2): 7-23	Objective: To determine quality of life (QOL) and health in Danish CFS patients 9 years after diagnosis. Methods: Thirty-four adults with CFS responded to questions regarding QOL at diagnosis, and again 5 and 9 years later. At 9-year followup patients also responded to questions regarding health, fatigue, use of Health Care system, alcohol and exercise. Results: Two patients (6%) had recovered and 3 patients (10%) had received secondary diagnoses. Overall, there was no improvement, except with depression/anxiety. The order of severity among disabilities remained the same. Work had the highest disability score, followed by post-exertional malaise. Patients slept and

		Personal Lives		rested 13.6 hours a day (mean). Self-reported physical health correlated with hours sleeping and resting. Rheumatic symptoms dominated the health symptoms. Alcohol consumption was low, and the use of the Health Care system was modest. Conclusion: After 9 years QOL was the same as at diagnosis, only mental health had improved.
Appel S, Chapman J, Shoenfeld Y.	Department of Neurology, Sheba Medical Center, Tel Hashomer, Israel.	Infection and vaccination in chronic fatigue syndrome: myth or reality?	Autoimmunity. 2007 Feb;40(1):48-53.	Chronic fatigue syndrome (CFS) is characterized by severe disabling fatigue lasting for more than 6 months associated with physical and mental disturbances such as headache, arthralgia, myalgia, memory impairment, sore throat and tender lymph nodes. The exact pathogenesis is still unknown. Several models were proposed to explain its etiology including chronic infection, endocrine dysfunction, autonomic imbalance, depression, decreased immunity states and an aberrant reaction to infection. No convincing evidence was found to support any of the suggested pathogenic mechanisms. The current concept is that CFS pathogenesis is a multi factorial condition in which an infective agent cause an aberrant immune response characterized by a shift to Th-2 dominant response. When the response fails to be switched-off, a chronic immune activation occurs and clinically expressed as the symptomatology of CFS. Vaccinations are used in order to stimulate the immune system to induce a persistent immunity against the favorable antigens. Several syndromes that contain chronic fatigue as one of their symptoms, such as "Gulf war syndrome" and macrophagic myofasciitis were related to vaccinations. Can vaccinations induce the aberrant immune response of CFS? Little is known about this issue. There are some reports on CFS occurring after vaccination, but few prospective and retrospective studies failed to find such an association. A working group of the Canadian Laboratory Center for Disease Control (LCDC) that was founded in order to examine the suspected association between CFS and vaccinations concluded that there is no evidence that relates CFS to vaccination. Further studies are requested to examine this issue since it is very conceivable that if infection can lead to CFS, vaccination may also lead to it in the same immune-mediated pathogenesis.
Armitage R, Landis C, Hoffmann R, Lentz M, Watson NF, Goldberg J, Buchwald D.	Department of Psychiatry, University of Michigan, Ann Arbor, MI 48105, USA. rosearmi@med.umich.edu	The impact of a 4-hour sleep delay on slow wave activity in twins discordant for chronic fatigue syndrome.	Sleep. 2007 May 1;30(5):657-62.	OBJECTIVES: Chronic fatigue syndrome (CFS) has been associated with altered amounts of slow wave sleep, which could reflect reduced delta electroencephalograph (EEG) activity and impaired sleep regulation. To evaluate this hypothesis, we examined the response to a sleep regulatory challenge in CFS. DESIGN: The first of 3 consecutive nights of study served as laboratory adaptation. Baseline sleep was assessed on the second night. On the third night, bedtime was delayed by 4 hours, followed by recovery sleep. Total available sleep time was held constant on all nights. SETTING: A research sleep laboratory. PARTICIPANTS: 13 pairs of monozygotic twins discordant for CFS. INTERVENTIONS: N/A. MEASUREMENTS AND RESULTS: Power spectral analysis quantified slow wave activity (SWA) in the 0.5-3.9 Hz band in successive NREM periods (stage 2, 3, or 4) on each night. To ensure comparability, analyses were restricted to the first 4 NREM periods on each night. Data were coded for NREM period and twin pair. Repeated-measures analysis of variance (ANOVA) contrasted sleep delay effects across NREM periods between twin pairs. A second ANOVA calculated the SWA in each NREM period in recovery sleep relative to baseline SWA. The 2 groups of twins were similar on baseline SWA power. After sleep delay, CFS twins exhibited significantly less SWA power in the first NREM period of recovery sleep and accumulated a smaller percentage of SWA in the first NREM period than their co-

				twins. CONCLUSIONS: CFS is associated with a blunted SWA response to sleep challenge, suggesting that the basic sleep drive and homeostatic response are impaired.
Arnold LD, Bachmann GA, Rosen R, Rhoads GG.	Department of Epidemiology, School of Public Health, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, USA.	Assessment of vulvodynia symptoms in a sample of US women: a prevalence survey with a nested case control study.	Am J Obstet Gynecol. 2007 Feb;196(2):128.e1-6.	OBJECTIVE: Vulvodynia is a chronic pain syndrome of unknown origin with scant data on frequency. This study assessed the prevalence of vulvodynia symptoms in a sample of US women and compared health characteristics of symptomatic and asymptomatic women. STUDY DESIGN: A phone survey contacted 2127 US households to identify 100 symptomatic women, who were matched on age and time zone to 325 asymptomatic controls. Odds ratios (ORs) and logistic regression were used to model associations between pain, medical conditions, and health care utilization variables. RESULTS: Current vulvar pain of at least 6 months duration was reported by 3.8% of respondents, with a 9.9% lifetime prevalence. Forty-five percent of women with pain reported an adverse effect on their sexual life and 27% an adverse effect on their lifestyle. Cases more frequently reported repeated urinary tract infections (OR, 6.15; 95% CI, 3.51-10.77) and yeast infections (OR, 4.24; 95% CI, 2.47-7.28). Associations existed with chronic fatigue syndrome (OR, 2.78; 95% CI, 1.33-6.19), fibromyalgia (OR, 2.15; 95% CI, 1.06-4.36), depression (OR, 2.99; 95% CI, 1.87-4.80), and irritable bowel syndrome (OR, 1.86; 95% CI, 1.07-3.23). CONCLUSION: Lifetime chronic vulvar pain was less prevalent in this national sample of women than previous data suggest and was correlated with several comorbid chronic medical conditions and substantial reduction in self-reported quality of life.
Bailey A.		Chronic fatigue syndrome: a tiresome illness.	Br J Nurs. 2007 Sep 13-27;16(16):967.	
Baker R, Shaw EJ.	Department of Health Sciences, University of Leicester, Leicester LE1 6TP.	Diagnosis and management of chronic fatigue syndrome or myalgic encephalomyelitis (or encephalopathy): summary of NICE guidance.	BMJ. 2007 Sep 1;335(7617):446-8. Comment in: BMJ. 2007 Sep 15;335(7619):528. BMJ. 2007 Sep 1;335(7617):411-2.	
Balon R.	Department of Psychiatry and Behavioral Neurosciences Wayne State University School of Medicine, Detroit, Mich., USA. rbalon@wayne.ed	Reflections on relevance: the fields of psychosomatics and psychotherapy in 2006.	Psychother Psychosom. 2007;76(4):203-12.	This article reviews several areas of new and interesting development in the fields of psychosomatics and psychotherapy published in the literature during 2006. These areas are: (1) cardiovascular illness and its interplay with depression; (2) risks and predisposing factors in the areas of mental illness and physical illness; (3) new developments in chronic fatigue syndrome, and (4) new or newly explored/modified (psycho)therapies, especially cognitive-behavioral therapy. In addition, an important area of conflict of interest in psychiatry in particular and in biomedical science in general is discussed, as this issue has reached prominence in the biomedical literature. Copyright 2007 S. Karger AG, Basel.

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Ban N, Saiki T, Ko G, Kuwahata A	. Department of General Medicine, Nagoya University School of Medicine	[Clinical features of chronic fatigue syndrome--symptoms] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1011-5.	. Chronic fatigue syndrome (CFS) is a clinically defined condition characterized by long-lasting disabling fatigue, resulting in severe impairment in daily functioning and associated symptoms such as memory and concentration difficulties, muscle aches, sleep disturbances, and headache. Common symptoms encountered in CFS patients were reviewed and top 10 common symptoms were described in detail with special reference to the particular features of each symptom helpful to diagnose CFS
Bennett B, Goldstein D, Friedlander M, Hickie I, Lloyd A.	Department of Medical Oncology, Prince of Wales Hospital, Sydney, Australia. Barbara.Bennett@sesiahs.health.nsw.gov.au	The experience of cancer-related fatigue and chronic fatigue syndrome: a qualitative and comparative study.	J Pain Symptom Manage. 2007 Aug;34(2):126-35. Epub 2007 Jun 4.	Cancer-related fatigue (CRF) is a common and disabling symptom complex reported by survivors. This study aimed to better understand the manifestations of CRF in women treated for breast cancer, and to compare them with those of women diagnosed with chronic fatigue syndrome (CFS). Women with CRF persisting 6 months after treatment for early stage breast cancer, and women with CFS participated in separate, audiotaped focus groups. Transcripts of the sessions were analyzed using the NUD*IST software, and interpreted using grounded theory. Twenty-eight women participated, 16 with CRF and 12 with CFS. Analysis of transcripts from both groups revealed a similar core set of symptoms, featuring fatigue, neurocognitive difficulties, and mood disturbances. Women with CFS reported additional symptoms including musculoskeletal pain and influenza-like manifestations. Both groups suffered disabling behavioral consequences of the symptom complex. Qualitatively, CRF appears closely related to CFS. These findings raise the emergent hypothesis of a conserved neurobehavioral symptom complex, which results from diverse triggering insults.
Beqaj SH, Lerner AM, Fitzgerald JT.	Pathgroup Labs, Nashville, TN, United States.	Immunoassay with cytomegalovirus early antigens from gene products p52 and CM2 (UL44 and UL57) detect active infection in patients with chronic fatigue syndrome.	J Clin Pathol. 2007 Dec 5 [Epub ahead of print]	AIMS: The purpose of this study is to demonstrate that the use of recombinant early antigens for detection of antibodies to cytomegalovirus (HCMV) gene products CM2 (UL44, UL57) and p52 (UL44) is specific in the diagnosis and differentiation of active HCMV infection in a subset of patients with chronic fatigue syndrome (CFS) which is often missed by the current ELISA assay that uses crude viral lysate antigen. METHODS: At a single clinic from 1999 - 2001 a total of 4,774 serologic tests were performed in 1135 CFS patients using two immunoassays; Copalis immunoassay and ELISA immunoassay. The Copalis immunoassay utilized HCMV Early gene products of UL44 and UL57 recombinant antigens for detection of HCMV IgM antibody, and viral capsid antigen for detection of HCMV IgG antibody. The ELISA immunoassay utilized viral crude lysate as antigen for detection of both HCMV IgG and IgM. RESULTS: Of the total, 1135 CFS patients, 517 patients (45.6%) were positive for HCMV IgG by both HCMV IgG by both assays. Of these, twelve CFS patients (2.2%) were positive for HCMV(V) IgM serum antibody by HCMV ELISA assay, and 61 CFS patients (11.8%) were positive for IgM HCMV serum antibody by Copalis assays. The Copalis assay that uses HCMV early recombinant gene products CM2 (UL44, UL57) and p52 (UL44) in comparison with ELISA was 98% specific. CONCLUSIONS: Immunoassays that use Early Antigen recombinant HCMV CM2 and p52 are five times more sensitive than HCMV ELISA assay using viral lysate and are specific in the detection and differentiation of active HCMV infection in a subset of CFS patients.
Bisbal C, Silverman RH.	IGH UPR CNRS 1142, 141 rue de la Cardonille, 34396 Montpellier, France.	Diverse functions of RNase L and implications in pathology.	Biochimie. 2007 Jun-Jul;89(6-7):789-98. Epub 2007 Feb 20.	The endoribonuclease L (RNase L) is the effector of the 2-5A system, a major enzymatic pathway involved in the molecular mechanism of interferons (IFNs). RNase L is a very unusual nuclease with a complex mechanism of regulation. It is a latent enzyme, expressed in nearly every mammalian cell type. Its activation requires its binding to a small oligonucleotide, 2-5A. 2-5A is a series of unique 5'-triphosphorylated oligoadenylates with 2'-5' phosphodiester bonds. By regulating viral and cellular

	catherine.bisbal@igh.cnrs.fr			RNA expression, RNase L plays an important role in the antiviral and antiproliferative activities of IFN and contributes to innate immunity and cell metabolism. The 2-5A/RNase L pathway is implicated in mediating apoptosis in response to viral infections and to several types of external stimuli. Several recent studies have suggested that RNase L could have a role in cancer biology and evidence of a tumor suppressor function of RNase L has emerged from studies on the genetics of hereditary prostate cancer.
Bogaerts K, Hubin M, Van Diest I, De Peuter S, Van Houdenhove B, Van Wambeke P, Crombez G, Van den Bergh O.	Research Group on Health Psychology, Department of Psychology, University of Leuven, Tiensestraat 102, 3000 Leuven, Belgium.	Hyperventilation in patients with chronic fatigue syndrome: the role of coping strategies.	Behav Res Ther. 2007 Nov;45(11):2679-90. Epub 2007 Jul 20.	Hyperventilation has been suggested as a concomitant and possible maintaining factor that may contribute to the symptom pattern of chronic fatigue syndrome (CFS). Because patients accepting the illness and trying to live with it seem to have a better prognosis than patients chronically fighting it, we investigated breathing behavior during different coping response sets towards the illness in patients with CFS (N=30, CDC criteria). Patients imagined a relaxation script (baseline), a script describing a coping response of hostile resistance, and a script depicting acceptance of the illness and its (future) consequences. During each imagery trial, end-tidal PCO2 (Handheld Capnograph, Oridion) was measured. After each trial, patients filled out a symptom checklist. Results showed low resting values of PetCO2 overall, while only imagery of hostile resistance triggered a decrease and deficient recovery of PetCO2. Also, more hyperventilation complaints and complaints of other origin were reported during hostile resistance imagery compared with acceptance and relaxation. In conclusion, hostile resistance seems to trigger both physiological and symptom perception processes contributing to the clinical picture of CFS.
Boiko AN, Batysheva TT, Matvievskaya OV, Manevich TM, Gusev EI.	Department of Neurology and Neurosurgery, Russian State Medical University.	Characteristics of the formation of chronic fatigue syndrome and approaches to its treatment in young patients with focal brain damage.	Neurosci Behav Physiol. 2007 Mar;37(3):221-8.	Chronic fatigue is among the manifestations of focal brain lesions. It is most often encountered in multiple sclerosis (MS) and patients with the sequelae of traumatic, inflammatory, and vascular brain damage (encephalopathies). The aim of the present work was to study the mechanisms of formation of this syndrome in 50 patients with focal brain lesions of different origins (in the inactive stage) and to assess the possibility of correcting it using the combined agent Fezam (2 capsules t.i.d. for one month), which contains piracetam and cinarrizine. In patients with encephalopathies, chronic fatigue syndrome was directly associated with the severity of depression. Patients with MS showed changes in the value-sense sphere. Neuropsychological testing showed that the psychological and personality components played a greater role in the origins of chronic fatigue in patients with encephalopathies than in those with MS. Fezam significantly decreased the severity of chronic fatigue, particularly in patients with MS; in the second group (non-MS patients) this was accompanied by a decrease in the severity of depression. Mild side effects (in six patients--12%) consisted generally of sleep disturbances. These results indicate that Fezam should be used in the treatment of chronic fatigue in patients with focal brain lesions; in encephalopathies it should be combined with psychoactive agents.
Boimel P, Check JH, Katsoff D.	Albert Enstein College of Medicine of Yeshiva University, Bronx, NY, USA.	Sympathomimetic amine therapy may improve refractory gastroparesis similar to its effect on chronic pelvic pain--case report.	Clin Exp Obstet Gynecol. 2007;34(3):185-7.	PURPOSE: To determine if treatment with sympathomimetic amines can effectively treat gastroparesis that was refractory to other medical therapy. METHODS: After failing a water load test, a 29-year-old female was treated with 20 mg/day of dextroamphetamine sulfate. RESULTS: After several weeks of therapy she noted that most of her symptoms of gastroparesis subsided and she has remained symptom free for eight months. CONCLUSIONS: Similar to its beneficial effect on chronic pelvic pain of both bladder and non bladder origin, refractory weight gain, esophageal pain, chronic fatigue syndrome, headaches and vasomotor symptoms, sympathomimetic amine therapy can also effectively

				treat gastroparesis refractory to other medical therapies at least in some cases.
Boneva RS, Decker MJ, Maloney EM, Lin JM, Jones JF, Helgason HG, Heim CM, Rye DB, Reeves WC.	Chronic Viral Diseases Branch, National Center for Zoonotic, Vector-borne and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30329, USA. rboneva@cdc.gov	Higher heart rate and reduced heart rate variability persist during sleep in chronic fatigue syndrome: a population-based study.	Auton Neurosci. 2007 Dec 30;137(1-2):94-101. Epub 2007 Sep 12.	Autonomic nervous system (ANS) dysfunction has been suggested in patients with chronic fatigue syndrome (CFS). In this study, we sought to determine whether increased heart rate (HR) and reduced heart rate variability (HRV) parameters observed in CFS patients during wakefulness persist during sleep. To this end, we compared heart rate (HR) and HRV as indicators of ANS function in CFS subjects and non-fatigued (NF) controls in a population-based, case-control study. Thirty subjects with CFS and 38 NF controls, matched for age-, sex- and body mass index, were eligible for analysis. Main outcome measures included mean RR interval (RRI), HR, and HRV parameters derived from overnight ECG. Plasma aldosterone and norepinephrine levels, medicines with cardiovascular effect, and reported physical activity were examined as covariates. General Linear Models were used to assess significance of associations and adjust for potential confounders. Compared to controls, CFS cases had significantly higher mean HR (71.4 vs 64.8 bpm), with a shorter mean RRI [840.4 (85.3) vs 925.4(97.8) ms] ($p<0.0004$, each), and reduced low frequency (LF), very low frequency (VLF), and total power (TP) of HRV ($p<0.02$, all). CFS cases had significantly lower plasma aldosterone ($p<0.05$), and tended to have higher plasma norepinephrine levels. HR correlated weakly with plasma norepinephrine ($r=0.23$, $p=0.05$) and moderately with vitality and fatigue scores ($r=-0.49$ and 0.46, respectively, $p<0.0001$). Limitation in moderate physical activity was strongly associated with increased HR and decreased HRV. Nevertheless, among 42 subjects with similar physical activity limitations, CFS cases still had higher HR (71.8 bpm) than respective controls (64.9 bpm), $p=0.023$, suggesting that reduced physical activity could not fully explain CFS-associated differences in HR and HRV. After adjusting for potential confounders case-control differences in HR and TP remained significant ($p<0.05$). Conclusion: the presence of increased HR and reduced HRV in CFS during sleep coupled with higher norepinephrine levels and lower plasma aldosterone suggest a state of sympathetic ANS predominance and neuroendocrine alterations. Future research on the underlying pathophysiologic mechanisms of the association is needed.
Britton S.		[Burnout in Greene-land] [Article in Swedish]	Lakartidningen. 2007 Aug 29-Sep 4;104(35):2446-7.	
Brown MM, Jason LA.	Department of Psychology, DePaul University, Center for Community Research, Chicago, IL, USA. mbrown59@depaul.edu.	Functioning in individuals with chronic fatigue syndrome: increased impairment with co-occurring multiple chemical sensitivity and fibromyalgia.	Dyn Med. 2007 Jul 30;6:9.	
Brown MM, Jason LA.	Department of Psychology, DePaul	Functioning in individuals with	Dyn Med. 2007 May 31;6:6.	BACKGROUND: Chronic fatigue syndrome (CFS), multiple chemical sensitivity (MCS), and fibromyalgia (FM) commonly co-occur. Some propose that CFS, MCS, and FM are manifestations of the same illness

	University, Center for Community Research, Chicago, IL, USA. mbrown59@depaul.edu	chronic fatigue syndrome: increased impairment with co-occurring multiple chemical sensitivity and fibromyalgia.		based on high rates of co-occurrence and overlapping diagnostic criteria. This study seeks to differentiate these diagnoses by comparing individuals with one or more illness on functioning, psychiatric comorbidity, coping style, and in vivo physical measures. METHODS: Participants included 114 men and women who met criteria for CFS. FM was diagnosed during a physical examination, and MCS was assessed using a questionnaire. Participants were divided into four groups: CFS alone, CFS-MCS, CFS-FM, and CFS-MCS-FM. Self-report measures, a psychiatric interview, and in vivo physical measures were given. RESULTS: 43.9% met criteria for CFS alone, 23.7% met criteria for CFS-MCS, 15.8% met criteria for CFS-FM, and 16.7% met criteria for CFS-MCS-FM. The CFS-MCS-FM group was more disabled than the CFS alone group on measures of physical functioning, general health, and bodily pain. In vivo measures did not differ, but the CFS-MCS-FM group rated exertion higher than the CFS alone group. CONCLUSION: Individuals with CFS alone were the highest functioning group across several domains, such as disability, depression, and severity of symptoms. Participants with three diagnoses experienced the greatest amount of disability. While substantial co-occurrence of these illnesses was found, this study provides evidence that having more than one illness exacerbates one's disability beyond CFS alone.
Brown RJ.		Introduction to the special issue on medically unexplained symptoms: background and future directions.	Clin Psychol Rev. 2007 Oct;27(7):769-80. Epub 2007 Jul 17.	This special issue is devoted to the topic of medically unexplained symptoms (MUS), a heterogeneous group of conditions characterized by persistent physical symptoms that cannot be explained by medical illness or injury. Although psychological factors have long been regarded as central to these problems, patients with MUS have typically been managed within medical settings and referrals to mental health services have been relatively rare. In recent years, however, interest in the psychological nature and treatment of MUS has expanded, culminating in the development of tailored psychological interventions for these conditions. This, coupled with the increasing willingness of practitioners to diagnose conditions such as chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome, has led to an increase in the number of patients who are referred for psychological treatment. At present, however, many psychological therapists are unfamiliar with the literature on MUS. With this in mind, this special issue presents a series of papers that provide an overview of what is known about the nature, aetiology and treatment of medically unexplained illness. This introductory paper provides general information about the clinical presentation, diagnosis, classification, terminology and epidemiology of MUS in adults, and concludes with an examination of important areas for future development in the field. Subsequent papers address the psychological mechanisms [Deary, V., Chalder, T., & Sharpe, M. (2007-this issue). The cognitive behavioural model of medically unexplained symptoms: A theoretical and empirical review. Clinical Psychology Review; Iverson, A., Chalder, T., & Wessely, S. (2007-this issue). Gulf war illness: Lessons from medically unexplained illness. Clinical Psychology Review; Rief, W., & Broadbent, E. (2007-this issue). Explaining medically unexplained symptoms: Models and mechanisms. Clinical Psychology Review; Roelofs, K., & Spinhoven, P. (2007-this issue). Trauma and medically unexplained symptoms: Towards an integration of cognitive and neuro-biological accounts. Clinical Psychology Review] and management [Deary, V., Chalder, T., & Sharpe, M. (2007-this issue). The cognitive behavioural model of medically unexplained symptoms: A theoretical and empirical review. Clinical Psychology Review] of these conditions. A separate overview of the literature on MUS in children and adolescents is provided by Eminson

				[Eminson, J. (2007-this issue). Medically unexplained symptoms in children and adolescents. Clinical Psychology Review].
Cameron B, Galbraith S, Zhang Y, Davenport T, Vollmer-Conna U, Wakefield D, Hickie I, Dunsmuir W, Whistler T, Vernon S, Reeves WC, Lloyd AR; Dubbo Infection Outcomes Study.	School of Medical Sciences, University of New South Wales, Sydney, Australia	Gene expression correlates of postinfective fatigue syndrome after infectious mononucleosis	J Infect Dis. 2007 Jul 1;196(1):56-66. Epub 2007 May 24. Comment in: J Infect Dis. 2007 Jul 1;196(1):4-5.	BACKGROUND: Infectious mononucleosis (IM) commonly triggers a protracted postinfective fatigue syndrome (PIFS) of unknown pathogenesis. METHODS: Seven subjects with PIFS with 6 or more months of disabling symptoms and 8 matched control subjects who had recovered promptly from documented IM were studied. The expression of 30,000 genes was examined in the peripheral blood by microarray analysis in 65 longitudinally collected samples. Gene expression patterns associated with PIFS were sought by correlation with symptom factor scores. RESULTS: Differential expression of 733 genes was identified when samples collected early during the illness and at the late (recovered) time point were compared. Of these genes, 234 were found to be significantly correlated with the reported severity of the fatigue symptom factor, and 180 were found to be correlated with the musculoskeletal pain symptom factor. Validation by analysis of the longitudinal expression pattern revealed 35 genes for which changes in expression were consistent with the illness course. These genes included several that are involved in signal transduction pathways, metal ion binding, and ion channel activity. CONCLUSIONS: Gene expression correlates of the cardinal symptoms of PIFS after IM have been identified. Further studies of these gene products may help to elucidate the pathogenesis of PIFS.
Capuron L, Pagnoni G, Demetrashvili MF, Lawson DH, Fornwalt FB, Woolwine B, Berns GS, Nemeroff CB, Miller AH	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA 30322, USA.	Basal ganglia hypermetabolism and symptoms of fatigue during interferon-alpha therapy.	Neuropsychopharmacology. 2007 Nov;32(11):2384-92. Epub 2007 Feb 28.	Interferon (IFN)-alpha is a cytokine of the innate immune response that is well known for inducing behavioral alterations and has been used to study effects of cytokines on the nervous system. Limited data, however, are available on the sites of action of IFN-alpha within the brain and their relationship with specific IFN-alpha-induced symptoms. Using a longitudinal design, whole-brain metabolic activity as assessed by fluorine-18-labeled fluorodeoxyglucose uptake and positron emission tomography was examined before and 4 weeks after IFN-alpha administration in patients with malignant melanoma. Changes in metabolic activity in relevant brain regions were then correlated with IFN-alpha-induced behavioral changes. IFN-alpha administration was associated with widespread bilateral increases in glucose metabolism in subcortical regions including the basal ganglia and cerebellum. Decreases in dorsal prefrontal cortex glucose metabolism were also observed. Prominent IFN-alpha-induced behavioral changes included lassitude, inability to feel, and fatigue. Correlational analyses revealed that self-reported fatigue (specifically as assessed by the 'energy' subscale of the Visual Analog Scale of Fatigue) was associated with increased glucose metabolism in the left nucleus accumbens and putamen. These data indicate that IFN-alpha as well as other cytokines of the innate immune response may target basal ganglia nuclei, thereby contributing to fatigue-related symptoms in medically ill patients.
Carpenter J, Hutchings A, Raine R, Sanderson C	Department of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, Keppel Street, London, UK.	An experimental study of the influence of individual participant characteristics on formal consensus	Technol Assess Health Care. 2007 Winter;23(1):108-15.	OBJECTIVES: The aim of this study was to examine the influence of participants' characteristics on the results produced by formal consensus methods. METHODS: The approach was an experimental study of 346 participants in 20 groups rating the appropriateness of four mental health interventions for the treatment of chronic fatigue syndrome, irritable bowel syndrome, and chronic back pain. There were four factors in the design: systematic literature review provided or not, decisions made under realistic or "ideal" resource assumptions, clinically mixed (general practitioners and mental health professionals) or homogenous group (general practitioners only), convened or mail-only group. A

	james.carpenter@lshtm.ac.uk	development		group's rating was defined as the median of participants' ratings. The influence of participants' characteristics (age, sex, and specialty) was examined using multilevel models. RESULTS: The largest differences were between the GPs and mental health professionals, both in their initial ratings of the different interventions, and in how much they altered their ratings between rounds. There were smaller but statistically significant (p<.05) differences between specialty and age groups in initial ratings for the treatment (by whatever means) of different conditions, and for certain conditions women increased their ratings more than men. Women rated intervention more favorably when assuming "ideal" rather than realistic levels of resources, but men did not. CONCLUSIONS: Our findings support the practice of treating professional specialty as an important determinant of the results in consensus panels.
Carville SF, Arendt-Nielsen S, Bliddal H, Blotman F, Branco JC, Buskila D, Da Silva JA, Danneskiold-Samsøe B, Dincer F, Henriksson C, Henriksson K, Kosek E, Longley K, McCarthy GM, Perrot S, Puszczewicz MJ, Sarzi-Puttini P, Silman A, Späth M, Choy EH.	King's College London, United Kingdom.	EULAR evidence based recommendations for the management of fibromyalgia syndrome.	Ann Rheum Dis. 2007 Oct 3 [Epub ahead of print]	OBJECTIVE: To develop evidence based recommendations for the management of fibromyalgia syndrome (FMS). METHODS: A multidisciplinary task force was formed representing eleven European Countries. The design of the study including search strategy, participants, interventions, outcome measures, data collection and analytical method was defined at the outset. A systematic review was undertaken with the keywords 'fibromyalgia', 'treatment or management' and 'trial'. Studies were excluded if they did not utilise the ACR classification criteria, were not clinical trials, or included patients with chronic fatigue syndrome or myalgic encephalomyelitis. Primary outcome measures were change in pain assessed by visual analogue scale (VAS) and fibromyalgia impact questionnaire (FIQ). The quality of the studies was categorised based on randomisation, blinding and allocation concealment. Only the highest quality studies were used to base recommendations on. When there was insufficient evidence from the literature, a Delphi process was used to provide basis for recommendation. RESULTS: One hundred and forty six studies were eligible for the review. Thirty nine pharmacologic intervention studies and 59 non-pharmacologic were included in the final recommendation summary tables once those of a lower quality or with insufficient data were separated. The categories of treatment identified were antidepressants, analgesics, and 'other pharmacological' and exercise, cognitive behavioural therapy, education, dietary interventions and 'other non-pharmacological'. In many studies sample size was small and the quality of the study was insufficient for strong recommendations to be made. CONCLUSION: Nine recommendations for the management of FMS were developed using a systematic review and expert consensus.
Chapenko S, Krumina A, Kozireva S, Nora Z, Sultanova A, Viksna L, Murovska M.	August Kirchenstein Institute of Microbiology and Virology, Riga Stradins University, Ratsupites St.1, Riga, LV-1067, Latvia. modra@latnet.lv	Activation of human herpesviruses 6 and 7 in patients with chronic fatigue syndrome.	J Clin Virol. 2006 Dec;37 Suppl 1:S47-51.	BACKGROUND: Human herpesvirus 6 (HHV-6) and 7 (HHV-7) have been suggested as possible triggering agents for chronic fatigue syndrome (CFS). OBJECTIVES: To determine the possible association of HHV-6 and HHV-7 infections with CFS. STUDY DESIGN: The prevalence of latent/persistent and active viral infections by nPCR, characteristic of HHV-6 variants using restriction endonuclease analysis and changes of lymphocyte subsets in peripheral blood by laser flow-cytometry in 17 CFS patients was examined. In addition, 12 patients with unexplained chronic fatigue and 20 blood donors (BD) were studied. RESULTS: No difference in prevalence of latent/persistent single viral infections between the patients and BD was found but dual infection rate was significantly higher in CFS patients. Active HHV-6 and dual (HHV-6 + HHV-7) infections were detected in CFS patients only and frequency of HHV-7 reactivation was also significantly higher in these patients. HHV-6 variant B was predominant in CFS patients (12/13). The changes of immunological parameters in CFS patients

				with active dual infection were characterized by significant decrease of CD3+ and CD4+ T cells, significant increase of CD95+ cells and decrease of CD4+/CD8+ ratio. CONCLUSIONS: HHV-6 and HHV-7 may be involved in the pathogenesis of CFS and reactivation of both viruses may provoke changes in the phenotype of circulating lymphocytes.
Chia JK, Chia AY.	EV Med Research, Lomita, California 90717, USA. evmed@sbcglobal.net	Chronic fatigue syndrome is associated with chronic enterovirus infection of the stomach.	J Clin Pathol. 2008 Jan;61(1):43-8. Epub 2007 Sep 13. Comment in: J Clin Pathol. 2008 Jan;61(1):1-2.	BACKGROUND AND AIMS: The aetiology for chronic fatigue syndrome (CFS) remains elusive although enteroviruses have been implicated as one of the causes by a number of studies. Since most CFS patients have persistent or intermittent gastrointestinal (GI) symptoms, the presence of viral capsid protein 1 (VP1), enterovirus (EV) RNA and culturable virus in the stomach biopsy specimens of patients with CFS was evaluated. METHODS: 165 consecutive patients with CFS underwent upper GI endoscopies and antrum biopsies. Immunoperoxidase staining was performed using EV-specific monoclonal antibody (mAb) or a control mAb specific for cytomegalovirus (CMV). RT-PCR ELISA was performed on RNA extracted from paraffin sections or samples preserved in RNA later. Biopsies from normal stomach and other gastric diseases served as controls. 75 samples were cultured for EV. RESULTS: 135/165 (82%) biopsies stained positive for VP1 within parietal cells, whereas 7/34 (20%) of the controls stained positive (p< or =0.001). CMV mAb failed to stain any of the biopsy specimens. Biopsies taken from six patients at the onset of the CFS/abdominal symptoms, and 2-8 years later showed positive staining in the paired specimens. EV RNA was detected in 9/24 (37%) paraffin-embedded biopsy samples; 1/21 controls had detectable EV RNA (p<0.01); 1/3 patients had detectable EV RNA from two samples taken 4 years apart; 5 patient samples showed transient growth of non-cytopathic enteroviruses. CONCLUSION: Enterovirus VP1, RNA and non-cytopathic viruses were detected in the stomach biopsy specimens of CFS patients with chronic abdominal complaints. A significant subset of CFS patients may have a chronic, disseminated, non-cytolytic form of enteroviral infection, which could be diagnosed by stomach biopsy.
Ciccolella Margaret, Staci R. Stevens, Christopher R. Snell, Mark Van Ness		Legal and Scientific Considerations of the Exercise Stress Test	Journal of Chronic Fatigue Syndrome 2007; 14(2): 61-75	This article examines the legal and scientific bases on which an exercise stress test can provide medically acceptable evidence of disability for the Chronic Fatigue Syndrome (CFS) patient. To qualify for disability benefits, a claimant must establish the existence of a serious medically determinable impairment (MDI) that causes the inability to work. The single stress test has been used to objectively establish whether a claimant can engage in "substantial gainful employment" and is an important determinant of the award or denial of benefits. A review of case law indicates problems associated with a single test protocol that may be remedied by a "test-retest" protocol. The results of a preliminary study employing this approach indicate that the test-retest protocol addresses problems inherent in a single test and therefore provides an assessment of CFS related disability consistent with both medical and legal considerations.
Claypoole KH, Noonan C, Mahurin RK, Goldberg J, Erickson T, Buchwald D.	Department of Psychology, University of Hawaii, Honolulu, HI, USA.	A twin study of cognitive function in chronic fatigue syndrome: the effects of sudden illness onset.	Neuropsychology. 2007 Jul;21(4):507-13.	Variable reports of neuropsychological deficits in individuals with chronic fatigue syndrome (CFS) may, in part, be attributable to methodological limitations. In this study, these limitations were addressed by controlling for genetic and environmental influences and by assessing the effects of comorbid depression and mode of illness onset. Specifically, the researchers conducted a co-twin control study of 22 pairs of monozygotic twins, in which 1 twin met strict criteria for CFS and the co-twin was healthy. Twins underwent a structured psychiatric interview and comprehensive neuropsychological assessment evaluating 6 cognitive domains. Results indicated that twin groups had similar intellectual

				and visual memory functioning, but fatigued twins exhibited decreases in motor functions (p = .05), speed of information processing (p = .02), verbal memory (p = .02), and executive functioning (p = .01). Major depression did not affect neuropsychological functioning among fatigued twins, although twins with sudden illness onset demonstrated slowed information processing compared with those with gradual onset (p = .01). Sudden onset CFS was associated with reduced speed of information processing. If confirmed, these findings suggest the need to distinguish illness onset in future CFS studies and may have implications for treatment, cognitive rehabilitation, and disability determination.
Cook DB, O'Connor PJ, Lange G, Steffener J.	Department of Veterans Affairs-William S. Middleton Memorial Veterans Hospital, Madison, WI 53706, USA. dcook@education.wisc.edu	Functional neuroimaging correlates of mental fatigue induced by cognition among chronic fatigue syndrome patients and controls.	Neuroimage. 2007 May 15;36(1):108-22. Epub 2007 Mar 3.	The neural mechanisms underlying feelings of fatigue are poorly understood. The primary purpose of the study was to use functional magnetic resonance imaging (fMRI) to determine the association between feelings of mental fatigue and blood oxygen level dependent (BOLD) brain responses during a mentally fatiguing cognitive task. Healthy, non-fatigued controls and chronic fatigue syndrome (CFS) patients were included to determine the influence of chronic levels of fatigue on brain responses. We hypothesized that mental fatigue would be significantly related to brain activity during a fatiguing cognitive task but not during either a non-fatiguing motor (finger tapping) or cognitive (auditory monitoring) task. Patients (n=9) and controls (n=11) completed a finger tapping task, a simple auditory monitoring task and a challenging working memory task, designed to induce mental fatigue, while undergoing fMRI. Fatigue was measured prior to scanning and following each task during fMRI data collection. Results showed that mental fatigue was significantly related to brain activity during the fatiguing cognitive task but not the finger tapping or simple auditory monitoring tasks. Significant (p< or =0.005) positive relationships were found for cerebellar, temporal, cingulate and frontal regions. A significant (p=0.001) negative relationship was found for the left posterior parietal cortex. CFS participants did not differ from controls for either finger tapping or auditory monitoring tasks, but exhibited significantly greater activity in several cortical and subcortical regions during the fatiguing cognitive task. Our results suggest an association between subjective feelings of mental fatigue and brain responses during fatiguing cognition.
Coucheron D.		[To be exhausted of? Not at all!] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2007 Sep 6;127(17):2278-9. Comment on: Tidsskr Nor Laegeforen. 2007 Jun 28;127(13):1797-9.	
Crawley E, Davey Smith G.	Centre for Child and Adolescent Health, Hampton House, Cotham Hill, Bristol BS6 6JS,	Is chronic fatigue syndrome (CFS/ME) heritable in children, and if so, why does it	Arch Dis Child. 2007 Dec;92(12):1058-61. Epub 2007 Sep 5.	

	UK. Esther.crawley@bristol.ac.uk	matter?		
Crofford LJ.	Center for the Advancement of Women's Health, University of Kentucky, USA. lcrofford@uky.edu	Violence, stress, and somatic syndromes.	Trauma Violence Abuse. 2007 Jul;8(3):299-313.	Syndromes characterized by pain, fatigue, mood disorder, cognitive dysfunction, and sleep disturbance have been referred to as stress-related somatic disorders by virtue of the observation that onset and exacerbation of symptoms occur with stress. These syndromes include but are not limited to fibromyalgia, chronic fatigue syndrome, temporomandibular disorder, and irritable bowel syndrome. As with most chronic illnesses, genetic susceptibility and lifetime environmental exposures play a role in creating vulnerability to disease. Cumulative lifetime stress has been associated with a number of physiologic changes in the brain and body that reflect dysregulated hormonal and autonomic activity. Exposure to the stressor of violence is likely to create a state of vulnerability for the stress-related somatic syndromes and also to contribute to symptom expression and severity. Understanding the relationship between violence, stress, and somatic syndromes will help in clarifying the consequences of violence exposure to long-term health and health-related quality of life.
Davies SM, Crawley EM.	Gloucester Royal Hospital, United Kingdom.	Chronic fatigue syndrome in children aged 11 years old and younger.	Arch Dis Child. 2008 Jan 11 [Epub ahead of print]	AIM: To describe children who presented to the Bath paediatric CFS/ME service under the age of 12. Method: Inventories measuring fatigue, pain, functional disability, anxiety, family history and symptoms were collected prospectively for all children presenting to the Bath CFS/ME service between September 2004 and April 2007. Data from children who presented to the service under the age of 12 were described and compared to those who presented at age 12 or older. RESULTS: 178 children (under the age of 18) were diagnosed as having CFS/ME using the RCPCH criteria out of 216 children assessed. The mean age at assessment for children with CFS/ME was 14.5 years old (SD 2.9). 32 (16%) children were under 12 years old at the time of assessment, four children were under 5 years old and the youngest child was 2 years old. Children under 12 were very disabled with mean school attendance of just over 40% (average 2 days a week), Chalder Fatigue score of 8.29 (CI 7.14 -9.43 maximum possible score=11) and pain visual analogue score of 39.7 (possible range 0-100). Comparison with the children aged 12 or older showed that both groups were remarkably similar at assessment. 24/26 children with complete symptom lists, would have been diagnosed as having CFS/ME using the stricter adult CDC criteria. CONCLUSION: Disability in the under 12 age group was high, with low levels of school attendance, high level of fatigue, anxiety, functional disability and pain. The clinical pattern seen is almost identical to that seen in older children and the majority of children would also be diagnosed as having CFS/ME using the stricter adult definition.
Deary V, Chalder T, Sharpe M.	Institute of Health and Society, University of Newcastle, 21 Claremont Place, Newcastle Upon Tyne NE2 4AA, UK. vincent.deary@ncl.ac.uk	The cognitive behavioural model of medically unexplained symptoms: a theoretical and empirical review.	Clin Psychol Rev. 2007 Oct;27(7):781-97. Epub 2007 Jul 17.	The article is a narrative review of the theoretical standing and empirical evidence for the cognitive behavioural model of medically unexplained symptoms (MUS) in general and for chronic fatigue syndrome (CFS) and irritable bowel syndrome (IBS) in particular. A literature search of Medline and Psychinfo from 1966 to the present day was conducted using MUS and related terms as search terms. All relevant articles were reviewed. The search was then limited in stages, by cognitive behavioural therapy (CBT), condition, treatment and type of trial. Evidence was found for genetic, neurological, psychophysiological, immunological, personality, attentional, attributional, affective, behavioural, social and inter-personal factors in the onset and maintenance of MUS. The evidence for the contribution of individual factors, and their autopoietic interaction in MUS (as hypothesised by the

				cognitive behavioural model) is examined. The evidence from the treatment trials of cognitive behavioural therapy for MUS, CFS and IBS is reviewed as an experimental test of the cognitive behavioural models. We conclude that a broadly conceptualized cognitive behavioural model of MUS suggests a novel and plausible mechanism of symptom generation and has heuristic value. We offer suggestions for further research.
Díaz-Caneja Greciano A, Rodríguez Sosa JT, Aguilera Albesa S, Sánchez-Carpintero R, Soutullo Esperón C.	Unidad de Psiquiatría Infantil y Adolescente, Departamento de Psiquiatría y Psicología Médica, Clínica Universitaria, Universidad de Navarra, España. adiazcaneja@hotmail.com	[Chronic fatigue syndrome in a 15-year-old girl] [Article in Spanish]	An Pediatr (Barc). 2007 Jul;67(1):74-7.	Fatigue and lack of energy are frequent symptoms in children and adolescents. A diagnosis of chronic fatigue syndrome should be considered in children and adolescents who complain of chronic fatigue associated with other symptoms without a demonstrable physical cause. Lack of knowledge about this syndrome and late diagnosis may have a negative impact on the normal development of affected children and adolescents. Treatment should be based on a rehabilitation program with cognitive behavioral therapy and a gradual increase in activities.
Donnelly DL, Rockland RH, Reisman SS, Quigley KS.	New Jersey Inst. of Technol., Newark, NJ, USA.	Continuous measurement of BRSI in chronic fatigue syndrome.	Conf Proc IEEE Eng Med Biol Soc. 2004;2:906-8.	This paper discusses the development of a system to measure continuous cardiac baroreceptor measurement during a 45-minute 70-degree head-up tilt (HUT) of five groups of subjects suffering the following: chronic fatigue syndrome (CFS), CFS with fibromyalgia (CFS-FM), CFS with postural orthostatic tachycardia syndrome (CFS-POTS), controls with POTS (CON-POTS), and controls (CON). The duration of the test was 56-minutes, which included a five-minute supine baseline, a 45-minute HUT and a six-minute recovery period. The system was developed in LabView, and can provide a comparative time analyses of weighted BRSI averages. Baroreflex effectiveness index (BEI) was also investigated over the course of lags 0, 1 and 2 as well as an assessment of overall BEI performance between groups.
Edwards CR, Thompson AR, Blair A.	Barnsley Primary Care Trust, UK. catherine.edwards@barnsleypct.nhs.uk	An 'overwhelming illness': women's experiences of learning to live with chronic fatigue syndrome/myalgic encephalomyelitis.	J Health Psychol. 2007 Mar;12(2):203-14.	The processes through which people learn to live with CFS/ME are poorly understood and have not been rigorously explored within the literature. Semi-structured interviews were conducted with eight women and analysed using interpretative phenomenological analysis. Participants initially described being 'overwhelmed' by CFS/ME. Attempts at seeking help were unsatisfactory and participants described feeling let down and disbelieved. Participants reacted to this by identifying types of 'self-help' and assertively taking more responsibility for their illness and its treatment. Acquiring social support and greater knowledge were key mediating factors in the emergence of control and acceptance. The relevance of the themes to existing research and the implications for clinical practice are considered.
Ellen A. Schur, Carolyn Noonan, Dedra S. Buchwald		Prospective Study of Body Mass Index, Weight Change, and Fatigue in Acute	Journal of Chronic Fatigue Syndrome 2007; 14(3):	Objective: To examine the influence of body mass index (BMI) and weight change on fatigue severity and failure to recover in individuals with acute infectious mononucleosis. Methods: We prospectively studied 148 individuals presenting with a positive monospot test. We obtained measured weights and vitality subscale scores from the Short Form-36 Health Survey (SF-36) at the index visit and at 6 months. Results: The mean age of the participants was 21 years and 24% were overweight or obese.

		Infectious Mononucleosis		During acute illness, overweight and obese participants had an adjusted odds ratio for low vitality scores of 2.9 (confidence interval 1.2-7.1) compared to normal weight subjects. Neither index BMI nor 6-month weight gain was significantly associated with prolonged fatigue or failure to recover. Conclusion: Overweight and obese patients with acute infectious mononucleosis are more likely to experience severe fatigue. In contrast, neither baseline weight nor weight gain appear to impede recovery.
Emmert-Streib F.	Stowers Institute for Medical Research, Kansas City, Missouri 64110, USA. fes@stowers-institute.org	The chronic fatigue syndrome: a comparative pathway analysis.	J Comput Biol. 2007 Sep;14(7):961-72.	In this paper, we introduce a method to detect pathological pathways of a disease. We aim to identify biological processes rather than single genes affected by the chronic fatigue syndrome (CFS). So far, CFS has neither diagnostic clinical signals nor abnormalities that could be diagnosed by laboratory examinations. It is also unclear if the CFS represents one disease or can be subdivided in different categories. We use information from clinical trials, the gene ontology (GO) database as well as gene expression data to identify undirected dependency graphs (UDGs) representing biological processes according to the GO database. The structural comparison of UDGs of sick versus non-sick patients allows us to make predictions about the modification of pathways due to pathogenesis.
Endresen GK.	Department of Rheumatology, The National Hospital Rikshospitalet, Forskningsvn. 2, Block B, 0027 Oslo, Norway. gerhard.endresen @rikshospitalet.no	Fibromyalgia: a rheumatologic diagnosis?	Rheumatol Int. 2007 Sep;27(11):999-1004. Epub 2007 Jul 20.	Fibromyalgia (FM) is a medically unexplained or functional somatic syndrome (FSS). The two classification criteria are chronic widespread pain (CWP) and the finding of 11/18 tender points (TP). FM overlaps and co-occurs with other FSSs, and auxiliary symptoms that are not included in the criteria may be clues to other FSSs. About ten FSSs include chronic fatigue syndrome, myofascial pain syndromes and irritable bowel syndrome. TP do not reflect demonstrable pathology, and are locations where everyone is generally more tender. In FM they are more tender than normal due to lowered pain threshold. High TP counts are associated with the extent of distress or unspecific somatic symptoms in the absence of chronic pain. TP lack validity and should be excluded. CWP and distress are outside the domain of rheumatology, and abnormal mechanisms in FM relate to the central nervous system, as compared to "peripheral" mechanisms studied in rheumatology. FM should not be considered as a rheumatologic condition but rather as part of a broader spectre of FSSs. Patients with FSSs should be considered and treated together across medical specialities by general physicians in primary health care.
Eva Libman, Laura Creti, Dorrie Rizzo, Melanie Jastremski, Sally Bailes, Catherine S. Fichten		Descriptors of Fatigue in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2007; 14(3):	Objective: To explore how individuals with chronic fatigue syndrome (CFS) describe their fatigue experience and examine how this differs from descriptions of fatigue in healthy controls. Methods: 52 individuals with CFS and 27 controls listed words that described their fatigue. These words were grouped into 18 categories. Results: Individuals with CFS used more categories to describe their fatigue and more descriptors within each category. The most popular category used by both groups was energy depletion/physical weakness. CFS participants also experienced their fatigue as limiting their ability to function, frustrating, permanent/ persistent, out of their control, depressing, and pervading all aspects of their lives. Controls reported that when they experienced fatigue, it was temporary, and they felt unmotivated, sleepy, and comfortable. Conclusion: Themultidimensional descriptive pattern characterizing the fatigue of individuals with CFS differs dramatically from the experienced fatigue of healthy individuals, suggesting their "language of fatigue" has a distinctive quality. Keywords: Fatigue, chronic fatigue syndrome, measure

Evengård B, Gräns H, Wahlund E, Nord CE.	Division of Clinical Microbiology, Department of Laboratory Medicine, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden.	Increased number of Candida albicans in the faecal microflora of chronic fatigue syndrome patients during the acute phase of illness.	Scand J Gastroenterol. 2007 Sep 18;:1-2 [Epub ahead of print]	
Faulkner S, Smith A.		A longitudinal study of the relationship between psychological distress and recurrence of upper respiratory tract infections in chronic fatigue syndrome.	Br J Health Psychol. 2006 Dec 18 [Epub ahead of print]	ObjectivesPrevious research has found that chronic fatigue syndrome (CFS) patients report increased susceptibility to upper respiratory tract illnesses (URTIs) when compared with healthy volunteers. This study aimed to replicate and extend this research by investigating the role of psychological distress (stress and negative mood) in the recurrence of URTIs in CFS patients as well as its role in the recurrence of CFS symptoms.DesignA 15-week diary study.MethodsMeasures of psychological stress, negative mood, recurrence of URTIs and symptoms were recorded each week for a 15-week period. CFS patients (N=21), who had been assessed and diagnosed according to the Oxford criteria, were recruited from the Cardiff Chronic Fatigue Clinic and compared with a matched group of healthy controls (N=18). Frequency of occurrence of infectious illness and the relationship between psychological stress/negative mood and occurrence of illness were assessed.ResultsCFS patients reported more URTIs than the controls. Stress scores (and negative mood) were significantly higher in the week prior to the occurrence of URTIs than in weeks when no subsequent illness occurred. High levels of psychological stress also preceded the severity of reported symptoms of fatigue in the CFS group.ConclusionsCFS patients reported more frequent URTIs than healthy controls and these recurrences were preceded by high levels of psychological stress. High levels of stress were also associated with greater subsequent fatigue. Possible explanations of these results are discussed.
Friedberg F, Quick J.	Stony Brook University, Stony Brook, NY 11794-8790, USA. fred.friedberg@stonybrook.edu	Alexithymia in chronic fatigue syndrome: associations with momentary, recall, and retrospective measures of somatic complaints and emotions.	Psychosom Med. 2007 Jan;69(1):54-60.	OBJECTIVE: The relationship between alexithymia and real-time momentary symptom assessments has not been reported. This cross-sectional study hypothesized that alexithymia would be a predictor of somatic symptoms using three different types of symptom measurement (momentary, recall, and retrospective) in the medically unexplained illness of chronic fatigue syndrome (CFS). In addition, it was hypothesized that negative affect would be a significant mediator of the relationship between alexithymia and somatic symptoms. Finally, the relation of alexithymia to physical illness attribution (a CFS illness predictor) was explored. METHODS: Participants were 111 adults with CFS. Alexithymia was assessed with the Toronto Alexithymia Scale. Momentary ratings of current symptoms and affect were recorded in electronic diaries carried for 3 weeks. Weekly recall of these momentary reports was also recorded. Retrospective measures included 6-month ratings of fatigue and pain, the Fatigue Severity Scale, the Brief Pain Inventory-Short Form, a CFS symptom measure, the Beck Depression Inventory-II, the Beck Anxiety Inventory, and an illness attribution rating. RESULTS: Partial correlations, controlling

				for age and sex, yielded no significant associations between general or specific forms of alexithymia and momentary ratings of fatigue or pain. On the other hand, a significant association, partially mediated by anxiety scores, was found between a specific form of alexithymia and a retrospective pain measure. Finally, physical illness attribution was not significantly associated with alexithymia. CONCLUSION: Based on assessments of real-time and retrospectively measured symptoms, these data provided only modest support for the alexithymia construct as a predictor of somatic symptoms in people with CFS.
Friedberg F, Sohl S, Schmeizer B.	Department of Psychiatry and Behavioral Medicine, Stony Brook University, NY 11794-8790, USA. fred.friedberg@stonybrook.edu	Publication trends in chronic fatigue syndrome: comparisons with fibromyalgia and fatigue: 1995-2004.	J Psychosom Res. 2007 Aug;63(2):143-6.	OBJECTIVE: In order to identify publishing patterns in chronic fatigue syndrome (CFS), we compared the annual number of peer review articles for CFS, fibromyalgia (FM), and non-CFS fatigue over a recent decade (1995-2004). METHOD: Citations were drawn from Ovid/Medline, PsychInfo, and the Journal of Chronic Fatigue Syndrome for peer review articles focusing on CFS, FM, and fatigue for each year of the decade ending in 2004. Statistics included chi-square, tests for differences in proportions, and regression-based curve estimation. RESULTS: The frequency of CFS peer review articles did not significantly change from the first half to the second half of the decade (1995-2004). By comparison, the output of both FM and fatigue articles significantly increased (P<.0001). A quadratic model (inverted U shape; P<.02) best fit the data for CFS annual publication frequency. By comparison, exponential models best fit the data for both FM (P<.0001) and fatigue (P<.0001) citations. The highest percentage of citations (15-16%) for both CFS and FM fell within the domains of diagnosis, physiopathology, and psychology. For fatigue, almost one third (31.4%) of the citations were focused on etiology, while psychology (11.5%) and physiopathology (10.4%) articles were the next most cited. Based on first-author affiliation, CFS articles were most likely to originate in the United States (37.7%), England (31.4%), and the Netherlands (4.9%). CONCLUSION: The output of CFS peer review articles has not increased over the past decade, while the number of FM and fatigue articles has increased substantially.
Galland BC, Jackson PM, Sayers RM, Taylor BJ.	Department of Women's & Children's Health, University of Otago, Dunedin 9015, New Zealand.	A Matched Case Control Study of Orthostatic Intolerance in Children/Adolescents With Chronic Fatigue Syndrome.	Pediatr Res. 2008 Feb;63(2):196-202.	This study aimed to define cardiovascular and heart rate variability (HRV) changes following head-up tilt (HUT) in children/adolescents with chronic fatigue syndrome (CFS) in comparison to age- and gender-matched controls. Twenty-six children/adolescents with CFS (11-19 y) and controls underwent 70-degree HUT for a maximum of 30 min, but returned to horizontal earlier at the participant's request with symptoms of orthostatic intolerance (OI) that included lightheadedness. Using electrocardiography and beat-beat finger blood pressure, a positive tilt was defined as OI with 1) neurally mediated hypotension (NMH); bradycardia (HR <75% of baseline), and hypotension [systolic pressure (SysP) drops >25 mm Hg)] or 2) postural orthostatic tachycardia syndrome (POTS); HR increase >30 bpm, or HR >120 bpm (with/without hypotension). Thirteen CFS and five controls exhibited OI generating a sensitivity and specificity for HUT of 50.0% and 80.8%, respectively. POTS without hypotension occurred in seven CFS subjects but no controls. POTS with hypotension and NMH occurred in both. Predominant sympathetic components to HRV on HUT were measured in CFS tilt-positive subjects. In conclusion, CFS subjects were more susceptible to OI than controls, the cardiovascular response predominantly manifest as POTS without hypotension, a response unique to CFS suggesting further investigation is warranted with respect to the pathophysiologic mechanisms involved. ABBREVIATIONS::

Gielissen MF, Knoop H, Servaes P, Kalkman JS, Huibers MJ, Verhagen S, Bleijenberg G.	Expert Centre Chronic Fatigue Nijmegen, Radboud University, Nijmegen Medical Centre, The Netherlands. m.gielissen@nkcv.umcn.nl	Differences in the experience of fatigue in patients and healthy controls: patients' descriptions.	Health Qual Life Outcomes. 2007 Jul 2;5:36.	BACKGROUND: The primary objective was to develop an adjective checklist, the Fatigue Quality List (FQL), aimed at assessing different perceptions of fatigue. METHODS: 961 participants filled out the FQL (28 adjectives). A component and confirmatory factor analyses were performed and psychometric properties were evaluated. Differences on factor scores between different patients' groups were investigated and pre- and post treatment scores were compared in demonstrating change of perceptions after treatment of fatigue. RESULTS: Four independent factors were found with adequate psychometric properties. Different perceptions were found between the patients' groups. Patients who were recovered after treatment for fatigue showed similar scores on the factors as healthy controls. CONCLUSION: The FQL appears to be a promising tool in measuring different perceptions of fatigue, which can be especially interesting for clinical practice.
Gilula MF.	President and Director, Life Energies Research Institute, 2510 Inagua Avenue, Miami, FL 33133, USA. mgilula@mindspring.com	Cranial electrotherapy stimulation and fibromyalgia.	Expert Rev Med Devices. 2007 Jul;4(4):489-95.	Cranial electrotherapy stimulation (CES) is a well-documented neuroelectrical modality that has been proven effective in some good studies of fibromyalgia (FM) patients. CES is no panacea but, for some FM patients, the modality can be valuable. This article discusses aspects of both CES and FM and how they relate to the individual with the condition. FM frequently has many comorbidities such as anxiety, depression, insomnia and a great variety of different rheumatologic and neurological symptoms that often resemble multiple sclerosis, dysautonomias, chronic fatigue syndrome and others. However, despite long-standing criteria from the American College of Rheumatology for FM, some physicians believe there is probably no single homogeneous condition that can be labeled as FM. Whether it is a disease, a syndrome or something else, sufferers feel like they are living one disaster after another. Active self-involvement in care usually enhances the therapeutic results of various treatments and also improves the patient's sense of being in control of the condition. D-ribose supplementation may prove to significantly enhance energy, sleep, mental clarity, pain control and well-being in FM patients. A form of evoked potential biofeedback, the EPFX, is a powerful stress reduction technique which assesses the chief stressors and risk factors for illness that can impede the FM patient's built-in healing abilities. Future healthcare will likely expand the diagnostic criteria of FM and/or illuminate a group of related conditions and the ways in which the conditions relate to each other. Future medicine for FM and related conditions may increasingly involve multimodality treatment that features CES as one significant part of the therapeutic regimen. Future medicine may also include CES as an invaluable, cost-effective add-on to many facets of clinical pharmacology and medical therapeutics.
Glover DS, Brown GP, Fairburn CG, Shafran R.	Royal Holloway University of London, UK.	A preliminary evaluation of cognitive-behaviour therapy for clinical perfectionism: a case series.	Br J Clin Psychol. 2007 Mar;46(Pt 1):85-94.	OBJECTIVE: The construct of 'clinical perfectionism' has been developed in response to criticisms that other approaches have failed to yield advances in the treatment of the type of self-oriented perfectionism that poses a clinical problem. The primary aim of this study was to conduct a preliminary investigation into the efficacy of a theory-driven, cognitive-behavioural intervention for 'clinical perfectionism'. DESIGN: A multiple baseline single case series design was used. METHOD: A specific, 10-session cognitive-behavioural intervention to address clinical perfectionism in eating disorders was adapted to allow its use in nine patients referred with a range of axis I disorders and clinical perfectionism. RESULTS: The intervention led to clinically significant improvements in self-referential perfectionism from pretreatment to follow-up for six of the nine participants on two perfectionism measures and for three of the nine participants on the measure of clinical

				perfectionism. Statistically significant improvements from pre- to post-intervention for the group as a whole were found on all three measures. The improvements were maintained at follow-up. CONCLUSIONS: The finding that clinical perfectionism is improved in the majority of participants is particularly encouraging given that perfectionism has traditionally been viewed as a personality characteristic resistant to change. These preliminary findings warrant replication in a larger study.
Godfrey E, Chalder T, Ridsdale L, Seed P, Ogden J.	Department of Psychology, Institute of Psychiatry, Kings College London, UK. emma.l.godfrey@kcl.ac.uk	Investigating the active ingredients of cognitive behaviour therapy and counselling for patients with chronic fatigue in primary care: developing a new process measure to assess treatment fidelity and predict outcome.	Br J Clin Psychol. 2007 Sep;46(Pt 3):253-72.	OBJECTIVES: To develop a brief measure of the therapy process and use it to examine which therapeutic ingredients were associated with outcome in a sample of patients from a randomized controlled trial (RCT) of cognitive behaviour therapy (CBT) versus counselling for patients with chronic fatigue in primary care. It was hypothesized that the two therapies would be clearly distinguishable and that in terms of process variables, the therapeutic alliance would be important in predicting outcome. DESIGN: The data for this study were collected alongside a RCT in primary care and included audiotaped therapy sessions. These tapes were assessed by two independent raters using a newly devised measure in order to evaluate therapy process and its relationship with outcome. METHODS: Tapes from 71 patients participating in the RCT were assessed to form the basis of the process analysis. Outcome was self-reported fatigue symptoms at 6 months follow-up. Data reduction was achieved via a principal component analysis (PCA). Factors were entered into a multiple regression analysis to produce a final model of predictors of outcome. RESULTS: The process measure showed that although the treatments could be distinguished, there was some overlap between them. The key predictor of a good fatigue outcome was emotional processing, including the expression, acknowledgement and acceptance of emotional distress. CONCLUSION: A new process measure was developed successfully which now warrants further testing. It was able to assess treatment adherence and unpack, and distinguish the common factor which predicted outcome across therapy modalities. The findings lend preliminary support to the view that the specific techniques associated with particular 'brand names' of therapy are not necessarily the 'active ingredients' that help patient's change within the primary care setting. Emotional processing predicted outcome for patients with chronic fatigue and therefore future research might explore this in more depth, in order to understand better how it can be facilitated.
Goudsmit EM.		Chronic fatigue syndrome	J R Soc Med. 2007 Jan;100(1):7. Comment on: J R Soc Med. 2006 Oct;99(10):506-20	
Guo J.	Hospital of Chengdu Jiuxing Company of Textile Group, Chengdu 610053, China.	Chronic fatigue syndrome treated by acupuncture and moxibustion in combination with psychological approaches in 310 cases.	J Tradit Chin Med. 2007 Jun;27(2):92-5.	OBJECTIVE: To observe clinical therapeutic effect of acupuncture and moxibustion combined with a psychological approach on chronic fatigue syndrome (CFS). METHODS: The treatment was given by acupuncture plus moxibustion combined with a psychological approach based on differentiation of symptoms and signs in 310 cases. RESULTS: Of 310 cases observed, 275 cases (88.7%) were clinically cured, 28 cases (9%) improved, and 7 cases (2.3%) failed. CONCLUSION: Acupuncture plus moxibustion combined with a psychological approach is an effective therapy for CFS.

Gupta S, Aslakson E, Gurbaxani BM, Vernon SD.	Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vector-Borne, and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. shaktig@gmail.com	Inclusion of the glucocorticoid receptor in a hypothalamic pituitary adrenal axis model reveals bistability.	Theor Biol Med Model. 2007 Feb 14;4:8.	BACKGROUND: The body's primary stress management system is the hypothalamic pituitary adrenal (HPA) axis. The HPA axis responds to physical and mental challenge to maintain homeostasis in part by controlling the body's cortisol level. Dysregulation of the HPA axis is implicated in numerous stress-related diseases. RESULTS: We developed a structured model of the HPA axis that includes the glucocorticoid receptor (GR). This model incorporates nonlinear kinetics of pituitary GR synthesis. The nonlinear effect arises from the fact that GR homodimerizes after cortisol activation and induces its own synthesis in the pituitary. This homodimerization makes possible two stable steady states (low and high) and one unstable state of cortisol production resulting in bistability of the HPA axis. In this model, low GR concentration represents the normal steady state, and high GR concentration represents a dysregulated steady state. A short stress in the normal steady state produces a small perturbation in the GR concentration that quickly returns to normal levels. Long, repeated stress produces persistent and high GR concentration that does not return to baseline forcing the HPA axis to an alternate steady state. One consequence of increased steady state GR is reduced steady state cortisol, which has been observed in some stress related disorders such as Chronic Fatigue Syndrome (CFS). CONCLUSION: Inclusion of pituitary GR expression resulted in a biologically plausible model of HPA axis bistability and hypocortisolism. High GR concentration enhanced cortisol negative feedback on the hypothalamus and forced the HPA axis into an alternative, low cortisol state. This model can be used to explore mechanisms underlying disorders of the HPA axis.
Hairon N; NICE.		NICE guidance on managing chronic fatigue syndrome/ME.	Nurs Times. 2007 Sep 25-Oct 1;103(39):21-2.	
Hakariya Y, Kuratsune H.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University.	[Chronic fatigue syndrome: biochemical examination of blood] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1071-6.	Though patients with chronic fatigue syndrome (CFS) have lots of complaints, abnormal findings cannot be detected by biochemical screening tests. However, some specialized blood tests have revealed neuroendocrine immune axis abnormalities, which is closely associated with each other. Recent studies indicate that CFS can be understood as a special condition based on abnormality of the psycho-neuro-endocrino-immunological system, with the distinguishing feature of CFS seeming to be the secondary brain dysfunction caused by several cytokines and/or autoantibodies. In this paper, we summarize these abnormalities found in CFS and show the neuro-molecular mechanism leading to chronic fatigue.
Hanna Grans, Birgetta Evengard, Peter Nilsson		Transcriptome Analysis of Peripheral Blood Mononuclear Cells from Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2007; 14(3):	Objective: Chronic fatigue syndrome (CFS) is an illness defined by unexplained disabling fatigue lasting longer than six months, together with at least four out of eight specified symptoms. The etiology and pathophysiology of CFS are to a large degree unknown. Since much remains unclear about CFS we wanted to investigate transcript expression levels in peripheral blood mononuclear cells to identify genes that are involved in CFS. Method: Transcript expression profiles for 20 CFS patients were compared with 14 healthy controls using microarray technology. Results were verified with real-time PCR. Results: We have identified significantly differentially expressed genes comparing a female CFS patient subgroup with gradual illness onset and no previously documented infection with female healthy controls. We have also created a list of genes with indicated, but not verified, expression differences from comparisons between other subgroups and healthy controls. These genes are

				candidates for further study of potential involvement in CFS. Conclusion: Our results stress the necessity of subgrouping the heterogeneous CFS patient cohort. The mRNA expression differences identified here may be causal factors for the illness or symptoms observed in these patients, or a result of altered functions of other cellular components involved in the illness. The role of these genes in the CFS pathology needs further investigation.
Harvey SB, Wadsworth M, Wessely S, Hotopf M.	Department of Psychological Medicine, Institute of Psychiatry, Kings College London, London, UK.	The relationship between prior psychiatric disorder and chronic fatigue: evidence from a national birth cohort study.	Psychol Med. 2007 Nov 2;:1-8 [Epub ahead of print]	BACKGROUND: Increased rates of psychiatric disorder have previously been reported in those diagnosed with chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME), although the direction of causation in this relationship has not been established. We aimed to test the hypothesis that individuals with self-reported CFS/ME have increased levels of psychiatric disorder prior to the onset of their fatigue symptoms.MethodA total of 5362 participants were prospectively followed with various measures of personality, psychiatric disorder and fatigue levels collected over the first 43 years of their life. CFS/ME was identified through self-report during a semi-structured interview at age 53 years. RESULTS: Thirty-four (1.1%) of the 3035 subjects assessed at age 53 years reported a diagnosis of CFS/ME. CFS/ME was more common among females, but there was no association between CFS/ME and either social class, social mobility or educational level. Those with psychiatric illness between the ages of 15 and 36 years were more likely to report CFS/ME later in life with an odds ratio (OR, adjusted for sex) of 2.65 [95% confidence interval (CI) 1.26-5.57, p=0.01]. Increased levels of psychiatric illness, in particular depression and anxiety, were present prior to the occurrence of fatigue symptoms. There was a dose-response relationship between the severity of psychiatric symptoms and the likelihood of later CFS/ME. Personality factors were not associated with a self-reported diagnosis of CFS/ME. CONCLUSIONS: This temporal, dose-response relationship suggests that psychiatric disorders, or shared risk factors for psychiatric disorders, are likely to have an aetiological role in some cases of CFS/ME.
Hashimoto N.	Center for Medical Education and Information.	[History of chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):975-82.	Chronic fatigue syndrome (CFS) is not a new disease. Similar morbidities have been known as different names since past several centuries. For example, neurasthenia, epidemic neuromyasthenia, myalgic encephalomyelitis, Akureyri disease, Royal Free disease, chronic EBV disease, post-viral fatigue syndrome etc. Much of the recent interest in CFS was generated by incidence of infection-like outbreak at Lake Tahoe in Nevada. The Center for Disease Control (USA) realized that correlation was poor between those patients who had virologic evidence of EBV infection and those who had the symptoms of chronic fatigue. This is a review of the history of CFS. (1) Historical perspectives in chronic fatigue cases in past old period, (2) Post-viral infectious fatigue and chronic fatigue (myalgic encephalomyelitis), (3) Recent trend of CFS studies and its clinical similar situation. Finally, I would like to state that we intend to draw up a new diagnostic guideline for CFS in Japan.
Heim ME, v d Malsburg ML, Niklas A.	Sonnenberg-Klinik, Bad Sooden-Allendorf, Germany. heim@sonnenberg-klinik.de <heim@sonnenber	Randomized controlled trial of a structured training program in breast cancer patients with tumor-related chronic fatigue.	Onkologie. 2007 Sep;30(8-9):429-34. Epub 2007 Sep 7.	BACKGROUND: Cancer-related fatigue is the most disabling symptom experienced by breast cancer patients following the cancer treatment. The positive effects of physical activity in the rehabilitation of breast cancer patients are documented in several studies. In a randomized controlled study the effects of a structured physical training program on fatigue and health-related quality of life were evaluated. PATIENTS AND METHODS: 63 breast cancer patients with cancer-related chronic fatigue were randomized at the beginning of the inpatient rehabilitation. The control group received the standard complex rehabilitation program, the intervention group a structured physical training program and

	g-klinik.de>			additional muscle strength and aerobic exercises. The effects of the treatment were evaluated by questionnaires at the start of rehabilitation (t1), end of rehabilitation (t2), and 3 months after t2 (t3). Isometric muscle strength and aerobic capacity were evaluated at t1 and t2. RESULTS: There was an improvement of muscle strength at the end of rehabilitation for both groups. The increase from t1 to t2 was significantly higher for the training group. The scores for global quality of life, physical well-being, and functionality increased from t1 to t2, but further improvement in the follow-up (t3) was only observed in the training group. The cancer-related fatigue was significantly reduced in the training group from t1 to t3, however, not in the control group. CONCLUSIONS: Structured physical training programs initiated during inpatient rehabilitation and continuously practiced in the time thereafter can improve symptoms of chronic fatigue and quality of life in breast cancer patients.
Hempel S, Chambers D, Bagnall AM, Forbes C.	Centre for Reviews and Dissemination, University of York, York, UK.	Risk factors for chronic fatigue syndrome/myalgic encephalomyelitis: a systematic scoping review of multiple predictor studies.	Psychol Med. 2007 Sep 25;:1-12 [Epub ahead of print]	BACKGROUND: The aetiology of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is still unknown. The identification of risk factors for CFS/ME is of great importance to practitioners.MethodA systematic scoping review was conducted to locate studies that analysed risk factors for CFS/ME using multiple predictors. We searched for published and unpublished literature in 11 electronic databases, reference lists of retrieved articles and guideline stakeholder submissions in conjunction with the development of a forthcoming national UK guideline. Risk factors and findings were extracted in a concise tabular overview and studies synthesized narratively. RESULTS: Eleven studies were identified that met inclusion criteria: two case-control studies, four cohort studies, three studies combining a cohort with a case-control study design, one case-control and twin study and one cross-sectional survey. The studies looked at a variety of demographic, medical, psychological, social and environmental factors to predict the development of CFS/ME. The existing body of evidence is characterized by factors that were analysed in several studies but without replication of a significant association in more than two studies, and by studies demonstrating significant associations of specific factors that were not assessed in other studies. None of the identified factors appear suitable for the timely identification of patients at risk of developing CFS/ME within clinical practice. CONCLUSIONS: Various potential risk factors for the development of CFS/ME have been assessed but definitive evidence that appears meaningful for clinicians is lacking.
Henningsen P, Zipfel S, Herzog W.	Department of Psychosomatic Medicine and Psychotherapy, University Hospital, Technical University of Munich, Langerstrasse 3, 81675 Munich, Germany. p.henningsen@tum.de	Management of functional somatic syndromes.	Lancet. 2007 Mar 17;369(9565):946-55. Comment in: Lancet. 2007 May 19;369(9574):1691-2.	Although functional somatic syndromes (FSS) show substantial overlap, treatment research is mostly confined to single syndromes, with a lack of valid and generally accepted diagnostic criteria across medical specialties. Here, we review management for the full variety of FSS, drawn from systematic reviews and meta-analyses since 2001, and give recommendations for a stepped care approach that differentiates between uncomplicated and complicated FSS. Non-pharmacological treatments involving active participation of patients, such as exercise and psychotherapy, seem to be more effective than those that involve passive physical measures, including injections and operations. Pharmacological agents with CNS action seem to be more consistently effective than drugs aiming at restoration of peripheral physiological dysfunction. A balance between biomedical, organ-oriented, and cognitive interpersonal approaches is most appropriate at this truly psychosomatic interface. In view of the iatrogenic component in the maintenance of FSS, doctor-centred interventions and close observation of the doctor-patient relationship are of particular importance.

Hepburn AL.		Adult coeliac disease: Rheumatic presentations are common	BMJ. 2007 Sep 29;335(7621):627. Comment on: BMJ. 2007 Sep 15;335(7619):558-62.	.
Hinton DE, Hinton L, Tran M, Nguyen M, Nguyen L, Hsia C, Pollack MH.	Harvard Medical School. devon_hinton@hms.harvard.edu.	Orthostatic panic attacks among vietnamese refugees.	Transcult Psychiatry. 2007 Dec;44(4):515-44.	Viewed historically and cross-culturally, orthostatic-induced dizziness, i.e., dizziness caused by standing up from a sitting or a lying position, forms a key aspect of many syndromes: irritable heart (American Civil War), effort syndrome (World War I and World War II), chronic fatigue syndrome (contemporary USA), Gulf War syndrome (contemporary USA), and orthostatic dysregulation (contemporary Japan). Among Vietnamese refugees attending a psychiatric clinic, this study documents a high rate of orthostatic panic (OP), as well as certain processes seemingly generating these panic attacks, viz., flashbacks and culturally specific catastrophic cognitions. Case examples are used to demonstrate OP's phenomenology and relevance to clinical care. To illustrate the mechanisms producing OP, we adduce the multiplex model of panic generation. Culturally appropriate care of Vietnamese refugees should include assessment and treatment of OP.
Hoseini SS, Gharibzadeh S.		Potential drugs for improving chronic fatigue syndrome.	J Neuropsychiatry Clin Neurosci. 2007 Fall;19(4):472.	
Iakupov RR, Safin VF.		[State of locomotory system under chronic functional overstrain in female manual workers] [Article in Russian]	Med Tr Prom Ekol. 2007;(7):37-9.	
Ismail K, Kent K, Sherwood R, Hull L, Seed P, David AS, Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK.	Chronic fatigue syndrome and related disorders in UK veterans of the Gulf War 1990-1991: results from a two-phase cohort study.	Psychol Med. 2007 Sep 25;:1-9 [Epub ahead of print]	BACKGROUND: The aim was to determine the prevalence of chronic fatigue syndrome (CFS), chronic fatigue and fibromyalgia in UK military personnel after the Gulf War 1990-1991.MethodA two-phase cohort study was used. Three randomly selected subsamples identified from a population-based cross-sectional postal survey of over 10 000 current and ex-service UK military personnel (Gulf veterans were those deployed to the Gulf War 1990-1991; non-Gulf veterans were Bosnia peacekeepers 1992-1997 and those on active duty during the Gulf War 1990-1991 but not deployed) were recruited. Their disability status was assessed using the Short Form 36 physical functioning scale; Gulf veterans who reported physical disability (n=111) were compared with non-Gulf (n=133) veterans who reported similar levels of physical disability. Screening for known medical and psychiatric conditions was conducted to exclude medical explanations for disability and symptomatic distress. Standardised criteria for CFS, chronic fatigue and fibromyalgia were used. RESULTS: Disabled Gulf veterans were more likely to be overweight, have elevated gamma-glutamyl transferase levels and screen positive for hypertension. There were no other clinically significant differences in clinical markers for medically

				explainable conditions. Disabled Gulf veterans were more likely than similarly disabled Bosnia and Era veterans (adjusted odds ratio 7.8, 95% confidence interval 2.5-24.5) to meet the criteria for CFS. Rates for other medically unexplained conditions were not significantly increased. CONCLUSIONS: Symptoms in keeping with CFS account for a significant part of the symptomatic distress in Gulf veterans.
Jansen NW, Huibers MJ, van Amelsvoort LG, Kant I.	Capaciteitsgroep Epidemiologie van de Universiteit Maastricht. Nicole.Jansen@epid.unimaas.nl	[Aetiology of prolonged fatigue among workers. An overview of findings from the Maastricht Cohort Study] [Article in Dutch]	Comment in: Tijdschr Psychiatr. 2007;49(8):555-7.	BACKGROUND: Considerable attention is being given to prolonged fatigue among workers because it occurs so frequently and is alleged to have serious consequences. AIM: To present an overview of the magnitude, causes and consequences of prolonged fatigue in the workplace with a view to preventing its occurrence. METHOD: On the basis of of the articles written as part of the Maastricht Cohort Study we present an overview of this study, a prospective cohort study (n=12,140) that covered a period of 4 years. results Prolonged fatigue seems to occur frequently among workers. Risk factors in the aetiology of prolonged fatigue were found in subjective and objective work-related factors, as well as in factors related to the health and private situation of the employee. CONCLUSION: The assumed multifactorial aetiology of prolonged fatigue was confirmed by means of prospective analyses in the Maastricht Cohort Study. The observed risk factors can be applied as tools for the development of effective preventive measures against prolonged fatigue.
Jansen Y, Koolhaas MP	Steungroep ME en Arbeidsongeschiktheidynskejansen@home.nl	[Fatigue, myalgic encephalomyelitis/ chronic fatigue syndrome and work] [Article in Dutch]	Tijdschr Psychiatr. 2007;49(8):555-7. Comment on: Tijdschr Psychiatr. 2007;49(8):537-45. Tijdschr Psychiatr. 2007;49(8):547-54.	.
Jedlicka F, Elbl L, Vásová I, Tomásková I, Vorlícek J, Spinar J.	Interní kardiologická klinika Lékarské fakulty MU a FN Brno. fjedlicka@fnbrno.cz	[Chronic fatigue syndrome in cancer patients. Diagnostic and treatment options] [Article in Czech]	Vnitr Lek. 2007 Sep;53(9):979-85. Comment in: Vnitr Lek. 2007 Sep;53(9):930.	Fatigue is the most frequent symptom accompanying a cancer disease and its treatment according to the visual analogue scale. Fatigue is reported by as many as 100% of patients in the course of cancer treatment and still by 40 to 70% of patients one year after the treatment has finished. This symptom has become known under the designation of "cancer-related fatigue" in the English language literature on the subject. The knowledge of the causes and mechanisms of fatigue is relatively limited. Based on practical guidelines, an algorithm has been used to detect, evaluate and influence by treatment the syndrome of fatigue caused by a cancer disease. Research in the field has been focused on both pharmacological and non-pharmacological approach. The highest efficiency in the treatment of fatigue syndrome has been recorded for the treatment of anaemia with erythropoietin, while aerobic exercise programmes have proven to be most efficient among the behavioural measures. In spite of a dramatically growing interest in the above problem in the past decade, a number of issues continue unresolved with respect to chronic fatigue syndrome related to a cancer disease or to its treatment. Based on their own experience and on the relevant literature, the authors deal with issues of chronic fatigue syndrome and the options for its diagnosing and treatment in patients undergoing cancer treatment.
Jerjes WK, Taylor NF, Wood PJ, Cleare AJ.	Department of Clinical Biochemistry,	Enhanced feedback sensitivity to	Psychoneuroendocrinology. 2007 Feb;32(2):192-8.	OBJECTIVE: Enhancement of negative feedback control of the HPA axis in patients with chronic fatigue syndrome (CFS) has been reported using the low dose dexamethasone suppression test. We have developed the use of prednisolone (5mg) as a more physiologically appropriate alternative to

	Guy's, King's and St Thomas' School of Medicine, Bessemer Road, London SE5 9RS, UK. w_jerjes@yahoo.co.uk	prednisolone in chronic fatigue syndrome.	Epub 2007 Feb 5.	dexamethasone in the investigation of mild degrees of glucocorticoid resistance or supersensitivity. The objective of the study was to use this test to look for alterations in negative feedback control of the HPA axis in CFS patients. METHODS: Fifteen patients with CFS were recruited after fulfilling strict criteria including the absence of comorbid psychiatric diagnosis. They collected urine between 0900 and 1800h and saliva at 0900h pre-prednisolone. At midnight, they took prednisolone (5mg) orally and then collected urine and saliva at the same intervals the following day. RESULTS: Salivary cortisol was lower in CFS subjects pre-prednisolone than controls. Urinary cortisol metabolites were lower in CFS subjects pre-prednisolone, but did not reach significance. Both measures were significantly lower in CFS subjects post-dose. Mean percentage suppression of both salivary cortisol and urinary cortisol metabolites was significantly higher in CFS compared to controls. CONCLUSION: There is enhanced sensitivity of the HPA axis to negative feedback in CFS as demonstrated using the prednisolone suppression test. This provides further evidence of alterations in the control of the HPA axis in patients with established CFS.
Johansson S, Ytterberg C, Claesson IM, Lindberg J, Hillert J, Andersson M, Widén Holmqvist L, von Koch L.	Division of Neurology, Dept. of Clinical Neuroscience, Karolinska Institutet, Karolinska University Hospital Huddinge, SE-141 86 Stockholm, Sweden. sverker.johansson@ki.se	High concurrent presence of disability in multiple sclerosis. Associations with perceived health.	J Neurol. 2007 Jun;254(6):767-73. Epub 2007 Apr 2.	OBJECTIVES : (1) To explore functioning and concurrent presence of disabilities - concerning cognition, manual dexterity, walking, energy, mood, activities of daily living (ADL), and social/lifestyle activities - in persons with multiple sclerosis (PwMS) cared for at an outpatient MS clinic. 2) To describe the PwMS' perceived physical and psychological impact and associations with the same disabilities. MATERIAL/METHODS : A descriptive cross-sectional study was carried out in 219 PwMS at the MS Centre, Karolinska University Hospital. Logistic regression employing proportional odds models was used to identify the associations of the disabilities with the perceived physical and psychological impact. RESULTS : In this sample the distribution with regard to disease severity as per Expanded Disability Status Scale was; mild 59.5%, moderate 17% and severe 23.5%. Despite the high proportion with mild disease severity disability regarding cognition was found in 49%, manual dexterity 76%, walking 43%, energy 67%, mood 29%, ADL 44% and social/lifestyle activities in 48%. Two or more disabilities were found in 80%, 24 % had six or seven disabilities. Disability regarding energy, mood, walking, manual dexterity and ADL was significantly associated with increase in the perceived physical impact, whereas disability in energy and mood was significantly associated with increase in the perceived psychological impact. CONCLUSIONS : The presence of several concurrent disabilities, some significantly associated with high perceived physical and psychological impact, in the majority of PwMS in outpatient clinics highlights the importance to identify disabilities, in particular fatigue and depressed mood, in order to supply health care interventions aiming to improve the life situation of PwMS.
Jones JF, Maloney EM, Boneva RS, Jones AB, Reeves WC.	Division of Viral and Rickettsial Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control	Complementary and alternative medical therapy utilization by people with chronic fatiguing illnesses in the United States.	BMC Complement Altern Med. 2007 Apr 25;7:12.	BACKGROUND: Chronic fatiguing illnesses, including chronic fatigue syndrome (CFS), pose a diagnostic and therapeutic challenge. Previous clinical reports addressed the utilization of health care provided to patients with CFS by a variety of practitioners with other than allopathic training, but did not examine the spectrum of complementary and alternative medicine (CAM) therapies used. This study was designed to measure CAM therapy use by persons with fatiguing illnesses in the United States population. METHODS: During a random-digit dialing survey to estimate the prevalence of CFS-like illness in urban and rural populations from different geographic regions of the United States, we queried the utilization of CAM including manipulation or body-based therapies, alternative medical

	and Prevention, Atlanta, GA 30333, USA. jaj9@cdc.gov			systems, mind-body, biologically-based, and energy modalities. RESULTS: Four hundred forty fatigued and 444 non-fatigued persons from 2,728 households completed screening. Fatigued subjects included 53 persons with prolonged fatigue, 338 with chronic fatigue, and 49 with CFS-like illness. Mind-body therapy (primarily personal prayer and prayer by others) was the most frequently used CAM across all groups. Among women, there was a significant trend of increasing overall CAM use across all subgroups (p-trend = 0.003). All categories of CAM use were associated with significantly poorer physical health scores, and all but one (alternative medicine systems) were associated with significantly poorer mental health scores. People with CFS-like illness were significantly more likely to use body-based therapy (chiropractic and massage) than non-fatigued participants (OR = 2.52, CI = 1.32, 4.82). Use of body-based therapies increased significantly in a linear trend across subgroups of non-fatigued, prolonged fatigued, chronic fatigued, and CFS-like subjects (p-trend = 0.002). People with chronic fatigue were also significantly more likely to use body-based therapy (OR = 1.52, CI = 1.07, 2.16) and mind-body (excluding prayer) therapy than non-fatigued participants (OR = 1.73, CI = 1.20 - 2.48). CONCLUSION: Utilization of CAM was common in fatiguing illnesses, and was largely accounted for by the presence of underlying conditions and poor physical and mental health. Compared to non-fatigued persons, those with CFS-like illness or chronic fatigue were most likely to use body-based and mind-body therapies. These observations have important implications for provider education programs and development of intervention strategies for CFS.
Jones JF.	Chronic Viral Diseases Branch, Division of Viral and Rickettsial Diseases, National Center for Zoonotic, Vectorborne, and Enteric Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.	An extended concept of altered self: Chronic fatigue and post-infection syndromes.	Psychoneuroendocrinology. 2007 Dec 24 [Epub ahead of print]	Sickness behavior in active infectious diseases is defined here as the responses to cytokines and other mediators of inflammation as well as the adaptability of a pre-existing integrated immunological, psychological, neurological, and philosophical self. These complex behaviors are biologically advantageous to the afflicted individual, but they also impact surrounding individuals. If chronic conditions, such as chronic fatigue syndrome or post-infection fatigue, exhibiting these behaviors follow infection in the absence of ongoing changes in immunological self associated with an active infection or subsequent injury, they are currently considered illness states rather than true diseases. Self-referential recognition (interoception) of bodily processes by the brain and subsequent unconscious and conscious adaptive responses arising in the brain, i.e., in the endocrine system and immune systems, which are initiated during the infection and would normally lead to positive maintenance, may become maladaptive and lead to an "extended altered self state." Exploratory measurements of such alterations using a "top-down" approach such as monitoring responses to appropriate challenges can be obtained using functional brain imaging techniques. Once identified, processes remediable to biological/pharmacologic and/or psychological intervention can be targeted in directed trials.
Jubeau M, Zory R, Gondin J, Martin A, Maffiuletti NA.	Laboratory INSERM U887, Faculty of Sport Sciences, University of Burgundy, BP 27877, 21078	Effect of electrostimulation training-detraining on neuromuscular fatigue mechanisms.	Neurosci Lett. 2007 Aug 31;424(1):41-6. Epub 2007 Aug 1.	The aim of this study was to evaluate the effects of neuromuscular electrical stimulation (NMES) training and subsequent detraining on neuromuscular fatigue mechanisms. Ten young healthy men completed one NMES fatigue protocol before and after a NMES training program of 4 weeks and again after 4 weeks of detraining. Muscle fatigue (maximal voluntary torque loss), central fatigue (activation failure), and peripheral fatigue (transmission failure and contractile failure) of the plantar flexor muscles were assessed by using a series of electrically evoked and voluntary contractions with concomitant electromyographic and torque recordings. At baseline, maximal voluntary torque

	Dijon, France. Marc.Jubeau@u-bourgogne.fr			decreased significantly with fatigue (P<0.001), due to both activation and transmission failure. After detraining, maximal voluntary torque loss was significantly reduced (P<0.05). In the same way, the relative decrease in muscle activation after training and detraining was significantly lower compared to baseline values (P<0.05). Short-term NMES training-detraining of the plantar flexor muscles significantly reduced the muscle fatigue associated to one single NMES exercise session. This was mainly attributable to a reduction in activation failure, i.e., lower central fatigue, probably as a result of subject's accommodation to pain and discomfort during NMES.
Juruena MF, Cleare AJ.	Seção de Neurobiologia dos Transtornos de Humor, Instituto de Psiquiatria, King's College, Universidade de Londres, UK. M.Juruena@iop.kcl.ac.uk	[Overlap between atypical depression, seasonal affective disorder and chronic fatigue syndrome] [Article in Portuguese]	Rev Bras Psiquiatr. 2007 May;29 Suppl 1:S19-26.	OBJECTIVE: We reviewed previous studies that have described an association between abnormal functioning of the hypothalamic-pituitary-adrenal axis and depression. In addition to melancholic depression, a spectrum of conditions may be associated with increased and prolonged activation of the hypothalamic-pituitary-adrenal axis. In contrast another group of states is characterized by hypoactivation of the stress system, rather than sustained activation, in which chronically reduced secretion of corticotropin releasing factor may result in pathological hypoarousal and an enhanced hypothalamic-pituitary-adrenal negative feedback. Patients with atypical depression, seasonal affective disorder and chronic fatigue syndrome fall in this category. METHOD: The literature data on the overlap between the key-words were reviewed, summarized and discussed. RESULTS: Many studies suggest that these conditions themselves overlap biologically, showing hypofunction of central corticotropin releasing factor neuronal systems. CONCLUSIONS: Therefore, in the real world of clinical practice, patients often present in a grey area between classical idiopathic fatigue and early chronic atypical depression and/or seasonal depression. This underscores the potential common biological links underpinning common symptom clusters not only between depression (atypical and seasonal) and chronic fatigue syndrome, but also other conditions characterized by the hypothalamic-pituitary-adrenal axis mainly diminished the corticotropin realising factor activity.
Kanaan RA, Lepine JP, Wessely SC.	King's College London, Department of Psychological Medicine, Institute of Psychiatry, London, UK.	The association or otherwise of the functional somatic syndromes.	Psychosom Med. 2007 Dec;69(9):855-9.	OBJECTIVE: To review the evidence for overlap in the phenomenology of the Functional Somatic Syndromes (FSS). The FSS show considerable comorbidity, leading some to suggest they may be aspects of the same disorder. METHODS: We conducted a selective review of peer-reviewed articles on the co-occurrence of FSS symptoms and diagnoses. RESULTS: Considerable evidence of overlap was found at the level of symptoms, diagnostic criteria, and clinical diagnoses made. CONCLUSIONS: Phenomenological commonalities support a close relationship between the FSS, although differences remain in other domains. Whether the FSS may best be considered the same or different will depend on the pragmatics of diagnosis.
Kant I, Jansen NW, van Amelsvoort LG, Huibers MJ.	Capaciteitsgroep Epidemiologie van de Universiteit Maastricht. IJ.Kant@epid.unimaas.nl	[Course, consequences and treatment of prolonged fatigue among workers: an overview of findings from the Maastricht Cohort Study] [Article in	Tijdschr Psychiatr. 2007;49(8):547-54. Comment in: Tijdschr Psychiatr. 2007;49(8):555-7.	summary background Although prolonged fatigue is a common complaint among workers, relatively little is known about its course and consequences. AIM: To present an overview of the course, consequences and treatment of prolonged fatigue in the work force. METHOD: We present an overview of the findings from the Maastricht Cohort Study, which was a prospective cohort (n=12.140) that covered a period of 4 years. results Fatigue runs an unfavourable course. In many workers symptoms of fatigue are present for a long time, and in some workers the symptoms even develop into those of chronic fatigue syndrome. The consequences of prolonged fatigue are also serious and are manifested in various ways: sick leave, work disability, accidents, immunological effects and reduction in work participation. A brief cognitive behaviour therapy administered by general

		Dutch]		practitioners to employees with prolonged fatigue proved ineffective. CONCLUSION: The severe consequences of prolonged fatigue and the current lack of effective therapies underline the importance of preventing the development of fatigue complaints, for which the Maastricht Cohort Study may provide the basic tools.
Karceski S.		Early Parkinson disease and depression.	Neurology. 2007 Jul 24;69(4):E2-3. Comment on: Neurology. 2007 Jul 24;69(4):342-7.	
Kasatkin DS, Spirin NN.	Yaroslavl State Medical Academy.	Possible mechanisms of the formation of chronic fatigue syndrome in the clinical picture of multiple sclerosis.	Neurosci Behav Physiol. 2007 Mar;37(3):215-9.	A frequent manifestation of multiple sclerosis (MS) is chronic fatigue syndrome, which can be defined as a subjective decrease in the level of physical and/or mental energy. Chronic fatigue syndrome can be divided into asthenia (fatigue at rest), pathological fatigability (fatigue on physical loading), and fatigue on the background of deterioration of other symptoms (exacerbation of MS). There are both central and peripheral mechanisms for the formation of fatigue. The combination of fatigue and affective disturbances, especially depression and sleep disorders (insomnia, restless legs syndrome) is common in MS and may provide evidence that they share common mechanisms--decreases in the activity of the serotoninergic and noradrenergic systems. An important component in the formation of chronic fatigue syndrome consists of endocrine and autoimmune factors, the latter having a greater effect on asthenia than on pathological fatigue. Further studies of the pathogenetic mechanisms of the formation of asthenia and pathological fatigue and clarification of their differential diagnostic signs should allow not only a better understanding of the nature of this syndrome, but also better selection of individual treatment.
Kawai T, Rokutan K.	Department of Stress Science, Institute of Health Biosciences, The University of Tokushima Graduate School.	[Identification and application of marker genes for differential diagnosis of chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1029-33.	Chronic fatigue syndrome (CFS) is a complex disease and has no laboratory biomarkers, which makes diagnosis of CFS difficult. Several research groups challenged to identify genes specific for CFS; however, there are no overlaps between studies. The U.S. Centers for Disease Control and Prevention reported remarkable gene expression profiles of a large scale cohort study recruited 227 people. Reported genes were mostly different from the previously reported genes, again featuring the complexity of CFS. Separately, we identified 9 genes that were significantly and differentially expressed between CFS patients and healthy subjects using an original microarray. The changes in expression of 9 genes were confirmed by quantitative PCR. We also demonstrated the usefulness of 9 genes for differential diagnosis of CFS.
Kent Holtorf		Diagnosis and Treatment of Hypothalamic-Pituitary-Adrenal (HPA) Axis Dysfunction in Patients with Chronic Fatigue Syndrome (CFS)	Journal of Chronic Fatigue Syndrome 2007; 14(3):	There is controversy regarding the incidence and significance of hypothalamic-pituitaryadrenal (HPA) axis dysfunction in chronic fatigue syndrome (CFS) and fibromyalgia (FM). Studies that utilize central acting stimulation tests, including CRH, IST, d-fenfluramine, ipsapirone, IL-6 and metyrapone testing, have demonstrated that HPA axis dysfunction of central origin is present in a majority of these patients. However, ACTH stimulation tests and baseline cortisol testing lack the sensitivity to detect this central dysfunction and have resulted in controversy and confusion regarding the incidence of HPA axis dysfunction in these conditions and the appropriateness of treatment. While both CFS and FM patients are shown to have central HPA dysfunction, the dysfunction in CFS appears to be at the pituitaryhypothalamic level while the dysfunction in FM is more related to dysfunction at the

		and Fibromyalgia (FM)		hypothalamic and supra-hypothalamic levels. Because treatment with low physiologic doses of cortisol (< 15 mg) has been shown to be safe and effective and routine dynamic ACTH testing does not appear to have significant diagnostic sensitivity, it is reasonable to give a therapeutic trial of physiologic doses of cortisol to the majority of patients with CFS and FM, especially to those who have symptoms that are consistent with adrenal dysfunction, have low blood pressure or have baseline cortisol levels in the low or low-normal range.
Kerr J, Burke B, Petty R, Gough J, Fear D, David M, Axford J, Dalgleish A, Nutt D.	St George's University of London, United Kingdom.	Seven genomic subtypes of Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME): a detailed analysis of gene networks and clinical phenotypes.	J Clin Pathol. 2007 Dec 5 [Epub ahead of print]	Chronic Fatigue Syndrome / myalgic encephalomyelitis (CFS/ME) is a multisystem disease, the pathogenesis of which remains undetermined. We have recently reported a study of gene expression which identified differential expression of 88 human genes in patients with CFS/ME. Clustering of QPCR data from CFS/ME patients revealed 7 distinct subtypes with distinct differences in SF-36 scores, clinical phenotypes and severity. In this study, for each CFS/ME subtype, we determined those genes whose expression differed significantly from that of normal blood donors, and then determined gene interactions, disease associations and molecular and cellular functions of those gene sets. Genomic analysis was then related to clinical data for each CFS/ME subtype. Genomic analysis revealed some common (neurological, cancer, immunological, inflammatory, haematological) and some distinct (metabolic, endocrine, dermatological, cardiovascular, connective tissue) disease associations among the subtypes. Subtypes 1, 2 and 7 were the most severe, and subtype 3 was the mildest. Clinical features of each subtype were as follows: subtype 1 (cognitive, musculoskeletal, sleep, anxiety / depression); subtype 2 (musculoskeletal, pain, anxiety / depression); subtype 3 (mild); subtype 4 (cognitive); subtype 5 (musculoskeletal, gastrointestinal); subtype 6 (postexertional); subtype 7 (pain, infectious, musculoskeletal, sleep, neurological, gastrointestinal, neurocognitive, anxiety / depression). It is particularly interesting that in these genomically derived subtypes, there were distinct clinical syndromes and that those which were most severe were also those with anxiety / depression, as would be expected in a disease with a biological basis.
Kerr JR.		Enterovirus infection of the stomach in chronic fatigue syndrome/myalgic encephalomyelitis.	J Clin Pathol. 2008 Jan;61(1):1-2. Epub 2007 Sep 14. Comment on: J Clin Pathol. 2008 Jan;61(1):43-8.	
Kirkengen AL, Getz L, Hetlevik I.	Allmennmedisinsk Forskningsenhet, Institutt for samfunnsmedisin, Norges teknisk-naturvitenskapelige universitet. anlui-k@online.no	[Exhausted because of] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2007 Jun 28;127(13):1797-9. Comment in: Tidsskr Nor Laegeforen. 2007 Sep 6;127(17):2278-9.	
Kirkengen AL,	Institutt for	[Heavy burdens	Tidsskr Nor	Complex chronic diseases require an increasing proportion of society's resources and represent a

Ulvestad E.	samfunnsmedisinske fag Universitetet i Tromsø. anlui-k@online.no	and complex disease--an integrated perspective] [Article in Norwegian]	Laegeforen. 2007 Dec 13;127(24):3228-31.	growing challenge. Valid biomedical models of etiology, pathogenesis, treatment and prognosis are inadequate for understanding these diseases. The article discusses current knowledge about the impact of stress on the immune-, hormonal - and central nervous systems, and integrates this knowledge with a phenomenological understanding of the body in an attempt to explain the complex chronic fatigue syndrome. The medical significance of the individual's biography is highlighted, and the inadequacy of statistically grounded biomedical research when aiming to understand complex disease is presented. By regarding human beings as persons who experience bodily and who both create and convey meaning, we claim to have transgressed the mind-body-dichotomy in complex disease development. The dichotomy converges in the living body.
Klimas NG, Koneru AO.	University of Miami Miller School of Medicine, 1201 NW 16th Street, VA Medical Center, 200 BMRC, 6th Floor, Miami, FL 33125, USA. nancy.klimas@va.gov	Chronic fatigue syndrome: inflammation, immune function, and neuroendocrine interactions.	Curr Rheumatol Rep. 2007 Dec;9(6):482-7.	Investigations into the underlying cause of chronic fatigue syndrome have advanced the field considerably in the past year. Gene microarray data have led to a better understanding of pathogenesis. Recent research has evaluated genetic signatures, described biologic subgroups, and suggested potential targeted treatments. Acute viral infection studies found that initial infection severity was the single best predictor of persistent fatigue. Genomic studies showed that persistent cases express Epstein Barr virus-specific genes and demonstrate abnormalities of mitochondrial function. Studies of immune dysfunction extended observations of natural killer cytotoxic cell dysfunction of the cytotoxic T cell through quantitative evaluation of intracellular perforins and granzymes. Other research has focused on a subgroup of patients with reactivated viral infection. These advances should result in targeted therapies that impact immune function, hypothalamic-pituitary-adrenal axis regulation, and persistent viral reactivation.
Knoop H, Bleijenberg G, Gielissen MF, van der Meer JW, White PD.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. j.knoop@nkcv.umcn.nl	Is a full recovery possible after cognitive behavioural therapy for chronic fatigue syndrome?	Psychother Psychosom. 2007;76(3):171-6.	BACKGROUND: Cognitive behavioural therapy (CBT) for chronic fatigue syndrome (CFS) leads to a decrease in symptoms and disabilities. There is controversy about the nature of the change following treatment; some suggest that patients improve by learning to adapt to a chronic condition, others think that recovery is possible. The objective of this study was to find out whether recovery from CFS is possible after CBT. METHODS: The outcome of a cohort of 96 patients treated for CFS with CBT was studied. The definition of recovery was based on the absence of the criteria for CFS set up by the Center for Disease Control (CDC), but also took into account the perception of the patients' fatigue and their own health. Data from healthy population norms were used in calculating conservative thresholds for recovery. RESULTS: After treatment, 69% of the patients no longer met the CDC criteria for CFS. The percentage of recovered patients depended on the criteria used for recovery. Using the most comprehensive definition of recovery, 23% of the patients fully recovered. Fewer patients with a co-morbid medical condition recovered. CONCLUSION: Significant improvement following CBT is probable and a full recovery is possible. Sharing this information with patients can raise the expectations of the treatment, which may enhance outcomes without raising false hopes. Copyright 2007 S. Karger AG, Basel.
Knoop H, Prins JB, Stulemeijer M, van der Meer JW, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical	The effect of cognitive behaviour therapy for chronic fatigue syndrome on self-	J Neurol Neurosurg Psychiatry. 2007 Apr;78(4):434-6.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) often have concentration and memory problems. Neuropsychological test performance is impaired in at least a subgroup of patients with CFS. Cognitive behavioural therapy (CBT) for CFS leads to a reduction in fatigue and disabilities. AIM: To test the hypothesis that CBT results in a reduction of self-reported cognitive impairment and in an improved neuropsychological test performance. METHODS: Data of two previous randomised

	Centre, P O Box 9011, 6525 EC Nijmegen, The Netherlands. j.knoop@nkcv.umcn.nl	reported cognitive impairments and neuropsychological test performance.		controlled trials were used. One study compared CBT for adult patients with CFS, with two control conditions. The second study compared CBT for adolescent patients with a waiting list condition. Self-reported cognitive impairment was assessed with questionnaires. Information speed was measured with simple and choice reaction time tasks. Adults also completed the symbol digit-modalities task, a measure of complex attentional function. RESULTS: In both studies, the level of self-reported cognitive impairment decreased significantly more after CBT than in the control conditions. Neuropsychological test performance did not improve. CONCLUSIONS: CBT leads to a reduction in self-reported cognitive impairment, but not to improved neuropsychological test performance. The findings of this study support the idea that the distorted perception of cognitive processes is more central to CFS than actual cognitive performance.
Knoop H, Stulemeijer M, Prins JB, van der Meer JW, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Post Box 9011, 6525 EC Nijmegen, The Netherlands. j.knoop@nkcv.umcn.nl	Is cognitive behaviour therapy for chronic fatigue syndrome also effective for pain symptoms?	Behav Res Ther. 2007 Sep;45(9):2034-43. Epub 2007 Mar 14.	Patients with chronic fatigue syndrome (CFS) frequently report chronic pain symptoms. Cognitive behavioural therapy (CBT) for CFS results in a reduction of fatigue, but is not aimed at pain symptoms. In this study, we tested the hypothesis that a successful treatment of CFS can also lead to a reduction of pain. The second objective was to explore possible mechanisms of changes in pain. The third objective was to assess the predictive value of pain for treatment outcome. Data from two previous CBT studies were used, one of adult CFS patients (n=96) and one of adolescent CFS patients (n=32). Pain severity was assessed with a daily self-observation list at baseline and post-treatment. The location of pain in adults was assessed with the McGill Pain Questionnaire (MPQ). Patients were divided into recovered and non-recovered groups. Recovery was defined as reaching a post-treatment level of fatigue within normal range. Recovered adult and adolescent CFS patients reported a significant reduction of pain severity compared to non-recovered patients. Recovered adult patients also had fewer pain locations following treatment. The decrease in fatigue predicted the change in pain severity. In adult patients, a higher pain severity at baseline was associated with a negative treatment outcome.
Kobelt A, Grosch E, Wasmus A, Ehlebracht-König I, Schwarze M, Krähling M, Gutenbrunner C.	Deutsche Rentenversicherung Braunschweig-Hannover, Arztlicher Dienst, Lange Weihe 2, 30880 Laatzen. axel.kobelt@drv.bsh.de	[Is it possible to predict approval of medical rehabilitation by the extent of fatigue and subjective need for rehabilitation? Development, results and acceptance of a short screening] [Article in German]	Rehabilitation (Stuttg). 2007 Feb;46(1):33-40.	OBJECTIVES: In earlier studies the lack of correlation between subjective need for rehabilitation of the applicant and the medically determined objective need for rehabilitation was reported again and again. The correlation between fatigue and subjective need for rehabilitation was not yet examined so far. Nevertheless fatigue is not defined sufficiently in the ICD, so interactions between chronic fatigue and somatic diseases are not taken into account appropriately. The following questions are considered: How high is the degree of chronic fatigue in insurees applying for rehabilitation? Is there a correlation between degree of fatigue and need for rehabilitation? Is it possible to predict approval of medical rehabilitation by fatigue and need for rehabilitation? How will insurees accept a screening accompanying their application for rehabilitation? METHOD: The study is based on data of 500 (response rate 85.6%) insurees of the pension insurance Braunschweig-Hannover, who had applied for medical rehabilitation between 1/2004 and 3/2004. The screening instrument included: scales on functional activity, mobility, social support, coping (IRES), the Chalder Fatigue Scale, SCL 14, Items concerning need for rehabilitation. As statistical methods t-, chi (2)-test, correlations, covariance-analysis and regression analysis are used. RESULTS: 70.2% of the patients claiming rehabilitation reported relevant clinical symptoms of chronic fatigue. There were no differences in age, work status, motivation, or expectations of returning to work, but differences in sex. Patients with chronic fatigue

				met more citeria of need for rehabilitation. But the approval of medical rehabilitation could not be predicted by fatigue and need for rehabilitation. Nevertheless the acceptance of the screening was high in the insurees. CONCLUSIONS: Patients with chronic fatigue met more criteria of need for rehabilitation. But the approval of medical rehabilitation could not be predicted by fatigue and need for rehabilitation. We assume that the reduction of activity and participation is associated with the degree of fatigue. It is discussed that the information an investigator may derive from a screening which is accepted by the insurees claiming medical rehabilitation will complete the collected clinical documents in a meaningful manner.
Kogelnik AM, Loomis K, Hoegh-Petersen M, Rosso F, Hischier C, Montoya JG.	Stanford University School of Medicine, Stanford, CA, USA.	Use of valganciclovir in patients with elevated antibody titers against Human Herpesvirus-6 (HHV-6) and Epstein-Barr Virus (EBV) who were experiencing central nervous system dysfunction including long-standing fatigue.	J Clin Virol. 2006 Dec;37 Suppl 1:S33-8.	BACKGROUND: Twelve patients with long-standing symptoms of central nervous system (CNS) dysfunction were found to have elevated antibody titres to human herpesvirus-6 (HHV-6) and Epstein-Barr virus (EBV). All patients had four or more of the following neurocognitive symptoms: impaired cognitive functioning, slowed processing speed, sleep disturbance, short-term memory deficit, fatigue and symptoms consistent with depression. OBJECTIVES: We sought to determine whether elevated antibodies to EBV and HHV-6 indicated chronic viral activation in patients with CNS dysfunction and if their symptoms could be improved by suppressing viral activity with oral valganciclovir. STUDY DESIGN: Patients with high IgG antibody titers against HHV-6 and EBV who were suffering from central nervous system dysfunction and debilitating fatigue for more than one year (median 3 years, range 1-8 years) were treated with 6 months of valganciclovir in an open label study. RESULTS: Nine out of 12 (75%) patients experienced near resolution of their symptoms, allowing them all to return to the workforce or full time activites. In the nine patients with a symptomatic response to treatment, EBV VCA IgG titers dropped from 1:2560 to 1:640 ($p = 0.008$) and HHV-6 IgG titers dropped from a median value of 1:1280 to 1:320 ($p = 0.271$). Clinically significant hematological toxicity or serious adverse events were not observed among the 12 patients. CONCLUSION: These preliminary clinical and laboratory observations merit additional studies to establish whether this clinical response is mediated by an antiviral effect of the drug, indirectly via immunomodulation or by placebo effect.
Komaroff AL.	Division of General Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 10 Shattuck Street, Suite 602, Boston, MA 02115, USA. komaroff@hms.harvard.edu	Is human herpesvirus-6 a trigger for chronic fatigue syndrome?	J Clin Virol. 2006 Dec;37 Suppl 1:S39-46.	Chronic fatigue syndrome (CFS) is an illness currently defined entirely by a combination of non-specific symptoms. Despite this subjective definition, CFS is associated with objective underlying biological abnormalities, particularly involving the nervous system and immune system. Most studies have found that active infection with human herpesvirus-6 (HHV-6)--a neurotropic, gliotropic and immunotropic virus--is present more often in patients with CFS than in healthy control and disease comparison subjects, yet it is not found in all patients at the time of testing. Moreover, HHV-6 has been associated with many of the neurological and immunological findings in patients with CFS. Finally, CFS, multiple sclerosis and seizure disorders share some clinical and laboratory features and, like CFS, the latter two disorders also are being associated increasingly with active HHV-6 infection. Therefore, it is plausible that active infection with HHV-6 may trigger and perpetuate CFS in a subset of patients.
Kondo K.	Department of Virology, The Jikei University School	[Chronic fatigue syndrome and herpesvirus	Nippon Rinsho. 2007 Jun;65(6):1043-8.	Human herpesvirus 6(HHV-6) and human herpesvirus 7(HHV-7) establish life-long latency, reactivate frequently, and are shed in saliva. To identify the factor(s) of their reactivation, we have studied the association with the reactivation and fatigue. Reactivation was examined for viral DNA by real-time

	of Medicine.	reactivation] [Article in Japanese]		PCR method. As a result, healthy adults shed the reactivated HHV-6 in the saliva during work -induced fatigue, and the copy number of HHV-6 DNA was reduced after holidays. However, no significant HHV-6 DNA increase was observed in chronic fatigue syndrome (CFS) patients. In contrast, increase of HHV-7 reactivation was observed both in the case of work-induced fatigue and CFS. These findings suggest that the amount of HHV-6 and HHV-7 reactivation can be an objective biomarker for fatigue.
Kumano-go T, Adachi H, Sugita Y.	Osaka University Health Care Center.	[Sleep disturbance in chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1017-22.	Attempts to elucidate the complex pathophysiology of chronic fatigue syndrome (CFS) must consider subjective and objective sleep. Several reports of CFS showed the high rate of sleep disturbance such as insomnia, hypersomnia, circadian rhythm sleep disorder, sleep apnea/hypopnea syndrome and so on. To analyze pulse wave continuously in sleep of CFS patients by laser blood flowmeter, we set base line component (0.01-0.08 Hz) and pulse wave component(0.70-1.50 Hz). Results of FFT analysis indicate that the CFS can have at least three subtypes of pulse dynamics in sleep. There probably are different types of illnesses now contained within the CFS construct, in which identifying subtypes of sleep disturbance can be one important key.
Kumor K, Pierzchała K.	Z Katedry i Kliniki Neurologii w Zabrzu Slaskiej Akademii Medycznej w Katowicach. kum2@poczta.onet.pl	[The problem of fatigue in neurological disorders] [Article in Polish]	Wiad Lek. 2006;59(9-10):685-91.	Fatigue or piercing feeling of weakness, lack of strength and energy or total exhaustion is a common complaint of patients with neurological disorders. From 40 to over 90 per cent of individuals with multiple sclerosis, Parkinson disease, amyotrophic lateral sclerosis, neuroboreliosis, post polio syndrome or stroke confirm its experience. It is not infrequently numbered among most disabling complaints. A separate entity, with fatigue as a cardinal sign, is a chronic fatigue syndrome, a disorder, though controversial, more and more frequently diagnosed. Fatigue ought to be discriminated from fatigability, paresis, somnolence and, first of all depression which commonly coexists in chronic disorders. The assessment is almost entirely based on self-estimate scales filled in by a patient. Attainable results of neuroimaging, electrophysiological, polisomnographic, vegetative, psychological and biochemical surveys have not allowed yet to define the pathogenesis of fatigue. The treatment basis consists of behavioral therapy, psychotherapy and a proper treatment of the basic disease.
Kuo DZ, Cheng TL, Rowe PC.	Maple Avenue Pediatrics, Fair Lawn, New Jersey, USA. dkuo5@jhmi.edu	Successful use of a primary care practice-specialty collaboration in the care of an adolescent with chronic fatigue syndrome.	Pediatrics. 2007 Dec;120(6):e1536-9.	We report on the successful collaborative care of an adolescent with chronic fatigue syndrome between a primary care pediatrician and an academic chronic fatigue syndrome specialist located in different cities. Regular telephone and e-mail communication and clearly defined patient-care roles allowed for timely management of symptoms and marked clinical improvement. We discuss ways to improve the collaboration of primary care and subspecialty physicians for patients with chronic fatigue syndrome and children with special health care needs.
Kuratsune H.	Faculty of Health Science for Welfare, Kansai University of Welfare Sciences.	[Overview of chronic fatigue syndrome focusing on prevalence and diagnostic criteria] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):983-90.	Chronic fatigue syndrome (CFS) is an operational concept proposed by Centers for Disease Control and Prevention to clarify the unknown etiology of the syndrome characterized by the sensation of abnormally prolonged fatigue. Lots of investigators reported various abnormalities such as virus infection, immune abnormalities, HPA axis abnormalities, metabolic abnormalities, etc., but there are a few abnormalities common to vast majority cases of CFS. Therefore, lots of people as well as medical doctors are still skeptical about the presence of CFS. However, recent studies reveal that CFS can be understood to be a special condition based on the abnormality of neuroendocrine-immunologic system caused by the psycho-social stress and some genetic components. Under these conditions, a

				reactivation of various kinds of herpes virus infections and/or chronic infections might occur as a result of immune dysfunction, causing the abnormal production of several cytokines. A distinctive feature of CFS is thought to be the secondary brain dysfunction caused by the abnormal production of several cytokines. In this paper, I show the overview of CFS focusing around prevalence, economic impact and diagnostic criteria in Japan.
Langelaan M, de Boer MR, van Nispen RM, Wouters B, Moll AC, van Rens GH.	Department of Ophthalmology, VU University Medical Center, Amsterdam, and Elkerliek Hospital, Helmond, The Netherlands. maaikelangelaan@visio.org	Impact of visual impairment on quality of life: a comparison with quality of life in the general population and with other chronic conditions.	Ophthalmic Epidemiol. 2007 May-Jun;14(3):119-26.	PURPOSE: Subjective evaluation of health-related quality of life (HRQoL) and health status is recognized as an important tool in the assessment and treatment of visually impaired patients. The aims of this study are to describe the generic HRQoL and health status of visually impaired patients and to compare the HRQoL of visually impaired patients with that of both the general population of the Netherlands and patients with other chronic conditions. METHODS: 128 persons attending a rehabilitation centre for visually impaired adults completed the EuroQol questionnaire (EQ-5D). These patients' EQ-5D scores were compared with EQ-5D norms of the Dutch population and of patients with other chronic conditions; both sets of data were taken from the literature. RESULTS: The average EQ-5Dindex score of the total study population was 0.73 (SD 0.22). Visually impaired patients reported more problems on every dimension of the EQ-5D than the general Dutch population. Only stroke patients and patients with chronic fatigue syndrome and reported more problems on every dimension of the EQ-5D than visually impaired patients. CONCLUSIONS: Visual impairment has a substantial impact on the quality of life; compared with other chronic conditions, it seems to affect the HRQoL, spoiling the quality of life more than diabetes type II, coronary syndrome, and hearing impairments, but less than stroke, multiple sclerosis, chronic fatigue syndrome, major depressive disorder, and severe mental illness.
Larun L, Malterud K.	Norwegian Knowledge Centre for the Health Services, Norway. lillebeth.larun@kunnskapssenteret.no	Identity and coping experiences in Chronic Fatigue Syndrome: a synthesis of qualitative studies.	Patient Educ Couns. 2007 Dec;69(1-3):20-8. Epub 2007 Aug 14.	OBJECTIVE: To provide insight into patients' and doctors' experiences with CFS. METHODS: We compiled available qualitative studies and applied meta-ethnography to identify and translate across the studies. Analysis provided second-order interpretation of the original findings and developed third-order constructs from a line of arguments. RESULTS: Twenty qualitative studies on CFS experiences were identified. Symptom experiences and the responses from significant others could jeopardise the patients' senses of identity. They felt severely ill, yet blamed and dismissed. Patients' beliefs and causal attributions oppose the doctor's understanding of the condition. For the patient, getting a diagnosis and knowing more was necessary for recovery. Doctors were reluctant towards the diagnosis, and struggle to maintain professional authority. For patients, experience of discreditation could lead to withdrawal and behavioural disengagement. CONCLUSION: The identities of CFS patients are challenged when the legitimacy of their illness is questioned. This significant burden adds to a loss of previously established identity and makes the patient more vulnerable than just suffering from the symptoms. CFS patients work hard to cope with their condition by knowing more, keeping a distance to protect themselves and learning more about their limits. PRACTICE IMPLICATIONS: Doctors can support patients' coping by supporting the strong sides of the patients instead of casting doubt upon them.
Le Bon Olivier MD, PhD, Daniel Neu MD, Filomena		HUParadoxical Nrems Distribution in "Pure" Chronic	Journal of Chronic Fatigue Syndrome 2007; 14(2): 45-59	Objective: The chronic fatigue syndrome (CFS) is a debated clinical entity, not presently associated with specific sleep abnormalities. However, higher levels of deep sleep and/or lower levels of light sleep have been reported in several all-night polysomnography studies in CFS patients. This

Valente PhD, Paul		Fatigue PAtients A Comparison With Sleep Apnea-Hypopnea Patients and Healthy Control Subjects UH		distribution of Non-Rapid Eye Movement Sleep (NREMS) contrasts with what would be expected if sleep was interrupted by microawakenings, such as in sleep apneas or periodic limb movements, where more light sleep and less deep sleep are commonly observed. This "paradoxical" distribution of NREMS could represent a characteristic feature of chronic fatigue and deserved to be investigated. Methods: A retrospective comparison of the NREMS distribution was performed between 28 "pure" Chronic Fatigue Syndrome patients (without primary sleep or psychiatric disorders), 27 Apneic-Hypopneic patients and 27 Healthy Controls. Results: Data showed CFS patients to have a higher stage 4/stage 2 or stage 4/light sleep ratios than the other two conditions. Conclusion: This sleep pattern is closer to what is observed in cases of infections than to what is seen after sleep fragmentation by primary sleep or in psychiatric disorders. Such a particular sleep pattern could provide insights into the pathophysiology of fatigue.
Ledina D, Bradarić N, Milas I, Ivić I, Brncić N, Kuzmicić N.	Department of Infectious Diseases, Split University Hospital, Split, Croatia. dledina@krizine.kbsplit.hr	Chronic fatigue syndrome after Q fever.	Med Sci Monit. 2007 Jul;13(7):CS88-92.	BACKGROUND: Q fever is a common and acute but rare chronic zoonosis caused by Coxiella burnetii. Its acute form manifests as atypical pneumonia, flu-like syndrome, or hepatitis. Some authors observed symptoms of chronic fatigue in a small number of patients after the acute phase of Q fever; in many cases serological assay confirmed the activity of Coxiella burnetii infection. The effect of antibiotic therapy on post-Q-fever fatigue syndrome has not been studied in south-east Europe thus far. CASE REPORTS: Three patients are presented with post-Q-fever fatigue syndrome. All fulfilled the CDC criteria for chronic fatigue syndrome. IgA antibodies to phase I of the growth cycle of Coxiella burnetii were positive in two patients and negative in one. Two patients were treated with doxycycline for two weeks in the acute phase of illness and one with a combination of erythromycin and gentamycin. After 4-12 months they developed post-Q-fever fatigue syndrome and were treated with intracellular active antibiotics (fluoroquinolones and tetracycline) for 3-12 months. Efficacy of the treatment was observed in two patients, but in one patient the results were not encouraging. CONCLUSIONS: These results suggest the possibility of the involvement of Coxiella burnetii infection in the evolution of chronic fatigue syndrome. This is the first report on post-Q-fever fatigue syndrome in Mediterranean countries. Evidence of IgA antibodies to phase I of the growth cycle of Coxiella burnetii is not a prerequisite for establishing a diagnosis of CFS. The recommendation of antibiotic treatment in post-Q-fever fatigue syndrome requires further investigation.
Leiblum S, Seehuus M, Goldmeier D, Brown C.	UNDNJ-Robert Wood Johnson Medical School-Psychiatry, Piscataway, NJ 08854, USA. leiblum@umdnj.edu	Psychological, medical, and pharmacological correlates of persistent genital arousal disorder.	J Sex Med. 2007 Sep;4(5):1358-66. Epub 2007 Aug 2.	INTRODUCTION: Little is known about the etiology or medical/psychological correlates of persistent genital arousal disorder (PGAD). AIM: The aims of this article were (i) to replicate the findings of earlier research identifying two subtypes of women with persistent arousal-those who meet all features of the condition and are at least moderately distressed, and those who meet only some features and are less distressed; and (ii) to identify the medical, psychological and/or pharmacological correlates of the condition. METHOD: A comprehensive web-based survey of persistent genital arousal (PGA) was posted on several Internet websites. Of the 156 women who completed the survey, 76 met all five features qualifying for a persistent genital arousal disorder (PGAD) group, and 48 met only some features (non-PGAD group). MAIN OUTCOME MEASURES: The main outcome measures were endorsement of diagnostic signs of depression, anxiety, obsessive-compulsive disorder, and panic attack as well as medical illnesses and pharmacological preparations. RESULTS: Compared to non-PGA subjects, women with PGA were significantly more likely to be depressed (55% vs. 38%) and to report

				panic attacks (31.6% vs. 14.6%). They were more anxious and more likely to monitor their physical sensations. Both groups reported high rates of childhood and adult sexual abuse, although the PGA women reported a higher prevalence of sexual victimization. They were significantly more likely to endorse negative feelings about their genital sensations and also more likely to complain of chronic fatigue syndrome than women without the condition (10% vs. 0%). There were no significant relationships with pharmacologic agents and symptoms. CONCLUSIONS: Women who met all the criteria of PGAD were more likely than women who only met some of the criteria to report depression, anxiety, panic attacks, and certain obsessive-compulsive symptoms such as monitoring their physical sensations. It is hypothesized that for a subset of women, psychological factors, namely anxiety, reinforce exacerbate and maintain PGAD.
Lerdal A, Celius EG, Krupp L, Dahl AA.	Department of Health, Buskerud University College, Drammen, Norway. Anners.Lerdal@hibu.no	A prospective study of patterns of fatigue in multiple sclerosis.	Eur J Neurol. 2007 Dec;14(12):1338-43. Epub 2007 Sep 26.	We sought to identify clinical characteristics and socio-demographic variables associated with longitudinal patterns of fatigue in multiple sclerosis (MS) patients. A questionnaire including the Fatigue Severity Scale (FSS) was mailed to a community sample of 502 MS patients three times 1 year apart. Three patterns of fatigue were defined: persistent fatigue (PF) (mean FSS score > or = 5 at all time-points), sporadic fatigue (SF) (mean FSS score > or = 5 at one or two time-points) and no fatigue (mean FSS score < 5 at all time-points). Among the 267 (53%) patients who responded at all time-points, 101 [38%, 95% confidence intervals (CI) 32-44] had persistent, 98 (37%, 95% CI 31-43) sporadic and 68 (25%, 95% CI 20-31) no fatigue. Persistent and sporadic fatigue were more common in patients with, increased neurological impairment (P < 0.001), primary progressive MS (P = 0.01), insomnia (P < 0.001), heat sensitivity (P < 0.001), sudden-onset fatigue (P < 0.001) or mood disturbance (P < 0.001) compared with patients without fatigue. Multivariable analysis showed that depression (PF P = 0.02, SF P < 0.001), heat sensitivity (PF P = 0.04, SF P = 0.02) and physical impairment (PF P = 0.004, SF P = 0.01) were associated with both sporadic and persistent fatigue. About 75% of the patients had persistent or sporadic fatigue over a 2 years observation period. Multivariable analyses confirmed a significant association between levels of depression, physical impairment and persistent fatigue.
Lerner AM, Beqaj SH, Deeter RG, Fitzgerald JT.	Department of Medicine, William Beaumont Hospital, Royal Oak, MI, USA. amartinlerner@yahoo.com	Valacyclovir treatment in Epstein-Barr virus subset chronic fatigue syndrome: thirty-six months follow-up.	In Vivo. 2007 Sep-Oct;21(5):707-13.	BACKGROUND: We hypothesized that subset classification of Epstein-Barr virus (EBV) in chronic fatigue syndrome (CFS) is required. At first, a blinded-random placebo-controlled trial of valacyclovir in EBV CFS subset was performed (Group 1), and this EBV subset was followed for thirty-six months (Group 2). Patients were given valacyclovir at 14.3 mg/kg every 6 hours. The validated Energy Index (EI) point score assessing physical functional capacity, Holter monitor, multigated (radionuclide) MUGA rest/stress ventriculographic examination, EBV serum IgM viral capsid antibodies (VCA), and EBV early antigen diffuse (EA) were followed. After six-months, Group 1 CFS patients receiving valacyclovir experienced an increased mean least square EI point score +1.12 units (122 kcal/day), while the placebo cohort increased +0.42 EI units (65 kcal/day). EI point scores at Group 2 increased progressively. Sinus tachycardias decreased and abnormal cardiac wall motion improved. Serum antibody titers to EBV VCA IgM decreased. Patients resumed normal activities.
Linde A.	Abteilung für Psychosomatik, Bereich Medizin, Universitätsspital	[Chronic fatigue syndrome--a functional somatic syndrome] [Article	Ther Umsch. 2007 Oct;64(10):567-74.	Chronic fatigue can be categorized as a functional somatic syndrome (fss), because there are findings of typical preconditions, trigger mechanisms and maintaining conditions. With relevance for therapy it makes sense to see it as an medical-psychiatric interface-disorder Subsyndromal short episodes of chronic fatigue are many more frequent as three or six month during clearly diagnosed episodes of

	Basel. alinde@uhbs.ch	in German]		"neurasthenia" or "chronic fatigue syndrome". Their descriptions are very similar and obvious those means the same matter. For original aetiological assumptions it wasn't any evidence. But there are findings of charcteristical patterns of changed neurhumeral and immunological interactions for the chronic fatigue syndrome, common for fss. Especially changes of HPA-Axis and its interactions with other systems of functional regulation. Another importent fact are increased senzitation in neuronal and neurocognitive regulation. Increased critical appraisal of somatic funtions and dysfunctional coping strategies are maintaining factors at least. Patterns of dysfuntional coping are not a problem of patients alone. There are also experiences, that some doctors shows the same dysfunctional somatizing management of fss in general and especially for chronic fatigue. In fact, a single and specific cause of chronic fatigue doesn't exist. But the above-mentioned facts allows a starting point for a more successful treatment. There are reviews that shows a good evidence for therapeutic procedures wich are calling for acticvity by patients, such cognitive behavioral therapy and graduated activation. Antidepressants, especialy SSRI, are helpful with a small evidence. They can be used to increase treatment effects. There is no evidence for therapies without patients activation.
Lu Tony V. Susan R. Torres-Harding, Leonard A Jason		HUThe Effectiveness of Early Educational Intervention in Improving Future Physicians' Attitudes Regarding CFS/FM UH	Journal of Chronic Fatigue Syndrome 2007; 14(2): 25-30	Objective: To assess the effects of an early educational intervention program's ability to alter the perceptions and attitudes of future physicians regarding chronic fatigue syndrome/fibromyalgia (CFS/FM), improve their understanding and acceptance of these diseases, make them feel more comfortable in diagnosing and treating patients. Method: Third-year medical students were surveyed before and after an educational intervention program. The three questions posed to the students in the survey were: (1) How comfortable do you feel you are in diagnosing and treating patients with CFS /FM?, (2) Do you consider CFS/FM legitimate illnesses?, and (3) Do you want to treat patients with CFS/FM? Results: The educational intervention program helped about half of the future physicians feel comfortable in diagnosing and treating patients with CFS/FM and improved by over 25% their willingness to treat patients with CFS. Conclusion: An educational intervention program appeared to improve future physicians' understanding and appreciation of CFS/FM, made them feel more comfortable diagnosing and treating these diseases, and increased their willingness to treat patients with CFS/FM.
Maes M, Coucke F, Leunis JC.	MCare4U Outpatient Clinics, Belgium. crc.mh@telenet.be	Normalization of the increased translocation of endotoxin from gram negative enterobacteria (leaky gut) is accompanied by a remission of chronic fatigue syndrome.	Neuro Endocrinol Lett. 2007 Dec;28(6):739-44.	There is now evidence that chronic fatigue syndrome (CFS) is accompanied by an increased translocation of endotoxins from gram-negative enterobacteria through the gut wall, as demonstrated by increased prevalences and median values for serum IgM and IgA against the endotoxins of gram-negative enterobacteria. This condition can also be described as increased gut permeability or leaky gut and indicates intestinal mucosal dysfunction (IMD). Here we report a case of a 13 year old girl with CFS who showed very high values for serum IgM against the LPS of some enterobacteria and signs of oxidative and nitrosative stress, activation of the inflammatory response system, and IgG3 subclass deficiency. Upon treatment with specific antioxidants and a "leaky gut diet", which both aim to treat increased gut permeability, and immunoglobins intravenously, the increased translocation of the LPS of gram negative enterobacteria normalized and this normalization was accompanied by a complete remission of the CFS symptoms.
Maes M, Mihaylova I,	MCare4U Outpatient Clinics,	Not in the mind of neurasthenic	Neuro Endocrinol Lett. 2007	There is now some evidence that chronic fatigue syndrome is accompanied by an activation of the inflammatory response system and by increased oxidative and nitrosative stress. Nuclear factor kappa

Bosmans E.	Olmenlaan 9, 2610 Wilrijk, Belgium. crc.mh@telenet.be	lazybones but in the cell nucleus: patients with chronic fatigue syndrome have increased production of nuclear factor kappa beta.	Aug;28(4):456-62.	beta (NFkappabeta) is the major upstream, intracellular mechanism which regulates inflammatory and oxidative stress mediators. In order to examine the role of NFkappabeta in the pathophysiology of CFS, this study examines the production of NFkappabeta p50 in unstimulated, 10 ng/mL TNF-alpha (tumor necrosis factor alpha) and 50 ng/mL PMA (phorbolmyristate acetate) stimulated peripheral blood lymphocytes of 18 unmedicated patients with CFS and 18 age-sex matched controls. The unstimulated (F=19.4, df=1/34, p=0.0002), TNF-alpha-(F=14.0, df=1/34, p=0.0009) and PMA-(F=7.9, df=1/34, p=0.008) stimulated production of NFkappabeta were significantly higher in CFS patients than in controls. There were significant and positive correlations between the production of NFkappabeta and the severity of illness as measured with the FibroFatigue scale and with symptoms, such as aches and pain, muscular tension, fatigue, irritability, sadness, and the subjective feeling of infection. The results show that an intracellular inflammatory response in the white blood cells plays an important role in the pathophysiology of CFS and that previous findings on increased oxidative stress and inflammation in CFS may be attributed to an increased production of NFkappabeta. The results suggest that the symptoms of CFS, such as fatigue, muscular tension, depressive symptoms and the feeling of infection reflect a genuine inflammatory response in those patients. It is suggested that CFS patients should be treated with antioxidants, which inhibit the production of NFkappabeta, such as curcumin, N-Acetyl-Cysteine, quercitin, silimarin, lipoic acid and omega-3 fatty acids.
Maes M, Mihaylova I, Kubera M, Bosmans E.	MCare4U Outpatient Clinics, Olmenlaan 9, 2610 Wilrijk, Belgium. crc.mh@telenet.be	Not in the mind but in the cell: increased production of cyclo-oxygenase-2 and inducible NO synthase in chronic fatigue syndrome.	Neuro Endocrinol Lett. 2007 Aug;28(4):463-9.	Chronic fatigue syndrome (CFS) is a medically unexplained disorder, characterized by profound fatigue, infectious, rheumatological and neuropsychiatric symptoms. There is, however, some evidence that CFS is accompanied by signs of increased oxidative stress and inflammation in the peripheral blood. This paper examines the role of the inducible enzymes cyclo-oxygenase (COX-2) and inducible NO synthase (iNOS) in the pathophysiology of CFS. Toward this end we examined the production of COX-2 and iNOS by peripheral blood lymphocytes (PBMC) in 18 CFS patients and 18 normal volunteers and examined the relationships between those inflammatory markers and the severity of illness as measured by means of the FibroFatigue scale and the production of the transcription factor nuclear factor kappa beta (NFkappabeta). We found that the production of COX-2 and iNOS was significantly higher in CFS patients than in normal controls. There were significant and positive intercorrelations between COX-2, iNOS and NFkappabeta and between COX-2 and iNOS, on the one hand, and the severity of illness, on the other. The production of COX-2 and iNOS by PBMCs was significantly related to aches and pain, muscular tension, fatigue, concentration difficulties, failing memory, sadness and a subjective experience of infection. The results suggest that a) an intracellular inflammatory response in the white blood cells plays an important role in the pathophysiology of CFS; b) the inflammatory response in CFS is driven by the transcription factor NFkappabeta; c) symptoms, such as fatigue, pain, cognitive defects and the subjective feeling of infection, indicates the presence of a genuine inflammatory response in CFS patients; and d) CFS patients may be treated with substances that inhibit the production of COX-2 and iNOS.
Maes M, Mihaylova I, Leunis JC.	MCare4U Outpatient Clinics, Belgium. crc.mh@telenet.be	Increased serum IgM antibodies directed against phosphatidyl	Neuro Endocrinol Lett. 2007 Dec;28(6):861-7.	Major depression and chronic fatigue syndrome (CFS) are accompanied by signs of oxidative and nitrosative stress (O&NS) and an inflammatory response. Phosphatidyl inositol (Pi) is thought to play a role in depression. The aim of the present study is to examine whether depression and CFS are characterized by an IgM-mediated immune response directed against Pi. Toward this end, this study

		inositol (Pi) in chronic fatigue syndrome (CFS) and major depression: evidence that an IgM-mediated immune response against Pi is one factor underpinning the comorbidity between both CFS and depression.		examines the serum IgM antibodies directed against Pi in 14 patients with major depression, 14 patients with CFS, 14 subjects with partial CFS, and in 11 normal controls. We found that the prevalence and mean value for the serum IgM levels directed against Pi were significantly greater in patients with major depression and CFS than in normal controls and patients with partial CFS. There were significant and positive correlations between serum IgM levels directed against Pi and two symptoms of the FibroFatigue Scale, i.e. fatigue and depression. The results show that an IgM-related immune response directed against Pi may occur in both depression and CFS and may play a role in the pathophysiology of the key symptom of CFS and major depression. It is suggested that the above disorders in Pi result from increased O&NS in both depression and CFS. Autoanti-Pi antibodies may have biological effects, for example, by changing inositol 1,4,5-triphosphate (IP3), phosphatidylinositol-4,5-bisphosphate (PIP2), diacylglycerol and phosphatidylinositol-3,4,5-triphosphate (PIP3) production, thus interfering with intracellular signalling processes. Future research in major depression and CFS should focus on the functional consequences of the immune responses directed against Pi.
Majer M, Jones JF, Unger ER, Solomon Youngblood L, Decker MJ, Gurbaxani B, Heim C, Reeves WC.		Perception versus polysomnographic assessment of sleep in CFS and non-fatigued control subjects: results from a population-based study.	BMC Neurol. 2007 Dec 5;7(1):40 [Epub ahead of print]	ABSTRACT: BACKGROUND: Complaints of unrefreshing sleep are a prominent component of chronic fatigue syndrome (CFS); yet, polysomnographic studies have not consistently documented sleep abnormalities in CFS patients. We conducted this study to determine whether alterations in objective sleep characteristics are associated with subjective measures of poor sleep quality in persons with CFS. METHODS: We examined the relationship between perceived sleep quality and polysomnographic measures of nighttime and daytime sleep in 35 people with CFS and 40 non-fatigued control subjects, identified from the general population of Wichita, Kansas and defined by empiric criteria. Perceived sleep quality and daytime sleepiness were assessed using clinical sleep questionnaires. Objective sleep characteristics were assessed by nocturnal polysomnography and daytime multiple sleep latency testing. RESULTS: Participants with CFS reported unrefreshing sleep and problems sleeping during the preceding month significantly more often than did non-fatigued controls. Participants with CFS also rated their quality of sleep during the overnight sleep study as significantly worse than did control subjects. Control subjects reported significantly longer sleep onset latency than latency to fall asleep as measured by PSG and MSLT. There were no significant differences in sleep pathology or architecture between subjects with CFS and control subjects. CONCLUSION: People with CFS reported sleep problems significantly more often than control subjects. Yet, when measured these parameters and sleep architecture did not differ between the two subject groups. A unique finding requiring further study is that control, but not CFS subjects, significantly over reported sleep latency suggesting CFS subjects may have an increased appreciation of sleep behaviour that may contribute to their perceived sleep problems.
Malaguarnera M, Gargante MP, Cristaldi E, Colonna V, Messano M, Koverech A, Neri	Centro di Ricerca "La Grande Senescenza", Università degli Studi di Catania, Via Messina 829, I-	Acetyl l-carnitine (ALC) treatment in elderly patients with fatigue.	Arch Gerontol Geriatr. 2007 Jul 19 [Epub ahead of print]	Fatigue is one of the conditions most frequently complained by the elderly. There are few effective treatment options for patients with chronic fatigue syndrome. To determine the efficacy, tolerability and impact on the fatigue, as well as on cognitive and functional status of elderly subjects with acetyl l-carnitine (ALC), 96 aged subjects (>70 years, range 71-88) were investigated (50 females and 46 males; mean age 76.2+/-7.6 and 78.4+/-6.4 years, respectively). They met four or more of the Holmes major criteria or at least six of Fukuda minor criteria. Fatigue was measured with the Wessely and

S, Vacante M, Cammalleri L, Motta M.	95126 Catania, Italy.			Powell [Wessely, S., Powell, R., 1989. Fatigue syndromes: a comparison of chronic postviral fatigue with neuromuscular and affective disorders. J. Neurol. Neurosurg. Psychiatry 52, 940-948] scores, with the fatigue severity scale. At the end of the treatment, we observed a decrease of physical fatigue: 6.2 ($p<0.001$), of mental fatigue: 2.8 ($p<0.001$), of severity fatigue: 21.0 ($p<0.001$) and improvements in functional status: 16.1 ($p<0.001$) and cognitive functions: 2.7 ($p<0.001$). By the end of the treatment, significant differences between the two groups were found for the following parameters: muscle pain -27% versus -3% ($p<0.05$); prolonged fatigue after exercise: 51% versus -4% ($p<0.0001$); sleep disorders: 28% versus 4% ($p<0.05$); physical fatigue: 7 versus -0.5 ($p<0.0001$); mental fatigue: -3.3 versus 0.6 ($p<0.0001$); fatigue severity scale: -22.5 versus 1.2 ($p<0.0001$); functional status 17.1 versus 0.6 ($p<0.0001$); mini mental state examination (MMSE) improvements: 3.4 versus 0.5 ($p<0.0001$). Our data show that administering ALC may reduce both physical and mental fatigue in elderly and improves both the cognitive status and physical functions.
Malouff JM, Thorsteinsson EB, Rooke SE, Bhullar N, Schutte NS.	University of New England, Armidale, Australia.	Efficacy of cognitive behavioral therapy for chronic fatigue syndrome: A meta-analysis.	Clin Psychol Rev. 2007 Nov 1 [Epub ahead of print]	A meta-analysis of the efficacy of cognitive behavioral therapy (CBT) in treating chronic fatigue included 15 effect sizes for between-group outcome comparisons. Across analyses, which included a total of 1371 participants, there was a significant difference, d=0.48, in post-treatment fatigue between participants receiving CBT and those in control conditions. Results indicate that CBT for chronic fatigue syndrome tends to be moderately efficacious. Dropout rates in CBT varied from 0-42%, with a mean of 16%. In the five studies that reported the number of CBT clients who were no longer in the clinical range with regard to fatigue at the latest follow-up, the percentage varied from 33% to 73% of those assigned to CBT, with a mean of 50%. Moderator results suggest directions for future investigations.
Maquet D, Demoulin C, Croisier JL, Crielaard JM.	Department of Motricity Sciences, University of Liege, ISEPK, B21, allée des sports 4, 4000 Liege, Belgium. D.Maquet@ulg.ac.be	Benefits of physical training in fibromyalgia and related syndromes. [Article in English, French]	Ann Readapt Med Phys. 2007 Jul;50(6):363-8, 356-62. Epub 2007 Apr 13.	OBJECTIVE: To review the published information on physical training for fibromyalgia (FM) and related syndromes. METHODS: A search of Medline literature (via Ovid and PubMed) with the following keywords: FM, chronic fatigue syndrome, therapy, rehabilitation, aerobic, exercise, and cognitive behavioral therapy. The reference lists of articles were examined for additional related articles. RESULTS: Several studies investigated the benefits of graded exercise therapy for patients with FM or related syndromes. Although some systematic reviews have not established an unequivocal benefit of physical training, most authors report a benefit for patients with chronic pain or fatigue. Ideally, such a therapy should be a part of multidisciplinary program. Muscular rehabilitation is reserved for preventing the deconditioning syndrome often reported in patients and the vicious cycle of pain, avoidance and inactivity behaviors, or even kinesiophobia, deconditioning, incapacity and psychological distress. CONCLUSION: This review emphasizes the relevance of graded physical training for treating FM and related syndromes. The development of rehabilitation centers, with experts able to propose a relevant therapy to patients with chronic pain or fatigue, should help alleviate this public health problem.
Martin A, Chalder T, Rief W, Braehler E.	Section for Clinical Psychology and Psychotherapy, Philipps University, Marburg,	The relationship between chronic fatigue and somatization syndrome: a	J Psychosom Res. 2007 Aug;63(2):147-56.	OBJECTIVE: The objective of this study was to assess the prevalence of chronic fatigue (CF) and its association with somatization syndrome [Somatization Syndrome Index (SSI) 4/6: >/=4 somatoform symptoms in men, 6 in women] in the general population. METHODS: A representative sample of the German population (N=2412) completed a fatigue questionnaire and a screening instrument for current somatoform symptoms (Screening for Somatoform Symptoms 7). RESULTS: The prevalence

	Germany. martin@staff.uni-marburg.de	general population survey.		rate of CF was 6.1% (n=147). Females were affected significantly more often as compared with males (7% vs. 5.1%). The mean number of somatoform symptoms was higher in CF cases than in control subjects without CF (11 vs. 2; P<.001). Seventy-two percent of the subjects with CF fulfilled the SSI4/6 criterion for somatization syndrome. Quality of life (EUROHIS-QOL and 8-item Short-Form Health Survey) and well-being (5-item WHO Well-Being Index) were markedly decreased in CF and SSI4/6. The results of regression analyses suggest that fatigue and somatization severity had a similar impact on quality of life. CONCLUSIONS: The results suggest that CF is relevant in the general population. Its substantial overlap with somatization syndrome supports the hypothesis that the two syndromes are only partially different manifestations of the same underlying processes.
Martinez-Lavin M, Infante O, Lerma C.	National Institute of Cardiology, Mexico City, Mexico.	Hypothesis: The Chaos and Complexity Theory May Help our Understanding of Fibromyalgia and Similar Maladies.	Semin Arthritis Rheum. 2008 Feb;37(4):260-4. Epub 2007 Jun 14.	BACKGROUND: Modern clinicians are often frustrated by their inability to understand fibromyalgia and similar maladies since these illnesses cannot be explained by the prevailing linear-reductionist medical paradigm. OBJECTIVE: This article proposes that new concepts derived from the Complexity Theory may help understand the pathogenesis of fibromyalgia, chronic fatigue syndrome, and Gulf War syndrome. METHODS: This hypothesis is based on the recent recognition of chaos fractals and complex systems in human physiology. RESULTS: These nonlinear dynamics concepts offer a different perspective to the notion of homeostasis and disease. They propose that the essence of disease is dysfunction and not structural damage. Studies using novel nonlinear instruments have shown that fibromyalgia and similar maladies may be caused by the degraded performance of our main complex adaptive system. This dysfunction explains the multifaceted manifestations of these entities. CONCLUSIONS: To understand and alleviate the suffering associated with these complex illnesses, a paradigm shift from reductionism to holism based on the Complexity Theory is suggested. This shift perceives health as resilient adaptation and some chronic illnesses as rigid dysfunction.
Masuda A, Munemoto T, Tei C.	Masuda Clinic.	[A new treatment: thermal therapy for chronic fatigue syndrome] [Article in Japanese	Nippon Rinsho. 2007 Jun;65(6):1093-8.	Thermal therapy using far-infrared ray dry sauna was performed for patients with chronic fatigue syndrome (CFS). Symptoms such as fatigue, pain, and low-grade fever were dramatically improved on two patients. And prednisolone administration was discontinued and became socially rehabilitated 6 months after discharge. On other 11 patients with CFS, physical symptoms such as fatigue and pain improved, too. Furthermore, we reported that repeated thermal therapy had relaxation effect and diminishes appetite loss and subjective complaints in mildly depressed patients. These results suggest that repeated thermal therapy may be a promising method for the treatment of CFS.
Mihaylova I, DeRuyter M, Rummens JL, Bosmans E, Maes M.	MCare4U Outpatient Clinics, Olmenlaan 9, 2610 Wilrijk, Belgium. crc.mh@telenet.be	Decreased expression of CD69 in chronic fatigue syndrome in relation to inflammatory markers: evidence for a severe disorder in the early activation of T lymphocytes and	Neuro Endocrinol Lett. 2007 Aug;28(4):477-83.	There is some evidence that patients with chronic fatigue syndrome (CFS) suffer from immune abnormalities, such as immune activation and decreased immune cell responsivity upon polyclonal stimili. This study was designed to evaluate lymphocyte activation in CFS by using a CD69 expression assay. CD69 acts as a costimulatory molecule for T- and natural killer (NK) cell activation. We collected whole blood from CFS patients, who met CDC criteria, and healthy volunteers. The blood samples were stimulated with mitogens during 18 h and the levels of activated T and NK cells expressing CD69 were measured on a Coulter Epics flow cytometer using a three color immunofluorescence staining protocol. The expression of the CD69 activation marker on T cells (CD3+, CD3+CD4+, and CD3+CD8+) and on NK cells (CD45+CD56+) was significantly lower in CFS patients than in healthy subjects. These differences were significant to the extent that a significant diagnostic performance was obtained, i.e. the area under the ROC curve was around 89%. No differences either in the number of leukocytes or

		natural killer cells.		in the number or percentage of lymphocytes, i.e. CD3, CD4, CD8 and CD19, could be found between CFS patients and the controls. Patients with CFS show defects in T- and NK cell activation. Since induction of CD69 surface expression is dependent on the activation of the protein kinase C (PKC) activation pathway, it is suggested that in CFS there is a disorder in the early activation of the immune system involving PKC.
Miike T.	Department of Child Development, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University Graduate School.	[Childhood chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1099-104.	Chronic fatigue syndrome in childhood and adolescents(CCFS) is a complex and debilitation with severe morbidity and confusion. It is common condition with up to 3-5% of children and adolescents showing strange fatigue and confusion for more than 30 days. In this condition, four major symptoms are important: sleep disorders, easy fatigability, disturbed learning and memorization and immunological problems. Routine laboratory studies are similar to adult CFS, although abnormalities can be seen on serum pyruvic acid level, OGTT pattern, deep body temperature rhythm, hormonal secretion rhythm, and cerebral blood flow. For a diagnosis of CCFS, a research group supported by Japanese ministry of health, labor and welfare developed CCFS case definition on 2004. Treatment focused to correct disrupted circadian rhythms and supply of energy.
Mirkin D, Murphy-Barron C, Iwasaki K.	Milliman, Inc, New York, NY 10119, USA. david.mirkin@milliman.com	Actuarial analysis of private payer administrative claims data for women with endometriosis.	J Manag Care Pharm. 2007 Apr;13(3):262-72.	BACKGROUND: Endometriosis is a painful, chronic disease affecting 5.5 million women and girls in the United States and Canada and millions more worldwide. The usual age range of women diagnosed with endometriosis is 20 to 45 years. Endometriosis has an estimated prevalence of 10% among women of reproductive age, although estimates of prevalence vary greatly. Endometriosis is the most common gynecological cause of chronic pelvic pain, but published information on its associated medical care costs is scarce. OBJECTIVE: The aim of this study was to determine (1) the prevalence of endometriosis in the United States, (2) the amount of health care services used by women coded with endometriosis in a commercial medical claims database during 1999 to 2003, and (3) the endometriosis-related costs for 2003, the most recent data available at the time the study was performed. METHODS: This study was a retrospective review of administrative data for commercial payers, which included enrollment, eligibility, and claims payment data contained in the Medstat Marketscan database for approximately 4 million commercial insurance members. All claims and membership data were extracted for each woman aged 18 to 55 years who had at least 1 medical or hospital claim with a diagnosis code for endometriosis (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes 617.00-617.99) for 1999 through 2003. Claims data from 1999 through 2003 were used to determine prevalence and health care resource utilization (i.e., annual admission rate, annual surgical rate, distribution of endometriosis-related surgeries, and prevalence of comorbid conditions). The cost analysis was based on claims from 2003 only. Cost was defined as the payer-allowed charge, which equals the net payer cost plus member cost share. RESULTS: The prevalence of women with medical claims (inpatient and/or outpatient) containing ICD-9-CM codes for endometriosis was 1.1% for the age band of 30 to 39 years and 0.7% over the entire age span of 18 to 55 years. The medical costs per patient per month (PPPM) for women with endometriosis were 63% greater ($706 PPPM) than those of the average woman per member per month ($433) in 2003; inpatient hospital costs accounted for 32% of total direct medical costs. Between 1999 and 2003, these women with endometriosis who were identified by either inpatient

				and/or outpatient claims had high rates of hospital admission (53% for any reason; 38% for an endometriosis-related reason) and a high annual surgical procedure rate (64%). Additionally, women with endometriosis frequently suffered from comorbid conditions, and these conditions were associated with greater PPPM costs of 15% to 50% for women with an endometriosis diagnosis code, depending on the condition. Interstitial cystitis was associated with 50% greater cost ($1,061 PPPM); depression, 41% ($997 PPPM); migraine, 40% ($988 PPPM); irritable bowel syndrome, 34% ($943 PPPM); chronic fatigue syndrome, 29% ($913 PPPM); abdominal pain, 20% ($846 PPPM); and infertility, 15% ($813 PPPM). CONCLUSIONS: Women with endometriosis have a high hospital admission rate and surgical procedure rate and a high incidence of comorbid conditions. Consequently, these women incur total medical costs that are, on average, 63% higher than medical costs for the average woman in a commercially insured group.
Miwa S, Takikawa O.	Department of Cellular Pharmacology, Hokkaido University Graduate School of Medicine.	[Chronic fatigue syndrome and neurotransmitters] [Article in Japanese	Nippon Rinsho. 2007 Jun;65(6):1005-10.	Chronic fatigue syndrome (CFS) is an idiopathic illness characterized by persistent fatigue, which could be caused by a variety of etiologic factors including viral infection, abnormal production of cytokines and abnormal acylcarnitine metabolism. Recent studies suggest that CFS is closely associated with attenuation of central synaptic transmission mediated by neurotransmitters such as serotonin and glutamate. Attenuation of serotonin neurotransmission can be caused by increased expression of serotonin transporter, which results either from viral infection and subsequent production of interferon--alpha or from abnormal promoter for serotonin transporter gene. Other neurotransmitter systems may be also involved in CFS mediated by abnormal acylcarnitine metabolism and autoantibodies for neurotransmitter receptors. In this review, we focus recent data on CFS in terms of neurotransmitters.
Murakami M.	Department of Psychosomatic Internal Medicine, Nihon University Itabashi Hospital.	[Considerations for the treatment of chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1089-92.	The etiology of chronic fatigue syndrome(CFS) is still unknown and under active discussion, but involvement of psychosocial factors appear to be essential for the onset and clinical course of CFS. As CFS patients complain of many stress-related physical and psychological symptom, it is important to understand the CFS from psychosomatic point of view. Not only for the pharmaceutical treatment, attentive consideration is required for treatment of exhaustion of body and mind of CFS patients. Use of anti-depressants or oriental herb medicine is often effective to relieve the anxiety and depressive condition. Furthermore to augment the self-healing potential, psychosomatic approach is important to modify the life style and behavioral characteristics.
Mutter J, Naumann J, Guethlin C.	Institute for Environmental Medicine and Hospital Epidemiology, Freiburg i.Br., Deutschland. joachim.mutter@uniklinik-freiburg.de	Elimination of xenobiotics in a female patient with fibromyalgia, chronic fatigue, and trunk obesity.	Forsch Komplement Med (2006). 2007 Feb;14(1):39-44. Epub 2007 Mar 6.	We describe the case of a 28-year-old woman, who had been suffering for more than 5 years from severe fatigue, myofascial pain, obstipation, obesity of trunk, abdominal striae, oedema, tinnitus, folliculitis, and facial swelling. The patient also showed a secondary adrenocortical insufficiency. From the anamnesis we assumed that environmental factors could account for the symptoms. The therapy consisted of dietary advise, chelating agents, supplements, and acupuncture. Under this therapy the patient became completely symptom-free. No such case has ever been reported before. We report mainly on the CAM diagnostic and therapeutic procedures, which are discussed together with the assumed pathogenetic factors.
Narita M, Narita N.	'Graduate School of Medicine, Mie	[Genetic background of	Nippon Rinsho. 2007	Although previous twin and family studies have suggested the involvement of genetic factor(s) in the pathogenesis of chronic fatigue syndrome (CFS), responsible gene for CFS was not known. We have

	University.	chronic fatigue syndrome] [Article in Japanese]	Jun;65(6):997-1002.	recently reported the association of serotonin transporter gene polymorphism in CFS. A significant increase of longer (L and XL) alleic variants was found in the CFS patients compared to the controls. Compared to S allele, the L allele is believed to retain higher transcriptional activity, which causes decreased concentration of serotonin in the extracellular space, namely, active serotonin in CFS. These results thus support the serotonin hypothesis in the pathogenesis of CFS.
Natelson BH, Intriligator R, Cherniack NS, Chandler HK, Stewart JM.	Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark NJ, USA. natelson@njneuromed.org	Hypocapnia is a biological marker for orthostatic intolerance in some patients with chronic fatigue syndrome.	Dyn Med. 2007 Jan 30;6:2.	CONTEXT: Patients with chronic fatigue syndrome and those with orthostatic intolerance share many symptoms, yet questions exist as to whether CFS patients have physiological evidence of orthostatic intolerance. OBJECTIVE: To determine if some CFS patients have increased rates of orthostatic hypotension, hypertension, tachycardia, or hypocapnia relative to age-matched controls. DESIGN: Assess blood pressure, heart rate, respiratory rate, end tidal CO2 and visual analog scales for orthostatic symptoms when supine and when standing for 8 minutes without moving legs. SETTING: Referral practice and research center. PARTICIPANTS: 60 women and 15 men with CFS and 36 women and 4 men serving as age matched controls with analyses confined to 62 patients and 35 controls showing either normal orthostatic testing or a physiological abnormal test. MAIN OUTCOME MEASURES: Orthostatic tachycardia; orthostatic hypotension; orthostatic hypertension; orthostatic hypocapnia or combinations thereof. RESULTS: CFS patients had higher rates of abnormal tests than controls (53% vs 20%, $p < .002$), but rates of orthostatic tachycardia, orthostatic hypotension, and orthostatic hypertension did not differ significantly between patients and controls (11.3% vs 5.7%, 6.5% vs 2.9%, 19.4% vs 11.4%, respectively). In contrast, rates of orthostatic hypocapnia were significantly higher in CFS than in controls (20.6% vs 2.9%, $p < .02$). This CFS group reported significantly more feelings of illness and shortness of breath than either controls or CFS patients with normal physiological tests. CONCLUSION: A substantial number of CFS patients have orthostatic intolerance in the form of orthostatic hypocapnia. This allows subgrouping of patients with CFS and thus reduces patient pool heterogeneity engendered by use of a clinical case definition.
Nater UM, Maloney E, Boneva RS, Gurbaxani BM, Lin JM, Jones JF, Reeves WC, Heim C.	Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control & Prevention, Atlanta, GA; Department of Psychiatry & Behavioral Sciences, Emory University School of Medicine, Atlanta, GA;	Attenuated Morning Salivary Cortisol Concentrations in a Population-based Study of Persons with Chronic Fatigue Syndrome and Well Controls.	J Clin Endocrinol Metab. 2007 Dec 26 [Epub ahead of print]	Context A substantial body of research on the pathophysiology of chronic fatigue syndrome (CFS) has focused on hypothalamic-pituitary-adrenal (HPA) axis dysregulation. The cortisol awakening response has received particular attention as a marker of HPA axis dysregulation. Objective The objective of the current study was to evaluate morning salivary cortisol profiles in persons with CFS and well controls identified from the general population. Design Case-control study. Setting This study was conducted at an outpatient research clinic. Cases and Other Participants We screened a sample of 19,381 residents of Georgia and identified those with CFS and a matched sample of well controls. Seventy-five medication-free CFS cases and 110 medication-free well controls provided complete sets of saliva samples. Main Outcome Measures Free cortisol concentrations in saliva collected on a regular workday, immediately upon awakening, 30 minutes and 60 minutes after awakening. Results There was a significant interaction effect, indicating different profiles of cortisol concentrations over time between groups, with the CFS group showing an attenuated morning cortisol profile. Notably, we observed a sex difference in this effect. Women with CFS exhibited significantly attenuated morning cortisol profiles compared with well women. In contrast, cortisol profiles were similar in men with CFS and male controls. Conclusions CFS was associated with an attenuated morning cortisol response but the effect was limited to women. Our results suggest that a sex difference in hypocortisolism may

	Department of Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, GA.			contribute to increased risk of CFS in women.
Naumann UK, Nigg C, Suter P, Käser L, Vetter W.	Medizinische Poliklinik, Universitätsspital Zürich. urania.kolyvanos@usz.ch	[Fatigue] [Article in German]	Schweiz Rundsch Med Prax. 2007 Aug 2;96(31-32):1159-65; quiz 1166-7.	
Neu D, Mairesse O, Hoffmann G, Dris A, Lambrecht LJ, Linkowski P, Verbanck P, Le Bon O.	Sleep Laboratory, Department of Psychiatry, University Hospital Brugmann, Brussels, Belgium. daniel.neu@skynet.be	Sleep quality perception in the chronic fatigue syndrome: correlations with sleep efficiency, affective symptoms and intensity of fatigue.	Neuropsychobiology. 2007;56(1):40-6. Epub 2007 Nov 6.	BACKGROUND/AIMS: One of the core symptoms of the chronic fatigue syndrome (CFS) is unrefreshing sleep and a subjective sensation of poor sleep quality. Whether this perception can be expressed, in a standardized questionnaire as the Pittsburgh Sleep Quality Index (PSQI), has to our knowledge never been documented in CFS. Furthermore, correlations of subjective fatigue, PSQI, affective symptoms and objective parameters such as sleep efficiency are poorly described in the literature. METHODS: Using a cross-sectional paradigm, we studied subjective measures like PSQI, Fatigue Severity Scale scores and intensity of affective symptoms rated by the Hamilton Depression and Anxiety scales as well as objective sleep quality parameters measured by polysomnography of 28 'pure' (no primary sleep and no psychiatric disorders) CFS patients compared to age- and gender-matched healthy controls. RESULTS: The PSQI showed significantly poorer subjective sleep quality in CFS patients than in healthy controls. In contrast, objective sleep quality parameters, like the Sleep Efficiency Index (SEI) or the amount of slow-wave sleep did not differ significantly. Subjective sleep quality showed a correlation trend with severity of fatigue and was not correlated with the intensity of affective symptoms in CFS. CONCLUSION: Our findings indicate that a sleep quality misperception exists in CFS or that potential nocturnal neurophysiological disturbances involved in the nonrecovering sensation in CFS are not expressed by sleep variables such as the SEI or sleep stage distributions and proportions. (c) 2007 S. Karger AG, Basel.
Newton JL, Okonkwo O, Sutcliffe K, Seth A, Shin J, Jones DE.	Fatigue Interest group and Liver Research Group, Institute for Cellular Medicine, University of Newcastle, Newcastle, UK. julia.newton@nuth.nhs.uk	Symptoms of autonomic dysfunction in chronic fatigue syndrome.	QJM. 2007 Aug;100(8):519-26. Epub 2007 Jul 7.	BACKGROUND: Chronic fatigue syndrome (CFS) is common and its cause is unknown. AIM: To study the prevalence of autonomic dysfunction in CFS, and to develop diagnostic criteria. DESIGN: Cross-sectional study with independent derivation and validation phases. METHODS: Symptoms of autonomic dysfunction were assessed using the Composite Autonomic Symptom Scale (COMPASS). Fatigue was assessed using the Fatigue Impact Scale (FIS). Subjects were studied in two groups: phase 1 (derivation phase), 40 CFS patients and 40 age- and sex-matched controls; phase 2 (validation phase), 30 CFS patients, 37 normal controls and 60 patients with primary biliary cirrhosis. RESULTS: Symptoms of autonomic dysfunction were strongly and reproducibly associated with the presence of CFS or primary biliary cirrhosis (PBC), and correlated with severity of fatigue. Total COMPASS score >32.5 was identified in phase 1 as a diagnostic criterion for autonomic dysfunction in CFS patients, and

				was shown in phase 2 to have a positive predictive value of 0.96 (95%CI 0.86-0.99) and a negative predictive value of 0.84 (0.70-0.93) for the diagnosis of CFS. DISCUSSION: Autonomic dysfunction is strongly associated with fatigue in some, but not all, CFS and PBC patients. We postulate the existence of a 'cross-cutting' aetiological process of dysautonomia-associated fatigue (DAF). COMPASS >32.5 is a valid diagnostic criterion for autonomic dysfunction in CFS and PBC, and can be used to identify patients for targeted intervention studies.
Niblett SH, King KE, Dunstan RH, Clifton-Bligh P, Hoskin LA, Roberts TK, Fulcher GR, McGregor NR, Dunsmore JC, Butt HL, Klineberg I, Rothkirch TB.	Environmental and Pathogenic Microbiology Laboratory, School of Environmental and Life Sciences, The University of Newcastle, Callaghan, NSW 2308, Australia.	Hematologic and urinary excretion anomalies in patients with chronic fatigue syndrome.	Exp Biol Med (Maywood). 2007 Sep;232(8):1041-9.	Patients with chronic fatigue syndrome (CFS) have a broad and variable spectrum of signs and symptoms with variable onsets. This report outlines the results of a single-blind, cross-sectional research project that extensively investigated a large cohort of 100 CFS patients and 82 non fatigued control subjects with the aim of performing a case-control evaluation of alterations in standard blood parameters and urinary amino and organic acid excretion profiles. Blood biochemistry and full blood counts were unremarkable and fell within normal laboratory ranges. However, the case-control comparison of the blood cell data revealed that CFS patients had a significant decrease in red cell distribution width and increases in mean platelet volume, neutrophil counts, and the neutrophil-lymphocyte ratio. Evaluation of the urine excretion parameters also revealed a number of anomalies. The overnight urine output and rate of amino acid excretion were both reduced in the CFS group ($P < 0.01$). Significant decreases in the urinary excretion of asparagine ($P < 0.0001$), phenylalanine ($P < 0.003$), the branch chain amino acids ($P < 0.005$), and succinic acid ($P < 0.0001$), as well as increases in 3-methylhistidine ($P < 0.05$) and tyrosine ($P < 0.05$) were observed. It was concluded that the urinary excretion and blood parameters data supported the hypothesis that alterations in physiologic homeostasis exist in CFS patients.
Nijs J, Demol S, Wallman K.	Department of Human Physiology, Faculty of Physical Education & Physiotherapy, Vrije Universiteit, Brussels, Belgium. Jo.Nijs@vub.ac.be	Can submaximal exercise variables predict peak exercise performance in women with chronic fatigue syndrome?	Arch Med Res. 2007 Apr;38(3):350-3. Epub 2007 Jan 30.	This study aimed at examining whether physiological exercise variables at the submaximal level, defined as 75% of the age-predicted target heart rate, are able to predict peak exercise performance in women with chronic fatigue syndrome (CFS) (n=222). Subjects performed a bicycle ergometric test against a graded increase in workload until exhaustion with continuous monitoring of electrocardiographic and ventilatory variables. Oxygen uptake at the submaximal level (VO2SUBMAX) correlated strongly with peak oxygen uptake (VO2PEAK) (r=0.70). For the prediction of VO2PEAK, linear regression analysis determined the line of best fit as: VO2PEAK=0.95xVO2SUBMAX+372.3. Using this equation, the mean error in the prediction was 14.6+/-11.2% (range 0.1-63.7%). It is concluded that the prediction of VO2PEAK based on VO2SUBMAX might be useful for analyzing group differences or treatment effects but not for individual (clinical) purposes.
Nishikai M.	National Hospital Organization Tokyo Medical Center.	[Antinuclear antibodies in patients with chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1067-70.	Significance of antinuclear antibodies (ANA) in the patients with chronic fatigue syndrome (CFS) was reviewed. When indirect immunofluorescence with the HEp-2 cells as the substrates was used, prevalence of the positive ANA was reportedly 15-25%. The ANA titers were low and the immunofluorescent staining patterns were heterogeneous. One group in the USA reported that 'nuclear envelope staining pattern' was found in more than 50% of the patients with CFS. This results, however, have not been confirmed by any other research groups. Clinical significance of the positive ANA in the CFS patients resides in differential diagnoses of systemic lupus erythematosus and other diffuse connective tissue diseases. Recently, several ANAs specific to CFS have been described. We reported anti-68/48kD protein antibodies utilizing SDS-PAGE/ immunoblot method. These

				autoantibodies were found in 13% of 114 CFS patients and 0% in healthy subjects ($p < 0.05$). Hypersomnia and difficulty in concentration were found more frequently in the CFS patients with this specific autoantibody.
Njoku MG, Jason LA, Torres-Harding SR.	DePaul University, Chicago, IL 60614, USA. nmgloria@depaul.edu	The prevalence of chronic fatigue syndrome in Nigeria.	J Health Psychol. 2007 May;12(3):461-74.	The present study found adult rates of chronic fatigue syndrome (CFS) in Nigeria that were somewhat higher than rates from community-based CFS epidemiologic studies in the USA. The rates of chronic fatigue for both adults and children were also higher than in existing community-based studies. It is possible that the presence of several fatiguing illnesses such as malaria and typhoid, the lack of adequate healthcare resources and poverty in Nigeria, place individuals at greater risk for fatigue and its syndromes. There is a need for more epidemiologic studies on the prevalence and sociodemographic characteristics of CFS in developing countries.
Nogué S, Fernández-Solá J, Rovira E, Montori E, Fernández-Huerta JM, Munné P.	Unidades de Toxicología y de Fatiga Crónica, Hospital Clínic, IDIBAPS, Universidad de Barcelona, Barcelona, España. SNOGUE@clinic.ub.es	[Multiple chemical sensitivity: study of 52 cases[Article in Spanish]]	Med Clin (Barc). 2007 Jun 16;129(3):96-8; quiz 99. Comment in: Med Clin (Barc). 2007 Jun 16;129(3):94-5.	BACKGROUND AND OBJECTIVE: Multiple chemical sensitivity (MCS) is characterized by a loss of tolerance to various environmental chemicals. The objective of this study was to describe patients with MCS seen in our hospital. PATIENTS AND METHOD: Patients consecutively seen by the Toxicology and Chronic Fatigue Units who presented symptoms of MCS were included. The diagnosis was clinical. All patients completed the Quick Environmental Exposure and Sensitivity Inventory (QEESI) questionnaire. RESULTS: Fifty-two patients were included. The average age (standard deviation) was 47.2 (7.6) years, and 46 (88%) were females. The origin of the syndrome was related to occupational exposure to various chemical agents in 31 cases (59.6%), including occupational accidents in 14 patients (fumigation of the workplace with insecticides). In 20 patients (38.5%), the syndrome could not be associated with any toxic exposure and was considered a manifestation of chronic fatigue syndrome. The QEESI showed mean scores of 72.9 (18.6) on the chemical inhalant intolerance scale, 45.5 (20.6) on the other intolerances scale, 69.8 (20.6) on the symptom severity scale, 4.4 (1.8) on the masking index and 66.6 (21.7) on the life impact scale. All patients were followed up for a minimum of 12 months, and during this period they remained stable with no deaths. CONCLUSIONS: MCS normally affects middle-aged women. It is frequently triggered by exposure to chemical agents, especially insecticides. An association with chronic fatigue syndrome is common. The prognosis is good but the patients' quality of life is seriously affected.
Nunez Juarez Montserrat, Esther Nunez Juarez, Jose Luis Del Val Garcia, Jose Manuel Fernandez Huerta, Cayetano Alegre de Miguel, Maria Bonet Llorach, Daniel Roig, Esther Gomez Gil, Teresa Godas Sieso, Joaquim		HUHealth-Related Quality of Life in Chronic Fatigue Syndrome versus Rheumatoid Arthritis as Control Group UH	Journal of Chronic Fatigue Syndrome 2007; 14(2): 31-43	The objectives of this study were (1) evaluate health-related quality of life (HRQL) in patients with chronic fatigue syndrome (CFS); (2) to compare the HRQL of these patients with that of rheumatoid arthritis (RA) patients and healthy Spanish reference population values (RPV); and (3) to identify the influence of sociodemographic and clinical variables on HRQL in CFS patients. We included 216 outpatients: 94 females/14 males (age 42.9 ± 9.9 years) with CFS and 94 females/14 males with RA (age 42.9 ± 9.9 years). We used a cross-sectional, observational design. Sociodemographic data, comorbidities, pain (VAS) and global functional status were determined. HRQL was measured by the SF-36 and HAQ questionnaires. CFS patients had worse scores than RA patients in all SF36 dimensions except emotional role ($p < 0.01$). Both CFS and RA patients had worse scores in all SF36 dimensions than RPV. In CFS patients, pain negatively influenced HRQL ($p < 0.05$) except for physical role, social function and emotional role. Global functional status negatively influenced HRQL ($p < 0.05$) except for bodily pain, general health and mental health. Comorbidities worsened scores for physical and social functions and mental health. In conclusion, HRQL was worse in patients with CFS than in those with

Fernandez Sola				RA. Both CFS and RA patients had worse HRQL compared with RPV. Comorbidities, pain and global functional status influenced HRQL in CFS patients. Standardised HRQL instruments are of value in determining the quality of life in these patients.
Nye F.		Chronic fatigue syndrome and myalgic encephalomyelitis: the 2007 guidelines from the National Institute of Clinical Excellence.	J Infect. 2007 Dec;55(6):569-71. Epub 2007 Oct 22.	
Ohinata J, Suzuki N, Araki A, Takahashi S, Fujieda K, Tanaka H.	Department of Pediatrics, Asahikawa Medical College, Japan.	Actigraphic assessment of sleep disorders in children with chronic fatigue syndrome.	Brain Dev. 2007 Nov 19 [Epub ahead of print]	Children with chronic fatigue syndrome (CFS) often suffer from sleep disorders, which cause many physiological and psychological problems. Understanding sleep characteristics in children with CFS is important for establishing a therapeutic strategy. We conducted an actigraphic study to clarify the problems in sleep/wake rhythm and physical activity in children with CFS. Methods. Actigraphic recordings were performed for 1-2 weeks in 12 CFS children. The obtained data were compared with those of healthy age-matched children used as the control. Results. Sleep patterns were divided into two groups based on subjects' sleep logs: irregular sleep type and delayed sleep phase type. Compared to the control group, total sleep time was longer and physical activity was lower in both groups of CFS. Continuous sleep for more than 10h was not uncommon in CFS. In the irregular sleep type, impaired daily sleep/wake rhythms and disrupted sleep were observed. Conclusion. Using actigraphy, we could identify several characteristics of the sleep patterns in CFS children. Actigraphic analysis proved to be useful in detecting sleep/wake problems in children with CFS.
Ojima K, Watanabe N, Narita N, Narita M.	Graduate School Human Sciences, University of Tsukuba, Ibaraki, Japan. narita_m@doc.medic.mie-u.ac.jp.	Temporomandibular disorder is associated with a serotonin transporter gene polymorphism in the Japanese population.	Biopsychosoc Med. 2007 Jan 10;1:3.	ABSTRACT: AIMS: Recent genetic studies have linked serotonin-related genetic polymorphisms with diverse disorders characterized by functional somatic symptoms, including chronic fatigue syndrome, irritable bowel syndrome, and premenstrual dysphoric disorder. METHODS: We investigated three serotonin-related genetic polymorphisms by screening genomic DNA of 36 temporomandibular disorder (TMD) patients. RESULTS: A significant increase of longer alleles (l and xl) was found in the TMD patients compared to the controls both by the genotype-wise and the allele-wise analyses (both $p < 0.01$ by chi2 test and Fisher's exact test). CONCLUSION: Genetic factors that involve the serotonergic system may play a role in the pathogenesis of TMD.
Oki J, Okubo J.	Department of Pediatrics, Asahikawa Kosei Hospital.	[Usefulness of growth chart in children and adolescents with chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1113-9.	We presented three sheets of growth chart in children with chronic fatigue syndrome. The growth chart in 14-year-old boy (patient 1) showed decreased weight gain because of too much exercise. After that he complained nausea, abdominal pain, sleep disturbance and debilitating fatigue. The growth chart in 12-year-old girl (patient 2) revealed increased weight gain because of overeating due to the divorce of her parents. She developed syncope, sleep disturbance, and fatigue during overeating. The growth chart in 13-year-old girl (patient 3) showed decreased weight gain after she developed lymph node enlargement. We diagnosed her as autoimmune fatigue syndrome because of persistent positive antinuclear antibody. Although growth chart will not be able to detect childhood

				chronic fatigue syndrome prospectively, the chart may be useful for detecting some life events in these children.
Olson K, Turner AR, Courneya KS, Field C, Man G, Cree M, Hanson J.	Faculty of Nursing, University of Alberta, Edmonton, Alberta, Canada.	Possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion in advanced cancer.	Support Care Cancer. 2007 Jul 24 [Epub ahead of print]	GOALS: In this theoretical paper, we present the Edmonton Fatigue Framework (EFF), a new framework for the study of tiredness, fatigue, and exhaustion in advanced cancer. MATERIALS AND METHODS: The Fatigue Adaptation Model (FAM), the starting point for the EFF, was drawn from a literature review pertaining to fatigue in depression, chronic fatigue syndrome, cancer, shift workers, and athletes published in the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Medical Literature Analysis and Retrieval System Online (MEDLINE), PubMed, PsychINFO, SPORTdiscus, and CancerLit between 1995 and 2004, and from seven qualitative studies conducted by our group. The EFF, an elaboration of the FAM, was constructed after an expansion of our literature review to 2006 and team discussion. The EFF provides new insights into possible links between behavioral and physiological indices of tiredness, fatigue, and exhaustion as they occur in both ill and non-ill states. In this paper, however, we consider only possible links in advanced cancer. CONCLUSIONS: We propose that stressors associated with advanced cancer and its supportive treatment trigger declines in four systems-cognitive function, sleep quality, nutrition, and muscle endurance-and that these declines reduce one's ability to adapt. While these systems each likely has its own effect on adaptation, we propose that the most important and serious effects arise from interactions among declines in cognitive function, sleep quality, nutrition, and muscle endurance. CONCLUSIONS: Interventions for fatigue have been limited by a lack of understanding about its etiology. Hypotheses arising from the EFF; suggest a new direction for further study that focuses on interactions among cognitive function, sleep quality, nutrition, and muscle endurance.
Ondo WG, Sethi KD, Kricorian G.	Baylor College of Medicine, Department of Neurology, 6550 Fannin, Houston, TX 77030, USA. wondo@bcm.tmc.edu	Selegiline orally disintegrating tablets in patients with Parkinson disease and "wearing off" symptoms.	Clin Neuropharmacol. 2007 Sep-Oct;30(5):295-300. Comment in: Clin Neuropharmacol. 2007 Sep-Oct;30(5):301-4. Clin Neuropharmacol. 2007 Sep-Oct;30(5):305-7	BACKGROUND: Selegiline orally disintegrating tablet (ODT; Zelapar) is a selective monoamine oxidase B inhibitor developed as an adjunct to levodopa (LD) for Parkinson disease. Most patients on long-term LD therapy eventually experience deterioration at the end of the LD dosing interval, with predictable "wearing off" and "on-off" fluctuations. METHODS: We conducted a 12-week, double-blind, placebo-controlled, parallel-design trial of selegiline ODT. The primary efficacy point was reduction in the percentage of average daily "off" time. Secondary measures included reductions in daily off hours and total daily off time, Clinical Global Impressions-Improvement (CGI-I), and Patient Global Impression-Improvement (PGI-I). Patients on LD received selegiline ODT (1.25 mg/d for 6 weeks, then 2.5 mg/d for 6 weeks) or placebo. Safety and tolerability were measured. RESULTS: The intent-to-treat population included 98 patients receiving selegiline ODT and 50 patients receiving placebo. Combined efficacy results for weeks 10 and 12 revealed an 11.6% reduction in percentage of daily off time for selegiline ODT versus a 9.8% reduction for placebo (NS). PGI-I detected a statistically significant difference between treatment groups in favor of selegiline ODT (P = 0.02), whereas CGI-I detected a strong trend toward improvement (P = 0.06). Selegiline ODT was safe and well tolerated. CONCLUSIONS: This study showed no significant difference in improvement in percentage of off time with selegiline ODT versus placebo. Some clinical impressions (e.g., PGI-I, CGI-I) improved. This result contrasts with an identically designed study that showed a significant improvement in off time with selegiline ODT. A combined analysis of both studies suggested overall efficacy.
Osipenko MF,		[Cirrhotic	Klin Med (Mosk).	Modern studies have shown that hepatic cirrhosis (HC) is accompanied by moderate cardiac

Bikbulatova EA.		cardiomyopathy] [Article in Russian]	2007;85(9):80-3.	dysfunction. The character and degree of these changes do not depend on the etiology of HC and manifest by an increased ventricular wall thickness and diastolic dysfunction, which deteriorate with ascite and physical labor, as well as basal hyperdynamic systolic dysfunction with pathologic response to physical stress. The latter decreases physical tolerance, which contributes to the development of chronic fatigue syndrome and lowered working ability in HC patients. Cardiovascular changes get reversed in 6 to 12 months after hepatic transplantation.
Page WF.	Medical Follow-up Agency, Institute of Medicine, 500 Fifth Street NW, Washington, DC 20001, USA. wpage@nas.edu	Update on the NAS-NRC Twin Registry	Twin Res Hum Genet. 2006 Dec;9(6):985-7	The National Academy of Sciences-National Research Council (NAS-NRC) Twin Registry is one of the oldest, national population-based twin registries in the United States. It consists of 15,924 white male twin pairs born in the years 1917 to 1927 (inclusive), both of whom served in the armed forces, mostly during World War II. This article updates activity in this registry since the earlier 2002 article in Twin Research. The results of clinically based studies on dementia, Parkinson's disease, age-related macular degeneration, and primary osteoarthritis were published, as well as articles based on previously collected questionnaire data on chronic fatigue syndrome, functional limitations, and healthy aging. In addition, risk factor studies are being planned to merge clinical data with earlier collected risk factor data from questionnaires. Examination data from the subset of National Heart, Lung, and Blood Institute (NHLBI) twins resulted in a number of articles, including the relationship of endogenous sex hormones to coronary heart disease and morphological changes in aging brain structures. The NEO Five-Factor Personality Inventory (a paper-and-pencil self-administered questionnaire) has been fielded for the first time. A push to consolidate the various data holdings of the registry is being made.
Pall ML.	School of Molecular Biosciences, Washington State University, Pullman, WA 99164-4234, USA. martin_pall@wsu.edu	Nitric oxide synthase partial uncoupling as a key switching mechanism for the NO/ONOO- cycle.	Med Hypotheses. 2007;69(4):821-5. Epub 2007 Apr 19.	Short-term stressors, capable of increasing nitric oxide levels, act to initiate cases of illnesses including chronic fatigue syndrome, multiple chemical sensitivity, fibromyalgia and posttraumatic stress disorder. These stressors, acting primarily through the nitric oxide product, peroxynitrite, are thought to initiate a complex vicious cycle mechanism, known as the NO/ONOO- cycle that is responsible for chronic illness. The complexity of the NO/ONOO- cycle raises the question as to whether the mechanism that switches on this cycle is this complex cycle itself or whether a simpler mechanism is the primary switch. It is proposed here that the switch involves a combination of two variable switches, the increase of nitric oxide synthase (NOS) activity and the partial uncoupling of the NOS activity, with uncoupling caused by a tetrahydrobiopterin (BH4) deficiency. NOS uncoupling causes the NOS enzymes to produce superoxide, the other precursor of peroxynitrite, in place of nitric oxide. Thus partial uncoupling will cause NOS proteins to act like peroxynitrite synthases, leading, in turn to increased NF-kappaB activity. Peroxynitrite is known to oxidize BH4, and consequently partial uncoupling may initiate a vicious cycle, propagating the partial uncoupling over time. The combination of high NOS activity and BH4 depletion will lead to a potential vicious cycle that may be expected to switch on the larger NO/ONOO- cycle, thus producing the symptoms and signs of chronic illness. The role of peroxynitrite in the NO/ONOO- cycle also implies that such uncoupling is part of the chronic phase cycle mechanism such that agents that lower uncoupling will be useful in treatment.
Papo T.	Service de Médecine Interne, Hôpital Bichat, Paris.	[Macrophage mediated myofasciites: a systemic disease or	Rev Neurol (Paris). 2007 Oct;163(10):981-4.	

	papo@bch.ap-hop-paris.fr	post-vaccinial tatoo?] [Article in French]		
Paralikar V, Sarmukaddam S, Agashe M, Weiss MG.	Maharashtra Institute of Mental Health, Pune, India. vasudeop@vsnl.com	Diagnostic concordance of neurasthenia spectrum disorders in Pune, India.	Soc Psychiatry Psychiatr Epidemiol. 2007 Jul;42(7):561-72. Epub 2007 May 2.	BACKGROUND: Clinically significant fatigue or weakness is a common but understudied clinical problem in India. The applicability and relevance of Western clinical criteria in this setting are not studied. Alternative criteria sets used in different clinical contexts suggest a range of conditions constituting neurasthenia spectrum disorders (NSDs). We therefore aimed to determine frequency of patients with these complaints in four specialty outpatient clinics of an urban general hospital. We compared the concordance of four diagnostic criteria sets of fatigue disorders among the same patients. METHODS: Patients from the clinics of Psychiatry, Medicine, Dermatology, and Ayurved were screened for clinically significant fatigue or weakness and assessed for CFS, ICD-10 neurasthenia, DSM-IV draft criteria for neurasthenia, and CCMD-2 neurasthenia. RESULTS: For 352 patients, sensitivity of CDC criteria for CFS (13.4%) was poorest. CFS was most frequent in the Medicine clinic. CCMD-2 criteria were the most frequently met (77.6%) with no significant difference across clinics. Two-way concordance of neurasthenia categories was no better than fair (< or =0.4) and few patients (8.0%) met criteria for all four categories. DISCUSSION: Four NSD criteria sets identified different clinical subgroups. CFS, considering fatigue and ignoring weakness, was least relevant for identifying NSD patients in these clinics. Poor concordance among the four diagnostic systems studied indicates the need for reviewing the nosology of these disorders. Focus on clinical significance alone is likely to avoid the discordant confusion arising from cross-cultural differences.
Park J, Knudson S.	Health Statistics Division, Statistics Canada, Ottawa, Ontario. Jungwee.Park@statcan.ca	Medically unexplained physical symptoms.	Health Rep. 2007 Feb;18(1):43-7.	
Perrin RN.	The Perrin Clinic, 11 St John St, Manchester, Greater Manchester, M3 4DW, UK. rayperrin@btconnect.com	Lymphatic drainage of the neuraxis in chronic fatigue syndrome: a hypothetical model for the cranial rhythmic impulse.	J Am Osteopath Assoc. 2007 Jun;107(6):218-24.	The cranial rhythmic impulse is a palpable, rhythmic fluctuation believed to be synchronous with the primary respiratory mechanism. The precise physiologic mechanism of the cranial rhythmic impulse is not fully understood. Based on traditional and current views of the cranial rhythmic impulse, animal studies, and clinical findings in patients with chronic fatigue syndrome, the author argues that the cranial rhythmic impulse is the rhythm produced by a combination of cerebrospinal fluid drainage from the neuraxis (brain and spinal cord) and pulsations of central lymphatic drainage induced by the sympathetic nervous system. In addition, evidence is provided to demonstrate that a disturbed, palpable, and visible neurolymphatic process leads to chronic fatigue syndrome. This process may also explain the pathophysiologic mechanisms leading to other disease states. Finally, the author's proposed manual treatment protocol for patients with chronic fatigue syndrome is described.
Pieczenik SR, Neustadt J.	drneustadt@gmail.com	Mitochondrial dysfunction and molecular pathways of	Exp Mol Pathol. 2007 Aug;83(1):84-92. Epub 2007 Jan 18.	Since the first mitochondrial dysfunction was described in the 1960s, the medicine has advanced in its understanding the role mitochondria play in health, disease, and aging. A wide range of seemingly unrelated disorders, such as schizophrenia, bipolar disease, dementia, Alzheimer's disease, epilepsy, migraine headaches, strokes, neuropathic pain, Parkinson's disease, ataxia, transient ischemic attack,

		disease		cardiomyopathy, coronary artery disease, chronic fatigue syndrome, fibromyalgia, retinitis pigmentosa, diabetes, hepatitis C, and primary biliary cirrhosis, have underlying pathophysiological mechanisms in common, namely reactive oxygen species (ROS) production, the accumulation of mitochondrial DNA (mtDNA) damage, resulting in mitochondrial dysfunction. Antioxidant therapies hold promise for improving mitochondrial performance. Physicians seeking systematic treatments for their patients might consider testing urinary organic acids to determine how best to treat them. If in the next 50 years advances in mitochondrial treatments match the immense increase in knowledge about mitochondrial function that has occurred in the last 50 years, mitochondrial diseases and dysfunction will largely be a medical triumph.
Pohar SL, Jones CA, Warren S, Turpin KV, Warren K.	Institute of Health Economics, Faculty of Rehabilitation Medicine, Edmonton, Alberta, Canada.	Health status and health care utilization of multiple sclerosis in Canada.	Can J Neurol Sci. 2007 May;34(2):167-74. Comment in: Can J Neurol Sci. 2007 May;34(2):120.	BACKGROUND: Persons with multiple sclerosis (MS) represent a small segment of the population, but given the progression of the disease, they experience substantial physical, psychosocial and economic burdens. OBJECTIVE: The primary aim was to compare demographic characteristics, health status, health behaviours, health care resource utilization and access to health care of the community dwelling populations with and without MS. METHODS: Cross-sectional survey using data from the Canadian Community Health Survey (CCHS 1.1). Adjusted analyses were performed to assess differences between persons with MS and the general population, after controlling for age and sex. Normalized sampling weights and bootstrap variance estimates were used. RESULTS: Respondents with MS were 7.6 times (95% CI: 5.4, 10.7) more likely to have health-related quality of life scores that reflected severe impairment than respondents without MS. Respondents with MS were 12.2 times (95% CI: 8.6, 17.2) to rate their health as 'poor' or 'fair' than the general population. Urinary incontinence and chronic fatigue syndrome were 18.7 times (95% CI: 12.5, 28.2) and 21.9 times (95% CI: 11.9, 40.3), more likely to be reported by respondents with MS than those without. Differences between the two populations also existed in terms of health care resource utilization and access and health behaviours. CONCLUSION: Large discrepancies in health status and health care utilization existed between persons with MS who reside in the community and the general population according to all indicators used. Health care needs of persons with MS were also not met.
Rees RJ, Bellon ML.	Disability Studies, School of Medicine, Flinders University, Adelaide, Australia. rees1@iinet.net.au	Post concussion syndrome ebb and flow: longitudinal effects and management.	NeuroRehabilitation. 2007;22(3):229-42.	This research identified persistent post concussion symptoms (PCS) in a group of 20 adult subjects. PCS generally lasted for two years with a mean of 3.35 years. Typical symptoms included physical and cognitive fatigue, depressive behaviors, sensitivity to noise, social withdrawal, irritability, concentration and problem solving difficulties, loss of libido and much difficulty making decisions at even the simplest strategic level. They represented a hard core group for whom the original symptoms persisted well beyond the 6~month period. Participants identified their PCS according to sensory, somatic affective and cognitive items immediately following their trauma (01) and two years later (02). Counseling and psychotherapy intervention took place between 01 and 02. Items on the PCS schedules and the Beck Depression Inventory (II) demonstrated significant decline in the presence of overall symptoms most noticeably in reduction of agitation, irritability and suicidal wishes. However, subjects throughout generally experienced the feeling that they were being punished which equated with behaviors comparable with learned helplessness. The PCS group considered themselves to be different people after trauma. They had different goals, changing lifestyle, relationships and employment and were more often in a dependent state. Comparability with other conditions such as

				PTSD and chronic fatigue syndrome (CFS) was demonstrated by individuals who experienced persistent and invasive post concussion symptoms.
Reeves WC, Jones JF, Maloney E, Heim C, Hoaglin DC, Boneva RS, Morrissey M, Devlin R.	Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. wcr1@cdc.gov	Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia.	Popul Health Metr. 2007 Jun 8;5:5. Comment in: Popul Health Metr. 2007;5:6.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating illness with no known cause or effective therapy. Population-based epidemiologic data on CFS prevalence are critical to put CFS in a realistic context for public health officials and others responsible for allocating resources. METHODS: Based on a random-digit dialing survey we ascertained CFS cases and controls to estimate the prevalence of CFS in metropolitan, urban, and rural populations of Georgia. This report focuses on the 5,623 of 19,381 respondents ages 18 to 59 years old. Fatigued (2,438), randomly selected unwell not fatigued (1,429) and randomly selected well (1,756) respondents completed telephone questionnaires concerning fatigue, other symptoms, and medical history. Subsets of those identified by interview as having CFS-like illness (292), chronic unwellness which was not CFS-like (268 - randomly selected), and well subjects (223, matched to those with CFS-like illness on sex, race, and age) completed a clinical evaluation. RESULTS: We estimated that 2.54% of persons 18 to 59 years of age suffered from CFS. There were no significant differences in prevalence of CFS between metropolitan, urban or rural populations or between white and black residents of the three regions. However, there were significant differences in female-to-male ratios of prevalence across the strata (metropolitan female: male 11.2 : 1, urban 1.7 : 1, rural 0.8 : 1). CONCLUSION: We estimated that 2.54% of the Georgia population suffers from CFS, which is 6- to 10-fold higher than previous population-based estimates in other geographic areas. These differences may reflect broader screening criteria and differences in the application of the case definition. However, we cannot exclude the possibility that CFS prevalence may be higher in Georgia than other areas where it has been measured. Although the study did not identify differences in overall prevalence between metropolitan, urban, and rural Georgia populations, it did suggest the need for additional stratified analyses by geographic strata.
Rimes KA, Goodman R, Hotopf M, Wessely S, Meltzer H, Chalder T.	King's College London, Institute of Psychiatry, Section of General Hospital Psychiatry, Weston Education Centre, Cutcombe Rd, London SE5 9RJ, United Kingdom. K.Rimes@iop.kcl.ac.uk	Incidence, prognosis, and risk factors for fatigue and chronic fatigue syndrome in adolescents: a prospective community study.	Pediatrics. 2007 Mar;119(3):e603-9.	OBJECTIVE: The objective of this study was to describe the incidence, prevalence, risk factors, and prognosis of fatigue, chronic fatigue, and chronic fatigue syndrome in 11- to 15-year-olds. METHODS: A random general population sample (n = 842) of British adolescents and their parents were assessed at baseline and 4 to 6 months later. The main outcomes were fatigue, chronic fatigue, and chronic fatigue syndrome, operationally defined. RESULTS: The incidence over 4 to 6 months was 30.3% for fatigue, 1.1% for chronic fatigue, and 0.5% for chronic fatigue syndrome. The point prevalence was 34.1% and 38.1% for fatigue, 0.4% and 1.1% for chronic fatigue, and 0.1% and 0.5% for chronic fatigue syndrome at time 1 and time 2, respectively. Of participants who were fatigued at time 1, 53% remained fatigued at time 2. The 3 cases of chronic fatigue and 1 case of chronic fatigue syndrome at time 1 had recovered by time 2. Higher risk for development of chronic fatigue at time 2 was associated with time 1 anxiety or depression, conduct disorder, and maternal distress; in multivariate analysis, baseline anxiety or depression remained a significant predictor of chronic fatigue. Increased risk for development of fatigue at time 2 was associated with time 1 anxiety or depression, conduct disorder, and older age; in multivariate analyses, these factors and female gender all were significant predictors of fatigue. CONCLUSIONS: The incidence rates for chronic fatigue and chronic fatigue syndrome in this adolescent sample were relatively high, but the prognosis for these conditions was good. This prospective study provides evidence for an association between emotional/behavioral

				problems and subsequent onset of fatigue/chronic fatigue.
Ring D, McCarthy M.	Department of Orthopaedic Surgery, Massachusetts General Hospital, ACC 525, 15 Parkman St., Boston, MA 02114, USA. dring@partners.org	Opinion: pseudoscientific explanations of arm pain.	J Surg Orthop Adv. 2007 Fall;16(3):105-10.	
Rodríguez Vidigal FF, Vera Tomé A, Muñoz Sanz A.		[Chlamydophila pneumoniae, a possible cause of mononucleosis syndrome] [Article in Spanish]	Med Clin (Barc). 2007 Jun 23;129(4):156.	
Roscoe JA, Kaufman ME, Matteson-Rusby SE, Palesh OG, Ryan JL, Kohli S, Perlis ML, Morrow GR.	Department of Radiation Oncology, University of Rochester School of Medicine and Dentistry, James P Wilmot Cancer Center, Rochester, NY 14642, USA. Joseph_Roscoe@URMC.Rochester.edu	Cancer-related fatigue and sleep disorders.	Oncologist. 2007;12 Suppl 1:35-42.	Sleep disorders, such as difficulty falling asleep, problems maintaining sleep, poor sleep efficiency, early awakening, and excessive daytime sleepiness, are prevalent in patients with cancer. Such problems can become chronic in some patients, persisting for many months or years after completion of cancer therapy. For patients with cancer, sleep is potentially affected by a variety of factors, including the biochemical changes associated with the process of neoplastic growth and anticancer treatments, and symptoms that frequently accompany cancer, such as pain, fatigue, and depression.Fatigue is highly prevalent and persistent in patients with cancer and cancer survivors. Although cancer-related fatigue and cancer-related sleep disorders are distinct, a strong interrelationship exists between these symptoms, and a strong possibility exists that they may be reciprocally related. The majority of studies that have assessed both sleep and fatigue in patients with cancer provide evidence supporting a strong correlation between cancer-related fatigue and various sleep parameters, including poor sleep quality, disrupted initiation and maintenance of sleep, nighttime awakening, restless sleep, and excessive daytime sleepiness.This paper reviews the data from these studies with a view toward suggesting further research that could advance our scientific understanding both of potential interrelationships between sleep disturbance and cancer-related fatigue and of clinical interventions to help with both fatigue and sleep disturbance.Disclosure of potential conflicts of interest is found at the end of this article.
Rosenhagen MC, Schmidt U, Ebinger M, Nickel T, Uhr M.	Max Planck Institute of Psychiatry Munich, Germany.	Successful treatment of chronic fatigue syndrome with duloxetine and	J Clin Psychopharmacol. 2008 Feb;28(1):105-7.	

		trijodthyronine-a case study.		
Rowe PC, Lucas KE.		Orthostatic intolerance in chronic fatigue syndrome.	Am J Med. 2007 Mar;120(3):e13. Comment on: Am J Med. 2005 Dec;118(12):1415.	
Ryan JL, Carroll JK, Ryan EP, Mustian KM, Fiscella K, Morrow GR.	Department of Radiation Oncology, University of Rochester School of Medicine and Dentistry, James P Wilmot Cancer Center, Rochester, NY 14642, USA. Julie_Ryan@urmc.rochester.edu	Mechanisms of cancer-related fatigue.	Oncologist. 2007;12 Suppl 1:22-34.	Cancer-related fatigue (CRF) is one of the most prevalent symptoms patients with cancer experience, both during and after treatment. CRF is pervasive and affects patients' quality of life considerably. It is important, therefore, to understand the underlying pathophysiology of CRF in order to develop useful strategies for prevention and treatment. At present, the etiology of CRF is poorly understood and the relative contributions of the neoplastic disease, various forms of cancer therapy, and comorbid conditions (e.g., anemia, cachexia, sleep disorders, depression) remain unclear. In any individual, the etiology of CRF probably involves the dysregulation of several physiological and biochemical systems. Mechanisms proposed as underlying CRF include 5-HT neurotransmitter dysregulation, vagal afferent activation, alterations in muscle and ATP metabolism, hypothalamic-pituitary-adrenal axis dysfunction, circadian rhythm disruption, and cytokine dysregulation. Currently, these hypotheses are largely based on evidence from other conditions in which fatigue is a characteristic, in particular chronic fatigue syndrome and exercise-induced fatigue. The mechanisms that lead to fatigue in these conditions provide a theoretical basis for future research into the complex etiology of this distressing and debilitating symptom. An understanding of relevant mechanisms may offer potential routes for its prevention and treatment in patients with cancer.Disclosure of potential conflicts of interest is found at the end of this article.
Sairenji T, Nagata K.	Division of Biosignaling, Department of Biomedical Sciences, School of Life Science, Faculty of Medicine, Tottori University.	[Viral infections in chronic fatigue syndrome] [Article in Japanese	Nippon Rinsho. 2007 Jun;65(6):991-6.	Chronic fatigue syndrome (CFS) is a heterogeneous illness in which patients can have different, overlapping signs and symptoms. No single underlying cause has been established for all CFS patients. Epidemiological studies reveal that a flu-like sickness precedes the onset in the majority of cases. The major hypothesis of the pathogenesis of CFS is that infectious agents such as viruses, may trigger and lead to chronic activation of the immune system with abnormal regulation of cytokine production. Many studies have been performed to identify the possible microbial triggers and to understand the epidemiological microbial agents. We have summarized the recent progressive literature of virus, rickettsia, and mycoplasma implicated in the pathogenesis of CFS.
Sakudo A, Kuratsune H, Hakariya Y, Kobayashi T, Ikuta K.	Department of Virology, Research Institute for Microbial Diseases, Osaka University.	[Spectroscopic diagnosis of chronic fatigue syndrome by multivariate analysis of visible and near-infrared spectra] [Article in	Nippon Rinsho. 2007 Jun;65(6):1051-6.	We have recently evaluated the possibility of visible and near-infrared (Vis-NIR) spectroscopy for diagnosis of chronic fatigue syndrome(CFS). Vis-NIR spectra in the 600-1,100 nm region for sera from CFS patients and healthy donors were subjected to principal component analysis (PCA) and soft independent modeling of class analogy (SIMCA) to develop multivariate models to discriminate between CFS patients and healthy donors. The PCA and SIMCA model predicted successful prediction of the masked samples. Furthermore, taking advantage of Vis-NIR spectroscopy to enable noninvasive analysis, our preliminary results have shown that SIMCA model from Vis-NIR spectra of thumb has achieved 70-80% correct determinations. In this review, we will introduce the potential of the Vis-NIR

		Japanese]		spectroscopy for CFS diagnosis.
Samer Koutoubi, John W. Cartmell, Mark Kestin, Geoffrey Lecovin		Protein Nutrition in Fibromyalgia	Journal of Chronic Fatigue Syndrome 2007; 14(3):	Background: Fibromyalgia (FM) is a soft-tissue disease of unknown origin. It causes soft-tissue pain and stiffness, often with chronic fatigue, disrupted sleep, headaches and irritable bowel. Fibromyalgia affects an estimated six million Americans of which 80 to 90 percent are female. Objective: To determine whether dietary intake of protein, Tryptophan, and Branched Chain Amino Acids (BCAA) meet Dietary Reference Intake (DRI) recommendations, and whether there is a difference in animal and vegetable protein intake in subjects with FM compared to healthy controls. Methods: Thirty subjects with FM and an equal number of controls completed a Food Frequency Questionnaire (FFQ) regarding dietary intake over the previous month. The FFQs were then computer analyzed to determine dietary intake. Results: Protein intake of all subjects was more than adequate to meet DRI recommendations and there was no significant difference in intake of protein, BCAA, Tryptophan, animal or vegetable protein. Subjects with FM had significantly higher body weight and Body Mass Index (BMI) than controls, and reported having a higher incidence of Irritable Bowel Syndrome (IBS) symptoms than controls. Conclusion: There was no significant difference in dietary intake of protein, Tryptophan, BCAA, or amounts of animal or vegetable protein in FM subjects compared to healthy controls. Significant differences in body weight and BMI in FM subjects might be related to less physical activity or possibly to malabsorption problems associated with IBS. Malabsorption related to IBS might increase the potential for protein malnutrition, FM, and associated symptoms like chronic fatigue.
Sanders P, Korf J.	University Centre of Psychiatry, University of Groningen, Groningen, The Netherlands.	Neuroaetiology of chronic fatigue syndrome: An overview.	World J Biol Psychiatry. 2007 May 8;:1-7 [Epub ahead of print]	Chronic fatigue syndrome (CFS) is now recognized as a medial disorder. In contrast to recent related reports, the present review focuses primarily on aetiological aspects of CFS. Four major hypotheses are reviewed. (1) Although CFS is often associated with viral infection, the presence of viruses has as yet not consistently been detected. (2) It is not clear whether anomalies of the HPA axis often observed in CFS, are cause or the consequences of the disorder. (3) Immune dysfunction as the cause of CFS is thus far the weakest hypothesis. (4) The psychiatric and psychosocial hypothesis denies the existence of CFS as a disease entity. Accordingly, the fatigue symptoms are assumed to be the consequence of other (somatic) diseases. Other possible causes of CFS are oxidative stress and genetic predisposition. In CFS cognitive behavioural therapy is most commonly used. This therapy, however, appears to be ineffective in many patients. The suggested causes of CFS and the divergent reactions to therapy may be explained by the lack of recognition of subgroups. Identification of subtypes may lead to more effective therapeutic interventions.
Scheeres K, Wensing M, Mes C, Bleijenberg G.	Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, The Netherlands. K.Scheeres@nkcv.	The impact of informational interventions about cognitive behavioral therapy for chronic fatigue syndrome on GPs referral behavior.	Patient Educ Couns. 2007 Sep;68(1):29-32. Epub 2007 May 22.	OBJECTIVE: This study investigated the impact of an informational intervention among general practitioners (GPs) about a new treatment with cognitive behavioral therapy (CBT) for chronic fatigue syndrome (CFS) in a mental health center (MHC). The outcome measures concerned GPs knowledge and attitudes towards CFS and their actual referrals of CFS patients to this new treatment setting. METHODS: Three hundred and one GPs, who all had received written information about CFS four times, and who partly had also visited an informational group session, completed a short questionnaire survey on CFS knowledge and attitudes. Referral data were obtained from the mental health center. RESULTS: During 16 months 22% of all GPs in the concerning region had referred at

	umcn.nl			least one CFS patient. Concerning knowledge and attitude, the survey results showed that 70% of the GPs had remembered the intervention's main message, namely the new treatment possibility. These informed GPs reported better knowledge and more positive attitudes towards CFS than the non-informed GPs, who had not seen and read the intervention's information. CONCLUSION: This study showed that disseminating written materials can be a useful method for stimulating GPs to refer CFS patients for CBT. PRACTICE IMPLICATIONS: In future implementation projects concerning CBT for CFS (or other 'new' treatments for a disputed illness) in a MHC or other institution, the informational intervention evaluated here can be a suitable and efficient method to inform GPs and let them refer patients.
Schur E, Afari N, Goldberg J, Buchwald D, Sullivan PF.	Department of Medicine, University of Washington School of Medicine, Seattle,Washington, USA. ellschur@washington.edu	Twin analyses of fatigue.	Twin Res Hum Genet. 2007 Oct;10(5):729-33.	Prolonged fatigue equal to or greater than 1 month duration and chronic fatigue equal to or greater than 6 months duration are both commonly seen in clinical practice, yet little is known about the etiology or epidemiology of either symptom. Chronic fatigue syndrome (CFS), while rarer, presents similar challenges in determining cause and epidemiology. Twin studies can be useful in elucidating genetic and environmental influences on fatigue and CFS. The goal of this article was to use biometrical structural equation twin modeling to examine genetic and environmental influences on fatigue, and to investigate whether these influences varied by gender. A total of 1042 monozygotic (MZ) twin pairs and 828 dizygotic (DZ) twin pairs who had completed the University of Washington Twin Registry survey were assessed for three fatigue-related variables: prolonged fatigue, chronic fatigue, and CFS. Structural equation twin modeling was used to determine the relative contributions of additive genetic effects, shared environmental effects, and individual-specific environmental effects to the 3 fatigue conditions. In women, tetrachoric correlations were similar for MZ and DZ pairs for prolonged and chronic fatigue, but not for CFS. In men, however, the correlations for prolonged and chronic fatigue were higher in MZ pairs than in DZ pairs. About half the variance for both prolonged and chronic fatigue in males was due to genetic effects, and half due to individual-specific environmental effects. For females, most variance was due to individual environmental effects.
Schur EA, Afari N, Furberg H, Olarte M, Goldberg J, Sullivan PF, Buchwald D.	Department of Medicine, University of Washington School of Medicine, Seattle, WA, USA. ellschur@u.washington.edu	Feeling bad in more ways than one: comorbidity patterns of medically unexplained and psychiatric conditions.	J Gen Intern Med. 2007 Jun;22(6):818-21.	BACKGROUND: Considerable overlap in symptoms and disease comorbidity has been noted among medically unexplained and psychiatric conditions seen in the primary care setting, such as chronic fatigue syndrome, low back pain, irritable bowel syndrome, chronic tension headache, fibromyalgia, temporomandibular joint disorder, major depression, panic attacks, and posttraumatic stress disorder. OBJECTIVE: To examine interrelationships among these 9 conditions. DESIGN: Using data from a cross-sectional survey, we described associations and used latent class analysis to investigate complex interrelationships. PARTICIPANTS: 3,982 twins from the University of Washington Twin Registry. MEASUREMENTS: Twins self-reported a doctor's diagnosis of the conditions. RESULTS: Comorbidity among these 9 conditions far exceeded chance expectations; 31 of 36 associations were significant. Latent class analysis yielded a 4-class solution. Class I (2% prevalence) had high frequencies of each of the 9 conditions. Class II (8% prevalence) had high proportions of multiple psychiatric diagnoses. Class III (17% prevalence) participants reported high proportions of depression, low back pain, and headache. Participants in class IV (73% prevalence) were generally healthy. Class I participants had the poorest markers of health status. CONCLUSIONS: These results support theories suggesting that medically unexplained conditions share a common etiology. Understanding patterns of comorbidity

				can help clinicians care for challenging patients.
Shepherd CB.		NICE behaviour: ME guideline is unworkable.	BMJ. 2007 Sep 15;335(7619):528. Comment on: BMJ. 2007 Sep 1;335(7617):446-8.	
Shevchuk NA.	Molecular Radiobiology Section, the Department of Radiation Oncology, Virginia Commonwealth University School of Medicine, 401 College St, Richmond, VA 23298, USA. nshevchuk@comcast.net.	Possible use of repeated cold stress for reducing fatigue in chronic fatigue syndrome: a hypothesis.	Behav Brain Funct. 2007 Oct 24;3:55.	ABSTRACT: BACKGROUND: Physiological fatigue can be defined as a reduction in the force output and/or energy-generating capacity of skeletal muscle after exertion, which may manifest itself as an inability to continue exercise or usual activities at the same intensity. A typical example of a fatigue-related disorder is chronic fatigue syndrome (CFS), a disabling condition of unknown etiology and with uncertain therapeutic options. Recent advances in elucidating pathophysiology of this disorder revealed hypofunction of the hypothalamic-pituitary-adrenal axis and that fatigue in CFS patients appears to be associated with reduced motor neurotransmission in the central nervous system (CNS) and to a smaller extent with increased fatigability of skeletal muscle. There is also some limited evidence that CFS patients may have excessive serotonergic activity in the brain and low opioid tone. PRESENTATION OF THE HYPOTHESIS: This work hypothesizes that repeated cold stress may reduce fatigue in CFS because brief exposure to cold may transiently reverse some physiological changes associated with this illness. For example, exposure to cold can activate components of the reticular activating system such as raphe nuclei and locus ceruleus, which can result in activation of behavior and increased capacity of the CNS to recruit motoneurons. Cold stress has also been shown to reduce the level of serotonin in most regions of the brain (except brainstem), which would be consistent with reduced fatigue according to animal models of exercise-related fatigue. Finally, exposure to cold increases metabolic rate and transiently activates the hypothalamic-pituitary-adrenal axis as evidenced by a temporary increase in the plasma levels of adrenocorticotropic hormone, beta-endorphin and a modest increase in cortisol. The increased opioid tone and high metabolic rate could diminish fatigue by reducing muscle pain and accelerating recovery of fatigued muscle, respectively. TESTING THE HYPOTHESIS: To test the hypothesis, a treatment is proposed that consists of adapted cold showers (20 degrees Celsius, 3 minutes, preceded by a 5-minute gradual adaptation to make the procedure more comfortable) used twice daily. IMPLICATIONS OF THE HYPOTHESIS: If testing supports the proposed hypothesis, this could advance our understanding of the mechanisms of fatigue in CFS.
Shin JI, Lee JS.		Can chronic fatigue symptoms associated with nutcracker phenomenon be treated with aspirin?	Med Hypotheses. 2007;69(3):704-5. Epub 2007 Feb 27. Comment on: Med Hypotheses. 2007;68(6):1318-27.	
Shinchuk LM, Holick MF.	Spaulding Rehabilitation Hospital, Boston,	Vitamin d and rehabilitation: improving	Nutr Clin Pract. 2007 Jun;22(3):297-304.	Vitamin D inadequacy is pandemic among rehabilitation patients in both inpatient and outpatient settings. Male and female patients of all ages and ethnic backgrounds are affected. Vitamin D deficiency causes osteopenia, precipitates and exacerbates osteoporosis, causes the painful bone

	MA, USA.	functional outcomes.	Erratum in: Nutr Clin Pract. 2007 Aug;22(4):table of contents. Shinchuk, Leonid [corrected to Shinchuk, Leonid M].	disease osteomalacia, and worsens proximal muscle strength and postural sway. Vitamin D inadequacy can be prevented by sensible sun exposure and adequate dietary intake with supplementation. Vitamin D status is determined by measurement of serum 25-hydroxyvitamin D. The recommended healthful serum level is between 30 and 60 ng/mL. 25-Hydroxyvitamin D levels of >30 ng/mL are sufficient to suppress parathyroid hormone production and to maximize the efficiency of dietary calcium absorption from the small intestine. This can be accomplished by ingesting 1000 IU of vitamin D(3) per day, or by taking 50,000 IU of vitamin D(2) every 2 weeks. Vitamin D toxicity is observed when 25-hydroxyvitamin D levels exceed 150 ng/mL. Identification and treatment of vitamin D deficiency reduces the risk of vertebral and nonvertebral fractures by improving bone health and musculoskeletal function. Vitamin D deficiency and osteomalacia should be considered in the differential diagnosis of patients with musculoskeletal pain, fibromyalgia, chronic fatigue syndrome, or myositis. There is a need for better education of health professionals and the general public regarding the optimization of vitamin D status in the care of rehabilitation patients.
Sleigh KM, Danforth DG, Hall RT, Fleming JA, Stiver HG.	Division of Infectious Disease, Department of Medicine;	Double-blind, randomized study of the effects of influenza vaccination on the specific antibody response and clinical course of patients with chronic fatigue syndrome.	Can J Infect Dis. 2000 Sep;11(5):267-73.	OBJECTIVE: To determine whether influenza immunization is associated with early side effects, a deleterious impact on the illness course and depressed antibody response in patients with chronic fatigue syndrome (CFS). DESIGN: Prospective, randomized, double-blind, placebo controlled trial. CFS patients and healthy volunteers filled out a questionnaire on immunization side effects and had hemagglutination-inhibiting (HI) antibody titres measured pre- and three weeks after immunization. CFS patients completed symptom and function questionnaires before and during the six-week, postimmunization period. SETTING: Ambulatory care. POPULATION STUDIED: Convenience sample of 40 CFS patients fulfilling the Centers for Disease Control and Prevention criteria and 21 demographically matched healthy volunteers. INTERVENTIONS: CFS patients were randomly selected to receive commercially available whole virus influenza vaccine (n=19) or an injection of saline placebo (n=21). Healthy volunteers received vaccine only. MAIN RESULTS: As a group, immunized CFS patients had lower geometric mean HI antibody rises than healthy volunteers (P<0.001). However, there was no difference in the rates of fourfold titre rises, and immunization did achieve a probably protective titre (1:32 or greater) in most CFS patients. No difference could be detected between immunized and placebo CFS patients in immunization side effects, although CFS patients as a group reported four times as many side effects as healthy volunteers. Further, in the six weeks following immunization, placebo and immunized CFS patients did not demonstrate any differences in terms of functioning, symptom severity and sleep disturbance. CONCLUSIONS: In patients with CFS, influenza immunization is safe, not associated with any excess early reactions, and stimulates an immunizing response comparable with that of healthy volunteers.
Smith AK, Dimulescu I, Falkenberg VR, Narasimhan S, Heim C, Vernon SD, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control	Genetic evaluation of the serotonergic system in chronic fatigue syndrome.	Psychoneuroendocrinology. 2007 Dec 11 [Epub ahead of print]	Chronic fatigue syndrome (CFS) is a debilitating disorder of unknown etiology with no known lesions, diagnostic markers or therapeutic intervention. The pathophysiology of CFS remains elusive, although abnormalities in the central nervous system (CNS) have been implicated, particularly hyperactivity of the serotonergic (5-hydroxytryptamine; 5-HT) system and hypoactivity of the hypothalamic-pituitary-adrenal (HPA) axis. Since alterations in 5-HT signaling can lead to physiologic and behavioral changes, a genetic evaluation of the 5-HT system was undertaken to identify serotonergic markers associated with CFS and potential mechanisms for CNS abnormality. A total of 77 polymorphisms in genes related

	and Prevention, 1600 Clifton Road, MSG41, Atlanta, GA 30333, USA.			to serotonin synthesis (TPH2), signaling (HTR1A, HTR1E, HTR2A, HTR2B, HTR2C, HTR3A, HTR3B, HTR4, HTR5A, HTR6, and HTR7), transport (SLC6A4), and catabolism (MAOA) were examined in 137 clinically evaluated subjects (40 CFS, 55 with insufficient fatigue, and 42 non-fatigued, NF, controls) derived from a population-based CFS surveillance study in Wichita, Kansas. Of the polymorphisms examined, three markers (-1438G/A, C102T, and rs1923884) all located in the 5-HT receptor subtype HTR2A were associated with CFS when compared to NF controls. Additionally, consistent associations were observed between HTR2A variants and quantitative measures of disability and fatigue in all subjects. The most compelling of these associations was with the A allele of -1438G/A (rs6311) which is suggested to have increased promoter activity in functional studies. Further, in silico analysis revealed that the -1438 A allele creates a consensus binding site for Th1/E47, a transcription factor implicated in the development of the nervous system. Electrophoretic mobility shift assay supports allele-specific binding of E47 to the A allele but not the G allele at this locus. These data indicate that sequence variation in HTR2A, potentially resulting in its enhanced activity, may be involved in the pathophysiology of CFS.
Spain LA, Tubridy N, Kilpatrick TJ, Adams SJ, Holmes AC.	Department of Neurology, Royal Melbourne Hospital, Parkville, Vic., Australia.	Illness perception and health-related quality of life in multiple sclerosis.	Acta Neurol Scand. 2007 Nov;116(5):293-9. Epub 2007 Sep 11.	AIMS - A number of physical and psychological factors have been shown to affect health-related quality of life (HRQoL) in patients with multiple sclerosis (MS). Among these, the role of illness perceptions has not been established as an independent factor. This study, the first of its kind in an Australian population, aimed to use a large sample to determine the relative importance of individual factors to each domain of HRQoL, in particular the role of illness perception. MATERIALS AND METHODS - 580 patients with confirmed MS were assessed cross sectionally in a designated research clinic to determine the relative impact of physical factors (illness severity, duration, age, fatigue and pain) and psychological factors (mood, cognition and illness representations) on each domain of the SF-36. RESULTS - Categorical regression analysis showed that a combination of physical and psychological factors predicted 38-71% of variance in HRQoL. Illness perception was shown to have an independent effect on HRQoL in MS. The Extended Disability Status Scale was a significant determinant in all domains except for mental health. Depression was less prevalent than anxiety, but had a greater effect on function. CONCLUSION - Illness perception is an independent factor contributing to HRQoL in people with MS. Individual domains of HRQoL are associated with different patterns of physical and psychological factors. In the domains of role and social function, activities most highly valued by patients with MS, depression, anxiety, fatigue and illness perceptions are key determinants, all of which have the potential to be improved through specific interventions.
Spence VA, Kennedy G, Belch JJ, Hill A, Khan F.		Low grade inflammation and arterial wave reflection in patients with chronic fatigue syndrome.	Clin Sci (Lond). 2007 Nov 21 [Epub ahead of print]	Some of the symptoms reported by people with chronic fatigue syndrome (CFS) are associated with various cardiovascular phenomena. Markers of cardiovascular risk, including inflammation and oxidative stress, have been demonstrated in some CFS patients but little is known about the relationship of these and prognostic indicators of cardiovascular risk in this patient group. We sought to investigate the relationship between inflammation and oxidative stress and augmentation index, a measure of arterial stiffness, in 41 well characterised CFS patients and in 30 healthy subjects. The augmentation index, normalised for a heart rate of 75 beats per minute (AIx@75), was significantly greater in CFS patients than in control subjects (22.5 +/- 1.7 versus 13.3 +/- 2.3%, P=0.002). CFS patients also had significantly increased levels of C-reactive protein (2.58 +/- 2.91 versus 1.07 +/- 2.16

				g/mL, P<0.01) and 8-iso-prostaglandin F 2alpha isoprostanes (470.7 +/- 250.9 versus 331.1 +/- 97.6 pg/mL, P<0.005). In CFS patients, AIx@75 significantly correlated with log C-reactive protein (r=0.507, P=0.001), isoprostanes (r=0.366, P=0.026), oxidised LDL (r=0.333, P=0.039) and systolic blood pressure (r=0.371, P=0.017). In a stepwise multiple regression model, (including systolic and diastolic blood pressure, body mass index, C-reactive protein, TNFalpha, IL-1, oxidised LDL, HDL cholesterol levels, isoprostanes, age and gender), AIx@75 was independently associated with log CRP (beta=0.385, P=0.006), age (beta=0.363, P=0.022), and female gender (beta=0.302, P=0.03) in CFS patients. The combination of increased arterial wave reflection, inflammation and oxidative stress may result in an increased risk of future cardiovascular events. Assessment of arterial wave reflection might be useful for determining cardiovascular risk in this patient group.
Stenlund T, Ahlgren C, Lindahl B, Burell G, Knutsson A, Stegmayr B, Birgander LS.	Department of Public Health and Clinical Medicine, Umeå University, Sweden. therese.stenlund@vll.se	Patients with burnout in relation to gender and a general population.	Scand J Public Health. 2007;35(5):516-23.	AIMS: The aims of this study were to describe gender differences in patients with burnout and compare these patients with a general population with respect to physical, psychosocial and work variables. METHODS: Data were collected from a total of 136 patients (96 women and 40 men, 41.6 +/- 7.4 years), diagnosed with stress-related disease and burnout at the Stress Clinic, University Hospital of Umeå. Data on burnout, physical, psychosocial and work characteristics were compared with similar data from a geographical and age-matched population based survey, the 2004 Northern Sweden MONICA study. The survey sample included a total of 573 participants (283 women and 290 men, 40.7 +/- 8.5 years). RESULTS: Women with burnout reported a higher rate of impaired awakening, lower job control, greater proportion of unpaid work and worked to a greater extent "with people" compared to men. Men with burnout had a more restricted social network and reported working more overtime than women. Patients with burnout reported a higher rate of unemployment, a more restricted social network and higher work demands compared to a general population. Women with burnout reported less emotional support, a more sedentary work situation, high job strain and worked to a greater extent "with people" than women from the general population. CONCLUSIONS: There are some differences in working conditions and social network between women and men with burnout. Patients with burnout differ from a general population regarding individual and social factors as well as work-related factors.
Tackenberg B, Himmerich H, Wellek A, Oertel WH, Sommer N.	Philipps Universität Marburg und Universitäts-klinikum Giessen. tackenbb@med.uni-marburg.de	[Advances in the treatment of multiple sclerosis?] [Article in German]	MMW Fortschr Med. 2007 May 21;149 Suppl 2:51-5.	The natural course of multiple sclerosis (MS) is probably more favourable than previously assumed years ago. Since the introduction of interferons in Germany, the establishment and further development of new diagnostic criteria (McDonald criteria), the causal and symptomatic treatment possibilities and initiation of therapy early in the course of the disease have led to a considerable change in the treatment of MS. MS attacks are usually treated with the intravenous administration of high-dosed steroids. When the attack symptoms do not sufficiently subside, plasmapheresis can be considered. For long-term treatment of MS, beta interferon, glatirameracetate and natalizumab are available as basic causal therapy and natalizumab and mitoxantrone are available for escalation therapy. Frequently occurring spasticity, chronic fatigue syndrome, depression, cognitive disturbances, incontinence, pain, ataxia and sexual disorders must be treated symptomatically. Overall, the outpatient treatment of MS is complex and should be carried out with close cooperation between the family doctor, neurological practices and outpatient departments specialized in treating MS.
Tajima S,	Fatigue Clinical	[Estimation of	Nippon Rinsho.	OBJECTIVES: In this study, we try to estimate the fatigue state using actigraphy and R-R interval power

Kuratsune H, Yamaguti K, Takahashi A, Takashima S, Watanabe Y, Nishizawa Y.	Center, Osaka City University Graduate School of Medicine.	fatigue state in patient with CFS using actigraph and R-R interval power spectrum analysis] [Article in Japanese]	2007 Jun;65(6):1057-64.	spectrum analysis. RESULTS: Actigraphy analysis showed that mean awake activity was decreased and duration of sleep was prolonged in patients with chronic fatigue syndrome (CFS), significantly ($p < 0.001$). Both of sleep episodes in wake period and wake episodes in sleep period were significantly increased in CFS patients in comparison with healthy volunteers ($p < 0.001$) In autonomic nerve analysis, sleep/awake ratio of high frequency component was significantly decreased in patients with CFS ($p < 0.05$). CONCLUSION: The quality of sleep in patients with CFS was decreased because of increase of wake episodes in sleep period. Also the lack of parasympathetic activation during sleep period might be associated with the deterioration of sleep quality in patients with CFS.
Takken T, Henneken T, van de Putte E, Helders P, Engelbert R.	Pediatric Physical Therapy and Exercise Physiology, UMC Utrecht, Utrecht, Netherlands. t.takken@umcutrecht.nl	Exercise testing in children and adolescents with chronic fatigue syndrome.	Int J Sports Med. 2007 Jul;28(7):580-4. Epub 2007 Mar 15.	The objective of this study was to evaluate exercise capacity in children and adolescents diagnosed with Chronic Fatigue Syndrome (CFS). We examined 20 patients (12 girls and 8 boys; mean age 14.9 +/- 3.7 years) diagnosed with CFS. Exercise capacity was measured using a maximal exercise test on a bicycle ergometer and an expired gas analysis system. Fatigue was assessed using a questionnaire and a daily activity diary was used to describe activities for three days. Z-scores were calculated using age- and sex-matched reference values. Z-scores in children and adolescents with CFS were - 0.33 +/- 1.0 ($p = 0.17$) for peak oxygen uptake, - 1.13 +/- 1.41 ($p = 0.002$) for relative peak oxygen uptake [ml/kg/min] and - 0.93 +/- 1.29 ($p = 0.07$) for maximal work load. Both heart rate and blood pressure at peak performance were significantly reduced compared to reference values. Fatigue levels were significantly positively associated with age and negatively with blood pressure at peak exercise ($p < 0.05$). In conclusion maximum exercise testing was feasible in young people with CFS. Maximal exercise capacity was only reduced in a minority of the patients and was related to current physical activity levels.
Tanaka H.	Department of Pediatrics, Osaka Medical College.	[Autonomic function and child chronic fatigue syndrome] [Article in Japanese	Nippon Rinsho. 2007 Jun;65(6):1105-12.	It is postulated that child chronic fatigue syndrome (CFS) involves the autonomic nervous system, although the precise mechanism has not been clearly indicated. This paper reviews recent reports focusing the role of the autonomic nervous system which plays in CFS. Many of the method for measuring autonomic function have appeared in the clinical setting in parallel with advancing computer technology, but these are limited when applied in children. In these blood pressure and heart rate changes during orthostatic stress and these variability are favorably used. As a result, one third of children with CFS showed abnormal cardiovascular adjustment during posture change (orthostatic dysregulation: OD) which is characterized by instantaneous orhthostatic hypotension, postural tachycardia or neurally-mediated syncope. Most of the studies using power spectral analysis of heart rate variability showed sympathetic activation, however no consistent finding has been obtained. In conclusion, autonomic function might be partly involved in CFS such as OD, but its priority in causing CFS is unclear.
Tanriverdi F, Karaca Z, Unluhizarci K, Kelestimur F.	Department of Endocrinology, Medical School, Erciyes University, Kayseri, Turkey.	The hypothalamo-pituitary-adrenal axis in chronic fatigue syndrome and fibromyalgia syndrome.	Stress. 2007 Mar;10(1):13-25.	The hypothalamo-pituitary-adrenal (HPA) axis plays a major role in the regulation of responses to stress. Human stress-related disorders such as chronic fatigue syndrome (CFS), fibromyalgia syndrome (FMS), chronic pelvic pain and post-traumatic stress disorder are characterized by alterations in HPA axis activity. However, the role of the HPA axis alterations in these stress-related disorders is not clear. Most studies have shown that the HPA axis is underactive in the stress-related disorders, but contradictory results have also been reported, which may be due to the patients selected for the study, the methods used for the investigation of the HPA axis, the stage of the syndrome when the

				tests have been done and the interpretation of the results. There is no structural abnormality in the endocrine organs which comprise the HPA axis, thus it seems that hypocortisolemia found in the patients with stress-related disorder is functional. It may be also an adaptive response of the body to chronic stress. In this review, tests used in the assessment of HPA axis function and the HPA axis alterations found in CFS and FMS are discussed in detail.
Ter Wolbeek M, van Doornen LJ, Coffeng LE, Kavelaars A, Heijnen CJ.	Laboratory of Psychoneuroimmunology, University Medical Center Utrecht, Office KC03.068.0, P.O. Box 85090, 3508 AB, Utrecht, The Netherlands.	Cortisol and severe fatigue: a longitudinal study in adolescent girls.	Psychoneuroendocrinology. 2007 Feb;32(2):171-82. Epub 2007 Feb 6.	Fatigue is a common complaint among adolescents, especially in girls, and is associated with high rates of school absenteeism. Severe fatigue is often accompanied by psychological and physical symptoms. In the chronic fatigue syndrome (CFS) functioning of the hypothalamic-pituitary-adrenal (HPA)-axis has previously been found to be altered. The aim of the present study was to investigate whether cortisol production is deviant in fatigued adolescent girls from the general population and to study longitudinal changes in fatigue in association with possible changes in HPA-axis functioning. In the cross-sectional part of the study the cortisol response to awakening (CAR) and to a low-dose oral dexamethasone were examined in a group of fatigued adolescent girls (n=87) in comparison to a non-fatigued control group (n=77). Questionnaires regarding fatigue, depression, anxiety, sleep quality, somatic symptoms and CFS-related symptoms were filled out. Follow up measurements were performed after 6 and 12 months. While the fatigued and non-fatigued group differed remarkably on all symptom self-reports, no differences between groups in CAR and response to dexamethasone were observed. Girls in the fatigued group remained fatigued over time and reported high levels of other psychological and physical symptoms during the whole year of the study. The CAR varied between time points but correlated non-systematically with situational characteristics or symptom reports. We conclude that trait-like fatigue, as measured in a sample of adolescent girls from a high school population, is not reflected in a dysregulation as assessed on the level of salivary cortisol after awakening.
ter Wolbeek M, van Doornen LJ, Kavelaars A, van de Putte EM, Schedlowski M, Heijnen CJ.	Laboratory of Psychoneuroimmunology, University Medical Center Utrecht, 3508 AB Utrecht, The Netherlands.	Longitudinal analysis of pro- and anti-inflammatory cytokine production in severely fatigued adolescents.	Brain Behav Immun. 2007 Nov;21(8):1063-74. Epub 2007 Jun 1.	In the adolescent population, fatigue is associated with somatic complaints, unrefreshing sleep, cognitive disturbances and symptoms of depression and anxiety. This pattern of symptoms resembles the one described in chronic fatigue syndrome (CFS). Since immunological alterations have been reported in CFS patients, we wondered whether also severely fatigued girls from a healthy population would show comparable alterations in psychological and immunological parameters. We tested this hypothesis in a longitudinal design, allowing a reliable assessment of the participants' characteristic immune status. Groups of severely fatigued (N=67) and non-fatigued (N=61) participants were selected. Severely fatigued girls reported more depressive symptoms, anxiety, reduced sleep quality, and somatic and CFS-related symptoms than non-fatigued participants across three measurements during one year (T1: spring, T2: autumn, T3: spring). In contrast, no group differences in mitogen-induced cytokine production or T-cell proliferation in vitro or in leukocyte subset counts were observed. Although absolute cytokine production and cell counts were affected by seasonal variation, the within-subject values, relatively to the rest of the participants, were fairly stable. Data from a small group of CFS patients (N=11) showed similarities in self-reported complaints between CFS patients and fatigued participants. Interestingly, CFS patients showed a distinct immune profile when compared to the severely fatigued or non-fatigued participants, i.e. increased levels of anti-inflammatory cytokines (IL-10, decreased IFN-gamma/IL-10 ratio) and reduced levels of pro-inflammatory cytokines (IL-6, TNF-

				alpha) over all three time points analyzed. These results show that, although overlap in symptomatology between the general population and patients with CFS was observed, only CFS patients show a skewing of the cytokine balance towards an anti-inflammatory profile.
Thanawala Sachi, Renee R. Taylor		Service Utilization, Barriers to Service Access, and Coping in Adults with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2007; 14(1): 5 - 21	Objective: In a sample of 47 adults with CFS, we aimed to describe patterns of service utilization, identify barriers to service access, and explore the relationship between service utilization and coping styles. Method: A questionnaire assessing service utilization frequency and barriers to service access was administered to a sample of 47 individuals with CFS. The Illness Management Questionnaire was used to assess relationships between coping styles and service utilization. Results: A Cochran's Q test of homogeneity revealed that medical and CFS self-help services were most frequently used and rehabilitation services were least frequently used. In terms of service accessibility, 80.9% of participants reported at least one barrier. Lack of financial (including insurance) resources and lack of knowledge about service availability were the two most frequently reported. In terms of coping styles, symptom focusing was positively associated with use of CFS self-help services and with use of in-home services and social service agencies. Information seeking was negatively associated with use of in-home and social service agencies and with use of mental health services. Conclusion: These findings can be used by health-care professionals and advocacy-based organizations to develop programs focused on mass education campaigns for health-care providers, increase knowledge of service availability among individuals with CFS, and to understand relationships between certain types of coping styles and service preferences.
The GK, Bleijenberg G, van der Meer JW.	Department of General Internal Medicine, Nijmegen Expert Centre Chronic Fatigue, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. g.the@aig.umcn.nl	The effect of acclydine in chronic fatigue syndrome: a randomized controlled trial.	PLoS Clin Trials. 2007 May 18;2(5):e19.	OBJECTIVES: It is unclear whether insulin-like growth factor (IGF) function is involved in the pathophysiology of chronic fatigue syndrome (CFS). Unpublished data and reports in patient organization newsletters suggest that Acclydine, a food supplement, could be effective in the treatment of CFS by increasing biologically active IGF1 levels. Here we aimed to measure the IGF1 and IGF binding protein (IGFBP) 3 status of CFS patients compared to age- and gender-matched neighborhood controls, and to assess the effect of Acclydine on fatigue severity, functional impairment, and biologically active IGF1 level (IGFBP3/IGF1 ratio). DESIGN: A randomized, placebo-controlled, double-blind clinical trial. SETTING: Radboud University Nijmegen Medical Centre, The Netherlands. PARTICIPANTS: Fifty-seven adult patients who fulfilled the US Centers for Disease Control and Prevention criteria for CFS. IGF status of 22 CFS patients was compared to that of 22 healthy age- and gender-matched neighborhood control individuals. INTERVENTION: Acclydine or placebo for 14 wk. OUTCOME MEASURES: Outcomes were fatigue severity (Checklist Individual Strength, subscale fatigue severity [CIS-fatigue]), functional impairment (Sickness Impact Profile-8 [SIP-8]), and biologically active IGF1 serum concentrations. Analyses were on an intention-to-treat basis. RESULTS: There was no difference in IGF status in 22 CFS patients compared to healthy age- and gender-matched control individuals. Treatment with Acclydine did not result in significant differences compared with the placebo group on any of the outcome measures: CIS-fatigue +1.1 (95% CI -4.4 to +6.5, p = 0.70), SIP-8 +59.1 (95% CI -201.7 to +319.8, p = 0.65), and IGFBP3/IGF1 ratio -0.5 (95% CI -2.8 to +1.7, p = 0.63). CONCLUSION: We found no differences in IGF1 status in CFS patients compared to healthy matched neighborhood controls. In addition, the results of this clinical trial do not demonstrate any benefit of Acclydine over placebo in the treatment of CFS.

Tietjen GE, Bushnell CD, Herial NA, Utley C, White L, Hafeez F.	Department of Neurology, University of Toledo Medical Center, Health Science Campus, 3120 Glendale Avenue, Toledo, OH 43614, USA.	Endometriosis is associated with prevalence of comorbid conditions in migraine.	Headache. 2007 Jul-Aug;47(7):1069-78.	OBJECTIVE: To examine the headache characteristics of women with migraine and endometriosis (EM), and differences in the prevalence of comorbid conditions between female migraineurs with EM, without EM and nonheadache controls. BACKGROUND: Migraine and EM are common conditions in women of reproductive age, and both are influenced by ovarian hormones. The comorbidity of migraine and EM is newly recognized, but reasons for the association are uncertain. METHODS: This is a cross-sectional study of female headache outpatients and healthy controls conducted at University of Toledo and Duke University in 2005 and 2006. After a headache specialist determined headache frequency and diagnosis (based on criteria of the second International Classification of Headache Disorders), patients completed a self-administered electronic survey with information on demographics, headache-related disability, menstrual disorders, premenstrual dysphoric disorder (PMDD), vascular event risk, and comorbid conditions, including irritable bowel syndrome (IBS), fibromyalgia (FM), chronic fatigue syndrome (CFS), interstitial cystitis (IC), depression, and anxiety. RESULTS: Study enrolled 171 women with migraine and 104 controls. EM was reported more commonly in migraineurs than in controls (22% vs 9.6%, P < .01). Frequency of chronic headache was higher in migraineurs with EM compared to without EM (P= .002) and median headache-related disability scores were also higher in the EM group (P= .025). Symptoms of PMDD were more common in migraineurs, but frequency did not differ by EM status. Migraineurs with EM reported more menorrhagia, dysmenorrhea, and infertility compared to the migraine cohort without EM and to controls. Depression, anxiety, IBS, FM, CFS, and IC were more common in migraine with EM group than in controls. Anxiety (OR = 2.2, 95% CI 1.0-4.7), IC (OR = 10.6, 95% CI 1.9-56.5), and CFS (OR = 3.6, 95% CI 1.1-11.5) were more common in migraine with EM group, than in the cohort with migraine without EM. CONCLUSION: Prevalence of EM is higher in women with migraine than in nonheadache controls. Migraineurs with EM have more frequent and disabling headaches, and are more likely to have other comorbid conditions affecting mood and pain, compared to migraineurs without EM.
Tietjen GE, Herial NA, Hardgrove J, Utley C, White L.	Department of Neurology, The University of Toledo College of Medicine, Toledo, OH 43614, USA.	Migraine comorbidity constellations.	Headache. 2007 Jun;47(6):857-65. Comment in: Headache. 2007 Jun;47(6):876-7.	OBJECTIVES: To identify distinct constellations of comorbid disorders occurring in migraineurs, and to examine differences in demographics, headache profiles, and psychosocial features between the comorbidity constellations. METHODS: This is a retrospective electronic chart review of consecutive new female outpatients diagnosed with migraine (n = 223) using International Classification of Headache Disorders (ICHD)-II criteria. Questionnaire collected information on comorbid diagnoses, current depression, somatic symptoms, psychosocial stressors, and antidepressant use, social and abuse history. Cluster analysis, based on nonheadache disorders, was performed and differences between the resulting groups were examined. RESULTS: We identified 3 groups. Group 1 (n = 55) was defined by hypertension, hyperlipidemia, diabetes mellitus, and hypothyroidism; Group 2 (n = 83) by depression, anxiety, and fibromyalgia; Group 3 (n = 85) by the absence of defining comorbidities. Group 1 had more males (22% vs 5% vs 12%, P < .05), was older (median years: 52 vs 36 vs 32, P < .01), and had later age of headache onset (median years: 22 vs 16 vs 18, P < .05). Group 2 had the greatest disability (P < .05), and the lowest quality of life (P < .001). Persons in Group 2 more commonly reported sexual abuse (OR = 2.7, 95% CI: 1.1 to 6.5), physical abuse (OR = 2.5, 95% CI: 1.2 to 5.1), and emotional abuse (OR = 4.3, 95% CI: 1.9 to 8.9). CONCLUSION: Within a headache clinic population, we identified 3 different migraine comorbidity constellations, with differing headache and psychosocial

				profiles, suggesting heterogeneity of genetic and environmental factors. This may have implications for diagnosis and disease management.
Tjørve E, Tjørve KM, Olsen JO, Senum R, Oftebro H.	Lillehammer University College, 2626 Lillehammer, Norway. even.tjorve@hil.no	On commonness and rarity of thyroid hormone resistance: a discussion based on mechanisms of reduced sensitivity in peripheral tissues.	Med Hypotheses. 2007;69(4):913-21. Epub 2007 Mar 26.	Reduced sensitivity to thyroid hormone (TH) in peripheral tissues can occur as defects in TH transport into the cell, intracellular TH metabolism, cytosolic mechanisms, TH entry into the nucleus, thyroxin receptors (TRs) and receptor binding, transcription and post-transcriptional mechanisms. Current literature reveals an extensive list of mutations, drugs, toxins, metabolites and autoimmune antibodies that may impair TH action in the cell, but such impairment may not be picked up by assays of TH and TSH in blood plasma. Substances may induce tissue specific resistance to thyroid hormone (RTH), e.g. by affecting numbers of different TR isoforms. Recent literature also indicates mechanisms by which different conditions, for example, chronic fatigue syndrome (CFS), chronic renal failure (CRF) and nonthyroidal illness, can be accompanied by acquired RTH caused by inhibition of TH metabolism, cell uptake, TR binding and transcription. This prompts us to reassess commonness and rarity of congenital vs. acquired RTH. We hypothesise that observed clinical symptoms of hypothyroidism in chemically euthyroid patients are typically caused by changes in hormonal systems, autoimmune antibodies, metabolites or other substances in the body, leading to reduced sensitivity to TH in peripheral tissues. These changes may be a by-product of other processes and a reversible biological response in the body, and may also result in chronic acquired RTH. Antibodies may prove to be the most common cause of chronic reduction in TH sensitivity. It is argued that the acquired form of RTH, caused by endogenous and exogenous sources, may indeed be more common than the congenital, as in insulin resistance. If acquired RTH exists, then it may not be picked up by blood assays of TH and TSH. An appropriate test to assess TH action in peripheral tissues is therefore greatly desired.
Tomoda A.	Department of Child Developmental Sociology, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University.	[School phobia and childhood chronic fatigue syndrome (CCFS)] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1121-33.	Chronic fatigue occurring in previously healthy children and adolescents is a vexing problem encountered by pediatric practitioners and the impact of fatigue in youngsters should not be underestimated. In its severe form, it is often associated with mood disorders. Findings in children and adolescent cases suggest that severe unexplained fatigue might precede the development of fatigue-related illness, such as childhood chronic fatigue syndrome (CCFS). This is a disabling condition characterized by severe disabling fatigue and a combination of symptoms, the prominent features being self-reported impairments in concentration and short-term memory, sleep disturbances and autonomic symptoms that cannot be explained by medical or psychiatric illness. We have encountered such patients with these complaints; their major symptoms include: general fatigue, fever, headache (not migraine), and memory disturbance. From our clinical experience, we have inferred that patients with CCFS might experience changes in brain function levels, which induce an autonomic imbalance and engender symptoms such as general fatigue, higher-order level cognitive dysfunction, and memory disturbance.
Torpy DJ, Ho JT.	Endocrine and Metabolic Unit, and the Hanson Institute, Royal Adelaide Hospital, Adelaide, South	Corticosteroid-binding globulin gene polymorphisms: clinical implications and	Clin Endocrinol (Oxf). 2007 Aug;67(2):161-7. Epub 2007 Jun 4.	Corticosteroid-binding globulin (CBG) binds cortisol with high affinity, facilitating transport of cortisol in blood, although tissue-specific CBG-cortisol interactions have long been postulated. There are three heritable, human CBG gene mutations that can reduce CBG-cortisol binding affinity and/or reduce circulating CBG levels. In some families, fatigue and low blood pressure have been associated with affinity altering or CBG level reducing mutations. The limited numbers of reports raise the possibility of ascertainment bias as many cases presented with features suggesting cortisol deficiency. The recent

	Australia, Australia. dtorpy@mail.rah.sa.gov.au	links to idiopathic chronic fatigue disorders.		description of a genetically CBG-deficient mouse listed fatigue, manifest as reduced activity levels, as part of the phenotype, which also included immune aberrations. Severe CBG mutations may produce fatigue, but one study suggests that these are a rare cause of idiopathic fatigue. A mechanism for the effect of CBG mutations on fatigue is not readily apparent because free cortisol levels are normal, although we speculate that CBG may have an effect on cortisol-brain transport.
Travers MK, Lawler J.	Faculty of Nursing & Midwifery, University of Sydney, Australia.	Self within a climate of contention: Experiences of chronic fatigue syndrome.	Soc Sci Med. 2008 Jan;66(2):315-26. Epub 2007 Oct 24.	Chronic fatigue syndrome (CFS) is a contested condition associated with scepticism and dispute. This qualitative project examines the illness experiences, and specifically the experiences of self, for people affected with CFS living in Australia. Using grounded theory methods, theory related to the process of self-renewal and adaptation associated with CFS is explicated. Narratives were derived from semi-structured interviews with 19 adults, including 3 people recovered from CFS. Analysis generated the narrative of the struggling self seeking renewal that defined the illness experience of CFS. The struggling self articulated the negative effects to self and personhood associated with CFS, defined as the violation of self, and the consequent efforts of participants to manage symptoms and decrease their violation by use of what was termed the Guardian Response and the Reconstructing Response. The Guardian Response provided protection and self-reclamation. The Reconstructing Response fostered self-renewal and meaning. The struggling self occurred within a climate of threats, and it was these threats which provided the catalyst for violation and the responses. Under different conditions the relative strengths of violation, guardianship or reconstruction fluctuated, and it was these fluctuations that presented the participants with the ongoing struggle of CFS.
Ullrich PM, Afari N, Jacobsen C, Goldberg J, Buchwald D.	Department of Rehabilitation Medicine, University of Washington, Seattle, WA 98104, USA. pullrich@u.washington.edu	Cold pressor pain sensitivity in monozygotic twins discordant for chronic fatigue syndrome.	Pain Med. 2007 Apr;8(3):216-22.	OBJECTIVE: Individuals with chronic fatigue syndrome (CFS) experience many pain symptoms. The present study examined whether pain and fatigue ratings and pain threshold and tolerance levels for cold pain differed between twins with CFS and their cotwins without CFS. DESIGN: Cotwin control design to assess cold pain sensitivity, pain, and fatigue in monozygotic twins discordant for CFS. PATIENTS AND SETTING: Fifteen monozygotic twin pairs discordant for CFS recruited from the volunteer Chronic Fatigue Twin Registry at the University of Washington. RESULTS: Although cold pain threshold and tolerance levels were slightly lower in twins with CFS than their cotwins without CFS, these differences failed to reach statistical significance. Subjective ratings of pain and fatigue at multiple time points during the experimental protocol among twins with CFS were significantly higher than ratings of pain ($P = 0.003$) and fatigue ($P < 0.001$) by their cotwins without CFS. CONCLUSIONS: These results, while preliminary, highlight the perceptual and cognitive components to the pain experience in CFS. Future studies should focus on examining the heritability of pain sensitivity and the underlying mechanisms involved in the perception of pain sensitivity in CFS.
van de Glind G, de Vries M, Rodenburg R, Hol F, Smeitink J, Morava E.	Department of Pediatrics, Nijmegen Centre for Mitochondrial Disorders, Radboud University Nijmegen Medical	Resting muscle pain as the first clinical symptom in children carrying the MTTK A8344G mutation.	Eur J Paediatr Neurol. 2007 Jul;11(4):243-6. Epub 2007 Feb 12.	The characteristic clinical presentation, especially the appearance of muscle symptoms, is quite unique in children carrying the mtA8344G mutation. The diagnosis of MERRF syndrome is seldom made in the pediatric age. Fatigue is a common finding in children of pubertal age. Fatigue in combination with recurrent resting muscle pain occurs frequently in the initial phase of various hereditary muscle disorders and in several autoimmune, endocrine and metabolic syndromes. In the absence of obvious biochemical/metabolic abnormalities and in the lack of neurological symptoms the complaints are frequently labelled as fibromyalgia or chronic fatigue syndrome. In patients with behavioural or psychiatric abnormalities one might even start to question the organic etiology of the

	Centre, 6500 HB Nijmegen, The Netherlands.			complaints. We describe a family carrying the classic MTTK mutation with a variable degree of heteroplasmy, presenting in childhood as isolated recurrent muscle pain as the first symptom of the disease.
van de Putte EM, Engelbert RH, Kuis W, Kimpen JL, Uiterwaal CS.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Center Utrecht; The Netherlands. e.vandeputte@umcutrecht.nl	Alexithymia in adolescents with chronic fatigue syndrome.	J Psychosom Res. 2007 Oct;63(4):377-80.	BACKGROUND: Alexithymia is postulated as an important factor in the development of medically unexplained physical symptoms. Chronic fatigue syndrome (CFS) is presently medically unexplained. The aim of this study was to investigate whether the prevalence of alexithymia was higher in adolescents with CFS compared to healthy adolescents. Comorbidity such as anxiety and depression were analyzed as possible confounding factors. Secondly, alexithymia was investigated as a prognostic factor for the recovery of CFS. METHODS: A cross-sectional study was performed among 40 adolescent outpatients diagnosed with CFS and 36 healthy controls. The 20-item Toronto Alexithymia Scale was used to assess all participants for alexithymia. Additionally, all participants completed a number of questionnaires regarding fatigue (Checklist Individual Strength), somatic complaints (Checklist Somatization Inventory), depression (Children's Depression Inventory), and trait anxiety (Spielberger State Trait Anxiety Questionnaire). A follow-up study was performed among the CFS adolescents 1 1/2 years after the initial assessment. RESULTS: CFS adolescents scored higher only on the subscale identifying feelings of the TAS-20 [mean difference after adjustment for depression and anxiety 2.8 (95% CI: 0.6; 4.9]. Twelve CFS adolescents (30%) fulfilled criteria for alexithymia. This subgroup was characterized by higher scores for depression and anxiety and equal scores for fatigue and somatic complaints. At follow-up, no differences in recovery were established between the alexithymic and nonalexithymic CFS adolescents. CONCLUSIONS: Alexithymia neither appears to be a unique correlate of CFS nor to be a prognostic factor for recovery of the CFS illness.
Van Den Eede F, Moorkens G, Hulstijn W, Van Houdenhove B, Cosyns P, Sabbe BG, Claes SJ.	Department of Molecular Genetics VIB8, Flanders Interuniversity Institute for Biotechnology, University of Antwerp, Antwerp, Belgium.	Combined dexamethasone/corticotropin-releasing factor test in chronic fatigue syndrome.	Psychol Med. 2007 Sep 6;:1-11 [Epub ahead of print]	BACKGROUND: Studies of hypothalamic-pituitary-adrenal (HPA) axis function in chronic fatigue syndrome (CFS) point to hypofunction, although there are negative reports. Suggested mechanisms include a reduced hypothalamic or supra-hypothalamic stimulus to the HPA axis and enhanced sensitivity to the negative feedback of glucocorticoids. The aim of the current study was to investigate HPA axis function in CFS with the dexamethasone/corticotropin-releasing factor (Dex/CRF) test, in analogy with research in affective disorders.MethodThirty-four well-characterized female CFS patients and 25 healthy control subjects participated in the low-dose Dex/CRF test. Current major depressive episode was an exclusion criterion. History of early-life stress (ELS) was assessed with the Structured Trauma Interview. RESULTS: Salivary cortisol responses after 0.5 mg Dex were lower in CFS patients than in controls (before 100 mug CRF, p=0.038; after 100 mug CRF, p=0.015). A secondary analysis revealed an influence of early-life stress and of oestrogen intake. After removal of the 10 participants who were taking an oral oestrogen, patients without a history of ELS showed lower cortisol responses than patients with ELS and controls (before CRF, p=0.005; after CRF, p=0.008). CONCLUSIONS: CFS is globally associated with reduced cortisol responses in the combined low-dose Dex/CRF test, but this effect is only clearly present in CFS patients without a history of ELS. This study provides further support for an enhanced glucocorticoid negative feedback and/or a reduced central HPA axis drive in CFS. Furthermore, it demonstrates that ELS is an important variable to consider in CFS research.
Van Den Eede F, Moorkens G, Van	Department of Psychiatry,	Hypothalamic-pituitary-adrenal	Neuropsychobiology.	There is evidence for a hypofunction of the hypothalamic-pituitary-adrenal (HPA) axis in a proportion of the patients with chronic fatigue syndrome (CFS), despite the negative studies and methodological

Houdenhove B, Cosyns P, Claes SJ.	University Hospital Antwerp, Edegem, Belgium. filip.van.den.eede@uza.be	axis function in chronic fatigue syndrome.	2007;55(2):112-20. Epub 2007 Jun 27.	difficulties. In this review, we focus on challenge studies and on the role of the HPA axis in the pathogenesis of CFS. Mild hypocortisolism, blunted adrenocorticotropin response to stressors and enhanced negative feedback sensitivity to glucocorticoids are the main findings. Several underlying mechanisms have been proposed. Currently, it is a matter of debate whether these disturbances have a primary role in the pathogenesis of CFS. However, even if the HPA axis dysfunctions are secondary to other factors, they are probably a relevant factor in symptom propagation in CFS.
van Geelen SM, Sinnema G, Hermans HJ, Kuis W.	Department of Psychology, Wilhelmina Children's Hospital, University Medical Center Utrecht, The Netherlands.	Personality and chronic fatigue syndrome: methodological and conceptual issues.	Clin Psychol Rev. 2007 Dec;27(8):885-903. Epub 2007 Jan 27.	Among clinical psychologists, consulting physicians, scientific researchers and society in general an image has emerged of patients with chronic fatigue syndrome (CFS) as perfectionist, conscientious, hardworking, somewhat neurotic and introverted individuals with high personal standards, a great desire to be socially accepted and with a history of continuously pushing themselves past their limits. The aim of this article is to (a) give a concise review of the main recent studies on personality and CFS, (b) address the major methodological problems in the study of personality in CFS and (c) discuss some of the conceptual assumptions that seem to limit the research on personality and CFS. The results of the reviewed studies range from no evidence of major differences between the personalities of patients with CFS and controls, to evidence of severe psychopathology and personality disorder in patients with CFS. Although personality seems to play a role in CFS, it is difficult to draw general conclusions on the relation between personality and CFS. It is argued that this is partially due to the diversity and heterogeneity in study methods, patient populations, control groups and CFS case definitions. Personality should be regarded as an important factor to be studied in CFS. However, additional studies are needed, not focusing exclusively on personality disorder, or personality considered on a general trait level. In recent developments in personality research, the continually evolving life narrative that makes sense of, and gives direction to, an individual's life is also regarded as an important aspect of personality. New insights into personality and CFS might be gained by systematically studying the self-narratives of patients with the syndrome.
Van Hoof E, De Becker P, Lapp C, Cluydts R, De Meirleir K.	Department of Human Physiology, Vrije Universiteit, Brussels, Belgium. Van.Hoof@vub.ac.be	Defining the occurrence and influence of alpha-delta sleep in chronic fatigue syndrome.	Am J Med Sci. 2007 Feb;333(2):78-84.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) present a disordered sleep pattern and frequently undergo polysomnography to exclude a primary sleep disorder. Such studies have shown reduced sleep efficiency, a reduction of deep sleep, prolonged sleep initiation, and alpha-wave intrusion during deep sleep. Deregulation of the 2-5A synthetase/RNase L antiviral pathway and a potential acquired channelopathy are also found in a subset of CFS patients and could lead to sleep disturbances. This article compiles a large sleep study database on CFS patients and correlates these data with a limited number of immune parameters as it has been thought that RNase L could be associated with these sleep disturbances. METHODS: Forty-eight patients who fulfilled 1994 Centers for Disease Control and Prevention criteria for CFS underwent extensive medical evaluation, routine laboratory testing, and a structured psychiatric interview. Subjects then completed a complaint checklist and a two-night polysomnographic investigation. RNase L analysis was performed by gel electrophoresis using a radiolabeled 2',5'-oligoadenylate trimer. Basic descriptive statistical parameters were calculated. RESULTS: Patients experienced a prolonged sleep latency, showed a low sleep efficiency index, and had a low percentage of slow wave sleep. The present alpha-delta intrusion correlated with anxiety; no correlations appeared, however, between alpha-delta sleep and immunologic parameters, including RNase L. CONCLUSIONS: The main findings are 1) validation of

				sleep latency problems and other sleep disturbances as already suggested by several authors; 2) alpha-delta intrusion seems associated with anxiety; and 3) elevated RNase L did not correlate with alpha-delta sleep.
Van Hootegem H.	henk.van.hootegem@skynet.be	Can homeopathy learn something from psychoanalysis?	Homeopathy. 2007 Apr;96(2):108-12.	This paper attempts to demonstrate how some insights from psychoanalysis can be useful in homeopathic treatment. I discuss three concepts: I illustrate these concepts with the case of a 23-year-old woman with chronic fatigue syndrome. (1) The working alliance: comparing medical alliance with a psychodynamic alliance. (2) The dream-function: serious somatic disorders can be the result of a blocked dream function, the restoration of the capacity to dream may lead to the disappearance of these disorders, homeopathy can help in this process. (3) The transgenerational influence: some traumatic, concealed events from the lives of ancestors can influence their descendants.
Van Houdenhove B, Verheyen L, Pardaens K, Luyten P, Van Wambeke P.	Faculty of Medicine. boudewijn.vanhoudenhove@uz.kuleuven.ac.be.	Rehabilitation of decreased motor performance in patients with chronic fatigue syndrome: should we treat low effort capacity or reduced effort tolerance?	Clin Rehabil. 2007 Dec;21(12):1121-42.	Aim: The aetiology, pathophysiology, diagnostic delineation and treatment of chronic fatigue syndrome (CFS) remain a matter of debate. Here some aspects of the debate are elucidated, with a particular focus on the patients' decreased motor performance.Hypothesis: The pathophysiological basis of decreased motor performance in CFS may, theoretically, involve three components: (1) a peripheral energetic deficit (impaired oxidative metabolism and/or physical deconditioning); (2) a central perceptual disturbance (higher effort sense or increased ;interoception'); and (3) a fundamental failure of the neurobiological stress system, leading to an abnormal ;sickness response'. It is proposed that the first two components may lead to low effort capacity, while the third component may lead to reduced effort tolerance. Although there is evidence for low effort capacity influencing symptoms and functional limitations in CFS, it is assumed that reduced effort tolerance might be the primary disturbance in CFS.Diagnostic implications: Distinguishing low effort capacity and reduced effort tolerance may contribute to a refinement of current diagnostic criteria of CFS and the identification of subgroups.Therapeutic implications: The above-mentioned distinction may make it possible to formulate a rationale for an effective implementation and adequate outcome evaluation of rehabilitation strategies in CFS.Research implications: This new heuristic framework may inform future research aimed at disentangling the complex determination of impaired motor performance in CFS, as well as studies aimed at customizing treatment to different subtypes of patients.
Van Ness Mark, Christopher R. Snell, Staci R. Stevens		HUDiminished Cardiopulmonary Capacity During Post-Exertional Malaise UH	Journal of Chronic Fatigue Syndrome 2007; 14(2): 77-85	Reduced functional capacity and post-exertional malaise following physical activity are hallmark symptoms of Chronic Fatigue Syndrome (CFS). That these symptoms are often delayed may explain the equivocal results for clinical cardiopulmonary exercise testing with CFS patients. The reproducibility of VO2max in healthy subjects is well documented. This may not be the case with CFS due to delayed recovery symptoms. Purpose: To compare results from repeated exercise tests as indicators of post-exertional malaise in CFS. Methods: Peak oxygen consumption (VO2 peak), percentage of predicted peak heart rate (HR%), and VO2 at anaerobic threshold (AT), were compared between six CFS patients and six control subjects for two maximal exercise tests separated by 24 hours. Results: Multivariate analysis showed no significant differences between control and CFS, respectively, for test 1: VO2 peak (28.4 ± 7.2 ml/ kg/min; 26.2 ± 4.9 ml/kg/min), AT (17.5 ± 4.8 ml/kg/min; 15.0 ± 4.9 ml/ kg/min) or HR% (87.0 ± 25.4%; 94.8 ± 8.8%). However, for test 2 the CFS patients achieved significantly lower values for both VO2peak (28.9 ± 8.0 ml/kg/min; 20.5 ± 1.8 ml/kg/min, p = 0.031) and AT (18.0 ± 5.2 ml/kg/min; 11.0 ± 3.4 ml/kg/min, p = 0.021). HR% was not

				significantly different (97.6 ± 27.2%; 87.8 ± 9.3%, p = 0.07). A follow-up classification analysis differentiated between CFS patients and controls with an overall accuracy of 92%. Conclusion: In the absence of a second exercise test, the lack of any significant differences for the first test would appear to suggest no functional impairment in CFS patients. However, the results from the second test indicate the presence of a CFS related post-exertional malaise. It might be concluded then that a single exercise test is insufficient to demonstrate functional impairment in CFS patients. A second test may be necessary to document the atypical recovery response and protracted malaise unique to CFS
Vanheule S, Vandenbergen J, Desmet M, Rosseel Y, Insleghers R.	Faculty of Psychology and Educational Sciences, Department of Psychoanalysis and Clinical Consulting, Ghent University, Belgium. stijn.Vanheule@UGent.be	Alexithymia and core conflictual relationship themes: a study in a chronically fatigued primary care population.	Int J Psychiatry Med. 2007;37(1):87-98.	OBJECTIVE: Clinical studies have indicated that concomitant to problems with affect regulation interpersonal problems can be observed in alexithymic patients. We test whether this is the case, and determine a parsimonious set of typical relationship themes. METHOD: Relationship themes were assessed by means of the Core Conflictual Relationship Theme (CCRT) method. This method examines transference patterns, and was applied to clinical interview data collected from a sample (n = 30) of chronically fatigued primary care patients. Alexithymia was assessed by means of a score on the 20-item Toronto Alexithymia Scale. The data were analyzed by means of the leaps and bounds regression algorithm for selecting optimal subsets of indicators, and by bootstrapping to determine 95% confidence intervals. RESULTS: Alexithymia can be meaningfully explained by typical relationship themes. A set of two wishes and one response of the self to the other that is most representative of alexithymia was mapped. The wishes demonstrate that the more alexithymic someone is, the less likely it is that this person wishes to be helped by others and the less likely it is that he/she interacts with others in order to feel good about him/herself. The selected response of the self indicates that it is typical of alexithymia that interactions with others do not result in good or happy feelings. CONCLUSION: Linking alexithymia to typical relationship themes is valid. Limitations of the study are indicated.
Vodvárka P.		[Chronic fatigue syndrome in oncology--editorial] [Article in Czech]	Vnitr Lek. 2007 Sep;53(9):930. Comment on: Vnitr Lek. 2007 Sep;53(9):979-85.	
Vollmer-Conna U, Cameron B, Hadzi-Pavlovic D, Singletary K, Davenport T, Vernon S, Reeves WC, Hickie I, Wakefield D, Lloyd AR; Dubbo Infective Outcomes Study Group.	School of Psychiatry, University of New South Wales, Sydney University, Sydney, Australia. ute@unsw.edu.au	Postinfective fatigue syndrome is not associated with altered cytokine production.	Clin Infect Dis. 2007 Sep 15;45(6):732-5. Epub 2007 Aug 6.	Peripheral blood specimens and clinical data were obtained over a 12-month period from subjects in the Dubbo Infection Outcomes Study to examine cytokine production in postinfective fatigue syndrome. Ex vivo production of 8 cytokines was examined in 22 case patients and in 42 control subjects who recovered promptly. No significant differences were found. Ongoing production of the cytokines examined does not play a role in postinfective fatigue syndrome.

Von Heuft G, Schneider G, Klaiberg A, Brähler E.	Klinik und Poliklinik für Psychosomatik und Psychotherapie, Universitätsklinikum Münster. heuftge@mednet.uni-muenster.de	[Bombed out--psychic and psychosomatic long term consequences of World War II for the cohort born until 1945 in the year 2004] [Article in German]	Z Psychosom Med Psychother. 2007;53(3):228-43.	OBJECTIVES: In a population-based study the hypothesis was pursued as to what extent psychiatric consequences of specific war experiences of the cohort born up to 1945, exemplified through the fate of those bombed out during World War II, can be proven. METHODS: A representative sample of 2552 participants (1206 men and 1346 women) with an age range from 14 to 92 years were questioned using the random-route-technique by an opinion research institute. The subsample of the cohort born until 1945 was comprised of 776 participants (30.4 % of the complete sample), of whom 375 were men (48.3 %) and 401 women. RESULTS: 161 participants (20.7 % of the cohort born until 1945) had been bombed out (66 men and 95 women). Comparing those who had been bombed out to those who had not been did not show any significant differences concerning their age, their place of residence (Eastern vs. Western Germany), marital status, education level or income level. From a gender perspective women had been bombed out more frequently ($p < .05$). Four predictors rendered in a multiple regression analysis significant contributions for the prediction of negative body functioning: age, having been bombed out, low income level and low education level (9 % of the variance could be explained). CONCLUSIONS: The results show the necessity for a new approach to the long-term consequences of severe strain and traumata concerning psychopathology of older people. For this purpose the concept of ambivalence must be further developed.
Wallman KE, Sacco P.	School of Human Movement & Exercise Science, The University of Western Australia, Crawley, Western Australia. kwallman@cyllene.uwa.edu.au	Sense of effort during a fatiguing exercise protocol in chronic fatigue syndrome.	Res Sports Med. 2007 Jan-Mar;15(1):47-59.	The purpose of this study was to determine whether chronic fatigue syndrome (CFS) subjects would produce greater force production in their matching limb during a fatiguing contralateral limb-matching task of the elbow flexors, compared with healthy, matched controls. Eight CFS subjects and 8 healthy, matched control subjects participated in a fatiguing task that consisted of intermittent submaximal contractions (30% maximal voluntary contraction) of the nondominant arm performed over a 45 min duration. Each minute, the subject attempted to match the force of the nondominant arm with their dominant arm (without visual feedback for the dominant arm). Results showed that average matching force and ratings of perceived effort values were significantly higher in the CFS group during the fatiguing task ($P = 0.04$, $P = 0.02$, respectively). This study demonstrated objectively that CFS subjects experienced a greater sense of effort in the elbow flexors while performing a fatiguing task.
Watanabe Y.	Department of Physiology, Osaka City University Graduate School of Medicine, Molecular Imaging Research Program, RIKEN.	[Molecular/neural mechanisms of fatigue] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):972-4.	
Watanabe Y.	Molecular Imaging Research Program, FRS, RIKEN, 6-7-3 Minatojima-minamimachi, Chuo-ku, Kobe,	[Molecular imaging for drug development] [Article in Japanese]	Brain Nerve. 2007 Mar;59(3):209-14.	In vivo molecular imaging has become a key technology for drug development and pathophysiological science. We are mostly utilizing PET (positron emission tomography) as a first-choice modality, because of its ultra-high sensitivity for molecules, adequate temporal and spatial resolution, and especially broad spectrum of target molecules. The present status for development of PET molecular probes, instrumentations including microPET, and the methods for quantitative analyses will be introduced with some examples. In vivo molecular imaging could bring the high-quality information

	Hyogo 650-0047, Japan.			about: (1) Molecular diagnosis for living patients with symptoms (2) Closer approach for etiology and differential diagnosis (3) Direct follow-up of key molecules as disease markers (4) Pharmacokinetics/Pharmacodynamics in primates/human (5) Dose finding information for individuals, corresponding to SNP (6) Direct evidence for accumulation in non-target organs: Related to adverse effects (7) Drug effects with surrogate markers (8) Early decision of dropout substances (drug candidates). In 2005, RIKEN and National Institute of Radiological Science were selected as the key centers for development of All-Japan research network to further promote mutual international and multi-disciplinary collaboration on in vivo molecular imaging. On this occasion, the concept and project themes will also be introduced.
Watanabe Y.		[Molecular/neural mechanisms of fatigue and the way to overcome fatigue[Article in Japanese]	Nippon Yakurigaku Zasshi. 2007 Feb;129(2):94-8.	
Weissmann G.		"Chronic Lyme" and other medically unexplained syndromes.	FASEB J. 2007 Feb;21(2):299-301.	
White P, Murphy M, Moss J, Armstrong G, Spencer P.		Chronic fatigue syndrome or myalgic encephalomyelitis.	BMJ. 2007 Sep 1;335(7617):411-2. Comment on: BMJ. 2007 Sep 1;335(7617):446-8.	
White PD, Sharpe MC, Chalder T, DeCesare JC, Walwyn R; PACE trial group.	Department of Psychological Medicine, Queen Mary School of Medicine and Dentistry, St Bartholomew's Hospital, London, UK. p.d.white@qmul.ac.uk <p.d.white@qmul.ac.uk>	Protocol for the PACE trial: a randomised controlled trial of adaptive pacing, cognitive behaviour therapy, and graded exercise, as supplements to standardised specialist medical care versus standardised specialist medical	BMC Neurol. 2007 Mar 8;7:6.	BACKGROUND: Chronic fatigue syndrome (CFS, also called myalgic encephalomyelitis /encephalopathy or ME) is a debilitating condition with no known cause or cure. Improvement may occur with medical care and additional therapies of pacing, cognitive behavioural therapy and graded exercise therapy. The latter two therapies have been found to be efficacious in small trials, but patient organisations surveys have reported adverse effects. Although pacing has been advocated by patient organisations, it lacks empirical support. Specialist medical care is commonly provided but its efficacy when given alone is not established. This trial compares the efficacy of the additional therapies when added to specialist medical care against specialist medical care alone. METHODS: 600 patients, who meet operationalised diagnostic criteria for CFS, will be recruited from secondary care into a randomised trial of four treatments, stratified by current co morbid depressive episode and different CFS/ME criteria. The four treatments are standardised specialist medical care either given alone, or with adaptive pacing therapy or cognitive behaviour therapy or graded exercise therapy. Supplementary therapies will involve fourteen sessions over 23 weeks and a booster session at 36 weeks. Outcome will be assessed at 12, 24, and 52 weeks after randomisation. Two primary outcomes of self-rated fatigue and physical function will assess differential effects of each treatment on these measures.

		care alone for patients with the chronic fatigue syndrome/myalgic encephalomyelitis or encephalopathy.		Secondary outcomes include adverse events and reactions, subjective measures of symptoms, mood, sleep and function and objective measures of physical activity, fitness, cost-effectiveness and cost-utility. The primary analysis will be based on intention to treat and will use logistic regression models to compare treatments. Secondary outcomes will be analysed by repeated measures analysis of variance with a linear mixed model. All analyses will allow for stratification factors. Mediators and moderators will be explored using multiple linear and logistic regression techniques with interactive terms, with the sample split into two to allow validation of the initial models. Economic analyses will incorporate sensitivity measures. DISCUSSION: The results of the trial will provide information about the benefits and adverse effects of these treatments, their cost-effectiveness and cost-utility, the process of clinical improvement and the predictors of efficacy.
White PD.	Wolfson Institute of Preventive Medicine, Barts and the London, Queen Mary's School of Medicine and Dentistry, University of London, London, UK. p.d.white@qmul.ac.uk	What causes prolonged fatigue after infectious mononucleosis: and does it tell us anything about chronic fatigue syndrome?	J Infect Dis. 2007 Jul 1;196(1):4-5. Epub 2007 May 24. Comment on: J Infect Dis. 2007 Jul 1;196(1):56-66.	
White PD.		How common is chronic fatigue syndrome; how long is a piece of string?	Popul Health Metr. 2007 Jun 8;5:6. Comment on: Popul Health Metr. 2007;5:5.	
Wikland B, Sandberg PO.		[Chronic fatigue and "burnout"--time for stringency of diagnosis] [Article in Swedish]	Lakartidningen. 2007 Aug 29-Sep 4;104(35):2445-6.	
Wyller VB, Due R, Saul JP, Amlie JP, Thaulow E.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Centre, and Department of Physiology, University of Oslo,	Usefulness of an abnormal cardiovascular response during low-grade head-up tilt-test for discriminating adolescents with	Am J Cardiol. 2007 Apr 1;99(7):997-1001. Epub 2007 Feb 16.	Hemodynamic dysfunction is documented in chronic fatigue syndrome (CFS). This study was conducted to investigate cardiovascular responses to orthostatic stress in adolescents with CFS, using a novel procedure for tilt-table testing. A total of 27 adolescents with CFS and 33 healthy control subjects with equal age and gender distribution underwent 15 minutes of 20 degrees head-up tilt testing. Heart rate, systolic blood pressure (BP), mean BP, diastolic BP, stroke index, total peripheral resistance index, end-diastolic volume index, and acceleration index were continuously and noninvasively recorded. At rest, patients with CFS had higher total peripheral resistance index values ($p<0.01$) and lower stroke index and end-diastolic volume index values ($p<0.05$) than controls. During

	Oslo, Norway. brwylle@online.no	chronic fatigue from healthy controls.		20 degrees head-up tilt testing, patients with CFS had greater increases in heart rate, diastolic BP (p<0.001), mean BP (p<0.01), and total peripheral resistance index (p<0.05) than controls and greater decreases in stroke index (p<0.05). Syncope or near syncope was not observed. In conclusion, this study found that adolescents with CFS have significant abnormalities of cardiovascular regulation in response to mild orthostatic stress, differentiating them from healthy controls.
Wyller VB, Godang K, Mørkrid L, Saul JP, Thaulow E, Walløe L.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Center, N-0027 Oslo, Norway. brwylle@online.no	Abnormal thermoregulatory responses in adolescents with chronic fatigue syndrome: relation to clinical symptoms.	Pediatrics. 2007 Jul;120(1):e129-37.	OBJECTIVES: Chronic fatigue syndrome is a common and disabling disease of unknown etiology. Accumulating evidence indicates dysfunction of the autonomic nervous system. To further explore the pathophysiology of chronic fatigue syndrome, we investigated thermoregulatory responses dependent on catecholaminergic effector systems in adolescent patients with chronic fatigue syndrome. PATIENTS AND METHODS: A consecutive sample of 15 patients with chronic fatigue syndrome aged 12 to 18 years and a volunteer sample of 57 healthy control subjects of equal gender and age distribution were included. Plasma catecholamines and metanephrines were measured before and after strong cooling of 1 hand. Acral skin blood flow, tympanic temperature, heart rate, and mean blood pressure were measured during moderate cooling of 1 hand. In addition, clinical symptoms indicative of thermoregulatory disturbances were recorded. RESULTS: Patients with chronic fatigue syndrome reported significantly more shivering, sweating, sudden change of skin color, and feeling unusually warm. At baseline, patients with chronic fatigue syndrome had higher levels of norepinephrine, heart rate, epinephrine, and tympanic temperature than control subjects. During cooling of 1 hand, acral skin blood flow was less reduced, vasoconstrictor events occurred at lower temperatures, and tympanic temperature decreased more in patients with chronic fatigue syndrome compared with control subjects. Catecholamines increased and metanephrines decreased similarly in the 2 groups. CONCLUSIONS: Adolescent patients with chronic fatigue syndrome have abnormal catecholaminergic-dependent thermoregulatory responses both at rest and during local skin cooling, supporting a hypothesis of sympathetic dysfunction and possibly explaining important clinical symptoms.
Wyller VB, Saul JP, Amlie JP, Thaulow E.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, and Department of Pysiology, University of Oslo, Oslo, Norway. brwylle@online.no	Sympathetic predominance of cardiovascular regulation during mild orthostatic stress in adolescents with chronic fatigue.	Clin Physiol Funct Imaging. 2007 Jul;27(4):231-8.	Haemodynamic abnormalities have been documented in the chronic fatigue syndrome (CFS), indicating functional disturbances of the autonomic nervous system responsible for cardiovascular control. This study was designed to explore the pathophysiology in adolescent CFS-patients by analysing RR-interval (RRI) variability and diastolic blood pressure (DBP) variability during mild orthostatic stress, using an algorithm which accounts for non-stationary biosignals. A total of 27 adolescents with CFS and 33 healthy control subjects having equal age- and sex distribution underwent 15 min of 20 degrees head-up tilt (HUT). The spectral power densities of RRI and DBP were computed in the low-frequency (LF) band (0.04-0.15 Hz) and the high-frequency (HF) band (0.15-0.4 Hz) using an adaptive autoregressive algorithm to obtain a time-varying spectrum. RMSSD, a time domain index of RRI variability, was also computed. At rest, all indices of variability were similar in the two groups. During tilt, CFS patients had a larger increase in the LF/HF ratio (P<or=0.001) and normalized LF power of RRI (P<or=0.01), and a larger decrease in normalized HF power (P<or=0.01) of RRI than controls. CFS patients also had trends towards a larger decrease in absolute HF power of RRI and a larger increase in normalized LF power of DBP. These findings suggest that adolescents with CFS have sympathetic predominance of cardiovascular regulation during very mild orthostatic stress. Possible underlying mechanisms are moderate hypovolemia, abnormalities of reflex control or

				physical de-conditioning.
Wyller VB, Saul JP, Walløe L, Thaulow E.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Center, 0027, Oslo, Norway.	Sympathetic cardiovascular control during orthostatic stress and isometric exercise in adolescent chronic fatigue syndrome.	Eur J Appl Physiol. 2007 Dec 8 [Epub ahead of print]	The chronic fatigue syndrome (CFS) has been shown to be associated with orthostatic intolerance and cardiovascular dysregulation. We investigated the cardiovascular responses to combined orthostatic stress and isometric exercise in adolescents with CFS. We included a consecutive sample of 15 adolescents 12-18 years old with CFS diagnosed according to a thorough and standardized set of investigations, and a volunteer sample of 56 healthy control subjects of equal sex and age distribution. Heart rate, systolic, mean and diastolic blood pressure, stroke index, and total peripheral resistance index were non-invasively recorded during lower body negative pressure (LBNP) combined with two consecutive periods of handgrip. In addition, we measured baseline plasma catecholamines, and recorded symptoms. At rest, CFS patients had higher heart rate, diastolic blood pressure, plasma norepinephrine ($P < 0.01$), mean blood pressure and plasma epinephrine ($P < 0.05$) than controls. During LBNP, CFS patients had a greater increase in heart rate, diastolic blood pressure, mean blood pressure ($P < 0.05$) and total peripheral resistance index (n.s.) than controls. During handgrip, CFS patients had a smaller increase in heart rate, diastolic blood pressure ($P < 0.05$), mean blood pressure and total peripheral resistance index (n.s.) than controls. Our results indicate that adolescents with CFS have increased sympathetic activity at rest with exaggerated cardiovascular response to orthostatic stress, but attenuated cardiovascular response when performing isometric exercise during orthostatic stress. This suggests that CFS might be causally related to sympathetic dysfunction.
Wyller VB, Thaulow E, Amlie JP.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, Norway. brwylle@online.no	Treatment of chronic fatigue and orthostatic intolerance with propranolol.	J Pediatr. 2007 Jun;150(6):654-5.	We describe the effect of propranolol in an adolescent with chronic fatigue syndrome and orthostatic intolerance. Our observations suggest that the head-up tilt-test and beta-blocker treatment might be considered in patients with chronic fatigue syndrome and that enhanced sympathetic nervous activity might be part of the underlying pathophysiology.
Wyller VB.	Department of Pediatrics, Rikshospitalet-Radiumhospitalet Medical Centre, Oslo, Norway. brwylle@online.no	The chronic fatigue syndrome--an update.	Acta Neurol Scand Suppl. 2007;187:7-14.	BACKGROUND: In this article, current scientific knowledge on the chronic fatigue syndrome (CFS) is reviewed. The US case definition of CFS (the CDC-definition) is most widespread in research and clinical practice. Estimates of prevalence vary from 0.2% to above 2%. The female-male ratio is approximately 3:1. CLINICAL FEATURES: Severe fatigue is the dominating complaint; it is worsened from exertions and not substantially relieved by rest. In addition, the patients might have a varying combination of accompanying symptoms. Clinical evaluation should be based upon standardized guidelines, including an assessment of functional impairments. PATHOPHYSIOLOGY: The pathophysiology should be interpreted within a biopsychosocial framework. Present knowledge suggests that certain genetic polymorphisms and personality traits might be regarded as predisposing factors, some infections and severe psychosocial stress constitute precipitating factors, whereas disturbances of immunity, skeletal muscle, cognitive abilities, endocrine control and cardiovascular homeostasis are possible perpetuating factors. TREATMENT: Cognitive behavioural therapy and graded exercise therapy are of proven value in randomized controlled trials. Several pharmaceutical measures have been explored and found to have no beneficial effect. Most patients might expect long-term improvement, but full recovery is rare; however, the prognosis is better among adolescents.

Yamadera W, Itoh H.	Department of Psychiatry, Jikei University School of Medicine.	[Overview of psychiatric therapy for chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1082-6.	Chronic fatigue syndrome (CFS) is recognized as a special condition based on abnormality of psycho-neuro-endocrine-immunological system, which is caused by several cytokines and autoantibodies. For CFS diagnosis, it is required to exclude psychiatric diseases which could cause chronic fatigue. On the other hand, recent studies proved the effectiveness cognitive behavioral therapy(CBT) for CFS. Distorted cognition relevant to CFS includes the characteristics such as over adaptation, perfectionism, avoidance and so on. In the CBT for CFS, it is important to quit seeking physical causes, to accept the pathological state as it is, to monitor daily activity and recognize the cognitive and behavioral patterns which might prolong fatigue, to maintain a constant activity level and to make planned increases in activity.
Yamaguti K.	Department of Physiology, Graduate School of Medicine, Osaka City University.	[Evaluation of fatigue by using acceleration plethysmography] [Article in Japanese	Nippon Rinsho. 2007 Jun;65(6):1034-42.	We evaluated the fatigue of patients with chronic fatigue syndrome by using acceleration plethysmography. The changes in the acceleration plethysmography were relatively dominant in the sympathetic nervous system from the viewpoint of the autonomic nervous system, and the fluctuation in the time-series data of the acceleration plethysmography was decreased from the viewpoint of chaos or complexity system. We found the relation between the level of fatigue and the changes in acceleration plethysmography. Therefore, the acceleration plethysmography might be useful for the evaluation of fatigue.
Yao F, Ji Q, Zhao Y, Feng JL.	College of Acupuncture and Massage, Shanghai University of TCM, Shanghai 201203, China. yaofei@tuina.com.cn	[Observation on therapeutic effect of point pressure combined with massage on chronic fatigue syndrome] [Article in Chinese]	Zhongguo Zhen Jiu. 2007 Nov;27(11):819-20.	OBJECTIVE: To search for an effective therapy for chronic fatigue syndrome (CFS). METHODS: Eighty-five cases of CFS were treated with massage and pressing of Back-shu points, combined with pressing acupoints on the head. The therapeutic effect was observed. RESULTS: After treatment of 3 courses, 26 cases were markedly effective, 52 cases were effective, and 7 cases were ineffective, with a total effective rate of 91.8% and a markedly effective rate of 30.6%. CONCLUSION: Pressing acupoints and massage can effectively improve clinical symptoms of the patient with chronic fatigue syndrome.
Yao R.	College of Traditional Chinese Medicine of Hong Kong University, China.	The thoughts and methods for clinical research on acupuncture treatment of chronic fatigue syndrome.	J Tradit Chin Med. 2007 Sep;27(3):163-5.	The general situation of chronic fatigue syndrome (CFS) and the criteria for its diagnosis are discussed, and it is put forward that making qi and blood of the zang-fu organs balanced is the key to acupuncture treatment of the disease. Such aspects as case selection, point selection and therapeutic assessment are also discussed in the present paper.
Yiu YM, Ng SM, Tsui YL, Chan YL.	School of Chinese Medicine, University of Hong Kong, China. yoyo@hku.hk	[A clinical trial of acupuncture for treating chronic fatigue syndrome in Hong Kong] [Article in Chinese]	Zhong Xi Yi Jie He Xue Bao. 2007 Nov;5(6):630-3.	OBJECTIVE: To evaluate the efficacy of acupuncture in treating chronic fatigue syndrome (CFS) in Hong Kong. METHODS: A single-blinded, randomized controlled trial design was adopted. Participants meeting inclusion criteria were randomly assigned to a treatment and a control group according to 1:1 ratio, resulting in an effective sample size of 99, with 50 and 49 patients in treatment and control group respectively. The same set of acupuncture points, which were selected according to traditional Chinese medicine theories, was applied in both groups, while conventional needle acupuncture was applied in treatment group and sham acupuncture (without skin penetration) was applied in control group. Schedule of treatment was the same in both groups, i.e. twice a week for 4 weeks. Key outcome measures were Chalder's Fatigue Scale, diagnostic criteria for CFS of the US's Centre for

				Disease Control and SF-12 health-related quality of life (HQOL) questionnaire. Adverse events, if any, were recorded. RESULTS: Improvements in physical and mental fatigue and HQOL in both groups were observed, but the improvements in treatment group were significantly bigger than in control group (P<0.01 or P<0.05). No adverse events occurred. CONCLUSION: Acupuncture is a safe, effective treatment for CFS.
Yokoyama T, Lisi TL, Moore SA, Sluka KA.	Physical Therapy and Rehabilitation Science Graduate Program, Department of Pathology, Pain Research Program, University of Iowa, Iowa City, Iowa 52242, USA.	Muscle fatigue increases the probability of developing hyperalgesia in mice.	J Pain. 2007 Sep;8(9):692-9. Epub 2007 Jul 12.	Chronic muscle pain is a major clinical problem that is often associated with fatigue. Conversely, chronic fatigue conditions are commonly associated with muscle pain. We tested the hypothesis that muscle fatigue enhances hyperalgesia associated with injection of acidic saline into muscle. We evaluated mechanical sensitivity of the paw (von Frey) in mice after 2 intramuscular injections of saline (20 microL; pH 4, pH 5, pH 6, pH 7.2) in a fatigue and a control group. To induce fatigue, mice were run for 2 h/day for 2 days prior to the first injection and 2 h/day for 2 days prior to the second injection. Muscle lactate, pCO(2), pO(2), creatinine kinase, phosphate, and histology were examined after the fatigue task and compared to a control group. Grip force was significantly decreased after 2 h of running indicating fatigue. The fatigue task did not induce muscle damage as there was no difference in muscle lactate, pCO(2), pO(2), creatinine kinase, phosphate, or histology. The fatigue task altered the dose-response relationship to intramuscular acidic saline injections. Mechanical hyperalgesia was observed in both fatigue and control groups after intramuscular injection of pH 4.0, but only the fatigue group after injection of pH 5. Neither the fatigue nor the control group developed hyperalgesia in response to intramuscular injection of pH 6 or pH 7.2. In conclusion, fatigue modified the susceptibility of mice to acid injection of pH 5.0 to result in mechanical hyperalgesia after 2 injections of pH 5.0. The fatigue task did not produce measurable changes in the muscle tissue suggesting a central mechanism mediating the enhancement of hyperalgesia. PERSPECTIVE: These data therefore show that muscle fatigue can enhance the likelihood that one develops pain to a mild insult. Clinically, this could relate to the development of pain from such conditions as repetitive strain injury, and may relate to the interrelationship between chronic pain and fatigue.
Yoshihara K, Kubo C.	Department of Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University.	[Overview of medical treatment and management of chronic fatigue syndrome] [Article in Japanese	Nippon Rinsho. 2007 Jun;65(6):1077-81.	A tailor-made management plan that includes various combinations of non-pharmacologic and pharmacologic therapy for patients with chronic fatigue syndrome (CFS) is important. We present an overview of four aspects of our medical treatment and management for CFS: introduction of our medical management system, summary of our management strategy, non-pharmacologic therapy, and pharmacologic therapy; according to foreign guidelines and the latest studies. The main non-pharmacologic therapies for CFS are rehabilitation and lifestyle guidance. Using a graded exercise therapy, we have constructed a broad management strategy for CFS. Herein we introduce our graded exercise therapy. If the symptoms continue despite careful management of the program by the physician, consultation with a psychiatrist or psychosomatic medicine specialist is necessary.
Yoshiuchi K, Cook DB, Ohashi K, Kumano H, Kuboki T, Yamamoto Y, Natelson BH.	Department of Neurosciences, University of Medicine and Dentistry of New Jersey - New Jersey	A real-time assessment of the effect of exercise in chronic fatigue syndrome.	Physiol Behav. 2007 Dec 5;92(5):963-8. Epub 2007 Jul 25.	Patients with chronic fatigue syndrome (CFS) report substantial symptom worsening after exercise. However, the time course over which this develops has not been explored. Therefore, the objective of this study was to investigate the influence of exercise on subjective symptoms and on cognitive function in CFS patients in natural settings using a computerized ecological momentary assessment method, which allowed us to track the effects of exercise within and across days. Subjects were 9 female patients with CFS and 9 healthy women. A watch-type computer was used to collect real-time

	Medical School, United States. kyoshiuc-tky@umin.ac.jp			data on physical and psychological symptoms and cognitive function for 1week before and 2weeks after a maximal exercise test. For each variable, we investigated temporal changes after exercise using multilevel modeling. Following exercise, physical symptoms did get worse but not until a five-day delay in CFS patients. Despite this, there was no difference in the temporal pattern of changes in psychological symptoms or in cognitive function after exercise between CFS patients and controls. In conclusion, physical symptoms worsened after several days delay in patients with CFS following exercise while psychological symptoms or cognitive function did not change after exercise.
Yoshiuchi K.	Department of Psychosomatic Medicine, The University of Tokyo.	[Psychological symptoms in chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2007 Jun;65(6):1023-7.	Patients with chronic fatigue syndrome (CFS) frequently complain of psychological symptoms including depression, anxiety, and neuropsychological impairment. In addition, patients with CFS have been reported to be more likely to have psychiatric diseases such as major depressive disorder, panic disorder, generalized anxiety disorder, and personality disorder. In the present review article, psychological symptoms and psychiatric comorbidity in CFS patients were introduced. In addition, differentiation between CFS and psychiatric disorders were discussed, because there have been few studies on comorbidity and differentiation between CFS and undifferentiated somatoform disorder although there has been heated debate about the existence of CFS itself.
Young JL, Redmond JC.	Rochester Center for Behavioral Medicine, Rochester Hills, MI. judithcredmond@aol.com	Fibromylagia, chronic fatigue, and adult attention deficit hyperactivity disorder in the adult: a case study.	Psychopharmacol Bull. 2007;40(1):118-26.	Adult attention deficit hyperactivity disorder (ADHD) may share common features with fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS). In an outpatient psychiatric clinic, a number of adult patients who presented primarily with symptoms of ADHD, predominately inattentive type, also reported unexplained fatigue, widespread musculoskeletal pain or a pre-existing diagnosis of CFS or FMS. As expected, ADHD pharmacotherapy usually attenuated the core ADHD symptoms of inattention, distractibility, hyperactivity, and impulsivity. Less expected was the observation that some patients also reported amelioration of pain and fatigue symptoms. The utility of ADHD medications in FMS and CFS states may be their innate arousal and enhanced filtering properties. This model supposes that FMS and CFS are central processing problems rather than peripheral disorders of muscles and joints.
Yunus MB.	Section of Rheumatology, The University of Illinois College of Medicine at Peoria, One Illini Drive, Peoria, IL 61605, USA.	Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes.	Semin Arthritis Rheum. 2007 Jun;36(6):339-56. Epub 2007 Mar 13.	OBJECTIVES: To discuss fibromyalgia syndrome (FMS) and overlapping conditions, eg, irritable bowel syndrome, headaches, and chronic fatigue syndrome, within the concept of central sensitivity syndromes (CSS). METHODS: A critical overview of the literature and incorporation of the author's own views. RESULTS: The concept of CSS seems viable. It is based on mutual associations among the CSS conditions as well as the evidence for central sensitization (CS) among several CSS members. However, such evidence is weak or not available in other members at this time, requiring further studies. The biology of CSS is based on neuroendocrine aberrations, including CS, that interact with psychosocial factors to cause a number of symptoms. CONCLUSIONS: CSS is an important new concept that embraces the biopsychosocial model of disease. Further critical studies are warranted to fully test this concept. However, it seems to have important significance for new directions for research and patient care involving physician and patient education. Each patient, irrespective of diagnosis, should be treated as an individual considering both the biological and psychosocial contributions to his or her symptoms and suffering.
Zuckerman AJ.	WHO Collaborating Centre for	Safety of hepatitis B vaccines.	Travel Med Infect Dis. 2004	Although concerns about vaccine safety have increased, true adverse reactions associated with hepatitis B vaccines are few, apart from minor symptoms at the site of injection and occasionally

	Reference and Research on Viral Diseases, Royal Free and University College Medical School, Rowland Hill Street, London NW3 2PF, UK.		May;2(2):81-4.	systemic reactions. There is no evidence of an association with hepatitis B vaccination and Sudden Infant Death Syndrome, Multiple Sclerosis and the Chronic Fatigue Syndrome. Hepatitis B vaccines are safe and essential for the prevention of this important and common infection.
Zwarts MJ, Bleijenberg G, van Engelen BG.	University Medical Centre Nijmegen, Institute of Neurology, 920 Department of Clinical Neurophysiology, PO Box 9101, 6500 HB Nijmegen, The Netherlands; Neuromuscular Centre Nijmegen, Department of Neurology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands.	Clinical neurophysiology of fatigue.	Clin Neurophysiol. 2008 Jan;119(1):2-10. Epub 2007 Nov 26.	Fatigue is a multidimensional concept covering both physiological and psychological aspects. Chronic fatigue is a typical symptom of diseases such as cancer, multiple sclerosis (MS), Parkinson's disease (PD) and cerebrovascular disorders but is also presented by people in whom no defined somatic disease has been established. If certain criteria are met, chronic fatigue syndrome can be diagnosed. The 4-item Abbreviated Fatigue Questionnaire allows the extent of the experienced fatigue to be assessed with a high degree of reliability and validity. Physiological fatigue has been well defined and originates in both the peripheral and central nervous system. The condition can be assessed by combining force and surface-EMG measurements (including frequency analyses and muscle-fibre conduction estimations), twitch interpolation, magnetic stimulation of the motor cortex and analysis of changes in the readiness potential. Fatigue is a well-known phenomenon in both central and peripheral neurological disorders. Examples of the former conditions are multiple sclerosis, Parkinson's disease and stroke. Although it seems to be a universal symptom of many brain disorders, the unique characteristics of the concomitant fatigue also point to a specific relationship with several of these syndromes. As regards neuromuscular disorders, fatigue has been reported in patients with post-polio syndrome, myasthenia gravis, Guillain-Barré syndrome, facioscapulohumeral dystrophy, myotonic dystrophy and hereditary motor and sensory neuropathy type-I. More than 60% of all neuromuscular patients suffer from severe fatigue, a prevalence resembling that of patients with MS. Except for several rare myopathies with specific metabolic derangements leading to exercise-induced muscle fatigue, most studies have not identified a prominent peripheral cause for the fatigue in this population. In contrast, the central activation of the diseased neuromuscular system is generally found to be suboptimal. The reliability of the psychological and clinical neurophysiological assessment techniques available today allows a multidisciplinary approach to fatigue in neurological patients, which may contribute to the elucidation of the pathophysiological mechanisms of chronic fatigue, with the ultimate goal to develop tailored treatments for fatigue in neurological patients. The present report discusses the different manifestations of fatigue and the available tools to assess peripheral and central fatigue.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Ablin JN, Shoenfeld Y, Buskila D.	Department of Rheumatology, Tel-Aviv Sourasky Medical Center and Sackler Faculty of Medicine, Tel-Aviv University, 6 Weizman St., 64239 Tel-Aviv, Israel.	Fibromyalgia, infection and vaccination: Two more parts in the etiological puzzle.	J Autoimmun. 2006 Nov;27(3):145-52. Epub 2006 Oct 30.	As the pathogenesis of fibromyalgia continues to raise debate, multiple putative triggers have been implicated. The current review summarizes the available data linking fibromyalgia to either infection or vaccination. Multiple infectious agents have been associated with the development of either full-blown fibromyalgia (e.g. hepatits C), or with symptom complexes extensively overlapping with that syndrome (e.g. chronic Lyme disease). The cases of Lyme disease, mycoplasma, hepatits C and HIV are detailed. Despite the described associations, no evidence is available demonstrating the utility of antibiotic or anti-viral treatment in the management of fibromyalgia. Possible mechanistic links between fibromyalgia and HIV are reviewed. Associations have been described between various vaccinations and symptom complexes including fibromyalgia and chronic fatigue syndrome. The case of Gulf War syndrome, a functional multisystem entity sharing many clinical characteristics with fibromyalgia is discussed, with emphasis on the possibility of association with administration of multiple vaccinations during deployment in the Persian Gulf and the interaction with stress and trauma. Based on this example a model is proposed, wherein vaccinations function as co-triggers for the development of functional disorders including fibromyalgia, in conjunction with additional contributing factors.
Arnold Llamosas PA, Arrizabalaga Clemente P, Bonet Agusti M, de la Fuente Brull X.	Inmunologia y Medicina Interna, Servicio de Reumatologia, Centro Internacional Medicina Avanzada (CIMA), Servei Acreditat Cat Salut, Barcelona, Spain.	[Multiple chemical sensitivity in sick-building syndrome] [Article in Spanish]	Med Clin (Barc). 2006 May 27;126(20):774-8.	The sick building syndrome includes irritation of the eyes and the respiratory tract neurotoxicity affectation and skin problems, which can occur in individuals under improperly ventilated buildings. Poor air quality, as shown in CO2 atmospheric levels of more than 1,000 ppm, results in a pathological exposure to biological and chemical products. We present a work-related case of multiple chemical hypersensitivity from a dialysis unit that had no air renewal. This person, who was summitted to continuous exposure despite having taken corrective measures in the ventilation, developed chronic fatigue syndrome. An acoustic voice observation alerted of the case which led to the analysis of the environmental conditions which confirmed the relationship between multiple chemical hypersensitivity and chronic fatigue syndrome. This case stresses the neglected fact that all health service centres pose a high risk of chemical exposure and that there exists a lack of rigoroursness in putting in practice scientific medical knowledge.
Aslakson E, Vollmer-Conna U, White PD.	Centers for Disease Control and Prevention, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Atlanta, GA 30333, USA. EAslakson@cdc.gov	The validity of an empirical delineation of heterogeneity in chronic unexplained fatigue.	Pharmacogenomics. 2006 Apr;7(3):365-73.	OBJECTIVES: To validate a latent class structure derived empirically from a clinical data set obtained from persons with chronic medically unexplained fatigue. METHODS: The strategies utilized in this validation study included: recalculating latent class analysis (LCA) results varying random seeds and the number of initial random starting sets; recalculating LCA results by substituting alternate variables to demonstrate a robust solution; determining the statistical significance of between-class differences on disability, fatigue and demographic measures omitted from the data set used for LCA; cross-classifying class membership using established Centers for Disease Control and Prevention (CDC) research criteria for chronic fatigue syndrome (CFS) to compare the relative proportions of subjects designated CFS, chronic fatigue (not CFS) or healthy controls captured by the latent classes. RESULTS: Recalculation of results and substitution of variables for low-loading variables demonstrated a robust LCA result. Highly significant between-class differences were confirmed between Class 2 (well) and those interpreted as ill/fatigued. Analysis of between-class differences for the fatigue groups revealed

				significant differences for all disability and fatigue variables, but with equivalent levels of reported activity and reduction in motivation. Cross-classification against established CDC criteria demonstrated that 89% of subjects constituting Class 2 (well) were indeed nonfatigued controls. A general tendency for grouping CFS cases in the multiple symptomatic classes was noted. CONCLUSION: This study established reasonably good validity for an empirically-derived latent class solution reflecting considerable heterogeneity among subjects with medically unexplained chronic fatigue. This work strengthens the growing understanding of CFS as a heterogeneous entity comprised of several conditions with different underlying pathophysiological mechanisms.
Authier FJ, Gherardi RK.	Centre de Reference pour Maladies Neuromusculaires Garches-Necker-Mondor-Hendaye (GNMH), Hopital Henri-Mondor, AP-HP, Creteil. francois-jerome.authier@hmn.aphp.fr	[Muscular complications of human immunodeficiency virus (HIV) infection in the era of effective anti-retroviral therapy] [Article in French]	Rev Neurol (Paris). 2006 Jan;162(1):71-81.	Introduction of highly active antiretroviral therapy (HAART) has dramatically modified the natural history of HIV disease, but lengthening the survival of HIV-infected individuals has been associated with an increasing prevalence of iatrogenic conditions. Muscular complications of HIV infection are classified as follows: (1) HIV-associated myopathies and related conditions including polymyositis, inclusion-body myositis, nemaline myopathy, diffuse infiltrative lymphocytosis syndrome (DILS), HIV-wasting syndrome, vasculitis, myasthenic syndromes, and chronic fatigue; (2) iatrogenic conditions including mitochondrial myopathies, HIV-associated lipodystrophy syndrome, and immune restoration syndrome; (3) opportunistic infections and tumor infiltrations of skeletal muscle; and (4) rhabdomyolysis. These features are described in the present review.
Axelrod FB, Chelimsky GG, Weese-Mayer DE.	Dysautonomia Treatment and Evaluation Center, Department of Pediatrics and Neurology, New York University School of Medicine, 530 First Ave, Suite 9Q, New York, New York 10016, USA. felicia.axelrod@med.nyu.edu	Pediatric autonomic disorders.	Pediatrics. 2006 Jul;118(1):309-21.	The scope of pediatric autonomic disorders is not well recognized. The goal of this review is to increase awareness of the expanding spectrum of pediatric autonomic disorders by providing an overview of the autonomic nervous system, including the roles of its various components and its pervasive influence, as well as its intimate relationship with sensory function. To illustrate further the breadth and complexities of autonomic dysfunction, some pediatric disorders are described, concentrating on those that present at birth or appear in early childhood.
Bailes S, Libman E, Baltzan M, Amsel R, Schondorf R, Fichten CS.	SMBD-Jewish General Hospital, Montreal, Canada. sally.bailes@mail.mcgill.ca	Brief and distinct empirical sleepiness and fatigue scales.	J Psychosom Res. 2006 Jun;60(6):605-13.	OBJECTIVE: Sleepiness and fatigue are conceptually distinct but pervasively confounded in research, measurement instruments, clinical settings, and everyday spoken language. The purpose of the present study was to construct two scales that represent unconfounded measures of sleepiness and fatigue, using widely used questionnaires. METHOD: Four questionnaires purporting to measure sleepiness [Stanford Sleepiness Scale (SSS); Epworth Sleepiness Scale (ESS)] or fatigue [Fatigue Severity Scale (FSS); Chalder Fatigue Scale (CFS)] were administered, as well as a battery measuring

				sleep, psychological, and health functioning variables, to three samples: 19 individuals with chronic fatigue syndrome, 14 with narcolepsy, and 11 normal control subjects. RESULTS: Analyses revealed two distinct sets of items (six sleepiness and three fatigue items) that were combined into two scales. These newly formed scales are only minimally correlated and represent separate constructs that have reasonably distinctive patterns of association. Findings were replicated and validated in a sample of 128 older individuals complaining of daytime sleepiness and/or fatigue. CONCLUSIONS: We conclude that (a) it is possible to derive empirically distinct sleepiness and fatigue scales from existing, commonly used self-report instruments, (b) the Empirical Sleepiness Scale is limited to the experience of daytime sleep tendency, while (c) the Empirical Fatigue Scale is associated more broadly with insomnia, psychological maladjustment, and poorer perceived health function. The important clinical implication of the new Empirical Sleepiness and Fatigue Scales is in the ability to identify "sleepiness which is not fatigue," a construct closely related to primary sleep disorders, such as sleep apnea/hypopnea syndrome, for which there is both available and effective treatment.
Barat M, Dehail P, de Seze M.	Unite de Reeducation Neurologique, Universite Victor-Segalen Bordeaux-II et Federation des Neurosciences Cliniques, CHU de Bordeaux, 146, rue Leo-Saignat, 33076 Bordeaux cedex, France. michel.barat@chu-bordeaux.fr	Fatigue after spinal cord injury. [Article in English, French]	Ann Readapt Med Phys. 2006 Jul;49(6):277-82, 365-9. Epub 2006 Apr 25.	OBJECTIVES: To identify variables increasing fatigue following spinal cord injury (SCI) and their functional consequences. METHODS: A search of the Medline and Reedoc databases with the keywords SCI, fatigue, intrinsic muscular fatigue, chronic fatigue, aging, training, electrostimulation, quality of life and the same words in French. RESULTS: Two kinds of fatigue are identified following SCI. Intrinsic fatigue in muscles totally or partially paralysed at the level of or below the spinal cord lesion; this peripheral fatigue is due to denervation, total or partial loss of motoneurons, or histological and metabolical changes in muscle; it is well-defined by electrophysiological technology; spasticity and spasms have little influence on its development; it is reversible in part with long term electrostimulation, but at this time, electroneuroprosthetic techniques do not reduce the excessive energetic cost to stand up and walk. Chronic fatigue appears in the long term following SCI; it is linked with aging, physiological, and psychological deconditioning; some data point to chronic fatigue after SCI similar to post-polio syndrome and chronic fatigue syndrome, which may explain the central nature of the fatigue; training programs could be useful in delaying this chronic fatigue and as a consequence, increasing the latent quality of life. CONCLUSION: Muscular intrinsic fatigue after SCI is always of a peripherical nature in muscles partially or totally paralysed. Chronic fatigue during aging greatly decreases quality of life. Both intrinsic and chronic fatigue could be anticipated by electrostimulation technique on the one hand and long term training on the other.
Barbado Hernandez FJ, Gomez Cerezo J, Lopez Rodriguez M, Vazquez Rodriguez JJ.	Servicio de Medicina Interna, Hospital Universitario La Paz, Universidad Autonoma, Madrid.	[The chronic fatigue syndrome and its diagnosis in internal medicine] [Article in Spanish]	An Med Interna. 2006 May;23(5):238-44.	
Baschetti R.		Chronic fatigue. Comment on: CMAJ. 2006 Mar	CMAJ. 2006 Aug 15;175(4):386; author reply 387-8.	

		14;174(6):765-7.		
Bates MN.	Division of Environmental Health Sciences, School of Public Health, 140 Warren Hall, University of California, Berkeley, CA 94720-7360, USA. m_bates@berkeley.edu	Mercury amalgam dental fillings: an epidemiologic assessment.	Int J Hyg Environ Health. 2006 Jul;209(4):309-16. Epub 2006 Jan 30.	Dental amalgam fillings containing approximately 50% mercury have been used for almost 200 years and have been controversial for almost the same time. Allegations of effects caused by amalgams have involved many diseases. Recent evidence that small amounts of mercury are continuously released from amalgam fillings has fuelled the controversy. This is a comprehensive review of the epidemiologic evidence for the safety of dental amalgam fillings, with an emphasis on methodological issues and identifying gaps in the literature. Studies show little evidence of effects on general chronic disease incidence or mortality. Limited evidence exists for an association with multiple sclerosis, but few studies on either Alzheimer's or Parkinson's diseases. The preponderance of evidence suggests no renal effects and that ill-defined symptom complexes, including chronic fatigue syndrome, are not caused by amalgams. There is little direct evidence that can be used to assess reproductive hazards. Overall, few relevant epidemiologic studies are available. Most prior assessments of possible amalgam health effects have been based on comparisons of dental mercury exposures with occupational exposures causing harm. However, the amalgam-exposed population contains a broader, possibly more susceptible, spectrum of people. Common limitations of population-based studies of dental amalgam effects include inadequate longitudinal exposure assessment and negative confounding by better access to dental care in higher socioeconomic groups. Better designed studies are needed, particularly for investigation of neurodegenerative diseases and effects on infants and children.
Bell SD, Van Hoof E.		Guidelines for the Diagnosis of Pediatric Chronic Fatigue Syndrome: Things Parents Need to Know This	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 79-88	In this special issue of the Journal of Chronic Fatigue Syndrome, chronic fatigue syndrome (CFS) in children and adolescents is specifically addressed. It is a topic long overdue. It is my sincere hope that the criteria presented here will begin a process of rigorous clinical testing and refinement so that pediatricians and other medical providers will come to have a reliable and accepted way of making the diagnosis of ME/CFS in a person under 18 years of age. This short review is meant for parents and other caregivers as a brief summary of the guidelines that may be of value. The primary role of these guidelines is to present a strict and rigorous definition that can be tried and tested. This summary is to make the process of diagnosis somewhat easier for parents and caregivers alike until the testing process is completed. Therefore, for more detailed symptom description and exclusionary illness description, I would refer the reader to the primary article. Professional caregivers and clinicians may offer this article available to inform parents with a child or/ adolescent suffering from CFS.
Blockmans D, Persoons P, Van Houdenhove B, Bobbaers H.	Department of Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium. daniel.blockmans@uz.kuleuven.ac.be	Does methylphenidate reduce the symptoms of chronic fatigue syndrome?	Am J Med. 2006 Feb;119(2):167.e23-30.	PURPOSE: Chronic fatigue syndrome is a clinical entity consisting of prolonged and debilitating fatigue in which concentration disturbances are very frequent. Until now, no medical treatment has shown any efficacy. The objectives of this study were to investigate the short-term effects of methylphenidate, an amphetamine derivative, on fatigue, concentration disturbances, and quality of life. SUBJECTS AND METHODS: A double-blind randomized placebo-controlled crossover study was conducted in 60 patients who fulfilled the 1994 Centers for Disease Control criteria for chronic fatigue syndrome and had concentration difficulties. Patients were enrolled between March 2003 and March 2004 at the outpatient department of a university hospital referral center for chronic fatigue syndrome patients. Random assignment to 4 weeks treatment with methylphenidate 2 x 10 mg/day, followed by 4 weeks of placebo treatment, or 4 weeks of placebo treatment, followed by methylphenidate treatment. Fatigue and concentration were measured with a Checklist Individual

				Strength (CIS) and a Visual Analogue Scale (VAS). RESULTS: Fatigue scores fell significantly during methylphenidate intake in comparison with baseline (mean difference: -0.7, P = .010 for VAS; mean difference: -11.8, P <.0001 for CIS) and in comparison with placebo (mean difference: -1.0, P = .001 for VAS; mean difference: -9.7, P <.0001 for CIS). Concentration disturbances, measured with a VAS improved significantly under methylphenidate treatment compared with baseline (mean difference: -1.3, P <.0001) and compared with placebo (mean difference: -1.1, P <.0001). A clinical significant effect (> or =33% improvement or CIS < or =76) on fatigue was achieved in 17% of patients, who were considered responders; on concentration in 22% of patients. CONCLUSIONS: Methylphenidate at a dose of 2 x 10 mg/day is significantly better than placebo in relieving fatigue and concentration disturbances in a minority of chronic fatigue syndrome patients. Further studies are needed to investigate the long-term effects of this treatment.
Bond PA, Dinan TG.		Antibodies to Herpes Simplex Types 1 and 2 in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2006;13(1): 35-40	Background. It has been suggested that Herpes simplex virus (HSV) could play a role in the aetiology of chronic fatigue syndrome (CFS). An immune system that has been compromised, could account for HSV reactivating or infecting for the first time, and also being insufficiently under control in the body. Another consequence of inadequate control could be that several strains of HSV could simultaneously infect the body. Objectives. To look for the presence of antibodies to HSV-1 and HSV-2 in patients with CSF and in controls. The presence of antibodies to both types of HSV could reflect infection by multiple strains of HSV. Methods. Antibodies to HSV-1 and HSV-2 were measured in sera from 27 CSF patients and 26 ageand sex-matched controls. CFS was diagnosed using the CDC criteria. Results. More CFS patients had antibodies to HSV-1, HSV-2 and both types simultaneously, than did the controls (all p < .019). Conclusions. More CFS patients have antibodies to both HSV-1 and HSV-2 than do controls. The possibility that multiple strains could
Broderick G, Craddock RC, Whistler T, Taylor R, Klimas N, Unger ER.	University of Alberta, Institute for Biomolecular Design, Edmonton, Alberta, T6G 2H7, Canada. gordon.broderick @ualberta.ca	Identifying illness parameters in fatiguing syndromes using classical projection methods.	Pharmacogenomics. 2006 Apr;7(3):407-19.	OBJECTIVES: To examine the potential of multivariate projection methods in identifying common patterns of change in clinical and gene expression data that capture the illness state of subjects with unexplained fatigue and nonfatigued control participants. METHODS: Data for 111 female subjects was examined. A total of 59 indicators, including multidimensional fatigue inventory (MFI), medical outcome Short Form 36 (SF-36), Centers for Disease Control and Prevention (CDC) symptom inventory and cognitive response described illness. Partial least squares (PLS) was used to construct two feature spaces: one describing the symptom space from gene expression in peripheral blood mononuclear cells (PBMC) and one based on 117 clinical variables. Multiplicative scatter correction followed by quantile normalization was applied for trend removal and range adjustment of microarray data. Microarray quality was assessed using mean Pearson correlation between samples. Benjamini-Hochberg multiple testing criteria served to identify significantly expressed probes. RESULTS: A single common trend in 59 symptom constructs isolates of nonfatigued subjects from the overall group. This segregation is supported by two co-regulation patterns representing 10% of the overall microarray variation. Of the 39 principal contributors, the 17 probes annotated related to basic cellular processes involved in cell signaling, ion transport and immune system function. The single most influential gene was sestrin 1 (SESN1), supporting recent evidence of oxidative stress involvement in chronic fatigue syndrome (CFS). Dominant variables in the clinical feature space described heart rate variability (HRV) during sleep. Potassium and free thyroxine (T4) also figure prominently. CONCLUSION: Combining

				multiple symptom, gene or clinical variables into composite features provides better discrimination of the illness state than even the most influential variable used alone. Although the exact mechanism is unclear, results suggest a common link between oxidative stress, immune system dysfunction and potassium imbalance in CFS patients leading to impaired sympatho-vagal balance strongly reflected in abnormal HRV.
Brooks JK, Francis LA.	Department of Diagnostic Sciences and Pathology, Baltimore College of Dental Surgery, Dental School, University of Maryland, Baltimore, MD 21201, USA. Oralpath5@aol.com	Postural orthostatic tachycardia syndrome: Dental treatment considerations.	J Am Dent Assoc. 2006 Apr;137(4):488-93.	BACKGROUND: Postural orthostatic tachycardia syndrome (POTS) is a chronic, relatively common autonomic disorder typically affecting younger females. It is distinguished by a dramatic increase in heart rate on the assumption of an upright posture from the supine position. METHODS: The authors provide an overview of the demographics, clinical assessment, diagnostic features, differential diagnoses, pathogeneses and medical treatment of patients with POTS, with an emphasis on the clinical treatment of the dental patient affected by the syndrome. CONCLUSION: Patients frequently exhibit symptoms of lightheadedness, fatigue, palpitations and syncope. Patients with POTS may have Ehlers-Danlos syndrome, mitral valve prolapse, chronic fatigue syndrome or, rarely, the Brugada syndrome. Despite widespread dissemination of information regarding POTS in the medical literature, scant information on it has appeared in dental publications. PRACTICE IMPLICATIONS: Dentists need to be familiar with the clinical features of POTS and be prepared to treat patients at risk of developing syncope.
Bruusgaard D.	Institutt for allmenn- og samfunnsmedisin, Universitetet i Oslo, Postboks 1130 Blindern O318, Oslo, Norway. HUdag.bruusgaard@medisin.uio.noUH	[With the back to the future] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2006 Oct 19;126(20):2686.	
Capuron L, Welberg L, Heim C, Wagner D, Solomon L, Papanicolaou DA, Craddock RC, Miller AH, Reeves WC.	Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, GA, USA.	Cognitive dysfunction relates to subjective report of mental fatigue in patients with chronic fatigue syndrome.	Neuropsychopharmacology. 2006 Aug;31(8):1777-84. Epub 2006 Jan 4.	Patients with chronic fatigue syndrome (CFS) frequently complain of cognitive dysfunction. However, evidence of cognitive impairment in CFS patients has been found in some, but not other, studies. This heterogeneity in findings may stem from the relative presence of mental fatigue in the patient populations examined. The present study assessed this possibility in a population-based sample of CFS patients. In all, 43 patients with CFS defined by the criteria of the 1994 research case definition using measurements recommended by the 2003 International CFS Study Group, and 53 age-, sex-, and race/ethnicity-matched nonfatigued subjects were included in the study. Mental fatigue was assessed using the mental fatigue subscale of the multidimensional fatigue inventory. Cognitive function was evaluated using an automated battery of computerized tests (Cambridge neuropsychological test automated battery (CANTAB)) that assessed psychomotor function, planning and problem-solving abilities, and memory and attentional performance. CFS patients with significant complaints of mental

				fatigue (score of mental fatigue 2 standard deviations above the mean of nonfatigued subjects) exhibited significant impairment in the spatial working memory and sustained attention (rapid visual information processing) tasks when compared to CFS patients with low complaints of mental fatigue and nonfatigued subjects. In CFS patients with significant mental fatigue, sustained attention performance was impaired only in the final stages of the test, indicating greater cognitive fatigability in these patients. CFS patients with low mental fatigue displayed performance comparable to nonfatigued subjects on all tests of the CANTAB battery. These findings show strong concordance between subjective complaints of mental fatigue and objective measurement of cognitive impairment in CFS patients and suggest that mental fatigue is an important component of CFS-related cognitive dysfunction.
Carlo-Stella N, Badulli C, De Silvestri A, Bazzichi L, Martinetti M, Lorusso L, Bombardieri S, Salvaneschi L, Cuccia M.	Immunogenetics Laboratory, Dept. of Genetics and Microbiology, University of Pavia, Italy. nickics@ipvgen.unipv.it	A first study of cytokine genomic polymorphisms in CFS: Positive association of TNF-857 and IFNgamma 874 rare alleles.	Clin Exp Rheumatol. 2006 Mar-Apr;24(2):179-82.	OBJECTIVE: In the past two years we have developed a biological bank of genomic DNA, cDNA, serum and red blood cells of Italian patients with certified CFS from the two Italian referral centers for the syndrome. Recent studies have shown an imbalance in cytokine production in disease states similar to Chronic Fatigue Syndrome (CFS), such as sickness behavior, both in animals and in humans. However we notice that serum cytokine concentrations are often inconstant and degrade rapidly. With this in mind, we investigated cytokine gene polymorphisms in 80 Italian patients with CFS in order to ascertain whether in this group of patients it is possible to describe a genetic predisposition to an inflammatory response. METHODS: We analyzed the promoter polymorphisms of IL-10, IL-6 and the IFNgamma 874 T/A polymorphism in intron 1 with a PCR-SSP method (Cytogen One Lambda Inc. Canoga Park, CA, U.S.A) in 54 patients and TNF-308 G/A and -857 C/T promoter polymorphisms with a PCR-RFLP method (in 54 and 80 patients respectively). RESULTS: There is a highly significant increase of TNF -857 TT and CT genotypes (p = 0.002) among patients with respect to controls and a significant decrease of IFN gamma low producers (A/A) (p = 0.04) among patients with respect to controls. CONCLUSIONS: We hypothesize that CFS patients can have a genetic predisposition to an immunomodulatory response of an inflammatory nature probably secondary to one or more environmental insults of unknown nature.
Carmel L, Efroni S, White PD, Aslakson E, Vollmer-Conna U, Rajeevan MS.	National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, Maryland, USA.	Gene expression profile of empirically delineated classes of unexplained chronic fatigue.	Pharmacogenomics. 2006 Apr;7(3):375-86.	OBJECTIVES: To identify the underlying gene expression profiles of unexplained chronic fatigue subjects classified into five or six class solutions by principal component (PCA) and latent class analyses (LCA). METHODS: Microarray expression data were available for 15,315 genes and 111 female subjects enrolled from a population-based study on chronic fatigue syndrome. Algorithms were developed to assign gene scores and threshold values that signified the contribution of each gene to discriminate the multiclasses in each LCA solution. Unsupervised dimensionality reduction was first used to remove noise or otherwise uninformative gene combinations, followed by supervised dimensionality reduction to isolate gene combinations that best separate the classes. RESULTS: The authors' gene score and threshold algorithms identified 32 and 26 genes capable of discriminating the five and six multiclass solutions, respectively. Pair-wise comparisons suggested that some genes (zinc finger protein 350 [ZNF350], solute carrier family 1, member 6 [SLC1A6], F-box protein 7 [FBX07] and vacuole 14 protein homolog [VAC14]) distinguished most classes of fatigued subjects from healthy subjects, whereas others (patched homolog 2 [PTCH2] and T-cell leukemia/lymphoma [TCL1A]) differentiated specific fatigue classes. CONCLUSION: A computational approach was developed for

				general use to identify discriminatory genes in any multiclass problem. Using this approach, differences in gene expression were found to discriminate some classes of unexplained chronic fatigue, particularly one termed interoception.
Caseras X, Mataix-Cols D, Giampietro V, Rimes KA, Brammer M, Zelaya F, Chalder T, Godfrey EL.	Unitat de Psicologia Medica, Institut de Neurociencies, Universitat Autonoma de Barcelona, Barcelona, Spain. x.caseras@iop.kcl.ac.uk	Probing the working memory system in chronic fatigue syndrome: a functional magnetic resonance imaging study using the n-back task.	Psychosom Med. 2006 Nov-Dec;68(6):947-55. Epub 2006 Nov 1.	OBJECTIVE: Up to 90% of patients with chronic fatigue syndrome (CFS) report substantial cognitive difficulties. However, objective evidence supporting these claims is inconsistent. The present functional magnetic resonance imaging study examined the neural correlates of working memory in patients with CFS compared with controls. METHODS: Seventeen patients with CFS and 12 healthy control subjects were scanned while performing a parametric version of the n-back task (0-, 1-, 2-, and 3-back). RESULTS: Both groups performed comparably well and activated the verbal working memory network during all task levels. However, during the 1-back condition, patients with CFS showed greater activation than control subjects in medial prefrontal regions, including the anterior cingulate gyrus. Conversely, on the more challenging conditions, patients with CFS demonstrated reduced activation in dorsolateral prefrontal and parietal cortices. Furthermore, on the 2- and 3-back conditions, patients but not control subjects significantly activated a large cluster in the right inferior/medial temporal cortex. Trend analyses of task load demonstrated statistically significant differences in brain activation between the two groups as the demands of the task increased. CONCLUSIONS: These results suggest that patients with CFS show both quantitative and qualitative differences in activation of the working memory network compared with healthy control subjects. It remains to be determined whether these findings stay stable after successful treatment.
Chalmers RA, Jones MG, Goodwin CS, Amjad S.	St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, UK. rachalmers@cimoa.org.uk	CFSUM1 and CFSUM2 in urine from patients with chronic fatigue syndrome are methodological artefacts.	Clin Chim Acta. 2006 Feb;364(1-2):148-58. Epub 2005 Aug 10.	McGregor et al. reported increased levels of an unidentified urinary compound (CFSUM1) in patients with chronic fatigue syndrome (CFS), with reduced excretion of another unidentified compound (CFSUM2), and suggested the possibility of chemical or metabolic 'markers' for CFS. The identity of CFSUM1 as reported was erroneous and the identities of these compounds have remained unknown until now. Urine samples were obtained from 30 patients with ME/CFS, 30 age- and sex-matched healthy controls, 20 control patients with depression and 22 control patients with rheumatoid arthritis. Samples were prepared using the published methods of McGregor et al. to produce heptafluorobutyryl-isobutyl derivatives of urinary metabolites. Alternative preparations utilised isopropyl, n-butyl and trifluoroacetyl derivatives. These were separated and identified using gas chromatography-mass spectrometry. CFSUM2 was identified as being partially derivatised [isobutyl ester-mono-heptafluorobutyryl (HFB)] serine. CFSUM1 was identified as partially derivatised pyroglutamic acid, being the isobutyl ester without formation of a HFB derivative. Both CFSUM1 and CFSUM2 are artefacts of the sample preparation procedure and previously reported quantitative abnormalities of CFSUM1 and CFSUM2 in urine from patients with ME/CFS are also artefactual. Pyroglutamic acid may be of primarily dietary origin. The methods used cannot provide reliable qualitative or quantitative data on urinary metabolites. No clinical or biochemical significance can be drawn between these compounds in ME/CFS or any other clinical conditions.
Chambers D, Bagnall AM, Hempel S, Forbes C.	Centre for Reviews and Dissemination, University of York, York YO10 5DD,	Interventions for the treatment, management and rehabilitation of	J R Soc Med. 2006 Oct;99(10):506-20.	OBJECTIVES: To determine whether any particular intervention or combination of interventions is effective in the treatment, management and rehabilitation of adults and children with a diagnosis of chronic fatigue syndrome / myalgic encephalomyelitis (CFS/ME). DESIGN: Substantive update of a systematic review published in 2002. Randomized (RCTs) and non-randomized controlled trials of any

	UK. dc510@york.ac.uk	patients with chronic fatigue syndrome/myalgic encephalomyelitis: an updated systematic review.		intervention or combination of interventions were eligible for inclusion. Study participants could be adults or children with a diagnosis of CFS/ME based on any criteria. We searched eleven electronic databases, reference lists of articles and reviews, and textbooks on CFS/ME. Additional references were sought by contact with experts. RESULTS: Seventy studies met the inclusion criteria. Studies on behavioural, immunological, pharmacological and complementary therapies, nutritional supplements and miscellaneous other interventions were identified. Graded exercise therapy and cognitive behaviour therapy appeared to reduce symptoms and improve function based on evidence from RCTs. For most other interventions, evidence of effectiveness was inconclusive and some interventions were associated with significant adverse effects. CONCLUSIONS: Over the last five years, there has been a marked increase in the size and quality of the evidence base on interventions for CFS/ME. Some behavioural interventions have shown promising results in reducing the symptoms of CFS/ME and improving physical functioning. There is a need for research to define the characteristics of patients who would benefit from specific interventions and to develop clinically relevant objective outcome measures.
Chapenko S, Krumina A, Kozireva S, Nora Z, Sultanova A, Viksna L, Murovska M.	August Kirchenstein Institute of Microbiology and Virology, Riga Stradins University, Ratsupites St.1, Riga, LV-1067, Latvia.	Activation of human herpesviruses 6 and 7 in patients with chronic fatigue syndrome.	J Clin Virol. 2006 Dec;37 Suppl 1:S47-51.	BACKGROUND: Human herpesvirus 6 (HHV-6) and 7 (HHV-7) have been suggested as possible triggering agents for chronic fatigue syndrome (CFS). OBJECTIVES: To determine the possible association of HHV-6 and HHV-7 infections with CFS. STUDY DESIGN: The prevalence of latent/persistent and active viral infections by nPCR, characteristic of HHV-6 variants using restriction endonuclease analysis and changes of lymphocyte subsets in peripheral blood by laser flow-cytometry in 17 CFS patients was examined. In addition, 12 patients with unexplained chronic fatigue and 20 blood donors (BD) were studied. RESULTS: No difference in prevalence of latent/persistent single viral infections between the patients and BD was found but dual infection rate was significantly higher in CFS patients. Active HHV-6 and dual (HHV-6 + HHV-7) infections were detected in CFS patients only and frequency of HHV-7 reactivation was also significantly higher in these patients. HHV-6 variant B was predominant in CFS patients (12/13). The changes of immunological parameters in CFS patients with active dual infection were characterized by significant decrease of CD3+ and CD4+ T cells, significant increase of CD95+ cells and decrease of CD4+/CD8+ ratio. CONCLUSIONS: HHV-6 and HHV-7 may be involved in the pathogenesis of CFS and reactivation of both viruses may provoke changes in the phenotype of circulating lymphocytes.
Chaudhuri A.	Essex Centre for Neurological Sciences, Oldchurch Hospital, Romford, Essex.	Diagnosing chronic fatigue.	Practitioner. 2006 Oct;250(1687):33-4, 37.	Review
Cho HJ, Skowera A, Cleare A, Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, King's College	Chronic fatigue syndrome: an update focusing on phenomenology and	Curr Opin Psychiatry. 2006 Jan;19(1):67-73.	PURPOSE OF REVIEW: Chronic fatigue syndrome is a controversial condition especially concerning its clinical definition and aetiopathogenesis. Most recent research progress has been made in phenomenology and pathophysiology and we focused our review on these two areas. RECENT FINDINGS: The phenomenology research supports the notion of a discrete fatigue syndrome which can be distinguished from depression and anxiety. The current case definition, however, may need an

	London, London, UK. h.cho@iop.kcl.ac.uk	pathophysiology.		improvement based on empirical data. Recent advances in understanding the pathophysiology of chronic fatigue syndrome continue to demonstrate the involvement of the central nervous system. Hyperserotonergic state and hypoactivity of the hypothalamic-pituitary-adrenal axis constitute other findings, but the question of whether these alterations are a cause or consequence of chronic fatigue syndrome still remains unanswered. Immune system involvement in the pathogenesis seems certain but the findings on the specific mechanisms are still inconsistent. Genetic studies provide some evidence of the syndrome being a partly genetic condition, but environmental effects seem to be still predominant and identification of specific genes is still at a very early stage. SUMMARY: The recent findings suggest that further research is needed in improving the current case definition; investigating overlaps and boundaries among various functional somatic syndromes; answering the question of whether the pathophysiologic findings are a cause or consequence; and elucidating the involvement of the central nervous system, immune system and genetic factors.
Cook DB, Nagelkirk PR, Poluri A, Mores J, Natelson BH.	University of Wisconsin, Madison, WI 53706, USA. dcook@education.wisc.edu	The influence of aerobic fitness and fibromyalgia on cardiorespiratory and perceptual responses to exercise in patients with chronic fatigue syndrome.	Arthritis Rheum. 2006 Oct;54(10):3351-62.	OBJECTIVE: To investigate cardiorespiratory and perceptual responses to exercise in patients with chronic fatigue syndrome (CFS), accounting for comorbid fibromyalgia (FM) and controlling for aerobic fitness. METHODS: Twenty-nine patients with CFS only, 23 patients with CFS plus FM, and 32 controls completed an incremental bicycle test to exhaustion. Cardiorespiratory and perceptual responses were measured. Results were determined for the entire sample and for 18 subjects from each group matched for peak oxygen consumption. RESULTS: In the overall sample, there were no significant differences in cardiorespiratory parameters between the CFS only group and the controls. However, the CFS plus FM group exhibited lower ventilation, lower end-tidal CO2, and higher ventilatory equivalent of carbon dioxide compared with controls, and slower increases in heart rate compared with both patients with CFS only and controls. Peak oxygen consumption, ventilation, and workload were lower in the CFS plus FM group. Subjects in both the CFS only group and the CFS plus FM group rated exercise as more effortful than did controls. Patients with CFS plus FM rated exercise as significantly more painful than did patients with CFS only or controls. In the subgroups matched for aerobic fitness, there were no significant differences among the groups for any measured cardiorespiratory response, but perceptual differences in the CFS plus FM group remained. CONCLUSION: With matching for aerobic fitness, cardiorespiratory responses to exercise in patients with CFS only and CFS plus FM are not different from those in sedentary healthy subjects. While CFS patients with comorbid FM perceive exercise as more effortful and painful than do controls, those with CFS alone do not. These results suggest that aerobic fitness and a concurrent diagnosis of FM are likely explanations for currently conflicting data and challenge ideas implicating metabolic disease in the pathogenesis of CFS.
Craddock RC, Taylor R, Broderick G, Whistler T, Klimas N, Unger ER.	Centers for Disease Control and Prevention, Viral Exanthems and Herpesvirus Branch, Atlanta, GA 30333, USA.	Exploration of statistical dependence between illness parameters using the entropy correlation	Pharmacogenomics. 2006 Apr;7(3):421-8.	The entropy correlation coefficient (ECC) is a useful tool for measuring statistical dependence between variables. We employed this tool to search for pairs of variables that correlated in the chronic fatigue syndrome (CFS) Computational Challenge dataset. Highly related variables are candidates for data reduction, and novel relationships could lead to hypotheses regarding the pathogenesis of CFS. METHODS: Data for 130 female participants in the Wichita (KS, USA) clinical study [1] was coded into numerical values. Metric data was grouped using Gaussian mixture models; the number of groups was chosen using Bayesian information content. The pair-wise correlation

	cmi5@cdc.gov	coefficient.		between all variables was computed using the ECC. Significance was estimated from 1000 iterations of a permutation test and a threshold of 0.01 was used to identify significantly correlated variables. RESULTS: The five dimensions of multidimensional fatigue inventory (MFI) were all highly correlated with each other. Seven Short Form (SF)-36 measures, four CFS case-defining symptoms and the Zung self-rating depression scale all correlated with all MFI dimensions. No physiological variables correlate with more than one MFI dimension. MFI, SF-36, CDC symptom inventory, the Zung self-rating depression scale and three Cambridge Neuropsychological Test Automated Battery (CANTAB) measures are highly correlated with CFS disease status. DISCUSSION: Correlations between the five dimensions of MFI are expected since they are measured from the same instrument. The relationship between MFI and Zung depression index has been previously reported. MFI, SF-36, and Centers for Disease Control and Prevention (CDC) symptom inventory are used to classify CFS; it is not surprising that they are correlated with disease status. Only one of the three CANTAB measures that correlate with disease status has been previously found, indicating the ECC identifies relationships not found with other statistical tools. CONCLUSION: The ECC is a useful tool for measuring statistical dependence between variables in clinical and laboratory datasets. The ECC needs to be further studied to gain a better understanding of its meaning for clinical data.
Crawley E.		Chronic fatigue syndrome in young people: the spectrum and the myths.	Br J Hosp Med (Lond). 2006 Sep;67(9):452-3.	Editorial
Demitrack MA.	Neuronetics, Inc., One Great Valley Parkway, Suite 2, Malvern, Pennsylvania 19355, USA. mdemitrack@neuronetics.com	Clinical methodology and its implications for the study of therapeutic interventions for chronic fatigue syndrome: a commentary.	Pharmacogenomics. 2006 Apr;7(3):521-8.	Chronic fatigue syndrome (CFS) is a complex, multisymptom illness of unknown etiology. A variety of operational case definitions based on symptom report have been developed that share some common clinical features. Patients often come to clinical presentation after months or, more typically, years of symptomatic distress. Comorbid presentation with psychiatric illnesses has been noted. Due to these fundamental issues, the impact of patient selection and the specification of the methods of outcome assessment loom large in therapeutic studies of CFS. While a substantial body of research has focused on increasing our understanding of the basic pathobiology of CFS, there have been comparatively fewer studies that have addressed the problems of patient characterization and outcome assessment. The role of clinical methodology in the study of the therapeutics of CFS is not trivial, and may confound our understanding of pragmatic recommendations for treatment.
Devanur LD, Kerr JR.	Chronic Fatigue Syndrome (CFS) Group, Department of Cellular & Molecular Medicine, St. George's University of	Chronic fatigue syndrome.	J Clin Virol. 2006 Nov;37(3):139-50. Epub 2006 Sep 15.	Chronic fatigue syndrome (CFS) is thought to have a worldwide prevalence of 0.4-1% with approximately 240,000 patients in the UK. Diagnosis is based on clinical criteria and critically depends on exclusion of other physical and psychiatric diseases. Studies of pathogenesis have revealed immune system abnormalities and chronic immune activation, dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis, brain abnormalities, evidence of emotional stress (comprising host aspects) and evidence of exogenous insults, for example, various microbial infections (Epstein-Barr virus, enteroviruses, parvovirus B19, Coxiella burnetii and Chlamydia pneumoniae), vaccinations and exposure to organophosphate chemicals and other toxins (comprising environmental aspects). Emotional stress appears to be very important as it reduces the ability of the immune system to clear

	London, Cranmer Terrace, London SW17 0RE, United Kingdom.			infections, it's presence has been shown to determine whether or not an individual develops symptoms upon virus infection, and it leads to activation of the HPA axis. But, emotional stress is distinct from depression, the presence of which precludes a diagnosis of CFS. There is no specific treatment for CFS other than the much underutilised approach of specific treatment of virus infections. Current priorities are to understand the molecular pathogenesis of disease in terms of human and virus gene expression, to develop a diagnostic test based on protein biomarkers, and to develop specific curative treatments.
Dumit J.	Program in Science, Technology & Society, Massachusetts Institute of Technology, E51-296D MIT, Cambridge, MA 02139-4307, USA. dumit@mit.edu	Illnesses you have to fight to get: facts as forces in uncertain, emergent illnesses.	Soc Sci Med. 2006 Feb;62(3):577-90. Epub 2005 Aug 8.	Chronic fatigue syndrome and multiple chemical sensitivity are two clusters of illnesses that are pervaded by medical, social and political uncertainty. This article examines how facts are talked about and experienced in struggles over these emergent, contested illnesses in the US. Based principally on a large archive of internet newsgroup postings, and also on fieldwork and on published debates, it finds that (1) sufferers describe their experiences of being denied healthcare and legitimacy through bureaucratic categories of exclusion as dependent upon their lack of biological facts; (2) institutions manage these exclusions rhetorically through exploiting the open-endedness of science to deny efficacy to new facts; (3) collective patient action responds by archiving the systematic nature of these exclusions and developing counter-tactics. The result is the maintenance of these very expensive struggles for all involved.
Dyer C.		GMC must consider case against paediatricians who suspected parents of fabricating child's illness.	BMJ. 2006 May 13;332(7550):1110 .	
Engel CC.	Department of Psychiatry, F. Edward Hebert School of Medicine of Uniformed Services University of Health Sciences, Bethesda, MD 20814-4799, USA. cengel@usuhs.mil	Explanatory and pragmatic perspectives regarding idiopathic physical symptoms and related syndromes.	CNS Spectr. 2006 Mar;11(3):225-32.	In recent years, research-methods literature mainly addressing controlled clinical trials has arisen regarding explanatory and pragmatic treatment trials. Explanatory trials tend to examine causal mechanisms and questions of efficacy and value internal validity (creating optimal study conditions) over generalizability (using study results to understand treatment effects in real-life patient populations). In contrast, pragmatic trials value "external relevance" (generalizability) of study results over "internal elegance" so that clinicians and health policymakers can better understand how treatments might impact their patients and policies. This review draws inspiration from these contrasting explanatory and pragmatic perspectives and develops them for clinical and research pertaining to idiopathic physical symptoms and related syndromes (eg, somatization disorder, chronic fatigue syndrome, multiple chemical sensitivities, irritable bowel syndrome). Explanatory and pragmatic perspectives are used to examine these idiopathies with regard to causation, case definition, labels, and treatment. It is concluded that idiopathic symptom syndromes are fundamentally pragmatic clinical and research challenges. For epidemiologic and methodologic reasons, the complex explanations for these syndromes remain largely elusive. Even so, scientific and clinical pragmatism offers the opportunity to reduce disagreement between competing medical

				disciplines and between clinicians and affected patients with regard to irreconcilable etiologic questions and to remain evidence-based in the care of patients.
Fang H, Xie Q, Boneva R, Fostel J, Perkins R, Tong W.	Z-Tech Corporation at NCTR, Division of Bioinformatics, 3900 NCTR Road, Jefferson, AR 72079, USA.	Gene expression profile exploration of a large dataset on chronic fatigue syndrome.	Pharmacogenomics. 2006 Apr;7(3):429-40.	OBJECTIVE: To gain understanding of the molecular basis of chronic fatigue syndrome (CFS) through gene expression analysis using a large microarray data set in conjunction with clinically administrated questionnaires. METHOD: Data from the Wichita (KS, USA) CFS Surveillance Study was used, comprising 167 participants with two self-report questionnaires (multidimensional fatigue inventory [MFI] and Zung depression scale [Zung]), microarray data, empiric classification, and others. Microarray data was analyzed using bioinformatics tools from ArrayTrack. RESULTS: Correspondence analysis was applied to the MFI questionnaire to select the 23 samples having either the most or the least fatigue, and to the Zung questionnaire to select the 26 samples having either the most or least depression; ten samples were common, resulting in a total of 39 samples. The MFI and Zung-based CFS/non-CFS (NF) classifications on the 39 samples were consistent with the empiric classification. Two differentially-expressed gene lists were determined, 188 fatigue-related genes and 164 depression-related genes, which shared 24 common genes and involved 11 common pathways. Principal component analysis based on 24 genes clearly separates 39 samples with respect to their likelihood to be CFS. Most of the 24 genes are not previously reported for CFS, yet their functions are consistent with the prevailing model of CFS, such as immune response, apoptosis, ion channel activity, signal transduction, cell-cell signaling, regulation of cell growth and neuronal activity. Hierarchical cluster analysis was performed based on 24 genes to classify 128 (=167-39) unassigned samples. Several of the 11 identified common pathways are supported by earlier findings for CFS, such as cytokine-cytokine receptor interaction and neuroactive ligand-receptor interaction. Importantly, most of the 11 common pathways are interrelated, suggesting complex biological mechanisms associated with CFS. CONCLUSION: Bioinformatics is critical in this study to select definitive sample groups, analyze gene expression data and gain insight into biological mechanisms. The 24 identified common genes and 11 common pathways could be important in future studies of CFS at the molecular level.
Fenske M.		Comment on "diurnal excretion of urinary cortisol, cortisone, and cortisol metabolites in chronic fatigue syndrome".	J Psychosom Res. 2006 Jun;60(6):627-8; author reply 629.	
Fostel J, Boneva R, Lloyd A.	National Center for Toxicogenomics, NIEHS MD F1-05, 111 Alexander Drive, PO Box 12233, Research Triangle Park, NC	Exploration of the gene expression correlates of chronic unexplained fatigue using factor analysis.	Pharmacogenomics. 2006 Apr;7(3):441-54.	OBJECTIVE: To identify biomarkers of chronic fatigue syndrome (CFS) and related disorders through analysis of microarray data, pathology test results and self-report symptom profiles. METHOD: To empirically derive the symptom domains of the illnesses, factor analysis was performed on responses to self-report questionnaires (multidimensional fatigue inventory, Centers for Disease Control and Prevention (CDC) symptom inventory and Zung depression scale) before validation with independent datasets. Gene expression patterns that distinguished subjects across each factor dimension were then sought. RESULTS: A four-factor solution was favored, featuring 'fatigue' and 'mood disturbance'

	27709-2233, USA. fostel@niehs.nih.gov			factors. Scores on these factors correlated with measures of disability on the Short Form (SF)-36. A total of 57 genes that distinguished subjects along each factor dimension were identified, although the separation was significant only for subjects beyond the extreme (15th and 85th) percentiles of severity. Clustering of laboratory parameters with expression of these genes revealed associations with serum measurements of pH, electrolytes, glucose, urea, creatinine, and liver enzymes (aspartate amino transferase [AST] and alanine amino transferase [AST]); as well as hematocrit and white cell count. CONCLUSION: CFS is a complex syndrome that cannot simply be associated with changes in individual laboratory tests or expression levels of individual genes. No clear association with gene expression and individual symptom domains was found. However, analysis of such multifacetted datasets is likely to be an important means to elucidate the pathogenesis of CFS.
Frémont M, Freya Vaeyens, C. Vincent Herst, Kenny De Meirleir, Patrick Englebienne		Antiviral Pathway Deregulation of Chronic Fatigue Syndrome Induces Nitric Oxide Production in Immune Cells that Precludes a Resolution of the Inflammatory Response	Journal of Chronic Fatigue Syndrome 2006; 13(4): 19-30	Chronic fatigue syndrome (CFS) is a poorly defined medical condition diagnosed by exclusion, which, besides severe chronic fatigue as the hallmark symptom, involves inflammatory and immune activation stigma. Although viral infections are not systematically found in CFS patients, the type I interferon antiviral pathway has been repeatedly shown to be activated in peripheral blood mononuclear cells (PBMC) of the most afflicted patients. An abnormal truncated form of ribonuclease L (37-kDa RNase L) is also found in the PBMC of CFS patients and this protein has been proposed as a biological marker for CFS. Recently, the levels of this abnormal protein have been significantly correlated to the extent of inflammatory symptoms displayed by CFS patients. We report here that active double-stranded RNA-dependent kinase (PKR) is expressed and activated in parallel to the presence of the 37-kDa RNase L and to an increase in nitric oxide production by immune cells. However, PKR upregulation results also in a significant increase followed by a decrease in caspase 3 activity for the samples containing the highest levels of 37-kDa RNase L. This caspase 3 downregulation does not result from increased expression of the anti-apoptotic proteins Bcl-2 and Bcl-XL. These results therefore suggest that chronic inflammation due to excess nitric oxide production plays a role in CFS and that the normal resolution of the inflammatory process by NF-KB activation and apoptotic induction is impaired. These observations draw new directions for the therapeutic approach of CFS.
Fremont M, Vaeyens F, Herst CV, De Meirleir K, Englebienne P.		Antiviral Pathway Deregulation of Chronic Fatigue Syndrome Induces Nitric Oxide Production in Immune Cells That Precludes a Resolution of the Inflammatory Response	Journal of Chronic Fatigue Syndrome 2006;13(4):	No abstract available at September 2006
Garcia-Campayo J, Pascual A, Alda M,	Department of Psychiatry, Miguel	The Spanish version of the	Gen Hosp Psychiatry. 2006	OBJECTIVE: To examine some of the psychometric properties of the Spanish version of the FibroFatigue Scale (FFS). METHODS: FFS was administered to 120 patients diagnosed with fibromyalgia

Marzo J, Magallon R, Fortes S.	Servet University Hospital and University of Zaragoza Faculty of Medicine, Avenida Isabel La Catolica, s/n 50.009 Zaragoza, Spain. jgarcamp@arrakis.es	FibroFatigue Scale: validation of a questionnaire for the observer's assessment of fibromyalgia and chronic fatigue syndrome.	Mar-Apr;28(2):154-60.	and chronic fatigue syndrome. Internal consistency was evaluated by using Cronbach's alpha, test-retest reliability with weighted kappa and construct validity by correlations among FFS, the Fibromyalgia Impact Questionnaire (FIQ), the EuroQol 5D (EQ-5D) and the Hospital Anxiety and Depression Scale (HADS). The interrater reliability was tested using analysis of variance with patients and raters as independent factors. RESULTS: Internal consistency (alpha) was .88, test-retest reliability was .91, and interrater reliability was .93. Significant correlations were obtained between overall FFS and the FIQ (.55, P<.01), the EQ-5D (-.48, P<.01) and the HADS depression subscale (.25, P<.01), but not with the HADS anxiety subscale. CONCLUSION: These results support the reliability and validity of the data obtained with the Spanish version of the FSS.
Geisser ME, Gracely RH, Giesecke T, Petzke FW, Williams DA, Clauw DJ.	Chronic Pain and Fatigue Research Center, Department of Internal Medicine, Division of Rheumatology, University of Michigan, Ann Arbor, MI, United States; Department of Physical Medicine and Rehabilitation, University of Michigan Health System, 325 E. Eisenhower Parkway, Ann Arbor, MI 48108, United States.	The association between experimental and clinical pain measures among persons with fibromyalgia and chronic fatigue syndrome.	Eur J Pain. 2006 Mar 16; [Epub ahead of print]	Evoked or experimental pain is often used as a model for the study of clinical pain, yet there are little data regarding the relationship between the two. In addition, there are few data regarding the types of stimuli and stimulus intensities that are most closely related to clinical pain. In this study, 36 subjects with fibromyalgia (FM), chronic fatigue syndrome (CFS), or both syndromes were administered measures of clinical pain and underwent a dolorimetry evaluation. Subjects also underwent experimental pain testing utilizing heat and pressure stimulation. Stimulation levels evoking low, moderate and high sensory intensity, and comparable levels of unpleasantness, were determined for both types of stimuli using random staircase methods. Clinical pain was assessed using visual analogue ratings and the short form of the McGill Pain Questionnaire (MPQ). Ratings of heat pain sensation were not significantly associated with clinical pain ratings, with the exception of unpleasantness ratings at high stimulus intensities. Pain threshold and tolerance as assessed by dolorimetry were significantly associated with average measures of clinical pain. Both intensity and unpleasantness ratings of pressure delivered using random staircase methods were significantly associated with clinical pain at low, moderate and high levels, and the strength of the association was greater at increasingly noxious stimulus intensities. These findings suggest that random pressure stimulation as an experimental pain model in these populations more closely reflects the clinical pain for these conditions. These findings merit consideration when designing experimental studies of clinical pain associated with FM and CFS.
Gharibzadeh S, Hoseini SS.		Is there any relation between moldy building exposure and chronic fatigue syndrome?	Med Hypotheses. 2006;66(6):1243-4. Epub 2006 Mar 9.	
Gharibzadeh S, Hoseini SS.		The potential role of nitric oxide metabolites in	Med Hypotheses. 2006;67(1):197-8. Epub 2006 Mar 15.	

		diagnosing chronic fatigue syndrome.		
Gibson I.	House of Commons, United Kingdom.	A new look at Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME).	J Clin Pathol. 2006 Aug 25; [Epub ahead of print]	It has been three years since the Chief Medical Office reported on CFS/ME and the time has come for a thorough investigation by an All Party Group drawn from the House of Commons and the House of Lords. We have received many written submissions and are engaged in taking oral evidence in 2-hour sessions, which we open to the public as well as interested groups. The group has received a fantastic response to its requests for written evidence over the last few months. Questions that arise for a government response are the lack of provision and support for CFS/ME patients, the issue of the clinical definition of CFS/ME, the need for a diagnostic test for CFS/ME, effectiveness of the NICE guidelines, and criteria used to decide which treatments are best for patients with CFS/ME.
Glass JM.	University of Michigan, Institute for Social Research and Department of Psychiatry, 426 Thompson Street, Room 5256, Ann Arbor, MI 48106-1248, USA. jglass@umich.edu	Cognitive dysfunction in fibromyalgia and chronic fatigue syndrome: new trends and future directions.	Curr Rheumatol Rep. 2006 Dec;8(6):425-9.	Fibromyalgia (FM) and chronic fatigue syndrome (CFS) patients often have memory and cognitive complaints. Objective cognitive testing demonstrates long-term and working memory impairments. In addition, CFS patients have slow information-processing, and FM patients have impaired control of attention, perhaps due to chronic pain. Neuroimaging studies demonstrate cerebral abnormalities and a pattern of increased neural recruitment during cognitive tasks. Future work should focus on the specific neurocognitive systems involved in cognitive dysfunction in each syndrome.
Goertzel BN, Pennachin C, de Souza Coelho L, Gurbaxani B, Maloney EM, Jones JF.	Virginia Tech, National Capital Region, Arlington, VA, USA. ben@goertzel.org	Combinations of single nucleotide polymorphisms in neuroendocrine effector and receptor genes predict chronic fatigue syndrome.	Pharmacogenomics. 2006 Apr;7(3):475-83.	OBJECTIVE: This paper asks whether the presence of chronic fatigue syndrome (CFS) can be more accurately predicted from single nucleotide polymorphism (SNP) profiles than would occur by chance. METHODS: Specifically, given SNP profiles for 43 CFS patients, together with 58 controls, we used an enumerative search to identify an ensemble of conjunctive rules that predict whether a patient has CFS. RESULTS: The accuracy of the rules reached 76.3%, with the highest accuracy rules yielding 49 true negatives, 15 false negatives, 28 true positives and nine false positives (odds ratio [OR] 8.94, $p < 0.0001$). Analysis of the SNPs used most frequently in the overall ensemble of rules gave rise to a list of 'most important SNPs', which was not identical to the list of 'most differentiating SNPs' that one would calculate via studying each SNP independently. The top three genes containing the SNPs accounting for the highest accumulated importances were neuronal tryptophan hydroxylase (TPH2), catechol-O-methyltransferase (COMT) and nuclear receptor subfamily 3, group C, member 1 glucocorticoid receptor (NR3C1). CONCLUSION: The fact that only 28 out of several million possible SNPs predict whether a person has CFS with 76% accuracy indicates that CFS has a genetic component that may help to explain some aspects of the illness.
Goertzel BN, Pennachin C, de Souza Coelho L, Maloney EM, Jones JF, Gurbaxani B.	Virginia Tech, National Capital Region, Arlington, Virginia, USA. ben@goertzel.org	Allostatic load is associated with symptoms in chronic fatigue syndrome patients.	Pharmacogenomics. 2006 Apr;7(3):485-94.	OBJECTIVES: To further explore the relationship between chronic fatigue syndrome (CFS) and allostatic load (AL), we conducted a computational analysis involving 43 patients with CFS and 60 nonfatigued, healthy controls (NF) enrolled in a population-based case-control study in Wichita (KS, USA). We used traditional biostatistical methods to measure the association of high AL to standardized measures of physical and mental functioning, disability, fatigue and general symptom severity. We also used nonlinear regression technology embedded in machine learning algorithms to

				learn equations predicting various CFS symptoms based on the individual components of the allostatic load index (ALI). METHODS: An ALI was computed for all study participants using available laboratory and clinical data on metabolic, cardiovascular and hypothalamic-pituitary-adrenal (HPA) axis factors. Physical and mental functioning/impairment was measured using the Medical Outcomes Study 36-item Short Form Health Survey (SF-36); current fatigue was measured using the 20-item multidimensional fatigue inventory (MFI); frequency and intensity of symptoms was measured using the 19-item symptom inventory (SI). Genetic programming, a nonlinear regression technique, was used to learn an ensemble of different predictive equations rather just than a single one. Statistical analysis was based on the calculation of the percentage of equations in the ensemble that utilized each input variable, producing a measure of the 'utility' of the variable for the predictive problem at hand. Traditional biostatistics methods include the median and Wilcoxon tests for comparing the median levels of subscale scores obtained on the SF-36, the MFI and the SI summary score. RESULTS: Among CFS patients, but not controls, a high level of AL was significantly associated with lower median values (indicating worse health) of bodily pain, physical functioning and general symptom frequency/intensity. Using genetic programming, the ALI was determined to be a better predictor of these three health measures than any subcombination of ALI components among cases, but not controls.
Goodwin GM.	Oxford University, Warneford Hospital, United Kingdom. guy.goodwin@psychiatry.oxford.ac.uk	Depression and associated physical diseases and symptoms.	Dialogues Clin Neurosci. 2006;8(2):259-65.	Depression can occur in association with virtually all the other psychiatric and physical diagnoses. Physical illness increases the risk of developing severe depressive illness. There are two broadly different mechanisms. The most obvious has a psychological or cognitive mechanism. Thus, the illness may provide the life event or chronic difficulty that triggers a depressive episode in a vulnerable individual. Secondly, more specific associations appear to exist between depression and particular physical disorders. These may turn out to be of particular etiological interest. The best examples are probably stroke and cardiovascular disease. Finally, major depression, but especially minor depression, dysthymia, and depressive symptoms merge with other manifestations of human distress with which patients present to their doctors. Such somatic presentations test the conventional distinction between physical and mental disorder and are a perennial source of controversy.
Gottfries CG, Hager O, Regland B, Zachrisson O.		Long-Term Treatment with a Staphylococcus Toxoid Vaccine in Patients with Fibromyalgia and Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2006;13(4):	No abstract available at September 2006
Gottfries CG, Ove Häger, Björn Regland, Olof Zachrisson		Long-Term Treatment with a Staphylococcus Toxoid Vaccine in Patients with	Journal of Chronic Fatigue Syndrome 2006; 13(4): 31-43	One hundred and sixty patients with fibromyalgia and chronic fatigue syndrome, who were on a continuous treatment with a Staphylococcus vaccine, were followed during one year with repeated consultation visits. The patients had participated in controlled studies and been on continuous treatment with the vaccine for 22 ±10 months before inclusion into this follow-up study. They were treated with 1 mL of the vaccine subcutaneously every third to fourth week. Adverse events were few.

		Fibromyalgia and Chronic Fatigue Syndrome		The adherence to the treatment was very good. Over a period of one year, 8% withdrew, and in only 5%, the withdrawal was due to insufficient clinical effect. Only in two cases where the patients were allergic to the preservative of the vaccine, the side effects caused the withdrawal of the treatment. Ratings with scales (CPRS-15 and FibroFatigue) showed improvement from start of treatment and also further improvement during the follow-up year. In view of the natural history for these disorders the result is of interest.
Grans H, Nilsson M, Dahlman-Wright K, Evengard B.	Karolinska Institutet, Sweden.	Reduced levels of oestrogen receptor {beta} mRNA in Swedish patients with chronic fatigue syndrome.	J Clin Pathol. 2006 May 26; [Epub ahead of print]	BACKGROUND: Chronic fatigue syndrome (CFS) is an illness with unknown aetiology and pathophysiology. The sex difference observed for CFS indicates a role for oestrogen and oestrogen receptors (ERs) for disease development. Furthermore, an immuno-mediated pathogenesis has been suggested for CFS which provides an additional connection to oestrogen, which display immunomodular functions. AIMS: The aim of this study was to investigate a possible association of ER mRNAs and two ERbeta single nucleotide polymorphisms (SNPs) with CFS. METHODS: Messenger RNA levels of ERalpha, ERbetawt and ERbetacx were investigated in peripheral blood mononuclear cells (PBMCs) from 30 CFS patients and 36 healthy controls by quantitative real-time PCR. Two ERbeta SNPs were scored in the same material. RESULTS: The CFS patient group showed significantly lower mRNA expression levels of ERbetawt compared with the healthy control group. No differences were observed for ERalpha or ERbetacx between patients and controls. There were no significant differences in frequency for the investigated ERbeta SNPs between cases and controls. CONCLUSIONS: The reduced ERbetawt expression levels observed in this study is consistent with an immune-mediated pathogenesis of CFS. Additionally, the observation that ERbetawt expression is decreased in CFS could provide an entry point to identify interesting, potentially disease causing, candidate molecules for further study. A possible connection between oestrogen, ERs and CFS should be further evaluated.
Greenberg S, Frid M.	Cardiac Rehabilitation and Prevention Unit, Tel Aviv Medical Center, Israel. shaigr@zahav.net.il	[Chronic fatigue syndrome--exercise and physical activity] [Article in Hebrew]	Harefuah. 2006 Apr;145(4):276-80, 318.	One of the major symptoms of chronic fatigue syndrome (CFS) is reduced exercise and functional capacity and increased fatigue symptoms following physical effort. A review of the literature indicates that patients that suffer from CFS are characterized by: low aerobic capacity, higher heart rate during sub-maximal exercise, higher subjective effort prescription, reduced muscle strength, and prolonged recovery period. Although several symptoms are a result of lack of physical activity, several mechanisms were suggested to explain those symptoms: pathological heart rate control, reduced aerobic metabolic capacity, reduced blood supply to the working muscles and nerve system dysfunction. Participating in guided exercise programs was found to be the most effective treatment in improving exercise and functional capacity, reducing fatigue syndromes and improving patients' daily function.
Greenfield JR, Samaras K.	Department of Endocrinology, St Vincent's Hospital and St Vincent's Clinic and the Garvan Institute of Medical Research,	Evaluation of pituitary function in the fatigued patient: a review of 59 cases.	38: Eur J Endocrinol. 2006 Jan;154(1):147-57.	OBJECTIVE: The aim of this study was to review the results of dynamic pituitary testing in patients presenting with fatigue. METHODS: We reviewed clinical histories and insulin tolerance test (ITT) results of 59 patients who presented with fatigue and other symptoms of glucocorticoid insufficiency over a 4-year period. All patients referred for ITT had an early-morning cortisol level of <400 nM and a low or normal ACTH level. RESULTS: Peak cortisol and GH responses following insulin-induced hypoglycaemia were normal in only seven patients (12%). Median age of the remaining 52 patients was 47 years (range, 17-67 years); all but five were female. Common presenting symptoms were

	Sydney, Australia.			neuroglycopaenia (n = 47), depression (n = 37), arthralgia and myalgia (n = 28), weight gain (n = 25), weight loss (n = 9), postural dizziness (n = 15) and headaches (n = 13). Other medical history included autoimmune disease (n = 20; particularly Hashimoto's thyroiditis, Graves' disease and coeliac disease), postpartum (n = 8) and gastrointestinal (n = 2) haemorrhage and hyperprolactinaemia (n = 13). 31 subjects had peak cortisol levels of <500 nM (suggestive of ACTH deficiency; 18 of whom had levels < 400 nM) and a further six had indeterminate results (500-550 nM). The remaining 15 subjects had normal cortisol responses (median 654 nM; range, 553-1062 nM) but had low GH levels following hypoglycaemic stimulation (5.9 mU/l; 3-11.6 mU/l). CONCLUSION: Our results suggest that patients presenting with fatigue and symptoms suggestive of hypocortisolism should be considered for screening for secondary adrenal insufficiency, particularly in the presence of autoimmune disease or a history of postpartum or gastrointestinal haemorrhage. Whether physiological glucocorticoid replacement improves symptoms in this patient group is yet to be established.
Guilleminault C, Poyares D, Rosa A, Kirisoglu C, Almeida T, Lopes MC.	Stanford University Sleep Disorders Clinic, 401 Quarry road, suite 3301, Stanford, CA 94305, USA. cguil@stanford.edu	Chronic fatigue, unrefreshing sleep and nocturnal polysomnography.	Sleep Med. 2006 Sep;7(6):513-20. Epub 2006 Aug 24.	BACKGROUND AND PURPOSE: To investigate the complaint of unrefreshing sleep with study of sleep electroencephalogram (EEG) in patients with chronic fatigue. PATIENTS AND METHODS: Fourteen successively seen patients (mean age: 41.1 9.8) who complained of chronic fatigue but denied sleepiness and agreed to participate were compared to 14 controls (33.6+/-10.2 years) who were monitored during sleep recorded in parallel. After performing conventional sleep scoring we applied Fast Fourier Transformation (FFT) for the delta 1, delta 2, theta, alpha, sigma 1, sigma 2, beta EEG frequency bands. The presence of non-rapid eye movement (NREM) sleep instability was studied with calculation of cyclic alternating pattern (CAP) rate. Two-way analysis of variance (ANOVA) was performed to analyze FFT results and Mann-Whitney U-test to compare CAP rate in both groups of subjects. RESULTS: Slow wave sleep (SWS) percentage and sleep efficiency were lower, but there was a significant increase in delta 1 (slow delta) relative power in the chronic fatigue group when compared to normals (P<0.01). All the other frequency bands were proportionally and significantly decreased compared to controls. CAP rate was also significantly greater in subjects with chronic fatigue than in normals (P=0.04). An increase in respiratory effort and nasal flow limitation were noted with chronic fatigue. CONCLUSIONS: The complaints of chronic fatigue and unrefreshing sleep were associated with an abnormal CAP rate, with increase in slow delta power spectrum, affirming the presence of an abnormal sleep progression and NREM sleep instability. These specific patterns were related to subtle, undiagnosed sleep-disordered breathing.
Gurbaxani BM, Jones JF, Goertzel BN, Maloney EM.	1Centers for Disease Control and Prevention, 600 Clifton Road, MS A-15, Atlanta, GA 30333, USA. buw8@cdc.gov	Linear data mining the Wichita clinical matrix suggests sleep and allostatic load involvement in chronic fatigue syndrome.	Pharmacogenomics. 2006 Apr;7(3):455-65.	OBJECTIVES: To provide a mathematical introduction to the Wichita (KS, USA) clinical dataset, which is all of the nongenetic data (no microarray or single nucleotide polymorphism data) from the 2-day clinical evaluation, and show the preliminary findings and limitations, of popular, matrix algebra-based data mining techniques. METHODS: An initial matrix of 440 variables by 227 human subjects was reduced to 183 variables by 164 subjects. Variables were excluded that strongly correlated with chronic fatigue syndrome (CFS) case classification by design (for example, the multidimensional fatigue inventory [MFI] data), that were otherwise self reporting in nature and also tended to correlate strongly with CFS classification, or were sparse or nonvarying between case and control. Subjects were excluded if they did not clearly fall into well-defined CFS classifications, had comorbid depression with melancholic features, or other medical or psychiatric exclusions. The popular data

				mining techniques, principle components analysis (PCA) and linear discriminant analysis (LDA), were used to determine how well the data separated into groups. Two different feature selection methods helped identify the most discriminating parameters. RESULTS: Although purely biological features (variables) were found to separate CFS cases from controls, including many allostatic load and sleep-related variables, most parameters were not statistically significant individually. However, biological correlates of CFS, such as heart rate and heart rate variability, require further investigation. CONCLUSIONS: Feature selection of a limited number of variables from the purely biological dataset produced better separation between groups than a PCA of the entire dataset. Feature selection highlighted the importance of many of the allostatic load variables studied in more detail by Maloney and colleagues in this issue [1] , as well as some sleep-related variables. Nonetheless, matrix linear algebra-based data mining approaches appeared to be of limited utility when compared with more sophisticated nonlinear analyses on richer data types, such as those found in Maloney and colleagues [1] and Goertzel and colleagues [2] in this issue.
Hampton T.		Chronic fatigue syndrome answers sought.	JAMA. 2006 Dec 27;296(24):2915.	News
Hampton T.		Researchers find genetic clues to chronic fatigue syndrome.	JAMA. 2006 Jun 7;295(21):2466-7.	
Hanna EZ.		Comments on guest editorial, "Chronic fatigue syndrome, mast cells, and tricyclic antidepressants". J Clin Psychopharmacol. 2005 Dec;25(6):515-20	J Clin Psychopharmacol. 2006 Dec;26(6):690; author reply 690-1.	Letter
Hannestad U, Theodorsson E, Evengard B.	Faculty of Health Science, Division of Clinical Chemistry, Linkoping University, SE-581 85 Linkoping, Sweden.	beta-Alanine and gamma-aminobutyric acid in chronic fatigue syndrome.	Clin Chim Acta. 2006 Jul 14; [Epub ahead of print]	BACKGROUND: Due to the occurrence of sleep disturbances and fatigue in chronic fatigue syndrome (CFS), an investigation was performed to examine if there is an abnormal excretion of gamma-aminobutyric acid (GABA) and/or its structural analogue beta-alanine in the urine from CFS patients. Both GABA and beta-alanine are inhibitory neurotransmitters in the mammalian central nervous system. METHODS: The 24 h urine excretion of GABA and beta-alanine was determined by isotope dilution gas chromatography mass spectrometry in 33 CFS patients and 43 healthy controls. The degree of symptoms in both patients and controls was measured by grading of three typical CFS symptoms using a Visual Analogue Scale. RESULTS: Men had a significantly higher excretion of both beta-alanine and GABA than women. Comparing CFS patients with healthy controls showed no significant difference in excretion of neither beta-alanine nor GABA. No correlation was found

				between the excretion of beta-alanine or GABA and any of the three characteristic CFS symptoms measured. However, two female and two male CFS patients excreted considerably higher amounts of beta-alanine in their 24 h urine samples than control subjects. CONCLUSIONS: Increased excretion of beta-alanine was found in a subgroup of CFS patients, indicating that there may be a link between CFS and beta-alanine in some CFS patients.
Hawk C, Jason LA, Torres-Harding SR.		Reliability of a Chronic Fatigue Syndrome Questionnaire	Journal of Chronic Fatigue Syndrome 2006;13(4):	No abstract available at September 2006
Heesen C, Nawrath L, Reich C, Bauer N, Schulz KH, Gold SM.	Department of Neurology, University Hospital Eppendorf, Martinistrasse 52, D-20246 Hamburg, Germany. heesen@uke.uni-hamburg.de	Fatigue in multiple sclerosis: an example of cytokine mediated sickness behaviour?	J Neurol Neurosurg Psychiatry. 2006 Jan;77(1):34-9. Comment in: J Neurol Neurosurg Psychiatry. 2006 Jan;77(1):2-3.	BACKGROUND: Fatigue is a major complaint of multiple sclerosis (MS) patients. However, little is known about its pathophysiological mechanisms. Evidence from chronic fatigue syndrome and studies on sickness behaviour suggest that immune and neuroendocrine factors may play a causative role in the development of fatigue. METHODS: We compared whole blood stimulatory capacity for pro- (TNFalpha, IFNgamma) and anti-inflammatory cytokines (IL-10) as well as hypothalamo-pituitary-adrenal (HPA) axis function in 15 MS patients with marked fatigue and 15 patients without fatigue as determined by the Fatigue Severity Scale (FSS). RESULTS: Proinflammatory cytokines were significantly higher (TNFalpha: 478.9 v 228.2 pg/ml, p = 0.01; IFNgamma: 57.6 v 27.8 pg/ml; p = 0.01) in MS patients with fatigue. Furthermore, TNFalpha values significantly correlated with daytime sleepiness as measured by the Epworth Sleepiness Scale (r = 0.64, p = 0.001). Controlling for disease activity (as measured by the Cambridge Multiple Sclerosis Basic Score), disease duration, Expanded Disability Status Scale, and depression further increased the correlation of cytokine production and fatigue. HPA axis activity was not related to fatigue but was modestly correlated with cognitive impairment. CONCLUSION: Our data suggest that fatigue in MS is at least partially mediated through activation of proinflammatory cytokines. In line with earlier findings, HPA axis dysfunction seems not to be relevant in MS fatigue pathogenesis but appears to be linked to cognitive impairment. Our findings suggest that increased levels of inflammatory cytokines may be involved in MS fatigue. Investigation of cytokine profiles may increase the understanding of fatigue pathogenesis in MS.
Heim C, Wagner D, Maloney E, Papanicolaou DA, Solomon L, Jones JF, Unger ER, Reeves WC.	Viral Exanthems and Herpesvirus Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30322, USA.	Early adverse experience and risk for chronic fatigue syndrome: results from a population-based study.	Arch Gen Psychiatry. 2006 Nov;63(11):1258-66.	CONTEXT: Chronic fatigue syndrome (CFS) is an important public health problem. The causes of CFS are unknown and effective prevention strategies remain elusive. A growing literature suggests that early adverse experience increases the risk for a range of negative health outcomes, including fatiguing illnesses. Identification of developmental risk factors for CFS is critical to inform pathophysiological research and devise targets for primary prevention. OBJECTIVE: To examine the relationship between early adverse experience and risk for CFS in a population-based sample of clinically confirmed CFS cases and nonfatigued control subjects. DESIGN, SETTING, AND PARTICIPANTS: A case-control study of 43 cases with current CFS and 60 nonfatigued controls identified from a general population sample of 56 146 adult residents from Wichita, Kan. MAIN OUTCOME MEASURES: Self-reported childhood trauma (sexual, physical, and emotional abuse and emotional and physical neglect) and psychopathology (depression, anxiety, and posttraumatic stress disorder) by CFS status. RESULTS: The CFS cases reported significantly higher levels of childhood trauma and psychopathology compared with the controls. Exposure to childhood trauma was

	cmheim@emory.edu			associated with a 3- to 8-fold increased risk for CFS across different trauma types. There was a graded relationship between the degree of trauma exposure and CFS risk. Childhood trauma was associated with greater CFS symptom severity and with symptoms of depression, anxiety, and posttraumatic stress disorder. The risk for CFS conveyed by childhood trauma increased with the presence of concurrent psychopathology. CONCLUSIONS: This study provides evidence of increased levels of multiple types of childhood trauma in a population-based sample of clinically confirmed CFS cases compared with nonfatigued controls. Our results suggest that childhood trauma is an important risk factor for CFS. This risk was in part associated with altered emotional state. Studies scrutinizing the psychological and neurobiological mechanisms that translate childhood adversity into CFS risk may provide direct targets for the early prevention of CFS.
Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, Reeves WC, Lloyd A; Dubbo Infection Outcomes Study Group.	Brain and Mind Research Institute, Sydney University, Sydney, NSW 2050, Australia.	Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study.	BMJ. 2006 Sep 16;333(7568):575. Epub 2006 Sep 1.	OBJECTIVE: To delineate the risk factors, symptom patterns, and longitudinal course of prolonged illnesses after a variety of acute infections. DESIGN: Prospective cohort study following patients from the time of acute infection with Epstein-Barr virus (glandular fever), Coxiella burnetii (Q fever), or Ross River virus (epidemic polyarthritis). SETTING: The region surrounding the township of Dubbo in rural Australia, encompassing a 200 km geographical radius and 104,400 residents. PARTICIPANTS: 253 patients enrolled and followed at regular intervals over 12 months by self report, structured interview, and clinical assessment. OUTCOME MEASURES: Detailed medical, psychiatric, and laboratory evaluations at six months to apply diagnostic criteria for chronic fatigue syndrome. Premorbid and intercurrent illness characteristics recorded to define risk factors for chronic fatigue syndrome. Self reported illness phenotypes compared between infective groups. RESULTS: Prolonged illness characterised by disabling fatigue, musculoskeletal pain, neurocognitive difficulties, and mood disturbance was evident in 29 (12%) of 253 participants at six months, of whom 28 (11%) met the diagnostic criteria for chronic fatigue syndrome. This post-infective fatigue syndrome phenotype was stereotyped and occurred at a similar incidence after each infection. The syndrome was predicted largely by the severity of the acute illness rather than by demographic, psychological, or microbiological factors. CONCLUSIONS: A relatively uniform post-infective fatigue syndrome persists in a significant minority of patients for six months or more after clinical infection with several different viral and non-viral micro-organisms. Post-infective fatigue syndrome is a valid illness model for investigating one pathophysiological pathway to chronic fatigue syndrome.
Hines CH, Leonard A. Jason, Susan R. Torres-Harding		Reliability of a Chronic Fatigue Syndrome Questionnaire	Journal of Chronic Fatigue Syndrome 2006; 13(4): 45-71	Background: A diagnostic instrument, the CFS Questionnaire, was developed for clinicians and researchers to administer to their patients as a screening instrument for CFS. The CFS Questionnaire is comprehensive, covering the inclusionary and exclusionary self-report criteria of the current U.S. case definition (Fukuda et al. 199). The instrument also assesses past and current activity levels, and symptoms of post-exertional malaise to ensure these items are adequately assessed. Objectives: The goal of the present study was to evaluate the diagnostic reliability of an experimental measure for assessing chronic fatigue syndrome (CFS). Methods: This instrument was administered to 15 persons with CFS, 15 persons with major depressive disorder (MDD), and 15 controls. Using the Fukuda et al. (1994) diagnostic criteria, raters independently reviewed participants' CFS Questionnaire responses and rated whether each study participant met criteria for chronic fatigue syndrome. Results: This instrument demonstrated good inter-rater reliability. Further, this instrument demonstrated adequate

				classification accuracy, with a 9.3 positive likelihood ratio and a .08 negative likelihood ratio. Overall, the CFS Questionnaire demonstrated good test-retest reliability, with intra-class correlation coefficients and kappa coefficients at .70 or higher for most items. Lower test-retest reliability coefficients were found for some items assessing temporal symptoms or items requiring an estimate of time. Conclusion: The present study suggests that the CFS Questionnaire is a reliable diagnostic tool. Use of the CFS Questionnaire should promote higher levels of diagnostic reliability because it allows for accurate classification of individuals with CFS
Horng-Shiuann Wu HS, Mengel MB.		Unexplained Prolonged Fatigue in Primary Care	Journal of Chronic Fatigue Syndrome 2006;13(1): 15-34	Background: Unexplained prolonged fatigue (UPF) is one of the most common complaints in primary care. UPF is difficult to manage because of its nonspecific nature and unknown mechanism. UPF frequently frustrates health care professionals and has negative impacts on the physician-patient relationship. Although it is nonfatal, fatigueassociated functional impairments and economic consequences are substantial, negatively impacting patients' quality of life. Objectives: To evaluate current knowledge development of UPF and to help focus the direction of future investigations. Methods: A literature review was undertaken with the MEDLINE databases chosen as the primary electronic resources to retrieve the literature. Results: Current understanding of UPF is limited. Lack of consistent scientific language is a major problem. There is no consensus about the case definition of UPF even for the most widely studied chronic fatigue syndrome (CFS). Various sets of classification have been developed, each with similar but not identical criteria. Clinicians are dubious about perceiving fatigue as a clinical entity and ignore the diagnosis criteria. Many more patients are excluded than included from the current classifications and lack appropriate evaluation and treatment. The predisposing factors are not well established with the exception of being female and relatively young. Laboratory testing and immune and endocrine abnormalities are inconsistent in determining the causes. Psychological and social factors play an important but inconclusive role in mediating fatigue status. Conclusions: The high prevalence, persistence, and disability-associated consequences of UPF warrant more attention. Further investigations of the symptoms, psychosocial-based symptom experiences, and a search for effective management are needed. Keywords: Unexplained fatigue, prolonged fatigue, primary care
Hoseini SS, Gharibzadeh S.		Anakinra: a potential treatment for chronic fatigue syndrome.	Med Hypotheses. 2006;67(1):196-7. Epub 2006 Mar 13.	
Huibers MJ, Leone SS, Kant IJ, Knottnerus JA.	Department of Medical, Clinical and Experimental Psychology, Maastricht University, Maastricht, Netherlands.	Chronic fatigue syndrome-like caseness as a predictor of work status in fatigued employees on sick leave: four year follow up study.	Occup Environ Med. 2006 Aug;63(8):570-2. Epub 2006 May 12.	OBJECTIVE: To assess whether CFS-like caseness (meeting the criteria for chronic fatigue syndrome (CFS)) predicts work status in the long term. METHODS: Prospective study in a sample of fatigued employees absent from work. Data were collected at baseline and four years later, and included CFS-like caseness and work status (inactive work status and full work incapacity). RESULTS: CFS-like cases at baseline were three times more likely to be unable to work at follow up than fatigued employees who did not meet CFS criteria at baseline (ORs 3-3.3). These associations grew even stronger when demographic and clinical confounders were controlled for (ORs 3.4-4.4). CONCLUSION: A CFS-like status (compared to non-CFS fatigue) proved to be a strong predictor of an inactive work status and

	m.huibers@dmkep.unimaas.nl			full work incapacity in the long term. Since little is known about effective interventions that prevent absenteeism and work incapacity or facilitate return to work in subjects with chronic fatigue, there is a great need for powerful early interventions that restore or preserve the ability to work, especially for workers who meet criteria for CFS.
Huibers MJ, Wessely S.	Department of Medical, Clinical & Experimental Psychology, Maastricht University, The Netherlands. m.huibers@dmkep.unimaas.nl	The act of diagnosis: pros and cons of labelling chronic fatigue syndrome.	Psychol Med. 2006 Jul;36(7):895-900. Epub 2006 Jan 10.	BACKGROUND: One of the many controversies surrounding chronic fatigue syndrome (CFS) is the possible impact of the diagnostic label: is it disabling or enabling? In this paper, we discuss the pros and cons of labelling CFS. METHOD: A narrative synthesis of the literature. RESULTS: Diagnosed CFS patients have a worse prognosis than fatigue syndrome patients without such a label. The ways in which CFS patients perceive themselves, label their symptoms and appraise stressors may perpetuate or exacerbate their symptoms, a process that involves psychological, psychosocial and cultural factors. Labels can also lead to conflicts with doctors who fear diagnosis might lead to worse outcomes. However, on the other hand, finding a label that fits one's condition can provide meaning, emotional relief and recognition, whilst the denial of the diagnosis of CFS in those who have already reached their own conclusion can be very counter productive. The act of diagnosis therefore seems to be a trade-off between empowerment, illness validation and group support, contrasted with the risk of diagnosis as self-fulfilling prophecy of non-recovery. CONCLUSIONS: The answer to the question of 'to label or not to label' may turn out to depend not on the label, but on what that label implies. It is acceptable and often beneficial to make diagnoses such as CFS, provided that this is the beginning, and not the end, of the therapeutic encounter.
Hunsaker DH, Riffenburgh RH.	Department of Otolaryngology, Naval Medical Center San Diego, San Diego, California 92109, USA. tripwest@earthlink.net	Snoring significance in patients undergoing home sleep studies.	Otolaryngol Head Neck Surg. 2006 May;134(5):756-60.	OBJECTIVE: To analyze the impact of snoring, independent of obstructive sleep apnea syndrome on patients referred for home sleep studies and to report a new technology for the reporting of snoring, using sophisticated sound collection and noise-canceling technology. STUDY DESIGN AND SETTING: A retrospective statistical review of consecutive anonymous data compiled from questionnaires and digital data of snoring loudness and duration measured at the upper lip during unattended home sleep studies in 4,860 patients referred for snoring and sleep-disturbed breathing. RESULTS: A strong relationship exists between a history of snoring and complaints of daytime sleepiness (80%), obesity (73%), and chronic fatigue (78%) (all yield P<0.001). By contrast, only 42% to 48% of patients without these symptoms complain of snoring. In 3 multiple-regression analyses, the percent of time snoring, average loudness, and peak loudness are all significantly predicted by the apnea hypopnea index (all P<0.003), body mass index (all P<0.001), and age (P=0.014). Daytime sleepiness was strongly predicted by percent time snoring (P=0.014), weakly by average loudness (P=0.046), and not at all by peak loudness (P=0.303). CONCLUSION: By using a pair of microphones placed at the upper lip, one that samples breath sounds and the other ambient sound and artifact noise, the NovaSOM QSG measures snoring while canceling ambient noise. The clinical impact of snoring on the patient as well as the bed partner, independent of obstructive sleep apnea syndrome, is an unrecognized factor in sleep-disturbed breathing. SIGNIFICANCE: Measurable criteria to define snoring are suggested. Snoring loudness is not measured in most laboratory Polysomnograms. EBM rating: B-3b.
Hyland ME, Sodergren SC, Lewith GT.	School of Psychology, University of	Chronic fatigue syndrome: the role of positivity to	J Health Psychol. 2006 Sep;11(5):731-41.	Fifty-three chronic fatigue syndrome patients treated at a complementary medical centre were assessed over 12 months. Measures included the Chalder Fatigue scale, the General Health Questionnaire (GHQ) and positivity in illness (Silver Lining Questionnaire, SLQ). The SLQ measured at 6

	Plymouth, Plymouth, UK. mhyland@plymouth.ac.uk	illness in chronic fatigue syndrome patients.		and 9 months predicted (p < .01) mental (but not physical) fatigue at 12 months independently of current mental fatigue, initial mental fatigue, duration since diagnosis and time between start of treatment and entry to the study. The GHQ did not predict fatigue at any time point. The results suggest that a caring therapeutic intervention increases positive interpretations of illness prior to improvements in mental fatigue, but that positivity does not play a causal role in the reduction of fatigue.
Hyland ME, Sodergren SC, Lewith GT.	University of Plymouth, UK. mhyland@plymouth.ac.uk.	Chronic fatigue syndrome: the role of positivity to illness in chronic fatigue syndrome patients.	J Health Psychol. 2006 Sep;11(5):731-41.	Fifty-three chronic fatigue syndrome patients treated at a complementary medical centre were assessed over 12 months. Measures included the Chalder Fatigue scale, the General Health Questionnaire (GHQ) and positivity in illness (Silver Lining Questionnaire, SLQ). The SLQ measured at 6 and 9 months predicted (p < .01) mental (but not physical) fatigue at 12 months independently of current mental fatigue, initial mental fatigue, duration since diagnosis and time between start of treatment and entry to the study. The GHQ did not predict fatigue at any time point. The results suggest that a caring therapeutic intervention increases positive interpretations of illness prior to improvements in mental fatigue, but that positivity does not play a causal role in the reduction of fatigue.
Hyland ME, Whalley B.		Chronic fatigue syndrome.	Comment on: Lancet. 2006 Jan 28;367(9507):346-55. Lancet. 2006 May 13;367(9522):1573-4; author reply 1575.	
Iasiukiavichene L, Vasiliauskas D.		[Chronic fatigue syndrome in cardiology neurohumoral changes] [Article in Russian]	Kardiologiia. 2006;46(1):58-64.	Chronic fatigue markedly worsens quality of life of cardiological patients. Chronic fatigue and chronic fatigue syndrome are neuro-immuno-endocrine disorders which manifest as moderate and severe even invalidizing fatigue with psychosomatic symptoms. External and internal stress such as psychological stress, stress after major surgery and trauma, depressive states, inadequate physical exercise, chronic heart failure, chronic viral infection, oncologic diseases, -- can promote development of chronic fatigue. Immune and hypothalamic-pituitary-adrenal (HPA) axis abnormalities were found to be associated with this condition. Measurement of plasma cortisol concentration is used as basic characteristic of HPA axis function. Measures aimed at detection of chronic fatigue in cardiological patients and its appropriate management should supplement programs of integrated rehabilitation in order to improve quality of life and facilitate return to work.
Ismail K, Lewis G.	Department of Psychological Medicine, Institute of Psychiatry, King's College London, Weston Education Centre,	Multi-symptom illnesses, unexplained illness and Gulf War Syndrome.	Philos Trans R Soc Lond B Biol Sci. 2006 Apr 29;361(1468):543-51.	Explanatory models for the increased prevalence of ill health in Gulf veterans compared to those not deployed to the Gulf War 1990-1991 remain elusive. This article addresses whether multi-symptom reporting in Gulf veterans are types of medically unexplained symptoms and whether the alleged Gulf War Syndrome is best understood as a medically unexplained syndrome. A review of the epidemiological studies, overwhelmingly cross-sectional, describing ill health was conducted including those that used factor analysis to search for underlying or latent clinical constructs. The overwhelming evidence was that symptoms in Gulf veterans were either in keeping with currently defined psychiatric

	UK. k.ismail@iop.kcl.ac.uk			disorders such as depression and anxiety or were medically unexplained. The application of factor analysis methods had varied widely with a risk of over interpretation in some studies and limiting the validity of their findings. We concluded that ill health in Gulf veterans and the alleged Gulf War Syndrome is best understood within the medically unexplained symptoms and syndromes constructs. The cause of increased reporting in Gulf veterans are still not clear and requires further inquiry into the interaction between sociological factors and symptomatic distress.
Ito N, Nagai T, Yabe T, Nunome S, Hanawa T, Yamada H.	Kitasato Institute for Life Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108-8641, Japan.	Antidepressant-like activity of a Kampo (Japanese herbal) medicine, Koso-san (Xiang-Su-San), and its mode of action via the hypothalamic-pituitary-adrenal axis.	Phytomedicine. 2006 Nov;13(9-10):658-67. Epub 2006 Mar 3.	Koso-san (Xiang-Su-San in Chinese), a Kampo (Japanese herbal) medicine, is used clinically in East Asia for the treatment of depression-like symptoms associated with the initial stage of the common cold, allergic urticaria due to food ingestion, irritable bowel syndrome, chronic fatigue syndrome, insomnia, and autonomic imbalance. However, the antidepressant-like activity of Koso-san has never been evaluated scientifically. In this study, ddY mice subjected to a combination of forced swimming and chronic mild stresses were termed depression-like model mice. The degree of the depression-like state was measured by the animal's duration of immobility using the forced swimming test (FST). Oral administration of Koso-san (1.0 g/kg/body wt./day, 9 days) significantly shortened the duration of immobility of the depression-like model mice in the FST; however, locomotor activity was not affected. Hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis plays an important role in the pathophysiology of depression. Levels of corticotropin-releasing hormone mRNA expression in the hypothalamus and proopiomelanocortin mRNA expression in the pituitary were significantly increased, and glucocorticoid receptor protein expression in the hypothalamus paraventricular nucleus was downregulated in the depression-like model mice. However, Koso-san ameliorated these alterations to the normal conditions. The results of this study suggest that Koso-san shows the antidepressant-like effect through suppressing the hyperactivity of the HPA axis in depression-like model mice.
Jackson JL, O'Malley PG, Kroenke K.	Department of Medicine, Uniformed Services University of Health Sciences, Bethesda, MD 20814, USA. jejackson@usuhs.mil	Antidepressants and cognitive-behavioral therapy for symptom syndromes.	CNS Spectr. 2006 Mar;11(3):212-22.	Somatic symptoms are common in primary care and clinicians often prescribe antidepressants as adjunctive therapy. There are many possible reasons why this may work, including treating comorbid depression or anxiety, inhibition of ascending pain pathways, inhibition of prefrontal cortical areas that are responsible for "attention" to noxious stimuli, and the direct effects of the medications on the syndrome. There are good theoretical reasons why antidepressants with balanced norepinephrine and serotonin effects may be more effective than those that act predominantly on one pathway, though head-to-head comparisons are lacking. For the 11 painful syndromes review in this article, cognitive-behavioral therapy is most consistently demonstrated to be effective, with various antidepressants having more or less randomized controlled data supporting or refuting effectiveness. This article reviews the randomized controlled trial data for the use of antidepressant and cognitive-behavior therapy for 11 somatic syndromes: irritable bowel syndrome, chronic back pain, headache, fibromyalgia, chronic fatigue syndrome, tinnitus, menopausal symptoms, chronic facial pain, noncardiac chest pain, interstitial cystitis, and chronic pelvic pain. For some syndromes, the data for or against treatment effectiveness is relatively robust, for many, however, the data, one way or the other is scanty.
Janal MN, Ciccone DS, Natelson BH.	Fatigue Research Center and	Sub-typing CFS patients on the	Biol Psychol. 2006 Aug;73(2):124-31.	The diagnosis of chronic fatigue syndrome (CFS), an illness characterized by medically unexplained fatigue, depends on a clinical case definition representing one or more pathophysiological

	Department of Psychiatry, New Jersey Medical School, BHSB-F1522, Box 1709, University of Medicine and Dentistry of New Jersey, Newark, NJ 07101, United States.	basis of 'minor' symptoms.	Epub 2006 Feb 10.	mechanisms. To prepare for studies of these mechanisms, this study sought to identify subtypes of CFS. In 161 women meeting 1994 criteria for CFS, principal components analysis of the 10 'minor' symptoms of CFS produced three factors interpreted to indicate musculoskeletal, infectious and neurological subtypes. Extreme scores on one or more of these factors characterized about 2/3 of the sample. Those characterized by the neurological factor were at increased risk of reduced scores on cognitive tests requiring attention, working memory, long-term memory or rapid performance. In addition, the neurological subtype was associated with reduced levels of function. Those characterized by the musculoskeletal factor were at increased risk for the diagnosis of fibromyalgia (chronic widespread pain and mechanical allodynia) and reduced physical function. Those characterized by the infectious factor were less likely to evidence co-occurring fibromyalgia, and showed lesser risk of functional impairment. The prevalence of disability was increased in those with the highest scores on any of the subtypes, as well as in those with high scores on multiple factors. Depression and anxiety, while frequently present, were not more prevalent in any particular subtype, and did not increase with the severity of specific symptom reports. Results suggest that subtypes of CFS may be identified from reports of the minor diagnostic symptoms, and that these subtypes demonstrate construct validity.
Jason LA, Bell DS, Row J, Van Hoof EL, Jordan K, Lapp C, Gurwitt A, Miike T, Torres-Harding S, De Meirleir K.		A Pediatric Case Definition for Myalgic Encephalomyelitis and Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 1-44	For a diagnosis chronic fatigue syndrome (CFS), most researchers use criteria that were developed by Fukuda et al. (1994), with modifications suggested by Reeves et al. (2003). However, this case definition was established for adults rather than children. A Canadian Case Definition (ME/CFS; Myalgic Encephalomyelitis/CFS) has recently been developed, with more specific inclusion criteria (Carruthers et al., 2003). Again, the primary aim of this case definition is to diagnose adult CFS. A significant problem in the literature is the lack of both a pediatric definition of ME/CFS and a reliable instrument to assess it. These deficiencies can lead to criterion variance problems resulting in studies labeling children with a wide variety of symptoms as having ME/CFS. Subsequently, comparisons between articles become more difficult, decreasing the possibility of conducting a meta-analysis. This article presents recommendations developed by the International Association of Chronic Fatigue Syndrome Pediatric Case Definition Working group for a ME/CFS pediatric case definition. It is hoped that this pediatric case definition will lead to more appropriate identification of children and adolescents with ME/CFS.
Jason LA, Corradi K, Gress S, Williams S, Torres-Harding S.	DePaul University, Chicago, IL 60614, USA. Ljason@depaul.edu	Causes of death among patients with chronic fatigue syndrome.	Health Care Women Int. 2006 Aug;27(7):615-26.	Chronic fatigue syndrome (CFS) is a debilitating illness affecting thousands of individuals. At the present time, there are few studies that have investigated causes of death for those with this syndrome. The authors analyzed a memorial list tabulated by the National CFIDS Foundation of 166 deceased individuals who had had CFS. There were approximately three times more women than men on the list. The three most prevalent causes of death were heart failure, suicide, and cancer, which accounted for 59.6% of all deaths. The mean age of those who died from cancer and suicide was 47.8 and 39.3 years, respectively, which is considerably younger than those who died from cancer and suicide in the general population. The implications of these findings are discussed.
Jerjes WK, Peters TJ, Taylor NF, Wood PJ, Wessely	Department of Clinical Biochemistry,	Diurnal excretion of urinary cortisol, cortisone, and	J Psychosom Res. 2006 Feb;60(2):145-53.	OBJECTIVE: The aim of this study was to obtain comprehensive information on basal hypothalamic-pituitary-adrenal (HPA) axis activity in chronic fatigue syndrome (CFS) patients who were not affected by medication or comorbid psychiatric disorder likely to influence the HPA axis. METHOD: Steroid

S, Cleare AJ.	Guy's, King's and St Thomas' School of Medicine, Bessemer Road, SE5 9RS London, UK. jerjes@kcl.ac.uk	cortisol metabolites in chronic fatigue syndrome.	Comment in: J Psychosom Res. 2006 Jun;60(6):627-8; author reply 629.	analysis of urine collections from 0600 to 2100 h at 3-h intervals in CFS patients and in controls. RESULTS: Urinary free cortisol and cortisone concentrations showed a significant normal diurnal rhythm, but levels were lower across the cycle in CFS. In contrast, while urinary cortisol metabolites also showed a normal diurnal rhythm, levels were not significantly different between the CFS and controls at any time. Derived metabolite ratios were similar in both groups. CONCLUSION: This study provides further evidence for reduced basal HPA axis function in patients with CFS, based on lower free cortisol and cortisone levels, but this is not corroborated by cortisol metabolite data. The difference between these measures cannot be explained by an altered timing of the diurnal rhythm.
Jerjes WK, Taylor NF, Peters TJ, Wessely S, Cleare AJ.	Department of Clinical Biochemistry, Guy's, King's and St. Thomas' School of Medicine, King's College London, UK. walid.jerjes@kcl.ac.uk	Urinary cortisol and cortisol metabolite excretion in chronic fatigue syndrome.	Psychosom Med. 2006 Jul-Aug;68(4):578-82.	OBJECTIVES: Reduced basal hypothalamic-pituitary-adrenal (HPA) axis output in chronic fatigue syndrome (CFS) has been inferred from low cortisol levels in blood, saliva, and urine in some studies. Because > 95% of cortisol is metabolized before excretion, we assessed cortisol output by assay of both cortisol metabolites and free cortisol in 24-hour urine collections and also investigated sex differences in these between CFS and control groups. METHOD: We calculated total urinary cortisol metabolites (TCM) and cortisol metabolite ratios from individual steroid data in 40 patients (20 males and 20 females) with CFS who were free of medication or comorbid psychiatric disorder likely to influence the HPA axis. Results were compared with those of 40 healthy volunteers (20 males and 20 females) well matched for age and body mass index. Data for free cortisol was obtained on 28 of the patients and 27 of the controls. RESULTS: The mean of TCM and cortisol metabolite ratios was not significantly different between patients and controls for either sex ($p > .05$ for all parameters). Previously established sex differences were confirmed in our controls and were found to be similar in CFS for TCM and the ratios 11OH/11OXO, 5alpha/5beta THF, and 20OH/20OXO (see text) ($p < .005$, $p < .05$, $p < .05$, and $p < .005$, respectively). Urinary free cortisol values were numerically (but not statistically) lower in patients with CFS than controls, and correlated inversely with fatigue levels in patients. CONCLUSION: The finding of normal urinary cortisol metabolite excretion in patients with CFS is at variance with earlier reports that CFS is a hypocortisolemic state. If serum and saliva cortisol levels are lower in CFS, this would suggest that metabolic clearance of cortisol is faster in patients with CFS than controls. This study also demonstrates that sex differences must be taken into account when interpreting results in patients with CFS.
Jones G, Godlee F.		Chronic Fatigue Syndrome: Editorial Bias in the British Medical Journal. Letter	Journal of Chronic Fatigue Syndrome 2006;13(1): 69-70	
Jonker K, van Hemert AM.	Parnassiagroep-PsyQ, afd Somatiek en Psyche, Den Haag.	[Treatment of patients with the chronic-fatigue syndrome] [Article in Dutch]	Ned Tijdschr Geneeskd. 2006 Sep 23;150(38):2067-8. Comment on: Ned Tijdschr Geneeskd. 2006 Sep	In the last few years, the chronic-fatigue syndrome has been recognised as an important health problem. In a recent report, the Health Council of the Netherlands suggested that the capacity for treatment be increased. Cognitive behavioural therapy and graded exercise training are treatment options of first choice. A recently published, uncontrolled evaluation of a Dutch clinical rehabilitation programme based partly on these methods proved to be successful. Unfortunately, due to the uncontrolled character of the study, it remains unclear which elements in the treatment were responsible for the success. Which patients should be included in a costly clinical rehabilitation

			23;150(38):2088-94.	programme also remains unclear. More in general, there is room for empirical studies of treatment allocation, not in the least because of the frequently occurring comorbidity. Good progress has been made in the treatment of the chronic-fatigue syndrome, but we are still far removed from evidence-based, stepped care, treatment programmes.
Jordan KM, Jason LA, Mears CJ, Katz BZ, Rademaker A, Huang CF, Richman J, McCready W, Ayers PM, Taylor KK		Prevalence of Pediatric Chronic Fatigue Syndrome in a Community-Based Sample	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 75-77	No abstract available
Kaiser J.		Biomedicine. Genes and chronic fatigue: how strong is the evidence?	Science. 2006 May 5;312(5774):669-71.	
Katafuchi T, Kondo T, Take S, Yoshimura M.	Department of Integrative Physiology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, 812-8582, Japan. kataf@physiol.med.kyushu-u.ac.jp	Brain cytokines and the 5-HT system during poly I:C-induced fatigue.	Ann N Y Acad Sci. 2006 Nov;1088:230-7.	Fatigue is evoked not only by peripheral factors, such as muscle fatigue, but also by the central nervous system (CNS). For example, it is generally known that the feeling of fatigue is greatly influenced by psychological aspects, such as motivation. However, little is known about the central mechanisms of fatigue. The clinical symptoms of chronic fatigue syndrome (CFS) are shown to include disorders in neuroendocrine, autonomic, and immune systems. On the other hand, it has been demonstrated that cytokines produced in the brain play significant roles in neural-immune interactions through their various central actions, including hypothalamo-pituitary and sympathetic activation, as well as immunosuppression. In this article, using the immunologically induced fatigue model, which was achieved by intraperitoneal (i.p.) injection of synthetic double-stranded RNAs, polyriboinosinic: polyribocytidylic acid (poly I:C) in rats, we show an involvement of brain interferon-alpha (IFN-alpha) and serotonin (5-HT) transporter (5-HTT) in the central mechanisms of fatigue. In the poly I:C-induced fatigue rats, expression of IFN-alpha and 5-HTT increased, while extracellular concentration of 5-HT in the medial prefrontal cortex decreased, probably on account of the enhanced expression of 5-HTT. Since the poly I:C-induced reduction of the running wheel activity was attenuated by a 5-HT(1A) receptor agonist, but not by 5-HT(2), 5-HT(3), or dopamine D(3) receptor agonists, it is suggested that the decrease in 5-HT actions on 5-HT(1A) receptors may at least partly contribute to the poly I:C-induced fatigue.
Kato K, Sullivan PF, Evengard B, Pedersen NL.	Department of Medical Epidemiology and Biostatistics, Karolinska University Hospital	Premorbid predictors of chronic fatigue.	Arch Gen Psychiatry. 2006 Nov;63(11):1267-72.	CONTEXT: Chronic fatigue syndrome is a disabling problem characterized by persistent fatigue lasting at least 6 months with a number of ancillary symptoms. Although the etiology of chronic fatiguing illness is unknown, some evidence suggests that stress may confer increased risk for development of the disorder. Moreover, subjects with chronic fatiguing illness may have distinctive personality traits, although this finding could reflect confounding by other mechanisms. OBJECTIVE: To assess the prospective association of premorbid self-reported stress and personality with chronic fatigue-like

	Huddinge, Karolinska Institutet, Stockholm, Sweden.			illness. DESIGN: Prospective nested case-control study in a population-based sample. SETTING: General community. PARTICIPANTS: From the Swedish Twin Registry, 19,192 twins born between January 1, 1935, and December 31, 1958. MAIN OUTCOME MEASURES: Information about current chronic fatiguing illnesses was obtained from computer-assisted telephone interviews conducted between 1998 and 2002. Self-reported stress (based on a single question) and personality scales (emotional instability and extraversion in the Eysenck Personality Inventory) were measured from 1972 to 1973 by a mailed questionnaire. Relative risks were estimated with case-control analyses (matched for age and sex) and co-twin control analyses (comparing discordant pairs). RESULTS: Higher emotional instability and self-reported stress in the premorbid period were associated with higher risk for chronic fatigue-like illness in matched case-control analyses (odds ratios, 1.72 and 1.64, respectively). In co-twin control analyses, relative risk of emotional instability decreased to 1.02 whereas that of stress increased considerably to 5.81. There was no association between extraversion and fatigue. CONCLUSIONS: Elevated premorbid stress is a significant risk factor for chronic fatigue-like illness, the effect of which may be buffered by genetic influences. Emotional instability assessed 25 years earlier is associated with chronic fatigue through genetic mechanisms contributing to both personality style and expression of the disorder. These findings suggest plausible mechanisms for chronic fatiguing illness.
Kato K, Sullivan PF, Evengard B, Pedersen NL.	Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, SE-171 77 Stockholm, Sweden. Kenji.Kato@ki.se	Chronic widespread pain and its comorbidities: a population-based study.	Arch Intern Med. 2006 Aug 14-28;166(15):1649-54.	BACKGROUND: Chronic widespread pain (CWP), the cardinal symptom of fibromyalgia, is prevalent and co-occurs with numerous symptom-based conditions such as chronic fatigue syndrome, joint pain, headache, irritable bowel syndrome, and psychiatric disorders. Few studies have examined the comorbidities of CWP in the general population. Furthermore, little is known about the importance of familial (genetic and family environmental) factors in the etiology of co-occurrence. METHODS: Data were obtained from 44 897 individuals in the Swedish Twin Registry via computer-assisted telephone interview from 1998 through 2002 (age >/=42 years; 73.2% response rate). Screening for CWP was based on the American College of Rheumatology criteria without clinical evaluation. Measures for comorbidities were based on standard criteria when available. Odds ratios (ORs) were calculated in case-control and co-twin control designs to assess the effect of familial confounding in the associations. RESULTS: Considerable co-occurrences were found in CWP cases for chronic fatigue (OR, 23.53; 95% confidence interval [CI], 19.67-28.16), joint pain (OR, 7.41; 95% CI, 6.70-8.21), depressive symptoms (OR, 5.26; 95% CI, 4.75-5.82), and irritable bowel syndrome (OR, 5.17; 95% CI, 4.55-5.88). In co-twin control analyses, ORs were no longer significant for psychiatric disorders, whereas they decreased but remained significant for most other comorbidities. No changes in ORs were observed for headache. CONCLUSIONS: Associations between CWP and most comorbidities are mediated by unmeasured genetic and family environmental factors in the general population. The extent of mediation via familial factors is likely to be disorder specific.
Kaufman FR, Goodnick PJ		Depression, Chronic Fatigue Syndrome, and Fibromyalgia: An Update	Journal of Chronic Fatigue Syndrome 2006; 13(4): 83-112	Centers for Disease Control criteria for chronic fatigue syndrome (CFS) specifically recognize that patients can have both CFS and depression. The clinician's challenge is to judge for each individual patient whether the complaint of fatigue is primarily depression, physical illness, such as CFS, or a combination of both. This review differentiates CFS and fibromyalgia, discussed as "chronic fatigue syndrome and related immune deficiency syndromes" (CFIDS), from depression in terms of physical

				signs, symptoms, biological parameters, brain imaging, immunology, and treatment. The review focuses on practical applications of research findings with a further focus on future ability to show clear biologic separation and specific treatment. When depressive symptoms exist with those of CFS, accurate differentiation can usually be accomplished by focusing on diagnostic criteria. Presence of multiple physical signs and symptoms of CFIDS may be of great value. In terms of laboratory testing, a single helpful test may be measuring the plasma cortisol, which is usually high in depression and low in CFS. Future research should focus on the combination of plasma cortisol with an index of serotonin function, which is high in CFIDS and low in depression. Additional research should focus on neuroimaging and immune differentiation. Combination of multiple tests should result in a significant and clinically useful separation between CFIDS and major depressive disorder (MDD). In treating patients with significant depression or MDD with CFIDS, one should think of the noradrenergic approach using bupropion or low-dose tricyclic antidepressants in combination with a selective serotonin reuptake inhibitor, especially sertraline, to aid improvement of global, pain, and immunologic parameters. Alternatively, serotonin norepinephrine reuptake inhibitors (venlafaxine and duloxetine) should be considered. Future treatment research should focus on larger placebo-controlled, double-blind trials of these and other antidepressants as well as the evaluation of psychostimulants, electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS).
Kaufman KR, Goodnick PJ.		Depression, Chronic Fatigue Syndrome and Fibromyalgia An Update	Journal of Chronic Fatigue Syndrome 2006;13(4):	No abstract available at September 2006
Kelsall H, Sim M, McKenzie D, Forbes A, Leder K, Glass D, Ikin J, McFarlane A.	Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Victoria, Australia. helen.kelsall@med.monash.edu.au	Medically evaluated psychological and physical health of Australian Gulf War veterans with chronic fatigue.	J Psychosom Res. 2006 Jun;60(6):575-84.	OBJECTIVE: The aim of this study was to evaluate fatigue in Australian Gulf War veterans and a military comparison group according to the 1994 chronic fatigue syndrome (CFS) definition and investigate the relation with exposures. METHODS: Comprehensive medical, psychological and reported exposure assessments of 1,456 veterans and 1,588 comparison group in a cross-sectional study. RESULTS: More Gulf War veterans had fatigue at all levels than did the military comparison group. The findings may be at least partly explained as an "active-deployment effect." The odds ratios increased with increasing clinical evaluation of the nature of the fatigue, even after adjustment for current psychiatric disorders in addition to other possible confounding factors. CONCLUSION: Medically unexplained chronic fatigue was more common, but not more disabling, in veterans than in the comparison group, but veterans with unexplained chronic fatigue had poorer health than veterans without. Within both populations, CFS is uncommon and at a similar level to the general community.
Kennedy G, Norris G, Spence V, McLaren M, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital	Is chronic fatigue syndrome associated with platelet activation?	Blood Coagul Fibrinolysis. 2006 Mar;17(2):89-92.	Chronic fatigue syndrome (CFS) is a debilitating condition that has no known aetiology or pathophysiology. Recent investigations by other workers have suggested that individuals with CFS may have a hypercoagulable state. This study investigated various aspects of platelet activation and function in 17 patients with CFS and in 16 age-matched and sex-matched healthy controls. Platelet aggregation, platelet volume and coagulation tests were performed. Platelet aggregation was investigated by means of the photometric changes using citrated platelet-rich plasma, whole blood

	& Medical School, Dundee, UK. g.y.kennedy@dundee.ac.uk			aggregation was calculated as the percentage fall in single platelet counts and the coagulation tests were performed on an automatic microcentrifugal analyser.A trend was observed for the patients to have lower aggregation results and a reduced mean platelet volume. However, this only reached statistical significance for one result; the rate of the aggregation slope by 1.0 microg/ml collagen [CFS patients, 18 (9-28) versus controls, 32.5 (19-36); Mann-Whitney U test, P = 0.029]. No significant differences were found for any of the measurements of coagulation.These results are in contrast to previously reported findings. However, due to the heterogeneous nature of the disease, and the resulting lifestyles of the patients, caution should be taken when comparing one group of patients with another. Nevertheless, we certainly found no evidence of increased platelet activation or of a hypercoagulable state in patients with CFS and, on the basis of these results, anti-platelet or anti-coagulant therapy is not warranted.
Kerr JR, Christian P, Hodgetts A, Langford PR, Devanur LD, Petty R, Burke B, Sinclair LI, Richards SC, Montgomery J, McDermott C, Harrison TJ, Kellam P, Nutt DJ, Holgate ST.	St George's University of London, United Kingdom.	Current research priorities in Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (CFS/ME): disease mechanisms, a diagnostic test and specific treatments.	J Clin Pathol. 2006 Aug 25; [Epub ahead of print]	Chronic fatigue syndrome (CFS) is an illness characterised by disabling fatigue of at least 6 months duration which is accompanied by various rheumatological, infectious and neuropsychiatric symptoms. A collaborative study group has been formed in order to address the current areas for development in CFS research, namely, to develop an understanding of the molecular pathogenesis of CFS, to develop a diagnostic test, and to develop specific and curative treatments. Various groups have studied the gene expression in peripheral blood of CFS patients and of those studies which have been confirmed using polymerase chain reaction (PCR), it is clear that the most predominant functional theme is that of immunity and defense. However, we do not yet know the precise gene signature and metabolic pathways involved. Currently, this is being addressed using a microarray representing 47,000 human genes and variants, massive parallel signature sequencing (MPSS) and real-time PCR. It will be important to ensure that once a gene signature has been identified, that it is specific to CFS and does not occur in other diseases and infections. A diagnostic test is being developed using Surface-Enhanced, Laser-Desorption and Ionisation - Time of Flight (SELDI-TOF) mass spectrometry following a pilot study in which putative biomarkers were identified. And, finally, clinical trials are being planned; novel treatments which we believe are important to trial in CFS patients are interferon-a and one of the anti-tumour necrosis factor-a drugs.
Kodama M, Kodama T.	Kodama Research Institute of Preventive Medicine, 50-5 Chiyogaoka, Chikusaku, Nagoya 464-0005, Japan.	Four problems with the clinical control of interstitial pneumonia, or chronic fatigue syndrome, using the megadose vitamin C infusion system with dehydroepiandrosterone-cortisol annex.	In Vivo. 2006 Mar-Apr;20(2):285-91.	Since 1996 in our clinic, the regular practice of megadose vitamin C infusion with dehydroepiandrosterone-cortisol annex and the continuous intake of erythromycin and chloramphenicol have been found useful for the clinical control of the autoimmune disease interstitial pneumonia, also known as chronic fatigue syndrome. The long-term use of these two systems for the treatment of the autoimmune disease has led to the emergence of four problems of theoretical or practical importance, as described below: i) Should maintenance of the above core treatments be continued for prophylactic purposes in the absence of acute signs of pneumonia? Evidence indicated that their use was essential to arrest the dynamic activity of an intrapulmonary bacterial colony in the immunodeficient host, and that the 5-year survival rate of interstitial pneumonia patients would have been worse without the prophylactic practice of the 2 treatments. ii) Evidence was presented to suggest that the activity of the intrapulmonary bacterial colony was becoming less responsive because of the emergence of a drug-resistent mutant bacterium. The introduction of new antibiotics (kanamycin) was found to improve the acute signs of pneumonia. iii) The bone marrow function of

				one male patient with interstitial pneumonia was found to decline during the observation period of 9 years. It was speculated that his bone marrow, like his lungs, was in the course of fibrosis. iv) One female patient was diagnosed with breast cancer in the course of interstitial pneumonia treatment--an example indicating that the persistence of an autoimmune disease in an elderly subject might be associated with the emergence of malignancy. Dehydroepiandrosterone was shown to promote the recovery of hepatic function in the course of cancer chemotherapy with cyclophosphamide. The beneficial effect of the adrenal androgen was dose-dependent. The significance of this finding is discussed in the light of the steroid carcinogenesis concept. The reasoning behind the view that interstitial pneumonia and chronic fatigue syndrome are one disease is also discussed.
Komaroff AL, Jacobson S, Ablashi DV, Yamanishi K.	Harvard Medical School, Boston, MA, USA.	Highlights from 5th International Conference on HHV-6 and -7.	Herpes. 2006 Nov;13(3):81-2.	This article reports on key presentations at the 5th International Conference on Human Herpesvirus (HHV)-6 and -7, organized by the HHV-6 Foundation. New assays for HHV-6 and -7 promise to be more accurate and better able to distinguish between HHV-6A and B or differentiate active from latent infection. Nevertheless, more research is needed to enhance the sensitivity and specificity of these assays. Cellular receptors for both HHV-6 and -7 have been identified. Both viruses have in vitro tropism for neurons and dendritic cells of the central nervous system (CNS), and their role in producing CNS disease in the immunocompromised (particularly transplant recipients and the HIV-infected) is well established. HHV-6 may enhance the progression of simian immunodeficiency virus in monkeys, as suggested by in vivo data. In immunocompetent children and adults, HHV-6 and/or -7 may play a role in triggering and perpetuating several diseases of the nervous system, namely encephalitis, multiple sclerosis, chronic fatigue syndrome and epilepsy.
Komaroff AL.	Division of General Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 10 Shattuck Street, Suite 602, Boston, MA 02115, USA.	Is human herpesvirus-6 a trigger for chronic fatigue syndrome?	J Clin Virol. 2006 Dec;37 Suppl 1:S39-46.	Chronic fatigue syndrome (CFS) is an illness currently defined entirely by a combination of non-specific symptoms. Despite this subjective definition, CFS is associated with objective underlying biological abnormalities, particularly involving the nervous system and immune system. Most studies have found that active infection with human herpesvirus-6 (HHV-6) - a neurotropic, gliotropic and immunotropic virus - is present more often in patients with CFS than in healthy control and disease comparison subjects, yet it is not found in all patients at the time of testing. Moreover, HHV-6 has been associated with many of the neurological and immunological findings in patients with CFS. Finally, CFS, multiple sclerosis and seizure disorders share some clinical and laboratory features and, like CFS, the latter two disorders also are being associated increasingly with active HHV-6 infection. Therefore, it is plausible that active infection with HHV-6 may trigger and perpetuate CFS in a subset of patients.
Komaroff AL.		By the way, doctor. I would be most grateful for information concerning chronic fatigue syndrome, a disorder from which I have suffered for the past 10 years. Do	Harv Health Lett. 2006 Aug;31(10):8.	

		you see any help on the horizon?		
Kondo K.	Department of Microbiology, The Jikei University School of Medicine.	[Chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2006 Mar;64 Suppl 3:490-5.	
Lapp CW		Recognizing Pediatric CFS in the Primary Care Practice: A Practicing Clinician's Approach This Article is	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 89-96	Pediatricians and primary care physicians may be uncomfortable diagnosing Chronic Fatigue Syndrome in children because a good diagnostic tool has not been available. Deferring a diagnosis, however, may lead to apprehension, over-utilization of medical resources in a search for validity, a delay in treatment, and possibly inappropriate coping techniques. This case-based article discusses symptoms and signs seen in adolescent patients with CFS, evaluation of suspect cases, and both current and future diagnostic case definitions
Le Bon O.	Unite du sommeil, Service de Psychiatrie, C.H.U. Brugmann.	[Chronic fatigue syndrome] [Article in French]	Rev Med Brux. 2006 Mar-Apr;27(2):S115-7.	
Leone SS, Huibers MJ, Kant I, van Amelsvoort LG, van Schayck CP, Bleijenberg G, Knottnerus JA.	Department of Epidemiology, Maastricht University, Maastricht, The Netherlands. stephanie.leone@epid.unimaas.nl	Long-term efficacy of cognitive-behavioral therapy by general practitioners for fatigue: a 4-year follow-up study.	J Psychosom Res. 2006 Nov;61(5):601-7.	OBJECTIVE: In an earlier study, we found that cognitive-behavioral therapy (CBT) delivered by general practitioners (GPs) for fatigue among employees on sick leave was not effective after 12 months. In this study we aim to assess the long-term efficacy of CBT by GPs for fatigue. It was hypothesized that the intervention could prevent deterioration as well as relapse of fatigue complaints and relapse into absenteeism in the long term. METHODS: Patients who participated in the original randomized controlled trial were followed up 4 years later. Fatigue and absenteeism were the main outcomes. RESULTS: Fatigue and absenteeism were high in the intervention and control groups at the 4-year follow-up. There was no significant difference between the intervention group and the control group on fatigue and absenteeism. The intervention group however tended toward less-favorable outcomes as compared with the control group. CONCLUSIONS: Like that of chronic fatigue syndrome, the prognosis of less-advanced fatigue is rather poor. CBT delivered by GPs is not effective in the long term.
Leone SS, Huibers MJ, Kant I, Van Schayck CP, Bleijenberg G, Andre Knottnerus J.	Department of Epidemiology, Maastricht University, The Netherlands. Stephanie.Leone@epid.unimaas.nl	Long-term predictors of outcome in fatigued employees on sick leave: a 4-year follow-up study.	Psychol Med. 2006 Sep;36(9):1293-300. Epub 2006 Jun 6.	BACKGROUND: Persistent fatigue is strongly associated with functional status and can lead to absenteeism and work disability. Despite several prognostic studies on chronic fatigue, little attention has been paid to occupational outcomes. METHOD: A total of 127 fatigued employees on sick leave were followed-up after 4 years to determine long-term predictors of work disability, fatigue caseness and chronic fatigue syndrome (CFS)-like caseness. Measures included fatigue, physical functioning, illness attributions, psychological problems and emotional exhaustion. RESULTS: Thirty-three participants (26%) were receiving work disability benefits at the 4-year follow-up. Older age and lower levels of physical functioning predicted work disability. Weaker psychological attributions and lower levels of physical functioning were predictors of fatigue caseness. CFS-like caseness was predicted by

				female gender and lower levels of physical functioning. Self-reported physical functioning remained a strong and statistically significant determinant of work disability [odds ratio (OR) 0.45, 95% confidence interval (CI) 0.24-0.87] and CFS-like caseness (OR 0.20, 95% CI 0.09-0.43) after controlling for confounders. CONCLUSIONS: This study suggests that physical functioning plays an important role in the persistence of fatigue complaints and work disability in employees on sick leave. The course of fatigue is a complex process, and exploring temporal relationships between fatigue, functional status and work status in future research could provide valuable information for the improvement of fatigue management.
Leppavuori A.	HYKS Psykiatrian klinikka, HUS. antero.leppavuori@hus.fi	[Chronic fatigue syndrome] [Article in Finnish]	Duodecim. 2006;122(5):545-53.	
Lin SM, Devakumar J, Kibbe WA.	Northwestern University, Robert H Lurie Cancer Center, Chicago, IL 60611, USA. S-Lin2@northwestern.edu	Improved prediction of treatment response using microarrays and existing biological knowledge.	Pharmacogenomics. 2006 Apr;7(3):495-501.	A desired application for microarrays in the clinic is to predict treatment response from an often diverse patient population. We present a method for analyzing microarray data that is predicated on biological pathway and function knowledge as opposed to a purely data-driven initial analysis. From an analysis perspective, this methodology takes advantage of information that is available across genes on a single array, as well as differences in those patterns across measurements. By using biological knowledge in the initial analysis, the accuracy and robustness of microarray profile classification is enhanced, especially when low numbers of samples are available. For clinical studies, particularly Phase I or I/II studies, this technique is exceptionally advantageous.
Lincoln AE, Helmer DA, Schneiderman AI, Li M, Copeland HL, Prisco MK, Wallin MT, Kang HK, Natelson BH.	War-Related Illness and Injury Study Center, Washington DC Veterans Affairs Medical Center, 50 Irving Street, NW, Washington, DC 20422, USA.	The war-related illness and injury study centers: a resource for deployment-related health concerns.	Mil Med. 2006 Jul;171(7):577-85.	Combat veterans often return from deployment having experienced a wide range of exposures, symptoms, and medical conditions. The Department of Veterans Affairs established war-related illness and injury study centers to serve combat veterans with unexplained illnesses. We report the exposures, clinical status, and utilization of 53 combat veterans who participated in the National Referral Program (NRP) from January 2002 until March 2004. Participants were primarily male (81%) and served in the Persian Gulf War (79%). Common diagnoses were chronic fatigue syndrome (n = 23, 43%), neurotic depression (n = 21, 40%), and post-traumatic stress disorder (n = 20, 38%). Self-reported exposures related to weaponry, disease prophylaxis, environmental hazards, stress, and poor hygiene. A small increase in mean SF-36V mental component scores (2.8 points, p = 0.009) and use of rehabilitation therapies (1.6 additional visits, p = 0.018) followed the NRP referral. The small gain in mental function suggests that the NRP may benefit combat veterans with long and complex medical histories.
Lindal E, Stefansson JG, Bergmann S.		The prevalence of chronic fatigue syndrome in Iceland--a national comparison by gender drawing on four different criteria.	Nord J Psychiatry. 2006;60(2):183.	

Lundell K, Qazi S, Eddy L, Uckun FM.	Parker Hughes Institute and Parker Hughes Clinics, St. Paul, MN 55113, USA.	Clinical activity of folinic acid in patients with chronic fatigue syndrome.	Arzneimittelforschung. 2006;56(6):399-404.	A high incidence of severe B-cell immunodeficiency and chronic reactivated Epstein-Barr virus (EBV) infection in patients with chronic fatigue syndrome (CFS) is reported herein. Of the 58 patients evaluated, 100% had evidence of prior EBV exposure and 72% had evidence for reactivated EBV infection. Notably, 94% of CFS patients had B-cell immunodeficiency with a marked depletion of their CD19+IgM+ mature B-lymphocyte population. A remarkable 81% of CFS patients experienced subjective improvement of their symptoms after treatment with folinic acid (CAS 58-05-9, leucovorin). The findings provide unprecedented evidence that CFS frequently is a folinic acid responsive clinical entity accompanied by B-cell immunodeficiency and inappropriate antibody responses to EBV.
Madhavan G, Stewart JM, McLeod KJ.	Department of Orthopaedics, School of Medicine, Health Sciences Center, State University of New York, Stony Brook, USA. guru@binghamton.edu	Cardiovascular systemic regulation by plantar surface stimulation.	Biomed Instrum Technol. 2006 Jan-Feb;40(1):78-84.	The decreased blood pressure and flow rates associated with orthostasis have been implicated in the etiology of numerous clinical conditions, including deep vein thrombosis, chronic fatigue syndrome, and more recently osteoporosis. Here, we investigate the potential of low-magnitude vibration, applied at the plantar surface, to inhibit the cardiovascular responses of adult women to the orthostatic stress associated with quiet sitting. METHODS: Thirty healthy women, aged 22-82 years, were exposed to a plantar-based vibration immediately after taking a seated position. Seven stimulus frequencies (0, 15, 22, 44, 60, 90, and 120 Hz, all at 0.2g) were tested on each subject, and cardiovascular responses were followed for 20 minutes. Each subject experienced only a single test frequency on any day. Pre- and poststimulus blood pressures and continuous electrocardiogram results were obtained, from which mean arterial pressure (MAP) and heart rate variability (HRV) were calculated. RESULTS: In the per-protocol study population (n = 25), 20 minutes of quiet sitting was associated with an average depression of 8.95 mm Hg in systolic pressure and of 1.9 mm Hg in diastolic blood pressure, corresponding to an average decrease in MAP of 5.15 mm Hg. These orthostasis-based changes in blood pressure were significantly reduced by exposure to plantar vibration, in a frequency-dependent manner, with essentially complete suppression of the drop in MAP achieved with plantar stimulation at 44 Hz (P < or = . 01). In the orthostatically hypotensive subpopulation (n = 15), both the 9.3-mm Hg depression in MAP and the decline in HRV were eliminated by exposure to plantar vibrations in the 40- to 60-Hz range (P = .01 and P = .03, respectively). These results are consistent with the hypothesis that the plantar vibration may be stimulating type IIA muscle fiber activity in the leg, which is critical for effective skeletal muscle pumping in the absence of locomotion. CONCLUSIONS: Our findings lead us to suggest that noninvasive, low-level, plantar-based vibration in the regime of 30-60 Hz can significantly inhibit the effects of the orthostatic stress of quiet sitting on the cardiovascular system.
Maes M, Mihaylova I, De Ruyter M.	M-Care4U Outpatient Clinics, Olmenlaan 9, 2610 Antwerp-Wilrijk, Belgium. crc.mh@telenet.be	Lower serum zinc in Chronic Fatigue Syndrome (CFS): relationships to immune dysfunctions and relevance for the oxidative stress status in CFS.	J Affect Disord. 2006 Feb;90(2-3):141-7. Epub 2005 Dec 9.	The present study examines serum zinc concentrations in patients with chronic fatigue syndrome (CFS) versus normal volunteers. Serum zinc levels were determined by means of an atomic absorption method. We found that serum zinc was significantly lower in the CFS patients than in the normal controls. There was a trend toward a significant negative correlation between serum zinc and the severity of CFS and there was a significant and negative correlation between serum zinc and the subjective experience of infection. We found that serum zinc was significantly and negatively correlated to the increase in the alpha2 protein fraction and positively correlated to decreases in the expression of mitogen-induced CD69+ (a T cell activation marker) on CD3+ as well as CD3+CD8+ T cells. These results show that CFS is accompanied by a low serum zinc status and that the latter is

				related to signs of inflammation and defects in early T cell activation pathways. Since zinc is a strong anti-oxidant, the present results further support the findings that CFS is accompanied by increased oxidative stress. The results of these reports suggest that some patients with CFS should be treated with specific antioxidants, including zinc supplements.
Maes M, Mihaylova I, Leunis JC.	MCare4U Outpatient Clinics, Antwerp, Belgium.	Chronic fatigue syndrome is accompanied by an IgM-related immune response directed against neopitopes formed by oxidative or nitrosative damage to lipids and proteins.	Neuro Endocrinol Lett. 2006 Oct;27(5):615-21.	There is now some evidence that chronic fatigue syndrome (CFS) is accompanied by signs of oxidative stress and by a decreased antioxidant status. The aim of the present study was to examine whether CFS is accompanied by an immune response to neoepitopes of a variety of modified lipids and proteins indicating damage caused by oxidative and nitrosative stress. Toward this end we examined serum antibodies to fatty acids (oleic, palmitic and myristic acid), by-products of lipid peroxidation, i.e. azelaic acid and malondialdehyde (MDA), acetylcholine, S-farnesyl-L-cysteine, and N-oxide modified amino-acids in 14 patients with CFS, 14 subjects with partial CFS and 11 normal controls. We found that the prevalences and mean values for the serum IgM levels directed against oleic, palmitic and myristic acid, MDA, azelaic acid, S-farnesyl-L-cysteine, and the N-oxide derivates, nitro-tyrosine, nitro-phenylalanine, nitro-arginine, nitro-tryptophan, and nitro-cysteinyl were significantly greater in CFS patients than in normal controls, whereas patients with partial CFS took up an intermediate position. There were significant and positive correlations between the serum IgM levels directed against fatty acids, MDA and azelaic acid and the above N-oxide-derivates and the severity of illness (as measured by the FibroFatigue scale) and symptoms, such as aches and pain, muscular tension and fatigue. The results show that CFS is characterized by an IgM-related immune response directed against disrupted lipid membrane components, by-products of lipid peroxidation, S-farnesyl-L-cysteine, and NO-modified amino-acids, which are normally not detected by the immune system but due to oxidative and nitrosative damage have become immunogenic.
Malaguarnera M, Di Mauro A, Gargante PM, Rampello L.		L-carnitine reduces severity of physical and mental fatigue and improves daily activities in the elderly.	South Med J. 2006 Mar;99(3):315-6.	
Maloney EM, Gurbaxani BM, Jones JF, de Souza Coelho L, Pennachin C, Goertzel BN.	Centers for Disease Control and Prevention, 1600 Clifton Road, MS A-15, Atlanta, GA 30333, USA. evm3@cdc.gov	Chronic fatigue syndrome and high allostatic load.	Pharmacogenomics. 2006 Apr;7(3):467-73.	STUDY POPULATION: We examined the relationship between chronic fatigue syndrome (CFS) and allostatic load in a population-based, case-control study of 43 CFS patients and 60 nonfatigued, healthy controls from Wichita, KS, USA. METHODS: An allostatic load index was computed for all study participants using available laboratory and clinical data, according to a standard algorithm for allostatic load. Logistic regression analysis was used to compute odds ratios (ORs) as estimates of relative risk in models that included adjustment for matching factors and education; 95% confidence intervals (CIs) were computed to estimate the precision of the ORs. RESULTS: CFS patients were 1.9-times more likely to have a high allostatic load index than controls (95% CI = 0.75, 4.75) after adjusting for education level, in addition to matching factors. The strength of this association increased in a linear trend across categories of low, medium and high levels of allostatic load (p = 0.06). CONCLUSION: CFS was associated with a high level of allostatic load. The three allostatic load components that best discriminated cases from controls were waist:hip ratio, aldosterone and urinary

				cortisol.
Maoz D, Shoenfeld Y.		[Chronic fatigue syndrome] [Article in Hebrew]	Harefuah. 2006 Apr;145(4):272-5, 319, 318.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by severe fatigue and other non-specific symptoms. It causes disturbance of normal function. Uncertainty about etiology and the appropriate treatment, combined with high prevalence of psychiatric comorbidity, cause a problem in the perception of the disease by the patient, physician and society. OBJECTIVES: This review recapitulates the updated information regarding CFS. It addresses the following aspects: definitions, diagnosis, demographic figures, etiology and treatment options. Since much about CFS is yet to be known, a large amount of work has recently been performed on this subject. Current perceptions, as recognized today, are also presented. METHODS: A literature search was performed using Medline. RESULTS: Accurate diagnosis of CFS patients is low despite the disabling fatigue. CFS patients present certain demographic characteristics and the illness etiology is as yet unclear. Nonetheless, many possible directions exist with inconclusive evidence about certain suspected causes. There are no treatment guidelines available. Different treatment approaches were investigated without consensus on the results. CONCLUSIONS: CFS is an illness that should be taken seriously by the medical establishment. Conscious awareness of the malady might reduce rates of undiagnosed patients. The different etiologic factors showing some degree of involvement in CFS, might suggest that this syndrome is a multi-factorial condition. Despite the fact that there is no distinct undisputed treatment, there are 2 treatments (cognitive behavioral therapy and graded exercise therapy) that might be effective.
Maquet D, Demoulin C, Crielaard JM.	Departement des Sciences de la Motricite, Unite de Medecine Physique et Kinesitherapie-Readaptation, Universite de Liege, CHU Sart-Tilman, ISEPK, Belgique. D.Maquet@ulg.ac.be	Chronic fatigue syndrome: a systematic review. [Article in English, French]	Ann Readapt Med Phys. 2006 Jul;49(6):337-47, 418-27. Epub 2006 Apr 19.	OBJECTIVE: A systematic review of the literature about chronic fatigue syndrome (CFS). METHODS: A search of the Medline database (via Ovid and PubMed) with the key words chronic fatigue syndrome, diagnosis, classification, epidemiology, etiology, physiopathology, metabolism, microbiology, immunology, virology, psychology, drug therapy, rehabilitation, and therapy. The reference lists of each article were examined for additional related articles. RESULTS: CFS was defined in 1988 by the US Centes for Disease Control and Prevention. The prevalence of chronic fatigue syndrome has ranged from 0.2% to 0.7% in the general population. In 1994, the definition of CFS was revised by Fukuda et al. Despite various research in several topics (e.g. infection, immune systems, neuroendocrinology, autonomic activity, neuromuscular involvement), the pathophysiology remains unknown. CONCLUSION: CFS, with its various major clinical and functional impacts, should be associated with a "biopsychosocial model". Progressive muscular rehabilitation, combined with behavioral and cognitive treatment, is an essential part of therapy.
Margutti P, Delunardo F, Ortona E.	Dipartimento di Malattie Infettive, Parassitarie e Immunomediate, Istituto Superiore di Sanita, Rome, Italy. ortona@iss.it.	Autoantibodies associated with psychiatric disorders.	Curr Neurovasc Res. 2006 May;3(2):149-57.	Growing evidence suggests that autoantibodies to neuronal or endothelial targets in psychiatric disorders exist and may be pathogenic. This review describes and discusses the possible role of autoantibodies related to the psychiatric manifestations in autoimmune diseases, autoantibodies related to the psychiatric disorders present in post-streptococcal diseases, celiac disease, chronic fatigue syndrome and substance abuse, and autoantibodies related to schizophrenia and autism, disorders now considered of autoimmune origin.

McCue P, Buchanan T, Martin CR.	Department of Psychology, Northumbria University, UK.	Screening for psychological distress using internet administration of the Hospital Anxiety and Depression Scale (HADS) in individuals with chronic fatigue syndrome.	Br J Clin Psychol. 2006 Nov;45(Pt 4):483-98.	OBJECTIVES: To investigate the factor structure and internal consistency of the Hospital Anxiety and Depression Scale (HADS) in individuals with Chronic Fatigue Syndrome (CFS) using an Internet administered version of the instrument. DESIGN: Between subjects. METHOD: Confirmatory factor analysis (CFA) and internal consistency analysis of the HADS was used to determine the psychometric characteristics of the instrument in individuals with CFS and a control group with data captured via an Internet data collection protocol. RESULTS: CFA revealed that a 3-factor solution offered the most parsimonious account of the data. Internal consistency estimations of the anxiety and depression subscales were found to be acceptable for both groups. The CFS group was found to have significantly higher HADS-assessed anxiety and depression scores compared with controls, however, there was also evidence found that Internet administration of the instrument may inflate HADS subscale scores as an artifact of testing medium. CONCLUSIONS: The HADS is suitable for use for screening individuals with CFS in terms of the factor structure of the instrument, however, clinicians should be aware that this instrument assesses 3 domains of affective disturbance rather than 2 as is interpreted within the current HADS anxiety and depression subscale scoring system. Researchers need also be aware that Internet administration of negative affective state measures such as the HADS is likely to inflate scores and need to ensure that comparisons between clinical groups are made with control group data gathered using the same collection methodology.
McCully KK, Malucelli E, Iotti S.	Department of Kinesiology, University of Georgia, Athens GA 30602. mccully@uga.edu.	Increase of free Mg2+ in the skeletal muscle of chronic fatigue syndrome patients.	Dyn Med. 2006 Jan 11;5:1.	ABSTRACT : In a previous study we evaluated muscle blood flow and muscle metabolism in patients diagnosed with chronic fatigue syndrome (CFS). To better understand muscle metabolism in CFS, we re-evaluated our data to calculate free Magnesium levels in skeletal muscle. Magnesium is an essential cofactor in a number of cell processes. A total of 20 CFS patients and 11 controls were evaluated. Phosphorus magnetic resonance spectroscopy from the medial gastrocnemius muscle was used to calculate free Mg2+ from the concentrations and chemical shifts of Pi, PCr, and beta ATP peaks. CFS patients had higher magnesium levels in their muscles relative to controls (0.47 + 0.07 vs 0.36 + 0.06 mM, $P < 0.01$), although there was no difference in the rate of phosphocreatine recovery in these subjects, as reported earlier. This finding was not associated with abnormal oxidative metabolism as measured by the rate of recovery of phosphocreatine after exercise. In summary, calculation of free Mg2+ levels from previous data showed CFS patients had higher resting free Mg2+ levels compared to sedentary controls.
McDermott C, Richards SC, Thomas PW, Montgomery J, Lewith G.	University of Southampton, UK. crm202@soton.ac.uk	A placebo-controlled, double-blind, randomized controlled trial of a natural killer cell stimulant (BioBran MGN-3) in chronic fatigue syndrome.	QJM. 2006 Jul;99(7):461-8. Epub 2006 Jun 29.	BACKGROUND: Previous research has suggested that natural killer (NK) cell activity may be reduced in patients with chronic fatigue syndrome (CFS). AIM: To evaluate the effectiveness of a putative NK cell stimulant, BioBran MGN-3, in reducing fatigue in CFS patients. DESIGN: Randomized, double-blind, placebo-controlled trial. METHODS: We recruited 71 patients with CFS (according to the Centers for Disease Control 1994 criteria) attending an out-patient specialist CFS service. Participants were given oral BioBran MGN-3 for 8 weeks (2 g three times per day) or placebo equivalent. The primary outcome measure was the Chalder physical fatigue score. Self-reported fatigue measures, self-assessment of improvement, change in key symptoms, quality of life, anxiety and depression measures were also included. RESULTS: Data were complete in 64/71 patients. Both groups showed marked improvement over the study duration, but without significant differences. Mean improvement in the Chalder fatigue score (physical scale) was 0.3 (95%CI -2.6 to 3.2) lower in the BioBran group. DISCUSSION: The findings

				do not support a specific therapeutic effect for BioBran in CFS. The improvement showed by both groups over time highlights the importance of placebo controls when evaluating interventions in CFS.
McIntyre RS, Konarski JZ, Soczynska JK, Wilkins K, Panjwani G, Bouffard B, Bottas A, Kennedy SH.	Department of Psychiatry, University of Toronto, Ontario, Canada. roger.mcintyre@uhn.on.ca	Medical comorbidity in bipolar disorder: implications for functional outcomes and health service utilization.	Psychiatr Serv. 2006 Aug;57(8):1140-4.	OBJECTIVE: This is the first cross-national population-based investigation exploring the prevalence and functional implications of comorbid general medical disorders in bipolar disorder. METHODS: Data were extracted from the Canadian Community Health Survey (N = 36,984). Analyses were conducted to ascertain the prevalence and prognostic implications of predetermined comorbid general medical disorders among persons who screened positive for a lifetime manic episode (indicative of a diagnosis of bipolar disorder). Within the subpopulation of people who screened positive for a manic episode, the effect of medical comorbidity on employment, functional role, psychiatric care, and medication use was examined. RESULTS: When the data were weighted to be representative of the household population of the ten provinces in 2002, an estimated 2.4 percent of respondents screened positive for a lifetime manic episode. Rates of chronic fatigue syndrome, migraine, asthma, chronic bronchitis, multiple chemical sensitivities, hypertension, and gastric ulcer were significantly higher in the bipolar disorder group (all $p < .05$). Chronic medical disorders were associated with a more severe course of bipolar disorder, increased household and work maladjustment, receipt of disability payments, reduced employment, and more frequent medical service utilization. CONCLUSIONS: Comorbid medical disorders in bipolar disorder are associated with several indices of harmful dysfunction, decrements in functional outcomes, and increased utilization of medical services.
McLean SA, Williams DA, Stein PK, Harris RE, Lyden AK, Whalen G, Park KM, Liberzon I, Sen A, Gracely RH, Baraniuk JN, Clauw DJ.	Department of Emergency Medicine, University of Michigan Medical Center, Ann Arbor, MI, USA. samclean@umich.edu	Cerebrospinal fluid corticotropin-releasing factor concentration is associated with pain but not fatigue symptoms in patients with fibromyalgia.	Neuropsychopharmacology. 2006 Dec;31(12):2776-82. Epub 2006 Aug 23.	Previous studies have identified stress system dysregulation in fibromyalgia (FM) patients; such dysregulation may be involved in the generation and/or maintenance of pain and other symptoms. Corticotropin-releasing factor (CRF) is the principal known central nervous system mediator of the stress response; however, to date no studies have examined cerebrospinal fluid (CSF) CRF levels in patients with FM. The relationship between CSF CRF level, heart rate variability (HRV), and pain, fatigue, and depressive symptoms was examined in patients with FM. Among participants (n=26), CSF CRF levels were associated with sensory pain symptoms ($r=0.574$, $p=0.003$) and affective pain symptoms ($r=0.497$, $p=0.011$), but not fatigue symptoms. Increased HRV was also strongly associated with increased CSF CRF and FM pain. In multivariate analyses adjusting for age, sex, and depressive symptoms, the association between CSF CRF and sensory pain symptoms ($t=2.54$, $p=0.027$) persisted. Women with FM who reported a history of physical or sexual abuse had lower CSF CRF levels than women who did not report such a history. CSF CRF levels are associated with both pain symptoms and variation in autonomic function in FM. Differences in CSF CRF levels among women with and without a self-reported history of physical or sexual abuse suggest that subgroups of FM patients may exist with different neurobiological characteristics. Further studies are needed to better understand the nature of the association between CSF CRF and pain symptoms in FM.
Meeus M, Nijs J, Meirleir KD.	Division of Musculoskeletal Physiotherapy, Higher Institute of Physiotherapy, Department of	Chronic musculoskeletal pain in patients with the chronic fatigue syndrome: A systematic	Eur J Pain. 2006 Jul 12; [Epub ahead of print]	BACKGROUND: In addition to debilitating fatigue the majority of patients with chronic fatigue syndrome (CFS) experience chronic widespread pain. AIMS: Conducting a systematic review to critically assess the existing knowledge on chronic pain in CFS. We focussed on the definition, the prevalence and incidence, the aetiology, the relevance and the therapy strategy for chronic musculoskeletal pain and post-exertional pain in CFS. METHODS: To identify relevant articles, we searched eight medical search engines. The search terms "chronic fatigue syndrome" AND "pain",

	Health Care Sciences, Hogeschool Antwerpen (HA), Van Aertselaerstraat 31, 2170 Merksem, Belgium; Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel (VUB), Belgium.	review.		"nociception", "arthralgia" and "myalgia", were used to identify articles concerning pain in CFS. Included articles were reviewed by two blinded researchers. RESULTS: Twenty-five articles and two abstract were identified and selected for further appraisal. Only 11 search results focussed on musculoskeletal pain in CFS patients. Regarding the standardized review of the articles, a 96% agreement between the researchers was observed. There is no consensus in defining chronic widespread pain in CFS, and although there is little or no strong proof for the exact prevalence, chronic pain is strongly disabling in CFS. Aetiological theories are proposed (sleep abnormalities, tryptophan, parovirus-B, hormonal and brain abnormalities and central sensitisation) and a reduction of pain threshold after exercise has been shown. Furthermore depression seemed not related to pain in CFS and a staphylococcus toxoid vaccine caused no significant pain reduction. CONCLUSIONS: The results from the systematic review highlight the clinical importance of chronic pain in CFS, but only few studies addressing the aetiology or treatment of chronic pain in CFS are currently available.
Meeus M, Nijs J.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel (VUB), Brussel, Belgium.	Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome.	Clin Rheumatol. 2006 Nov 18; [Epub ahead of print]	In addition to the debilitating fatigue, the majority of patients with chronic fatigue syndrome (CFS) experience chronic widespread pain. These pain complaints show the greatest overlap between CFS and fibromyalgia (FM). Although the literature provides evidence for central sensitization as cause for the musculoskeletal pain in FM, in CFS this evidence is currently lacking, despite the observed similarities in both diseases. The knowledge concerning the physiological mechanism of central sensitization, the pathophysiology and the pain processing in FM, and the knowledge on the pathophysiology of CFS lead to the hypothesis that central sensitization is also responsible for the sustaining pain complaints in CFS. This hypothesis is based on the hyperalgesia and allodynia reported in CFS, on the elevated concentrations of nitric oxide presented in the blood of CFS patients, on the typical personality styles seen in CFS and on the brain abnormalities shown on brain images. To examine the present hypothesis more research is required. Further investigations could use similar protocols to those already used in studies on pain in FM like, for example, studies on temporal summation, spatial summation, the role of psychosocial aspects in chronic pain, etc.
Michielsen HJ, Van Houdenhove B, Leirs I, Vandenbroeck A, Onghena P.	Department of Psychology and Health, Tilburg University, Tilburg, The Netherlands.	Depression, attribution style and self-esteem in chronic fatigue syndrome and fibromyalgia patients: is there a link?	Clin Rheumatol. 2006 Mar;25(2):183-8. Epub 2005 Jul 12.	The aims of the present study were to compare a single diagnosis (chronic fatigue syndrome, CFS) and a double diagnosis (CFS + fibromyalgia, CFS+FM) group regarding depression, attribution style and self-esteem as well as to examine whether attribution style is a mediator in the relationship between self-esteem and depression. Eighty-five patients (CFS: 47, CFS+FM: 38) completed questionnaires on attribution style, self-esteem and depression. The single and double diagnosis groups tended to differ slightly, but the differences were never statistically significant. In addition, only one condition was met of the four conditions mentioned by Baron and Kenny to establish that mediation exists between two variables. In conclusion, an external attribution style does not protect the CFS or CFS+FM patients with a low self-esteem from depression. The prevalence rate of depression was high in both patient samples, of which clinicians should be aware.
Miike T.	miketeru@kaiju.m	[Brain science,	No To Hattatsu.	

	edic.kumamoto-u.ac.jp	education and living environment] [Article in Japanese]	2006 Mar;38(2):85-91.	
Mommersteeg PM, Heijnen CJ, Verbraak MJ, van Doornen LJ.	Department of Health Psychology, Utrecht University, P.O. Box 80.140, 3508 TC Utrecht, The Netherlands. p.mommersteeg@fss.uu.nl	Clinical burnout is not reflected in the cortisol awakening response, the day-curve or the response to a low-dose dexamethasone suppression test.	Psychoneuroendocrinology. 2006 Feb;31(2):216-25. Epub 2005 Sep 16.	Burnout is presumed to be the result of chronic stress, and chronic stress is known to affect the HPA-axis. To date, studies on HPA-axis functioning in burnout have showed inconsistent results. In the present study, a large sample (n=74) of clinically diagnosed burnout individuals, mostly on sick-leave, were included and compared with 35 healthy controls. Salivary cortisol was sampled on 2 days to determine the cortisol awakening response (CAR) and the day-curve. In addition, the dexamethasone suppression test (DST) was applied to assess the feedback efficacy of the HPA-axis. There were no differences observed in the CAR, day-curve or CAR after DST in the burnout group as compared to a healthy control group. Burnout shows overlap in symptoms with chronic fatigue syndrome (CFS) and depression. Therefore, differential changes in HPA-axis functioning that resemble the hypo-functioning of the HPA-axis in CFS, or rather the hyper-functioning of the HPA-axis in depression, might have obscured the findings. However, no effect of fatigue or depressive mood on HPA-axis functioning was found in the burnout group. We concluded that HPA-axis functioning in clinically diagnosed burnout participants as tested in the present study, seems to be normal.
Moss-Morris R, Spence M.	School of Psychology, University of Southampton, Highfield, Southampton, SO17 1BJ, United Kingdom. R.E.Moss-Morris@soton.ac.uk	To "lump" or to "split" the functional somatic syndromes: can infectious and emotional risk factors differentiate between the onset of chronic fatigue syndrome and irritable bowel syndrome?	Psychosom Med. 2006 May-Jun;68(3):463-9.	OBJECTIVES: Recent academic debate has centered on whether functional somatic syndromes should be defined as separate entities or as one syndrome. The aim of this study was to investigate whether there may be significant differences in the etiology or precipitating factors associated with two common functional syndromes, irritable bowel syndrome (IBS) and chronic fatigue syndrome (CFS). METHODS: We prospectively studied 592 patients with an acute episode of Campylobacter gastroenteritis and 243 with an acute episode of infectious mononucleosis who had no previous history of CFS or IBS. At the time of infection, patients completed a baseline questionnaire that measured their levels of distress using the Hospital Anxiety and Depression scale. At 3- and 6-month follow-up, they completed questionnaires to determine whether they met published diagnostic criteria for chronic fatigue (CF), CFS, and/or IBS. RESULTS: The odds of developing IBS were significantly greater post-Campylobacter than post-infectious mononucleosis at both 3- (odds ratio, 3.45 [95% confidence interval (CI), 1.75-6.67]) and 6- (2.22 [95% CI, 1.11-6.67]) month follow-up. In contrast, the odds for developing CF/CFS were significantly greater after infectious mononucleosis than after Campylobacter at 3 (2.77 [95% CI, 1.08-7.11]) but not 6 (1.48 [95% CI, 0.62-3.55]) months postinfection. Anxiety and depression were the strongest predictors of CF/CFS, whereas the nature of the infection was the strongest predictor of IBS. CONCLUSIONS: These results support the argument to distinguish between postinfectious IBS and CFS. The nature of the precipitating infection appears to be important, and premorbid levels of distress appear to be more strongly associated with CFS than IBS, particularly levels of depression.
Naschitz J, Fields M, Isseroff H, Sharif D, Sabo E,	Department of Internal Medicine A, Bnai Zion	Shortened QT interval: a distinctive feature	J Electrocardiol. 2006 Oct;39(4):389-94.	PURPOSE: Because autonomic nervous functioning is frequently abnormal in chronic fatigue syndrome (CFS), we examined whether the corrected QT interval (QTc) in CFS differs from QTc in other populations. METHODS: The QTc was calculated at the end of 10 minutes of recumbence and the end

Rosner I.	Medical Center and Rappaport Family Faculty of Medicine, Technion-Israel Institute of Technology, P.O. Box 4940, Haifa 31048, Israel. naschitz@tx.technion.ac.il	of the dysautonomia of chronic fatigue syndrome.	Epub 2006 Feb 28.	of 10 minutes of head-up tilt. In a pilot study, groups of 15 subjects, CFS, and controls, matched for age and sex, were investigated. In a second phase of the study, the QTc was measured in larger groups of CFS (n = 30) and control patients (n = 96) not matched for demographic features. RESULTS: In the pilot study, the average supine QTc in CFS was 0.371 +/- 0.02 seconds and QTc on tilt, 0.385 +/- 0.02 seconds, significantly shorter than in controls (P = .0002 and .0003, respectively). Results of phase II confirmed this data. CONCLUSIONS: Relative short QTc intervals are features of the CFS-related dysautonomia. The significance of this finding is discussed.
Naschitz JE, Mussafia-Priselac R, Kovalev Y, Zaigraykin N, Slobodin G, Elias N, Rosner I.	Department of Internal Medicine A, the Bnai-Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. Naschitz@tx.technion.ac.il	Patterns of hypocapnia on tilt in patients with fibromyalgia, chronic fatigue syndrome, nonspecific dizziness, and neurally mediated syncope.	Am J Med Sci. 2006 Jun;331(6):295-303.	OBJECTIVES: To assess whether head-up tilt-induced hyperventilation is seen more often in patients with chronic fatigue syndrome (CFS), fibromyalgia, dizziness, or neurally mediated syncope (NMS) as compared to healthy subjects or those with familial Mediterranean fever (FMF). PATIENTS AND METHODS: A total of 585 patients were assessed with a 10-minute supine, 30-minute head-up tilt test combined with capnography. Experimental groups included CFS (n = 90), non-CFS fatigue (n = 50), fibromyalgia (n = 70), nonspecific dizziness (n = 75), and NMS (n =160); control groups were FMF (n = 90) and healthy (n = 50). Hypocapnia, the objective measure of hyperventilation, was diagnosed when end-tidal pressure of CO2 (PETCO2) less than 30 mm Hg was recorded consecutively for 10 minutes or longer. When tilting was discontinued because of syncope, one PETCO2 measurement of 25 or less was accepted as hyperventilation. RESULTS: Hypocapnia was diagnosed on tilt test in 9% to 27% of patients with fibromyalgia, CFS, dizziness, and NMS versus 0% to 2% of control subjects. Three patterns of hypocapnia were recognized: supine hypocapnia (n = 14), sustained hypocapnia on tilt (n = 76), and mixed hypotensive-hypocapnic events (n = 80). Hypocapnia associated with postural tachycardia syndrome (POTS) occurred in 8 of 41 patients. CONCLUSIONS: Hyperventilation appears to be the major abnormal response to postural challenge in sustained hypocapnia but possibly merely an epiphenomenon in hypotensive-hypocapnic events. Our study does not support an essential role for hypocapnia in NMS or in postural symptoms associated with POTS. Because unrecognized hypocapnia is common in CFS, fibromyalgia, and nonspecific dizziness, capnography should be a part of the evaluation of patients with such conditions.
Nater UM, Wagner D, Solomon L, Jones JF, Unger ER, Papanicolaou DA, Reeves WC, Heim C.	Viral Exanthems and Herpesvirus Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control	Coping styles in people with chronic fatigue syndrome identified from the general population of Wichita, KS.	J Psychosom Res. 2006 Jun;60(6):567-73.	OBJECTIVE: Studies of primary and tertiary care patients suggest that maladaptive coping styles contribute to the pathogenesis and maintenance of chronic fatigue syndrome (CFS). We assessed coping styles in persons with unexplained fatigue and nonfatigued controls in a population-based study. METHODS: We enrolled 43 subjects meeting the 1994 Research Case Definition of CFS, matching them with 61 subjects with chronic unexplained fatigue who did not meet criteria for CFS [we term them insufficient symptoms or fatigue (ISF)] and 60 non-ill (NI) controls. Coping styles and clinical features of CFS were assessed using standard rating scales. RESULTS: Subjects with CFS and ISF reported significantly more escape-avoiding behavior than NI controls. There were no differences between the CFS and ISF subjects. Among participants with CFS, escape-avoiding behavior was associated with fatigue severity, pain, and disability. CONCLUSIONS: We demonstrate significantly

	and Prevention, Atlanta, GA, USA.			higher reporting of maladaptive coping in a population-based sample of people with CFS and other unexplained fatiguing illnesses defined by reproducible standardized clinical empirical means in comparison to NI controls.
Nicolson GL, Ellithorpe R.		Lipid Replacement and Antioxidant Nutritional Therapy for Restoring Mitochondrial Function and Reducing Fatigue in Chronic Fatigue Syndrome and Other Fatiguing Illnesses	Journal of Chronic Fatigue Syndrome 2006;13(1): 57-68	Evidence in the literature indicates that diminished mitochondrial function through loss of efficiency in the electron transport chain caused by oxidation occurs during aging and in fatiguing illnesses. Lipid Replacement Therapy (LRT) administered as a nutritional supplement with antioxidants can prevent oxidative membrane damage, and LRT can be used to restore mitochondrial and other cellular membrane functions via delivery of undamaged replacement lipids to cellular organelles. Recent clinical trials using patients with chronic fatigue have shown the benefit of LRT plus antioxidants in restoring mitochondrial electron transport function and reducing moderate to severe chronic fatigue. These studies indicate the benefits of LRT plus antioxidants in reducing fatigue and preventing loss of mitochondrial function, most likely by protecting mitochondrial and other cellular membranes from oxidative and other damage and removing damaged lipids by lipid replacement. In one clinical study we determined if mitochondrial function is reduced in subjects with mild to severe chronic fatigue, and if this can be reversed with NT Factor(r), a nutritional supplement that replaces damaged cellular lipids. With the use of the Piper Fatigue Scale, there was a significant time-dependent reduction in overall fatigue in moderately or severely fatigued subjects while on the dietary supplement for 4-8 weeks. Analysis of mitochrondrial function indicated that four and eight weeks of the dietary supplement in moderately or severely fatigued subjects significantly increased mitochondrial function. Similarly, chronic fatigue syndrome patients administered antioxidants plus LRT also show reductions in fatigue. The results indicate that LRT plus antioxidants can significantly reduce moderate to severe chronic fatigue and restore mitochondrial function. Dietary use of unoxidized membrane lipids plus antioxidants is recommended for patients with moderate to severe chronic fatigue.
Nijs J, Aerts A, De Meirleir K.	Department of Human Physiology-Faculty of Physical Education and Physiotherapy Vrije Universiteit Brussel (VUB), Belgium. jo.Nijs@vub.ac.be	Generalized joint hypermobility is more common in chronic fatigue syndrome than in healthy control subjects.	J Manipulative Physiol Ther. 2006 Jan;29(1):32-9.	OBJECTIVES: This study aimed at (1) comparing the prevalence of generalized hypermobility in patients with chronic fatigue syndrome (CFS) and healthy volunteers, (2) examining the clinical importance of generalized hypermobility in patients with CFS, and (3) examining whether knee proprioception is associated with hypermobility in patients with CFS. METHODS: Sixty-eight patients with CFS filled out two self-reported measures (for the assessment of symptom severity and disability), were questioned about muscle and joint pain, and were screened for generalized hypermobility. Afterward, the patients performed a knee repositioning test (assessment of knee proprioception), and it was examined whether or not they fulfilled the criteria for benign joint hypermobility syndrome (BJHS). Sixty-nine age- and sex-matched healthy volunteers were screened for generalized joint hypermobility and performed the same knee repositioning test. RESULTS: Compared with the healthy volunteers (4.3%, 3/68), significantly more patients with CFS (20.6%, 14/69) fulfilled the criteria for generalized joint hypermobility (Fisher exact test, $P < .004$). No associations were found between generalized joint hypermobility and the self-reported measures (including pain severity) or knee proprioception (Spearman correlation analysis). Knee proprioception was similar in both groups (Mann-Whitney $U = 1961$, $z = -1.745$, $P = .81$). Forty patients with CFS (58.8%) fulfilled the criteria for BJHS. CONCLUSIONS: These data indicate that a subgroup of patients with CFS present with generalized joint hypermobility and most patients with of CFS fulfill the

				diagnostic criteria for BJHS. There appears to be no association between musculoskeletal pain and joint hypermobility in patients with CFS.
Nijs J, De Meirleir K.		Nitric oxide and chronic fatigue syndrome: Are we caring for our patients or are we practicing selfcare?	Med Hypotheses. 2006;66(2):449-50. Epub 2005 Oct 10. Comment on: Med Hypotheses. 2005;65(3):631-3.	
Nijs J, Meeus M, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Belgium; Department of Health Sciences, Division of Musculoskeletal Physiotherapy, Higher Institute of Physiotherapy, Hogeschool Antwerpen, Belgium.	Chronic musculoskeletal pain in chronic fatigue syndrome: Recent developments and therapeutic implications.	Man Ther. 2006 Aug;11(3):187-191. Epub 2006 Jun 14.	Patients with chronic fatigue syndrome (CFS) experience chronic musculoskeletal pain which is even more debilitating than fatigue. Scientific research data gathered around the world enables clinicians to understand, at least in part, chronic musculoskeletal pain in CFS patients. Generalized joint hypermobility and benign joint hypermobility syndrome appear to be highly prevalent among CFS sufferers, but they do not seem to be of any clinical importance. On the other hand, pain catastrophizing accounts for a substantial portion of musculoskeletal pain and is a predictor of exercise performance in CFS patients. The evidence concerning pain catastrophizing is supportive of the indirect evidence of a dysfunctional pain processing system in CFS patients with musculoskeletal pain. CFS sufferers respond to incremental exercise with a lengthened and accentuated oxidative stress response, explaining muscle pain, postexertional malaise, and the decrease in pain threshold following graded exercise in CFS patients. Applying the scientific evidence to the manual physiotherapy profession, pacing self-management techniques and pain neurophysiology education are indicated for the treatment of musculoskeletal pain in CFS patients. Studies examining the effectiveness of these strategies for CFS patients are warranted.
O'Dowd H, Gladwell P, Rogers CA, Hollinghurst S, Gregory A.	Pain Management Centre, Frenchay Hospital, Bristol, UK.	Cognitive behavioural therapy in chronic fatigue syndrome: a randomised controlled trial of an outpatient group programme.	Health Technol Assess. 2006 Oct;10(37):iii-iv, ix-x, 1-121.	OBJECTIVES: To test the hypothesis that group cognitive behavioural therapy (CBT) will produce an effective and cost-effective management strategy for patients in primary care with chronic fatigue syndrome/myalgic encephalopathy (CFS/ME). DESIGN: A double-blind, randomised controlled trial was adopted with three arms. Outcomes were assessed at baseline and 6 and 12 months after first assessment and results were analysed on an intention-to-treat basis. SETTING: A health psychology department for the management of chronic illness in a general hospital in Bristol, UK. PARTICIPANTS: Adults with a diagnosis of CFS/ME referred by their GP. INTERVENTIONS: The three interventions were group CBT incorporating graded activity scheduling, education and support group (EAS) and standard medical care (SMC). OUTCOME MEASURES: The primary outcome measure was the Short Form with 36 Items (SF-36) physical and mental health summary scales. Other outcome measures included the Chalder fatigue scale, Hospital Anxiety and Depression Scale, General Health Questionnaire, physical function (shuttles walked, walking speed and perceived fatigue), health utilities index and cognitive function (mood, recall and reaction times). RESULTS: A total of 153 patients were recruited to the trial and 52 were randomised to receive CBT, 50 to EAS and 51 to SMC. Twelve patients failed to attend for the 12-month follow-up and 19 patients attended one follow-up, but not both. The sample was found

				to be representative of the patient group and the characteristics of the three groups were similar at baseline. Three outcome measures, SF-36 mental health score, Chalder fatigue scale and walking speed, showed statistically significant differences between the groups. Patients in the CBT group had significantly higher mental health scores [difference +4.35, 95% confidence interval (CI) +0.72 to +7.97, p = 0.019], less fatigue (difference -2.61, 95% CI -4.92 to -0.30, p = 0.027) and were able to walk faster (difference +2.83 shuttles, 95% CI +1.12 to +5.53, p = 0.0013) than patients in the SMC group. CBT patients also walked faster and were less fatigued than those randomised to EAS (walking speed: difference +1.77, 95% CI +0.025 to +3.51, p = 0.047; fatigue: difference -3.16, 95% CI -5.59 to -0.74, p = 0.011). Overall, no other statistically significant difference across the groups was found, although for many measures a trend towards an improved outcome with CBT was seen. Except for walking speed, which, on average, increased by +0.87 shuttles (95% CI +0.09 to +1.65, p = 0.029) between the 6- and 12-month follow-ups, the scores were similar at 6 and 12 months. At baseline, 30% of patients had an SF-36 physical score within the normal range and 52% had an SF-36 mental health score in the normal range. At 12 months, the physical score was in the normal range for 46% of the CBT group, 26% of the EAS group and 44% of SMC patients. For mental health score the percentages were CBT 74%, EAS 67% and SMC 70%. Of the CBT group, 32% showed at least a 15% increase in physical function and 64% achieved a similar improvement in their mental health. For the EAS and SMC groups, this improvement in physical and mental health was achieved for 40 and 60% (EAS) and 49 and 53% (SMC), respectively. The cost-effectiveness of the intervention proved very difficult to assess and did not yield reliable conclusions. CONCLUSIONS: Group CBT did not achieve the expected change in the primary outcome measure as a significant number did not achieve scores within the normal range post-intervention. The treatment did not return a significant number of subjects to within the normal range on this domain; however, significant improvements were evident in some areas. Group CBT was effective in treating symptoms of fatigue, mood and physical fitness in CFS/ME. It was found to be as effective as trials using individual therapy in these domains. However, it did not bring about improvement in cognitive function or quality of life. There was also evidence of improvement in the EAS group, which indicates that there is limited value in the non-specific effects of therapy. Further research is needed to develop better outcome measures, assessments of the broader costs of the illness and a clearer picture of the characteristics best fitted to this type of intervention.
Oleske JM, Friedman KJ, Kaufman KK, Palumbo D, Sterling J, Evans TL		REVIEW Chronic Fatigue Syndrome in Children and Adolescents	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 97-115	Objective: An overview of the unique aspects of Chronic Fatigue Syndrome in children and adolescents (CACFS) is herein provided for healthcare professionals who may be called upon to diagnose and/or treat this illness. Young age of onset, puberty, and interactions with peers and the educational system provide greater diagnostic and treatment challenges than found with adult onset CFS. Method: A review of diagnostic procedures and treatment protocols found in the contemporary literature is coupled with the professional experiences of the authors in treating CACFS to delineate the roles and responsibilities of family, healthcare providers and educators in diagnosing, treating and supporting the CACFS patient. Results: Areas discussed include: pathogenesis, patient evaluation, clinical evaluation, laboratory evaluation, treatment options, psychological issues, role of schools, and the roles of primary and tertiary care providers. Conclusion: CACFS can be diagnosed and treated with varying levels of success if all the professionals involved in the treatment program have a clear

				understanding of their roles and responsibilities. Primary care physicians, pediatricians, other subspecialists, family members, social workers and educators, may all be called upon to participate in the treatment program of CACFS. While it is best to have one, compassionate physician in charge of care, the CACFS may benefit from the inclusion of specialized treatment options available from or through a tertiary care provider. To the extent possible, socialization, education and psychological support of the CACFS should be provided.
Ouyang A, Wrzos HF.	Division of Gastroenterology and Hepatology, The Milton S. Hershey Medical Center, College of Medicine, Pennsylvania State University, Hershey, Pennsylvania.	Contribution of Gender to Pathophysiology and Clinical Presentation of IBS: Should Management Be Different in Women?	Am J Gastroenterol. 2006 Dec;101 Suppl 3:S602-9.	The irritable bowel syndrome (IBS) is found more commonly in women than men. It is more prevalent in patients with chronic fatigue syndrome, fibromyalgia, and chronic pelvic pain, all syndromes characterized by pain and found predominantly in women. This article reviews evidence for a role of biological sex factors and gender on the pathways mediating visceral pain. The effect of gonadal hormones on gastrointestinal motility and the sensory afferent pathway and central processing of visceral stimuli and the contribution of gender role to the clinical presentation are discussed. Although differences in responses to treatment modalities between genders exist, the approach to IBS patients in both genders is quite similar. Nevertheless, a special attention to gender role and stress-related factors should be addressed. New developments in research, outlined in the paper, might bring more gender-specific treatments in the future.
Padhan P.		Chronic fatigue.	CMAJ. 2006 Aug 15;175(4):386-7; author reply 387-8. Comment on: CMAJ. 2006 Mar 14;174(6):765-7.	
Page WF.	Medical Follow-up Agency, Institute of Medicine, 500 Fifth Street NW, Washington, DC 20001, USA. wpage@nas.edu	Update on the NAS-NRC Twin Registry.	Twin Res Hum Genet. 2006 Dec;9(6):985-7.	The National Academy of Sciences-National Research Council (NAS-NRC) Twin Registry is one of the oldest, national population-based twin registries in the United States. It consists of 15,924 white male twin pairs born in the years 1917 to 1927 (inclusive), both of whom served in the armed forces, mostly during World War II. This article updates activity in this registry since the earlier 2002 article in Twin Research. The results of clinically based studies on dementia, Parkinson's disease, age-related macular degeneration, and primary osteoarthritis were published, as well as articles based on previously collected questionnaire data on chronic fatigue syndrome, functional limitations, and healthy aging. In addition, risk factor studies are being planned to merge clinical data with earlier collected risk factor data from questionnaires. Examination data from the subset of National Heart, Lung, and Blood Institute (NHLBI) twins resulted in a number of articles, including the relationship of endogenous sex hormones to coronary heart disease and morphological changes in aging brain structures. The NEO Five-Factor Personality Inventory (a paper-and-pencil self-administered questionnaire) has been fielded for the first time. A push to consolidate the various data holdings of the registry is being made.
Pardaens K, Haagdorens L, Van Wambeke P, Van den Broeck A, Van	Chronic Fatigue Reference Centre, University Hospitals and	How relevant are exercise capacity measures for evaluating	Clin Rehabil. 2006 Jan;20(1):56-66.	OBJECTIVE: To evaluate the outcome of a multidisciplinary treatment programme for patients with chronic fatigue syndrome, including health-related quality of life (HRQoL) and psychosocial variables, and exercise capacity measures. DESIGN: A six-month prospective outcome study. SETTING: University outpatient rehabilitation clinic; group setting. SUBJECTS: One hundred and sixteen women fulfilling

Houdenhove B.	Department of Rehabilitation Sciences, KU Leuven, Belgium.	treatment effects in chronic fatigue syndrome? Results from a prospective, multidisciplinary outcome study.		chronic fatigue syndrome criteria. INTERVENTIONS: Cognitive behaviourally and graded exercise-based strategies; emphasis on adaptive lifestyle changes. MEASURES: Short Form General Health Survey (SF-36); Symptom Checklist (SCL-90); Causal Attribution List (CAL); Self-Efficacy Scale (SE); maximum progressive bicycle ergometer test with respiratory gas analysis; and isokinetic leg strength test, before and after treatment. RESULTS: The total group significantly improved on nearly all reported HRQoL/psychosocial variables. Changes in exercise capacity measures were rather modest and did not correlate or only weakly correlated with HRQoL/psychosocial variables. Subgroup analyses indicated that less fit patients improved significantly more on exercise capacity measures than their more fit counterparts. Patients who were fitter at baseline scored better on pretreatment HRQoL/psychosocial variables, but both subgroups improved similarly on these variables. CONCLUSIONS: Health-related quality of life and psychosocial functioning in patients with chronic fatigue syndrome improves after a six-month cognitive behaviourally and graded exercise-based multidisciplinary treatment programme. Increase in exercise capacity measures is not a necessary condition for reported improvements, except for less fit patients.
Parker NR, Barralet JH, Bell AM.	Darling Downs Public Health Unit, Queensland Health, Australia. neil_parker@health.qld.gov.au	Q fever.	Lancet. 2006 Feb 25;367(9511):679-88.	Q fever is a zoonosis with many manifestations. The most common clinical presentation is an influenza-like illness with varying degrees of pneumonia and hepatitis. Although acute disease is usually self-limiting, people do occasionally die from this condition. Endocarditis is the most frequent chronic presentation. Although Q fever is widespread, practitioner awareness and clinical manifestations vary from region to region. Geographically limited studies suggest that chronic fatigue syndrome and cardiovascular disease are long-term sequelae. An effective whole-cell vaccine is licensed in Australia. Live and acellular vaccines have also been studied, but are not currently licensed.
Peakman M, Skowera A, Hotopf M.	Department of Immunobiology, King's College London, School of Medicine at Guy's, UK.	Immunological dysfunction, vaccination and Gulf War illness.	Philos Trans R Soc Lond B Biol Sci. 2006 Apr 29;361(1468):681-7.	One candidate cause of Gulf War illness is vaccination against infectious diseases including medical counter-measures against biological weapons. One influential theory has suggested that such mass-vaccination caused a shift in immune response to a Type 2 cytokine pattern (Th2), which it was suggested was accompanied by a chronic fatigue syndrome-like illness. This article critically appraises this theory. We start by examining epidemiological evidence, which indicates that single vaccines are unlikely to be a substantial cause of Gulf War illness, but that there was a modest relationship with multiple vaccines, which was strongest in those vaccinated while deployed to the Gulf. These relationships may be affected by recall bias. We conclude by examining the results of immunological studies carried out in veterans or in a relevant setting in vitro. The balance of evidence from immunological studies on veterans returning from the War, including those developing multi-symptom illness, is that the immune response has not become polarized towards Th2. In summary, the epidemiological evidence for a multiple vaccine effect on Gulf War-related illness remains a potentially important aetiological lead, but mechanistic studies available at this stage do not identify any immunological basis for it.
Pedersen BK, Saltin B.	The Centre of Inflammation and Metabolism, Department of Infectious	Evidence for prescribing exercise as therapy in chronic disease.	Scand J Med Sci Sports. 2006 Feb;16 Suppl 1:3-63.	Considerable knowledge has accumulated in recent decades concerning the significance of physical activity in the treatment of a number of diseases, including diseases that do not primarily manifest as disorders of the locomotive apparatus. In this review we present the evidence for prescribing exercise therapy in the treatment of metabolic syndrome-related disorders (insulin resistance, type 2 diabetes, dyslipidemia, hypertension, obesity), heart and pulmonary diseases (chronic obstructive pulmonary

	Diseases, Copenhagen, Denmark. bkp@rh.dk			disease, coronary heart disease, chronic heart failure, intermittent claudication), muscle, bone and joint diseases (osteoarthritis, rheumatoid arthritis, osteoporosis, fibromyalgia, chronic fatigue syndrome) and cancer, depression, asthma and type 1 diabetes. For each disease, we review the effect of exercise therapy on disease pathogenesis, on symptoms specific to the diagnosis, on physical fitness or strength and on quality of life. The possible mechanisms of action are briefly examined and the principles for prescribing exercise therapy are discussed, focusing on the type and amount of exercise and possible contraindications.
Petersen I, Thomas JM, Hamilton WT, White PD.	Centre for Psychiatry, Barts and The London, Queen Mary's School of Medicine and Dentistry, UK.	Risk and predictors of fatigue after infectious mononucleosis in a large primary-care cohort.	QJM. 2006 Jan;99(1):49-55. Epub 2005 Dec 5.	BACKGROUND: Fatigue has been found to complicate infectious mononucleosis (IM) when patients are directly asked about it. We do not know whether such fatigue is clinically significant, nor whether IM is a specific risk for fatigue (or whether it can follow other common infections). Various risk markers for post-infectious fatigue have been identified, but findings are inconsistent. AIM: To determine the risk of clinically reported fatigue (compared with depression) after IM (compared with both influenza and tonsillitis) in patients attending primary care, and to examine risk markers for post-IM fatigue. DESIGN: Comparison of matched primary-care cohorts. METHODS: We identified 1438 adult patients with a positive heterophil antibody test for IM from the UK General Practice Research Database. These patients were individually matched on age, sex and practice to two comparison groups; one with a clinical diagnosis of influenza and the other of tonsillitis. RESULTS: The odds ratios (ORs) (95%CI) for reported fatigue after IM vs. influenza and tonsillitis were 4.4 (2.9-6.9) and 6.6 (4.2-10.4), respectively. Risk markers for post-IM fatigue included female sex and premorbid mood disorder. By comparison, the ORs for depression after IM vs. influenza and tonsillitis were 1.6 (0.9-2.6) and 2.3 (1.4-3.9), respectively. DISCUSSION: IM is a specific and significant risk for clinically reported fatigue, which is both separate from, and more common than, depression. Female sex and premorbid mood disorder are risk markers for fatigue. These can be used both to target prevention strategies and to explore aetiological mechanisms.
Pittion-Vouyovitch S, Debouverie M, Guillemin F, Vandenberghe N, Anxionnat R, Vespignani H.	Department of Neurology, Central Hospital, 54000 Nancy, France. sophie-pittion@wanadoo.fr	Fatigue in multiple sclerosis is related to disability, depression and quality of life.	J Neurol Sci. 2006 Apr 15;243(1-2):39-45. Epub 2006 Jan 24.	Fatigue in multiple sclerosis is a frequent and disabling symptom that can interfere in daily functioning. The aim of this study is to demonstrate the relationship between fatigue and disability, disease course, depression and quality of life. We administered French valid versions of the Fatigue Impact Scale (EMIF-SEP), the short form of the Beck depression inventory (13 items) and the SF-36 to 237 out of 312 patients with clinically definite multiple sclerosis with EDSS<or=6.5. The EMIF-SEP is composed of four dimensions (cognitive, physical, social role and psychological) and allows a multidimensional evaluation. Using a multivariate analysis, EMIF-SEP total scores with physical and social role subscales were highly correlated with EDSS ($p < 0.0001$). Cognitive and psychological dimensions of the EMIF-SEP were not linked to EDSS. EMIF-SEP was not correlated with disease course after adjusting for EDSS. EMIF-SEP scores were significantly associated with depression scores ($r = 0.74$, $p < 0.0001$). The multivariate analysis also showed a significant impact of fatigue on each scale of quality of life of the SF-36. These data confirm that fatigue is correlated with disability, but cognitive and psychological dimensions of fatigue remain independent. Fatigue is also associated with depression and quality of life.
Prins JB, van der Meer JW,	Department of Medical	Chronic fatigue syndrome.	Lancet. 2006 Jan 28;367(9507):346-	During the past two decades, there has been heated debate about chronic fatigue syndrome (CFS) among researchers, practitioners, and patients. Few illnesses have been discussed so extensively. The

Bleijenberg G.	Psychology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands. j.prins@mps.umcn.nl		55. Comment in: Lancet. 2006 May 13;367(9522):1573-4; author reply 1575. Lancet. 2006 May 13;367(9522):1574; author reply 1575	existence of the disorder has been questioned, its underlying pathophysiology debated, and an effective treatment opposed; patients' organisations have participated in scientific discussions. In this review, we look back on several controversies over CFS with respect to its definition, diagnosis, pathophysiology, and treatment. We review issues of epidemiology and clinical manifestations, focusing on the scientific status of CFS. Modern neuroscience and genetics research offer interesting findings for new hypotheses on the aetiology and pathogenesis of the illness. We also discuss promising future issues, such as psychopathophysiology and mechanisms of improvement, and suggest multidisciplinary prospective studies of CFS and fatigue in the general population. These studies should pay particular attention to similarities to and differences from functional somatic syndromes and other fatiguing conditions.
Puri BK.	MRC Clinical Sciences Centre, Imperial College, Hammersmith Hospital, London, UK. basant.puri@csc.mrc.ac.uk	Proton and 31-phosphorus neurospectroscopy in the study of membrane phospholipids and fatty acid intervention in schizophrenia, depression, chronic fatigue syndrome (myalgic encephalomyelitis) and dyslexia.	Int Rev Psychiatry. 2006 Apr;18(2):145-7.	Neurospectroscopy allows biochemical processes in the brain to be studied non-invasively. At magnetic field strengths of 1.5 T or higher, cerebral proton neurospectroscopy allows the ascertainment of values of myo-inositol, choline-containing compounds, creatine, glutamate, glutamine, and N-acetyl aspartate. At similar field strengths, cerebral 31-phosphorus neurospectroscopy allows the ascertainment of values of phosphomonoesters, inorganic phosphate, phosphodiesters, phosphocreatine, and the gamma, alpha and beta nucleotide triphosphate (mainly adenosine triphosphate) resonances. Since choline is a common polar head group at the Sn3 position of membrane phospholipid molecules, a raised level of free choline, as indexed by proton neurospectroscopy, can indicate relatively low anabolism of membrane phospholipid molecules. Furthermore, the choline peak includes phosphorylcholine and glycerophosphorylcholine and even ethanolamine. The phosphomonoesters peak measured using 31-phosphorus spectroscopy includes major contributions from phosphocholine, phosphoethanolamine and L-phosphoserine, which are important precursors of membrane phospholipids, while the phosphodiesters peak includes contributions from glycerophosphocholine and glycerophosphoethanolamine, which are important products of membrane phospholipid catabolism. Hence proton neurospectroscopy and 31-phosphorus neurospectroscopy can yield important information relating to the metabolism of cerebral membrane phospholipids. The application of these techniques to the investigation of membrane phospholipid metabolism in schizophrenia, depression, chronic fatigue syndrome (myalgic encephalomyelitis or M.E.) and dyslexia is described.
Puri BK.	MRC Clinical Sciences Centre, Imperial College, Hammersmith Hospital, London, UK. basant.puri@csc.mrc.ac.uk	High-resolution magnetic resonance imaging sinc-interpolation-based subvoxel registration and semi-automated quantitative lateral ventricular morphology employing	Int Rev Psychiatry. 2006 Apr;18(2):149-54.	Serial high-resolution structural magnetic resonance imaging scans of the brain can now be precisely aligned, with six degrees of freedom (three mutually orthogonal translational and three rotational degrees of freedom around three mutually orthogonal axes), using a rigid-body subvoxel registration technique. This is driven by the in-plane point spread function for images acquired in the Fourier domain with data obtained over a bounded region of k-space, namely the sinc interpolation function, where sinc z = (sin z)/z, with z being any complex number (including zero). Computational subtraction of the three-dimensional Cartesian spatial representation matrices of serially acquired scan data allows for the determination of structural cerebral changes with great precision, since voxel signals from unchanged structures are almost completely cancelled. Thus changes readily show up against a background of noise. Furthermore, lateral ventricular changes can now be accurately quantified using a semi-automated method involving contour production, threshold computation, binary image

		threshold computation and binary image creation in the study of fatty acid interventions in schizophrenia, depression, chronic fatigue syndrome and Huntington's disease.		creation and ventricular extraction. These techniques have been applied to the investigation of the effects on cerebral structure of intervention with fatty acids, particularly the long-chain polyunsaturated n-3 fatty acid eicosapentaenoic acid (EPA), in disorders such as schizophrenia, treatment-resistant depression, chronic fatigue syndrome (myalgic encephalomyelitis or ME), and Huntington's disease.
Puri BK.	Hammersmith Hospital, United Kingdom.	Long-chain polyunsaturated fatty acids and the pathophysiology of myalgic encephalomyelitis (chronic fatigue syndrome).	J Clin Pathol. 2006 Aug 25; [Epub ahead of print]	Evidence is put forward to suggest that myalgic encephalomyelitis, also known as chronic fatigue syndrome, may be associated with persistent viral infection. In turn, such infections are likely to impair the ability of the body to biosynthesize n-3 and n-6 long-chain polyunsaturated fatty acids by inhibiting the delta-6 desaturation of the precursor essential fatty acids alpha-linolenic acid and linoleic acid. In turn, this would impair the proper functioning of cell membranes, including cell signalling, and have an adverse effect of the biosynthesis of eicosanoids from the long-chain polyunsaturated fatty acids dihomo-a-linolenic acid, arachidonic acid and eicosapentaenoic acid. These actions might offer an explanation for some of the symptoms and signs of myalgic encephalomyelitis. A potential therapeutic avenue may be offered by bypassing the inhibition of the enzyme delta-6-desaturase by administering both virgin cold-pressed non-raffinated evening primrose oil and eicosapentaenoic acid. The former would supply gamma-linolenic acid and lipophilic pentacyclic triterpenes. The gamma-linolenic acid can readily be converted into dihomo-a-linolenic acid and thence arachidonic acid, while triterpenes have important free radical scavenging, cyclooxygenase and neutrophil elastase inhibitory activities. Furthermore, both arachidonic acid and eicosapentaenoic acid are, at relatively low concentrations, directly virucidal.
Quarmby L, Rimes KA, Deale A, Wessely S, Chalder T.	King's College London, Academic Department of Psychological Medicine, Weston Education Centre, Cutcombe Road, London SE5 9RJ, UK.	Cognitive-behaviour therapy for chronic fatigue syndrome: Comparison of outcomes within and outside the confines of a randomised controlled trial.	Behav Res Ther. 2006 Oct 27; [Epub ahead of print]	Outcomes for cognitive-behaviour therapy (CBT) in randomised controlled trials (RCTs) have rarely been compared to those in routine clinical practice. Taking the case of CBT for chronic fatigue syndrome (CFS), we evaluated the results of a successful RCT against those of the same treatment given in the same setting as part of routine practice. Fatigue and social adjustment scores were compared for patients who received CBT for CFS as part of a RCT (N=30) and patients who received CBT as part of everyday clinical practice (N=384). The results in the RCT were superior to those in routine clinical practice. Between pre-treatment and 6-month follow-up, the RCT showed a larger reduction in fatigue and greater improvement in social adjustment than those in routine treatment. The changes in fatigue scores were similar for both groups during treatment but were greater in the RCT between post-treatment and follow-up. Potential reasons for the superior results of the RCT include patient selection, therapist factors and the use of a manualised treatment protocol. Practitioners need to pay particular attention to relapse prevention and ensuring adequate follow-up in addition to encouraging patients to continue with cognitive-behavioural strategies once treatment

				has ended.
Rajeevan MS, Smith AK, Dimulescu I, Unger ER, Vernon SD, Heim C, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA.	Glucocorticoid receptor polymorphisms and haplotypes associated with chronic fatigue syndrome.	Genes Brain Behav. 2006 Jun 1; [Epub ahead of print]	Chronic fatigue syndrome (CFS) is a significant public health problem of unknown etiology, the pathophysiology has not been elucidated, and there are no characteristic physical signs or laboratory abnormalities. Some studies have indicated an association of CFS with deregulation of immune functions and hypothalamic-pituitary-adrenal (HPA) axis activity. In this study, we examined the association of sequence variations in the glucocorticoid receptor gene (NR3C1) with CFS because NR3C1 is a major effector of the HPA axis. There were 137 study participants (40 with CFS, 55 with insufficient symptoms or fatigue, termed as ISF, and 42 non-fatigued controls) who were clinically evaluated and identified from the general population of Wichita, KS. Nine single nucleotide polymorphisms (SNPs) in NR3C1 were tested for association of polymorphisms and haplotypes with CFS. We observed an association of multiple SNPs with chronic fatigue compared to non-fatigued (NF) subjects ($P < 0.05$) and found similar associations with quantitative assessments of functional impairment (by the SF-36), with fatigue (by the Multidimensional Fatigue Inventory) and with symptoms (assessed by the Centers for Disease Control Symptom Inventory). Subjects homozygous for the major allele of all associated SNPs were at increased risk for CFS with odds ratios ranging from 2.61 (CI 1.05-6.45) to 3.00 (CI 1.12-8.05). Five SNPs, covering a region of approximately 80 kb, demonstrated high linkage disequilibrium (LD) in CFS, but LD gradually declined in ISF to NF subjects. Furthermore, haplotype analysis of the region in LD identified two associated haplotypes with opposite alleles: one protective and the other conferring risk of CFS. These results demonstrate NR3C1 as a potential mediator of chronic fatigue, and implicate variations in the 5' region of NR3C1 as a possible mechanism through which the alterations in HPA axis regulation and behavioural characteristics of CFS may manifest.
Reeves WC, Heim C, Maloney EM, Youngblood LS, Unger ER, Decker MJ, Jones JF, Rye DB.	Viral Exanthems & Herpesvirus Branch, Division of Viral & Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control & Prevention, Atlanta, GA, USA. wcr1@cdc.gov	Sleep characteristics of persons with chronic fatigue syndrome and non-fatigued controls: results from a population-based study.	BMC Neurol. 2006 Nov 16;6:41.	BACKGROUND: The etiology and pathophysiology of chronic fatigue syndrome (CFS) remain inchoate. Attempts to elucidate the pathophysiology must consider sleep physiology, as unrefreshing sleep is the most commonly reported of the 8 case-defining symptoms of CFS. Although published studies have consistently reported inefficient sleep and documented a variable occurrence of previously undiagnosed primary sleep disorders, they have not identified characteristic disturbances in sleep architecture or a distinctive pattern of polysomnographic abnormalities associated with CFS. METHODS: This study recruited CFS cases and non-fatigued controls from a population based study of CFS in Wichita, Kansas. Participants spent two nights in the research unit of a local hospital and underwent overnight polysomnographic and daytime multiple sleep latency testing in order to characterize sleep architecture. RESULTS: Approximately 18% of persons with CFS and 7% of asymptomatic controls were diagnosed with severe primary sleep disorders and were excluded from further analysis. These rates were not significantly different. Persons with CFS had a significantly higher mean frequency of obstructive apnea per hour ($p = .003$); however, the difference was not clinically meaningful. Other characteristics of sleep architecture did not differ between persons with CFS and controls. CONCLUSION: Although disordered breathing during sleep may be associated with CFS, this study generally did not provide evidence that altered sleep architecture is a critical factor in CFS. Future studies should further scrutinize the relationship between subjective sleep quality relative to objective polysomnographic measures.

Ryall C, Coggon D, Peveler R, Reading I, Palmer KT.	MRC Epidemiology Resource Centre, University of Southampton, Southampton General Hospital, Tremona Road, Southampton SO16 6YD, UK.	A case-control study of risk factors for arm pain presenting to primary care services.	Occup Med (Lond). 2006 Mar;56(2):137-43. Epub 2006 Feb 1.	OBJECTIVES: To investigate the association of occupational activities, mental health and comorbidity with care seeking for arm pain, and to test the hypothesis that specific disorders arise from physical risk factors and non-specific pain from psychological ones. METHODS: Patients with a new episode of arm pain and matched controls were recruited from eight general practices. A questionnaire about risk factors was completed and cases were classified using a validated examination schedule. Questions were asked about occupational activities and psychosocial stressors. Mental health was assessed using the Hospital Anxiety Depression Scale, elements of the Brief Symptom Inventory (somatizing tendency) and the Whiteley Index (health anxiety); comorbidity from chronic fatigue syndrome (CFS) and chronic widespread pain (CWP) was ascertained using standard definitions. Associations were explored using logistic regression and summarized as odds ratios (ORs) with 95% confidence intervals (95% CIs). RESULTS: Altogether, 132 cases and 127 controls were studied. Consulting with arm pain was strongly associated with all of the mental health variables and with CFS and CWP, irrespective of the site of arm pain or diagnosis. The OR in those with >3 versus <3 distressing somatic symptoms was 3.9 (95% CI 1.7-9.0). There were several significant associations with physical activity, but none with occupational psychosocial stressors. Repeated wrist/finger movements and carrying weights were more strongly associated with specific diagnoses than with non-specific pain. CONCLUSIONS: Somatizing tendency, health anxiety, low mood, CFS and CWP are more common in arm pain consulters. Certain mechanical activities are also overrepresented, particularly in those with specific pathology.
Saggini R, Vecchiet J, Iezzi S, Racciatti D, Affaitati G, Bellomo RG, Pizzigallo E.	Physical Therapy Institute, Department of Medicine and Aging, G. D'Annunzio University, Chieti, Italy.	Submaximal aerobic exercise with mechanical vibrations improves the functional status of patients with chronic fatigue syndrome.	Eura Medicophys. 2006 Jun;42(2):97-102.	AIM: Chronic fatigue syndrome (CFS) is an illness characterised by disabling fatigue of uncertain aetiology and other nonspecific symptoms. Typically CFS patients complain of a severe fatigue made worse by exercise, with a consistent reduction of working activity. A physical deconditioning could explain CFS features as well as a neuromuscular dysfunction, of central or peripheric origin. METHODS: Ten CFS patients were enrolled in a protocol of a rehabilitative treatment over a six-month period: they underwent a submaximal and predominantly aerobic exercise with a reduced O2 consumption using a Galileo 2000 system that provides mechanical vibrations characterised by sinusoid vertical sollecitations. Before and after such treatment, all patients underwent a pressure pain thresholds profile, an evaluation of physical and psychosocial parameters using the visual analogue scale (VAS) of Scott-Huskisson, and a muscle performance analysis by the CIBEX 6000 dynamometer. RESULTS: After the six-month period of study there was an overall improvement of the above described parameters as compared to the basal determinations. CONCLUSION: We conclude that the rehabilitative exertion provides an useful treatment for CFS patients particularly to realize an effective training of the explosive strength.
Saidi G, Haines L.	Research Division, Royal College of Paediatrics and Child Health, 50 Hallam Street, London W1W 6DE, UK.	The management of children with chronic fatigue syndrome-like illness in primary care: a cross-sectional study.	Br J Gen Pract. 2006 Jan;56(522):43-7.	BACKGROUND: Most studies on children with chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) have been undertaken in tertiary care and little is known about their management in primary care. AIM: To describe the characteristics of patients aged 5-19 years with CFS-like illness in primary care and to examine how GPs investigate and manage patients. DESIGN OF STUDY: Descriptive retrospective questionnaire study. SETTING: Sixty-two UK GP practices in the MRC General Practice Research Framework (GPRF). METHOD: One hundred and twenty-two practices were approached; 62 identified 116 patients consulting a GP with severe fatigue lasting over 3 months.

				Practice nurses and GPs completed questionnaires from medical notes and patients completed postal questionnaires. RESULTS: Ninety-four patients were considered by a clinical panel, blind to diagnosis, to meet the Oxford CFS criteria with a fatigue duration of 3 months. Seventy-three per cent were girls, 94% white, mean age was 12.9 years and median illness duration 3.3 years. GPs had principal responsibility for 62%. A diagnosis of CFS/ME was made in 55%, 30% of these within 6 months. Fifty per cent had a moderate illness severity. Paediatric referrals were made in 82% and psychiatric referrals in 46% (median time of 2 and 13 months respectively). Advice given included setting activity goals, pacing, rest and graded exercise. CONCLUSIONS: Patient characteristics are comparable to those reported in tertiary care, although fewer are severe cases. GPs have responsibility for the majority of patients, are diagnosing CFS/ME within a short time and applying a range of referral and advice strategies.
Sakudo A, Kuratsune H, Kobayashi T, Tajima S, Watanabe Y, Ikuta K.	Department of Virology, Center for Infectious Disease Control, Research Institute for Microbial Diseases, Osaka University, Yamadaoka, Suita, Japan.	Spectroscopic diagnosis of chronic fatigue syndrome by visible and near-infrared spectroscopy in serum samples.	Biochem Biophys Res Commun. 2006 Jul 14;345(4):1513-6. Epub 2006 May 22.	To investigate visible and near-infrared (Vis-NIR) spectroscopy enabling chronic fatigue syndrome (CFS) diagnosis, we subjected sera from CFS patients as well as healthy donors to Vis-NIR spectroscopy. Vis-NIR spectra in the 600-1100 nm region for sera from 77 CFS patients and 71 healthy donors were subjected to principal component analysis (PCA) and soft independent modeling of class analogy (SIMCA) to develop multivariate models to discriminate between CFS patients and healthy donors. The model was further assessed by the prediction of 99 masked other determinations (54 in the healthy group and 45 in the CFS patient group). The PCA model predicted successful discrimination of the masked samples. The SIMCA model predicted 54 of 54 (100%) healthy donors and 42 of 45 (93.3%) CFS patients of Vis-NIR spectra from masked serum samples correctly. These results suggest that Vis-NIR spectroscopy for sera combined with chemometrics analysis could provide a promising tool to objectively diagnose CFS.
Schikler KN.		Potential polygenic influences on chronic fatigue syndrome.	Pediatrics. 2006 Oct;118(4):1799-800; author reply 1800. Comment on: Pediatrics. 2006 Jun;117(6):2074-9.	Letter
Schonfeldt-Lecuona C, Connemann BJ, Wolf RC, Braun M, Freudenmann RW.		Bupropion augmentation in the treatment of chronic fatigue syndrome with coexistent major depression episode.	Pharmacopsychiatry. 2006 Jul;39(4):152-4.	While psychoeducational strategies and general support are always indicated for the treatment of chronic fatigue syndrome (CFS), pharmacological strategies are yet not well established. Antidepressants such as selective serotonin re-uptake inhibitors have been shown to influence positively symptoms and immunological parameters. However, a considerable part of CFS patients do not satisfactorily respond to them. Bupropion, a centrally acting catecholamine-transporter blocker without classic psycho-analeptic properties, shows theoretical potential to improve fatigue symptoms. In the reported case paroxetine was augmented with bupropion at high dosage, a strategy which consecutively led to a rapid relief of CFS-symptoms.
Sene D, Saadoun D, Limal N, Piette JC, Cacoub P.	Service de medecine interne, hopital de la Pitie-	[Update in Hepatitis C virus associated	Rev Med Interne. 2006 Nov 7; [Epub ahead of print]	INTRODUCTION: Since the discovery of the hepatitis C virus, many manifestations, so called extra-hepatic manifestations (EHM), are largely reported with more or less relationship proofs. ACTUALITIES AND MAIN POINTS: This article proposes a review of the main extra-hepatic manifestations associated

	Salpetriere, 91, boulevard de l'Hopital, 75651 Paris cedex 13, France.	extrahepatic manifestations.] [Article in French]		with the Hepatis C Virus infection and which remain a topical subject, more than fifteen years after the discovery of this virus. Mixed cryoglobulin and its vasculitic manifestations are still one of the more frequent Hepatis C Virus associated-extra-hepatic manifestations. Its management may be critically changed due to the increasing use of anti-CD20 therapy. Among other HCV-EHM, the following extra-hepatic manifestations are still of interest: the chronic fatigue syndrome, the sicca syndrome, the non-insulin-dependent diabetes mellitus, malignant B cell proliferations, mainly the Hepatis C Virus-related splenic lymphoma with villous lymphocytes and the production of auto-antibodies. PERSPECTIVES AND PROJECTS: The mechanisms underlying these HCV-associated EHM are ill-elucidated and still remain of great interest as proved by current studies. The use of anti-CD20 antibodies in the treatment of cryoglobulinemic vasculitis is also under investigation.
Shapiro CM.		Chronic fatigue and chronic fatigue syndrome: pathogenesis and measurement scales.	J Psychosom Res. 2006 Jun;60(6):549-50.	
Shepherd C.		The debate: myalgic encephalomyelitis and chronic fatigue syndrome.	Br J Nurs. 2006 Jun 22-Jul 12;15(12):662-9.	Almost every aspect of myalgic encephalomyelitis (or encephalopathy) and chronic fatigue syndrome is the subject of disagreement and uncertainty -- something that has undoubtedly hampered recognition, understanding and research. Although the pathogenesis remains the subject of intense medical debate, a number of predisposing, precipitating and perpetuating factors are now starting to emerge. Therapeutic nihilism is no longer appropriate as there is a great deal that can be done to alleviate some of the more distressing symptoms and improve quality of life for these patients.
Shor S		Lyme Disease Presenting as Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2006; 13(4): 73-82	Objective: Chronic Fatigue Syndrome (CFS) by definition represents a diagnosis of exclusion. Late stage or "Chronic Lyme" infection with or without "co-infections" is a difficult diagnosis to establish. The symptom complex of both conditions can be very similar. This case study represents an attempt to support serious consideration for a subpopulation of patients otherwise diagnosed with "CFS," as actually representing chronic Lyme disease. Method: A case study is presented of a 33-year-old man, who for two years, was being managed as having CFS. However, after ~2 years of utilizing multiple modalities of management with limited success, the diagnosis of Lyme was reconsidered. Historical exposure risks to Lyme in this individual were high. He had prolonged exposure in the highly tick-infested mountains of North Carolina for 18 months, several years prior to becoming ill. More aggressive investigation confirmed the diagnosis of Lyme. Appropriate changes in management were associated with an improved level of functioning that was far in excess of what maximal management of CFS was able to achieve. The features of CFS and chronic Lyme can be very similar and include the following: Profound fatigue often associated with cognitive impairment. Other common symptoms related to both of these conditions include sleep disturbances, fibromyalgia, and dysautonomias. In pursuing clarification of this diagnosis, the author was exposed to a contrast in medical opinion regarding diagnostic tools and criteria that were perceived as creating potential barriers to the management of patients presenting with these symptoms. Conclusion: Acceptance and awareness of the possibility that Lyme disease can present as CFS has important therapeutic and prognostic

				implications.
Shor S.		Lyme Disease Presenting as Chronic Fatigue Syndrome Profile A Case Report	Journal of Chronic Fatigue Syndrome 2006;13(4):	No abstract available at September 2006
Shuttleworth A.		Understanding chronic fatigue.	Nurs Times. 2006 Jan 17-23;102(3):20-1.	
Siegel SD, Antoni MH, Fletcher MA, Maher K, Segota MC, Klimas N.	Department of Psychology, Behavioral Medicine Research Center, University of Miami, FL, USA.	Impaired natural immunity, cognitive dysfunction, and physical symptoms in patients with chronic fatigue syndrome: preliminary evidence for a subgroup?	J Psychosom Res. 2006 Jun;60(6):559-66.	OBJECTIVE: The diagnostic criteria of chronic fatigue syndrome (CFS) define a heterogeneous population composed of several subgroups. Past efforts to identify subgroup markers have met with mixed success. This study was designed to examine natural killer cell activity (NKCA) as a potential subgroup marker by comparing the clinical presentations of CFS patients with and without clinically reduced NKCA. METHODS: Forty-one female CFS patients were classified into having either low or normal NKCA levels. These subgroups were then compared on objective measures of cognitive functioning and subjective assessments of fatigue, vigor, cognitive impairment, and daytime dysfunction. RESULTS: Relative to CFS patients in the normal-NKCA subgroup, low-NKCA patients reported less vigor, more daytime dysfunction, and more cognitive impairment. In addition, low-NKCA patients performed less on objective measures of cognitive functioning relative to normal-NKCA patients. CONCLUSIONS: The results are offered as preliminary evidence in support of using NKCA as an immunological subgroup marker in CFS. Findings are also discussed in terms of known associations between dysregulated immune functions, somatic symptoms, and psychological stress.
Smith AK, White PD, Aslakson E, Vollmer-Conna U, Rajeevan MS.	Centers for Disease Control and Prevention, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, 1600 Clifton Road, MSG41, Atlanta, GA 30333, USA.	Polymorphisms in genes regulating the HPA axis associated with empirically delineated classes of unexplained chronic fatigue.	Pharmacogenomics. 2006 Apr;7(3):387-94.	Chronic fatigue syndrome (CFS) is characterized by persistent or relapsing fatigue that is not alleviated by rest, causes substantial reduction in activities and is accompanied by a variety of symptoms. Its unknown etiology may reflect that CFS is heterogeneous. Latent class analyses of symptoms and physiological systems were used to delineate subgroups within a population-based sample of fatigued and nonfatigued subjects [1] . This study examined whether genetic differences underlie the individual subgroups of the latent class solution. Polymorphisms in 11 candidate genes related to both hypothalamic-pituitary-adrenal (HPA) axis function and mood-related neurotransmitter systems were evaluated by comparing each of the five ill classes (Class 1, n = 33; Class 3, n = 22; Class 4, n = 22; Class 5, n = 17; Class 6, n = 11) of fatigued subjects with subjects defined as well (Class 2, n = 35). Of the five classes of subjects with unexplained fatigue, three classes were distinguished by gene polymorphsims involved in either HPA axis function or neurotransmitter systems, including proopiomelanocortin (POMC), nuclear receptor subfamily 3, group C, member 1 (NR3C1), monoamine oxidase A (MAOA), monoamine oxidase B (MAOB), and tryptophan hydroxylase 2 (TPH2). These data support the hypothesis that medically unexplained chronic fatigue is heterogeneous and presents preliminary evidence of the genetic mechanisms underlying some of the putative conditions.
Smith WR, Noonan C, Buchwald D.	Department of Psychiatry, University of	Mortality in a cohort of chronically	Psychol Med. 2006 Sep;36(9):1301-6.	BACKGROUND: Comprehensive studies of mortality among patients with chronic fatigue (CF) and chronic fatigue syndrome (CFS) have not been published, but several sources suggest that CFS is associated with an elevated risk for suicide. METHOD: Data on 1201 chronically fatigued patients

	Washington, Seattle, WA, USA. wrsmith@u.washington.edu	fatigued patients.		followed in a university-affiliated tertiary-care clinic for up to 14 years were submitted to the Center for Disease Control and Prevention (CDC) National Death Index (NDI) to evaluate all-cause and suicide-caused death rates against standardized mortality rates (SMRs). We used Life Table Analysis to examine the influence of sex and diagnoses of CFS and depression. RESULTS: All-cause mortality in chronically fatigued patients was no higher than expected, but suicide-caused death rates were more than eight times higher than in the US general population. The significant elevation in the SMR of suicide was restricted to those who did not meet criteria for CFS [SMR(CF)=14.2, 95% confidence interval (CI) 5.7-29.3 versus SMR(CFS)=3.6, 95% CI 0.4-12.9]. Among chronically fatigued patients who did not meet CFS criteria, those with a lifetime history of major depression (MD) had higher suicide-caused death rates than among their non-depressed counterparts (SMR(MD)=19.1, 95% CI 7.0-41.5 versus SMR(NMD)=5.6, 95% CI 0.1-31.4), although the difference was not significant. CONCLUSIONS: CFS does not appear to be associated with increased all-cause mortality or suicide rates. Clinicians, however, should carefully evaluate patients with CF for depression and suicidality.
Smith WR, White PD, Buchwald D.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA. wrsmith@u.washington.edu	A case control study of premorbid and currently reported physical activity levels in chronic fatigue syndrome.	BMC Psychiatry. 2006 Nov 13;6:53.	BACKGROUND: Patients with chronic fatigue syndrome typically report high levels of physical activity before becoming ill. Few studies have examined premorbid and current activity levels in chronically fatigued patients. METHODS: In a case-control study, 33 patients with chronic, unexplained, disabling fatigue attending a university-based clinic specializing in fatigue were compared to 33 healthy, age- and sex-matched controls. Patients rated their activity levels before their illness and currently, using scales designed for this purpose. Controls reported their level of activity of 2 years previously and currently. Chi-square analyses, Student's t tests, and Wilcoxon signed rank tests were used in pair matched analyses. RESULTS: Compared to healthy controls, patients with chronic, unexplained fatigue rated themselves as more active before their illness ($p < or = 0.001$) and less active currently ($p < or = 0.001$). The patients also reported they currently stood or walked less than the controls (median [inter-quartile range] = 4 2345 versus 9 [7.5-12] hours, $p < or = 0.001$), and spent more time reclining (median [inter-quartile range] = 12 10111213141516 versus 8 [8-9.5] hours, $p < or = 0.001$). These differences remained significant for the subset of patients who met strict criteria for chronic fatigue syndrome or fibromyalgia. CONCLUSION: Patients with chronic, unexplained, disabling fatigue reported being more active before becoming ill than healthy controls. This finding could be explained by greater premorbid activity levels that could predispose to illness, or by an overestimation of previous activity. Either possibility could influence patients' perceptions of their current activity levels and their judgments of recovery. Perceived activity should be addressed as part of management of the illness.
St Clair Gibson A, Grobler LA, Collins M, Lambert MI, Sharwood K, Derman EW, Noakes TD.	UCT/MRC Research Unit of Exercise Science and Sports Medicine, Department of Human Biology, University of Cape	Evaluation of maximal exercise performance, fatigue, and depression in athletes with acquired chronic training	Clin J Sport Med. 2006 Jan;16(1):39-45.	OBJECTIVE: This study compared differences in maximal strength and aerobic capacity and symptoms of fatigue and depression in athletes with acquired training intolerance (ATI) and control athletes (CON) matched for age and current training volume who did not have symptoms of excessive or chronic fatigue associated with their sporting activity. SETTING: University of Cape Town, Sports Science Institute of South Africa. PARTICIPANTS: Twenty ATI and 10 CON athletes participated in the trial. Although the ATI athletes reported symptoms of excessive fatigue during exercise, or symptoms of fatigue that occurred at rest and during activities of daily living, they did not fulfill the criteria for a diagnosis of chronic fatigue syndrome. MAIN OUTCOME MEASURES: A training and comprehensive

	Town, Cape Town, South Africa. agibson@sports.uct.ac.za	intolerance.		medical history was recorded from all subjects. The Beck Depression Inventory Short Form (BDI-SF) was used to assess levels of depression in both ATI and control subjects. Maximal force output during a 5-second isometric voluntary knee extensor muscle contraction, and maximal aerobic capacity (VO2max), maximal heart rate (HRmax), and maximal blood lactate concentrations during a treadmill running test were measured in all subjects. RESULTS: There were no differences in maximal isometric force output, peak treadmill running speed, VO2max, HRmax, or blood lactate concentration at rest or after maximal exercise testing between the ATI and CON athletes. However, the BDI-SF scores were higher in the ATI (7.7 +/- 6.6 arbitrary units) than in the CON athletes (1.7 +/- 1.5 arbitrary units; (P = 0.0052). CONCLUSIONS: These findings suggest that the symptoms of excessive fatigue and acquired training intolerance described by these ATI athletes do not affect their maximal isometric and maximal aerobic capacity, and may be associated with psychologic depression in these athletes.
Staines DR.		Phosphodiesterase inhibitors may be indicated in the treatment of postulated vasoactive neuropeptide autoimmune fatigue-related disorders.	Med Hypotheses. 2006;66(1):203-4. Epub 2005 Sep 19.	
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport, Qld, 4215, Australia. don_staines@health.qld.gov.au	Postulated vasoactive neuropeptide autoimmunity in fatigue-related conditions: a brief review and hypothesis.	Clin Dev Immunol. 2006 Mar;13(1):25-39.	Disorders such as chronic fatigue syndrome (CFS) and gulf war syndrome (GWS) are characterised by prolonged fatigue and a range of debilitating symptoms of pain, intellectual and emotional impairment, chemical sensitivities and immunological dysfunction. Sudden infant death syndrome (SIDS) surprisingly may have certain features in common with these conditions. Post-infection sequelae may be possible contributing factors although ongoing infection is unproven. Immunological aberration may prove to be associated with certain vasoactive neuropeptides (VN) in the context of molecular mimicry, inappropriate immunological memory and autoimmunity. Adenylate cyclase-activating VNs including pituitary adenylate cyclase-activating polypeptide (PACAP), vasoactive intestinal peptide (VIP) and calcitonin gene-related peptide (CGRP) act as hormones, neurotransmitters, neuroregulators, immune modulators and neurotrophic substances. They and their receptors are potentially immunogenic. VNs are widely distributed in the body particularly in the central and peripheral nervous systems and have been identified in the gut, adrenal gland, blood cells, reproductive system, lung, heart and other tissues. They have a vital role in maintaining cardio-respiratory function, thermoregulation, memory, concentration and executive functions such as emotional responses including social cues and appropriate behaviour. They are co-transmitters for a number of neurotransmitters including acetylcholine and gaseous transmitters, are potent immune regulators with primarily anti-inflammatory activity, and have a significant role in protection of the nervous system against toxic assault as well as being important in the maintenance of homeostasis. This paper describes a biologically plausible mechanism for the development of certain fatigue-related

				syndromes based on loss of immunological tolerance to these VNs or their receptors following infection, other events or de novo resulting in significant pathophysiology possibly mediated via CpG fragments and heat shock (stress) proteins. These conditions extend the public health context of autoimmunity and VN dysregulation and have implications for military medicine where radiological, biological and chemical agents may have a role in pathogenesis. Possible treatment and prevention options are considered.
Stormorken E.		[A step backwards for the patients] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2006 Oct 19;126(20):2688-9; author reply 2689.	Letter
Stouten B, Goudsmit E, Howes S.		Chronic Fatigue Syndrome: Editorial Bias in the British Medical Journal. Response to the Letter to the Editor	Journal of Chronic Fatigue Syndrome 2006;13(1): 71-73	
Takahashi T, Yu F, Zhu SJ, Moriya J, Sumino H, Morimoto S, Yamaguchi N, Kanda T.	Department of General Medicine, Kanazawa Medical University, Kahoku-gun, Ishikawa, Japan.	Beneficial effect of brewers' yeast extract on daily activity in a murine model of chronic fatigue syndrome.	Evid Based Complement Alternat Med. 2006 Mar;3(1):109-15. Epub 2006 Jan 23.	The aim of this study was to assess the effect of Brewers' yeast extract (BYE) on daily activity in a mouse model of chronic fatigue syndrome (CFS). CFS was induced by repeated injection of Brucella abortus (BA) antigen every 2 weeks. BYE was orally administered to mice in a dose of 2 g per kg per day for 2 weeks before injecting BA and for 4 weeks thereafter. We evaluated daily running activity in mice receiving BYE as compared with that in untreated mice. Weekly variation of body weight (BW) and survival in both groups was monitored during the observation period. Spleen weight (SW), SW/BW ratio, percent splenic follicular area and expression levels of interferon-gamma (IFN-gamma) and interleukin-10 (IL-10) mRNA in spleen were determined in both groups at the time of sacrifice. The daily activity during 2 weeks after the second BA injection was significantly higher in the treated group than in the control. There was no difference in BW between both groups through the experimental course. Two mice in the control died 2 and 7 days after the second injection, whereas no mice in the treated group died. Significantly decreased SW and SW/BW ratio were observed in the treated mice together with elevation of splenic follicular area. There were suppressed IFN-gamma and IL-10 mRNA levels in spleens from the treated mice. Our results suggest that BYE might have a protective effect on the marked reduction in activity following repeated BA injection via normalization of host immune responses.
Tanaka M, Sadato N, Okada T, Mizuno K, Sasabe T, Tanabe HC, Saito DN, Onoe H,	Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3	Reduced responsiveness is an essential feature of chronic fatigue syndrome:	BMC Neurol. 2006 Feb 22;6:9.	BACKGROUND: Although the neural mechanism of chronic fatigue syndrome has been investigated by a number of researchers, it remains poorly understood. METHODS: Using functional magnetic resonance imaging, we studied brain responsiveness in 6 male chronic fatigue syndrome patients and in 7 age-matched male healthy volunteers. Responsiveness of auditory cortices to transient, short-lived, noise reduction was measured while subjects performed a fatigue-inducing continual visual

Kuratsune H, Watanabe Y.	Asahimachi, Osaka 545-8585, Japan. masa-t@msic.med.osaka-cu.ac.jp	a fMRI study.		search task. RESULTS: Responsiveness of the task-dependent brain regions was decreased after the fatigue-inducing task in the normal and chronic fatigue syndrome subjects and the decrement of the responsiveness was equivalent between the 2 groups. In contrast, during the fatigue-inducing period, although responsiveness of auditory cortices remained constant in the normal subjects, it was attenuated in the chronic fatigue syndrome patients. In addition, the rate of this attenuation was positively correlated with the subjective sensation of fatigue as measured using a fatigue visual analogue scale, immediately before the magnetic resonance imaging session. CONCLUSION: Chronic fatigue syndrome may be characterised by attenuation of the responsiveness to stimuli not directly related to the fatigue-inducing task.
Taylor RR		Rehabilitation Programs for Individuals with Chronic Fatigue Syndrome A Review	Journal of Chronic Fatigue Syndrome 2006;13(1): 41-55	Over the past two decades, a small but growing number of rehabilitation programs for individuals with chronic fatigue syndrome (CFS) have been initiated. The aims of this paper were to review existing literature on these programs, to compare and contrast findings emerging from inpatient and outpatient programs, and to comment on the rigor and quality of methodologies used in outcomes research in this area. The studies reviewed herein varied widely in case selection criteria, program intensity, length of participation, program content, and outcome variables measured. Moreover, many were limited by selection bias, the absence of valid and reliable measures, and the absence of a control group. These limitations made it difficult to draw definitive conclusions regarding the effectiveness of any single approach to rehabilitation (whether inpatient or outpatient). However, there is some preliminary evidence that both inpatient and outpatient rehabilitation programs may lead to improvements in physical and occupational functioning, decreased perception of symptom severity, improved quality of life, and greater resource acquisition-at least for certain subgroups of individuals with CFS that participate in specific types of programs. Taken together, these preliminary findings support the need for additional funding and support for the development of comprehensive rehabilitative program centers that include both inpatient and outpatient programs with follow-up sessions and ongoing evaluation. Recommendations for future program development and outcomes research in this area are discussed.
Taylor RR, Kulkarni S, Shiraishi Y.		Conservation of Resources and Quality of Life in Individuals with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2006;13(4):	No abstract available at September 2006
Taylor RR, Supriya Kulkarni, Yukiko Shiraishi		Conservation of Resources and Quality of Life in Individuals with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2006; 13(4): 5-18	Objective: To examine the relationship between resources and quality of life in individuals with chronic fatigue syndrome (CFS). Participants and Study Design: A cross-sectional design was used to describe associations between resource loss and gain and quality of life for 47 individuals diagnosed with CFS. Main Outcome Measures: The Conservation of Resources Evaluation was used to measure resources in terms of perceived loss and gain. Health-related quality of life was assessed with the Quality of Life Index. Results: Total resource loss and total resource gain were significant correlates of overall quality of life. Gains in self-esteem, energy, and work resources were associated with higher-perceived quality of life. Material loss and energy loss were associated with lower-perceived quality of

				life. Conclusions: Findings for the relationships between perceived resources of self-esteem, work, material items, and energy and perceived quality of life can be used inform future rehabilitation efforts. These relationships appear to occur independently of illness severity among individuals CFS
Taylor RR, Thanawala SG, Shiraishi Y, Schoeny ME.	Department of Occupational Therapy, College of Applied Health Sciences, University of Illinois at Chicago, Chicago, IL 60612, USA. rtaylor@uic.edu	Long-term outcomes of an integrative rehabilitation program on quality of life: a follow-up study.	J Psychosom Res. 2006 Dec;61(6):835-9.	OBJECTIVE: To assess the long-term effects of an integrative rehabilitation program on the overall quality of life of individuals with chronic fatigue syndrome (CFS). METHODS: This study utilized a within-subjects, repeated measures cohort design. Twenty-three subjects diagnosed with CFS attended eight sessions of an illness-management group followed by 7 months of goal-oriented, individualized counseling that occurred once weekly for 30 min per session. Quality of life was assessed at five time points (baseline, following the group phase, following the one-on-one phase, and 4 and 12 months following program completion). RESULTS: A within-subjects repeated measures ANOVA revealed significant increases in overall quality of life for up to 1 year following program completion [F(4, 21)=23.5, P<.001]. CONCLUSIONS: Definitive conclusions about program efficacy are limited by design issues. However, findings suggest that the program may have led to improvement in quality of life for up to 1 year following program completion.
Teitelbaum JE, Johnson C, St Cyr J.	Fibromyalgia and Fatigue Centers, Dallas, TX, USA. Endfatigue@aol.com	The use of D-ribose in chronic fatigue syndrome and fibromyalgia: a pilot study.	J Altern Complement Med. 2006 Nov;12(9):857-62.	OBJECTIVES: Fibromyalgia (FMS) and chronic fatigue syndrome (CFS) are debilitating syndromes that are often associated with impaired cellular energy metabolism. As D-ribose has been shown to increase cellular energy synthesis in heart and skeletal muscle, this open-label uncontrolled pilot study was done to evaluate if D-ribose could improve symptoms in fibromyalgia and/or chronic fatigue syndrome patients. DESIGN: Forty-one (41) patients with a diagnosis of FMS and/or CFS were given D-ribose, a naturally occurring pentose carbohydrate, at a dose of 5 g t.i.d. for a total of 280 g. All patients completed questionnaires containing discrete visual analog scales and a global assessment pre- and post-D-ribose administration. RESULTS: D-ribose, which was well-tolerated, resulted in a significant improvement in all five visual analog scale (VAS) categories: energy; sleep; mental clarity; pain intensity; and well-being, as well as an improvement in patients' global assessment. Approximately 66% of patients experienced significant improvement while on D-ribose, with an average increase in energy on the VAS of 45% and an average improvement in overall well-being of 30% ($p < 0.0001$). CONCLUSIONS: D-ribose significantly reduced clinical symptoms in patients suffering from fibromyalgia and chronic fatigue syndrome.
ter Wolbeek M, van Doornen LJ, Kavelaars A, Heijnen CJ.	Laboratory of Psychoneuroimmunology, University Medical Center Utrecht, Utrecht, The Netherlands.	Severe fatigue in adolescents: a common phenomenon?	Pediatrics. 2006 Jun;117(6):e1078-86.	OBJECTIVE: The purpose of this study was to determine the prevalence of severe fatigue in adolescent boys and girls, to explore the role of lifestyle factors in fatigue, and to investigate whether severe fatigue in a healthy population is associated with depression, anxiety, and comorbid factors also observed in chronic fatigue syndrome patients. METHODS: In a sample of 1718 boys and 1749 girls, fatigue severity and duration were measured using a multidimensional questionnaire (Checklist Individual Strength). In addition, self-reports of depressive symptoms, anxiety, chronic fatigue syndrome-related symptoms, and lifestyle characteristics were assessed by means of questionnaires. Prevalence rates of severe fatigue and severe fatigue for > or =1 month, based on a clinical cutoff score of the Checklist Individual Strength, were determined for boys and girls separately, and gender-specific predictors of fatigue were identified by multiple regression analysis. RESULTS: The data showed high prevalence rates of severe fatigue in adolescents. Remarkable differences between boys and girls were observed: 20.5% of girls and 6.5% of the boys scored above the clinical cutoff score on

				the Checklist Individual Strength. Of these subjects 80.0% of the girls and 61.5% of the boys reported severe fatigue for > or =1 month. Of the examined lifestyle characteristics, only sleep characteristics and the participation in sports played a role in predicting fatigue in both genders. Moreover, in girls, fatigue was associated with higher age, an early menarche, medication use, and the absence of an additional job. Overall, girls scored higher on depression, anxiety, and chronic fatigue syndrome-related symptoms. However, the relation between fatigue and these comorbid symptoms did not differ between genders. In both girls and boys, the duration of fatigue was positively related to fatigue severity, severity of depression and anxiety, and the number of chronic fatigue syndrome-related symptoms. CONCLUSIONS: Fatigue prevalence among adolescents is high, especially in girls. Adolescent girls seem to be more vulnerable to symptoms of fatigue and comorbidity than boys. Interestingly, despite a female predominance in complaints, the relation between fatigue and depression, anxiety, and chronic fatigue syndrome-related symptoms was not gender specific and emerged as a cluster. In both genders, fatigue duration was associated with the severity of fatigue and the level of psychological comorbidity and chronic fatigue syndrome-related symptoms, and we, therefore, hypothesize that enduring severe fatigue may form a risk factor for the development of chronic fatigue syndrome.
Tharakan B, Dhanasekaran M, Brown-Borg HM, Manyam BV.	Plummer Movement Disorders Center, Department of Neurology, Scott & White Clinic, Temple, TX 76508, USA.	Trichopus zeylanicus combats fatigue without amphetamine-mimetic activity.	Phytother Res. 2006 Mar;20(3):165-8.	Chronic fatigue is a complex and little understood symptom for which there is no safe and effective pharmacotherapy. The present study was conducted to investigate the effectiveness of Trichopus zeylanicus whole plant powder on fatigue in young Sprague Dawley rats, and aged normal and long-living mutant Ames dwarf mice. Fatigue was evaluated by subjecting the animals to a forced swim test. Trichopus zeylanicus (250 and 500 mg/kg) treated young Sprague-Dawley rats resisted fatigue at a significant level ($p < 0.005$) compared with controls by an extended swim time in the forced swim test. Oral Trichopus zeylanicus (500 mg/kg) treatment for 2 weeks significantly increased the mobility time in the aged mutant ($p < 0.05$) and normal mice ($p < 0.01$) and significantly increased the swim time in the forced swim test in the aged normal mice ($p < 0.05$). Amphetamine-mimetic activity in Trichopus zeylanicus was excluded by suitable tests. These results show that Trichopus zeylanicus whole plant powder has anti-fatigue effects in young Sprague-Dawley rats and aged normal and mutant Ames dwarf mice providing scientific evidence for the Kani tribal practice in India. Copyright 2006 John Wiley & Sons, Ltd.
Tharakan B, Manyam BV.	Plummer Movement Disorders Center, Department of Neurology, Scott and White Clinic and the Texas A&M University System, HSC College of Medicine, Temple,	Botanical therapies in chronic fatigue.	Phytother Res. 2006 Feb;20(2):91-5.	Chronic fatigue often occurs in aging and in various neurological, psychiatric and systemic diseases. The available therapies in modern medicine are limited. The exploration of potential alternative therapies from traditional medicine is reviewed, as there are several botanicals with experimental evidence of efficacy based on animal models and clinical studies. Copyright 2006 John Wiley & Sons, Ltd.

	Texas, USA.			
Thomas HV, Stimpson NJ, Weightman AL, Dunstan F, Lewis G.	Department of Psychological Medicine, School of Medicine, Cardiff University, UK.	Systematic review of multi-symptom conditions in Gulf War veterans.	Psychol Med. 2006 Jun;36(6):735-47. Epub 2006 Jan 26.	BACKGROUND: Gulf War veterans have a number of health complaints. We therefore decided to carry out a systematic review to identify and summarize the findings from studies that have assessed multi-symptom conditions in Gulf War veterans and in an unexposed comparison group. METHOD: Studies published between January 1990 and May 2004 were identified by searching a large number of electronic databases. Reference lists and websites were also searched and key researchers were contacted. Studies were included if they compared the prevalence of chronic fatigue syndrome, multiple chemical sensitivity, CDC-defined chronic multi-symptom illness, fibromyalgia, or symptoms of either fatigue or numbness and tingling in Gulf War veterans and non-Gulf veterans. A total of 2401 abstracts were independently reviewed by two authors. RESULTS: Twenty-three publications fulfilled the inclusion criteria. Gulf deployment was most strongly associated with chronic fatigue syndrome (OR 3.8, 95% CI 2.2-6.7). Gulf War veterans were also approximately three and a half times more likely than non-Gulf veterans to report multiple chemical sensitivity or chronic multi-symptom illness as defined by CDC. The methodological quality of the studies varied but the later and larger studies were of a high methodological standard with robust sampling strategies, adequate response rates and good adjustment for confounders. CONCLUSIONS: The results support the hypothesis that deployment to the Gulf War is associated with greater reporting of multi-symptom conditions.
Thomas MA, Smith AP.	Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, UK. thomasma@cf.ac.uk	An investigation of the long-term benefits of antidepressant medication in the recovery of patients with chronic fatigue syndrome.	Hum Psychopharmacol. 2006 Dec;21(8):503-9.	Two hundred and seventy-five patients fulfilling the Centre for Disease Control (CDC) criteria for Chronic Fatigue Syndrome (CFS) completed measures assessing illness history, global ratings of well being, sleep, activity and psychopathology at baseline, 6 months, 18 months and 3 year follow-up. Forty-nine of these patients had been prescribed antidepressant medication, namely Tricyclic drugs or Selective Serotonin Re-uptake Inhibitors (SSRI). Data from the current study suggests that patients in the antidepressant medication group recover at a faster rate over time when compared to the untreated patient sample. In addition, the positive effects of antidepressant therapy are maintained at the 3-year follow-up point. It appears from these data that the SSRI in particular are responsible for improvements in the condition. Most importantly, these improvements include a reduction in the levels of fatigue recorded by patients. These findings have not been demonstrated in previous studies of the effect of antidepressant therapy for patients with this illness and this may reflect the short time periods studied in the earlier research.
Thompson TD, Weiss M.	Academic Unit of Primary Care, Cotham House, Cotham Hill, Bristol BS6 6JL, UK. trevor.thompson@bris.ac.uk	Homeopathy--what are the active ingredients? An exploratory study using the UK Medical Research Council's framework for the evaluation of complex interventions.	BMC Complement Altern Med. 2006 Nov 13;6:37.	BACKGROUND: Research in homeopathy has traditionally addressed itself to defining the effectiveness of homeopathic potencies in comparison to placebo medication. There is now increasing awareness that the homeopathic consultation is in itself a therapeutic intervention working independently or synergistically with the prescribed remedy. Our objective was to identify and evalute potential "active ingredients" of the homeopathic approach as a whole, in a prospective formal case series, which draws on actual consultation data, and is based on the MRC framework for the evaluation of complex interventions. METHODS: Following on from a theoretical review of how homeopathic care might mediate its effects, 18 patients were prospectively recruited to a case series based at Bristol Homeopathic Hospital. Patients, who lived with one of three index conditions, were interviewed before and after a five visit "package of care". All consultations were recorded and transcribed verbatim. Additional data, including generic and condition-specific questionnaires, artwork and

				"significant other" reports were collected. Textual data was subject to thematic analysis and triangulated with other sources. RESULTS: We judged that around one third of patients had experienced a major improvement in their health over the study period, a third had some improvement and a third had no improvement. Putative active ingredients included the patients' "openness to the mind-body connection", consultational empathy, in-depth enquiry into bodily complaints, disclosure, the remedy matching process and, potentially, the homeopathic remedies themselves. CONCLUSION: This study has has identified, using primary consultation and other data, a range of factors that might account for the effectiveness of homeopathic care. Some of these, such as empathy, are non-specific. Others, such as the remedy matching process, are specific to homeopathy. These findings counsel against the use of placebo-controlled RCT designs in which both arms would potentially be receiving specific active ingredients. Future research in homeopathy should focus on pragmatic trials and seek to confirm or refute the therapeutic role of constructs such as patient "openness", disclosure and homeopathicity.
Toda K, Kimura H.	Department of Rehabilitation, Hiroshima Prefectural Rehabilitation Center, Higashi-Hiroshima, Hiroshima, Japan.	Efficacy of neurotropin in chronic fatigue syndrome: a case report.	Hiroshima J Med Sci. 2006 Mar;55(1):35-7.	Chronic fatigue syndrome (CFS) is a disorder that causes general fatigue and chronic widespread pain. A 28-year-old male visited an outpatient department due to general fatigue and pain involving the entire body. He did not suffer from fibromyalgia, but he was diagnosed with CFS. At the initial visit, he complained of lack of concentration, memory decline, frequent urination, insomnia and occasional difficulty of emotional control, as well as general fatigue and pain involving the entire body. Four tablets of Neurotropin per day alone were administered. General fatigue and pain were gradually alleviated one week later. His sleep condition, concentration power, and memory also improved two weeks later. Medication was discontinued from 11 weeks based on the patient's judgment as he felt little general fatigue and pain involving the entire body. Treatment was completed 3 months later. The symptoms disappeared and did not recur five months after the discontinuation of Neurotropin. He was looking for a job without fatigue and pain 8 months later (5 months after the cessation of treatment). The functional mechanisms of Neurotropin in CFS are unknown.
Torenbeek M, Mes CA, van Liere MJ, Schreurs KM, ter Meer R, Kortleven GC, Warmerdam CG.	Het Roessingh, Centrum voor Revalidatie, divisie Pijnrevalidatie, Enschede. m.torenbeek@roessingh.nl	[Favourable results of a rehabilitation programme with cognitive behavioural therapy and graded physical activity in patients with the chronic-fatigue syndrome] [Article in Dutch]	Ned Tijdschr Geneeskd. 2006 Sep 23;150(38):2088-94. Comment in: Ned Tijdschr Geneeskd. 2006 Sep 23;150(38):2067-8.	OBJECTIVE: To determine whether a specific course of interdisciplinary rehabilitation might lead to clinically significant changes in fatigue, experienced disability and physical function in patients with the chronic-fatigue syndrome (CFS). DESIGN: Prospective and uncontrolled. METHOD: 'Het Roessingh', a rehabilitation centre in Enschede, the Netherlands, has developed an interdisciplinary clinical rehabilitation programme for patients with CFS in cooperation with the 'Nijmeegs Kenniscentrum Chronische Vermoeidheid' [Chronic-Fatigue Knowledge Centre] in Nijmegen, the Netherlands. In this programme, physical, mental and social activities are gradually increased on the basis of cognitive behavioural principles and graded activity. Of the 127 successive persons who enrolled for the therapy during the period from August 2000 to December 2004, 99 fulfilled the inclusion criteria; they had a median duration of symptoms of 6 years. The results of treatment were evaluated by a measurement with the 'Checklist individuele spankracht' [Checklist individual muscle tone] before and after treatment and the scores on the 'Patientspecifieke beperkingen' [Patient-specific disability] and the Short form-36. The measured data were complete in 74 patients. RESULTS: Before rehabilitation, the levels of fatigue, disability and distress were high. After treatment, the studied population showed significant improvement in fatigue, experienced disability and physical function. The magnitude of the

				improvement was generally 'average'. At the end of treatment, 70% of the patients were clinically less fatigued, 68% experienced less disability and 55% functioned better physically. In 34% the level of fatigue was normalised after treatment, but 9.5% of the patients was more fatigue. CONCLUSION: The rehabilitation programme offered for CFS led to significant improvements in function and fatigue.
Torres-Harding SR, Jordan J, Jason LA, Arias R.		Psychosocial and Physical Impact of Chronic Fatigue in a Community-Based Sample of Children and Adolescents	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 55-74	Background: Few studies have examined the problem of chronic fatigue in children and adolescents and its potential impact on functioning. Chronic fatigue may have a negative impact on school functioning, family activities, psychological well-being, physical functioning, and severity of medical symptomatology. Objectives: This study compared psychosocial, family, and physical functioning between a randomly selected community based sample of 36 children and adolescents with chronic fatigue and a group of 21 children and adolescents without fatigue. Methods: Children and parents completed a comprehensive medical history questionnaire and questionnaires assessing psychological functioning, family functioning, and school attendance. Results: Results indicated that children with chronic fatigue tended to have more difficulties in overall physical and psychological functioning, as measured by the Child Health Questionnaire and the Child Behavior Checklist. In addition, children in the chronic fatigue group experienced disruptions in a range of activities and reported more severe physical symptomatology when compared to children without fatigue. Conclusions: Findings suggest that children and adolescents with chronic fatigue may have a range of associated difficulties, including limitations in physical and psychosocial functioning and a negative impact on the ability to engage in normative activities.
Underhill RA, O'Gorman RL		Prevalence of Chronic Fatigue Syndrome and Chronic Fatigue Within Families of CFS Patients	Journal of Chronic Fatigue Syndrome 2006;13(1): 3-13	The prevalence of CFS (Chronic Fatigue Syndrome) and chronic fatigue were investigated in family members of CFS patients using a questionnaire-based study. Significant differences were seen between the prevalence of CFS in all groups of family members relative to the published community prevalence of 0.422% (spouses/partners: 3.2%, $p < 0.001$; offspring: 5.1%, $p < .001$; parents and siblings: 1.1%, $p < 0.02$; second and third degree blood relatives 0.8%, $p < 0.02$). The prevalence of CFS was higher in genetically unrelated household contacts and in nonresident genetic relatives than in the community, indicating that both household contact and genetic relationship are risk factors for CFS
Van Damme S, Crombez G, Van Houdenhove B, Mariman A, Michielsen W.	Department of Experimental-Clinical and Health Psychology, Ghent University, Ghent, Belgium. stefaan.vandamme@ugent.be	Well-being in patients with chronic fatigue syndrome: the role of acceptance.	J Psychosom Res. 2006 Nov;61(5):595-9.	OBJECTIVE: Research in chronic pain patients has shown that accepting the chronic nature of their illness is positively related to quality of life. The aim of this study was to investigate whether acceptance is also associated with better well-being in patients suffering from chronic fatigue syndrome (CFS). METHODS: Ninety-seven patients completed a battery of questionnaires measuring fatigue, functional impairment, psychological distress, and acceptance. RESULTS: Results indicated that acceptance has a positive effect upon fatigue and psychological aspects of well-being. More specifically, acceptance was related to more emotional stability and less psychological distress, beyond the effects of demographic variables, and fatigue severity. CONCLUSION: We suggest that promoting acceptance in patients with CFS may often be more beneficial than trying to control largely uncontrollable symptoms.
van de Putte EM, Engelbert RH, Kuis	Department of Paediatrics,	How fatigue is related to other	Arch Dis Child. 2006	AIMS: To assess the relation between fatigue and somatic symptoms in healthy adolescents and adolescents with chronic fatigue syndrome/myalgic encephalopathy (CFS/ME). METHODS: Seventy

W, Kimpen JL, Uiterwaal CS.	Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, The Netherlands. E.vandePutte@umcutrecht.nl	somatic symptoms.	Oct;91(10):824-7. Epub 2006 Jun 5.	two adolescents with CFS were compared within a cross-sectional study design with 167 healthy controls. Fatigue and somatic complaints were measured using self-report questionnaires, respectively the subscale subjective fatigue of the Checklist Individual Strength (CIS-20) and the Children's Somatization Inventory. RESULTS: Healthy adolescents reported the same somatic symptoms as adolescents with CFS/ME, but with a lower score of severity. The top 10 somatic complaints were the same: low energy, headache, heaviness in arms/legs, dizziness, sore muscles, hot/cold spells, weakness in body parts, pain in joints, nausea/upset stomach, back pain. There was a clear positive relation between log somatic symptoms and fatigue (linear regression coefficient: 0.041 points log somatic complaints per score point fatigue, 95% CI 0.033 to 0.049) which did not depend on disease status. CONCLUSIONS: Results suggest a continuum with a gradual transition from fatigue with associated symptoms in healthy adolescents to the symptom complex of CFS/ME.
van de Putte EM, van Doornen LJ, Engelbert RH, Kuis W, Kimpen JL, Uiterwaal CS.	Department of Pediatrics, Wilhelmina Children's Hospital, University Medical Center, Utrecht, The Netherlands. e.vandeputte@wkz.azu.nl	Mirrored symptoms in mother and child with chronic fatigue syndrome.	Pediatrics. 2006 Jun;117(6):2074-9.	OBJECTIVE: Our aim with this study was to assess the relation between chronic fatigue syndrome in adolescents and fatigue and associated symptoms in their fathers and mothers, more specifically the presence of chronic fatigue syndrome-like symptoms and psychologic distress. METHOD: In this cross-sectional study, 40 adolescents with chronic fatigue syndrome according to the Centers for Disease Control and Prevention criteria were compared with 36 healthy control subjects and their respective parents. Questionnaires regarding fatigue (Checklist Individual Strength), fatigue-associated symptoms, and psychopathology (Symptom Checklist-90) were applied to the children and their parents. RESULTS: Psychologic distress in the mother corresponds with an adjusted odds ratio of 5.6 for the presence of CFS in the child. The presence of fatigue in the mother and dimensional assessment of fatigue with the Checklist Individual Strength revealed odds ratios of, respectively, 5.29 and 2.86 for the presence of chronic fatigue syndrome in the child. An increase of 1 SD of the hours spent by the working mother outside the home reduced the risk for chronic fatigue syndrome in their child with 61%. The fathers did not show any risk indicator for chronic fatigue syndrome in their child. CONCLUSIONS: Mothers of adolescents with chronic fatigue syndrome exhibit fatigue and psychologic symptoms similar to their child in contrast with the fathers. The striking difference between the absent association in fathers and the evident association in mothers suggests that the shared symptom complex of mother and child is the result of an interplay between genetic vulnerability and environmental factors.
van Heukelom RO, Prins JB, Smits MG, Bleijenberg G.	Department of Neurology, Sleep-Wake Disorders and Chronobiology, Hospital De Gelderse Vallei, Ede, and Department of Medical Psychology,	Influence of melatonin on fatigue severity in patients with chronic fatigue syndrome and late melatonin secretion.	Eur J Neurol. 2006 Jan;13(1):55-60.	The effect of melatonin, a chronobiotic drug, was explored in 29 patients with chronic fatigue syndrome (CFS) and Dim Light Melatonin onset (DLMO) later than 21.30 hours, reflective of delayed circadian rhythmicity. The patients took 5 mg of melatonin orally, 5 h before DLMO during 3 months. Their responses to the checklist individual strength (CIS), a reliable questionnaire measuring the severity of personally experienced fatigue, were assessed twice with a 6-week interval immediately before the treatment and once after 3 months treatment. In the pre-treatment period the fatigue sub-score improved significantly. After treatment, the total CIS score and the sub-scores for fatigue, concentration, motivation and activity improved significantly. The sub-score fatigue normalized in two of the 29 patients in the pre-treatment period and in eight of 27 patients during treatment. This change was significant. In the patients with DLMO later than 22.00 hours (n=21) the total CIS score and the sub-scores for fatigue, concentration and activity improved significantly more than in the

	Radbound University Medical Centre, Nijmegen, The Netherlands.			patients (n=8) with DLMO earlier than 22.00 hours. Melatonin may be an effective treatment for patients with CFS and late DLMO, especially in those with DLMO later than 22.00 hours.
Van Hoof E, De Becker P, De Meirleir K.		Pediatric Chronic Fatigue Syndrome and Muchausen-by-Proxy: A Case Study	Journal of Chronic Fatigue Syndrome 2006;13(2/3): 45-53	Pediatric chronic fatigue syndrome (CFS) posits even more challenges for professional caregivers in comparison with adult CFS samples. Most children with CFS display a decrease in school attendance and a decrease in social activities. As several conditions such as school phobia, primary psychiatric disorders or family disturbance present the same characteristics, the diagnostic process appears more complex. Family disturbance, moreover, is often specified as child abuse, neglect or even Muchausen-by-proxy. As skepticism is frequently associated with a diagnosis of CFS, patients and parents must fend for themselves fighting allegations of child abuse and neglect. This case study illustrates what happens when such allegations are put forward.
Van Houdenhove B, Bruyninckx K, Luyten P.	Chronic Fatigue Reference Centre, University Hospitals, K.U. Leuven, Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	In search of a new balance. Can high "action-proneness" in patients with chronic fatigue syndrome be changed by a multidisciplinary group treatment?	J Psychosom Res. 2006 Jun;60(6):623-5.	OBJECTIVE: The purpose of this study is to investigate changes in action-proneness (a cognitive and behavioral tendency toward direct action) after a multidisciplinary group intervention, including cognitive behaviour therapy (CBT) and graded exercise therapy (GET). METHODS: Patients with chronic fatigue syndrome (n=62) completed three versions of a Dutch self-report questionnaire evaluating action-proneness retrospectively that is (1) before illness onset, (2) before treatment and (3) after treatment. Significant others (n=62) also gave their opinion about the patients' action-proneness at time points 1 and 2. RESULTS: Premorbid action-proneness levels considerably dropped after illness onset. After treatment, action-proneness levels significantly increased again, although levels remained below premorbid levels. CONCLUSION: High action-proneness retrospectively reported by CFS patients can be adaptively modified by a multidisciplinary group treatment including CBT and GET.
Van Houdenhove B.		Psychiatric comorbidity and chronic fatigue syndrome.	Br J Psychiatry. 2006 Apr;188:395; author reply 396.	
van Staden WC.	Department of Psychiatry, University of Pretoria, Pretoria, South Africa. cwvanstaden@icon.co.za	Conceptual issues in undifferentiated somatoform disorder and chronic fatigue syndrome.	Curr Opin Psychiatry. 2006 Nov;19(6):613-8.	PURPOSE OF REVIEW: To review the conceptual problems in distinguishing between undifferentiated somatoform disorder and chronic fatigue syndrome, for both may present with fatigue as the main symptom. RECENT FINDINGS: The differences and/or similarities between undifferentiated somatoform disorder and chronic fatigue syndrome have not been studied, conceptually or empirically. The literature fails to present discriminant validity of chronic fatigue syndrome in relation to undifferentiated somatoform disorder. A critical feature is implied in the definition of undifferentiated somatoform disorder but absent from the definitions of chronic fatigue syndrome: some patients experience their fatigue as being exclusively physical and not as mental, which is prima facie peculiar, for fatigue is necessarily a mental experience. One is not able to experience fatigue without a mind (or a brain). This experience is characterized as a 'mindless' fatigue, underpinned by pathological reductionist thinking. By not recognizing this critical feature, diagnostic endeavours may perpetuate the problem as a function of the patient's difficulty. SUMMARY: Proponents of chronic fatigue syndrome should distinguish chronic fatigue syndrome from undifferentiated somatoform

				disorder, if chronic fatigue syndrome is a distinct entity at all. Further, the 'mindless' quality is a critical feature that needs consideration in refining the concept of undifferentiated somatoform disorder.
Vermeulen RC, Scholte HR.	CFS and Pain Research Center Amsterdam, Waalstraat 25-31, 1078 BR Amsterdam, The Netherlands. rv@cvscentrum.nl.	Azithromycin in Chronic Fatigue Syndrome (CFS), an analysis of clinical data.	J Transl Med. 2006 Aug 15;4:34.	ABSTRACT: BACKGROUND: CFS is a clinical state with defined symptoms, but undefined cause. The patients may show a chronic state of immune activation and treatment with an antibiotic in this subgroup has been suggested. METHODS: In a retrospective study, the response of CFS patients to azithromycin, an antibiotic and immunomodulating drug, has been scored from the patients records and compared with clinical and laboratory data. Azithromycin was not the first choice therapy, but offered when the effect of counseling and L-carnitine was considered insufficient by the patient and the clinician. RESULTS: Of the 99 patients investigated, 58 reported a decrease in the symptoms by the use of azithromycin. These responding patients had lower levels of plasma acetylcarnitine. CONCLUSION: The efficacy of azithromycin in the responsive patients could be explained by the modulating effect on a chronic primed state of the immune cells of the brain, or the activated peripheral immune system. Their lower acetylcarnitine levels may reflect a decreased antioxidant defense and/or an increased consumption of acetylcarnitine caused by oxidative stress.
Vermeulen RC.	CFS and Pain Research Center Amsterdam, Amsterdam, The Netherlands. rv@cvscentrum.nl.	Translation and validation of the Dutch language version of the CDC Symptom Inventory for assessment of Chronic Fatigue Syndrome (CFS).	Popul Health Metr. 2006 Oct 18;4:12.	ABSTRACT: BACKGROUND: In a study by Wagner et al., the CDC Symptom Inventory was validated in a population selected from the inhabitants of a city in the USA, and proofed reliable for the assessment of the accompanying symptoms of CFS. The Dutch translation of the CDC Symptom Inventory is compared to the original and the psychometric properties are presented for patients in a tertiary care setting. METHODS: One hundred thirty-nine consecutive patients who visited the CFS Center Amsterdam for the first time were asked to complete the CDC Symptom Inventory in the Dutch Language Version (DLV) together with the usual set of questionnaires. Sixty-one patients had Chronic Fatigue (CF) and 78 patients fulfilled the criteria for CFS. Forty-three healthy accompanying persons completed the CDC Symptom Inventory DLV, the Physical Functioning scale of the Medical Outcome Survey Short Form-36 DLV, and the Fatigue and Concentration scales of the Checklist Individual Strength (CIS-20). RESULTS: The healthy controls group contained fewer women and was overall older than the patient groups. The influence of gender on the CDC Symptom Inventory DLV was significant but the effect of age was not. The Dutch version had a good internal consistency and convergent validity. The results were comparable to the original English version, but the sex-related difference needs further study. CONCLUSION: The Dutch version of the CDC Symptom Inventory is a reliable tool for the assessment of the secondary criteria for CFS. The results show that it is comparable to the outcome of studies in English speaking countries.
Vernon SD, Reeves WC.	Centers for Disease Control and Prevention, National Center for Infectious Diseases, Atlanta, GA, USA. sdv2@cdc.gov	The challenge of integrating disparate high-content data: epidemiological, clinical and laboratory data collected during an in-hospital study of	Pharmacogenomics. 2006 Apr;7(3):345-54. Comment in: Pharmacogenomics. 2006 Apr;7(3):341-3.	Chronic fatigue syndrome (CFS) is a debilitating illness characterized by multiple unexplained symptoms including fatigue, cognitive impairment and pain. People with CFS have no characteristic physical signs or diagnostic laboratory abnormalities, and the etiology and pathophysiology remain unknown. CFS represents a complex illness that includes alterations in homeostatic systems, involves multiple body systems and results from the combined action of many genes, environmental factors and risk-conferring behavior. In order to achieve understanding of complex illnesses, such as CFS, studies must collect relevant epidemiological, clinical and laboratory data and then integrate, analyze and interpret the information so as to obtain meaningful clinical and biological insight. This issue of Pharmacogenomics represents such an approach to CFS. Data was collected during a 2-day in-hospital

		chronic fatigue syndrome.		study of persons with CFS, other medically and psychiatrically unexplained fatiguing illnesses and nonfatigued controls identified from the general population of Wichita, KS, USA. While in the hospital, the participants' psychiatric status, sleep characteristics and cognitive functioning was evaluated, and biological samples were collected to measure neuroendocrine status, autonomic nervous system function, systemic cytokines and peripheral blood gene expression. The data generated from these assessments was made available to a multidisciplinary group of 20 investigators from around the world who were challenged with revealing new insight and algorithms for integration of this complex, high-content data and, if possible, identifying molecular markers and elucidating pathophysiology of chronic fatigue. The group was divided into four teams with representation from the disciplines of medicine, mathematics, biology, engineering and computer science. The papers in this issue are the culmination of this 6-month challenge, and demonstrate that data integration and multidisciplinary collaboration can indeed yield novel approaches for handling large, complex datasets, and reveal new insight and relevance to a complex illness such as CFS.
Vernon SD, Whistler T, Aslakson E, Rajeevan M, Reeves WC.	Center for Infectious Diseases, Division of Viral and Rickettsial Diseases, National Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. svernon@cdc.gov	Challenges for molecular profiling of chronic fatigue syndrome.	Pharmacogenomics. 2006 Mar;7(2):211-8.	Chronic fatigue syndrome (CFS) is prevalent, disabling and costly. Despite extensive literature describing the epidemiology and clinical aspects of CFS, it has been recalcitrant to diagnostic biomarker discovery and therapeutic intervention. This is due to the fact that CFS is a complex illness defined by self-reported symptoms and diagnosed by the exclusion of medical and psychiatric diseases that may explain the symptoms. Studies attempting to dissect the pathophysiology are challenging to design as CFS affects multiple body systems, making the choice of which system to study dependent on an investigators area of expertise. However, the peripheral blood appears to be facilitating the molecular profiling of several diseases, such as CFS, that involve bodywide perturbations that are mediated by the CNS. Successful molecular profiling of CFS will require the integration of genetic, genomic and proteomic data with environmental and behavioral data to define the heterogeneity in order to optimize intervention.
Vervoort T, Crombez G, Buysse A, Goubert L, De Backer T, Ickes W.	Department of Experimental-Clinical and Health Psychology, Ghent University, Belgium; Research Institute for Psychology and Health, The Netherlands.	Brief Report: The Accuracy of Parents for the Thoughts and Feelings of Their Adolescent Suffering from Chronic Fatigue: A Preliminary Study of Empathy.	J Pediatr Psychol. 2006 Sep 29; [Epub ahead of print]	Objective This study examined the actual and estimated empathic accuracy (EA) of the parents of adolescents with chronic fatigue syndrome (CFS). Methods The actual EA of both parents (n = 24) was assessed in relation to the thoughts and feelings of their child (n = 14) about CFS and about other life events. Adolescents were also asked to estimate the parents' EA. Results For the actual EA, both parents were significantly less accurate regarding the adolescent's thoughts and feelings about CFS than about other life events. Fathers were just as empathically accurate as mothers. For the estimated EA, however, results indicated that adolescents perceived their mother to be more empathically accurate than their father. Actual EA and estimated EA about CFS were negatively correlated for fathers, not for mothers. Conclusions Results are discussed in terms of the importance of assessing EA in relation to other dimensions of empathic understanding and distress in the observer.
Vollmer-Conna U, Aslakson E, White PD.	University of New South Wales, School of Psychiatry, 30 Botany Street,	An empirical delineation of the heterogeneity of chronic unexplained	Pharmacogenomics. 2006 Apr;7(3):355-64.	OBJECTIVES: To test the hypothesis that medically unexplained chronic fatigue and chronic fatigue syndrome (CFS) are heterogeneous conditions, and to define the different conditions using both symptom and laboratory data. METHODS: We studied 159 women from KS, USA. A total of 51 of these suffered from fatigue consistent with established criteria for CFS, 55 had chronic fatigue of insufficient symptoms/severity for a CFS diagnosis and 53 were healthy controls matched by age and body mass

	Sydney UNSW 2052, Australia. ute@unsw.edu.au	fatigue in women.		index (BMI) against those with CFS. We used principal components analyses to define factors that best described the variable space and to reduce the number of variables. The 38 most explanatory variables were then used in latent class analyses to define discrete subject groups. RESULTS: Principal components analyses defined six discrete factors that explained 40% of the variance. Latent class analyses provided several interpretable solutions with four, five and six classes. The four-class solution was statistically most convincing, but the six-class solution was more interpretable. Class 1 defined 41 (26%) subjects with obesity and relative sleep hypnoea. Class 2 were 38 (24%) healthy subjects. Class 3 captured 24 (15%) obese relatively hypnoeic subjects, but with low heart rate variability and cortisol. Class 4 were 23 (14%) sleep-disturbed and myalgic subjects without obesity or significant depression. The two remaining classes with 22 (14%) and 11 (7%) subjects consisted of the most symptomatic and depressed, but without obesity or hypnoea. Class 5 had normal sleep indices. Class 6 was characterized by disturbed sleep, with low sleep heart rate variability, cortisol, and sex hormones. CONCLUSION: Chronic medically unexplained fatigue is heterogeneous. The putative syndromes were differentiated by obesity, sleep hypnoea, depression, physiological stress response, sleep disturbance, interoception and menopausal status. If these syndromes are externally validated and replicated, they may prove useful in determining the causes, pathophysiology and treatments of CFS.
Wallace DJ.	Cedars-Sinai/David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. dwallace@ucla.edu	Is there a role for cytokine based therapies in fibromyalgia.	Curr Pharm Des. 2006;12(1):17-22.	Cytokines are glycoproteins that serve as chemical messengers between cells. They assist in the regulation of cell growth and repair and also have immune modulating properties. Cytokines play a role in diverse clinical processes and phenomena such as fatigue, fever, sleep, pain, stress and aching. A review of the fibromyalgia literature and related studies suggest that IL-1, IL-6 and IL-8 are dysregulated in the syndrome. Therapies directed against these cytokines may be of potential importance in the management of fibromyalgia.
Wallesch CW.		[Fatigue and multiple sclerosis] [Article in German]	Fortschr Neurol Psychiatr. 2006 Sep;74(9):495-6.	Editorial
Waltman P, Pearlman A, Mishra B.	New York University, Courant Institute of Mathematical Sciences, 715 Broadway, New York, NY 10003, USA. mishra@nyu.edu	Interpreter of maladies: redescription mining applied to biomedical data analysis.	Pharmacogenomics. 2006 Apr;7(3):503-9.	Comprehensive, systematic and integrated data-centric statistical approaches to disease modeling can provide powerful frameworks for understanding disease etiology. Here, one such computational framework based on redescription mining in both its incarnations, static and dynamic, is discussed. The static framework provides bioinformatic tools applicable to multifaceted datasets, containing genetic, transcriptomic, proteomic, and clinical data for diseased patients and normal subjects. The dynamic redescription framework provides systems biology tools to model complex sets of regulatory, metabolic and signaling pathways in the initiation and progression of a disease. As an example, the case of chronic fatigue syndrome (CFS) is considered, which has so far remained intractable and unpredictable in its etiology and nosology. The redescription mining approaches can be applied to the Centers for Disease Control and Prevention's Wichita (KS, USA) dataset, integrating transcriptomic, epidemiological and clinical data, and can also be used to study how pathways in the hypothalamic-pituitary-adrenal axis affect CFS patients.
Wang JJ, Meng H, Cui CB, Song YJ,	Institute of Acupuncture &	[On the important role of Siguan	Zhongguo Zhen Jiu. 2006	OBJECTIVE: To probe into the role of Siguan points in treatment of chronic fatigue syndrome. METHODS: Based on diagnosis, pathogenesis and etiology of chronic fatigue syndrome in TCM, the

Wang XH, Wu ZC.	Moxibustion, China Academy of TCM, Beijing 100700, China. wjj751@sina.com	points in treatment of chronic fatigue syndrome] [Article in Chinese]	Feb;26(2):116-9.	role of Siguan points in treatment of chronic fatigue syndrome were induced by means of relative literatures of Siguan points in recent 10 years from 3 aspects. CONCLUSION: Acupuncture at Siguan as main points has a better therapeutic effect on chronic fatigue syndrome.
Wearden AJ, Riste L, Dowrick C, Chew-Graham C, Bentall RP, Morriss RK, Peters S, Dunn G, Richardson G, Lovell K, Powell P.	School of Psychological Sciences, University of Manchester, Manchester, M13 9PL, UK. alison.wearden@manchester.ac.uk	Fatigue Intervention by Nurses Evaluation--the FINE Trial. A randomised controlled trial of nurse led self-help treatment for patients in primary care with chronic fatigue syndrome: study protocol. [ISRCTN74156610].	BMC Med. 2006 Apr 7;4:9.	BACKGROUND: Chronic fatigue syndrome, also known as ME (CFS/ME), is a condition characterised primarily by severe, disabling fatigue, of unknown origin, which has a poor prognosis and serious personal and economic consequences. Evidence for the effectiveness of any treatment for CFS/ME in primary care, where most patients are seen, is sparse. Recently, a brief, pragmatic treatment for CFS/ME, based on a physiological dysregulation model of the condition, was shown to be successful in improving fatigue and physical functioning in patients in secondary care. The treatment involves providing patients with a readily understandable explanation of their symptoms, from which flows the rationale for a graded rehabilitative plan, developed collaboratively with the therapist. The present trial will test the effectiveness and cost-effectiveness of pragmatic rehabilitation when delivered by specially trained general nurses in primary care. We selected a client-centred counselling intervention, called supportive listening, as a comparison treatment. Counselling has been shown to be as effective as cognitive behaviour therapy for treating fatigue in primary care, is more readily available, and controls for supportive therapist contact time. Our control condition is treatment as usual by the general practitioner (GP). METHODS AND DESIGN: This study protocol describes the design of an ongoing, single-blind, pragmatic randomized controlled trial of a brief (18 week) self-help treatment, pragmatic rehabilitation, delivered by specially trained nurse-therapists in patients' homes, compared with nurse-therapist delivered supportive listening and treatment as usual by the GP. An economic evaluation, taking a societal viewpoint, is being carried out alongside the clinical trial. Three adult general nurses were trained over a six month period to deliver the two interventions. Patients aged over 18 and fulfilling the Oxford criteria for CFS are assessed at baseline, after the intervention, and again one year later. Primary outcomes are self-reported physical functioning and fatigue at one year, and will be analysed on an intention-to-treat basis. A qualitative study will examine the interventions' mechanisms of change, and also GPs' drivers and barriers towards referral.
Weidenhammer W, Wessel A, Hutter A, Melchart D, Schroder A.	Zentrum fur naturheilkundliche Forschung, II. Medizinische Klinik und Poliklinik, TU Munchen, Kaiserstrasse 9, 80801 Munich. Wolfgang.Weidenhammer@ltz.tu-muenchen.de	[Chronic fatigue in complementary rehabilitative medicine--predictors of the outcomes] [Article in German]	Rehabilitation (Stuttg). 2006 Oct;45(5):299-308.	Chronic exhaustion and fatigue are increasingly important in rehabilitation medicine. Objectives of this study were (a) to describe the effects of in-patient rehabilitation on patients with chronic fatigue syndromes, (b) to identify predictors for treatment outcome, and (c) to analyze the impact of comprehensive diagnosing on these issues. A total of 171 patients with chronic exhaustion or fatigue (90 % female, mean age 55 +/- 10 yrs) from a rehabilitation hospital with a complementary medicine-based treatment concept were included in a prospective observational study. Within the longitudinal study patients were examined three times (on admission to hospital, at discharge as well as six months later). Participation rate of the postal inquiry was 69 %. Besides items constructed ad hoc, Patient questionnaires included the Symptom Checklist and assessment instruments for depression, quality of life, sense of coherence as well as for changes in experience and behaviour. Treatment outcome was defined as sum score of binary-coded response criteria. The pattern of complaints differed clearly between diagnostic subgroups (neurasthenia, affective disorders, adjustment

				disorders) before treatment. At discharge from hospital patients showed clinically relevant improvements lasting for six months after rehabilitation. Multiple regression analyses revealed a statistically significant relationship (R (mult) = 0.59) between predictors and outcome at discharge from hospital. A better result was associated with higher trust in treatment success, active information seeking on complementary medicine, healthier feeding habits, better somatic health and a decreased mental status, with regard to the status before treatment. The prediction of outcome after six months was comparably poorer (R (mult) = 0.42). Treatment success was higher in the absence of a diagnosis of neurasthenia, in patients accepting the group-oriented treatment concept and in patients not believing that their disease was due to their own way of living. Trust in the success of the treatment was a highly ranked predictor for longer lasting outcome, too. The results underline the importance of motivation aspects for treatment outcome indicating that individual expectations and attitudes should be considered in a more distinct way when allocating patients to rehabilitative programmes.
Weir PT, Harlan GA, Nkoy FL, Jones SS, Hegmann KT, Gren LH, Lyon JL.	Department of Family and Preventive Medicine, University of Utah, Salt Lake City, Utah 84108, USA. peter.weir@hsc.utah.edu	The incidence of fibromyalgia and its associated comorbidities: a population-based retrospective cohort study based on International Classification of Diseases, 9th Revision codes.	J Clin Rheumatol. 2006 Jun;12(3):124-8.	BACKGROUND: The epidemiology of fibromyalgia is poorly defined. The incidence of fibromyalgia has not been determined using a large population base. Previous studies based on prevalence data demonstrated that females are 7 times more likely to have fibromyalgia than males and that the peak age for females is during the childbearing years. OBJECTIVE: We have calculated the incidence rate of fibromyalgia in a large, stable population and determined the strength of association between fibromyalgia and 7 comorbid conditions. METHODS: We conducted a retrospective cohort study of a large, stable health insurance claims database (62,000 nationwide enrollees per year). Claims from 1997 to 2002 were examined using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes to identify fibromyalgia cases (ICD code 729.1) and 7 predetermined comorbid conditions. RESULTS: A total of 2595 incident cases of fibromyalgia were identified between 1997 and 2002. Age-adjusted incidence rates were 6.88 cases per 1000 person-years for males and 11.28 cases per 1000 person-years for females. Females were 1.64 times (95% confidence interval = 1.59-1.69) more likely than males to have fibromyalgia. Patients with fibromyalgia were 2.14 to 7.05 times more likely to have one or more of the following comorbid conditions: depression, anxiety, headache, irritable bowel syndrome, chronic fatigue syndrome, systemic lupus erythematosus, and rheumatoid arthritis. CONCLUSION: Females are more likely to be diagnosed with fibromyalgia than males, although to a substantially smaller degree than previously reported, and there are strong associations for comorbid conditions that are commonly thought to be associated with fibromyalgia.
Whistler T, Taylor R, Craddock RC, Broderick G, Klimas N, Unger ER.	Centers for Disease Control and Prevention, Viral Exanthems and Herpesvirus Branch, Atlanta, GA 30333, USA. taw6@cdc.gov	Gene expression correlates of unexplained fatigue.	Pharmacogenomics. 2006 Apr;7(3):395-405.	Quantitative trait analysis (QTA) can be used to test whether the expression of a particular gene significantly correlates with some ordinal variable. To limit the number of false discoveries in the gene list, a multivariate permutation test can also be performed. The purpose of this study is to identify peripheral blood gene expression correlates of fatigue using quantitative trait analysis on gene expression data from 20,000 genes and fatigue traits measured using the multidimensional fatigue inventory (MFI). A total of 839 genes were statistically associated with fatigue measures. These mapped to biological pathways such as oxidative phosphorylation, gluconeogenesis, lipid metabolism, and several signal transduction pathways. However, more than 50% are not functionally annotated or associated with identified pathways. There is some overlap with genes implicated in other studies

				using differential gene expression. However, QTA allows detection of alterations that may not reach statistical significance in class comparison analyses, but which could contribute to disease pathophysiology. This study supports the use of phenotypic measures of chronic fatigue syndrome (CFS) and QTA as important for additional studies of this complex illness. Gene expression correlates of other phenotypic measures in the CFS Computational Challenge (C3) data set could be useful. Future studies of CFS should include as many precise measures of disease phenotype as is practical.
Whitehead L.	Department of Nursing and Midwifery, University of Stirling, Western Isles Hospital, Macaulay Road, Stornoway, UK. lw6@stir.ac.uk	Toward a trajectory of identity reconstruction in chronic fatigue syndrome/myalgic encephalomyelitis: a longitudinal qualitative study.	Int J Nurs Stud. 2006 Nov;43(8):1023-31. Epub 2006 Mar 9.	BACKGROUND: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is an illness associated with high levels of physical and cognitive disability over a prolonged period of time. Recovery from CFS/ME can be interspersed with relapses. Further, the legitimacy of the illness continues to be questioned within and beyond the health profession. AIM: This paper examines the reconstruction of self-identity for those experiencing CFS/ME. METHOD: This longitudinal qualitative study involved up to three in-depth interviews with 17 people with CFS/ME and family members. RESULTS: A trajectory that describes transitions in identity over time and the range of elements that influence these is proposed. During the acute phase of illness, characterised by total debility, people adopted the traditional sick role. The medium term phase highlighted movement between disability as part of the total self, total debility, and/or the adoption of a supernormal identity. The longer-term phase was defined for the majority of participants as the positive reconstruction of self. Identity was contingent with positive and negative experiences and responses co-existing with the potential to 'tip' the balance and perceived identity. In the longer term people's identity became more static with the development of coping strategies to maintain this. The trajectory can be described as pendular and movement between each type of identity was possible during all phases of the illness experience depending on the nature and impact of the illness and responses given to these. The proposed trajectory represents a dynamic model of identity reconstruction. CONCLUSION: Understanding the patients' experience and recognising that different stages may exist is important for health professionals. This awareness can enhance shared understanding and opportunities to work with people in negotiating the impact of illness.
Whitehead LC.	University of Stirling Stornoway, UK. lw6@stir.ac.uk	Quest, chaos and restitution: living with chronic fatigue syndrome/myalgic encephalomyelitis.	Soc Sci Med. 2006 May;62(9):2236-45. Epub 2005 Oct 19.	Chronic illness is disruptive, threatening people's sense of identity and taken for granted assumptions. Transformations in values, expectations and life priorities are likely to be experienced and in order to regain a coherent sense of self, people must interpret their experiences. People with difficult to diagnose illnesses can find themselves living with greater uncertainty and stigma. This paper explores how people with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) describe and interpret their illness experience by applying Arthur Frank's narrative typologies to analyse interviews with 17 British people with CFS/ME. The analysis proposes that a trajectory of narrative typologies is experienced, starting with a restitution narrative, moving to a chaos narrative and, for most, back to a restitution narrative and on to a quest narrative. The presentation of narrative types put forward by people living with CFS/ME differ to those presented by people who are HIV positive and have been treated for breast cancer.
Witkowski JA.		The postgenomic era and complex disease.	Pharmacogenomics. 2006 Apr;7(3):341-3.	

			Comment on: Pharmacogenomics. 2006 Apr;7(3):345-54.	
Yoshiuchi K, Farkas J, Natelson BH.	Department of Neurosciences, Fatigue Research Center, UMDNJ-New Jersey Medical School, Newark, USA. kyoshiuc-tky@umin.ac.jp	Patients with chronic fatigue syndrome have reduced absolute cortical blood flow.	Clin Physiol Funct Imaging. 2006 Mar;26(2):83-6.	Prior studies on brain blood flow in chronic fatigue syndrome (CFS) did not find consistent results. This may be because they used single-photon emission computed tomography to measure brain blood flow, which could not measure absolute blood flow. Therefore, the aim of this study was to test the hypothesis that patients with CFS have reduced absolute cerebral blood flow. Xenon-computed tomography blood flow studies were done on 25 CFS patients and seven healthy controls. Analyses were done after stratifying the CFS patients based on the presence or absence of a current psychiatric disorder. Flow was diminished in both groups as follows: patients with no current psychiatric disorders had reduced cortical blood flow in the distribution of both right and left middle cerebral arteries ($P<0.05$ for both) while those with current psychiatric disorders had reduced blood flow only in the left middle cerebral artery territory ($P<0.05$). These data indicate that patients with CFS have reduced absolute cortical blood flow in rather broad areas when compared with data from healthy controls and that those devoid of psychopathology had the most reductions in cortical flow. These data support, in part, our earlier findings that patients devoid of psychopathology are the group most at risk of having some of the symptoms of CFS due to brain dysfunction.
Yuemei L, Hongping L, Shulan F, Dongfang G.	First Hospital Affiliated to Guangzhou University of Traditional Chinese Medicine, Guangzhou 510405, China.	The therapeutic effects of electrical acupuncture and auricular-plaster in 32 cases of chronic fatigue syndrome.	J Tradit Chin Med. 2006 Sep;26(3):163-4.	OBJECTIVE: To observe the therapeutic effects of electrical acupuncture and auricular-plaster therapy for chronic fatigue syndrome (CFS). METHOD: 64 CFS patients were randomly divided into two groups. 32 cases in the treatment group were treated by the electrical acupuncture and auricular-plaster therapy, and 32 cases in the control group with oral hydrocortisone. RESULTS: The total effective rates were respectively 93.75% in the treatment group and 75.00% in the control group, with a statistically significant difference between the two groups ($P < 0.05$). CONCLUSION: Electrical acupuncture and auricular-plaster therapy may show a better anti-fatigue effect than that of routine Western drugs.
Zuckerman JN.	Academic Centre for Travel Medicine and Vaccines and WHO Collaborating Centre for Reference, Research and Training in Travel Medicine, Royal Free and University College Medical School, University College London,	Protective efficacy, immunotherapeutic potential, and safety of hepatitis B vaccines.	J Med Virol. 2006 Feb;78(2):169-77.	Hepatitis B vaccines are highly effective and safe and have been incorporated into national immunization programs in over 150 countries. The major humoral immune response is to the common a determinant of the surface antigen protein of the virus. Approximately 5-10% of healthy immunocompetent subjects do not mount an antibody response (anti-HBs). Non-response is associated with different HLA-DR alleles and impaired Th cell response, among other factors such as route of injection, age, gender, body mass, and other factors. Important hepatitis B surface antigen variants have also been identified, which may have a potential impact on immunization and routine screening of blood, blood products and tissues, and organs for transplantation. Strategies for hepatitis B immunization are reviewed. Over 1,000 million doses of hepatitis B vaccine have been used with an outstanding record of safety. There is no evidence of an association between hepatitis B vaccines and the sudden infant death syndrome, chronic fatigue syndrome, and multiple sclerosis (MS). Several studies are in progress on treatment of chronic hepatitis B infection by immunization with multiple antigenic components, combination of vaccine with antiviral drugs and cytokines, T cell vaccines, DNA vaccines alone or with DNA encoded immunomodulatory cytokines, and direct genetic manipulation

	United Kingdom. j.zuckerman@medsch.ucl.ac.uk			of antigen presenting cells. Copyright 2005 Wiley-Liss, Inc.
[No authors listed]		In this issue.	Psychol Med. 2006 Jul;36(7):893-4.	This issue contains two reviews, one on chronic fatigue syndrome and one on suicide and the menstrual cycle. Other sets of papers examine various aspects of suicide, addictive behaviours, and depression, and three individual papers examine a variety of topics.
[No authors listed]		Chronic fatigue syndrome.	Nurs Times. 2006 Apr 4-10;102(14):25.	
[No authors listed]		Global Advisory Committee on Vaccine Safety, 1-2 December 2005. [English, French]	Wkly Epidemiol Rec. 2006 Jan 13;81(2):15-9.	

2005				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No authors listed]		Summaries for patients. The health of Gulf War veterans. Original report in: Ann Intern Med. 2005 Jun 7;142(11):881-90.	Ann Intern Med. 2005 Jun 7;142(11):I22.	
[No authors listed]		Increased activity OK for chronic pain.	Health News. 2005 May;11(5):6.	
Armengaud D.	Service de pediatrie-medecine neonatale, CHI Poissy-Saint-Germain, 78300 Poissy. darmenga@chi-psg.com	[Chronic fatigue and sleep disorders in adolescents] [Article in French]	Rev Prat. 2005 May 31;55(10):1095-8.	To be, or to feel tired, is a frequent complaint at any age, and which does not seem in itself to be specific of the teenager. If it frequently lies within the scope of an organic pathology, acute or chronic, besides while being able to be a revealing element for it, it is often insulated and asks a rigorous step in the evaluation of its various possible components. It is then important to be in an active listening and patient, and not in a hasty regulation of a "cosmetic" treatment of this subjective allegation. It is all the work of the doctor whom to support the emergence of the subjacent complaint whose tensions and stakes of adolescence post there their singularity.
Aslangul E, Le Jeunne C.	Service de Medecine Interne, Hotel-Dieu, 75004 Paris. claire.le-jenne@htd.aphp.fr	[Diagnosing asthenia and chronic fatigue syndrome] [Article in French]	Rev Prat. 2005 May 15;55(9):1029-33.	
Axe EK, Satz P, Rasgon NL, Fawzy FI		ORIGINAL RESEARCH Major Depressive Disorder in Chronic Fatigue Syndrome: A CDC Surveillance Study	Journal of Chronic Fatigue Syndrome 2005 12 (3): 7-23	Background: Controversy continues to exist as to whether Chronic Fatigue Syndrome is a psychological/psychiatric disorder. To further understand this condition the Centers for Disease Control (CDC) conducted a Surveillance Study. The CDC partitioned 565 subjects with fatiguing illnesses into four diagnostic groups, one of which met the 1988 CDC criteria for CFS. The non-CFS groups had either insufficient severity (idiopathic), medical exclusions or prior psychiatric disorders. Objectives: The present study reports on the psychiatric features in that study, estimates the time of onset of Major Depressive Disorder (MDD) and looks for possible relationships between 1988 CDC criteria for Chronic Fatigue Syndrome and psychiatric disorders. Methods: The study design is cross-sectional. The Diagnostic Interview Schedule (DIS) assessed for four Axis I psychiatric disorders. Time of onset ofMDDwas estimated from the DIS and validated by an examination of the medical records. Odds ratios and confidence intervals were calculated as tests of association between 1988 CDC criteria and psychiatric disorders. Results: Subjects classified as CFS and non-CFS had similar rates of psychiatric disorders. A minority of subjects had preexisting MDD. Three 1988 CDC criteria were

				associated with current MDD whilst no criteria were associated with prior MDD. Conclusions: CFS subjects did not demonstrate any unique patterns of psychiatric disorders. MDD may not be an important predisposing factor for CFS or the other fatiguing illnesses. Some 1988 CDC criteria may be preferentially endorsed by subjects with current MDD.
Badawy AA, Morgan CJ, Llewelyn MB, Albuquerque SR, Farmer A.	Cardiff & Vale NHS Trust, Biomedical Research Laboratory, Whitchurch Hospital, Cardiff, Wales, UK. Abdulla.Badawy@cardiffandvale.wales.nhs.uk	Heterogeneity of serum tryptophan concentration and availability to the brain in patients with the chronic fatigue syndrome.	J Psychopharmacol. 2005 Jul;19(4):385-91.	We assessed the serotonin status of patients with the chronic fatigue syndrome (CFS). Tryptophan (Trp) availability to the brain, expressed as the ratio of concentration of serum Trp to the sum of those of its five competitors (CAA), and other parameters of Trp disposition were compared in 23 patients with the CFS and 42 healthy controls. The serum [free Trp]/[CAA] ratio was 43% higher in CFS patients, due to a 48% higher [free Trp]. [Total Trp] was also significantly higher (by 19%) in CFS patients, and, although the [total Trp]/[CAA] ratio did not differ significantly between the control and patient groups, the difference became significant when the results were co-varied with age and gender. [CAA] was not significantly different between groups, but was significantly lower in females, compared to males, of the CFS patient group. We have established normal ranges for Trp disposition parameters and propose criteria for defining the serotonin-biosynthetic status in humans. We have provisionally identified two subgroups of CFS patients, one with normal serotonin and the other with a high serotonin status. The relevance of our findings to, and their implications for, the pharmacological and other therapies of the chronic fatigue syndrome are discussed.
Baraniuk JN, Casado B, Maibach H, Clauw DJ, Pannell LK, Hess S S.	Georgetown University Proteomics Laboratory, Division of Rheumatology, Immunology & Allergy, Room B-105, Lower Level Kober-Cogan Building, Georgetown University, Washington, DC 20007-2197, USA. HUbaraniuj@georgetown.eduUH	A Chronic Fatigue Syndrome - related proteome in human cerebrospinal fluid.	BMC Neurol. 2005 Dec 1;5:22.	BACKGROUND: Chronic Fatigue Syndrome (CFS), Persian Gulf War Illness (PGI), and fibromyalgia are overlapping symptom complexes without objective markers or known pathophysiology. Neurological dysfunction is common. We assessed cerebrospinal fluid to find proteins that were differentially expressed in this CFS-spectrum of illnesses compared to control subjects. METHODS: Cerebrospinal fluid specimens from 10 CFS, 10 PGI, and 10 control subjects (50 mul/subject) were pooled into one sample per group (cohort 1). Cohort 2 of 12 control and 9 CFS subjects had their fluids (200 mul/subject) assessed individually. After trypsin digestion, peptides were analyzed by capillary chromatography, quadrupole-time-of-flight mass spectrometry, peptide sequencing, bioinformatic protein identification, and statistical analysis. RESULTS: Pooled CFS and PGI samples shared 20 proteins that were not detectable in the pooled control sample (cohort 1 CFS-related proteome). Multilogistic regression analysis (GLM) of cohort 2 detected 10 proteins that were shared by CFS individuals and the cohort 1 CFS-related proteome, but were not detected in control samples. Detection of >or=1 of a select set of 5 CFS-related proteins predicted CFS status with 80% concordance (logistic model). The proteins were alpha-1-macroglobulin, amyloid precursor-like protein 1, keratin 16, orosomucoid 2 and pigment epithelium-derived factor. Overall, 62 of 115 proteins were newly described. CONCLUSION: This pilot study detected an identical set of central nervous system, innate immune and amyloidogenic proteins in cerebrospinal fluids from two independent cohorts of subjects with overlapping CFS, PGI and fibromyalgia. Although syndrome names and definitions were different, the proteome and presumed pathological mechanism(s) may be shared.
Baraniuk JN, Petrie KN, Le U, Tai CF, Park YJ, Yuta A, Ali M, Vandenbussche	Division of Rheumatology, Immunology and Allergy,	Neuropathology in rhinosinusitis.	Am J Respir Crit Care Med. 2005 Jan 1;171(1):5-11. Epub 2004 Oct 11.	Pathophysiologic differences in neural responses to hypertonic saline (HTS) were investigated in subjects with acute sinusitis (n = 25), subjects with chronic fatigue syndrome (CFS) with nonallergic rhinitis (n = 14), subjects with active allergic rhinitis (AR; n = 17), and normal (n = 20) subjects. Increasing strengths of HTS were sprayed into their nostrils at 5-minute intervals. Sensations of nasal

CJ, Nelson B.	Georgetown University, 3800 Reservoir Road, N.W., Washington, DC 20007-2197, USA. baraniuj@georgetown.edu			pain, blockage, and drip increased with concentration and were significantly elevated above normal. These parallels suggested activation of similar subsets of afferent neurons. Urea and lysozyme secretion were dose dependent in all groups, suggesting that serous cell exocytosis was one source of urea after neural stimulation. Only AR and normal groups had mucin dose responses and correlations between symptoms and lysozyme secretion (R(2) = 0.12-0.23). The lysozyme dose responses may represent axon responses in these groups. The neurogenic stimulus did not alter albumin (vascular) exudation in any group. Albumin and mucin concentrations were correlated in sinusitis, suggesting that nonneurogenic factors predominated in sinusitis mucous hypersecretion. CFS had neural hypersensitivity (pain) but reduced serous cell secretion. HTS nasal provocations identified significant, unique patterns of neural and mucosal dysregulation in each rhinosinusitis syndrome.
Baschetti R.		Chronic fatigue syndrome, exercise, cortisol and lymphadenopathy.	J Intern Med. 2005 Sep;258(3):291-2.	Letter
Bazelmans E, Bleijenberg G, Voeten MJ, van der Meer JW, Folgering H.	Department of Medical Psychology, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands.	Impact of a maximal exercise test on symptoms and activity in chronic fatigue syndrome.	J Psychosom Res. 2005 Oct;59(4):201-8.	OBJECTIVE: This study examined the effects of exercise on symptoms and activity in chronic fatigue syndrome (CFS). METHODS: Twenty CFS patients and 20 neighborhood controls performed an incremental exercise test until exhaustion. Fatigue, muscle pain, minutes spent resting, and the level of physical activity were assessed with a self-observation list. Physical activity was assessed with an actometer as well. Data were obtained 3 days before the maximal exercise test (MET) up to 5 days thereafter. RESULTS: For CFS patients, daily observed fatigue was increased up to 2 days after the exercise test. For controls, self-observed fatigue returned to baseline after 2 h. Both CFS patients and controls spent more minutes resting on the day before and on the day after the MET. For CFS patients, self-observed minutes resting increased on the day of the exercise test. For neither group, a decrease of actometer recorded or self-observed physical activity after exercise was found. CONCLUSION: Fatigue in CFS patients increased after exercise, but the level of actual physical activity remained unchanged.
Bazelmans E, Bleijenberg G, Voeten MJ, van der Meer JW, Folgering H.	Department of Medical Psychology, Radboud University Nijmegen Medical Centre, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. HUe.bazelmans@mps.umcn.nlUH	Impact of a maximal exercise test on symptoms and activity in chronic fatigue syndrome.	J Psychosom Res. 2005 Oct;59(4):201-8.	OBJECTIVE: This study examined the effects of exercise on symptoms and activity in chronic fatigue syndrome (CFS). METHODS: Twenty CFS patients and 20 neighborhood controls performed an incremental exercise test until exhaustion. Fatigue, muscle pain, minutes spent resting, and the level of physical activity were assessed with a self-observation list. Physical activity was assessed with an actometer as well. Data were obtained 3 days before the maximal exercise test (MET) up to 5 days thereafter. RESULTS: For CFS patients, daily observed fatigue was increased up to 2 days after the exercise test. For controls, self-observed fatigue returned to baseline after 2 h. Both CFS patients and controls spent more minutes resting on the day before and on the day after the MET. For CFS patients, self-observed minutes resting increased on the day of the exercise test. For neither group, a decrease of actometer recorded or self-observed physical activity after exercise was found. CONCLUSION: Fatigue in CFS patients increased after exercise, but the level of actual physical activity remained unchanged.
Bazelmans E, Prins	Department of	Cognitive	Psychother	BACKGROUND: It has been demonstrated that individual cognitive behaviour therapy is an effective

JB, Lulofs R, van der Meer JW, Bleijenberg G; The Netherlands Fatigue Research Group Nijmegen.	Medical Psychology, University Medical Centre Nijmegen, Nijmegen, The Netherlands. E.Bazelmans@cukz.umcn.nl	behaviour group therapy for chronic fatigue syndrome: a non-randomised waiting list controlled study.	Psychosom. 2005;74(4):218-24.	treatment for chronic fatigue syndrome (CFS). The aim of the present study was to investigate the effectiveness of cognitive behaviour group therapy (CBGT) in an unselected group of CFS patients. Additionally, pretreatment characteristics of CFS patients who improve after CBGT were explored. METHODS: In a non-randomised waiting list controlled design, 31 patients were allocated to CBGT and 36 to the waiting list condition. CBGT consisted of 12 two-hour sessions during 6 months. Main outcome measures were fatigue (Checklist Individual Strength) and functional impairment (Sickness Impact Profile). RESULTS: A moderate effect on fatigue in favour of CBGT was found. For functional impairment, the effect was opposite to what was expected. Patients who improved after CBGT had less complaints at baseline compared to patients who did not improve. CONCLUSIONS: An explanation for the moderate effect might be that during CBGT, rest and relaxation were too much emphasised. Furthermore, an unselected group of CFS patients and therapists inexperienced in CB(G)T for CFS participated. Suggestions to improve CBGT for future research are given. Copyright (c) 2005 S. Karger AG, Basel.
Bell IR, Brooks AJ, Baldwin CM, Fernandez M, Figueredo AJ, Witten ML.	Research Service, Southern Arizona VA Health Care System, USA. HUibell@u.arizona.eduUH	JP-8 jet fuel exposure and divided attention test performance in 1991 Gulf War veterans.	Aviat Space Environ Med. 2005 Dec;76(12):1136-44.	INTRODUCTION: Previous research indicates that a large cohort of veterans from the 1991 Gulf War report polysymptomatic conditions. These syndromes often involve neurocognitive complaints, fatigue, and musculoskeletal symptoms, thus overlapping with civilian illnesses from low levels of environmental chemicals, chronic fatigue syndrome, and fibromyalgia. METHODS: To test for time-dependent changes over repeated intermittent exposures, we evaluated objective performance on a computerized visual divided attention test in chronically unhealthy Gulf War veterans (n = 22 ill with low-level chemical intolerance (CI); n = 24 ill without CI), healthy Gulf War veterans (n = 23), and healthy Gulf War era veterans (n = 20). Testing was done before and after each of three weekly, double blind, low-level JP-8 jet fuel or clean air sham exposure laboratory sessions, including acoustic startle stimuli. RESULTS: Unhealthy veterans receiving jet fuel had faster mean peripheral reaction times over sessions compared with unhealthy veterans receiving sham clean air exposures. Unhealthy Gulf veterans with CI exhibited faster post- vs. pre-session mean central reaction times compared with unhealthy Gulf veterans without CI. Findings were controlled for psychological distress variables. DISCUSSION: These data on unhealthy Gulf veterans show an acceleration of divided attention task performance over the course of repeated low-level JP-8 exposures. The present faster reaction times are consistent with rat neurobehavioral studies on environmental toxicant cross-sensitization and nonlinear dose-response patterns with stimulant drugs, as well as some previous civilian studies using other exposure agents. Together with previous research findings, the data suggest involvement of central nervous system dopaminergic pathways in affected Gulf veterans.
Bellanti JA, Sabra A, Castro HJ, Chavez JR, Malka-Rais J, de Inocencio JM.	Departments of Pediatrics , Georgetown University Medical Center, Washington, D.C. 20057, USA.	Are attention deficit hyperactivity disorder and chronic fatigue syndrome allergy related? what is fibromyalgia?	Allergy Asthma Proc. 2005 Jan-Feb;26(1):19-28.	Despite the progress made in the field of allergy-immunology in recent years, there are a group of diseases that the allergist-immunologist may be called on to manage in which their precise etiologies have not been identified but that appear to be initiated or exacerbated by allergic mechanisms. Attention deficit hyperactivity disorder (ADHD), chronic fatigue syndrome (CFS), and fibromyalgia (FM) fall into this category of disorders. Although the precise etiology of ADHD still remains unknown, the most prevalent theory is that it represents a neurobiologically based developmental disability leading to inadequate production of the neurotransmitter dopamine. In patients with CFS, there appears to be a fundamental dysfunction of the neuroendocrine-immunological system with deficiencies of

				immunological and neurological function, which, together with chronic viral infection, may lead to a sequence of events responsible for the symptoms of this disorder. FM appears to be a variant of CFS with a predominance of hypothalamic pituitary axis dysfunction. The disorder is characterized by chronic widespread pain and the finding of 11/18 tender points on examination. Now, there is emerging evidence to suggest that adverse reactions to foods or food components also may be associated with behavioral disturbances that may play a role in each of these disorders. An understanding of the interactive responses involved in the neuroendocrine-immunological network is essential for a comprehension of the pathophysiology of ADHD, CFS, and FM and the role of allergies appears to be an important triggering event in each of the disorders.
Bentler SE, Hartz AJ, Kuhn EM.	Department of Family Medicine, College of Medicine, University of Iowa, Iowa City, IA 52242-1097, USA.	Prospective observational study of treatments for unexplained chronic fatigue.	J Clin Psychiatry. 2005 May;66(5):625-32.	BACKGROUND: Unexplained chronic fatigue is a frequent complaint in primary care. A prospective observational study design was used to evaluate whether certain commonly used therapies for unexplained chronic fatigue may be effective. METHOD: Subjects with unexplained chronic fatigue of unknown etiology for at least 6 months were recruited from the Wisconsin Chronic Fatigue Syndrome Association, primary care clinics, and community chronic fatigue syndrome presentations. The primary outcome measure was change in a 5-question fatigue score from 6 months to 2 years. Self-reported interventions tested included prescribed medications, non-prescribed supplements and herbs, lifestyle changes, alternative therapies, and psychological support. Linear regression analysis was used to test the association of each therapy with the outcome measure after adjusting for statistically significant prognostic factors. RESULTS: 155 subjects provided information on fatigue and treatments at baseline and follow-up. Of these subjects, 87% were female and 79% were middle-aged. The median duration of fatigue was 6.7 years. The percentage of users who found a treatment helpful was greatest for coenzyme Q10 (69% of 13 subjects), dehydroepiandrosterone (DHEA) (65% of 17 subjects), and ginseng (56% of 18 subjects). Treatments at 6 months that predicted subsequent fatigue improvement were vitamins (p = .08), vigorous exercise (p = .09), and yoga (p = .002). Magnesium (p = .002) and support groups (p = .06) were strongly associated with fatigue worsening from 6 months to 2 years. Yoga appeared to be most effective for subjects who did not have unclear thinking associated with the fatigue. CONCLUSION: Certain alternative therapies for unexplained chronic fatigue, especially yoga, deserve testing in randomized controlled trials.
Black CD, McCully KK.	Department of Kinesiology, The University of Georgia, Athens, GA, USA. HUblackcd@uga.eduUH	Time course of exercise induced alterations in daily activity in chronic fatigue syndrome.	Dyn Med. 2005 Oct 28;4:10.	In a previous study we demonstrated that while people with CFS had lower daily activity levels than control subjects, they were able to increase daily activity via a daily walking program. We reanalyzed our data to determine the time course of activity changes during the walking program. Daily activity assessed via an accelometer worn at the hip was divided into sleep, active, and walking periods. Over the first 4-10 days of walking the subjects with CFS were able to reach the prescribed activity goals each day. After this time, walking and total activity counts decreased. Sedentary controls subjects were able to maintain their daily walking and total activity goals throughout the 4 weeks. Unlike our previous interpretation of the data, we feel this new analysis suggests that CFS patients may develop exercise intolerance as demonstrated by reduced total activity after 4-10 days. The inability to sustain target activity levels, associated with pronounced worsening of symptomology, suggests the subjects with CFS had reached their activity limit.
Black CD,	Department of	Increased daily	Dyn Med. 2005	Individuals with chronic fatigue syndrome (CFS) have been shown to have reduced activity levels

O'connor PJ, McCully KK.	Exercise Science, The University of Georgia, Athens, GA, USA. kmccully@coe.uga.edu.	physical activity and fatigue symptoms in chronic fatigue syndrome.	Mar 3;4(1):3.	associated with heightened feelings of fatigue. Previous research has demonstrated that exercise training has beneficial effects on fatigue-related symptoms in individuals with CFS. PURPOSE: The aim of this study was to sustain an increase in daily physical activity in CFS patients for 4 weeks and assess the effects on fatigue, muscle pain and overall mood. METHODS: Six CFS and seven sedentary controls were studied. Daily activity was assessed by a CSA accelerometer. Following a two week baseline period, CFS subjects were asked to increase their daily physical activity by 30% over baseline by walking a prescribed amount each day for a period of four weeks. Fatigue, muscle pain and overall mood were reported daily using a 0 to 100 visual analog scale and weekly using the Profile of Mood States (Bipolar) questionnaire. RESULTS: CFS patients had significantly lower daily activity counts than controls (162.5 +/- 51.7 x 103 counts/day vs. 267.2 +/- 79.5 x 103 counts/day) during a 2-week baseline period. At baseline, the CFS patients reported significantly ($P < 0.01$) higher fatigue and muscle pain intensity compared to controls but the groups did not differ in overall mood. CFS subjects increased their daily activity by 28+/-19.7% over a 4 week period. Overall mood and muscle pain worsened in +the CFS patients with increased activity. CONCLUSION: CFS patients were able to increase their daily physical activity for a period of four weeks. In contrast to previous studies fatigue, muscle pain, and overall mood did not improve with increased activity. Increased activity was not presented as a treatment which may account for the differential findings between this and previous studies. The results suggest that a daily "activity limit" may exist in this population. Future studies on the impact of physical activity on the symptoms of CFS patients are needed.
Blotman F, Thomas E, Myon E, Andre E, Caubere JP, Taieb C.	Rheumatology Department, Lapeyronie Hospital, Montpellier, France. francis.blotman@wanadoo.fr	Awareness and knowledge of fibromyalgia among french rheumatologists and general practitioners.	Clin Exp Rheumatol. 2005 Sep-Oct;23(5):697-700.	OBJECTIVES: Fibromyalgia is a chronic disorder characterized by widespread musculoskeletal pain and fatigue. Its prevalence is estimated to be at 3.4% in women and 0.5% in men. It is a major cause of morbidity. Our objective was to evaluate, using a self-questionnaire sent by mail, the level of knowledge of French physicians, general practitioners, and rheumatologists on fibromyalgia and to analyse their therapeutic approach. METHODS: The demographic characteristics of a sample of general practitioners and rheumatologists were compared to those of the overall data available. This comparison demonstrated the good representativeness of our sample. RESULTS: Fibromyalgia was considered as a disease by 23% of rheumatologists and 33% of general practitioners. While on average, each rheumatologist followed 30 fibromyalgia patients, each general practitioner followed 6.1 patients (i.e., 2 to 5% of their practice's patient base). Among rheumatologists, 6.4% made no distinction between this disease and depression vs. 13.1% of general practitioners. The diagnosis of fibromyalgia was made based on tenderness that occurs in precise, localized areas of the body (trigger points) by 94% of rheumatologists and 79.1% of general practitioners. Of general practitioners and rheumatologists, 93.7% and 73.7% respectively, have not received any medical school training on fibromyalgia or chronic fatigue syndrome. CONCLUSION: Given the lack of medical school training and continuing professional education concerning fibromyalgia (rare use of pain rating scales, confusion in the classification of rheumatic diseases), there is an urgent need to initiate an explicit teaching effort on chronic pain, and on fibromyalgia in particular.
Bolk JH.	Leids Universitair Medisch Centrum, afd Algemene	[Report from the Health Council of the Netherlands on	Ned Tijdschr Geneeskd. 2005 Apr 2;149(14):739-	The Health Council of the Netherlands has issued a report on the chronic fatigue syndrome (CFS). CFS is a real and seriously debilitating condition which imposes limitations on an individual's personal, occupational and social functioning. It is a syndrome of unknown aetiology without physical signs or

	Interne Geneeskunde, 2300 RC Leiden.	the chronic fatigue syndrome: moving away from the body-mind dichotomy with a view to effective prevention and treatment] [Article in Dutch]	41.	biological markers. Although there is no disease, patients both feel ill and give the appearance of being ill. There is no consensus on whether CSF patients are able to work or whether they should be entitled to social security benefits. An imbalance between demand and coping is central in CFS, with stress as an important intermediary factor. It is little use concluding that unexplained signs are 'psychological' or that 'I cannot find anything wrong with you so you must be healthy'. The classical view that mind and body are separate systems is outmoded. The bio-psycho-social model of disease may be helpful in describing the interaction between body, mind and circumstance. Putting the CFS patient at ease and explaining the pathophysiology of the symptoms is a useful approach but many patients and patient associations are still very somatically orientated, thereby sustaining the condition. However, in patients who accept that their problems may be stress-induced and are prepared to participate in therapy, some therapies have been proven to be effective, notably cognitive behavioural therapy.
Bowen J, Pheby D, Charlett A, McNulty C.	Health Protection Agency Primary Care Unit, Gloucester, UK. jill.whiting@hpa.org.uk	Chronic Fatigue Syndrome: a survey of GPs' attitudes and knowledge.	Fam Pract. 2005 Aug;22(4):389-93. Epub 2005 Apr 1.	BACKGROUND: GPs need evidence and guidance to help them diagnose and manage Chronic Fatigue Syndrome (CFS)/ME appropriately. OBJECTIVES: The aim of this survey was to obtain baseline data and identify the factors associated with GPs' attitudes to and knowledge of CFS/ME. The attitude of GPs to the condition is an important indicator of likely prognosis. METHODS: A postal questionnaire was sent to 1054 GPs served by Taunton, Bristol and Gloucester laboratories. GPs' attitudes to nine statements about CFS/ME were assessed and the factors associated with positive or negative responses were determined. Knowledge of the clinical features was also assessed. RESULTS: 811 GPs (77%) returned the questionnaire. 48% of GPs did not feel confident with making a diagnosis of CFS/ME and 41% did not feel confident in treatment. 72% of GPs accepted CFS/ME as a recognisable clinical entity and those GPs had significantly more positive attitudes. Three other key factors that were significantly, positively associated with GPs' attitudes were knowing someone socially with CFS/ME, being male and seeing more patients with the condition in the last year. CONCLUSION: Despite the publication of guidance for GPs on CFS/ME, confidence with making a diagnosis and management was found to be low. Educational initiatives and guidance for GPs should stress the importance of accepting CFS/ME as a recognisable clinical entity, as this is linked to having a positive attitude and could lead to improved confidence to make a diagnosis and treat CFS/ME patients.
Brimacombe M, Lange G, Bisuchio K, Ciccone DS, Natelson B		ORIGINAL RESEARCH Cognitive Function Index for Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2005 12 (4): 3 - 23	Background: A comprehensive approach to assessing neuropsychological deficits in CFS patients is developed by assessing cognitive function across a number of domains using a battery of tests, rather than relying on any single instrument. Objective: A factor analytic approach was employed to examine the underlying dimensionality of 15 standard cognitive function related test variables in CFS patients. A cognitive function index (CFI) was then developed using appropriately weighted and interpreted factors. Methods: Factor analysis was applied to an initial sample of 65 CFS patients, identifying eight factors accounting for over 70% of total variation. This factor structure was then independently verified on a separate sample of 124 CFS patients. An overall combined CFS sample of 212 was then used to derive the CFI using an appropriately interpreted and weighted average of the derived factors. Results: After including age and education as separate factors, the CFI consists of nine factors accounting for 70% of total variation in the overall CFS group. The CFI was not affected by the presence of current psychiatric comorbidity. A cut-off score for cognitive dysfunction was established

				using the lower quartile value of a group of sedentary controls on the same index. Conclusions: The CFI will provide a useful summary measure for researchers investigating cognitive function performance in CFS patients. It does not replace existing individual specialized tests.
Buskila D, Neumann L, Press J.	Department of Internal Medicine, Faculty of Health Sciences, Ben Gurion University of the Negev, Beer Sheva 84101, Israel. dbuskila@bgumail.bgu.ac.il	Genetic factors in neuromuscular pain.	CNS Spectr. 2005 Apr;10(4):281-4.	Recent evidence suggests that fibromyalgia, a chronic widespread pain condition and related syndromes (chronic fatigue syndrome, irritable bowel syndrome, etc.) may share heritable pathophysiologic features. We review the recent literature on genetic and familial factors found to participate in the pathogenesis of these syndromes, specifically fibromyalgia, including evidence suggesting that serotonin- and dopamine-related genes may play a role in the pathogenesis of these illnesses. The importance of environmental factors triggering these conditions in predisposed individuals is also discussed.
Cairns R, Hotopf M.	Department of Psychological Medicine, Institute of Psychiatry, London, UK.	A systematic review describing the prognosis of chronic fatigue syndrome.	Occup Med (Lond). 2005 Jan;55(1):20-31.	AIM: To perform a systematic review of studies describing the prognosis of chronic fatigue (CF) and chronic fatigue syndrome (CFS) and to identify occupational outcomes from such studies. METHOD: A literature search was used to identify all studies describing the clinical follow-up of patients following a diagnosis of CF or CFS. The prognosis is described in terms of the proportion of individuals improved during the period of follow-up. Return to work, other medical illnesses and death as outcomes are also considered, as are variables which may influence prognosis. RESULTS: Twenty-eight articles met the inclusion criteria and, for the 14 studies of subjects meeting operational criteria for CFS, the median full recovery rate was 5% (range 0-31%) and the median proportion of patients who improved during follow-up was 39.5% (range 8-63%). Less fatigue severity at baseline, a sense of control over symptoms and not attributing illness to a physical cause were all associated with a good outcome. Return to work at follow-up ranged from 8 to 30% in the three studies that considered this outcome. CONCLUSIONS: Full recovery from untreated CFS is rare. The prognosis for an improvement in symptoms is less gloomy. This review looks at the course of CF/CFS without systematic intervention. However, there is increasing evidence for the effectiveness of cognitive behavioural and graded exercise therapies. Medical retirement should be postponed until a trial of such treatment has been given.
Cairns V, Godwin J.	Consultant Statistician, Am Rothlauf 9, 61476 Kronberg, Germany.	Post-Lyme borreliosis syndrome: a meta-analysis of reported symptoms.	Int J Epidemiol. 2005 Jul 22; [Epub ahead of print]	BACKGROUND: This meta-analysis compares the prevalence of fatigue, musculoskeletal pain, and neurocognitive difficulties in patients who have had Lyme borreliosis (LB) and control subjects without LB. METHODS: Titles and abstracts in PubMed were reviewed for studies with data on the symptoms listed above that compared patients who had had LB with controls from the general population. Five studies with 504 patients and 530 controls were included in the meta-analysis. RESULTS: The prevalence of symptoms was significantly higher in the LB patients, with P-values between <0.00001 and 0.007 for 8 of the 10 symptoms in the three categories listed above. The higher prevalence of certain neurocognitive symptoms but not others, in the same pattern as reported in the literature, is further confirmation of this syndrome. The pattern of symptoms appears to be different from that seen in fibromyalgia, depression, and chronic fatigue syndrome. CONCLUSIONS: This meta-analysis provides strong evidence that some patients with LB have fatigue, musculoskeletal pain, and

				neurocognitive difficulties that may last for years despite antibiotic treatment.
Cairns V, Godwin J.	Clinical Trial Service Unit, University of Oxford, UK. HUcairns@t-online.deUH	Post-Lyme borreliosis syndrome: a meta-analysis of reported symptoms.	Int J Epidemiol. 2005 Dec;34(6):1340-5. Epub 2005 Jul 22.	BACKGROUND: This meta-analysis compares the prevalence of fatigue, musculoskeletal pain, and neurocognitive difficulties in patients who have had Lyme borreliosis (LB) and control subjects without LB. METHODS: Titles and abstracts in PubMed were reviewed for studies with data on the symptoms listed above that compared patients who had had LB with controls from the general population. Five studies with 504 patients and 530 controls were included in the meta-analysis. RESULTS: The prevalence of symptoms was significantly higher in the LB patients, with P-values between <0.00001 and 0.007 for 8 of the 10 symptoms in the three categories listed above. The higher prevalence of certain neurocognitive symptoms but not others, in the same pattern as reported in the literature, is further confirmation of this syndrome. The pattern of symptoms appears to be different from that seen in fibromyalgia, depression, and chronic fatigue syndrome. CONCLUSIONS: This meta-analysis provides strong evidence that some patients with LB have fatigue, musculoskeletal pain, and neurocognitive difficulties that may last for years despite antibiotic treatment.
Casado B, Zanone C, Annovazzi L, Iadarola P, Whalen G, Baraniuk JN.	Department of Biochemistry A. Castellani, University of Pavia, V.le Taramelli 3/B, 27100 Pavia, Italy. bc48@georgetown.edu	Urinary electrophoretic profiles from chronic fatigue syndrome and chronic fatigue syndrome/fibromyalgia patients: a pilot study for achieving their normalization.	J Chromatogr B Analyt Technol Biomed Life Sci. 2005 Jan 5;814(1):43-51.	Aim of our study was to determine if there were distinct, disease-related patterns of urinary analytes in chronic fatigue syndrome (CFS) and chronic fatigue syndrome/fibromyalgia (CFS/FM) compared to normal controls (NC). Urine was collected from these subjects for two consecutive 24 h periods and aliquots were submitted to micellar electrokinetic chromatography (MEKC). To compensate for the differences in peak migration times, these were normalized from the 35 min duration of run to a 100-point scale, and each peak was assigned its normalized time measure. Peak heights were also normalized by dividing the mAU by that of the internal standard (creatinine) and multiplying by 100. MEKC with normalization for peak height and migration time generated comparable results within each of the patient groups. CFS/FM and CFS had significant differences in peaks compared to NC that may be of significance as biomarkers of illnesses.
Cervera C, Alegre J, Ruiz E, Vasquez A, Armadans L, Garcia-Quintana AM, Aleman C, de Sevilla TF		Employment Status and Financial Repercussions in 60 Patients with Chronic Fatigue Syndrome in Spain: Utility of the Fatigue Impact Scale	Journal of Chronic Fatigue Syndrome 2005 12 (2): 35-45	Chronic fatigue syndrome (CFS) is a disabling disorder with implications in employment status. We enrolled 60 patients who fulfilled the CDC diagnostic criteria of Holmes and those of Fukuda. All patients underwent a protocol involving a structured questionnaire to record diagnostic criteria items, clinical features of fatigue, social features and associated symptoms; application of the Fatigue Impact Scale (FIS); an employment repercussion questionnaire; and information on evolution of the symptoms. Statistical comparisons were performed with the Mann-Whitney U test and correlations with the Spearman test. A close correlation was found between work inactivity and higher scores in the FIS cognitive dimension. Patient age and duration of symptoms also correlated with high cognitive scores. Chronic fatigue syndrome patients report a considerable decrease in quality of life, and most of them have work limitations, particularly those with poor overall FIS scores and cognitive function scores.
Chalmers RA, Jones MG, Goodwin CS, Amjad S.	St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, UK.	CFSUM1 and CFSUM2 in urine from patients with chronic fatigue syndrome are	Clin Chim Acta. 2005 Aug 8; [Epub ahead of print]	McGregor et al. reported increased levels of an unidentified urinary compound (CFSUM1) in patients with chronic fatigue syndrome (CFS), with reduced excretion of another unidentified compound (CFSUM2), and suggested the possibility of chemical or metabolic 'markers' for CFS. The identity of CFSUM1 as reported was erroneous and the identities of these compounds have remained unknown until now. Urine samples were obtained from 30 patients with ME/CFS, 30 age- and sex-matched

		methodological artefacts.		healthy controls, 20 control patients with depression and 22 control patients with rheumatoid arthritis. Samples were prepared using the published methods of McGregor et al. to produce heptafluorobutyryl-isobutyl derivatives of urinary metabolites. Alternative preparations utilised isopropyl, n-butyl and trifluoroacetyl derivatives. These were separated and identified using gas chromatography-mass spectrometry. CFSUM2 was identified as being partially derivatised [isobutyl ester-mono-heptafluorobutyryl (HFB)] serine. CFSUM1 was identified as partially derivatised pyroglutamic acid, being the isobutyl ester without formation of a HFB derivative. Both CFSUM1 and CFSUM2 are artefacts of the sample preparation procedure and previously reported quantitative abnormalities of CFSUM1 and CFSUM2 in urine from patients with ME/CFS are also artefactual. Pyroglutamic acid may be of primarily dietary origin. The methods used cannot provide reliable qualitative or quantitative data on urinary metabolites. No clinical or biochemical significance can be drawn between these compounds in ME/CFS or any other clinical conditions.
Chaudhuri A.		Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: data are insufficient and conclusion inappropriate. Comment on: BMJ. 2005 Jan 1;330(7481):14.	BMJ. 2005 Apr 2;330(7494):789-90; author reply 790.	Letter
Chia JK.	CEI Research Center, Torrance, CA 90505, USA. HUChiiasann@pol.netUH	The role of enterovirus in chronic fatigue syndrome.	J Clin Pathol. 2005 Nov;58(11):1126-32.	Two and a half decades after coining of the term chronic fatigue syndrome (CFS), the diagnosis of this illness is still symptom based and the aetiology remains elusive. Enteroviruses are well known causes of acute respiratory and gastrointestinal infections, with tropism for the central nervous system, muscles, and heart. Initial reports of chronic enteroviral infections causing debilitating symptoms in patients with CFS were met with skeptism, and had been largely forgotten for the past decade. Observations from in vitro experiments and from animal models clearly established a state of chronic persistence through the formation of double stranded RNA, similar to findings reported in muscle biopsies of patients with CFS. Recent evidence not only confirmed the earlier studies, but also clarified the pathogenic role of viral RNA through antiviral treatment. This review summarises the available experimental and clinical evidence that supports the role of enterovirus in chronic fatigue syndrome.
Cho HJ, Hotopf M, Wessely S.	Section of General Hospital Psychiatry, Institute of Psychiatry, King's College London,	The placebo response in the treatment of chronic fatigue syndrome: a systematic review	Psychosom Med. 2005 Mar-Apr;67(2):301-13.	OBJECTIVE: The placebo response is conventionally asserted to be high in chronic fatigue syndrome (CFS) because of the latter's subjective nature and obscure pathogenesis, but no systematic review of placebo responses has been undertaken. We report such a study. Patient expectation is known to be important in the placebo response. It is also known that CFS patients attending specialist clinics often have strong physical attributions regarding causation and hence skepticism about psychological or psychiatric interventions. If so, the placebo response in CFS may be influenced by the type of

	United Kingdom. h.cho@iop.kcl.ac.uk	and meta-analysis.		intervention according to its perceived rationale. We aimed to estimate the summary placebo response in clinical trials of CFS and to determine whether intervention type influences the placebo response in CFS. METHODS: We searched Medline, Embase, Cochrane Library, PsychInfo, and the references of the identified articles, and contacted experts for controlled trials (randomized or nonrandomized) of any intervention on CFS patients reporting the placebo response as a clinical improvement in physical or general outcomes. Data were extracted from the articles and validity assessment conducted by one reviewer and checked by a second. Meta-analysis and metaregression were performed. RESULTS: The pooled placebo response was 19.6% (95% confidence interval, 15.4-23.7), lower than predicted and lower than in some other medical conditions. The meta-regression revealed that intervention type significantly contributed to the heterogeneity of placebo response (p = .03). CONCLUSION: In contrast with the conventional wisdom, the placebo response in CFS is low. Psychological-psychiatric interventions were shown to have a lower placebo response, perhaps linked to patient expectations.
Cho HJ, Wessely S.		Chronic fatigue syndrome: an overview.	Rev Bras Psiquiatr. 2005 Sep;27(3):174-5. Epub 2005 Oct 4.	Editorial
Cho HJ, Wessely S.		Chronic fatigue syndrome: an overview.	Rev Bras Psiquiatr. 2005 Sep;27(3):174-5. Epub 2005 Oct 4.	Editorial
Christie D, Wilson C.	University College and Middlesex Hopsitals, London, UK. HUdeborah.christie@uclh.orgUH	CBT in paediatric and adolescent health settings: a review of practice-based evidence.	Pediatr Rehabil. 2005 Oct-Dec;8(4):241-7.	Cognitive Behavioural therapy (CBT) has strong theoretical underpinnings that facilitate the systematic evaluation of outcomes and process of change adults. CBT has been extensively adapted for use with children and young people with session content and method of delivery modified to acknowledge developmental stage and ability. Current approaches emphasise the psychological management of the impact of symptoms of particular types of physical health difficulties and prevention of the development of psychological difficulties, as well as in the alleviation of procedurally related stress. The need for collaboration with families and other parts of a child's network is particularly relevant in the paediatric setting. This review describes what we have found helpful in our work and provides a road map of where to go to find out more about how to do more. General CBT approaches are described as well as examples of how CBT has been used specifically for procedural distress, diabetes, sickle cell disease, chronic pain and chronic fatigue.
Chrousos GP, Kaltsas G.	Athens University, Athens, Greece and National Institutes of Health, Bethesda, MD, USA. HUchrousge@med.uoa.grUH	Post-SARS sickness syndrome manifestations and endocrinopathy: how, why, and so what?	Clin Endocrinol (Oxf). 2005 Oct;63(4):363-5. Comment on: Clin Endocrinol (Oxf). 2005 Aug;63(2):197-202.	Comment

Cleare AJ, Messa C, Rabiner EA, Grasby PM.	Section of Neurobiology of Mood Disorders, Division of Psychological Medicine, Institute of Psychiatry and Guy-s, King-s and St. Thomas- School of Medicine, London, United Kingdom. a.cleare@iop.kcl.ac.uk	Brain 5-HT1A receptor binding in chronic fatigue syndrome measured using positron emission tomography and [11C]WAY-100635.	Biol Psychiatry. 2005 Feb 1;57(3):239-46.	BACKGROUND: Research from neuroendocrine challenge and other indirect studies has suggested increased central 5-HT function in chronic fatigue syndrome (CFS) and increased 5-HT1A receptor sensitivity. We assessed brain 5-HT1A receptor binding potential directly using the specific radioligand [11C]WAY-100635 and positron emission tomography (PET). METHODS: We selected 10 patients from a tertiary referral clinic who fulfilled the CDC consensus criteria for CFS. To assemble a homogenous group and avoid confounding effects, we enrolled only subjects who were completely medication-free and did not have current comorbid psychiatric illness. We also scanned 10 healthy control subjects. RESULTS: There was a widespread reduction in 5-HT1A receptor binding potential in CFS relative to control subjects. This was particularly marked in the hippocampus bilaterally, where a 23% reduction was observed. CONCLUSIONS: There is evidence of decreased 5-HT1A receptor number or affinity in CFS. This may be a primary feature of CFS, related to the underlying pathophysiology, or a finding secondary to other processes, such as previous depression, other biological changes or the behavioral consequences of CFS.
Cook DB, Nagelkirk PR, Peckerman A, Poluri A, Mores J, Natelson BH.	University of Wisconsin-Madison, Department of Kinesiology, USA. cookdb@njneuromed.org	Exercise and cognitive performance in chronic fatigue syndrome.	Med Sci Sports Exerc. 2005 Sep;37(9):1460-7.	PURPOSE: To determine the effect of submaximal steady-state exercise on cognitive performance in patients with chronic fatigue syndrome (CFS) alone, CFS with comorbid fibromyalgia FM (CFS + FM), and sedentary healthy controls (CON). METHODS: Twenty CFS-only patients, 19 CFS + FM, and 26 CON completed a battery of cognitive tests designed to assess speed of information processing, variability, and efficiency. Tests were performed at baseline, immediately before, and twice following 25 min of either cycle ergometry set at 40% of peak oxygen capacity or quiet rest. RESULTS: There were no group differences in average percentage of peak oxygen consumption during exercise (CFS = 45%; CFS + FM = 47%; Control = 43%: P = 0.2). There were no significant effects of acute exercise on cognitive performance for any group. At baseline, one-way ANOVA indicated that CFS patients displayed deficits in speed of processing, performance variability, and task efficiency during several cognitive tests compared with healthy controls. However, the CFS + FM patients were not different than controls. Repeated measures ANOVA indicated that across all tests (pre- and postexercise) CFS, but not CFS + FM, were significantly less consistent ($F_{2,59} = 3.7$, $P = 0.03$) and less efficient ($F_{2,59} = 4.6$, $P = 0.01$) than controls. CONCLUSION: CFS patients without comorbid FM exhibit subtle cognitive deficits in terms of speed, consistency, and efficiency that are not improved or exacerbated by light exercise. Importantly, our data suggest that CFS + FM patients do not exhibit cognitive deficits either pre- or postexercise. These results highlight the importance of disease heterogeneity in studies determining acute exercise and cognitive function in CFS.
Covelli V, Passeri ME, Leogrande D, Jirillo E, Amati L.	Division of Neurology, Polyclinic Hospital, Bari Italy.	Drug targets in stress-related disorders.	Curr Med Chem. 2005;12(15):1801-9.	Nervous and immune systems mutually cooperate via release of mediators of both neurological and immunological derivation. Adrenocorticotropin hormone (ACTH) is a product of the hypothalamus-pituitary adrenal axis (HPAA) which stimulates secretion of corticosteroids from adrenals. In turn, corticosteroids modulate the immune response in virtue of their anti-inflammatory activity. On the other hand, catecholamines, products of the sympathetic nervous system (SNS), regulate immune function by acting on specific beta-adrenergic receptors. Conversely, cytokines released by monocytes/macrophages and lymphocytes, upon antigenic stimulation, are able to cross the blood-brain-barrier, thus modulating nervous functions (e.g., thermoregulation, sleep, and appetite).

				However, cytokines are locally produced in the brain, especially in the hypothalamus, thus contributing to the development of anorexic, pyrogenic, somnogenic and behavioural effects. Besides pathogens and/or their products, the so-called stressors are able to activate both HPAA and SNS, thus influencing immune responses. In this respect, many studies conducted in medical students taking exams have evidenced an array of stress-induced immune alterations. Phobic disorders and migraine without aura (MWA) represent examples of stress-related disorders in which phagocytic immune deficits, endotoxemia and exaggerated levels of proinflammatory cytokines [Tumor Necrosis Factor-alpha (TNF- alpha), and interleukin- 1 beta] have been detected. Quite interestingly, administration of a thymic hormone could ameliorate clinical symptoms in phobic patients. In MWA patients, a beta-blocker, propranolol, could mitigate migraine, whose cessation coincided with a drop of TNF-alpha serum concentration. In phobic disorders and in MWA, benzodiazepines are very often administered and, in this respect, some of them, such as diazepam, inhibit immune functions, while others, e.g., alprazolam, enhance immune responses. Alprazolam could improve clinical symptoms in MWA patients. Chronic Fatigue Syndrome (CFS) is a disorder whose etiology and pathogenesis are still unknown. In this syndrome both abnormalities of nervous and immune systems have been reported. Despite many immune parameters evaluated in CFS no specific biomarkers of disease have been found. Our own data are in agreement with current literature in that we found decreased levels of serum (IFN)-gamma in these patients, thus indicating a predominance of T helper (h)1 response in CFS. Also leptin, a hormone which regulates food intake, fluctuates within normal ranges in CFS individuals. Quite interestingly, in depressed patients, used as controls, leptinaemia was more elevated than in CFS. Finally, in a series of recent therapeutic trials several immunomodulating agents have been used, such as staphypan Berna, lactic acid bacteria, kuibitang and intravenous immunoglobulin. In conclusion, it seems that major drug targets in stress-related disorders are immune cells in terms of inhibition of proinflammatory cytokines and modulation of Th responses. In particular, according to recent evidences, antidepressants seem to exert beneficial effects in experimental autoimmune neuritis in rats by decreasing IFN- beta release or augmenting NK activity in depressed patients.
Crowhurst G.	25% Severe ME Group, Great Walsingham, Norfolk. gregcrowhurst@yahoo.co.uk	Supporting people with severe myalgic encephalomyelitis.	Nurs Stand. 2005 Feb 2-8;19(21):38-43.	This article aims to raise nurses' awareness of myalgic encephalomyelitis (ME) also known as chronic fatigue syndrome (CFS). Key symptoms are presented along with possible service responses and treatment options. It emphasises that this condition is often misunderstood but that it can be serious and more research is needed to promote better understanding of the physical symptoms.
Darbishire L, Seed P, Ridsdale L.	Department of General Practice and Primary Care, Guy's, King's and St Thomas' School ol of Medicine, 5 Lambeth Walk,	Predictors of outcome following treatment for chronic fatigue.	Br J Psychiatry. 2005 Apr;186:350-1.	We explored the role of baseline characteristics of 105 patients who presented with fatigue in primary care in determining outcome following either graded exercise or cognitive-behavioural therapy. Meeting the criteria for chronic fatigue syndrome was the most powerful predictor of poor outcome and this negative effect was enhanced by greater functional impairment or greater perceived negative consequences, but was not further enhanced by both.

	London, SE11 6SP, UK. lucy.clark@kcl.ac.uk			
Davidson J.	Department of Geography, Queen's University, Kingston, Ont., K7L 3N6, Canada. HUjoyce.davidson@queensu.caUH	Contesting stigma and contested emotions: personal experience and public perception of specific phobias.	Soc Sci Med. 2005 Nov;61(10):2155-64.	This paper draws on interviews with members of the United Kingdom National Phobics Society to explore the implications of the contested nature of specific phobias for their experience and perception. In common with other chronic and contested conditions such as Chronic Fatigue Syndrome, phobias are stigmatised and subjected to widespread judgmental attitudes in both medical and lay populations. In contrast, however, phobic experience is rarely characterised by difficulty in describing symptoms and obtaining a diagnosis: core fearful reaction to and avoidance of particular objects is usually obvious and uncontested. The crucial difference is that phobias are constituted by emotions and behaviours considered irrational and inconsequential, and it is their (perceived absence of) significance that raises questions and eyebrows. In other words, what does it matter and who cares if you happen to be scared of snakes? Using phobics' own words as far as possible, the paper explores the processes through which phobic emotions are constructed as contested, and examines phobic means of managing experience and perception of these emotions. It reveals that many respondents are resourceful and resistant, continually renegotiating their positioning as irrational, incapable and emotionally weak.
de Lange FP, Kalkman JS, Bleijenberg G, Hagoort P, van der Meer JW, Toni I.	F.C. Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, NL-6500 HB Nijmegen, The Netherlands. floris.delange@fcdonders.ru.nl	Gray matter volume reduction in the chronic fatigue syndrome.	Neuroimage. 2005 Jul 1;26(3):777-81. Epub 2005 Apr 7.	The chronic fatigue syndrome (CFS) is a disabling disorder of unknown etiology. The symptomatology of CFS (central fatigue, impaired concentration, attention and memory) suggests that this disorder could be related to alterations at the level of the central nervous system. In this study, we have used an automated and unbiased morphometric technique to test whether CFS patients display structural cerebral abnormalities. We mapped structural cerebral morphology and volume in two cohorts of CFS patients (in total 28 patients) and healthy controls (in total 28 controls) from high-resolution structural magnetic resonance images, using voxel-based morphometry. Additionally, we recorded physical activity levels to explore the relation between severity of CFS symptoms and cerebral abnormalities. We observed significant reductions in global gray matter volume in both cohorts of CFS patients, as compared to matched control participants. Moreover, the decline in gray matter volume was linked to the reduction in physical activity, a core aspect of CFS. These findings suggest that the central nervous system plays a key role in the pathophysiology of CFS and point to a new objective and quantitative tool for clinical diagnosis of this disabling disorder.
Di Giorgio A, Hudson M, Jerjes W, Cleare AJ.	Department of Neurological and Psychiatric Services, University of Bari, Bari, Italy	24-hour pituitary and adrenal hormone profiles in chronic fatigue syndrome.	Psychosom Med. 2005 May-Jun;67(3):433-40.	OBJECTIVES: Disturbances of neuroendocrine function, particularly the hypothalamo-pituitary-adrenal (HPA) axis, have been implicated in the pathophysiology of chronic fatigue syndrome (CFS). However, few studies have attempted to measure blood levels of pituitary or adrenal hormones across a whole 24-hour period in CFS, and those that did so have used infrequent sampling periods. Our aim was to assess 24-hour pituitary and adrenal function using frequent blood sampling. METHODS: We recruited 15 medication-free patients with CFS without comorbid psychiatric disorder and 10 healthy control subjects. Blood samples were collected over 24 hours and assayed for cortisol, corticotropin (ACTH), growth hormone (GH), and prolactin (PRL) levels on an hourly basis during daytime hours (10 am to 10 pm) and every 15 minutes thereafter (10 pm to 10 am). RESULTS: Repeated-measures analyses of

				variance were undertaken using hormone levels averaged over 2-hour blocks to smooth curves by reducing the influence of sample timing relative to secretory burst. For ACTH, there was both a main effect of group, suggesting reduced mean ACTH secretion in patients with CFS over the whole monitoring period, and a group-by-time interaction, suggesting a differential pattern of ACTH release. Post hoc analysis showed reduced ACTH levels in CFS during the 8 am to 10 am period. In contrast, there were no significant abnormalities in the levels of cortisol, GH, and PRL in patients with CFS over the full cycle compared with control subjects. Cosinor analysis found no differences in the cortisol circadian rhythm parameters, but the ACTH rhythm did differ, patients with CFS showing an earlier acrophase. CONCLUSIONS: Patients with CFS demonstrated subtle alterations in HPA axis activity characterized by reduced ACTH over a full circadian cycle and reduced levels during the usual morning physiological peak ACTH secretion. This provides further evidence of subtle dysregulation of the HPA axis in CFS. Whether this dysregulation is a primary feature of the illness or instead represents a biologic effect secondary to having the illness itself remains unclear.
Doljansky JT, Kannety H, Dagan Y.	The Institute for Sleep and Fatigue Medicine, Chaim Sheba Health Center, Tel-Hashomer, Israel. Julia.Tamir@Sheba.health.gov.il	Working under daylight intensity lamp: an occupational risk for developing circadian rhythm sleep disorder?	Chronobiol Int. 2005;22(3):597-605.	A 47-yr-old male was admitted to the Institute for Fatigue and Sleep Medicine complaining of severe fatigue and daytime sleepiness. His medical history included diagnosis of depression and chronic fatigue syndrome. Antidepressant drugs failed to improve his condition. He described a gradual evolvement of an irregular sleep-wake pattern within the past 20 yrs, causing marked distress and severe impairment of daily functioning. He had to change to a part-time position 7 yrs ago, because he was unable to maintain a regular full-time job schedule. A 10-day actigraphic record revealed an irregular sleep-wake pattern with extensive day-to-day variability in sleep onset time and sleep duration, and a 36 h sampling of both melatonin level and oral temperature (12 samples, once every 3 h) showed abnormal patterns, with the melatonin peak around noon and oral temperature peak around dawn. Thus, the patient was diagnosed as suffering from irregular sleep-wake pattern. Treatment with melatonin (5 mg, 2 h before bedtime) did not improve his condition. A further investigation of the patient's daily habits and environmental conditions revealed two important facts. First, his occupation required work under a daylight intensity lamp (professional diamond-grading equipment of more than 8000 lux), and second, since the patient tended to work late, the exposure to bright light occurred mostly at night. To recover his circadian rhythmicity and stabilize his sleep-wake pattern, we recommended combined treatment consisting of evening melatonin ingestion combined with morning (09:00 h) bright light therapy (0800 lux for 1 h) plus the avoidance of bright light in the evening. Another 10-day actigraphic study done only 1 wk after initiating the combined treatment protocol revealed stabilization of the sleep-wake pattern with advancement of sleep phase. In addition, the patient reported profound improvement in maintaining wakefulness during the day. This case study shows that chronic exposure to bright light at the wrong biological time, during the nighttime, may have serious effects on the circadian sleep-wake patterns and circadian time structure. Therefore, night bright light exposure must be considered to be a risk factor of previously unrecognized occupational diseases of altered circadian time structure manifested as irregularity of the 24 h sleep-wake cycle and melancholy.
Driver C.		An under-active or over-active	J Anal Psychol. 2005	This paper explores the dynamics brought into analytic work when there is a symmetric fusion between psyche and soma within the patient. It will consider how such a fusion may emerge from

		internal world? An exploration of parallel dynamics within psyche and soma, and the difficulty of internal regulation, in patients with Chronic Fatigue Syndrome and Myalgic Encephalomyelitis.	Apr;50(2):155-73.	reverberations between physical constitution and a lack of maternal attunement, containment and reflective function. I will describe the work with a patient, Jane, who was diagnosed with Myalgic Encephalomyelitis (ME) during the course of her analysis. The dynamic of her physical symptoms within the analytic work, and the impact of her internal affects and internal 'objects' within the transference and countertransference, indicated a difficulty in finding an homeostatic balance resulting in overactivity and underactivity at both somatic and psychological levels. Using the clinical work with Jane this paper will also examine the interrelationship between mother-infant attachment, an inadequate internalized maternal reflective function, affect dysregulation, unconscious fusion, the lack of psyche-soma differentiation and the impact of the latter in relation to internal regulation systems, or lack of, in patients with Chronic Fatigue Syndrome (CFS) and Myalgic Encephalomyelitis (ME). I will draw on similar work carried out by Holland (1997), Simpson (1997) and Simpson et al. (1997). The paper will also employ the concept of the reflective function (Fonagy 2001; Knox 2003), and consider Matte-Blanco's (1999) concepts of generalization and unconscious symmetry in relation to the patient's internal world. I go on to consider how analysis provides a point outside the 'fusion' that can enable the 'deadlock' to be broken.
Dumit J.	Program in Science, Technology & Society, Massachusetts Institute of Technology, E51-296D MIT, Cambridge, MA 02139-4307, USA.	Illnesses you have to fight to get: Facts as forces in uncertain, emergent illnesses.	Soc Sci Med. 2005 Aug 5; [Epub ahead of print]	Chronic fatigue syndrome and multiple chemical sensitivity are two clusters of illnesses that are pervaded by medical, social and political uncertainty. This article examines how facts are talked about and experienced in struggles over these emergent, contested illnesses in the US. Based principally on a large archive of internet newsgroup postings, and also on fieldwork and on published debates, it finds that (1) sufferers describe their experiences of being denied healthcare and legitimacy through bureaucratic categories of exclusion as dependent upon their lack of biological facts; (2) institutions manage these exclusions rhetorically through exploiting the open-endedness of science to deny efficacy to new facts; (3) collective patient action responds by archiving the systematic nature of these exclusions and developing counter-tactics. The result is the maintenance of these very expensive struggles for all involved.
Durlach J, Pages N, Bac P, Bara M, Guiet-Bara A.	SDRM, Universite Pierre et Marie Curie, 75252 Paris Cedex 05, France. jean.durlach@wanadoo.fr	Magnesium depletion with hypo- or hyper-function of the biological clock may be involved in chronopathological forms of asthma.	Magnes Res. 2005 Mar;18(1):19-34.	Asthma is a chronic, inflammatory disorder of the airways leading to airflow limitation. Its worldwide rise, mainly in developed countries, is a matter of concern. Nocturnal asthma (NA) frequently occurs and concerns two thirds of asthmatics. But, it remains controversial whether NA is a distinct entity or is a manifestation of more severe asthma. Generally, it is considered as an exacerbation of the underlying pathology. The pathological mechanisms most likely involve endogenous circadian rhythms with pathological consequences on both respiratory inflammation and hyperresponsiveness. A decrease in blood and tissue magnesium levels is frequently reported in asthma and often testifies to a true magnesium depletion. The link with magnesium status and chronobiology are well established. The quality of magnesium status directly influences the Biological Clock (BC) function, represented by the suprachiasmatic nuclei and the pineal gland. Conversely, BC dysrythmias influence the magnesium status. Two types of magnesium deficits must be clearly distinguished: deficiency corresponding to an insufficient intake which can be corrected through mere nutritional Mg supplementation and depletion due to a dysregulation of the magnesium status which cannot be corrected through nutritional supplementation only, but requires the more or less specific correction of the dysregulation mechanisms. Both in clinical and in animal experiments, the dysregulation mechanisms

				of magnesium depletion associate a reduced magnesium intake with various types of stress including biological clock dysrhythmias. The differenciation between Mg depletion forms with hyperfunction of BC (HBC) and forms with hypofunction of BC (hBC) is seminal and the main biological marker is melatonin (MT) production alteration. We hypothesize that magnesium depletion with HBC or hBC may be involved in chronopathological forms of asthma. Nocturnal asthma would be linked to HBC, represented by an increase in MT levels. The corresponding clinical forms associate diverse expressions of nervous hypoexcitability such as depression, cluster headaches, dyssomnia, mainly advanced sleep phase syndrome, some clinical forms of chronic fatigue syndrome and of fibromyalgia. The main comorbidities are depression and/or asthenia. They take place during the night or the "bad" seasons (autumn and winter) when sunshine is at a minimum. The corresponding chronopathological therapy relies on bright light phototherapy sometimes with additional psychoanaleptics. Conversely, asthma forms linked to hBC are less frequently studied as a whole and present a decrease in MT levels. They associate various signs of nervous hyperexcitability such as anxiety, diurnal cephalalgia (mainly migraine), dyssomnia, mainly delayed sleep phase syndrome, and some clinical forms of chronic fatigue syndrome and of fibromyalgia. The treatment relies on diverse forms of "darkness therapy", possibly with the help of some psycholeptics. Finally, the treatment of asthma involves the maintenance of a standard dosing schedule of anti-asthma drugs, a balanced magnesium intake and the appropriate treatment of the chronopathological disorders.
Ehrlich GE.		Silicone breast implants. Comment on: J Rheumatol. 2004 May;31(5):1015; author reply 1015-6.	J Rheumatol. 2005 Jun;32(6):1173-4; author reply 1174.	Letter
Eisen SA, Kang HK, Murphy FM, Blanchard MS, Reda DJ, Henderson WG, Toomey R, Jackson LW, Alpern R, Parks BJ, Klimas N, Hall C, Pak HS, Hunter J, Karlinsky J, Battistone MJ, Lyons MJ; Gulf War Study Participating Investigators.	Veterans Affairs Medical Center, Washington University School of Medicine, St. Louis, Missouri 63106, USA. seth.eisen@med.va.gov	Gulf War veterans' health: medical evaluation of a U.S. cohort.	Ann Intern Med. 2005 Jun 7;142(11):881-90.	BACKGROUND: United States military personnel reported various symptoms after deployment to the Persian Gulf during the 1991 Gulf War. However, the symptoms' long-term prevalence and association with deployment remain controversial. OBJECTIVE: To assess and compare the prevalence of selected medical conditions in a national cohort of deployed and nondeployed Gulf War veterans who were evaluated by direct medical and teledermatologic examinations. DESIGN: A cross-sectional prevalence study performed 10 years after the 1991 Gulf War. SETTING: Veterans were examined at 1 of 16 Veterans Affairs medical centers. PARTICIPANTS: Deployed (n = 1061) and nondeployed (n = 1128) veterans of the 1991 Gulf War. MEASUREMENTS: Primary outcome measures included fibromyalgia, the chronic fatigue syndrome, dermatologic conditions, dyspepsia, physical health-related quality of life (Short Form-36 [SF-36]), hypertension, obstructive lung disease, arthralgias, and peripheral neuropathy. RESULTS: Of 12 conditions, only 4 conditions were more prevalent among deployed than nondeployed veterans: fibromyalgia (deployed, 2.0%; nondeployed, 1.2%; odds ratio, 2.32 [95% CI, 1.02 to 5.27]); the chronic fatigue syndrome (deployed, 1.6%; nondeployed 0.1%; odds ratio, 40.6 [CI, 10.2 to 161]); dermatologic conditions (deployed, 34.6%; nondeployed, 26.8%; odds ratio, 1.38 [CI, 1.06 to 1.80]), and dyspepsia (deployed, 9.1%; nondeployed, 6.0%; odds ratio, 1.87 [CI, 1.16 to 2.99]).

				The mean physical component summary score of the SF-36 for deployed and nondeployed veterans was 49.3 and 50.8, respectively. LIMITATIONS: Relatively low participation rates introduce potential participation bias, and deployment-related illnesses that resolved before the research examination could not, by design, be detected. CONCLUSIONS: Ten years after the Gulf War, the physical health of deployed and nondeployed veterans is similar. However, Gulf War deployment is associated with an increased risk for fibromyalgia, the chronic fatigue syndrome, skin conditions, dyspepsia, and a clinically insignificant decrease in the SF-36 physical component score.
Elena Garralda M, Chalder T.	Imperial College, London, UK. HUegarralda@imperial.ac.ukUH	Practitioner review: chronic fatigue syndrome in childhood.	J Child Psychol Psychiatry. 2005 Nov;46(11):1143-51.	BACKGROUND: Chronic fatigue syndrome (CFS) is being increasingly recognized in children and adolescents. Yet comparatively little attention has been given in the literature to management. METHODS: Description of the main features of the disorder, precipitating and maintaining factors and diagnostic assessment. Outline of different views on the nature and treatment of CFS in childhood. Description of a rehabilitation program based on cognitive behavior therapy and graded activity. RESULTS: Using adult research criteria, CFS can be diagnosed in children and adolescents. In its severe form it is often triggered by infectious illness episodes. It is commonly associated with mood disorders in the child and with mental distress and high levels of emotional involvement in parents. A number of patient support groups hold the view that CFS is a medical disorder, contest a psychiatric contribution and advocate 'pacing' as an approach to rehabilitation which includes avoiding activities. To date there is no empirical evidence for the efficacy of this approach. Research in adults, open and clinical reports in children support the use of graded activity and family cognitive behavior therapy. The main aim is to enable children, with the help of their family, to carry out their own rehabilitation with some support and guidance from a health professional. Engaging the child and family in treatment and forming a therapeutic alliance is a continual process and a crucial aspect of management, as many families view the condition as a medical disorder and are initially ambivalent towards this approach. CONCLUSIONS: There is controversy about the nature and management of CFS in childhood but a rehabilitation program based on family cognitive behavior therapy can be implemented and seems to hold most promise in the management of children with CFS. Family engagement is a crucial aspect of management.
Evengard B, Jacks A, Pedersen NL, Sullivan PF.	Department of Laboratory Medicine, Karolinska Institutet at Karolinska University Hospital Huddinge, Stockholm, Sweden.	The epidemiology of chronic fatigue in the Swedish Twin Registry.	Psychol Med. 2005 Sep;35(9):1317-26.	BACKGROUND: Chronic fatigue syndrome (CFS) remains an idiopathic and controversial entity. METHOD: We screened 31405 individual members of the Swedish Twin Registry (aged 42-64 years) for the symptoms of fatiguing illness via a telephone questionnaire. We refined self-reported symptoms via data from several national registries and from physician review of all available medical records in order to approximate closely the dominant case definition of CFS. FINDINGS: The 6-month prevalence of CFS-like illness was 2.36% (95% CI 2.19-2.53) and was markedly higher in women than men, odds ratio 3.92 (95% CI 3.24-4.72) with no significant association with age or years of education. There was a highly significant association with occupation that disappeared after accounting for gender. INTERPRETATION: CFS-like illness may be more common that previously acknowledged. There is a marked increase in risk by gender. Previous reports that CFS is more prevalent in individuals in certain occupational categories were not confirmed and may have been due to confounding by gender.
Fernandez-Sola J, Lluis Padierna M,	Servicio de Medicina Interna.	[Chronic fatigue syndrome and	Med Clin (Barc). 2005 Apr	Background and objective: Chronic Fatigue Syndrome (CFS) and Multiple Chemical Sensitivity (MCS) are well-defined illnesses that may appear after some toxic exposures. Patients and method: We

Nogue Xarau S, Munne Mas P.	Unidad Multidisciplinar de Fatiga Cronica. Hospital Clinic de Barcelona. IDIBAPS. Universitat de Barcelona. Barcelona. Spain.	multiple chemical hypersensitivity after insecticide exposition.] [Article in Spanish]	2;124(12):451-3.	report a consecutive series of 26 patients who developed CFS after exposure to insecticide products. It was associated with MCS in a third of cases. RESULTS: Toxic exposure was of labour origin after returning to usual work place after a process of fumigation. In 42% of cases there was no fulfilment of fumigation safety rules. The majority of patients were mean-aged women who developed an acute upper airway inflammatory syndrome, without muscarinic or nicotinic manifestations, followed by digestive syndrome, neurocognitive, fibromyalgic and chronic fatigue manifestations. The course of disease was shorter than 1 year in 5 cases (19%), longer than 1 year in 15(58%), and disabling in 6 cases (23%). CONCLUSIONS: Due to the possible prevention of this toxic exposure, it is very important to carefully follow measures of environment isolation and ventilation after insecticide use in order to avoid the development of these diseases.
Ferre Ybarz L, Cardona Dahl V, Cadahia Garcia A, Ruiz E, Vazquez A, Fernandez de Sevilla T, Alegre Martin J.	Hospital Vall d'Hebron, Barcelona, Spain. laiafy@vodafone.es	[Prevalence of atopy in chronic fatigue syndrome] [Article in Spanish]	Allergol Immunopathol (Madr). 2005 Jan-Feb;33(1):42-7.	BACKGROUND: Several hypotheses have been postulated to explain the etiopathogenesis of chronic fatigue syndrome (CFS). Among these, immunologic dysfunction has been proposed. Up to 30 % of these patients have a history of allergic disease. The aim of this study was to investigate whether allergic sensitization is higher in patients with CFS than in the general population. METHODS: Twenty-five patients with CFS and 20 controls were evaluated. A clinical history for allergy was taken and immediate hypersensitivity tests were performed. RESULTS: Twelve patients (48 %) and eight controls (40 %) had a family history of atopy. Personal histories of atopy were as follows: rhinoconjunctivitis: 12 patients (48 %), seven controls (35 %); asthma: five patients (20 %), two controls (10 %); food allergy: three patients (12 %); atopic dermatitis: two patients; contact dermatitis: two patients. No statistically significant differences were found between the groups in any of the variables ($p > 0.05$). In the CSF group, 3.4 % (15/441) of the inhalant prick tests were positive, and in the control group 3.8 % (16/420) were positive. None of the tests for hypersensitivity to food or latex were positive. CONCLUSIONS: In our study atopy was not more prevalent in patients with CFS than in healthy controls, although the CSF group tended to report more respiratory symptoms and drug allergies.
Fowler T, Duthie P, Thapar A, Farmer A.	Department of Psychological Medicine, Wales College of Medicine, Cardiff University, UK. fowlerta@cardiff.ac.uk	The definition of disabling fatigue in children and adolescents.	BMC Fam Pract. 2005 Aug 9;6:33.	BACKGROUND: Disabling fatigue is the main illness related reason for prolonged absence from school. Although there are accepted criteria for diagnosing chronic fatigue in adults, it remains uncertain as to how best to define disabling fatigue and Chronic Fatigue Syndrome (CFS) in children and adolescents. In this population-based study, the aim was to identify children who had experienced an episode of disabling fatigue and examine the clinical and demographic differences between those individuals who fulfilled a narrow definition of disabling fatigue and those who fulfilled broader definitions of disabling fatigue. METHODS: Participants (aged 8-17 years) were identified from a population-based twin register. Parent report was used to identify children who had ever experienced a period of disabling fatigue. Standardised telephone interviews were then conducted with the parents of these affected children. Data on clinical and demographic characteristics, including age of onset, gender, days per week affected, hours per day spent resting, absence from school, comorbidity with depression and a global measure of impairment due to the fatigue, were examined. A narrow definition was defined as a minimum of 6 months disabling fatigue plus at least 4 associated symptoms, which is comparable to the operational criteria for CFS in adults. Broader definitions included those with at least 3 months of disabling fatigue and 4 or more of the associated symptoms and those with simply a minimum of 3 months of disabling fatigue. Groups were mutually exclusive. RESULTS: Questionnaires were returned

				by 1468 families (65% response rate) and telephone interviews were completed on 99 of the 129 participants (77%) who had experienced fatigue. There were no significant differences in demographic and clinical characteristics or levels of impairment between those who fulfilled the narrower definition and those who fulfilled the broader definitions. The only exception was the reported number of days per week that the child was affected by the fatigue. All groups demonstrated evidence of substantial impairment associated with the fatigue. CONCLUSION: Children and adolescents who do not fulfil the current narrow definition of CFS but do suffer from disabling fatigue show comparable and substantial impairment. In primary care settings, a broader definition of disabling fatigue would improve the identification of impaired children and adolescents who require support.
Fremont M, El Bakkouri K, Vaeyens F, Herst CV, De Meirleir K, Englebienne P.	RED Laboratories, Pontbeek 61, B-1731 Zellik, Belgium.	2',5'-Oligoadenylate size is critical to protect RNase L against proteolytic cleavage in chronic fatigue syndrome.	Exp Mol Pathol. 2005 Jun;78(3):239-46. Epub 2005 Mar 2.	A dysregulation in the 2',5'-oligoadenylate (2-5A)-dependent RNase L antiviral pathway has been detected in peripheral blood mononuclear cells (PBMC) of chronic fatigue syndrome (CFS) patients, which is characterized by upregulated 2-5A synthetase and RNase L activities, as well as by the presence of a low molecular weight (LMW) 2-5A-binding protein of 37-kDa related to RNase L. This truncated protein has been shown to originate from proteolytic cleavage of the native 83-kDa RNase L by m-calpain and human leukocyte elastase (HLE). We investigated the possible role of 2-5A oligomers in the proteolytic action toward the endonuclease and show that incubation of CFS PBMC extracts with 2-5A trimer and tetramer, but not with the dimer, results in a significant protection of the native 83-kDa RNase L against cleavage by endogenous and purified proteases. Similar results are obtained with a purified recombinant RNase L. An analysis of the size of 2-5A oligomers produced by the catalytic activity of the 2-5A synthetase present in PBMC extracts further shows that samples containing the 37-kDa RNase L preferentially produce 2-5A dimers instead of higher oligomers. Taken together, our results indicate that homodimerization of RNase L by 2-5A oligomers higher than the dimer prevents its cleavage by proteolytic enzymes. The presence of the truncated 37-kDa RNase L in PBMC extracts is therefore likely to result, not only from the abnormal activation of inflammatory proteases, but also from a dysregulation in 2-5A synthetase induction or activation towards the preferential production of 2-5A dimers.
Fremont M, Vaeyens F, Herst CV, De Meirleir K, Englebienne P, Tiev KP, Cabane J, Lebleu B. HUpenglebi@ulb.ac.beUH**.**		37-Kilodalton/83-Kilodalton RNase L Isoform Ratio in Peripheral Blood Mononuclear Cells: Analytical Performance and Relevance for Chronic Fatigue Syndrome.	Clin Diagn Lab Immunol. 2005 Oct;12(10):1259-60.	
Fremont M, Vaeyens F, Herst CV, De Meirleir K, Englebienne P.		37-Kilodalton/83-kilodalton RNase L isoform ratio in peripheral blood	Clin Diagn Lab Immunol. 2005 Oct;12(10):1259-60; author reply	Comment Letter

		mononuclear cells: analytical performance and relevance for chronic fatigue syndrome.	1260. Comment on: Clin Diagn Lab Immunol. 2003 Mar;10(2):315-6.	
Friedberg F, Leung DW, Quick J.	Department of Psychiatry, Stony Brook University, Stony Brook, New York 11794-8790, USA. HUfred.friedberg@stonybrook.eduUH	Do support groups help people with chronic fatigue syndrome and fibromyalgia? A comparison of active and inactive members.	J Rheumatol. 2005 Dec;32(12):2416-20.	OBJECTIVE: To examine the benefits and problems of a chronic fatigue syndrome (CFS) and fibromyalgia (FM) support organization as reported by its participants. METHODS: Active members (n = 32) and inactive members or dropouts (n = 135) of a regional support organization for people with CFS and FM completed a 26 item questionnaire by telephone interview or by self-completion and postal return. RESULTS: The most frequently endorsed benefits of membership were illness legitimization (67.8%), finding out helpful new information (66.4%), and feeling understood by others (62.2%). Lower frequency endorsements were given to: helped to find (35.0%) or deal with (38.5%) doctors, and helped to improve my illness (36.4%). The most frequently reported reasons for dropping out were inconvenient location (37.8%) or time (37.0%), too much negative talk or complaining (33.3%), too sick to attend (28.8%), and illness or coping improvement (29.6% each). The active-member group showed significantly higher ($p < 0.04$) symptom severity scores and less illness improvement ($p < 0.01$) in comparison to the inactive/dropout group. CONCLUSION: This cross-sectional study suggests that support groups for CFS are viewed as helpful by participants on a number of illness related issues. On the other hand, active members reported greater symptom severity and less illness improvement than inactive members or dropouts.
Fries E, Hesse J, Hellhammer J, Hellhammer DH.	Department for Psychobiology, University of Trier, Johanniterufer 15, 54290 Trier, Germany.	A new view on hypocortisolism.	Psychoneuroendocrinology. 2005 Nov;30(10):1010-6.	Low cortisol levels have been observed in patients with different stress-related disorders such as chronic fatigue syndrome, fibromyalgia, and post-traumatic stress disorder. Data suggest that these disorders are characterized by a symptom triad of enhanced stress sensitivity, pain, and fatigue. This overview will present data on the development, mechanisms and consequences of hypocortisolism on different bodily systems. We propose that the phenomenon of hypocortisolism may occur after a prolonged period of hyperactivity of the hypothalamic-pituitary-adrenal axis due to chronic stress as illustrated in an animal model. Further evidence suggests that despite symptoms such as pain, fatigue and high stress sensitivity, hypocortisolism may also have beneficial effects on the organism. This assumption will be underlined by some studies suggesting protective effects of hypocortisolism for the individual.
Frissora CL, Koch KL.	Department of Medicine, The Weill Medical College of Cornell University, 520 E. 70th Street, Suite J-314, New York, NY 10021, USA. cfrissor@med.corn	Symptom overlap and comorbidity of irritable bowel syndrome with other conditions.	Curr Gastroenterol Rep. 2005 Aug;7(4):264-71.	Irritable bowel syndrome (IBS) is one of several highly prevalent, multi-symptom gastrointestinal motility disorders that have a wide clinical spectrum and are associated with symptoms of gastrointestinal dysmotility and visceral hypersensitivity. Symptom overlap and comorbidity between IBS and other gastrointestinal motility disorders (eg, chronic constipation, functional dyspepsia, gastroesophageal reflux disease), with gastrointestinal disorders that are not related to motility (eg, celiac disease, lactose intolerance), and with somatic conditions (eg, fibromyalgia, chronic fatigue syndrome), are frequent. The clinical associations and pathophysiologic links between IBS and these disorders continue to be explored. This review discusses overlapping symptoms and comorbidity of IBS with select gastrointestinal and non-gastrointestinal disorders and attempts to identify

	ell.edu			commonalities among these conditions.
Furberg H, Olarte M, Afari N, Goldberg J, Buchwald D, Sullivan PF.	Department of Genetics, University of North Carolina, Chapel Hill, NC, USA.	The prevalence of self-reported chronic fatigue in a U.S. twin registry.	J Psychosom Res. 2005 Nov;59(5):283-90.	OBJECTIVE: To investigate the prevalence and correlates of various definitions of self-reported lifetime fatiguing illness in a U.S. twin registry. METHODS: Data from 4591 female and male twins from the population-based Mid-Atlantic Twin Registry were available for this study. Variables representing different definitions of lifetime fatiguing illness and personal characteristics were obtained through questionnaires. Odds ratios and 95% confidence intervals were calculated as measures of association between fatigue and gender. Kaplan-Meier curves were produced to examine the age at onset for lifetime fatiguing illnesses. RESULTS: Prevalences for different definitions of self-reported lifetime fatigue ranged from 36.7% for any fatigue to 2.7% for chronic fatigue syndrome-like illness. Females were two to three times more likely to report fatigue than males. Gender differences increased as fatigue definitions grew more restrictive. Ages at onset of chronic fatiguing illness were significantly earlier and the number of ancillary symptoms was greater for females than males. People with lifetime fatigue had significantly more compromised functional status than people without lifetime fatigue. CONCLUSION: The prevalence of self-reported lifetime fatiguing illness varied widely depending upon how it was defined. Given the debilitating consequences of fatiguing illnesses, the reasons for the female predominance and the earlier onset in women should receive increased research priority.
Gaab J, Rohleder N, Heitz V, Engert V, Schad T, Schurmeyer TH, Ehlert U.	Center for Psychobiological and Psychosomatic Research, University of Trier, Trier, Germany. j.gaab@psychology.unizh.ch	Stress-induced changes in LPS-induced pro-inflammatory cytokine production in chronic fatigue syndrome.	Psychoneuroendocrinology. 2005 Feb;30(2):188-98.	OBJECTIVE: It has been suggested that a hypofunctional hypothalamic-pituitary-adrenal (HPA) axis in chronic fatigue syndrome could result in an exaggerated release of pro-inflammatory cytokines during stress. As pro-inflammatory cytokines are involved in the induction of sickness behavior and thus constitute a potential physiological correlate of stress-induced symptom exacerbation in chronic fatigue syndrome, we set out to evaluate the LPS-induced production of pro-inflammatory cytokines during psychosocial stress in CFS and healthy controls. METHOD: Twenty-one CFS patients and 20 healthy controls matched for age and gender underwent a standardized psychosocial stress test (Trier social stress test, TSST). Adrenocorticotropine hormone (ACTH), salivary cortisol and plasma cortisol levels were measured before and repeatedly following exposure to the stressor. Lipopolysaccharide-stimulated production of interleukin-6 and tumor necrosis factor-alpha were assessed at baseline as well as 10 and 60 min after the stress test. RESULTS: CFS patients showed an inverse stress-induced response pattern of LPS-stimulated cytokines responses in comparison to healthy controls, i.e. stimulated cytokine production decreased shortly after stress in CFS patients, while it increased in controls. Fatigue scores and basal LPS-induced cytokine levels were significantly associated for TNF-alpha in controls and for both cytokines in CFS patients. Stress-induced changes in stimulated cytokine production were not associated with general fatigue scores in the control group, whereas in the CFS group, fatigue scores were significantly correlated with integrated levels of LPS-induced cytokines. However, partial correlations revealed that these results were due to the high correlations with basal LPS-induced cytokine levels. CONCLUSION: CFS patients do not show an exaggerated secretion of LPS-induced cytokines. Although cortisol responses to stress were normal, pro-inflammatory cytokine levels in CFS patients were significantly attenuated. Possible intracellular mechanisms, such as for example an enhanced sensitivity to inhibitory effects of glucocorticoids, a diminished responsivity to catecholaminergic stimulation, and a disruption of intracellular activation are discussed. Basal levels of

				stimulated pro-inflammatory Il-6 levels are generally related to fatigue scores. However, in CFS patients this association is of greater magnitude and can also be observed for TNF-alpha.
Gallagher AM, Coldrick AR, Hedge B, Weir WR, White PD.	Centre for Psychiatry, Institute of Community Health Sciences, Queen Mary School of Medicine and Dentistry, St. Bartholomew's Hospital, EC1A 7BE London, UK.	Is the chronic fatigue syndrome an exercise phobia? A case control study.	J Psychosom Res. 2005 Apr;58(4):367-73.	OBJECTIVE: The aim of this study was to test whether patients with chronic fatigue syndrome (CFS) have an exercise phobia, by measuring anxiety-related physiological and psychological reactions to ordinary activity and exercise. METHODS: Patients and healthy but sedentary controls were assessed over 8 h of an ordinary day, and before, during and after an incremental exercise test on a motorised treadmill. To avoid confounding effects, those with a comorbid psychiatric disorder were excluded. Heart rate, galvanic skin resistance (GSR) and the amount of activity undertaken were measured, along with state and trait measures of anxiety. RESULTS: Patients with CFS were more fatigued and sleep disturbed than were the controls and noted greater effort during the exercise test. No statistically significant differences were found in either heart rate or GSR both during a normal day and before, during and after the exercise test. Patients with CFS were more symptomatically anxious at all times, but this did not increase with exercise. CONCLUSION: The data suggest that CFS patients without a comorbid psychiatric disorder do not have an exercise phobia.
Garralda ME, Rangel L.	Academic Unit of Child and Adolescent Psychiatry, Faculty of Medicine, Imperial College London, St Mary's Campus, Norfolk Place, London W2 1PG, UK. HUe.garralda@imperial.ac.ukUH	Chronic fatigue syndrome of childhood. Comparative study with emotional disorders.	Eur Child Adolesc Psychiatry. 2005 Dec;14(8):424-30.	OBJECTIVE: To examine clinical specificity in chronic fatigue syndrome (CFS) of childhood, by comparing clinical features in childhood CFS and in emotional disorders (ED). METHOD SAMPLE: 28 children with CFS; 27 with ED. MEASURES: History of disorder; K-SADS psychiatric interviews; self-esteem and physical symptoms questionnaires; premorbid history, behavioural and personality assessments. RESULTS: There were high levels of comorbid emotional disorders in children with CFS, and the two groups were comparable on self-esteem, but CFS children endorsed more fatigue and other somatic symptoms. The two groups were comparable on age at illness onset, but parents of children with CSF reported more biological illness precipitants, more pre-morbid recurrent medical problems and infections. The CFS group had fewer pre-morbid psychological problems and less psychiatric comorbidity than the ED group. CONCLUSION: There is considerable clinical overlap between CFS and ED of childhood, but there are also differences in clinical presentation between these disorders.
Glaser R, Padgett DA, Litsky ML, Baiocchi RA, Yang EV, Chen M, Yeh PE, Klimas NG, Marshall GD, Whiteside T, Herberman R, Kiecolt-Glaser J, Williams MV.	Department of Molecular Virology, Immunology and Medical Genetics, The Ohio State University Medical Center, 333 W. 10th Avenue, Columbus, OH 43210, USA. glaser.1@osu.edu	Stress-associated changes in the steady-state expression of latent Epstein-Barr virus: implications for chronic fatigue syndrome and cancer.	Brain Behav Immun. 2005 Mar;19(2):91-103.	Antibodies to several Epstein-Barr virus (EBV)-encoded enzymes are observed in patients with different EBV-associated diseases. The reason for these antibody patterns and the role these proteins might play in the pathophysiology of disease, separate from their role in virus replication, is unknown. In this series of studies, we found that purified EBV deoxyuridine triphosphate nucleotidohydrolase (dUTPase) can inhibit the replication of human peripheral blood mononuclear cells in vitro and upregulate the production of TNF-alpha, IL-1beta, IL-6, IL-8, and IL-10. It also enhanced the ability of natural killer cells to lyse target cells. The EBV dUTPase also significantly inhibited the replication of mitogen-stimulated lymphocytes and the synthesis of IFN-gamma by cells isolated from lymph nodes and spleens obtained from mice inoculated with the protein. It also produced sickness behaviors known to be induced by some of the cytokines that were studied in the in vitro experiments. These symptoms include an increase in body temperature, a decrease in body mass and in physical activity. The data provide a new perspective on how an early nonstructural EBV-encoded protein can cause immune dysregulation and produce clinical symptoms observed in patients with chronic fatigue syndrome (CFS) separate from its role in virus replication and may serve as a new approach to help

				identify one of the etiological agents for CFS. The data also provide additional insight into the pathophysiology of EBV infection, inflammation, and cancer.
Glozier N.	Department of Occupational Health and Safety, Kings College Hospital, Denmark Hill, London SE5 9RS, UK. n.glozier@iop.kcl.ac.uk	Chronic fatigue syndrome: it's tiring not knowing much--an in-depth review for occupational health professionals.	Occup Med (Lond). 2005 Jan;55(1):10-2.	
Godas Sieso T, Gomez-Gil E, Fernandez-Sola J, Fernandez-Huertas JM.		[Significant increase of functional status and decrease of fatigue in patients with chronic fatigue syndrome after completing cognitive behavioural group therapy] [Article in Spanish]	Med Clin (Barc). 2005 Oct 22;125(14):556.	Letter
Gottschalk M, Kumpfel T, Flachenecker P, Uhr M, Trenkwalder C, Holsboer F, Weber F.	Max Planck Institute of Psychiatry, Munich, Germany.	Fatigue and regulation of the hypothalamo-pituitary-adrenal axis in multiple sclerosis.	Arch Neurol. 2005 Feb;62(2):277-80.	BACKGROUND: Fatigue is a common and disabling symptom in patients with multiple sclerosis (MS). Underlying mechanisms postulated so far have involved localization of brain lesions and abnormalities of the neuroendocrine system and cytokine regulation. OBJECTIVE: To investigate the relationship between fatigue and the hypothalamo-pituitary-adrenal (HPA) axis in patients with MS. DESIGN: A prospective survey. SETTING: Outpatient and inpatient study at the Max Planck Institute of Psychiatry, Munich, Germany. PATIENTS: Thirty-one patients with clinically definite MS, a relapsing-remitting disease course, and without MS-specific treatment. INTERVENTIONS: Assessment of fatigue with 3 questionnaires: the Fatigue Severity Scale (FSS), the Modified Fatigue Impact Scale (MFIS), and the Visual Analog Scale. Assessment of HPA axis regulation with the combined dexamethasone-corticotropin releasing hormone (Dex-CRH) test. RESULTS: The FSS score was significantly correlated with the MFIS score. Patients with fatigue had significantly elevated adrenocorticotropin (ACTH) levels in the combined Dex-CRH test. CONCLUSIONS: In contrast to results for chronic fatigue syndrome, where a hyporeactivity of the HPA axis has been shown, MS patients with fatigue exhibited a higher activity of the HPA axis than those without fatigue, as evidenced by significantly increased ACTH concentrations. Proinflammatory cytokines, known to be elevated in patients with MS, may cause both HPA axis alterations and fatigue.
Goudsmit E,		Chronic Fatigue	Journal of Chronic	A literature search identified all papers published on chronic fatigue syndrome (CFS) and myalgic

Stouten B		Syndrome: Editorial Bias in the British Medical Journal	Fatigue Syndrome 2005 12 (4): 47-59	encephalomyelitis (ME) in the British Medical Journal between 1995 and 2000. Analysis of the findings revealed a bias towards the views of one school of thought and a lack of papers on the immunological or virological aspects of CFS. This contrasts with the mainstream American journals, which generally covered a much wider range of subjects and views. We examine the arguments for and against covert editorial policies, and summarise the results of discussions with the relevant individuals and organisations.
Grans H, Nilsson P, Evengard B.		Gene expression profiling in the chronic fatigue syndrome.	J Intern Med. 2005 Oct;258(4):388-90.	Letter
Grans H, Nilsson P, Evengard B.		Gene expression profiling in the chronic fatigue syndrome.	J Intern Med. 2005 Oct;258(4):388-90.	Letter
Gutenbrunner C, Linden M, Gerdes N, Ehlebracht-Konig I, Grosch E.	Klinik fur Physikalische Medizin und Rehabilitation der Medizinischen Hochschule Hannover, Carl-Neuberg-Strasse 1, 30625 Hannover, Germany. gutenbrunner.christoph@mh-hannover.de	[Significance of the chronic fatigue syndrome in rehabilitation medicine--status and perspectives] [Article in German]	Rehabilitation (Stuttg). 2005 Jun;44(3):176-85.	It appears that from a clinical point of view chronic exhaustion or fatigue is an important factor in rehabilitation. This is, however, first of all a phenomenon that can be described as a function in accordance with the International Classification of Functioning, Disability and Health (JCF), caused by chronic illnesses or chronic excessive stress. The clinical and sociomedical ranking of chronic fatigue or exhaustion in respect of rehabilitation was discussed in the framework of a Workshop at the 12th Rehabilitation Science Colloquium, 2003 from the viewpoints of psychiatric rehabilitation, methodology, sociology and practical rehabilitation, and conclusions for future research were drawn. The definition of chronic fatigue is first of all mainly based on the feeling of chronic tiredness but also on phenomena of disturbed concentration, physical discomfort, headache and disorders of "drive" and mood. A psychiatric diagnosis linked with symptoms of chronic fatigue is neurasthenia, which is arrived at according to precisely defined criteria. Depressive disorder is one of the most important differential diagnoses in this sphere. Examinations by general practitioners revealed that about 90 % of the patients who had been diagnosed as suffering from psychovegetative disorders completely agreed with the diagnosis of neurasthenia. Neurasthenia resulted more often in work disability periods than disorders of somatisation and other psychosomatic diagnoses. Basing on the "IRES" scale "vital exhaustion", singular of even serious changes become evident in about 50 % to 90 % of the patients undergoing rehabilitation, depending on their individual range of indications. As was to be expected, the majority of pathologic findings concerns patients undergoing psychosomatic rehabilitation, since in such cases there is an overlapping with symptoms of psychosomatic diseases. It is, however, remarkable that also in somatically oriented orthopaedic rehabilitation symptoms of fatigue are seen in up to 50 % of the patients. Preliminary studies have shown that these symptoms can be definitely ameliorated within the rehabilitation framework, although pathological signs are still abundantly apparent in follow-up examinations. Markedly severe degrees of "vital exhaustion" and "vocational exhaustion" are also seen in rheumatology patients undergoing somatic rehabilitation. This agrees with case history details related by many female and male patients. Hence, it appears necessary to adapt rehabilitative intervention to both the psychovegetative and the medical

				behavioural aspects of this symptom. Scientific classification of the entire sphere of chronic fatigue in respect of rehabilitation requires classification of the relevant functions within the ICF framework. To this end it would be necessary to conduct patient inquiries within cross-sectional studies on the one hand and, on the other, a systematic consensus process among experts would have to be used for allocation to the relevant functions. This is the basis for development of suitable assessment tools for use in prospective studies in order to systematically evaluate the impact on functions and especially their effects on activities and participation.
Haines LC, Saidi G, Cooke RW.	Royal College of Paediatrics and Child Health, 50 Hallam Street, London W1W 6DE, UK. Linda.haines@rcpch.ac.uk	Prevalence of severe fatigue in primary care.	Arch Dis Child. 2005 Apr;90(4):367-8.	A postal survey of 1024 UK GP practices showed the prevalence of medically unexplained severe fatigue over three months in 5-19 year olds to be 62/100,000. Cases were predominantly adolescent girls and were more likely to come from practices in less deprived areas, which could reflect consulting behaviours.
Hamilton WT, Gallagher AM, Thomas JM, White PD.	The Grange, Bristol BS8 1AU, UK. w.hamilton@bristol.ac.uk	The prognosis of different fatigue diagnostic labels: a longitudinal survey.	Fam Pract. 2005 Aug;22(4):383-8. Epub 2005 Apr 1.	BACKGROUND: Several different diagnostic labels exist for the fatigue syndromes, including chronic fatigue syndrome (CFS), myalgic encephalomyelitis (ME) and postviral fatigue syndrome (PVFS). An allied condition is fibromyalgia. No study has examined prognostic differences across these different labels. OBJECTIVE: To compare the prognoses of patients labelled with different fatigue syndromes in primary care. METHODS: We performed a longitudinal survey, using electronic records from the General Practice Research Database. All 18,122 patients diagnosed by their GP with a fatigue syndrome from 1988-2001 with a minimum of one year of records after diagnosis were collated into four groups: CFS, ME, PVFS and fibromyalgia. CFS and ME were combined for the main analysis as no code for CFS was available until 1995. The length of illness was calculated as the interval between the diagnosis and the last recorded fatigue symptom, expressed as days per year, to account for differing lengths of record after diagnosis. RESULTS: Patients with CFS/ME combined had a worse prognosis (median length of illness 80 days per year; interquartile range 0-242) than fibromyalgia (51;0-244) or PVFS 0 (0-108), a significant difference, $P < 0.001$. In a subgroup analysis, ME had a worse prognosis (median length of illness in days per year 106; interquartile range 0-259) than CFS (33; 0-170), $P < 0.001$, in spite of a better course before diagnosis. Secondary outcome measures were consistent with these results. CONCLUSION: There were important differences in outcome between the various fatigue labels, with ME having the worst prognosis and PVFS the best. This could be an adverse effect of the label ME itself. Alternatively, patients who are destined to have a worse prognosis may preferentially attract the ME label. Our data support the first interpretation.
Henderson M, Tannock C.	Academic Department of Psychological Medicine, GKT School of Medicine and Institute of	Use of depression rating scales in chronic fatigue syndrome.	J Psychosom Res. 2005 Sep;59(3):181-4.	OBJECTIVE: The aim of this study was to examine the performance of three commonly used depression rating scales in a hospital sample of patients with chronic fatigue syndrome (CFS). METHODS: Sixty-one patients with CDC criteria for CFS completed the General Health Questionnaire (GHQ), the Hamilton Depression Scale (HAM-D) and the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D). Current psychiatric status was assessed using the Structured Clinical Interview for DSM-III-R. DISORDERS: Patient version (SCID-P). Receiver operating curves were drawn

	Psychiatry, Weston Education Centre, Cutcombe Road, London SE5 9RJ, United Kingdom.			for each of the depression rating scales. RESULTS: Thirty-one percent of the patients were depressed according to the SCID-P. Using the standard cut-offs, both GHQ and HAM-D overestimated the number of depressed patients, whilst the HADS-D underestimated the number. The receiver operating curves suggest that the optimum cut-offs for GHQ, HAM-D and HADS-D in this population are 7/8, 13/14 and 8/9, respectively. CONCLUSIONS: Standard cutoffs may not be appropriate when using depression rating scales in CFS patients in a tertiary care setting.
Hershfield NB.	Division of Gastroenterology, Department of Medicine, University of Calgary, Calgary, Alberta. gutdoc1@shaw.ca	Nongastrointestinal symptoms of irritable bowel syndrome: an office-based clinical survey.	Can J Gastroenterol. 2005 Apr;19(4):231-4.	Irritable bowel syndrome (IBS) is the most prevalent gastrointestinal problem faced by practicing gastroenterologists. For many years, nongastrointestinal symptoms have been documented in IBS patients, but the medical literature does not emphasize them. The present study explored how IBS and inflammatory bowel disease patients differ in their reporting of nongastrointestinal symptoms. Information from 200 consecutive patients with IBS and a similar number of patients with Crohn's disease (in a single gastroenterology practice) was obtained at the initial visit using a simple questionnaire. Comparison of the data revealed that IBS patients describe certain nongastrointestinal symptoms far more frequently than do those with inflammatory bowel disease. It is recommended that these symptoms be considered along with the generally accepted criteria for making a positive diagnosis of IBS.
Hutchings A, Raine R, Sanderson C, Black N.	Health Services Research Unit, London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK. andrew.hutchings@lshtm.ac.uk	An experimental study of determinants of the extent of disagreement within clinical guideline development groups.	Qual Saf Health Care. 2005 Aug;14(4):240-5.	OBJECTIVE: To assess the effect of design features and clinical and social cues on the extent of disagreement among participants in a formal consensus development process. METHODS: Factorial design involving 16 groups consisting of 135 general practitioners (GPs) and 42 mental health professionals from England. The groups rated the appropriateness of four mental health interventions for three conditions (chronic back pain, irritable bowel syndrome, and chronic fatigue syndrome) in the context of various clinical and social cues. The groups differed in three design features: provision of a systematic literature review (versus not provided), group composition (mixed versus GP only), and assumptions about the healthcare resources available (realistic versus idealistic). Disagreement was measured using the mean absolute deviation from a group's median rating for a scenario. RESULTS: None of the design features significantly affected the extent of disagreement within groups (all $p>0.3$). Disagreement did differ between treatments (closer consensus for cognitive behavioural therapy and behavioural therapy than for brief psychodynamic intervention therapy and antidepressants) and cues (closer consensus for depressed patients and patients willing to try any treatment). CONCLUSION: In terms of the extent of disagreement in the groups in this study, formal consensus development was a robust technique in that the results were not dependent on the way it was conducted.
Hvenegaard V.		[Chronic fatigue syndrome, an acknowledged neurologic diagnosis] [Article in Danish]	Ugeskr Laeger. 2005 Feb 14;167(7):784-5.	Letter
Inder WJ, Prickett TC, Mulder RT.	Department of Endocrinology, Christchurch	Normal opioid tone and hypothalamic-	Clin Endocrinol (Oxf). 2005 Mar;62(3):343-8.	OBJECTIVE: To determine whether the functional impairment seen in chronic fatigue syndrome (CFS) is associated with reduced levels of central opioids and/or deficiency of the hypothalamic-pituitary-adrenal (HPA) axis. DESIGN: Single-blinded case-control study measuring functional and psychological

	Hospital, and Department of Psychological Medicine, Christchurch School of Medicine, Christchurch, New Zealand. winder@medstv.unimelb.edu.au	pituitary-adrenal axis function in chronic fatigue syndrome despite marked functional impairment.		status, basal hormonal parameters and ACTH/cortisol response to naloxone and ovine corticotrophin-releasing hormone (oCRH) vs. placebo in people with CFS and healthy controls. PATIENTS: Twelve people with CFS and 11 age-matched controls. MEASUREMENTS: Hormonal parameters: basal levels of 09:00 h plasma cortisol, dehydroepiandrosterone sulfate (DHEAS) and IGF-1. 24-h urinary free cortisol. Plasma ACTH and cortisol response to naloxone 125 microg/kg, oCRH 1 microg/kg and placebo (normal saline). Psychological parameters: SF-36, Hamilton Depression Score, Hospital Anxiety and Depression Scale and Fatigue Scale. RESULTS: There were highly significant differences between the CFS subjects and the controls with respect to the measures of fatigue and physical functioning. However, there were no differences in basal levels of 09:00 h cortisol (367 +/- 37 vs. 331 +/- 39 nmol/l, P = 0.51), DHEAS (4.2 +/- 0.6 vs. 4.0 +/- 0.5 micromol/l, P = 0.81), 24-h urinary free cortisol (182 +/- 27 vs. 178 +/- 21 nmol/24 h, P = 0.91) or IGF-1 (145 +/- 19 vs. 130 +/- 11 microg/l, P = 0.52) between the CFS group and controls, respectively. There was also no difference between the groups with respect to the ACTH and cortisol response to either oCRH or naloxone. CONCLUSIONS: Our data do not support an aetiological role for deficiency in central opioids or the HPA axis in the symptoms of CFS.
Iwakami E, Arashima Y, Kato K, Komiya T, Matsukawa Y, Ikeda T, Arakawa Y, Oshida S.	Department of Legal Medicine, Nihon University School of Medicine, Tokyo, Japan.	Treatment of chronic fatigue syndrome with antibiotics: pilot study assessing the involvement of Coxiella burnetii infection.	Intern Med. 2005 Dec;44(12):1258-63.	OBJECTIVE: To examine whether Coxiella burnetii (C. burnetii) is involved in chronic fatigue syndrome (CFS), we administered tetracycline antibiotics to subjects with CFS, and followed changes in clinical symptoms, PCR findings, and C. burnetii antibody titers. PATIENTS AND METHODS: The subjects were 8 patients with CFS and 213 with nonspecific complaints such as chronic fatigue and low-grade fever for several months or longer but not meeting the diagnostic criteria for CFS. All were examined for C. burnetii infection by nested PCR and the indirect immunofluorescence test (IF). RESULTS: Four CFS patients (the CFS group) and 54 controls [the post-Q fever fatigue syndrome (QFS) group] positive for C. burnetii were treated mainly with minocycline or doxycycline (100 mg/day) for 3 months. After treatment, all 58 patients tested negative for C. burnetii infection. In the CFS group, no significant difference was noted between the mean pre- and post-treatment temperatures or headache scores. Similarly, there was no significant improvement in performance status (PS) scores. In the QFS group, however, mean temperatures and headache scores were significantly decreased after treatment ($p<0.001$). PS scores were also improved. CONCLUSION: These results suggest the possibility of direct involvement of C. burnetii in the pathological state of CFS to be low, despite the C. burnetii infection rate being high in CFS patients. This is a pilot study and further larger investigations are necessary to confirm our preliminary results.
J R Soc Med. 2004 Dec;97(12):571-5.	Berger E.	Brain imaging in fatigue syndromes. Comment on:	J R Soc Med. 2005 Mar;98(3):135.	Letter
Jammes Y, Steinberg JG, Mambrini O, Bregeon F, Delliaux S.	Laboratoire de Physiopathologie Respiratoire (UPRES EA 2201), Faculte de Medecine, Institut Federatif de	Chronic fatigue syndrome: assessment of increased oxidative stress and altered muscle excitability in response to	J Intern Med. 2005 Mar;257(3):299-310.	OBJECTIVES: Because the muscle response to incremental exercise is not well documented in patients suffering from chronic fatigue syndrome (CFS), we combined electrophysiological (compound-evoked muscle action potential, M wave), and biochemical (lactic acid production, oxidative stress) measurements to assess any muscle dysfunction in response to a routine cycling exercise. DESIGN: This case-control study compared 15 CFS patients to a gender-, age- and weight-matched control group (n=11) of healthy subjects. INTERVENTIONS: All subjects performed an incremental cycling exercise continued until exhaustion. MAIN OUTCOME MEASURES: We measured the oxygen uptake

	Recherche Jean Roche, Marseille, France. jammes.y@jean-roche.univ-mrs.fr	incremental exercise.		(VO2), heart rate (HR), systemic blood pressure, percutaneous O2 saturation (SpO2), M-wave recording from vastus lateralis, and venous blood sampling allowing measurements of pH (pHv), PO2 (PvO2), lactic acid (LA), and three markers of the oxidative stress (thiobarbituric acid-reactive substances, TBARS, reduced glutathione, GSH, and ascorbic acid, RAA). RESULTS: Compared with control, in CFS patients (i) the slope of VO2 versus work load relationship did not differ from control subjects and there was a tendency for an accentuated PvO2 fall at the same exercise intensity, indicating an increased oxygen uptake by the exercising muscles; (ii) the HR and blood pressure responses to exercise did not vary; (iii) the anaerobic pathways were not accentuated; (iv) the exercise-induced oxidative stress was enhanced with early changes in TBARS and RAA and enhanced maximal RAA consumption; and (v) the M-wave duration markedly increased during the recovery period. CONCLUSIONS: The response of CFS patients to incremental exercise associates a lengthened and accentuated oxidative stress together with marked alterations of the muscle membrane excitability. These two objective signs of muscle dysfunction are sufficient to explain muscle pain and postexertional malaise reported by our patients.
Jason LA, Corradi K, Torres-Harding S, Taylor RR, King C.	DePaul University, Chicago, Illinois 60614, USA. ljason@depaul.edu	Chronic fatigue syndrome: the need for subtypes.	Neuropsychol Rev. 2005 Mar;15(1):29-58.	Chronic fatigue syndrome (CFS) is an important condition confronting patients, clinicians, and researchers. This article provides information concerning the need for appropriate diagnosis of CFS subtypes. We first review findings suggesting that CFS is best conceptualized as a separate diagnostic entity rather than as part of a unitary model of functional somatic distress. Next, research involving the case definitions of CFS is reviewed. Findings suggest that whether a broad or more conservative case definition is employed, and whether clinic or community samples are recruited, these decisions will have a major influence in the types of patients selected. Review of further findings suggests that subtyping individuals with CFS on sociodemographic, functional disability, viral, immune, neuroendocrine, neurology, autonomic, and genetic biomarkers can provide clarification for researchers and clinicians who encounter CFS' characteristically confusing heterogeneous symptom profiles. Treatment studies that incorporate subtypes might be particularly helpful in better understanding the pathophysiology of CFS. This review suggests that there is a need for greater diagnostic clarity, and this might be accomplished by subgroups that integrate multiple variables including those in cognitive, emotional, and biological domains.
Jerjes WK, Cleare AJ, Wessely S, Wood PJ, Taylor NF.	Department of Clinical Biochemistry, King's College Hospital, Denmark Hill, London SE5 9RX, United Kingdom. w_jerjes@yahoo.co.uk	Diurnal patterns of salivary cortisol and cortisone output in chronic fatigue syndrome.	J Affect Disord. 2005 Aug;87(2-3):299-304.	BACKGROUND: The aim of the present study was to obtain a naturalistic measure of diurnal hypothalamic-pituitary-adrenal (HPA) axis output in CFS patients unaffected by medication or comorbid psychiatric disorder likely to influence the axis. METHOD: Cortisol and cortisone levels were measured in saliva samples collected from 0600 h to 2100 h at 3-h intervals in CFS patients and healthy controls. RESULTS: Mean cortisol and cortisone concentrations were significantly lower in patients than controls across the whole day, as were levels at each individual time point except 2100 h. Cosinor analysis showed a significant diurnal rhythm of cortisol and cortisone that was not phase-shifted in CFS compared to controls. However, there was a lower rhythm-adjusted mean and a lower amplitude in CFS patients. The cortisol/cortisone ratio showed no diurnal rhythm and did not differ between CFS subjects and controls. LIMITATIONS: The sample size was relatively small, and drawn from specialist referral patients who had been ill for some time; generalisation of these results to other populations is therefore unwarranted. CONCLUSION: The main findings of this study are to

				provide further evidence for reduced basal HPA axis function in at least some patients with CFS and to show for the first time that salivary cortisone is also reduced in CFS and has a diurnal rhythm similar to that of cortisol. We have also demonstrated that the cortisol/cortisone ratio remains unchanged in CFS, suggesting that increased conversion of cortisol to cortisone cannot account for the observed lowering of salivary cortisol.
Jones JF, Kulkarni PS, Butera ST, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. jaj9@cdc.gov	GB virus-C--a virus without a disease: we cannot give it chronic fatigue syndrome.	BMC Infect Dis. 2005 Sep 28;5:78.	BACKGROUND: Chronic fatigue syndrome (CFS) is an illness in search of an infectious etiology. GB virus-C (GBV-C) virus is a flavivirus with cell tropism and host defense induction qualities compatible with a role in producing the syndrome. The GBV-C genome is detectable in 4% of the population and 12% of the population is seropositive. The present study evaluated the association between infection with GBV and CFS. METHODS: We used a commercial EIA to detect antibodies against the GBV-C E2 protein and a quantitative real-time RT-PCR assay to detect active GBV-C infection. Sera were from a case control study of CFS in Atlanta, Georgia. The Fisher's exact two-tailed test was used for statistical analysis. RESULTS: Two of 12 CFS patients and one of 21 controls were seropositive for prior GBV-C infection and one control had viral RNA detected, indicating active infection. The results are not statistically different. CONCLUSION: We found no evidence that active or past infection with GBV is associated with CFS.
Jones JF, Nicholson A, Nisenbaum R, Papanicolaou DA, Solomon L, Boneva R, Heim C, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Ga 30333, USA. HUjaj9@cdc.govUH	Orthostatic instability in a population-based study of chronic fatigue syndrome.	Am J Med. 2005 Dec;118(12):1415.	PURPOSE: Autonomic nervous system dysfunction has been suggested as involved in the pathophysiology of chronic fatigue syndrome. This population-based case control study addressed the potential association between orthostatic instability (one sign of dysautonomia) and chronic fatigue syndrome. SUBJECTS AND METHODS: Fifty-eight subjects who fulfilled criteria of the 1994 chronic fatigue syndrome research case definition and 55 healthy controls participated in a 2-day inpatient evaluation. Subjects had been identified during a 4-year population-based chronic fatigue syndrome surveillance study in Wichita, Kan. The present study evaluated subjects' current medical and psychiatric status, reviewed past medical/psychiatric history and medication use, used a stand-up test to screen for orthostatic instability, and conducted a head-up tilt table test to diagnose orthostatic instability. RESULTS: No one manifested orthostatic instability in the stand-up test. The head-up tilt test elicited orthostatic instability in 30% of eligible chronic fatigue syndrome subjects (all with postural orthostatic tachycardia) and 48% of controls (50% with neurally mediated hypotension); intolerance was present in only nonfatigued (n=7) subjects. Neither fatigue nor illness severity were associated with outcome. CONCLUSIONS: Orthostatic instability was similar in persons with chronic fatigue syndrome and nonfatigued controls subjects recruited from the general Wichita population. Delayed responses to head-up tilt tests were common and may reflect hydration status. These findings suggest reappraisal of primary dysautonomia as a factor in the pathogenesis of chronic fatigue syndrome.
Jones MG, Cooper E, Amjad S, Goodwin CS, Barron JL, Chalmers RA.	St George's Hospital Medical School, Cranmer Terrace, London, SW17 0RE, UK.	Urinary and plasma organic acids and amino acids in chronic fatigue syndrome.	Clin Chim Acta. 2005 Nov;361(1-2):150-8.	Previous work by others have suggested the occurrence of one or more chemical or metabolic 'markers' for ME/CFS including specific amino acids and organic acids and a number of unidentified compounds (CFSUM1, CFSUM2). We have shown elsewhere that CFSUM1 is partially derivatised pyroglutamic acid and CFSUM2 partially derivatised serine and have suggested and demonstrated that the analytical methods used were unsuitable to identify or to accurately quantify urinary metabolites. We have now made a detailed analysis of plasma and urinary amino acids and of urinary organic acids

				from patients with ME/CFS and from three control groups. Fasting blood plasma and timed urine samples were obtained from 31 patients with CFS, 31 age and sex-matched healthy controls, 15 patients with depression and 22 patients with rheumatoid arthritis. Plasma and urinary amino acids and urinary organic acids were determined using established and validated methods and data compared by statistical analysis. None of the previously reported abnormalities in urinary amino acids or of organic acids could be confirmed. Results however provide some evidence in patients with ME/CFS for underlying inflammatory disease and for reduced intramuscular collagen with a lowered threshold for muscle micro-injury. These factors in combination may provide a basis for the fatigue and muscle pain that are the major symptoms in these patients.
Jones MG, Goodwin CS, Amjad S, Chalmers RA.	St. George's Hospital Medical School, Cranmer Terrace, London, SW17 0RE, UK.	Plasma and urinary carnitine and acylcarnitines in chronic fatigue syndrome.	Clin Chim Acta. 2005 Oct;360(1-2):173-7.	Contradictory reports have suggested that serum free carnitine and acylcarnitine concentrations are decreased in patients with chronic fatigue syndrome (CFS) and that this is a cause of the muscle fatigue observed in these patients. Others have shown normal serum free carnitine and acylcarnitines in similar patients. We report here studies on free, total and esterified (acyl) carnitines in urine and blood plasma from UK patients with CFS and three control groups. Plasma and timed urine samples were obtained from 31 patients with CFS, 31 healthy controls, 15 patients with depression and 22 patients with rheumatoid arthritis. Samples were analysed using an established radioenzymatic procedure for total, free and esterified (acyl) carnitine. There were no significant differences in plasma or urinary total, free or esterified (acyl) carnitine between UK patients with CFS and the control groups or in renal excretion rates of these compounds. The data presented here show that, in the CFS patients studied, there are no significant abnormalities of free or esterified (acyl) carnitine. It is thus unlikely that abnormalities in carnitine homeostasis have any significant role in the aetiology of their chronic fatigue.
Jones MG, Goodwin CS, Amjad S, Chalmers RA.	St. George's Hospital Medical School, Cranmer Terrace, London, SW17 0RE, UK.	Plasma and urinary carnitine and acylcarnitines in chronic fatigue syndrome.	Clin Chim Acta. 2005 Oct;360(1-2):173-7.	Contradictory reports have suggested that serum free carnitine and acylcarnitine concentrations are decreased in patients with chronic fatigue syndrome (CFS) and that this is a cause of the muscle fatigue observed in these patients. Others have shown normal serum free carnitine and acylcarnitines in similar patients. We report here studies on free, total and esterified (acyl) carnitines in urine and blood plasma from UK patients with CFS and three control groups. Plasma and timed urine samples were obtained from 31 patients with CFS, 31 healthy controls, 15 patients with depression and 22 patients with rheumatoid arthritis. Samples were analysed using an established radioenzymatic procedure for total, free and esterified (acyl) carnitine. There were no significant differences in plasma or urinary total, free or esterified (acyl) carnitine between UK patients with CFS and the control groups or in renal excretion rates of these compounds. The data presented here show that, in the CFS patients studied, there are no significant abnormalities of free or esterified (acyl) carnitine. It is thus unlikely that abnormalities in carnitine homeostasis have any significant role in the aetiology of their chronic fatigue.
Karmisholt K, Gotzsche PC.	Nordic Cochrane Centre, H:S Rigshospitalet, DK-2100 Kobenhavn O, Denmark.	Physical activity for secondary prevention of disease. Systematic reviews	Dan Med Bull. 2005 May;52(2):90-4.	BACKGROUND: Physical activity is recommended for secondary prevention of several diseases but it is not always clear how reliable the evidence is. METHODS: We searched MEDLINE and The Cochrane Library for systematic reviews of randomised clinical trials published 1998-2004. RESULTS: We identified 30 eligible systematic reviews and excluded 13 that contained trials covered in larger reviews or were older than other reviews on the same subject. Physical activity decreased all-cause

		of randomised clinical trials.		mortality in patients with coronary heart disease, odds ratio 0.73 (95% confidence interval 0.54 to 0.98), increased maximum walking time in patients with intermittent claudication by 6.5 min (4.4 to 8.7), and decreased pain in patients with osteoarthritis of the knee, standardised mean difference 0.34 (0.24 to 0.44). There were positive effects also in heart failure, chronic obstructive lung disease, type 2 diabetes and fibromyalgia, but they need confirmation in high-quality trials. Exercise improved quality of life in several conditions and generally led to improved physical performance. An effect was not shown in stroke, asthma, rheumatoid arthritis, acute or chronic low back pain, chronic fatigue syndrome, depression, cystic fibrosis or HIV/AIDS. The occurrence of harms was generally not reported. CONCLUSION: Physical activity can have important, and even life-saving, effects as secondary prevention of disease, but more and better trials are needed to fully assess its benefits and harms, in particular trials that compare exercise with drugs.
Kaushik N, Fear D, Richards SC, McDermott CR, Nuwaysir EF, Kellam P, Harrison TJ, Wilkinson RJ, Tyrrell DA, Holgate ST, Kerr JR.	Department of Paediatric Infectious Diseases, St Marys Campus, Imperial College, Norfolk Place, London W2 1PG, UK.	Gene expression in peripheral blood mononuclear cells from patients with chronic fatigue syndrome.	J Clin Pathol. 2005 Aug;58(8):826-32.	BACKGROUND: Chronic fatigue syndrome (CFS) is a multisystem disease, the pathogenesis of which remains undetermined. AIMS: To test the hypothesis that there are reproducible abnormalities of gene expression in patients with CFS compared with normal healthy persons. METHODS: To gain further insight into the pathogenesis of this disease, gene expression was analysed in peripheral blood mononuclear cells from 25 patients with CFS diagnosed according to the Centers for Disease Control criteria and 25 normal blood donors matched for age, sex, and geographical location, using a single colour microarray representing 9522 human genes. After normalisation, average difference values for each gene were compared between test and control groups using a cutoff fold difference of expression > or = 1.5 and a p value of 0.001. Genes showing differential expression were further analysed using Taqman real time polymerase chain reaction (PCR) in fresh samples. RESULTS: Analysis of microarray data revealed differential expression of 35 genes. Real time PCR confirmed differential expression in the same direction as array results for 16 of these genes, 15 of which were upregulated (ABCD4, PRKCL1, MRPL23, CD2BP2, GSN, NTE, POLR2G, PEX16, EIF2B4, EIF4G1, ANAPC11, PDCD2, KHSRP, BRMS1, and GABARAPL1) and one of which was downregulated (IL-10RA). This profile suggests T cell activation and perturbation of neuronal and mitochondrial function. Upregulation of neuropathy target esterase and eukaryotic translation initiation factor 4G1 may suggest links with organophosphate exposure and virus infection, respectively. CONCLUSION: These results suggest that patients with CFS have reproducible alterations in gene regulation.
Kazar J.	Research Base of the Slovak Medical University, Bratislava, Slovak Republic. HUjan.kazar@szu.skUH.	Coxiella burnetii Infection.	Ann N Y Acad Sci. 2005 Dec;1063:105-14.	Coxiella burnetii is an obligate intracellular bacterium that causes a worldwide zoonosis, Q fever, and can be misused as a biological warfare agent. Infection in animals (coxiellosis) is mostly persistent. Infection in humans is often asymptomatic, but it can manifest as an acute disease (usually a self-limited flu-like illness, pneumonia, or hepatitis) or as a chronic form (mainly endocarditis, but also hepatitis and chronic fatigue syndrome). C. burnetii infection in pregnant women may result in abortions, premature deliveries, and stillbirths. Infection in nature is maintained and transmitted by ticks as the principal vector and reservoir. Cattle, sheep, and goats are the most important source of human infections. Humans contract C. burnetii infection mostly by aerosol in contact with contaminated environs, wind playing an important factor in spreading the infection. The wide distribution of C. burnetii contributes to a high resistance of its extracellular small cell variant to environmental conditions. Its intracellular large cell variant, adapted to survive under harsh conditions

				of phagolysosomes, enables long-term survival and persistence of C. burnetii, namely in monocytes/macrophages. Host factors such as underlying disease and cell-mediated immunity play a decisive role in the clinical expression of C. burnetii infection. Complete genome analysis of C. burnetii will certainly contribute to better understanding of the pathogenesis of C. burnetii infection and will improve Q fever diagnosis and immunoprophylaxis.
Kennedy G, Spence VA, McLaren M, Hill A, Underwood C, Belch JJ.	Vascular Diseases Research Unit, The Institute of Cardiovascular Research, Ninewells Hospital and Medical School, Dundee, Scotland DD1 9SY, UK. g.y.kennedy@dundee.ac.uk	Oxidative stress levels are raised in chronic fatigue syndrome and are associated with clinical symptoms.	Free Radic Biol Med. 2005 Sep 1;39(5):584-9.	The aetiology of chronic fatigue syndrome (CFS) is unknown; however, recent evidence suggests excessive free radical (FR) generation may be involved. This study investigated for the first time levels of 8-iso-prostaglandin-F(2 alpha)-isoprostanes alongside other plasma markers of oxidative stress in CFS patients and control subjects. Forty-seven patients (18 males, 29 females, mean age 48 [19--63] years) who fulfilled the Centres for Disease Control classification for CFS and 34 healthy volunteers (13 males, 21 females, 46 [19--63] years) were enrolled in the study. The CFS patients were divided into two groups; one group had previously defined cardiovascular (CV) risk factors of obesity and hypertension (group 1) and the second were normotensive and nonobese (group 2). Patients had significantly increased levels of isoprostanes (group 1, P=0.007; group 2, P=0.03, unpaired t test compared to controls) and oxidised low-density lipoproteins (group 2, P=0.02) indicative of a FR attack on lipids. CFS patients also had significantly lower high-density lipoproteins (group 1, P=0.011; group 2, P=0.005). CFS symptoms correlated with isoprostane levels, but only in group 2 low CV risk CFS patients (isoprostanes correlated with; total symptom score P=0.005; joint pain P=0.002; postexertional malaise P=0.027, Pearson). This is the first time that raised levels of the gold standard measure of in vivo oxidative stress (isoprostanes) and their association with CFS symptoms have been reported.
Kim CH, Shin HC, Won CW.	Department of Family Medicine, Sungkyunkwan University School of Medicine, Korea. kchjp@hanafos.com	Prevalence of chronic fatigue and chronic fatigue syndrome in Korea: community-based primary care study.	J Korean Med Sci. 2005 Aug;20(4):529-34.	There have been many epidemiological and clinical researches on chronic fatigue (CF) and chronic fatigue syndrome (CFS) since the 1990s, but such studies have been quite limited in Korea. The aim of this study was to investigate the point prevalence of CF and CFS in patients who visited community-based eight primary care clinics in Korea. The study subjects were 1,648 patients aged 18 yr and over who visited one of eight primary care clinics in Korea between the 7th and 17th of May 2001. The physicians determined the status of the subjects through fatigue-related questionnaires, medical history, physical examination, and laboratory tests. The subjects were categorized into no fatigue, prolonged fatigue, CF and then CF were further classified to medically explained CF (Physical CF and Psychological CF) and medically unexplained CF (CFS and idiopathic chronic fatigue). The point prevalence of CF and CFS were 8.4% (95% CI 7.1-9.7%) and 0.6% (95% CI 0.2-1.0%). Medically explained CF was 80.5% of CF, of which 57.1% had psychological causes. The clinical characteristics of CFS were distinguished from explained CF. CF was common but CFS was rare in community-based primary care settings in Korea.
King C, Jason LA.	Spinal Cord Injury Service (128), Hines VA Hospital, P.O. Box 5000, Hines, IL 60141-5128, USA.	Improving the diagnostic criteria and procedures for chronic fatigue syndrome.	Biol Psychol. 2005 Feb;68(2):87-106.	Since the publication of the case definition for chronic fatigue syndrome (CFS) in 1988 the diagnostic criteria have been revised twice in the U.S. None of the case definitions were derived empirically. As a result, there is concern regarding the sensitivity, specificity, and reliability of the criteria. The goal of the present study was to identify methods for improving the diagnostic criteria for CFS. Three groups of 15 participants each were recruited: participants with (1) CFS, (2) major depressive disorder (MDD), and (3) healthy controls. Using statistical procedures, three methods for improving the diagnostic

	cpking@rcn.com			criteria were explored: identification of new diagnostic symptoms, the use of severity ratings for symptomatology, and the identification of standardized measures that differentiate cases of CFS from other conditions. Results of the present study suggest that these three methods hold promise for improving the sensitivity, specificity, and reliability of the diagnostic criteria for CFS.
Kodama M, Kodama T.	Kodama Research Institute of Preventive Medicine, 50-5 Chikusaku, Chikusaku, Nagoya 464-0005, Japan.	The clinical course of interstitial pneumonia alias chronic fatigue syndrome under the control of megadose vitamin C infusion system with dehydroepiandrosterone-cortisol annex.	Int J Mol Med. 2005 Jan;15(1):109-16.	The year 1995 marked the onset of interstitial pneumonia spread in Nagoya, Japan. For the last 9 years, we have been accumulating clinical experience with the disease control using the combination of prophylactic use of anti-biotics and regular practice of megadose vitamin C infusion with either dehydroepiandrosterone-annex or dehydroepiandrosterone-cortisol annex. The purpose of this study is to assess the usefulness of our new treatment system for the control of interstitial pneumonia alias chronic fatigue syndrome. The results obtained are given as follows: i) The long-term maintenance of the above treatment system was effective not only for decreasing the risk for recurrence of active form pneumonia, but also for prevention of malignancy emergence in aged patients with interstitial pneumonia. ii) Evidence is presented to indicate that interstitial pneumonia was associated with increased risk for depression of which the emergence is a candidate subject causally related to the long-term use of glucocorticoid. iii) A patient with both interstitial pneumonia and depression was found to be less responsive to our treatment system. It is suggested that the use of more dehydroepiandrosterone at the sacrifice of cortisol in the infusion annex may be a choice for the control of both interstitial pneumonia and depression. iv) The description of chronic fatigue syndrome as regards the endocrinological, epidemiological and psychiatric characteristics are in good agreement with our experience on patients having interstitial pneumonia, evidence in support of our proposal that there is no convincing reasoning to separate chronic fatigue syndrome from interstitial pneumonia. v) The long-term practice of our treatment system for the control of interstitial pneumonia (an autoimmune disease) was found to suppress the inflammatory process but not the fibrotic process in the long run. vi) A few innovations were made in our treatment system to reduce the risk of bleeding or thrombosis--vascular complications of pneumonia. vii) The merit of our treatment system is to create a new hormonal environment to improve the state of immunodeficiency by use of a non-steroid substance--vitamin C which encounters little resistance from the feedback mechanism of steroid metabolism in the in vivo system.
Kop WJ, Lyden A, Berlin AA, Ambrose K, Olsen C, Gracely RH, Williams DA, Clauw DJ.	Department of Medical and Clinical Psychology, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Road, Bethesda, MD 20814, USA. wjkop@usuhs.mil	Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome.	Arthritis Rheum. 2005 Jan;52(1):296-303.	OBJECTIVE: Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are associated with substantial physical disability. Determinants of self-reported physical disability are poorly understood. This investigation uses objective ambulatory activity monitoring to compare patients with FM and/or CFS with controls, and examines associations of ambulatory activity levels with both physical function and symptoms during activities of daily life. METHODS: Patients with FM and/or CFS (n = 38, mean +/- SD age 41.5 +/- 8.2 years, 74% women) completed a 5-day program of ambulatory monitoring of physical activity and symptoms (pain, fatigue, and distress) and results were compared with those in age-matched controls (n = 27, mean +/- SD age 38.0 +/- 8.6 years, 44% women). Activity levels were assessed continuously, ambulatory symptoms were determined using electronically time-stamped recordings at 5 time points during each day, and physical function was measured with the 36-item Short Form health survey at the end of the 5-day monitoring period. RESULTS: Patients had significantly lower peak activity levels than controls (mean +/- SEM 8,654 +/- 527 versus 12,913 +/-

				1,462 units; P = 0.003) and spent less time in high-level activities when compared with controls (P = 0.001). In contrast, patients had similar average activity levels as those of controls (mean +/- SEM 1,525 +/- 63 versus 1,602 +/- 89; P = 0.47). Among patients, low activity levels were associated with worse self-reported physical function over the preceding month. Activity levels were inversely related to concurrent ambulatory pain (P = 0.031) and fatigue (P < 0.001). Pain and fatigue were associated with reduced subsequent ambulatory activity levels, whereas activity levels were not predictive of subsequent symptoms. CONCLUSION: Patients with FM and/or CFS engaged in less high-intensity physical activities than that recorded for sedentary control subjects. This reduced peak activity was correlated with measures of poor physical function. The observed associations may be relevant to the design of behavioral activation programs, because activity levels appear to be contingent on, rather than predictive of, symptoms.
Lange G, Steffener J, Cook DB, Bly BM, Christodoulou C, Liu WC, Deluca J, Natelson BH.	Department of Radiology, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, 07103, USA. lange@njneurome d.org	Objective evidence of cognitive complaints in Chronic Fatigue Syndrome: a BOLD fMRI study of verbal working memory.	Neuroimage. 2005 Jun;26(2):513-24. Epub 2005 Apr 7.	Individuals with Chronic Fatigue Syndrome (CFS) often have difficulties with complex auditory information processing. In a series of two Blood Oxygen Level Dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) studies, we compared BOLD signal changes between Controls and individuals with CFS who had documented difficulties in complex auditory information processing (Study 1) and those who did not (Study 2) in response to performance on a simple auditory monitoring and a complex auditory information processing task (mPASAT). We hypothesized that under conditions of cognitive challenge: (1) individuals with CFS who have auditory information processing difficulties will utilize frontal and parietal brain regions to a greater extent than Controls and (2) these differences will be maintained even when objective difficulties in this domain are controlled for. Using blocked design fMRI paradigms in both studies, we first presented the auditory monitoring task followed by the mPASAT. Within and between regions of interest (ROI), group analyses were performed for both studies with statistical parametric mapping (SPM99). Findings showed that individuals with CFS are able to process challenging auditory information as accurately as Controls but utilize more extensive regions of the network associated with the verbal WM system. Individuals with CFS appear to have to exert greater effort to process auditory information as effectively as demographically similar healthy adults. Our findings provide objective evidence for the subjective experience of cognitive difficulties in individuals with CFS.
Li YJ, Gao XG, Wang DX, Lin T, Bai XL, Yang FZ.	Department of Neurology, People's Hospital, Peking University, Beijing 100044, China.	[Cognitive function and psychological characteristics of patients with chronic fatigue syndrome] [Article in Chinese]	Zhonghua Yi Xue Za Zhi. 2005 Nov 2;85(41):2926-9.	OBJECTIVE: To investigate the cognitive function and psychological characteristics of the patients with chronic fatigue syndrome (CFS) in China and analyze its relation with primary psychological diseases. METHODS: Ninety-one patients with CFS who visited the People's Hospital, Peking University, in Beijing from Beijing, Shanghai, Tianjin, Heilongjiang, Jilin, Hebei, Inner Mongolia, Shanxi, Shandong, Sichuan, Gansu, Fujian, and Guangdong, 42 males and 49 females, aged 37 +/- 7, 43% of which had the record of formal schooling of regular college course or over and 21 of which had the record of formal schooling of college for professional training, and 58% of which showed clear causes, diagnosed by the CDC criteria 1994, underwent case history collection, physical examination, necessary laboratory test, memory test, and SCL-90, Hamilton depression rating scale (HAMD), and Hamilton anxiety rating scale (HAMA) testing. Thirty healthy persons, 14 males and 16 females, aged 37 +/- 7, were used as controls., A table of case file was established based on the CDC criteria 1994 for each patient to record the relevant data. Independent-Samples T Test was used to compare the memory quotient, the total

				score and general mean score of SCL-90, the score of HAMD and HAMA. Analyzed the impairment of cognitive function and psychological characteristics of patients with CFS. RESULTS: The most common symptoms was descent of remembrance and/or attention (82/91, 90%). The memory quotient of the CFS patients was 85 +/- 14, significantly lower than that of the healthy controls (98 +/- 12, t = 4.627, P = 0.000). The total score of SCL-90 of the CFS patients was 192 +/- 47, significantly higher than that of the healthy controls (140 +/- 46, t = 5.297, P = 0.000). The symptoms with a factor score > or = 2.0 in SCL-90 included obsessive-compulsive symptoms (61/91, 67%), somatization (61/91, 67 %), depression (57/91, 63%), and anxiety (49/91, 54%). The HAMD score of the CFS patients was 9.9 +/- 6.1, significantly higher than that of the healthy controls (6.5 +/- 2.5, t = 2.948, P = 0.004). The HAMA score of the CFS patients was 9.9 +/- 7.0, significantly higher than that of the healthy controls (5.9 +/- 2.9, t = 3.015, P = 0.003). CONCLUSION: The CFS patients in China have an obvious impairment of remembrance and show different psychological abnormalities that are different from those of the patients with primary psychological diseases.
Li YJ, Wang DX, Bai XL, Chen J, Liu ZD, Feng ZJ, Zhao YM.	Department of Neurology, People's Hospital, Beijing University, Beijing 100044, China.	[Clinical characteristics of patients with chronic fatigue syndrome: analysis of 82 cases] [Article in Chinese]	Zhonghua Yi Xue Za Zhi. 2005 Mar 16;85(10):701-4.	OBJECTIVE: To analyze the clinical characteristics of Chinese patients suffering from chronic fatigue syndrome (CFS) and provide clinical and laboratory evidence for the study of its etiology and treatment. METHODS: 82 patients with CFS diagnosed based on the CDC criteria 1994 were recruited. History was collected, and physical examination was made. SCL-90 and memory test were used, and Hamilton Anxiety Rating Scale was used to those showing depression and/or anxiety. Laboratory examination, including examination of electrolytes, blood sugar, creatinine, bilirubin, alkaline phosphatase, alanine trasaminase, etc, was conducted. Western blotting was used to detect the protein-24 of Borna disease virus (BDV) in the plasma of 61 patients and 73 healthy controls. High-pressure chromatography was conducted to detect n-6 fatty acids on the membrane of erythrocytes of 42 patients and 37 healthy controls. Plasma L-carnitine in 61 patients and 73 healthy controls was detected by zymological analysis. In different examinations sex and age-matched controls were used. RESULTS: Most of the patients were 21 approximately 50 years old (74/82, 90.24%). No gender difference was found. The patients usually had 4 approximately 6 symptoms besides distinctive fatigue. Descent of remembrance and/or attention was the most conspicuous accompanying symptoms (69/82, 84.15%). Abnormalities in SCL-90 scores were present in 57 patients (69.51%), e.g, somatization existed most commonly (32/82, 39.02%), and anxiety and depression were 20.73% (17/82) and 18.29% (15/82) respectively. The prevalence of anti-BDV-p24 antibody was 20.73% (17/82), significantly higher than that of the controls (0%, chi(2) = 6.673, P = 0.010). The arachidonic acid level was significantly lower in the CFS group than in the controls (P > 0.05) and there were no differences in linoleic acid and ETA (both P > 0.05). The level of L-carnitine was 6.4336 +/- 3.4225, significantly lower than that of the control group (7.6666 +/- 3.5819, t = 2.025, P = 0.045) and the L-carnitine level was increased 2 weeks after supplementary treatment, together with improvement of symptoms. CONCLUSION: Most of the CFS patients are young and middle-aged. Descent of reorganization is common in these patients. Psychological abnormalities exist in most patients. Some patients are infected with BDV, some with deficiency of nutrition and/or abnormality of energy metabolism.
Lijue Z.	Affiliated Hospital	Acupuncture and	J Tradit Chin Med.	

	of Guiyang Medical College, Guiyang, Guizhou 550001, China.	Chinese patent drugs for treatment of chronic fatigue syndrome.	2005 Jun;25(2):99-101.	
Lo YL, Leong HN, Hsu LY, Tan TT, Kurup A, Fook-Chong S, Tan BH.		Autonomic dysfunction in recovered severe acute respiratory syndrome patients.	Can J Neurol Sci. 2005 May;32(2):264.	Letter
Maes M, Mihaylova I, De Ruyter M.	M-Care4U outpatient Clinics, and the Clinical Research Center for Mental Health, Olmenlaan 9, 2610 Antwerp, Belgium.	Decreased dehydroepiandrosterone sulfate but normal insulin-like growth factor in chronic fatigue syndrome (CFS): relevance for the inflammatory response in CFS.	Neuro Endocrinol Lett. 2005 Oct;26(5):487-92.	There are a few reports that chronic fatigue syndrome (CFS) may be accompanied by changes in hormones, such as dehydroepiandrosterone (DHEA) and insulin-like growth factor (IGF1). This study examines the serum concentrations of DHEA-sulfate (DHEAS), IGF1 and IGF1 binding protein-3 (IGFBP3) in 20 patients with CFS and in 12 normal controls. The IGFBP3/IGF1 ratio was computed as an index for IGF1 availability. We found significantly lower serum DHEAS concentrations in CFS, but no significant differences either in IGF1 or the IGFBP3/IGF1 ratio between CFS patients and normal controls. The decrease in serum DHEAS was highly sensitive and specific for CFS. There were significant and positive correlations between serum DHEAS and serum zinc and the mitogen-induced expression of the CD69 molecule on CD3+CD8+ T cells (an indicator of early T cell activation). There was a significant and negative correlation between serum DHEAS and the increase in the serum alpha-2 protein fraction (an inflammatory marker). Serum IGF1, but not DHEAS, was significantly and inversely correlated to age. The results show that CFS is accompanied by lowered levels of DHEAS and that the latter may play a role in the immune (defect in the early activation of T cells) and the inflammatory pathophysiology of CFS.
Maes M, Mihaylova I, Leunis JC.	M-Care4U Outpatient Clinics, and the Clinical Research Center for Mental Health, Belgium.	In chronic fatigue syndrome, the decreased levels of omega-3 poly-unsaturated fatty acids are related to lowered serum zinc and defects in T cell activation.	Neuro Endocrinol Lett. 2005 Dec 28;26(6):745-751 [Epub ahead of print]	There is now evidence that major depression is accompanied by decreased levels of omega3 poly-unsaturated fatty acids (PUFA), such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). There is a strong comorbidity between major depression and chronic fatigue syndrome (CFS). The present study has been carried out in order to examine PUFA levels in CFS. In twenty-two CFS patients and 12 normal controls we measured serum PUFA levels using gas chromatography and mass spectrometry. We found that CFS was accompanied by increased levels of omega6 PUFAs, i.e. linoleic acid and arachidonic acid (AA), and mono-unsaturated fatty acids (MUFAs), i.e. oleic acid. The EPA/AA and total omega3/omega6 ratios were significantly lower in CFS patients than in normal controls. The omega3/omega6 ratio was significantly and negatively correlated to the severity of illness and some items of the FibroFatigue scale, i.e. aches and pain, fatigue and failing memory. The severity of illness was significantly and positively correlated to linoleic and arachidonic acid, oleic acid, omega9 fatty acids and one of the saturated fatty acids, i.e. palmitic acid. In CFS subjects, we found significant positive correlations between the omega3/omega6 ratio and lowered serum zinc levels and the lowered mitogen-stimulated CD69 expression on CD3+, CD3+CD4+, and CD3+CD8+ T cells, which indicate defects in early T cell activation. The results of this study show that a decreased availability of omega3 PUFAs plays a role in the pathophysiology of CFS and is related to the immune

				pathophysiology of CFS. The results suggest that patients with CFS should respond favourably to treatment with - amongst other things - omega3 PUFAs, such as EPA and DHA.
Maher KJ, Klimas NG, Fletcher MA.	Department of Medicine, University of Miami Miller School of Medicine, Miami, FL 33176, USA.	Chronic fatigue syndrome is associated with diminished intracellular perforin.	Clin Exp Immunol. 2005 Dec;142(3):505-11.	Chronic fatigue syndrome (CFS) is an illness characterized by unexplained and prolonged fatigue that is often accompanied by abnormalities of immune, endocrine and cognitive functions. Diminished natural killer cell cytotoxicity (NKCC) is a frequently reported finding. However, the molecular basis of this defect of in vitro cytotoxicy has not been described. Perforin is a protein found within intracellular granules of NK and cytotoxic T cells and is a key factor in the lytic processes mediated by these cells. Quantitative fluorescence flow cytometry was used to the intracellular perforin content in CFS subjects and healthy controls. A significant reduction in the NK cell associated perforin levels in samples from CFS patients, compared to healthy controls, was observed. There was also an indication of a reduced perforin level within the cytotoxic T cells of CFS subjects, providing the first evidence, to our knowledge, to suggest a T cell associated cytotoxic deficit in CFS. Because perforin is important in immune surveillance and homeostasis of the immune system, its deficiency may prove to be an important factor in the pathogenesis of CFS and its analysis may prove useful as a biomarker in the study of CFS.
Masuda A, Kihara T, Fukudome T, Shinsato T, Minagoe S, Tei C.	Respiratory and Stress Care Center, Kagoshima University Hospital, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan. masudaak@m.kufm.kagoshima-u.ac.jp	The effects of repeated thermal therapy for two patients with chronic fatigue syndrome.	J Psychosom Res. 2005 Apr;58(4):383-7.	OBJECTIVE: This paper describes the successful treatment of two patients with chronic fatigue syndrome (CFS) using repeated thermal therapy. METHODS: Two patients with CFS underwent treatment with prednisolone (PSL), with no satisfactory effect. They were subjected to thermal therapy that consisted of a far-infrared ray dry sauna at 60 degrees C and postsauna warming. The therapy was performed once a day, for a total of 35 sessions. After discharge, these subjects continued the therapy once or twice a week on an outpatient basis for 1 year. RESULTS: Symptoms such as fatigue, pain, sleep disturbance, and low-grade fever were dramatically improved after 15 to 25 sessions of thermal therapy. Although PSL administration was discontinued, the subjects showed no relapse or exacerbation of symptoms during the first year after discharge. The patients became socially rehabilitated 6 months after discharge. CONCLUSIONS: These results suggest that repeated thermal therapy might be a promising method for the treatment of CFS.
McGhee SA, Kaska B, Liebhaber M, Stiehm ER.	Department of Pediatrics, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA. smcghee@mednet.ucla.edu	Persistent parvovirus-associated chronic fatigue treated with high dose intravenous immunoglobulin.	Pediatr Infect Dis J. 2005 Mar;24(3):272-4.	We report a 16-year-old boy with no evidence of immunodeficiency who had a 2-year history of chronic fatigue, low grade fever and slapped-cheek rash associated with chronic parvovirus B19 viremia. Prolonged intravenous immunoglobulin therapy resulted in resolution of his symptoms and viremia. Intravenous immunoglobulin may be useful in the resolution of parvovirus viremia regardless of immune status.
Metcalf LN, McGregor NR, Roberts TK		Membrane Damaging Toxins from Coagulase-Negative Staphylococcus Are Associated	Journal of Chronic Fatigue Syndrome 2005 12 (3): 25-43	Aim: To assess whether there is any association between membrane damaging toxin production by Staphylococcus spp. and self-reported TMD symptom expression in a group of patients selected to have CFS. Methods: Thirty-three defined Chronic Fatigue Syndrome (CFS) patients and 33 ageand sex-matched controls were assessed to evaluate the relationship between carriage of membrane damaging toxin producing staphylococcus, CFS and temporomandibular dysfunction (TMD) symptoms. Results: The CFS patients had an increased prevalence of face pain (Odds Ratio = 21.0, 95% CL 4.2-106,

		with Self-Reported Temporomandibular Disorder (TMD) in Patients with Chronic Fatigue Syndrome		P < .001) and temporomandibular joint (TMJ) clicking/locking (OR = 5.7, 95% CL 1.423.5, P < .007), and the coagulase-negative staphylococcus maximum% B*-toxin haemolysis per patient. Both multivariate and univariate analyses revealed an association between the membrane damaging o*-toxin producing CoNS (MDT-CoNS) species per subject and face pain prevalence and intensity within both the CFS patients and the control subjects. No association was found between CoNS toxin production and TMJ clicking/locking. Importantly, áand B*-toxin production by CoNS was associated with patient reporting of arthritis. Conclusions: These data confirm the original observations of the association between MDTCoNS and facial muscle pain (Butt et al, 1998; McGregor et al, 2003). These data also suggest that MDT-CoNS associated facial muscle pain expression represents a distinct clinical entity, which has an increased prevalence in CFS patients.
Michielsen HJ, Van Houdenhove B, Leirs I, Vandenbroeck A, Onghena P.	Department of Psychology and Health, Tilburg University, Tilburg, The Netherlands.	Depression, attribution style and self-esteem in chronic fatigue syndrome and fibromyalgia patients: is there a link?	Clin Rheumatol. 2005 Jul 12; [Epub ahead of print]	The aims of the present study were to compare a single diagnosis (chronic fatigue syndrome, CFS) and a double diagnosis (CFS + fibromyalgia, CFS+FM) group regarding depression, attribution style and self-esteem as well as to examine whether attribution style is a mediator in the relationship between self-esteem and depression. Eighty-five patients (CFS: 47, CFS+FM: 38) completed questionnaires on attribution style, self-esteem and depression. The single and double diagnosis groups tended to differ slightly, but the differences were never statistically significant. In addition, only one condition was met of the four conditions mentioned by Baron and Kenny to establish that mediation exists between two variables. In conclusion, an external attribution style does not protect the CFS or CFS+FM patients with a low self-esteem from depression. The prevalence rate of depression was high in both patient samples, of which clinicians should be aware.
Mihrshahi R, Beirman R.	Department of Biological Sciences, Macquarie University, Sydney, NSW, Australia. HUrbeirman@els.mq.edu.auUH	Aetiology and pathogenesis of chronic fatigue syndrome: a review.	N Z Med J. 2005 Dec 16;118(1227):U1780.	Chronic fatigue syndrome (CFS) is a debilitating disease of uncertain aetiology that is characterised by unexplained, severe fatigue associated with a number of typical symptoms. This paper reviews the scientific literature related to current theories about the aetiology and pathogenesis of CFS by focussing on what appear to be the four most significant aspects in the development and perpetuation of this disease: the role of infectious agents as well as immunological, neuroendocrine, and psychiatric factors. A multifactorial model for the aetiology of CFS, which includes and draws together these four aspects, is proposed; and suggestions are offered regarding approaches to the diagnosis and treatment of this disease.
Miller R.		Thimerosal, micromercurialism and chronic fatigue syndrome.	Med Hypotheses. 2005;64(5):1063-4.	Letter
Mommersteeg PM, Heijnen CJ, Verbraak MJ, van Doornen LJ.	Department of Health Psychology, Utrecht University, P.O. Box 80.140, 3508 TC Utrecht, The Netherlands.	Clinical burnout is not reflected in the cortisol awakening response, the day-curve or the response to a low-dose dexamethasone	Psychoneuroendocrinology. 2005 Sep 5; [Epub ahead of print]	Burnout is presumed to be the result of chronic stress, and chronic stress is known to affect the HPA-axis. To date, studies on HPA-axis functioning in burnout have showed inconsistent results. In the present study, a large sample (n=74) of clinically diagnosed burnout individuals, mostly on sick-leave, were included and compared with 35 healthy controls. Salivary cortisol was sampled on 2 days to determine the cortisol awakening response (CAR) and the day-curve. In addition, the dexamethasone suppression test (DST) was applied to assess the feedback efficacy of the HPA-axis. There were no differences observed in the CAR, day-curve or CAR after DST in the burnout group as compared to a healthy control group. Burnout shows overlap in symptoms with chronic fatigue syndrome (CFS) and

		suppression test.		depression. Therefore, differential changes in HPA-axis functioning that resemble the hypo-functioning of the HPA-axis in CFS, or rather the hyper-functioning of the HPA-axis in depression, might have obscured the findings. However, no effect of fatigue or depressive mood on HPA-axis functioning was found in the burnout group. We concluded that HPA-axis functioning in clinically diagnosed burnout participants as tested in the present study, seems to be normal.
Moss J.	Association of Young People with ME, Milton Keynes MK2 2XD, UK. jill@ayme.org.uk	Development of a functional ability scale for children and young people with myalgic encephalopathy (ME)/chronic fatigue syndrome (CFS).	J Child Health Care. 2005 Mar;9(1):20-30.	The numerous symptoms and unpredictable pattern of myalgic encephalopathy (ME) make it difficult to describe, especially for children. It was left to carers to guess what the child could achieve each day, often leading to over/underestimates. A functional ability scale was needed, which measured from 0 to 100 percent able and that children and young people themselves designed. A new scale was developed from the Moss Ability Scale using the critique of 251 children and young people from the Association of Young People with ME (AYME). Responding to the shift in emphasis towards patients taking an active role in their own care, it was felt these young people would know whether the scale measured what it had set out to measure, and were asked questions on the face and content validity of the scale. There was a 99 percent agreement between the young people that the final scale was 'workable' or better.
Moss-Morris R, Sharon C, Tobin R, Baldi JC.	Health Psychology, The Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92 019, Auckland, New Zealand. r.moss-morris@auckland.ac.nz	A randomized controlled graded exercise trial for chronic fatigue syndrome: outcomes and mechanisms of change.	J Health Psychol. 2005 Mar;10(2):245-59.	The aim of this study was to investigate the potential mechanisms underlying the efficacy of graded exercise therapy for chronic fatigue syndrome (CFS). Forty-nine CFS patients were randomized to a 12-week graded exercise programme or to standard medical care. At the end of treatment the exercise group rated themselves as significantly more improved and less fatigued than the control group. A decrease in symptom focusing rather than an increase in fitness mediated the treatment effect. Graded exercise appears to be an effective treatment for CFS and it operates in part by reducing the degree to which patients focus on their symptoms.
Naschitz JE, Mussafia-Priselac R, Peck ER, Peck S, Naftali N, Storch S, Slobodin G, Elias N, Rosner I.	Department of Internal Medicine A, Bnai-Zion Medical Center, Haifa, Israel. Naschitz@tx.technion.ac.il	Hyperventilation and amplified blood pressure response: is there a link?	J Hum Hypertens. 2005 May;19(5):381-7.	Based on prior studies, the hypothesis that hyperventilation (HV) may have a pressor effect and play a causal role in hypertension has been suggested. The objective of this study was to correlate HV with blood pressure (BP)-change during a postural challenge. Consecutive subjects referred for evaluation of syncope, dizziness, chronic fatigue syndrome (CFS), fibromyalgia, or non-CFS fatigue were assessed with a 10-min supine 30-min head-up tilt test combined with capnography. We selected for analysis the records of patients aged 17-70 years, not taking vasoactive medications, having sitting systolic BP (SBP) < 140 mmHg, sitting diastolic BP (DBP) < 90 mmHg, and who completed 30 min of tilt. HV was diagnosed when end-tidal pressure of CO2 < 30 mmHg was recorded consecutively for > or = 10 min. Postural hypertension (PHT) was diagnosed when DBP on tilt > or = 90 mmHg was recorded consecutively for > or = 10 min. DBP-change was computed as (median DBP on tilt) -(median DBP supine). PHT and DBP-change were correlated with HV. A total of 320 patient charts were reviewed. PHT was present in 30 cases. The mean DBP-change in patients with PHT was +9.9 mmHg (s.d. 5.8), with three patients manifesting HV. Of the remaining 290 patients, 56 had HV, their mean DBP-change was -0.3 mmHg (s.d. 7.2). The other 234 patients without HV had a mean DBP-change +0.95 mmHg

				(s.d. 5.7), comparable to the DBP-change in patients with HV. In, conclusion, posturally induced HV was not associated with an increase in BP, nor was PHT associated with HV, except in a small minority of cases.
Naschitz JE, Rozenbaum M, Fields M, Isseroff H, Enis S, Babich JP, Peck S, Peck ER, Gaitini L, Naschitz S, Sabo E, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. Naschitz@tx.technion.ac.il	Search for disease-specific cardiovascular reactivity patterns: developing the methodology.	Clin Sci (Lond). 2005 Jan;108(1):37-46.	Aberrations of CVR (cardiovascular reactivity), an expression of autonomic function, lack specificity for a particular disorder. Recently, a CVR pattern particular to chronic fatigue syndrome has been observed. In the present study, we aimed to develop methodologies for assessing disease-specific CVR patterns. As a prototype, a population of 50 consecutive patients with FMF (familial Mediterranean fever) was studied and compared with control populations. A 10 min supine/30 min head-up tilt test with recording of the heart rate and blood pressure or the pulse transit time was performed. Five studies were conducted applying different methods. In each study, statistical analysis identified independent predictors of CVR in FMF. Based on regression coefficients of these predictors, a linear DS (discriminant score) was computed for every subject. Each study established an equation to assess CVR, calculate DS for FMF and determine the sensitivity and specificity of the DS cut-off. In each of the five studies, abnormal CVR was observed in FMF patients. The best accuracy (88% sensitivity and 90.1% specificity for FMF) was obtained by a method based on beat-to-beat heart rate and pulse transit time recordings. Data was processed by fractal and recurrence quantitative analysis with recordings in FMF patients compared with a mixed control population. Identification of disease-specific CVR patterns was possible with the methodologies described in the present study. In FMF, disease-specific CVR may be explained by the interplay between neuroendocrine loops specific to FMF with cardiovascular homoeostatic mechanisms. Recognition of disease-specific CVR patterns may advance the understanding of homoeostatic mechanisms and have implications in clinical practice.
Naschitz JE, Rozenbaum M, Fields MC, Enis S, Manor H, Dreyfuss D, Peck S, Peck ER, Babich JP, Mintz EP, Sabo E, Slobodin G, Rosner I.	Department of Internal Medicine A and Rheumatology, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. Naschitz@tx.technion.ac.il	Cardiovascular reactivity in fibromyalgia: evidence for pathogenic heterogeneity.	J Rheumatol. 2005 Feb;32(2):335-9.	OBJECTIVE: To evaluate disease-specific cardiovascular reactivity patterns in patients with fibromyalgia (FM) using a recently described method called fractal and recurrence analysis score (FRAS). METHODS: The study group included 30 women with FM, average age 46.7 years (SD 7.03). An age matched group of 30 women with other rheumatic disorders or having a dysautonomic background [chronic fatigue syndrome (CFS), non-CFS fatigue, neurally mediated syncope, and psoriatic arthritis (PsA)] served as controls. Subjects were evaluated with a head-up tilt test with beat-to-beat recording of the heart rate (HR) and pulse transit time. A 10-minute supine phase was followed by 600 cardiac cycles recorded on tilt. Data were processed by recurrence plot and fractal analysis. Variables acting as independent predictors of the cardiovascular reactivity were identified in FM patients versus controls. RESULTS: No statistically significant differences were found between the groups by univariate analysis comparing 92 variables of cardiovascular reactivity in FM patients compared to controls. CONCLUSION: Study of cardiovascular reactivity utilizing a head-up tilt test and processing the data using the FRAS method did not reveal a specific FM-associated abnormality. Our data confirm studies that utilized other methodologies and reached similar conclusions. Patients with FM represent a heterogenous group with respect to their pattern of cardiovascular reactivity.
Natelson BH, Weaver SA, Tseng CL, Ottenweller JE.	CFS Cooperative Research Center and Department of Neurosciences,	Spinal fluid abnormalities in patients with chronic fatigue	Clin Diagn Lab Immunol. 2005 Jan;12(1):52-5.	Arguments exist as to the cause of chronic fatigue syndrome (CFS). Some think that it is an example of symptom amplification indicative of functional or psychogenic illness, while our group thinks that some CFS patients may have brain dysfunction. To further pursue our encephalopathy hypothesis, we did spinal taps on 31 women and 13 men fulfilling the 1994 case definition for CFS and on 8 women

	University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey, USA. bhn@njneuromed.org	syndrome.		and 5 men serving as healthy controls. Our outcome measures were white blood cell count, protein concentration in spinal fluid, and cytokines detectable in spinal fluid. We found that significantly more CFS patients had elevations in either protein levels or number of cells than healthy controls (30 versus 0%), and 13 CFS patients had protein levels and cell numbers that were higher than laboratory norms; patients with abnormal fluid had a lower rate of having comorbid depression than those with normal fluid. In addition, of the 11 cytokines detectable in spinal fluid, (i) levels of granulocyte-macrophage colony-stimulating factor were lower in patients than controls, (ii) levels of interleukin-8 (IL-8) were higher in patients with sudden, influenza-like onset than in patients with gradual onset or in controls, and (iii) IL-10 levels were higher in the patients with abnormal spinal fluids than in those with normal fluid or controls. The results support two hypotheses: that some CFS patients have a neurological abnormality that may contribute to the clinical picture of the illness and that immune dysregulation within the central nervous system may be involved in this process.
Nicolson GL, Gan R, Haier J.		ORIGINAL RESEARCH Evidence for Brucella spp. and Mycoplasmaspp. Co-Infections in Blood of Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 2005 12 (2): 5 - 17	We examined the blood of 94 North American Chronic Fatigue Syndrome (CFS) patients using forensic polymerase chain reaction and found that a subset (10.6%) of CFS patients show evidence of Brucella spp. infections compared to one of 70 control subjects (Odds Ratio = 8.2; 95% Confidence Limits (CL) 1-66; P < .01). Rural patients showed a higher incidence of Brucella spp. infections over urban patients (OR = 5.5, 95% CL 1.3-23.5, P < .02). Since CFS patients also have a high prevalence of one of four Mycoplasma species and sometimes show evidence of infections with Chlamydia pneumoniae, we examined Brucella-positive patients for other bacterial infections. Previously we found that 8% of the CFS patients showed evidence of C. pneumoniae and about 50% show evidence of Mycoplasma spp. infections. Since the presence of one or more chronic systemic infections may predispose patients to other infections, we examined the prevalence of C. pneumoniae and Mycoplasma spp. infections in Brucella-positive patients. We found only one Brucella-positive patient with C. pneumoniae and four other patients with evidence of Mycoplasma spp., suggesting that such bacterial infections occur independently in CFS patients. Control subjects (N = 70) had low rates of Brucella spp. (1.4%), Mycoplasma spp. (7.2%) or C. pneumoniae (1.4%) infections, and there were no co-infections in control subjects. The results indicate that a subset of CFS patients show evidence of infection with Brucella spp., and some of these patients also have other bacterial infections.
Nijs J, De Meirleir K		CRITICAL REVIEWS AND COMMENTS ON CURRENT RESEARCH Enterovirus Related Myopathy in a Subset of Chronic Fatigue Syndrome?	Journal of Chronic Fatigue Syndrome 2005 12 (2): 67-73	
Nijs J, De Meirleir K.	Department of Human Physiology,	Nitric oxide and chronic fatigue	Med Hypotheses. 2005 Oct 7; [Epub	LETTER

	Faculty of Physical Education and Physiotherapy, Vrije University Brussel, Belgium; Division of Musculoskeletal Physiotherapy, Higher Institute of Physiotherapy, Department of Health Sciences, Hogeschool Antwerpen, Belgium.	syndrome: Are we caring for our patients or are we practicing selfcare?	ahead of print]	
Nijs J, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium. HUJo.Nijs@vub.ac.beUH	Impairments of the 2-5A synthetase/RNase L pathway in chronic fatigue syndrome.	In Vivo. 2005 Nov-Dec;19(6):1013-21.	This paper provides an overview of the evidence addressing the impairments of the 2'-5' oligoadenylate (2-5 A) synthetase/RNase L pathway in Chronic Fatigue Syndrome (CFS) patients. The 2-5A synthetase/RNase L pathway in CFS patients appears to be both up-regulated (i.e. increased levels of bioactive 2-5A synthetase and increased activity of the RNase L enzyme) and deregulated (elastase and calpain initiate 83 kDa RNase L proteolysis, generating two major fragments with molecular masses of 37 and 30 kDa, respectively). The deregulation of the 2-5A synthetase/RNase L pathway in CFS accompanies decreased NK-function and deregulation of apoptotic pathways. Since various components of the pathway appear to be related to performance during a graded exercise stress test, some evidence supportive of the clinical importance of the impaired pathway in CFS patients has been provided. Studies addressing the treatment of the deregulation of the 2-5A synthetase/RNase L pathway in CFS are warranted.
Nijs J, Meeus M, McGregor NR, Meeusen R, de Schutter G, van Hoof E, de Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium.	Chronic fatigue syndrome: exercise performance related to immune dysfunction.	Med Sci Sports Exerc. 2005 Oct;37(10):1647-54.	PURPOSE: To date, the exact cause of abnormal exercise response in chronic fatigue syndrome (CFS) remains to be revealed, but evidence addressing intracellular immune deregulation in CFS is growing. Therefore, the aim of this cross-sectional study was to examine the interactions between several intracellular immune variables and exercise performance in CFS patients. METHODS: After venous blood sampling, subjects (16 CFS patients) performed a maximal exercise stress test on a bicycle ergometer with continuous monitoring of cardiorespiratory variables. The following immune variables were assessed: the ratio of 37 kDa Ribonuclease (RNase) L to the 83 kDa native RNase L (using a radiolabeled ligand/receptor assay), RNase L enzymatic activity (enzymatic assay), protein kinase R activity assay (comparison Western blot), elastase activity (enzymatic-colorimetric assay), the percent of monocytes, and nitric oxide determination (for monocytes and lymphocytes; flow cytometry, live cell assay). RESULTS: Forward stepwise multiple regression analysis revealed 1) that elastase activity was the only factor related to the reduction in oxygen uptake at a respiratory exchange ratio (RER) of 1.0 (regression model: $R = 0.53$, $F(1,14) = 15.5$, $P < 0.002$; elastase activity $P < 0.002$); 2) that the protein kinase R activity was the principle factor related to the reduction in workload at RER = 1.0; and

				3) that elastase activity was the principle factor related to the reduction in percent of target heart rate achieved. CONCLUSION: These data provide evidence for an association between intracellular immune deregulation and exercise performance in patients with CFS. To establish a causal relationship, further study of these interactions using a prospective longitudinal design is required.
Nijs J, Vaes P, De Meirleir K.	Department of Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel (VUB), Brussels, Belgium. Jo.Nijs@vub.ac.be	The Chronic Fatigue Syndrome Activities and Participation Questionnaire (CFS-APQ): an overview.	Occup Ther Int. 2005;12(2):107-21.	Chronic fatigue syndrome (CFS) is characterized by severe fatigue and a reduction in activity levels. The purpose of this study was to provide an overview of design, reliability, and validity of the CFS Activities and Participation Questionnaire (CFS-APQ). The CFS-APQ was constructed based on a retrospective analysis of the Karnofsky Performance Status Questionnaire and the Activities of Daily Living Questionnaire (n = 141). In a reliability study of 34 participants the test-retest reliability coefficient of the CFS-APQ was 0.95. In two different studies, the Cronbach alpha coefficient for internal consistency varied between 0.87 (n = 88) and 0.94 (n = 47). The CFS-APQ was administered to 47 patients who listed 183 activities that had become difficult due to their chronic symptoms, and 157 (85.8%) answers matched the content of the CFS-APQ. The outcome of a cross-sectional study (n = 88) studying the correlations between the Medical Outcomes Short Form 36 Health Status Survey subscale scores and the CFS-APQ supported the validity of the CFS-APQ. The CFS-APQ scores correlated with a behavioural assessment of the patients' performance of activities encompassed by the questionnaire (r = 0.29-0.55; n = 63), and correlated with exercise capacity parameters (r = 0.26-0.39; n = 77) obtained during a maximal exercise capacity stress test. Finally, the CFS-APQ correlated with visual analogue scales for pain (r = 0.51) and fatigue (r = 0.50; n = 47). It is concluded that the CFS-APQ generates reliable and valid data, and can be used as a clinical measure of disease severity in patients with CFS. Future studies should aim at examining the sensitivity of the CFS-APQ.
Nijs J, Van de Putte K, Louckx F, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Belgium. HUJo.Nijs@vub.ac.beUH	Employment status in chronic fatigue syndrome. A cross-sectional study examining the value of exercise testing and self-reported measures for the assessment of employment status.	Clin Rehabil. 2005 Dec;19(8):895-9.	OBJECTIVE: To examine the value of exercise testing and self-reported disability for the assessment of employment status in patients with chronic fatigue syndrome. DESIGN: Cross-sectional observational study. SETTING: A university-based chronic fatigue clinic. SUBJECTS: Fifty-four consecutive, Flemish, employed (not self-employed) chronic fatigue syndrome patients (49/54 female). INTERVENTIONS: Not applicable. MAIN OUTCOME MEASURES: Participants were questioned about their current and premorbid employment status, filled in the Chronic Fatigue Syndrome Activities and Participation Questionnaire (CFS-APQ), the Medical Outcomes Short Form 36 Health Status Survey (SF-36), and performed a maximal exercise test on a bicycle ergometer with continuous monitoring of cardiorespiratory variables. RESULTS: A significant association was observed between the current employment rate and two SF-36 subscales (i.e., role limitations due to physical functioning and social functioning; rho = 0.39 and 0.35 respectively) (n = 54). Analysing only the female chronic fatigue syndrome patients (n = 49), the current employment rate correlated significantly with the peak workload (rho = 0.38). CONCLUSIONS: The associations between either exercise testing or self-reported disability and employment status are too weak to predict employment status.
Nijs J, Van de Velde B, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy,	Pain in patients with chronic fatigue syndrome: does nitric oxide trigger central	Med Hypotheses. 2005;64(3):558-62.	Previous studies have provided evidence supportive of the clinical importance of widespread pain in patients with chronic fatigue syndrome (CFS): pain severity may account for 26-34% of the variability in the CFS patient's activity limitations and participation restrictions. The etiology of widespread pain in CFS remains to be elucidated, but sensitisation of the central nervous system has been suggested to take part of CFS pathophysiology. It is hypothesised that a nitric oxide (NO)-dependent reduction in

	Vrije Universiteit Brussel (VUB), Belgium. jo.nijs@vub.ac.be	sensitisation?		inhibitory activity of the central nervous system and consequent central sensitisation accounts for chronic widespread pain in CFS patients. In CFS patients, deregulation of the 2',5'-oligoadenylate synthetase/RNase L pathway is accompanied by activation of the protein kinase R enzyme. Activation of the protein kinase R and subsequent nuclear factor-kappaB activation might account for the increased production of NO, while infectious agents frequently associated with CFS (Coxsackie B virus, Epstein-Barr Virus, Mycoplasma) might initiate or accelerate this process. In addition, the evidence addressing behavioural changes in CFS patients fits the central sensitisation-hypothesis: catastrophizing, avoidance behaviour, and somatization may result in, or are initiated by sensitisation of the central nervous system.
Nijs J, Van Parijs M		CRITICAL REVIEWS AND COMMENTS ON CURRENT RESEARCH Long-Term Effectiveness of Pool Exercise Therapy and Education in Patients with Fibromyalgia	Journal of Chronic Fatigue Syndrome 2005 12 (3): 73 - 79	
Njoku MG, Jason LA, Torres-Harding SR.	Center for Community Research, Chronic Fatigue Research Study, Chicago, IL 60614, USA. HUnmgloria@depaul.eduUH	The relationships among coping styles and fatigue in an ethnically diverse sample.	Ethn Health. 2005 Nov;10(4):263-78.	The present study focused on coping strategies among African Americans, Latinos, and European Americans with chronic fatigue syndrome (CFS) and idiopathic chronic fatigue (ICF). The coping strategies examined were measured by using the COPE Scales, which assess Seeking Emotional Social Support, Positive Reinterpretation and Growth, Acceptance, Denial, Turning to Religion, Behavioral Disengagement, and Focusing on and Venting Emotions. In addition, the four coping strategies specifically designed for people with CFS, including maintaining activity, accommodating to the illness, focusing on symptoms, and information-seeking, were used in this study. It was hypothesized that African Americans and Latinos in comparison to European Americans would be more likely to use religious coping, behavioral disengagement, and denial. As predicted, African Americans were significantly more likely to turn to religion than European Americans, and Latinos and African Americans used denial significantly more often than European Americans. An additional finding was that focusing on symptoms was associated with greater fatigue and more physical disability among African Americans. Within the Latino sample, acceptance was related to greater fatigue and less physical disability, and greater optimism predicted less mental disability. Among European American participants, maintaining activity was related to less mental disability, whereas accommodating to the illness predicted more physical disability. These results indicate that coping varies among various ethnic groups with CFS and ICF; however, denial is consistently related to less adaptive outcomes. Therefore, healthcare professionals should find ways to reduce patient use of denial and promote alternative strategies for managing life events.
Ohayon MM.	Stanford Sleep Epidemiology	Prevalence and correlates of	Arch Intern Med. 2005 Jan	BACKGROUND: Nonrestorative sleep (NRS) has been little studied in the general population, even though this symptom has an important role in several medical conditions such as heart disease,

	Research Center, Stanford University School of Medicine, Stanford, Calif., USA. mohayon@stanford.edu	nonrestorative sleep complaints.	10;165(1):35-41.	fibromyalgia, and chronic fatigue syndrome, as well as various sleep disorders. METHODS: A total of 25,580 individuals (age range, 15-100 years) from the noninstitutionalized general population representative of 7 European countries (France, the United Kingdom, Germany, Italy, Portugal, Spain, and Finland) were interviewed by telephone using the Sleep-EVAL system. Nonrestorative sleep was analyzed in relationship to sociodemographic determinants, environmental factors, life habits, health, sleep-wake schedule, and psychological factors. RESULTS: The prevalence of NRS was 10.8% (95% confidence interval, 10.4%-11.2%) in the sample, was higher in women than in men (12.5% vs 9.0%; P<.001), and decreased with age. The United Kingdom (16.1%) and Germany (15.5%) had the highest prevalence of NRS and Spain (2.4%), the lowest. In multivariate analyses, several factors were positively associated with NRS. The most important were younger age, dissatisfaction with sleep, difficulty getting started in the morning, stressful life, presence of anxiety, bipolar or a depressive disorder, and having a physical disease. When compared with subjects who have difficulty initiating or maintaining sleep (without NRS), subjects with NRS reported more frequently a variety of daytime impairment (irritability, physical, and mental fatigue) and consulted a physician twice as frequently for their sleeping difficulties than did other subjects with insomnia. CONCLUSIONS: Nonrestorative sleep is a frequent symptom in the general population, but its prevalence largely varies between countries. It is often associated with mental disorders and characteristics of sleep deprivation (such as extra sleep time on weekends). Nonrestorative sleep affected more frequently the active classes of the population and caused greater daytime impairment than difficulty initiating or maintaining sleep.
Ong BN, Evans D, Bartlam A.	Health Services Research, Primary Care Sciences Research Centre, Keele University, Keele ST5 5BG. HUb.n.ong@keele.ac.ukUH	A patient's journey with myalgic encephalomyelitis.	BMJ. 2005 Mar 19;330(7492):648-50.	
Pall ML.		Nitric oxide and the etiology of chronic fatigue syndrome: giving credit where credit is due.	Med Hypotheses. 2005;65(3):631-3.	Letter
Patten SB, Beck CA, Kassam A, Williams JV, Barbui C, Metz LM.	Department of Community Health Sciences, University of Calgary, Alberta. patten@ucalgary.ca	Long-term medical conditions and major depression: strength of association for specific conditions in the general	Can J Psychiatry. 2005 Mar;50(4):195-202.	BACKGROUND: The prevalence of major depression (MD) in persons with nonpsychiatric medical conditions is an indicator of clinical need in those groups, an indicator of the feasibility of screening and case-finding efforts, and a source of etiologic hypotheses. This analysis explores the prevalence of MD in the general population in relation to various long-term medical conditions. METHODS: We used a dataset from a large-scale Canadian national health survey, the Canadian Community Health Survey (CCHS). The sample consisted of 115 071 subjects aged 18 years and over, randomly sampled from the Canadian population. The survey interview recorded self-reported diagnoses of various long-term

		population.		medical conditions and employed a brief predictive interview for MD, the Composite International Diagnostic Interview Short Form for Major Depression. Logistic regression was used to adjust estimates of association for age and sex. RESULTS: The conditions most strongly associated with MD were chronic fatigue syndrome (adjusted odds ratio [AOR] 7.2) and fibromyalgia (AOR 3.4). The conditions least strongly associated were hypertension (AOR 1.2), diabetes, heart disease, and thyroid disease (AOR 1.4 in each case). We found associations with various gastrointestinal, neurologic, and respiratory conditions. CONCLUSIONS: A diverse set of long-term medical conditions are associated with MD, although previous studies might have lacked power to detect some of these associations. The strength of association in prevalence data, however, varies across specific conditions.
Piche T, Vanbiervliet G, Cherikh F, Antoun Z, Huet PM, Gelsi E, Demarquay JF, Caroli-Bosc FX, Benzaken S, Rigault MC, Renou C, Rampal P, Tran A.	Department of Hepatogastroenterology, Chu de Nice, France. tpiche@fc.horus-medical.fr	Effect of ondansetron, a 5-HT3 receptor antagonist, on fatigue in chronic hepatitis C: a randomised, double blind, placebo controlled study.	Gut. 2005 Aug;54(8):1169-73.	BACKGROUND AND AIMS: There are no available effective therapies for fatigue associated with chronic hepatitis C (CHC). The serotonin antagonist ondansetron has been shown to be effective in the chronic fatigue syndrome. In this randomised, placebo controlled, double blind trial, we investigated the effect of orally administered ondansetron on fatigue in CHC. METHODS: Thirty six patients with CHC were included if fatigue was their predominant symptom and they scored more than 4 on a visual analogue scale (0-10). During the study, fatigue and depression were measured on days 0, 15, 30, and 60 using a validated self report questionnaire (fatigue impact scale and Beck depression inventory). Patients were randomised to receive ondansetron tablets 4 mg twice daily or placebo for one month followed by an additional four weeks of observation. RESULTS: Fatigue score was 85.4 (28.2) and 98.2 (26.9) in the ondansetron and placebo groups, respectively (NS). Ondansetron significantly reduced the fatigue score with more than 30% improvement on day 15 (57.1 (38.9); $p<0.01$), day 30 (54.5 (37.6); $p<0.01$), and day 60 (60.8 (37.3); $p<0.01$) whereas placebo did not. Overall, the reduction in fatigue was significantly higher with ondansetron compared with placebo (ANOVA for repeated measurements) for the whole follow up period ($p = 0.03$) or for the treatment period only ($p = 0.04$). Ondansetron also significantly reduced depression scores. CONCLUSIONS: The 5-hydroxytryptamine receptor type 3 antagonist ondansetron had a significant positive effect on fatigue in CHC. These observations support the concept that fatigue involves serotoninergic pathways and may encourage further evaluations of the efficacy of ondansetron on fatigue in chronic liver diseases.
Prins J, Bleijenberg G, Rouweler EK, van der Meer J.	Department of Psychology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. j.prins@mps.umcn.nl	Effect of psychiatric disorders on outcome of cognitive-behavioural therapy for chronic fatigue syndrome.	Br J Psychiatry. 2005 Aug;187:184-5.	Psychiatric disorders have been associated with poor outcome in individuals with chronic fatigue syndrome (CFS). This study examines the impact of psychiatric disorders on outcome of cognitive-behavioural therapy (CBT). Psychiatric diagnoses were assessed with a structured psychiatric interview in a CBT trial of 270 people with CFS. Lifetime and current psychiatric disorders were found in 50 and 32% respectively. No significant differences in fatigue severity and functional impairment following treatment were found between participants with and without psychiatric diagnoses.
Rakib A, White PD, Pinching AJ, Hedge B, Newbery N, Fakhoury WK,	Queen Mary's School of Medicine and Dentistry, Newham Centre	Subjective quality of life in patients with chronic fatigue syndrome.	Qual Life Res. 2005 Feb;14(1):11-9.	The aim of this study was to (1) assess Subjective Quality of Life (SQOL) of patients with Chronic Fatigue Syndrome (CFS) using a generic concept and to compare the findings with those in groups with mental disorders and healthy subjects, and (2) investigate whether and, if so, to what extent socio-demographic and clinical variables predict SQOL in CFS patients. Seventy-three patients diagnosed

Priebe S.	for Mental Health, London, UK.			with CFS were randomly selected and interviewed from two specialised clinics. CFS was diagnosed using the Oxford Criteria. SQOL was assessed on the Manchester Short Assessment of Quality of Life (MANSA) and Health-Related Quality of Life (HRQOL) on the Medical Outcome Study Short-Form 36 (MOS) SF-36. A battery of mood and symptom questionnaires, including the Symptom Checklist Questionnaire (SCL-90-R), was administered to assess various aspects of symptomatology as potential predictor variables. Multiple regression analyses were conducted to identify predictors of SQOL. Overall, SQOL was low in CFS patients and less favourable than in groups with mental disorders and healthy subjects. Satisfaction was particularly low with life as a whole, leisure activities and financial situation. Whilst SQOL was only moderately correlated with HRQOL, the SCL-90-R score, especially SCL-90-R Depression scale score, was the best predictor of SQOL explaining 35% of the variance. HRQOL and generic SQOL appear distinct despite some overlap. The findings underline that SQOL is significantly disrupted in CFS patients. Depressive symptoms are statistically the strongest 'predictor' of SQOL, although the direction of the relationship is not established. These data suggest that treatment of depression associated with CFS, regardless of causation, could help to improve SQOL in CFS patients.
Randall DC, Cafferty FH, Shneerson JM, Smith IE, Llewelyn MB, File SE.	Psychopharmacology Research Unit, Centre for Neuroscience Research, King's College London, London, UK.	Chronic treatment with modafinil may not be beneficial in patients with chronic fatigue syndrome.	J Psychopharmacol. 2005 Nov;19(6):647-60.	Fourteen patients (7 male, 7 female, 22-63 years), classified as having chronic fatigue syndrome (CFS), but without concurrent major depression, significant sleepiness or use of psychoactive medication, completed a double-blind, placebo-controlled, crossover study of the effects of the selective wakefulness-promoting agent, modafinil (200 and 400mg/day). The treatment periods were each 20 days, with washout periods of 2 weeks. The primary aim was to determine effects on cognition and the secondary aim was to determine effects on self-ratings of fatigue, quality of life and mood. Modafinil had mixed effects in two cognitive tasks. In a test of sustained attention, treatment with 200mg reduced the latency to correctly detect sequences, but 400mg increased the number of missed targets. In a test of spatial planning, the 200mg dose resulted in a slower initial thinking time for the easiest part of the task, whereas 400mg reduced the initial thinking time for the hardest part of the test. Lastly, in a test of mental flexibility and one of motor speed, patients performed worse whilst on modafinil (400mg), compared with the placebo period. No effects were observed on the performance of other psychometric tests or on self-ratings of fatigue, quality of life or mood, but this may have been due to insufficient statistical power. It is discussed whether the limited and mixed cognitive effects that we observed could have occurred by chance, or whether a subgroup of CFS patients with daytime sleepiness would have shown greater benefits.
Rangel L, Garralda ME, Jeffs J, Rose G.	Academic Unit of Child and Adolescent Psychiatry, Imperial College, London, UK.	Family health and characteristics in chronic fatigue syndrome, juvenile rheumatoid arthritis, and emotional disorders of childhood.	J Am Acad Child Adolesc Psychiatry. 2005 Feb;44(2):150-8.	OBJECTIVE: To compare family health and characteristics in children with chronic fatigue syndrome (CFS), in juvenile rheumatoid arthritis (JRA), and emotional disorders. METHOD: Parents of 28 children and adolescents aged 11 to 18 years with CFS, 30 with JRA, and 27 with emotional disorders (i.e., anxiety and/or depressive disorders) were recruited from specialty clinical settings and completed interviews and questionnaires assessing family health problems, parental mental distress, illness attitudes, and family burden of illness. RESULTS: Parents of children with CFS were significantly more likely than those of children with JRA to report a history of CFS-like illness, high levels of mental distress, and a tendency to experience functional impairment in response to physical symptoms. Families of children with CFS were characterized by significantly greater emotional involvement and

				reported greater family burden related to the child's illness in comparison with families of children with JRA. CONCLUSIONS: CFS in childhood and adolescence is associated with higher levels of parental CFS-like illness, mental distress, emotional involvement, and family illness burden than those observed in association with JRA, a chronic pediatric physical illness.
Ranjith G.	Department of Psychological Medicine, King's College Hospital, London, UK. g.ranjith@iop.kcl.ac.uk	Epidemiology of chronic fatigue syndrome.	Occup Med (Lond). 2005 Jan;55(1):13-9.	BACKGROUND: Chronic fatigue syndrome (CFS) is a controversial disorder with different case definitions, aetiological models and proposed treatments. An epidemiological approach is likely to bring some clarity to the field. AIM: The aim of this article is to review the literature on the epidemiology of fatigue, chronic fatigue and CFS. METHOD: A literature search was conducted using the databases Medline and Pubmed as well as the reference lists of recent reviews to identify the relevant studies. The aim was not to do a systematic review but to review the key studies in the area to highlight the methodological issues. RESULTS: The review is organized according to the following areas: the prevalence of fatigue and chronic fatigue, the prevalence and incidence of CFS, epidemiological associations such as gender, social class and psychiatric co-morbidity and CFS in special groups such as those recovering from a viral infection, specific occupational groups and Gulf War veterans. CONCLUSION: While fatigue as a symptom is very common, CFS is relatively rare. Many of the epidemiological associations seen in specialist clinics are not found in community samples. It is unlikely that one specific causal factor can explain CFS. Future studies should go beyond estimating the prevalence to testing more complex aetiological models.
Reeves WC, Wagner D, Nisenbaum R, Jones JF, Gurbaxani B, Solomon L, Papanicolaou DA, Unger ER, Vernon SD, Heim C.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. HUwcr1@cdc.govUH	Chronic fatigue syndrome--a clinically empirical approach to its definition and study.	BMC Med. 2005 Dec 15;3:19.	BACKGROUND: The lack of standardized criteria for defining chronic fatigue syndrome (CFS) has constrained research. The objective of this study was to apply the 1994 CFS criteria by standardized reproducible criteria. METHODS: This population-based case control study enrolled 227 adults identified from the population of Wichita with: (1) CFS (n = 58); (2) non-fatigued controls matched to CFS on sex, race, age and body mass index (n = 55); (3) persons with medically unexplained fatigue not CFS, which we term ISF (n = 59); (4) CFS accompanied by melancholic depression (n = 27); and (5) ISF plus melancholic depression (n = 28). Participants were admitted to a hospital for two days and underwent medical history and physical examination, the Diagnostic Interview Schedule, and laboratory testing to identify medical and psychiatric conditions exclusionary for CFS. Illness classification at the time of the clinical study utilized two algorithms: (1) the same criteria as in the surveillance study; (2) a standardized clinically empirical algorithm based on quantitative assessment of the major domains of CFS (impairment, fatigue, and accompanying symptoms). RESULTS: One hundred and sixty-four participants had no exclusionary conditions at the time of this study. Clinically empirical classification identified 43 subjects as CFS, 57 as ISF, and 64 as not ill. There was minimal association between the empirical classification and classification by the surveillance criteria. Subjects empirically classified as CFS had significantly worse impairment (evaluated by the SF-36), more severe fatigue (documented by the multidimensional fatigue inventory), more frequent and severe accompanying symptoms than those with ISF, who in turn had significantly worse scores than the not ill; this was not true for classification by the surveillance algorithm. CONCLUSION: The empirical definition includes all aspects of CFS specified in the 1994 case definition and identifies persons with CFS in a precise manner that can be readily reproduced by both investigators and clinicians.
Richards J, Turk J,	Child and Family	Children and	Eur Child Adolesc	BACKGROUND: Adolescents with Chronic Fatigue Syndrome (CFS) seen in specialist centres have

White S.	Clinic, Unit 5 Des Roches Square, Witan Way, Witney, OX28 4BE, Oxfordshire, UK.	adolescents with Chronic Fatigue Syndrome in non-specialist settings Beliefs, functional impairment and psychiatric disturbance.	Psychiatry. 2005 Sep;14(6):310-8.	substantial psychological and functional impairment. Beliefs about activity levels may be important in the development of CFS. METHOD: The aim was to investigate psychological and functional impairment, and beliefs in children and adolescents with CFS recruited from non-specialist services. A total of 30 such individuals participated, and 30 young people with Inflammatory Bowel Disease (IBD) formed the comparison group. RESULTS: Emotional symptoms and disorder were high in both groups. In all, 50% of those with CFS and 30% with IBD reached the threshold for emotional disorder according to the Strengths and Difficulties Questionnaire (SDQ) parent report, although this difference did not reach statistical significance. Participants with CFS scored statistically significantly higher on measures of functional impairment, including school non-attendance, compared to those with IBD. According to questionnaire responses, those with CFS were statistically significantly more likely to favour rest rather than exercise compared to those with IBD. Comparison of parental beliefs did not show such a difference. CONCLUSIONS: These young people with CFS were at high risk of psychiatric disorder. They were substantially disabled when compared to individuals with a known chronic illness. Also, as a group, they were characterised by a preference for rest rather than exercise.
Richards RS, McGregor NR, Roberts TK		Association Between Oxidative Damage Markers and Self-Reported Temporomandibular Dysfunction Symptoms in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2005 12 (3): 45 - 61	Full blood counts, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), haematinics and markers for oxidative stress were measured on thirty-three patients diagnosed with chronic fatigue syndrome (CFS) and twenty-seven age and sex matched controls. The CFS patients had increased prevalence of symptoms of temporomandibular dysfunction (TMD). Jaw muscle pain was associated with increases in methaemoglobin ($P < .002$), ferritin ($P < .02$) and malondialdehyde ($P < .007$) whilst temporomandibular joint (tmj) clicking and/or locking was associated with increases in methaemoglobin ($P < .001$), malondialdehyde ($P < .05$) and vitamin B12 ($P < .02$) levels. Multiple regression analysis found methaemoglobin to be the principle component associated with TMD symptoms in the CFS patients. Increases in scalar severity responses to jaw muscle pain and TMJ clicking and/or locking were positively correlated with methaemoglobin by multiple regression. These data indicate that oxidative stress due to excess free radical formation was associated with jaw muscle pain in CFS patients and suggest that these symptoms were likely to be associated with a pathogen-associated aetiology.
Rimes KA, Chalder T.	Department of Psychological Medicine, Institute of Psychiatry, London, UK. k.rimes@iop.kcl.ac.uk	Treatments for chronic fatigue syndrome.	Occup Med (Lond). 2005 Jan;55(1):32-9.	AIMS: To review studies evaluating the treatment of chronic fatigue and chronic fatigue syndrome, to describe predictors of response to treatment and to discuss the role of the occupational health physician. METHODS: A literature search was carried out using Medline and PsychInfo. RESULTS: Studies evaluating cognitive behaviour therapy, graded exercise therapy, pharmacological interventions (e.g. antidepressants and corticosteroids), immunological interventions and nutritional supplements were reviewed. The most promising results have been found with cognitive behaviour therapy and graded exercise therapy, and some predictors of outcome have been identified. Most of the other interventions were evaluated in just one or two studies and therefore evidence is insufficient to draw firm conclusions. CONCLUSIONS: By applying the models of fatigue that form the bases for cognitive behaviour therapy and graded exercise therapy, occupational health physicians may play an important role in helping the patients with chronic fatigue syndrome to reduce their symptoms, improve their functioning and return to work.
Robertson MJ,	Division of	Lymphocyte subset	Clin Exp Immunol.	Chronic fatigue syndrome (CFS) is a heterogeneous disorder of unknown aetiology characterized by

Schacterle RS, Mackin GA, Wilson SN, Bloomingdale KL, Ritz J, Komaroff AL.	Hematologic Malignancies, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA. mjrobert@iupui.edu	differences in patients with chronic fatigue syndrome, multiple sclerosis and major depression.	2005 Aug;141(2):326-32.	debilitating fatigue, along with other symptoms, for at least 6 months. Many studies demonstrate probable involvement of the central and autonomic nervous system, as well as a state of generalized immune activation and selective immune dysfunction in patients with CFS. The aim of this study was to compare the lymphocyte subsets of patients with chronic fatigue syndrome to those of patients with major depression and multiple sclerosis as well as those of healthy control subjects. No differences were found in total numbers of T cells, B cells or natural killer (NK) cells. However, differences were found in T, B and NK cell subsets. Patients with major depression had significantly fewer resting T (CD3(+)/CD25(-)) cells than the other groups. Patients with major depression also had significantly more CD20(+)/CD5(+) B cells, a subset associated with the production of autoantibodies. Compared to patients with multiple sclerosis, patients with CFS had greater numbers of CD16(+)/CD3(-) NK cells. Further study will be required to determine whether these alterations in lymphocyte subsets are directly involved in the pathophysiology of these disorders, or are secondary effects of the causal agent(s).
Rubin GJ, Hotopf M, Papadopoulos A, Cleare A.	Division of Psychological Medicine, Institute of Psychiatry and Guy's, King's and St. Thomas' School of Medicine, King's College London, London, UK. g.rubin@iop.kcl.ac.uk	Salivary cortisol as a predictor of postoperative fatigue.	Psychosom Med. 2005 May-Jun;67(3):441-7.	OBJECTIVE: Some patients with chronic fatigue syndrome (CFS) exhibit low basal cortisol levels, but it is not known whether low cortisol is a cause of CFS, predates the onset of CFS symptoms, or is an epiphenomenon caused by the behavioral changes typical of CFS. Because elective surgery is one of the few predictable risk factors for chronic fatigue, in this study, we followed a cohort of surgery patients from before to 6 months after their operation to test these theories. METHOD: One hundred sixty-one patients completed fatigue questionnaires and provided salivary cortisol samples before undergoing an elective inpatient surgical procedure, and then 2 days, 3 weeks, and 6 months afterward. RESULTS: Controlling for relevant demographic and surgical variables and for preoperative fatigue, low preoperative cortisol did not predict postoperative fatigue severity on any occasion ($p > .05$). Similarly, there was no correlation between low postoperative cortisol and postoperative fatigue severity at 3 weeks or 6 months ($p > .05$). Although 16 patients met our case definition for "chronic fatigue" at the 6-month follow up, low preoperative and low postoperative cortisol did not significantly predict fatigue caseness ($p > .05$). CONCLUSIONS: Any association between chronic fatigue and low cortisol would seem to develop after the onset of fatigue symptoms. Low cortisol is therefore unlikely to be the primary cause of chronic fatigue states.
Sanchez Rodriguez A, Gonzalez Marono C, Sanchez Ledesma M.	Servicio de Medicina Interna 1, Hospital Universitario de Salamanca, Salamanca.	[Chronic fatigue syndrome: a syndrome in search of definition] [Article in Spanish]	Rev Clin Esp. 2005 Feb;205(2):70-4.	
Segal TY, Hindmarsh PC, Viner RM.	University College London Hospitals, UK.	Disturbed adrenal function in adolescents with chronic fatigue syndrome.	J Pediatr Endocrinol Metab. 2005 Mar;18(3):295-301.	OBJECTIVE: To investigate adrenal function in children and adolescents with chronic fatigue syndrome (CFS) compared with age-matched controls. METHODS: Case-control study of low dose (500 ng/m2) synacthen tests (LDST) in 23 adolescents with CFS and 17 age-matched controls. Serum cortisol concentrations were measured at 5-min intervals from 10 to 45 minutes. Peak serum cortisol concentration, time to peak, rise in cortisol and area under the curve (AUC) were derived. RESULTS: Patients with CFS had significantly lower mean cortisol levels during the LDST ($p <0.001$), lower peak

				cortisol (p <0.025), reduced cortisol AUC (p <0.005) and longer time to peak cortisol (p <0.05). Abnormalities were seen in both sexes but were more pronounced in females. Unstimulated adrenal androgen and 17-hydroxyprogesterone concentrations were normal. CONCLUSIONS: Adolescents with CFS have subtle alterations in adrenal function suggesting a reduction in central stimulation of the adrenal glands. The more pronounced effects in females may reflect differential central effects of stress on hypothalamic-pituitary-adrenal axis regulation between the sexes.
Shephard RJ.	Faculty of Physical Education and Health and , Department of Public Health Sciences, Faculty of Medicine , University of Toronto, Toronto, ON, Canada.	Chronic fatigue syndrome. A brief review of functional disturbances and potential therapy.	J Sports Med Phys Fitness. 2005 Sep;45(3):381-92.	The chronic fatigue syndrome (CFS) is debilitating for both athletes and the general population. A review of etiology and mechanisms underlying functional disturbances is undertaken to provide a valid basis for therapeutic options. The review focuses on CFS as characterized by standard diagnostic criteria, building on previous reviews through use of articles identified by Medline search. Overtraining, a negative energy balance, excessive physical or environmental stress, disorders of personality and affect, dysfunction of the hypophyseal-pituitary adrenal axis, hormonal imbalance, nutritional deficits, immune suppression or activation and chronic infection have all been proposed as factors precipitating CFS, but none of these precipitants are observed consistently. Impairments of peak aerobic power and muscle strength, together with many functional disturbances, seem related to patient- or physician-imposed inactivity. Once CFS is established, treatment should aim at breaking the vicious cycle of effort avoidance, deterioration in physical condition and increasing fatigue through a combination of psychotherapy, general encouragement and a progressive exercise regimen.
Shin YI, Lee MS.	Department of Physical Medicine and Rehabilitation, Wonkwang University School of Medicine, Institute of Medical Science, Wonkwang University, Iksan 570-749, Republic of Korea.	Qi therapy (external qigong) for chronic fatigue syndrome: case studies.	Am J Chin Med. 2005;33(1):139-41.	The aim of this study was to examine the effects of Qi therapy (QT) on the symptoms of chronic fatigue syndrome (CFS), including fatigue and complications. QT affected the experience of mental and emotional relaxation in the subjects of these case studies, who also gained strength to overcome their pain and fatigue. Although the results of these two case studies may not constitute conclusive evidence, they provide a foundation for the exploration of QT as a complementary therapy in the reduction of negative symptoms of chronic fatigue syndrome.
Singal A, Kaur S, Tirkey N, Chopra K.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India.	Green tea extract and catechin ameliorate chronic fatigue-induced oxidative stress in mice.	J Med Food. 2005 Spring;8(1):47-52.	Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various body systems. The etiology of CFS remains unclear, but a number of studies have shown that oxidative stress may be involved in its pathogenesis. The present study was designed to investigate the protective effect of green tea extract (GTE) and catechin in the mouse model of CFS. Animals were subjected to a forced swimming test session of 6 minutes every day for 7 days; a significant increase in immobility time on successive days represented the CFS in mice. Biochemical analysis revealed that the chronic swim test significantly increased lipid peroxidation levels and decreased glutathione levels in mouse whole-brain homogenate. Treatment with GTE (25 or 50 mg/kg, i.p.) and catechin (50 or 100 mg/kg, i.p.) for 7 days reversed the increase in immobility time. Protection was correlated with the lowered levels of lipid peroxidation and

				restoration of reduced glutathione levels in the brains of fatigued mice. These findings strongly suggest the pivotal role of oxidative stress in the pathophysiology of CFS and that GTE and catechin could be used as potential agents in the management of CFS and warrant the inclusion of GTE and catechin in the treatment regimen of CFS patients.
Siniscalchi M, Iovino P, Tortora R, Forestiero S, Somma A, Capuano L, Franzese MD, Sabbatini F, Ciacci C.	Gastrointestinal Unit, Department of Clinical and Experimental Medicine, Federico II University of Naples, Italy.	Fatigue in adult coeliac disease.	Aliment Pharmacol Ther. 2005 Sep 1;22(5):489-94.	BACKGROUND: Fatigue is reported by many adults at the moment of diagnosis of coeliac disease and during follow-up. AIM: To evaluate the prevalence, characteristics and associations of fatigue in adult coeliac disease patients. METHODS: The investigated sample comprised adults from Campania, Italy. A total of 130 coeliac disease patients were consecutively recruited in both treated (59 on gluten-free diet) and untreated conditions (71 on normal diet). The control group was made up of 80 healthy controls. Coeliac disease patients and healthy controls underwent laboratory tests, a set of questionnaires for studying fatigue: visual analogue scale for fatigue, chronic fatigue syndrome questionnaire, fatigue severity scale and a modified version of the Zung self-rating depression scale. RESULTS: Coeliac disease patients showed a significantly lower body mass index than controls (P = 0.0001), lower serum iron (P = 0.04). The entire cohort of coeliac disease patients reported greater modified version of the Zung self-rating depression scale score (P = 0.001), greater visual analogue scale for fatigue score (P = 0.0001) and greater chronic fatigue syndrome questionnaire score (P = 0.0001) compared with healthy controls. Coeliac disease patients on a gluten-free diet had a significantly higher modified version of the Zung self-rating depression scale score than coeliacs on a normal diet (P = 0.001). The prevalence of pathological modified version of the Zung self-rating depression scale score was 17% in all coeliac disease patients and 0% in healthy controls. A significant correlation was found between modified version of the Zung self-rating depression scale score and fatigue scale scores in coeliacs on a normal diet. Presence/absence of gastrointestinal symptoms did not show any significant correlation with modified version of the Zung self-rating depression scale score and fatigue scale scores. In coeliacs on a gluten-free diet, modified version of the Zung self-rating depression scale and fatigue scales scores did not significantly differ from coeliacs on a normal diet and were not related to dietetic compliance. CONCLUSION: In coeliacs, fatigue is a common finding, which ameliorates with the gluten-free diet and is strictly correlated to depression although coeliacs on a gluten-free diet showed more frequent and more severe depression symptoms than coeliacs on a normal diet.
Smith J, Fritz EL, Kerr JR, Cleare AJ, Wessely S, Mattey DL.	Tissue Typing Laboratory, Harefield Hospital, Middlesex UB9 6JH, UK.	Association of chronic fatigue syndrome with human leucocyte antigen class II alleles.	J Clin Pathol. 2005 Aug;58(8):860-3.	BACKGROUND: A genetic component to the development of chronic fatigue syndrome (CFS) has been proposed, and a possible association between human leucocyte antigen (HLA) class II antigens and chronic fatigue immune dysfunction has been shown in some, but not all, studies. AIMS: To investigate the role of HLA class II antigens in CFS. METHODS: Forty nine patients with CFS were genotyped for the HLA-DRB1, HLA-DQA1, and HLA-DQB1 alleles and the frequency of these alleles was compared with a control group comprising 102 normal individuals from the UK. All patients and controls were from the same region of England and, apart from two patients, were white. RESULTS: Analysis by 2 x 2 contingency tables revealed an increased frequency of HLA-DQA1*01 alleles in patients with CFS (51.0% v 35%; odds ratio (OR), 1.93; p = 0.008). HLA-DQB1*06 was also increased in the patients with CFS (30.2% v 20.0%; OR, 1.73, p = 0.052). Only the association between HLA-DQA1*01 and CFS was significant in logistic regression models containing HLA-DQA1*01 and HLA-

				DRQB1*06, and this was independent of HLA-DRB1 alleles. There was a decreased expression of HLA-DRB1*11 in CFS, although this association disappeared after correction for multiple comparisons. CONCLUSIONS: CFS may be associated with HLA-DQA1*01, although a role for other genes in linkage disequilibrium cannot be ruled out.
Snell CR, Vanness JM, Strayer DR, Stevens SR.	University of the Pacific, Department of Sport Sciences, Stockton, CA 95211-0197, USA. snells@juno.com	Exercise capacity and immune function in male and female patients with chronic fatigue syndrome (CFS).	In Vivo. 2005 Mar-Apr;19(2):387-90.	Hyperactivition of an unwanted cellular cascade by the immune-related protein RNase L has been linked to reduced exercise capacity in persons with chronic fatigue syndrome (CFS). This investigation compares exercise capacities of CFS patients with deregulation of the RNase L pathway and CFS patients with normal regulation, while controlling for potentially confounding gender effects. Thirty-five male and seventy-one female CFS patients performed graded exercise tests to voluntary exhaustion. Measures of peak VO2, peak heart rate, body mass index, perceived exertion, and respiratory quotient were entered into a two-way factorial analysis with gender and immune status as independent variables. A significant multivariate main effect was found for immune status ($p < 0.01$), with no gender effect or interaction. Follow-up analyses identified VO2(peak) as contributing most to the difference. These results implicate abnormal immune activity in the pathology of exercise intolerance in CFS and are consistent with a channelopathy involving oxidative stress and nitric oxide-related toxicity.
Soderlund A, Malterud K.	Section for General Practice, Department of Public Health and Primary Health Care, University of Bergen, Norway. HUmpkat@msn.comUH	Why did I get chronic fatigue syndrome? A qualitative interview study of causal attributions in women patients.	Scand J Prim Health Care. 2005 Dec;23(4):242-7.	OBJECTIVES: To explore causal attributions among women with chronic fatigue syndrome (CFS). DESIGN: Qualitative study where data from individual semi-structured interviews were analysed according to Malterud's systematic text condensation. SETTING: Bergen, Norway. SUBJECTS: A purposeful sample of eight women aged 25-55, recruited among members of a self-help organization. MAIN OUTCOME MEASURES: Accounts of causal attribution for CFS among the informants, focusing on gender. RESULTS: The participants agreed that their way of living could have increased the vulnerability of their resistance resources. Pressure they put upon themselves, workload burdens without subsequent relaxation, emotional conflicts, or preparing for assumed problem-solving were mentioned as gendered dimensions. They presented different explanations regarding potential triggers encountering their fragile immune systems, most often a virus infection. The participants thought women might have a weaker immune system than men, or that CFS was caused by a virus that women are more likely to catch. In their experience, their symptoms were activated when people put pressure on them, such that they might be nervous as to whether they could live up to the demands of their surroundings, and in the case of emotional strain related to family and work. CONCLUSION: More studies are needed exploring hypotheses concerning the complex interplay between molecular predispositions and more or less gendered lifestyle issues in CFS. Doctors need to challenge their strong beliefs regarding medically unexplained conditions, where facts still remain unresolved. Recognizing this, the doctor may provide realistic support and advice, and contribute to the establishment of common ground for understanding and managing the condition.
Staevska M, Baraniuk JN.	Division of Rheumatology, Immunology and Allergy, Room B105, Georgetown	Persistent nonallergic rhinosinusitis.	Curr Allergy Asthma Rep. 2005 May;5(3):233-42.	Nonallergic rhinitis is a complex of syndromes that are united by the absence of atopic, T(H)2 lymphocyte, immunoglobulin E (IgE)-mediated mechanisms. We propose a classification system based on the presence or absence of inflammatory granulocytes. Eosinophilic nonallergic rhinosinusitis may also be called chronic eosinophilic sinusitis syndromes (CESS) to help classify these disorders in which diverse mechanisms of eosinophil chemoattraction and survival predominate. Allergic fungal sinusitis,

	University, Lower Level Kober-Cogan Building, 3800 Reservoir Road, NW, Washington, DC 20007-2197, USA.			eosinophilic nasal polyps, aspirin sensitivity, and related disorders would fit in this category. Accumulation of neutrophils occurs in chronic infectious rhinosinusitis, foreign body reactions, and immunodeficiencies. More complex and variable combinations of leukocytes are found in Wegner's granulomatosis and related syndromes, and during the evolution of viral infections. The noninflammatory disorders can be divided by mechanism into hormonal; sympathetic dysfunction (including antihypertensive adrenergic drug therapy); cholinergic rhinitis; and nociceptive syndromes with hyperalgesia and other features (eg, the nonallergic rhinitis of chronic fatigue syndrome). Therapy based on the most likely pathophysiologic mechanism is anticipated to have the most success, but requires acceptance of the wide differential diagnosis of nonallergic rhinitis and rejection of the obsolete term of "vasomotor rhinitis."
Staines D.	Gold Coast Public Health Unit, 10-12 Young Street, Southport 4215, Queensland, Australia. don_staines@health.qld.gov.au	Do vasoactive neuropeptide autoimmune disorders explain pyridostigmine's association with Gulf War syndrome?	Med Hypotheses. 2005;65(3):591-4.	Gulf War syndrome (GWS) is a perplexing multi-symptom condition comprising a constellation of signs and symptoms consistently described in the literature. These include muscle fatigue and tiredness, malaise, myalgia, impaired cognition, ataxia, diarrhoea, bladder dysfunction, sweating disturbances, headaches, fever, arthralgia, skin rashes, and gastrointestinal and sleep disturbances. Excessive chemical sensitivity and odour intolerance is reported. Epidemiological analysis suggests association with pyridostigmine bromide (PB) use as nerve gas prophylaxis, insect repellent, certain vaccination regimes, a variety of possible chemical exposures and physical and psychological stress. Pituitary adenylate cyclase-activating polypeptide (PACAP), calcitonin gene-related peptide (CGRP) and vasoactive intestinal peptide (VIP) are potent vasoactive (vasodilatory) neuropeptides (VNs) having pleiotropic functions as immunomodulators, neuroregulators and hormones. VNs also have neurotrophic and anti-apoptotic roles. VNs act on G protein-coupled receptors (GPCRs) to activate adenylate cyclase, an important step in cyclic AMP metabolism. Autoimmune dysfunction of these VNs or their receptors is postulated to give rise to fatigue-related conditions such as chronic fatigue syndrome (CFS). Complex mechanisms involving heat shock proteins (hsps) and cytosine-guanine dinucleotide (CpG) DNA fragments may also be associated with autoimmunity to VNs or their GPCRs in contributing to fatigue-related conditions. Dysfunction of certain VNs may be the missing link in explaining the nebulous nexus between PB and GWS. This paper explores a possible link between exposures to PB and other chemical, physical and psychological stressors in producing a fatigue-related illness possibly related to autoimmune dysfunction of certain VNs. Treatment options involving restoration of VN function are considered in the context of analogues with other neurotransmitter fatigue-related conditions such as myasthenia gravis (MG). While evidence associating these conditions is thin, vasoactive neuropeptide neurotransmitters of the VIP/PACAP family have acetylcholine co-transmission functions via specific GPCRs. Autoimmune reactions to these receptors may have parallels with muscarinic (e.g., Sjogren's syndrome) and nicotinic (e.g., MG) acetylcholine neurotransmission. Hence theoretically, treatment options such as thymectomy, corticosteroids, plasma exchange, anti-idiotype antibodies and receptor genomic expression reactivation/suppression may be considered. Paradoxically pyridostigmine may prove to have a role in therapy although VN treatment/replacement may be associated with tachyphylaxis.
Staines D.	Gold Coast Public Health Unit, 10-12	Are vasoactive neuropeptide	Med Hypotheses. 2005;65(1):29-31.	Vasoactive neuropeptides such as pituitary adenylate cyclase activating polypeptide (PACAP), calcitonin gene related peptide (CGRP) and vasoactive intestinal peptide (VIP) have been implicated in

	Young Street, Southport 4215, Qld., Australia. don_staines@health.qld.gov.au	autoimmune fatigue-related disorders mediated via G protein-coupled receptors?		a number of fatigue-related conditions. Associations of these vasoactive neuropeptides with heat shock proteins (hsps) and cytosine-guanosine dinucleotide (CpG) DNA fragments in autoimmune phenomena have been postulated to interfere with receptor signal activation for adenylate cyclase and other vital cellular processes. However, a specific mechanism for receptor dysfunction has not been explored to date. G protein-coupled receptors (GPCRs) constitute a high proportion of biological receptor mechanisms and serve a wide range of substances including nucleosides, nucleotides, catecholamines, calcium, histamine, serotonin and prostaglandins. They are complex transmembrane hepta-helical serpentine structures with specific binding capabilities resulting in conformational changes that activate cognate cyclic GMP (G proteins). GPCRs adapt to certain stimuli through desensitisation and changes in phosphorylation and are subject to distortions of signalling processes. Hence, these vital signalling structures are susceptible to impairment of function through a range of mechanisms. One of their vital functions is signalling through adenylate cyclase, a vital step in cyclic AMP metabolism. This step involves ATP metabolism and therefore is a crucial mediator of cellular energy pathways. Some GPCRs act to inhibit adenylate cyclase (Gi proteins). Also vasoactive neuropeptides, such as PACAP display a number of receptor isotypes including null variants. Overexpression of Gi proteins and null variant receptors may account for major disruptions of signal transduction and ATP/cAMP metabolism. This paper examines the possible role of GPCR dysfunction in contributing to fatigue-related vasoactive neuropeptide autoimmune disorders which may include chronic fatigue syndrome (CFS), Gulf War syndrome (GWS) and even sudden infant death syndrome (SIDS).
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport 4215, Queensland, Australia. don_staines@health.qld.gov.au	Therapeutic and preventive interventions for postulated vasoactive neuropeptide autoimmune fatigue-related disorders.	Med Hypotheses. 2005;65(4):797-803.	Major advances have been made in understanding the relatively novel group of vasoactive (vasodilatory) neuropeptides (VNs) in humans. VNs comprise a novel but expanding group of substances having immunoregulation, inflammation modulation, neurotransmitter, neurotrophic, hormonal and metabolic functions. These substances may control gene expression for mRNA for themselves and their receptors. They have complex relationships with gaseous and other neurotransmitters and xenobiotic substances. Theoretical arguments have implicated these substances in autoimmune phenomena resulting in fatigue-related conditions such as chronic fatigue syndrome (CFS), sudden infant death syndrome (SIDS), fibromyalgia (FM) and Gulf War syndrome (GWS) but remain unproven. As well as possibly spontaneous onset, the precipitating causes of VN autoimmune dysfunction are likely to be a combination of genetic predisposition, infection and xenobiotic substances. Therapeutic and preventive possibilities for postulated VN autoimmune conditions will be influenced by the complex pathophysiology underpinning them. Some speculative possibilities are VN substitution/replacement, preservation of biological effect, epigenetic DNA modifications, plasma exchange, anti-cholinesterases, e.g., pyridostigmine, corticosteroids and other drug treatments, thymectomy, intravenous immunoglobulin and anti-idiotype antibodies, and CpG/DNA vaccines. Prevention and treatment of possible VN autoimmune fatigue-related disorders may prove to be important areas for future research and development.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street,	Does dysregulation of key epigenetic and biochemical	Med Hypotheses. 2005;65(6):1154-60. Epub 2005 Jul	Autoimmune dysfunction of certain vasoactive neuropeptides (VNs) has been postulated as a contributing cause of sudden infant death syndrome (SIDS), chronic fatigue syndrome (CFS), Gulf War syndrome (GWS) and other fatigue-related disorders. This family of VNs includes pituitary adenylate

	Southport 4215, Queensland, Australia.	pathways occur in postulated vasoactive neuropeptide autoimmune disorders?	18.	cyclase activating polypeptide (PACAP), vasoactive intestinal peptide (VIP) and calcitonin gene related peptide (CGRP). The postulated mechanism is compromise of adenylate cyclase activation, a vital and unique step in cyclic AMP production from ATP, through autoimmune dysfunction of VNs, their receptors or their genes possibly involving cytosine-phosphate-guanine (CpG) fragments. CpG fragments are immunomodulatory dinucleotides serving as 'friend or foe' recognition systems to differentiate bacterial and viral (hypomethylated CpG) from mammalian (methylated CpG) DNA. However hypomethylation disorders affecting these fragments in mammals may convert them to dysfunctional states by promoting autoimmune inflammatory reactions. Epigenetic mechanisms acting on gene promoter regions may contribute to the development of VN autoimmune fatigue-related disorders through CpG fragments located in vital segments of VN/receptor genes by causing signalling defects with profound implications for VN function. Neurotransmitter dysfunction particularly glutamatergic transmission could also result with disruption of neuronal cellular biochemical functions such as ammonia regulation. Endosomal acidity and mitochondrial membrane potential modifiers such as chloroquine, together with immunoregulatory therapies, may have therapeutic implications in protecting against these apparent autoimmune disorders. This paper examines specific epigenetic and biochemical mechanisms possibly mediated by VN or receptor genes resulting in postulated VN autoimmune fatigue-related disorders. These mechanisms may have implications for treatment and prevention options for VN autoimmune disorders. VN autoimmune processes have implications for military medicine where radiological, chemical and biological agents may play an important role in pathogenesis.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport 4215, Qld., Australia. don_staines@health.qld.gov.au	Do cytosine guanine dinucleotide (CpG) fragments induce vasoactive neuropeptide mediated fatigue-related autoimmune disorders?	Med Hypotheses. 2005;65(2):370-3.	Autoimmune dysfunction of certain vasoactive neuropeptides (e.g., vasoactive intestinal peptide, pituitary adenylate cyclase activating polypeptide) may be implicated in a range of disorders associated with fatigue-like states (chronic fatigue syndrome, Gulf War syndrome) and even sudden infant death syndrome (SIDS). The important roles of these vasoactive neuropeptides make them a vulnerable target for autoimmune dysfunction. They are known to be associated with heat shock proteins for intracellular functioning with which they may form immunostimulating complexes. Cytosine guanine dinucleotide (CpG) fragments are potently immunogenic DNA fragments which serve as friend or foe recognition systems between bacterial (hypomethylated) and mammalian (methylated) DNA and are being assessed for suitability for use in human vaccines as adjuvants. Interactions between CpG fragments, heat shock proteins and vasoactive neuropeptides may be associated with fatigue-related autoimmune conditions.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport 4215, Qld, Australia. don_staines@health.qld.gov.au	Do vasoactive neuropeptides and heat shock proteins mediate fatigue-related autoimmune disorders?	Med Hypotheses. 2005;64(3):539-42.	Autoimmune dysfunction of certain vasoactive neuropeptides may be implicated in a range of disorders associated with fatigue like states (chronic fatigue syndrome, Gulf War syndrome) and even sudden infant death syndrome. These substances have neurotrophic, neuroregulatory, and neurotransmission functions, as well as that of immune modulators and hormones. They exert significant control over carbohydrate and lipid metabolism. The hypothesis is that because these substances have vital and indispensable roles in cellular processes, loss or compromise of these roles would lead to predictable and severe cellular and systemic effects. The important roles of certain VNs make them a vulnerable target for autoimmune dysfunction. They are known to be associated with heat shock proteins for intracellular functioning with which they may form immunostimulating

				complexes. While peptide-HSP complexes are a relatively new area for research, this paper asserts that attention could be focused on these substances and complexes in an effort to elucidate a number of perplexing fatigue-associated disorders.
Stang A, Korn K, Wildner O, Uberla K.	Department of Molecular and Medical Virology, Ruhr University Bochum, D-44780 Bochum, Germany.	Characterization of virus isolates by particle-associated nucleic acid PCR.	J Clin Microbiol. 2005 Feb;43(2):716-20.	Diagnostic virus isolation is still frequently used, particularly from respiratory tract secretions. Testing positive virus cultures for all possible viruses is time-consuming, and unexpected or unknown viruses may escape detection. Therefore, a novel random PCR approach was developed that allows sequence-independent amplification of viral nucleic acids from virus isolation-positive cultures. Selectivity for viral sequences is obtained by preferential isolation of nucleic acids that are particle associated and resistant to nucleases. Using primers with a degenerated 3' end, the isolated nucleic acids are amplified and the randomly amplified PCR products are cloned and sequenced. As proof of the concept, the PAN-PCR approach was applied to supernatants of coxsackievirus B3 and murine adenovirus type 1-infected cells. Enterovirus and adenovirus sequences were obtained, demonstrating that the random PCR approach allows detection of RNA and DNA viruses. As a first application of this PAN-PCR approach, we characterized a virus isolate from mouth-washing material of a patient with chronic fatigue syndrome and high antibody titers to coxsackievirus B2. The virus isolate had tested negative for enteroviruses and respiratory viruses (influenza viruses A and B, parainfluenza virus types 1 to 3, respiratory syncytial virus, and adenovirus) by immunofluorescence and PCR. Particle-associated, nuclease-resistant RNA and DNA were prepared from the supernatant of infected cells. The DNA and the reverse-transcribed RNA were randomly amplified, and PCR products were cloned and sequenced. Of 25 sequences obtained from the DNA preparation, 24 contained herpes simplex virus type 1 (HSV-1) sequences from 14 different loci spread over the HSV-1 genome. This result was confirmed by using a standard diagnostic HSV-PCR, demonstrating that the PAN-PCR correctly identified the virus isolate. Although the identification of HSV-1 in mouth-washing material is not surprising in retrospect, it clearly demonstrates the applicability of the PAN-PCR approach. This method should be particularly useful for characterizing virus isolates that have tested negative for all expected viruses and for identifying unknown viruses.
Stouten B.		Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution.	BMC Health Serv Res. 2005 May 13;5(1):37.	BACKGROUND: A recent article by Reeves et al. on the identification and resolution of ambiguities in the 1994 chronic fatigue syndrome (CFS) research case definition recommended the Checklist Individual Strength, the Chalder Fatigue Scale, and the Krupp Fatigue Severity Scale for evaluating fatigue in CFS studies. To be able to discriminate between various levels of severe fatigue, extreme scoring on the individual items of these questionnaires must not occur too often. METHODS: We derived an expression that allows us to compute a lower bound for the number of items with the maximum item score for a given study from the reported mean scale score, the number of reported subjects, and the properties of the fatigue rating scale. Several CFS studies that used the recommended fatigue rating scales were selected from literature and analyzed to verify whether abundant extreme scoring had occurred. RESULTS: Extreme scoring occurred on a large number of the items for all three recommended fatigue rating scales across several studies. The percentage of items with the maximum score exceeded 40% in several cases. The amount of extreme scoring for a certain scale varied from one study to another, which suggests heterogeneity in the selected subjects across studies. CONCLUSION: Because all three instruments easily reach the extreme ends of their scales on a

				large number of the individual items, they do not accurately represent the severe fatigue that is characteristic for CFS. This should lead to serious questions about the validity and suitability of the Checklist Individual Strength, the Chalder Fatigue Scale, and the Krupp Fatigue Severity Scale for evaluating fatigue in CFS research.
Stulemeijer M, de Jong LW, Fiselier TJ, Hoogveld SW, Bleijenberg G.	Expert Centre Chronic Fatigue, University Medical Centre Nijmegen, PO Box 9101, 6500 HB, Netherlands.	Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial.	BMJ. 2005 Jan 1;330(7481):14. Epub 2004 Dec 7.	OBJECTIVE: To evaluate the efficacy of cognitive behaviour therapy for adolescents aged 10-17 years with chronic fatigue syndrome. DESIGN: Randomised controlled trial. SETTING: Department of child psychology. PARTICIPANTS: 71 consecutively referred patients with chronic fatigue syndrome; 36 were randomly assigned to immediate cognitive behaviour therapy and 35 to the waiting list for therapy. INTERVENTION: 10 sessions of therapy over five months. Treatment protocols depended on the type of activity pattern (relatively active or passive). All participants were assessed again after five months. MAIN OUTCOME MEASURES: Fatigue severity (checklist individual strength), functional impairment (SF-36 physical functioning), and school attendance. RESULTS: 62 patients had complete data at five months (29 in the immediate therapy group and 33 on the waiting list). Patients in the therapy group reported significantly greater decrease in fatigue severity (difference in decrease on checklist individual strength was 14.5, 95% confidence interval 7.4 to 21.6) and functional impairment (difference in increase on SF-36 physical functioning was 17.3, 6.2 to 28.4) and their attendance at school increased significantly (difference in increase in percentage school attendance was 18.2, 0.8 to 35.5). They also reported a significant reduction in several accompanying symptoms. Self reported improvement was largest in the therapy group. CONCLUSION: Cognitive behaviour therapy is an effective treatment for chronic fatigue syndrome in adolescents.
Sullivan PF, Pedersen NL, Jacks A, Evengard B.	Department of Genetics, University of North Carolina at Chapel Hill, NC 27599-7264, USA. pfsulliv@med.unc.edu	Chronic fatigue in a population sample: definitions and heterogeneity.	Psychol Med. 2005 Sep;35(9):1337-48.	BACKGROUND: Numerous nosological decisions are made when moving from the common human symptom of unusual fatigue to the rare chronic fatigue syndrome (CFS). These decisions have infrequently been subjected to rigorous evaluation. METHOD: We obtained telephone interview data on fatiguing symptoms from 31406 individuals twins in the Swedish Twin Registry aged 42-64 years; 5330 subjects who endorsed fatigue and possessed no exclusionary condition formed the analytic group. We evaluated the definition and classification of CFS-like illness using graphical methods, regression models, and latent class analysis. RESULTS: Our results raise fundamental questions about the 1994 Centers for Disease Control criteria as (1) there was no empirical support for the requirement of four of eight cardinal CFS symptoms; (2) these eight symptoms were not equivalent in their capacity to predict fatigue; and (3) no combination of symptoms was markedly more heritable. Critically, latent class analysis identified a syndrome strongly resembling CFS-like illness. CONCLUSIONS: Our data are consistent with the 'existence' of CFS-like illness although the dominant nosological approach captures population-level variation poorly. We suggest that studying a more parsimonious case definition - impairing chronic fatigue not due to a known cause - would represent a way forward.
Swain NF, Kashikar-Zuck S, Brent Graham T, Prahalad S.	The Children's Hospital, Denver, CO 80218, USA. HUnicolefalvoswain@yahoo.comUH	Tender point assessment in juvenile primary fibromyalgia syndrome.	Arthritis Rheum. 2005 Oct 15;53(5):785-7.	

Theoharides TC, Papaliodis D, Tagen M, Konstantinidou A, Kempuraj D, Clemons A.		Chronic fatigue syndrome, mast cells, and tricyclic antidepressants.	J Clin Psychopharmacol. 2005 Dec;25(6):515-20.	Editorial
Thomas MA, Smith AP.	Centre for Occupational and Health Psychology, School of Psychology, Cardiff University, 63 Park Place, Cardiff, UK. HUthomasma@cf.ac.ukUH	Primary healthcare provision and Chronic Fatigue Syndrome: a survey of patients' and General Practitioners' beliefs.	BMC Fam Pract. 2005 Dec 13;6:49.	BACKGROUND: The current study was conducted as part of a research project into the evaluation and assessment of healthcare provision and education in Chronic Fatigue Syndrome (CFS). One aim of the study was the development of informative and educational literature for both General Practitioners (GP) and sufferers. Issues such as diagnosis, management and treatment of the syndrome should be included in information booklets written by healthcare professionals. It was important to begin the process by assessing the level of specialist knowledge that existed in typical GP surgeries. This data would then be compared to data from CFS patients. METHOD: 197 survey booklets were sent to CFS sufferers from an existing research panel. The patients approached for the purpose of the study had been recruited onto the panel following diagnosis of their illness at a specialised CFS outpatient clinic in South Wales. A further 120 booklets were sent to GP surgeries in the Gwent Health Authority region in Wales. RESULTS: Results from the study indicate that the level of specialist knowledge of CFS in primary care remains low. Only half the GP respondents believed that the condition actually exists. CONCLUSION: Steps are recommended to increase the knowledge base by compiling helpful and informative material for GPs and patient groups.
Tiev KP, Briant M, Ziani M, Cabane J, Demettre E, Lebleu B.		Variability of the RNase L isoform ratio (37 kiloDaltons/83 kiloDaltons) in diagnosis of chronic fatigue syndrome.	Clin Diagn Lab Immunol. 2005 Feb;12(2):366.	Letter
Tomoda A, Joudoi T, Rabab el-M, Matsumoto T, Park TH, Miike T.	Department of Child Development, School of Medicine, Kumamoto University, Kumamoto, Japan. atomoda@mclean.harvard.edu	Cytokine production and modulation: comparison of patients with chronic fatigue syndrome and normal controls.	Psychiatry Res. 2005 Mar 30;134(1):101-4.	We studied cytokine production in 15 patients with chronic fatigue syndrome (CFS) and 23 controls. CFS patients' peripheral blood mononuclear cells were cultured with lipopolysaccharide or phytohemagglutinin. Enzymatic immunoassay indicated cytokine concentration in culture supernatants. CFS patients showed significantly lower mRNA levels and transforming growth factor-beta1 (TGF-beta1) production. Cytokine dysregulation affects CFS pathogenesis. TGF-beta1 may aid treatment because it affects CFS inflammatory characteristics.
Torres-Harding SR, Jason LA, Dicle		Family Medical History of Persons	Journal of Chronic Fatigue Syndrome	Background: Little research has examined the family history of persons with CFS, although a few studies have found people with CFS may be more likely to have family members with fatigue or CFS-

Turkoglu O		with Chronic Fatigue Syndrome	2005 12 (4): 25-35	like conditions, cancers, autoimmune illness, and early parental death. Research into the family history of fatigue, chronic fatigue syndrome, and other medical or psychiatric illness may help inform the etiology of this illness. Objectives: The present investigation examined the occurrence of medical and psychiatric illness in the family history of persons with CFS, and then compared these results with the family history of medical illness reported by a control group of persons without fatigue. Methods: Family medical history data was obtained from questionnaire responses, a medical assessment, and medical records, and were then classified into specific illness categories, using the International Classification of Diseases, Tenth Revision (ICD-10). Family history data was compared among three groups using logistic regression analyses. Results: Results indicated that persons with chronic fatigue syndrome were significantly more likely to report a family history of endocrine/ metabolic disorders when compared to the control group. Conclusions: Findings suggest an underlying familial predisposition toward the development of both CFS and endocrine/metabolic disorders. This finding is consistent with the hypothesis that CFS represents a deregulation of the endocrine system.
Vallings R		Hypnosis in the Management of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2005 12 (4): 37-46	During the past 30 years hypnosis has become recognised as a useful adjunct to traditional medical therapies, and has become part of mainstream medicine. Hypnosis societies provide training for health professionals to obtain registrable qualifications. The modality has been incorporated in the management of many medical conditions and diseases, with opportunities for symptom control, building confidence and enhancing the benefits of regular therapies. There are many opportunities for using hypnosis as an adjunctive therapy in the management of Chronic Fatigue Syndrome, despite some early difficulties. Problems likely to be encountered are discussed and the structure of the hypnosis session is outlined. Suggestions are given for practitioners to construct useful scripts, which can be used to teach self-hypnosis.
Vallings R		CONFERENCE REPORTS Report on the AACFS 7th International Conference	Journal of Chronic Fatigue Syndrome 2005 12 (4): 61-79	
van de Putte EM, Engelbert RH, Kuis W, Sinnema G, Kimpen JL, Uiterwaal CS.	Department of Paediatrics, Wilhelmina Children's Hospital, University Medical Center, Utrecht, Netherlands. e.vandeputte@wkz.azu.nl	Chronic fatigue syndrome and health control in adolescents and parents.	Arch Dis Child. 2005 Oct;90(10):1020-4. Epub 2005 Jul 27.	AIMS: To explore the locus of health control in adolescents with chronic fatigue syndrome (CFS) and their parents in comparison with healthy adolescents and their parents. METHODS: In this cross-sectional study 32 adolescents with CFS were compared with 167 healthy controls and their respective parents. The Multidimensional Health Locus of Control (MHLC) questionnaire was applied to all participants. RESULTS: There was significantly less internal health control in adolescents with CFS than in healthy controls. An increase of internal health control of one standard deviation was associated with a 61% reduced risk for CFS (OR = 0.39, 95% CI 0.25 to 0.61). Internal health control of the parents was also protective (OR fathers: 0.57 (95% CI 0.38 to 0.87); OR mothers: 0.74 (95% CI 0.50 to 1.09)). The external loci of health control were higher in adolescents with CFS and in their parents. Increased levels of fatigue (56%) were found in the mothers of the adolescents with CFS, in contrast with the fathers who reported a normal percentage of 13. CONCLUSIONS: In comparison with healthy adolescents, adolescents with CFS and their parents show less internal health control. They attribute their health more to external factors, such as chance and physicians. This outcome is of relevance for

				treatment strategies such as cognitive behaviour therapy, for which health behaviour is the main focus.
van de Putte EM, Engelbert RH, Kuis W, Sinnema G, Kimpen JL, Uiterwaal CS.	Department of Paediatrics, Wilhelmina Children's Hospital, University Medical Center, Utrecht, Netherlands. HUe.vandeputte@wkz.azu.nlUH	Chronic fatigue syndrome and health control in adolescents and parents.	Arch Dis Child. 2005 Oct;90(10):1020-4. Epub 2005 Jul 27.	AIMS: To explore the locus of health control in adolescents with chronic fatigue syndrome (CFS) and their parents in comparison with healthy adolescents and their parents. METHODS: In this cross-sectional study 32 adolescents with CFS were compared with 167 healthy controls and their respective parents. The Multidimensional Health Locus of Control (MHLC) questionnaire was applied to all participants. RESULTS: There was significantly less internal health control in adolescents with CFS than in healthy controls. An increase of internal health control of one standard deviation was associated with a 61% reduced risk for CFS (OR = 0.39, 95% CI 0.25 to 0.61). Internal health control of the parents was also protective (OR fathers: 0.57 (95% CI 0.38 to 0.87); OR mothers: 0.74 (95% CI 0.50 to 1.09)). The external loci of health control were higher in adolescents with CFS and in their parents. Increased levels of fatigue (56%) were found in the mothers of the adolescents with CFS, in contrast with the fathers who reported a normal percentage of 13. CONCLUSIONS: In comparison with healthy adolescents, adolescents with CFS and their parents show less internal health control. They attribute their health more to external factors, such as chance and physicians. This outcome is of relevance for treatment strategies such as cognitive behaviour therapy, for which health behaviour is the main focus.
van de Putte EM, Uiterwaal CS, Bots ML, Kuis W, Kimpen JL, Engelbert RH.	Department of Pediatric, Wilhelmina Children's Hospital, University Medical Center Utrecht, Utrecht, Netherlands. e.vandeputte@wkz.azu.nl	Is chronic fatigue syndrome a connective tissue disorder? A cross-sectional study in adolescents.	Pediatrics. 2005 Apr;115(4):e415-22.	OBJECTIVES: To investigate whether constitutional laxity of the connective tissues is more frequently present in adolescents with chronic fatigue syndrome (CFS) than in healthy controls. Increased joint hypermobility in patients with CFS has been previously described, as has lower blood pressure in fatigued individuals, which raises the question of whether constitutional laxity is a possible biological predisposing factor for CFS. DESIGN: Cross-sectional study. PARTICIPANTS: Thirty-two adolescents with CFS (according to the criteria of the Centers for Disease Control and Prevention) referred to a tertiary hospital and 167 healthy controls. METHODS: The 32 adolescents with CFS were examined extensively regarding collagen-related parameters: joint mobility, blood pressure, arterial stiffness and arterial wall thickness, skin extensibility, and degradation products of collagen metabolism. Possible confounding factors (age, gender, height, weight, physical activity, muscle strength, diet, alcohol consumption, and cigarette smoking) were also measured. The results were compared with findings in 167 healthy adolescents who underwent the same examinations. RESULTS: Joint mobility, Beighton score, and collagen biochemistry, all indicators of connective tissue abnormality, were equal for both groups. Systolic blood pressure, however, was remarkably lower in patients with CFS (117.3 vs. 129.7 mm Hg; adjusted difference: -13.5 mm Hg; 95% confidence interval [CI]: -19.1, -7.0). Skin extensibility was higher in adolescents with CFS (mean z score: 0.5 vs. 0.1 SD; adjusted difference: 0.3 SD; 95% CI: 0.1, 0.5). Arterial stiffness, expressed as common carotid distension, was lower in adolescents with CFS, indicating stiffer arteries (670 vs 820 mum; adjusted difference: -110 mum; 95% CI: -220, -10). All analyses were adjusted for age, gender, body mass index, and physical activity. Additionally, arterial stiffness was adjusted for lumen diameter and pulse pressure. CONCLUSIONS: These findings do not consistently point in the same direction of an abnormality in connective tissue. Patients with CFS did have lower blood pressure and more extensible skin but lacked the most important parameter

				indicating constitutional laxity, ie, joint hypermobility. Moreover, the collagen metabolism measured by crosslinks and hydroxyproline in urine, mainly reflecting bone resorption, was not different. The unexpected finding of stiffer arteries in patients with CFS warrants additional investigation.
Van Hoof E, Coomans D, Cluydts R, De Meirleir K		Association Between Fennel Phase Inventory Scores and Immune and RNase-L Parameters in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2005 12 (2): 19 - 34	All patients suffering from a chronic condition, are challenged to manage the reality of their disease, the accompanying anxiety, the problems of daily living, and the effect on relationships. Therefore, when confronted with debilitating complaints, patients suffering from chronic fatigue syndrome (CFS) need to adapt to a new way of living during the course of their illness. Fennell developed an integrated model to manage CFS. This article is a follow-up of a study by Jason et al. (9, 10) to verify the existence of the different phases. Although not all differences are statistically significant, a clear distinction is made according to the conclusions drawn by Jason et al. (9, 10). Relationships between these distinctions and measures of symptoms, disability, psychological distress, coping, and immune parameters were revealed using non-parametric statistical tests.
Van Hoof E, De Meirleir K		The Influence of Chronic Fatigue Syndrome on the Personality Profile: A Case Report	Journal of Chronic Fatigue Syndrome 2005 12 (3): 63 - 71	Objective: Chronic fatigue syndrome (CFS) functionally impairs many patients. Despite numerous studies and reviews in CFS, little is known about the behavioral consequences. Several researchers have already suggested the influential role of personality as a possible predisposing or perpetuating factor. Method: Acase study is presented of a 34-year-old man with a history of CFS. Psychological profiling using the MMPI-2 was performed during the course of his condition. Results: His passive-aggressive manner during the medical encounter was underscored by his personality profile (code type 3-2). After his recovery, however, a spike 3 profile emerged indicating a fulfilled individual. Somatic items included in the inventory, created a secondary increase of the clinical scales. Physical complaints diminished as his condition improved and subsequently, decreased the clinical scales. Conclusion: The relevance of classifying personality characteristics in CFS patients as traits could not be supported by this case report.
Vernon SD, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA. svernon@cdc.gov	Evaluation of autoantibodies to common and neuronal cell antigens in Chronic Fatigue Syndrome.	J Autoimmune Dis. 2005 May 25;2:5.	People with chronic fatigue syndrome (CFS) suffer from multiple symptoms including fatigue, impaired memory and concentration, unrefreshing sleep and musculoskeletal pain. The exact causes of CFS are not known, but the symptom complex resembles that of several diseases that affect the immune system and autoantibodies may provide clues to the various etiologies of CFS. We used ELISA, immunoblot and commercially available assays to test serum from subjects enrolled in a physician-based surveillance study conducted in Atlanta, Georgia and a population-based study in Wichita, Kansas for a number of common autoantibodies and antibodies to neuron specific antigens. Subsets of those with CFS had higher rates of antibodies to microtubule-associated protein 2 (MAP2) ($p = 0.03$) and ssDNA ($p = 0.04$). There was no evidence of higher rates for several common nuclear and cellular antigens in people with CFS. Autoantibodies to specific host cell antigens may be a useful approach for identifying subsets of people with CFS, identify biomarkers, and provide clues to CFS etiologies.
Viner R, Christie D.	Middlesex Adolescent Unit, University College London Hospitals NHS Foundation Trust, London.	Fatigue and somatic symptoms.	BMJ. 2005 Apr 30;330(7498):1012 -5.	

	HUrviner@ich.ucl.ac.ukUH			
Vinjamury SP, Singh BB.	Southern California University of Health Sciences, Whittier, USA.	Ayurvedic treatment of chronic fatigue syndrome--a case report.	Altern Ther Health Med. 2005 Sep-Oct;11(5):76-8.	
Wagner D, Nisenbaum R, Heim C, Jones JF, Unger ER, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. dieter_krefeld@web.de	Psychometric properties of the CDC Symptom Inventory for assessment of chronic fatigue syndrome.	Popul Health Metr. 2005 Jul 22;3:8.	OBJECTIVES: Validated or standardized self-report questionnaires used in research studies and clinical evaluation of chronic fatigue syndrome (CFS) generally focus on the assessment of fatigue. There are relatively few published questionnaires that evaluate case defining and other accompanying symptoms in CFS. This paper introduces the self-report CDC CFS Symptom Inventory and analyzes its psychometric properties. METHODS: One hundred sixty-four subjects (with CFS, other fatiguing illnesses and non fatigued controls) identified from the general population of Wichita, Kansas were enrolled. Evaluation included a physical examination, a standardized psychiatric interview, three previously validated self-report questionnaires measuring fatigue and illness impact (Medical Outcomes Survey Short-Form-36 [MOS SF-36], Multidimensional Fatigue Inventory [MFI], Chalder Fatigue Scale), and the CDC CFS Symptom Inventory. Based on theoretical assumptions and statistical analyses, we developed several different Symptom Inventory scores and evaluated them on their ability to differentiate between participants with CFS and non-fatigued controls. RESULTS: The Symptom Inventory had good internal consistency and excellent convergent validity. A Total score (all symptoms), Case Definition score (CFS case defining symptoms) and Short Form score (6 symptoms with minimal correlation) differentiated CFS cases from controls. Furthermore, both the Case Definition and Short Form scores distinguished people with CFS from fatigued subjects who did not meet criteria for CFS. CONCLUSION: The Symptom Inventory appears to be a reliable and valid instrument to assess symptoms that accompany CFS. It is a positive addition to existing instruments measuring fatigue because it allows other dimensions of the illness to be assessed. Further research is needed to confirm and replicate the current findings in a normative population.
Wallman KE, Morton AR, Goodman C, Grove R.	Human Movement and Exercise Science, University of Western Australia, 35 Stirling Highway, Crawley, WA 6009. kwallman@cyllene.uwa.edu.au	Exercise prescription for individuals with chronic fatigue syndrome.	Med J Aust. 2005 Aug 1;183(3):142-3.	
Wang Q, Xiong JX.	The First Affiliated Hospital of Guangzhou University of TCM,	[Clinical observation on electroacupuncture for treatment of	Zhongguo Zhen Jiu. 2005 Oct;25(10):691-2.	OBJECTIVE: To observe clinical therapeutic effect of acupuncture at Back-shu acupoints of five zang-organs on chronic fatigue syndrome (CFS). METHODS: Forty cases of CFS were treated with electroacupuncture at main acupoints Back-shu, and Fatigue Assessment Instrument (FAI) and Mental State Self-rating Scale (SCL-90) were used for assessment of therapeutic effect. RESULTS: After

	Guangdong 510405, China. HUzxxjxl@hotmail.comUH	chronic fatigue syndrome] [Article in Chinese]		electroacupuncture treatment, clinical symptoms improved. The cumulative scores of FAI decreased from 148.36 +/- 26.53 before treatment to 98.63 +/- 28.36 after treatment (P < 0.01). And the scores of somatization, depression, anxiety and interpersonal relationship in SCL-90 reduced significantly (P < 0.01). CONCLUSION: Electroacupuncture has a definite therapeutic effect on chronic fatigue syndrome.
Wernham W, Pheby D, Saffron L.		SHORT COMMUNICATION /PILOT STUDIES Risk Factors for the Development of Severe ME/CFS–: A Pilot Study	Journal of Chronic Fatigue Syndrome 2005 12 (2): 47-50	The pilot phase is reported of a case-control study to determine risk factors for severe CFS/ME. One hundred fifty-seven members of the ME Association, selected at random, were sent postal questionnaires, with a 56% response. The Barthel index was used as a validated proxy measure to distinguish severe disease (cases) and those less severe. Thirteen of 88 respondents had severe disease, and 44 mild disease. Two matched controls from the 'mild' group were selected per case. Of possible risk factors, odds ratios greater than 2 were found for comorbidities, damaging initial treatment and occupational chemical exposure, although in this study they were not statistically significant. These data suggest that additional studies are warranted.
Wheatland R.	The Endocrine Research Project, 574 Sims Road, Santa Cruz, CA 95060, USA. rwheatla@query.com	Chronic ACTH autoantibodies are a significant pathological factor in the disruption of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome, anorexia nervosa and major depression.	Med Hypotheses. 2005;65(2):287-95.	Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis is a commonly recognized feature of many pathological conditions. Abnormal adrenal responses to experimental manipulation have been well documented in patients suffering from chronic fatigue syndrome, anorexia nervosa and major depression. Yet no defect of any single organ, gland or brain region has been identified as a cause of these abnormalities. The disruption of the HPA axis that occurs in these conditions can be understood if an interfering factor is present in these patients. Evidence indicates that this interfering factor is adrenocorticotropin hormone (ACTH) autoantibodies. Chronic high levels of ACTH autoantibodies will significantly disrupt the HPA axis and force the body to compensate for an impaired cortisol response. The resulting effect of chronic ACTH autoantibody interference is the manifestation of adrenocortical insufficient symptoms and psychological disturbances. Some symptoms of chronic fatigue syndrome, anorexia nervosa and major depression, such as anxiety, are the adverse effects of mechanisms compensating for less effective ACTH due to autoantibodies. Furthermore, these patients engage in extraordinary behaviors, such as self-injury, to increase their cortisol levels. When this compensation is inadequate, symptoms of adrenocortical insufficiency appear. Corticosteroid supplements have been demonstrated to be an effective treatment for chronic fatigue syndrome, anorexia nervosa and major depression. It allows the patients to have the corticosteroids they require for daily functioning and daily stressors. This therapy will relieve the patients of their symptoms of adrenocortical insufficiency and permit their cortisol-stimulating mechanisms to operate at levels that will not cause pathological problems.
Whistler T, Jones JF, Unger ER, Vernon SD.	Viral Exanthems and Herpesvirus Branch, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. taw6@cdc.gov	Exercise responsive genes measured in peripheral blood of women with chronic fatigue syndrome and matched control	BMC Physiol. 2005 Mar 24;5(1):5.	BACKGROUND: Chronic fatigue syndrome (CFS) is defined by debilitating fatigue that is exacerbated by physical or mental exertion. To search for markers of CFS-associated post-exertional fatigue, we measured peripheral blood gene expression profiles of women with CFS and matched controls before and after exercise challenge. RESULTS: Women with CFS and healthy, age-matched, sedentary controls were exercised on a stationary bicycle at 70% of their predicted maximum workload. Blood was obtained before and after the challenge, total RNA was extracted from mononuclear cells, and signal intensity of the labeled cDNA hybridized to a 3800-gene oligonucleotide microarray was measured. We identified differences in gene expression among and between subject groups before and after

		subjects.		exercise challenge and evaluated differences in terms of Gene Ontology categories. Exercise-responsive genes differed between CFS patients and controls. These were in genes classified in chromatin and nucleosome assembly, cytoplasmic vesicles, membrane transport, and G protein-coupled receptor ontologies. Differences in ion transport and ion channel activity were evident at baseline and were exaggerated after exercise, as evidenced by greater numbers of differentially expressed genes in these molecular functions. CONCLUSION: These results highlight the potential use of an exercise challenge combined with microarray gene expression analysis in identifying gene ontologies associated with CFS.
White PD, Nye KE, Pinching AJ, Yap TM, Power N, Vleck V, Bentley DJ, Thomas JM, Buckland M, Parkin JM		Immunological Changes After Both Exercise and Activity in Chronic Fatigue Syndrome: A Pilot Study	Journal of Chronic Fatigue Syndrome 2005 12 (2): 51-66	Background: The chronic fatigue syndrome (CFS) is characterized by post-exertional malaise and fatigue. We designed this pilot study to explore whether the illness was associated with alterations in immunological markers following exercise. Methods: We measured immunological markers before and up to three days after either a sub-maximal or maximal bicycle exercise test.We studied nine patients with CFS and nine ageand sex-matched healthy but sedentary controls. We also studied the same patients with CFS at home after a night's sleep and then after traveling to the study center. Results: There were no significant differences in any of the cell markers after a sub-maximal exercise test compared to a maximal test. However, we found elevated concentrations of plasma transforming growth factor beta (TGF-ß), even before exercise, in subjects with CFS (median (IQR) of 904 (182-1072) pg/ml) versus controls (median (IQR) of 50 (45-68) pg/ml) (P < .001). Traveling from home to the hospital significantly elevated TGF-ß concentrations from a resting median (IQR) concentration of 1161 (130-1246) pg/ml to a median (IQR) concentration of 1364 (1155-1768) pg/ml (P < .02). There was also a sustained increase in plasma tumor necrosis factor alpha (TNF-α) after exercise in CFS patients, but not in controls (P = .004 for the area under the curve), although traveling had no such effect. CD3, CD4 and HLA DR-expressing lymphocyte counts were lower in CFS patients, but exercise had the same effect in both groups, causing an immediate increase in circulating cell numbers that lasted less than three hours. Conclusions: These results suggest that the relationship between physical activity and both pro-inflammatory and anti-inflammatory cytokines merits further investigation in patients with CFS. The results also emphasize the importance of defining a truly resting baseline condition in such studies.
Whitehead LC.	University of Stirling Stornoway, UK.	Quest, chaos and restitution: Living with chronic fatigue syndrome/myalgic encephalomyelitis.	Soc Sci Med. 2005 Oct 15; [Epub ahead of print]	Chronic illness is disruptive, threatening people's sense of identity and taken for granted assumptions. Transformations in values, expectations and life priorities are likely to be experienced and in order to regain a coherent sense of self, people must interpret their experiences. People with difficult to diagnose illnesses can find themselves living with greater uncertainty and stigma. This paper explores how people with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) describe and interpret their illness experience by applying Arthur Frank's narrative typologies to analyse interviews with 17 British people with CFS/ME. The analysis proposes that a trajectory of narrative typologies is experienced, starting with a restitution narrative, moving to a chaos narrative and, for most, back to a restitution narrative and on to a quest narrative. The presentation of narrative types put forward by people living with CFS/ME differ to those presented by people who are HIV positive and have been treated for breast cancer.
Whitehead LC.	University of	Quest, chaos and	Soc Sci Med. 2005	Chronic illness is disruptive, threatening people's sense of identity and taken for granted

	Stirling Stornoway, UK.	restitution: Living with chronic fatigue syndrome/myalgic encephalomyelitis.	Oct 15; [Epub ahead of print]	assumptions. Transformations in values, expectations and life priorities are likely to be experienced and in order to regain a coherent sense of self, people must interpret their experiences. People with difficult to diagnose illnesses can find themselves living with greater uncertainty and stigma. This paper explores how people with chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) describe and interpret their illness experience by applying Arthur Frank's narrative typologies to analyse interviews with 17 British people with CFS/ME. The analysis proposes that a trajectory of narrative typologies is experienced, starting with a restitution narrative, moving to a chaos narrative and, for most, back to a restitution narrative and on to a quest narrative. The presentation of narrative types put forward by people living with CFS/ME differ to those presented by people who are HIV positive and have been treated for breast cancer.
Wright B, Ashby B, Beverley D, Calvert E, Jordan J, Miles J, Russell I, Williams C.	Lime Trees, Shipton Road, York, UK. barry.wright@sypct.nhs.uk	A feasibility study comparing two treatment approaches for chronic fatigue syndrome in adolescents.	Arch Dis Child. 2005 Apr;90(4):369-72.	
Yiu YM, Qiu MY.	School of Chinese Medicine, University of Hong Kong, Hong Kong, China. yoyo@hku.hk	[A preliminary epidemiological study and discussion on traditional Chinese medicine pathogenesis of chronic fatigue syndrome in Hong Kong] [Article in Chinese]	Zhong Xi Yi Jie He Xue Bao. 2005 Sep;3(5):359-62.	OBJECTIVE: Our purpose is to conduct an epidemiological study of chronic fatigue syndrome (CFS) and its syndrome types and symptoms of traditional Chinese medicine (TCM) among adults (20-50 years old) in Hong Kong, and to discuss the TCM pathogenesis. METHODS: Design: Cross-sectional questionnaire survey. Measures: Demographic data, CDC (1994) CFS diagnostic criteria, Trudie Chalder fatigue scale, and China national standard for TCM syndrome types criteria. Subjects: Twenty to fifty years old adults by convenient sampling. RESULTS: One thousand and thirteen subjects were successfully interviewed. Five hundred and eighty-five subjects (57.8%) had different levels of fatigue. Sixty-five subjects (6.4%) met CFS diagnostic criteria. In terms of TCM syndrome types, blood stasis due to qi deficiency had the highest prevalence (35.7%) among CFS. In the 54 symptoms investigated in total, the first eight symptoms in order of appearing rates were soreness of loins and weakness in knees, poor spirit, lassitude, pain, insomnia, forgetting, vessels blood stasis, vertigo and dazzle. The mostly appeared tongue figures were pale and corpulent or pale dim tongue proper, white and white greasy tongue coating, and the mostly appeared pulse figure was sunken-thin. CONCLUSION: The point prevalence of CFS among adults of 20 to 50 years old was found to be 6.4%. The most prevalent TCM syndrome type was blood stasis due to qi deficiency. The TCM pathogenesis of CFS was deficiency of origin, mainly deficiency of qi and kidney, with excess of superficiality.

2004				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Aboudiab T, Leke L, Skonieczny M, Chouraki JP.	Departement de pediatrie, unite de neonatologie, CHU, 80000 Amiens, France.	[Are IgE-independent food hypersensitivity and chronic fatigue syndrome related?][Article in French]	Arch Pediatr. 2004 Aug;11(8):975-977.	
Aceves-Avila FJ, Ferrari R, Ramos-Remus C.	Hospital General Regional No. 46, Instituto Mexicano del Seguro Social, Unidad de Investigacion en Enfermedades Cronico-Degenerativas SC, Guadalajara, Jalisco, Mexico.	New insights into culture driven disorders.	Best Pract Res Clin Rheumatol. 2004 Apr;18(2):155-71.	Rheumatologists frequently encounter patients whose illnesses lack face-value; that is, they lack the typical objective features of pathology that rheumatologists traditionally rely on for diagnosis and developing effective treatment approaches: namely fibromyalgia, chronic fatigue syndrome, Gulf War syndrome, chronic whiplash, chronic low back pain, etc. In this article, we examine this group of illnesses as culture-driven disorders to emphasize the central importance of various societal constraints in the ultimate presentation of patients with these illnesses. We will examine them by first understanding the purpose they serve, the underlying factors that compel societal institutions to sanctify these disorders as diseases, and how research is beginning to examine the behaviour that captures and packages these symptoms to produce their clinical presentation. With this research understanding, rheumatologists may be able to offer patients more useful action plans, but likely changes in societal approaches to the expressions of distress and changes in disability and compensation systems will also be required.
Adler RH.	University of Berne Medical School, Kehrsatz, Switzerland. rolf.adler@tele2.ch	Chronic fatigue syndrome (cfs).	Swiss Med Wkly. 2004 May 15;134(19-20):268-76.	The Chronic Fatigue Syndrome (CFS) is described based on the revision of Fukuda et al. The question "whether CFS can be discussed as a homogenous disorder?" has been reviewed and the answer is "no". Other overlapping syndromes are mentioned. Disorders with fatigue as a symptom are depression, somatisation, irritable bowel syndrome, effort-syndrome, hyperventilation, conservation-withdrawal. Among the pathogenetic factors of CFS immune systems disorders, neuroendocrine abnormalities, autonomic activity, neuroimaging, neuropsychological abnormalities, exercise capacity and muscle function and psychological processes (attribution, perception, symptom avoidance and neutralisation of conflicts) are discussed. Since CFS cannot be comprehended without knowledge of the ontogenetic development of the affect "fatigue", it is extensively described. Based on this knowledge, fatigue as an affect and the CFS are embedded in a context, which has as its basis the fight-flight reaction and the conservation-withdrawal reaction. Weighing the evidence, it is concluded that CFS in its varieties can best be understood as a manifestation of the activation of the two biological emergency reactions: fight-flight and conservation-withdrawal. The physician should interview and examine each individual patient according to the Harvey Cushing dictum: The physician should not only study the diseased organ, but the man with his diseased organ, and not only these. He should comprehend the man with his diseased organ in his environment. This leads to study of the biological, psychological and social factors contributing to each patient's illness. Work-up and therapy have to be based on this integrated approach. The latter encompasses conflict centred psychotherapy, stepwise increasing physical activation and antidepressive drugs.

Andersen MM, Permin H, Albrecht F.	Department of Infectious Diseases M5132, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark.	Illness and disability in Danish Chronic Fatigue Syndrome patients at diagnosis and 5-year follow-up.	J Psychosom Res. 2004 Feb;56(2):217-29.	OBJECTIVE: Evaluation of the life impact of Chronic Fatigue Syndrome (CFS) over 5 years. METHODS: Thirty-three adult patients meeting 1988 and 1994 CDC case criteria answered identical questionnaires at diagnosis and 5 years later, when a retrospective questionnaire was also completed. RESULTS: Work disability was very high and increased further, social isolation remained high, emotional adjustment improved. There were increased problems with reading and with allergies. Two measures of improvement were used: The relation between these measures was weak. Length of illness, extent of disability and emotional adjustment were poorly related to measures of improvement. Average illness scores were unchanged, but most individuals improved in some ways while worsening or remaining the same in others. Only one participant (3%) neared recovery, one other was substantially better but still severely disabled. CONCLUSION: CFS patients exhibit severe, long-term functional impairment. Substantial improvement is uncommon, less than 6%. Allergies and aspects of cognition may worsen, emotional adjustment often improves.
Arashima Y, Kato K, Komiya T, Kumasaka K, Matsukawa Y, Murakami M, Takahashi K, Ikeda T, Arakawa Y.	Department of Laboratory Medicine, Nihon University School of Medicine, Tokyo,	Improvement of chronic nonspecific symptoms by long-term minocycline treatment in Japanese patients with Coxiella burnetii infection considered to have post-Q fever fatigue syndrome.	Intern Med. 2004 Jan;43(1):49-54. Comment in: Intern Med. 2004 Jan;43(1):1-2.	OBJECTIVE: To address the presence of post-Q fever fatigue syndrome (post-QFS) in Japan, and to evaluate the efficacy of minocycline for this condition. PATIENTS AND METHODS: In 20 Coxiella burnetii (C. burnetii) seropositive patients with persistent nonspecific symptoms including general fatigue, low-grade fever, myalgia and arthralgia, changes in subjective symptoms, C. burnetii antibody titers and C. burnetii DNA were evaluated after antibiotic treatment. RESULTS: After treatment mainly with minocycline (100 mg/day for 3 months), the clinical picture improved in all 20 patients as evidenced by decreases in body temperature (13/17), general fatigue (20/20) and headache (9/12). The mean performance status (PS) score improved from 5.0 to 1.8 ($p<0.01$). All 7 who had been positive for C. burnetii DNA, became negative together with an improvement in subjective symptoms. Indirect immunofluorescence tests demonstrated 6 of the 20 patients to be positive for C. burnetii IgM antibody to phase II antigen (1:32), and 18 to be positive for IgG antibody (1:128, 1:256). Antibody titers of both IgM (6/6, 1:16) and IgG (18/18, 1:16) decreased markedly after treatment. CONCLUSION: These results of an open label study in Japan suggest that minocycline administration is useful for improving chronic nonspecific symptoms considered to be post-Q fever fatigue syndrome caused by C. burnetii infection.
Asbring P, Narvanen AL.	Stockholm Center of Public Health, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden.	Patient power and control: a study of women with uncertain illness trajectories.	Qual Health Res. 2004 Feb;14(2):226-40.	The authors interviewed 12 women diagnosed with chronic fatigue syndrome and 13 with fibromyalgia with the aim of determining the strategies they perceive themselves as using to gain control over their situation during the health care process. The results highlight various strategies that the women report applying to find a way of managing the illness and to influence caregivers. They describe, for example, how they try to gain control over their situation by acquiring knowledge about the illness. The women also describe various power strategies they use in their interaction with the caregivers to take command of their situation, namely exiting, noncompliance, confrontation, persuasion/insistence, making demands, and demonstrative distancing.
Ball N, Buchwald DS, Schmidt D, Goldberg J, Ashton S, Armitage R.	Virginia Mason Sleep Disorders Center, University of Washington,	Monozygotic twins discordant for chronic fatigue syndrome:	J Psychosom Res. 2004 Feb;56(2):207-12.	PURPOSE: Chronic fatigue syndrome (CFS) is characterized by profound fatigue accompanied by disturbances of sleep, cognition, mood, and other symptoms. Our objective was to describe sleep architecture in CFS-discordant twin pairs. METHODS: We conducted a co-twin control study of 22 pairs of monozygotic twins where one twin met criteria for CFS and the co-twin was healthy. Twins

	Seattle, WA, USA.	objective measures of sleep.		underwent two nights of polysomnography. RESULTS: The percentage of Stage 3 and REM sleep was greater among the CFS twins than their healthy co-twins (P< or = .05 for both), but no other differences in sleep architecture including sleep latency, REM latency, and total sleep time were observed. Compared to their co-twins, CFS twins had higher values for the apnea-hypopnea index and apnea-hypopnea arousal index (P< or =.05 for both). CONCLUSION: These results do not provide strong evidence for a major role for abnormalities in sleep architecture in CFS. Respiration appears impaired in CFS, but these clinical abnormalities cannot alone account for the prominence of sleep complaints in this illness. The co-twin control methodology highlights the importance of selecting well-matched control subjects.
Barlow JH, Ellard DR.	Interdisciplinary Research Centre in Health, School of Health and Social Sciences, Coventry University, Coventry, UK. j.barlow@coventry.ac.uk	Psycho-educational interventions for children with chronic disease, parents and siblings: an overview of the research evidence base.	Child Care Health Dev. 2004 Nov;30(6):637-45.	BACKGROUND: The role of psycho-educational interventions in facilitating adaptation to chronic disease has received growing recognition and is in keeping with policy developments advocating greater involvement of patients in their own care. The purpose of this paper is to provide an overview of the current literature regarding the effectiveness of psycho-educational interventions for children and adolescents with chronic disease, their parents and siblings. METHODS: Electronic searches were conducted using AMED, CINAHL, Cochrane Database, DARE, HTA, MEDLINE, NHS EED, PsycLIT, PsycINFO, and PubMED. Inclusion criteria were systematic reviews, meta-analyses and overviews based on traditional reviews of published literature. The titles of papers were reviewed, abstracts were obtained and reviewed, and full copies of selected papers were obtained. RESULTS: No reviews of psycho-educational interventions were found for either parents or siblings. Twelve reviews of interventions for children and adolescents were identified: chronic disease in general (three); chronic pain (one); asthma (three); chronic fatigue syndrome (CFS)/myalgic encephalomyelitis (ME) (one); diabetes (two); juvenile idiopathic arthritis (JIA) (one) and one informational intervention for paediatric cancer patients. The main focus was on disease management (particularly in asthma and diabetes) with less attention being paid to psychosocial aspects of life with a chronic condition. Overall, there is evidence of effectiveness for interventions incorporating cognitive-behavioural techniques on variables such as self-efficacy, self-management of disease, family functioning, psychosocial well-being, reduced isolation, social competence, knowledge, hope, pain (for chronic headache), lung function (asthma), days absent from school (asthma), visits to A & E (asthma), fatigue (CFS), and metabolic control (diabetes). A number of gaps and limitations were identified across all disease categories, such as inadequate description of interventions, small sample sizes, and lack of evidence regarding cost-effectiveness. CONCLUSION: This overview has highlighted the need to extend the evidence base for psycho-educational interventions, particularly in a UK context. It is essential that effective interventions are implemented and embedded in service provision in order to maximize empowerment through self-care for children, adolescents and their parents.
Baschetti R.		Cost-effectiveness of cognitive behaviour therapy for patients with chronic fatigue syndrome. [Letter]	QJM. 2004 Jun;97(6):378-9.	

Baschetti R.		Chronic fatigue syndrome, pregnancy, and Addison disease.	Arch Intern Med. 2004 Oct 11;164(18):2065. Comment on: Arch Intern Med. 2004 Feb 23;164(4):401-4.	
Bates MN, Fawcett J, Garrett N, Cutress T, Kjellstrom T.	Institute of Environmental Science and Research Ltd. (ESR), PO Box 50-348, Porirua, New Zealand.	Health effects of dental amalgam exposure: a retrospective cohort study.	Int J Epidemiol. 2004 Aug;33(4):894-902. Epub 2004 May 20.	BACKGROUND: Whether dental amalgam fillings (containing mercury) are hazardous is a long-standing issue, with few epidemiological investigations. Allegations have particularly involved nervous system disorders, such as multiple sclerosis, Alzheimer's disease, and chronic fatigue syndrome. This retrospective cohort study, the largest of its kind, contained people in the New Zealand Defence Force (NZDF) between 1977 and 1997. The NZDF has its own dental service, providing all personnel with regular and consistent treatment. Comprehensive treatment records are maintained and archived. METHODS: Yearly dental treatment histories, including amalgam filling placements, were compiled from individual records. To minimize amalgam exposure misclassification the cohort was restricted to people who, at NZDF entry, were aged <26 years and had all their posterior teeth. The cohort was linked with morbidity records. Data were analysed with a proportional hazards model, using a time-varying exposure unit of 100 amalgam surface-years. RESULTS: The final cohort contained 20 000 people, 84% males. Associations with medical diagnostic categories, particularly disorders of the nervous system and kidney, were examined. Of conditions allegedly associated with amalgam, multiple sclerosis had an adjusted hazard ratio (HR) of 1.24 (95% CI: 0.99, 1.53, P = 0.06), but there was no association with chronic fatigue syndrome (HR = 0.98, 95% CI: 0.94, 1.03), or kidney diseases. There were insufficient cases for investigation of Alzheimer's or Parkinson's diseases. CONCLUSIONS: Results were generally reassuring, and provide only limited evidence of an association between amalgam and disease. Further follow-up of the cohort will permit investigation of diseases more common in the elderly.
Benca RM, Ancoli-Israel S, Moldofsky H.	University of Wisconsin, Madison, USA.	Special considerations in insomnia diagnosis and management: depressed, elderly, and chronic pain populations.	J Clin Psychiatry. 2004;65 Suppl 8:26-35.	Patients with insomnia who also have chronic pain or depression or who are elderly represent segments of the population that are particularly difficult to treat. These populations tend to be at higher risk for experiencing difficulty sleeping and are more likely to experience chronic insomnia, sleep maintenance problems, and/or nonrestorative sleep. Worsening insomnia may exacerbate other somatic and psychological symptoms and vice versa. Conversely, there is evidence that appropriate recognition and management of the sleep complaint may alleviate other symptoms related to the associated condition and help interrupt this vicious cycle.
Berger J.		On chronic fatigue syndrome. Comment on: Am J Psychiatry. 2003 Feb;160(2):221-36.	Am J Psychiatry. 2004 Jun;161(6):1133; author reply 1133-4.	
Bierl C, Nisenbaum R, Hoaglin DC,	Division of Viral and Rickettsial	Regional distribution of	Popul Health Metr. 2004 Feb 4;2(1):1.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating illness with no known cause or effective therapy. Population-based epidemiologic data on CFS prevalence are critical to put CFS in a

Randall B, Jones AB, Unger ER, Reeves WC.	Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. wcr1@cdc.gov	fatiguing illnesses in the United States: a pilot study.		realistic context for public health officials and others responsible for allocating resources. METHODS: We conducted a pilot random-digit-dialing survey to estimate the prevalence of fatiguing illnesses in different geographic regions and in urban and rural populations of the United States. This report focuses on 884 of 7,317 respondents 18 to 69 years old. Fatigued (440) and randomly selected non-fatigued (444) respondents completed telephone questionnaires concerning fatigue, other symptoms, and medical history. RESULTS: We estimated 12,186 per 100,000 persons 18 to 69 years of age suffered from fatigue lasting for at least 6 months (chronic fatigue), and 1,197 per 100,000 described an illness that, though lacking clinical evaluation, met criteria for CFS (CFS-like). Chronic fatigue and CFS-like illness were more common in rural than in urban populations, although the differences were not significant. The prevalence of these fatiguing illnesses did not differ meaningfully among the four regions surveyed, and no significant geographic trends were observed. CONCLUSIONS: This investigation estimated that nearly 2.2 million American adults suffer from CFS-like illness. The study also suggested the need to focus future investigations of fatigue on populations with lower incomes and less education. There was no evidence for regional differences in the occurrence of fatiguing illnesses.
Blacker CV, Greenwood DT, Wesnes KA, Wilson R, Woodward C, Howe I, Ali T.	Department of Health and Social Sciences, University of Exeter, Exeter, England. c.v.r.blacker@btinternet.com	Effect of galantamine hydrobromide in chronic fatigue syndrome: a randomized controlled trial.	JAMA. 2004 Sep 8;292(10):1195-204.	CONTEXT: There is no established pharmacological treatment for the core symptoms of chronic fatigue syndrome (CFS). Galantamine hydrobromide, an acetyl cholesterone inhibitor, has pharmacological properties that might benefit patients with CFS. OBJECTIVE: To compare the efficacy and tolerability of galantamine hydrobromide in patients with CFS. DESIGN, SETTING, AND PATIENTS: Randomized, double-blind trial conducted June 1997 through July 1999 at 35 outpatient centers in the United Kingdom (n = 17), United States (n = 14), the Netherlands (n = 2), Sweden (n = 1), and Belgium (n = 1) involving 434 patients with a clinical diagnosis of CFS (modified US Centers for Disease Control and Prevention criteria). INTERVENTIONS: A total of 89 patients were randomly assigned to receive 2.5 mg of galantamine hydrobromide; 86 patients, 5.0 mg; 91 patients, 7.5 mg; and 86 patients, 10 mg (these patients received medicine in the tablet form 3 times per day); a total of 82 patients received matching placebo tablets 3 times per day. MAIN OUTCOME MEASURES: The primary efficacy variable was the global change on the Clinician Global Impression Scale after 4, 8, 12, and 16 weeks of treatment. Secondary outcomes were changes in core symptoms of CFS on the Chalder Fatigue Rating Scale, the Fibromyalgia Impact Questionnaire, and the Pittsburgh Sleep Quality Index; changes in quality of life on the Nottingham Health Profile; and assessment of plasma-free cortisol levels and cognitive performance on a computer-based battery of tests. RESULTS: After 16 weeks, there were no statistically significant differences between any of the galantamine or placebo groups in clinical condition on the Clinician Global Impression Scale, or for any of the secondary end points. Exploratory regression analysis failed to detect any consistent prognostic factor that might have influenced the primary or any secondary outcome measures. CONCLUSION: This trial did not demonstrate any benefit of galantamine over placebo in the treatment of patients with CFS.
Bobo WV, Hall WC.		On chronic fatigue syndrome. Comment on: Am J Psychiatry. 2003	Am J Psychiatry. 2004 Jun;161(6):1132-3; author reply 1133-	

		Feb;160(2):221-36.	4.	
Bruera E, Moyano JR, Sala R, Rico MA, Bosnjak S, Bertolino M, Willey J, Strasser F, Palmer JL.	Department of Palliative Care & Rehabilitation Medicine, The University of Texas MD Anderson Cancer Center, Houston 77030, USA.	Dexamethasone in addition to metoclopramide for chronic nausea in patients with advanced cancer: a randomized controlled trial.	J Pain Symptom Manage. 2004 Oct;28(4):381-8.	Chronic nausea occurs in most patients with advanced cancer. This study was done to assess the antiemetic effects of dexamethasone in patients with chronic nausea refractory to metoclopramide. Secondary outcomes included appetite, fatigue, and pain. Fifty-one patients who had nausea (> or = 3/10 on a 0-10 scale) for > or = 2 weeks despite 48 hours of oral metoclopramide therapy (40-60 mg/day) were enrolled. Patients received 20 mg/day dexamethasone (DM) orally (n = 25) or placebo (n = 26) for severe nausea in addition to metoclopramide (60 mg/day orally). At baseline the mean nausea intensity ratings in the DM and placebo groups were 8.0 and 7.4. At Day 8 they were 2.1 and 2.0, respectively. At Day 3 and Day 8, the mean difference in nausea intensity for the DM and placebo groups was 4.5 and 2.9 (P = 0.16) and 5.9 and 5.7 (P = 0.85), respectively. Improvement in appetite and fatigue were observed on Day 3 and Day 8 in both groups as compared with the baseline. Pain, vomiting, well-being, and quality of life remained unchanged in both groups at both times. We conclude that DM was not superior to placebo in the management of chronic nausea in our patients with advanced cancer.
Brustia D, Uglietti A, Garavelli PL.	SCDO Malattie Infettive, Azienda Sanitaria Ospedaliera Maggiore della Carita, Novara.	[Polyneuritis cranialis HHV-6 infection associated][Article in Italian]	Recenti Prog Med. 2004 May;95(5):257-8.	Human herpesvirus 6 (HHV-6) has been shown to be a common cause of acute febrile disease in young children, including exanthema subitum. HHV-6 has also been associated with a number of neurologic disorders including encephalitis and the virus has been postulated to play a role in acquired immunodeficiency syndrome, multiple sclerosis and chronic fatigue syndrome. The disorder of multiple cranial nerve palsies without spinal cord involvement is referred to as polyneuritis cranialis and is rare. The Authors describe a case of polyneuritis cranialis in a 52-year old woman treated with ganciclovir and only complete eradication of the virus.
Burnet RB, Chatterton BE.		Gastric Emptying is Slow in Chronic Fatigue Syndrome.	BMC Gastroenterol. 2004 Dec 26;4(1):32 [Epub ahead of print]	BACKGROUND: Gastrointestinal symptoms are common in patients with Chronic Fatigue Syndrome (CFS). The objective of this study was to determine the frequency of these symptoms and explore their relationship with objective (radionuclide) studies of upper GI function. METHODS: Thirty-two (32) patients with CFS and 45 control subjects completed a questionnaire on upper GI symptoms, and the 32 patients underwent oesophageal clearance, and simultaneous liquid and solid gastric emptying studies using radionuclide techniques compared with historical controls. RESULTS: The questionnaires showed a significant difference in gastric ($p>0.01$) symptoms and swallowing difficulty. Nocturnal diarrhoea was a significant symptom not previously reported. 5/32 CFS subjects showed slightly delayed oesophageal clearance, but overall there was no significant difference from the control subjects, nor correlation of oesophageal clearance with symptoms. 23/32 patients showed a delay in liquid gastric emptying, and 12/32 a delay in solid gastric emptying with the delay significantly correlated with the mean symptom score (for each $p<<0.001$). CONCLUSION: GI symptoms in patients with chronic fatigue syndrome are associated with objective changes of upper GI motility.
Busichio K, Tiersky LA, Deluca J, Natelson BH.	Chronic Fatigue Syndrome Center, Newark, New Jersey 07666, USA.	Neuropsychological deficits in patients with chronic fatigue syndrome.	J Int Neuropsychol Soc. 2004 Mar;10(2):278-85.	The degree of neuropsychological dysfunction across multiple domains was examined in individuals suffering from chronic fatigue syndrome (CFS). In this descriptive study, a similar series of neuropsychological tests was administered to a group of CFS patients and healthy participants. More specifically, CFS patients (n = 141) who met the 1994 Case Definition criteria were compared to 76 healthy control participants on tests of memory, attention (concentration), speed of information processing, motor speed, and executive functioning. On the 18 measures administered, CFS patients

				scored 1 standard deviation below the healthy mean on nine measures and scored 2 standard deviations below the healthy mean on four of the measures. Moreover, results indicated that CFS patients were more likely than healthy controls to fail (1.6 SD below the healthy mean) at least one test in each of the following domains: attention, speed of information processing, and motor speed, but not on measures of memory and executive functioning. Finally, CFS patients demonstrated a greater total number of tests failed across domains.
Busichio K, Tiersky LA, Deluca J, Natelson BH.	Chronic Fatigue Syndrome Center, Newark, New Jersey.	Neuropsychological deficits in patients with chronic fatigue syndrome.	J Int Neuropsychol Soc. 2004 Feb;:278-285. [Epub ahead of print]	The degree of neuropsychological dysfunction across multiple domains was examined in individuals suffering from chronic fatigue syndrome (CFS). In this descriptive study, a similar series of neuropsychological tests was administered to a group of CFS patients and healthy participants. More specifically, CFS patients (n = 141) who met the 1994 Case Definition criteria were compared to 76 healthy control participants on tests of memory, attention (concentration), speed of information processing, motor speed, and executive functioning. On the 18 measures administered, CFS patients scored 1 standard deviation below the healthy mean on nine measures and scored 2 standard deviations below the healthy mean on four of the measures. Moreover, results indicated that CFS patients were more likely than healthy controls to fail (1.6 SD below the healthy mean) at least one test in each of the following domains: attention, speed of information processing, and motor speed, but not on measures of memory and executive functioning. Finally, CFS patients demonstrated a greater total number of tests failed across domains. (JINS, 2004, 10, 278285.)
Candy B, Chalder T, Cleare AJ, Wessely S, Hotopf M.	Department of Psychological Medicine, Guy's, King's and St. Thomas' School of Medicine, 103 Denmark Hill, London SE5 8AZ, UK.	A randomised controlled trial of a psycho-educational intervention to aid recovery in infectious mononucleosis.	J Psychosom Res. 2004 Jul;57(1):89-94.	OBJECTIVES: Glandular fever is associated with an approximate fivefold increase in fatigue at 6 months. Reduced levels of fitness and illness beliefs may be important predictors of fatigue following glandular fever. We therefore developed a brief psycho-educational intervention aimed at improving recovery from infectious mononucleosis, and piloted a randomised controlled trial to evaluate the intervention. METHODS: We performed a randomised-controlled trial in primary health care in Southeast London and Kent. Sixty-nine patients aged between 16 and 45 years who were diagnosed, serologically and clinically, with acute infectious mononucleosis between December 1999 and December 2000 were randomised. The control group received a standardised fact-sheet about infectious mononucleosis, which gave no advice on rehabilitation. Patients who were randomised to the intervention received an individual treatment session, two follow-up telephone calls, and an information booklet. Fatigue score 6 months after the onset of infectious mononucleosis was the main outcome measure. RESULTS: Sixty-nine out of 139 patients referred were recruited and randomised. Eighty-seven percent of those recruited completed the Fatigue Questionnaire at 6 months. The intervention was acceptable to all who received it. There were fewer fatigue cases in the intervention group than the control group at 6 months follow-up (odds ratio 0.31, 95% confidence interval 0.09-0.91). CONCLUSIONS: A brief intervention at the diagnosis of infectious mononucleosis is acceptable, and may help prevent the development of chronic fatigue. Definitive randomised controlled trials are required to test the intervention.
Carlo-Stella N, Lorusso L, Candura SM, Cuccia M.	Laboratorio di Immunogenetica, Dipartimento di Genetica e	[Chronic fatigue syndrome: a review] [Article in Italian]	Recenti Prog Med. 2004 Nov;95(11):546-52;	Chronic fatigue sindrome is a relatively unknown and underdiagnosed entity in Italy where its epidemiology remains uncertain, as well as its etiology, although it causes important disability in those affected. Classification criteria by Fukuda are available to diagnose the syndrome. Its epidemiology indicates that it is probably more frequent in Northern countries and it is described in Gulf War

	Microbiologia, Universita, Pavia.			veterans. Etiological hypotheses include infectious diseases, immunology and neurology. Among these hypotheses sickness behavior mimes certain aspects of this syndrome and is characterized by a cytokine imbalance in the central nervous system and in the periphery. There are no valid therapies available at the moment. In the laboratory of Immunogenetics, we are constituting a biological bank of the syndrome to study the immunogenetic aspects of the disease in the hope of delucidating some of the obscure areas of its etiopathogenesis.
Cevik R, Gur A, Acar S, Nas K, Sarac AJ.	Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey. ftremzi@dicle.edu.tr	Hypothalamic-pituitary-gonadal axis hormones and cortisol in both menstrual phases of women with chronic fatigue syndrome and effect of depressive mood on these hormones.	BMC Musculoskelet Disord. 2004 Dec 08;5(1):47.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disease which defined as medically unexplained, disabling fatigue of 6 months or more duration and often accompanied by several of a long list of physical complaints. We aimed to investigate abnormalities of hypothalamic-pituitary-gonadal (HPG) axis hormones and cortisol concentrations in premenopausal women with CFS and find out effects of depression rate on these hormones. METHODS: We examined follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol, progesterone and cortisol concentrations in 43 premenopausal women (mean age: 32.86 +/- 7.11) with CFS and compared matched 35 healthy controls (mean age: 31.14 +/- 6.19). Patients were divided according to menstrual cycle phases (follicular and luteal) and compared with matched phase controls. Depression rate was assessed by Beck Depression Inventory (BDI), and patients with high BDI scores were compared to patients with low BDI scores. RESULTS: There were no significant differences in FSH, LH, estradiol and progesterone levels in both of menstrual phases of patients versus controls. Cortisol levels were significantly lower in patients compared to controls. There were no significant differences in all hormone levels in patients with high depression scores versus patients with low depression scores. CONCLUSION: In spite of high depression rate, low cortisol concentration and normal HPG axis hormones of both menstrual phases are detected in premenopausal women with CFS. There is no differentiation between patients with high and low depression rate in all hormone levels. Depression condition of CFS may be different from classical depression and evaluation of HPG and HPA axis should be performed for understanding of pathophysiology of CFS and planning of treatment.
Chaudhuri A, Behan PO.	Division of Clinical Neurosciences, Institute of Neurological Sciences, Southern General Hospital, University of Glasgow, 1345 Govan Road, Glasgow G51 4TF, UK. ac54p@udcf.gla.ac.uk	In vivo magnetic resonance spectroscopy in chronic fatigue syndrome.	Prostaglandins Leukot Essent Fatty Acids. 2004 Sep;71(3):181-3.	The pathogenic mechanisms of chronic fatigue syndrome (CFS) are not clearly known. Fatigue, poor short-term memory and muscle pain are the most disabling symptoms in CFS. Research data on magnetic resonance spectroscopy (MRS) of muscles and brain in CFS patients suggest a cellular metabolic abnormality in some cases. 31P MRS of skeletal muscles in a subset of patients indicate early intracellular acidosis in the exercising muscles. 1H MRS of the regional brain areas in CFS have shown increased peaks of choline derived from the cell membrane phospholipids. Cell membrane oxidative stress may offer a common explanation for the observed MRS changes in the muscles and brain of CFS patients and this may have important therapeutic implications. As a research tool, MRS may be used as an objective outcome measure in the intervention studies. In addition, regional brain 1H MRS has the potential for wider use to substantiate a clinical diagnosis of CFS from other disorders of unexplained chronic fatigue.
Chaudhuri A, Behan PO.	Division of Clinical Neurosciences,	Fatigue in neurological	Lancet. 2004 Mar 20;363(9413):978-	Chronic fatigue is a typical symptom of neurological diseases, and is most disabling in multiple sclerosis, postpoliomyelitis, poststroke, and in chronic fatigue syndrome. Disorders of neuromuscular

	University of Glasgow, Glasgow G51 4TF, UK. ac54p@udcf.gla.ac.uk	disorders.	88.	junction transmission and metabolic diseases cause muscle fatigability, which is characterised by failure to sustain the force of muscle contraction (peripheral fatigue). Fatigue is also seen in diseases that affect the central, peripheral, and autonomic nervous systems (central fatigue). Enhanced perception of effort and limited endurance of sustained physical and mental activities are the main characteristics of central fatigue. Metabolic and structural lesions that disrupt the usual process of activation in pathways interconnecting the basal ganglia, thalamus, limbic system, and higher cortical centre are implicated in the pathophysiological process of central fatigue. A state of pre-existing relative hypocortisolaemia might sensitise the hypothalamic-pituitary-adrenal axis to development of persistent central fatigue after stress. The contributions of physiological, cognitive, and affective changes underlying fatigue are variable, and treatment is largely symptomatic and rehabilitative.
Clark C.		Patient organisations in ME and CFS seek only understanding. Comment on: BMJ. 2004 Jun 5;328(7452):1354-7.	BMJ. 2004 Jul 10;329(7457):112-3.	
Cleare AJ, O'Keane V, Miell JP.	Division of Psychological Medicine, The Institute of Psychiatry and Guy's, King's and St Thomas' School of Medicine, London SE5 8AF, UK. a.cleare@iop.kcl.ac.uk	Levels of DHEA and DHEAS and responses to CRH stimulation and hydrocortisone treatment in chronic fatigue syndrome.	Psychoneuroendocrinology. 2004 Jul;29(6):724-32.	Background: An association between chronic fatigue syndrome (CFS) and abnormalities of the hypothalamo-pituitary-adrenal axis has been described, and other adrenal steroid abnormalities have been suggested. Dehydroepiandrostenedione (DHEA) and its sulphate (DHEA-S), apart from being a precursor of sex steroids, have other functions associated with memory, depression and sleep. It has been suggested that CFS may be associated with a state of relative DHEA(-S) deficiency. Therefore we investigated basal levels of DHEA(-S), the cortisol/DHEA molar ratio and the responsiveness of DHEA to stimulation by corticotrophin-releasing hormone (CRH). Recent studies have also suggested that low dose hydrocortisone may be effective at reducing fatigue in CFS. We therefore also assessed these parameters prior to and following treatment with low dose oral hydrocortisone. Methods: Basal levels of serum DHEA, DHEAS and cortisol were measured in 16 patients with CFS without depression and in 16 controls matched for age, gender, weight, body mass index and menstrual history. CRH tests (1 g/kg i.v.) were carried out on all subjects and DHEA measured at 0, +30 and +90 min. In the patient group, CRH tests were repeated on two further occasions following treatment with hydrocortisone (5 or 10 mg, p.o.) or placebo for 1 month each in a double-blind cross over study protocol. Results: Basal levels of DHEA were higher in the patient, compared to the control, group (14.1+/-2.2 vs. 9.0+/-0.90 ng/ml, P=0.04), while levels of DHEAS in patients (288.7+/-35.4 microg/dl) were not different from controls (293.7+/-53.8, P=NS). Higher DHEA levels were correlated with higher disability scores. Basal cortisol levels were higher in patients, and consequently the cortisol/DHEA molar ratio did not differ between patients and controls. Levels of DHEA (8.9+/-0.97 ng/ml, P=0.015) and DHEAS (233.4+/-41.6 microg/dl, P=0.03) were lower in patients following treatment with hydrocortisone. There was a rise in DHEA responsiveness to CRH in the patients after treatment but this did not attain significance (AUCc:

				2.5+/-1.7 ng/ml h pre-treatment vs. 6.4+/-1.2 ng/ml h post-hydrocortisone, P=0.053). However, those patients who responded fully to hydrocortisone in terms of reduced fatigue scores did show a significantly increased DHEA responsiveness to CRH (AUCc: -1.4+/-2.5 ng/ml h at baseline, 5.0+/-1.2 ng/ml h after active treatment, P=0.029). Conclusions: DHEA levels are raised in CFS and correlate with the degree of self-reported disability. Hydrocortisone therapy leads to a reduction in these levels towards normal, and an increased DHEA response to CRH, most marked in those who show a clinical response to this therapy.
Cleare AJ.	Section of Neurobiology of Mood Disorders, Division of Psychological Medicine, The Institute of Psychiatry, London, SE5 8AF, UK. a.cleare@iop.kcl.ac.uk	The HPA axis and the genesis of chronic fatigue syndrome.	Trends Endocrinol Metab. 2004 Mar;15(2):55-9.	Many studies of patients with long-standing chronic fatigue syndrome (CFS) have found alterations to the hypothalamo-pituitary-adrenal (HPA) axis, including mild hypocortisolism, heightened negative feedback and blunted responses to challenge. However, recent prospective studies of high-risk cohorts suggest that there are no HPA axis changes present during the early stages of the genesis of fatiguing illnesses. Moreover, HPA axis changes can be reversed by modifying behavioural features of the illness, such as inactivity, deconditioning and sleep disturbance. Nevertheless, raising levels of cortisol pharmacologically can temporarily alleviate symptoms of fatigue. This article presents the case that there is no specific change to the HPA axis in CFS and that the observed changes are of multifactorial aetiology, with some factors occurring as a consequence of the illness. Nevertheless, the HPA axis might play a role in exacerbating or perpetuating symptoms late on in the course of the illness.
Cook DB, Lange G, Ciccone DS, Liu WC, Steffener J, Natelson BH.	Chronic Fatigue Syndrome Cooperative Research Center, New Jersey Medical School, Newark, New Jersey 07018, USA. cookdb@njneurom ed.org	Functional imaging of pain in patients with primary fibromyalgia.	J Rheumatol. 2004 Feb;31(2):364-78.	OBJECTIVE: To examine the function of the nociceptive system in patients with fibromyalgia (FM) using functional magnetic resonance imaging (fMRI). METHODS: Two groups of women, 9 with FM and 9 pain-free, volunteered to participate. In Experiment 1, we assessed psychophysical responses to painful stimuli and prepared participants for fMRI testing. For Experiment 2, subjects underwent fMRI scanning while receiving painful and nonpainful heat stimuli. Conventional and functional MR images were acquired using a 1.5 T MR scanner. Scanning occurred over 5 conditions. Condition 1 served as a practice session (no stimuli). Conditions 2 and 5 consisted of nonpainful warm stimuli. Conditions 3 and 4 consisted of an absolute thermal pain stimulus (47 degrees C) and a perceptually equivalent pain stimulus delivered in counterbalanced order. RESULTS: Experiment 1 indicated that subjects with FM were significantly more sensitive to experimental heat pain than controls ($p < 0.001$). In Experiment 2, fMRI data indicated that the FM group exhibited greater activity than controls over multiple brain regions in response to both nonpainful and painful stimuli ($p < 0.01$). Specifically, in response to nonpainful warm stimuli, FM subjects had significantly greater activity than controls in prefrontal, supplemental motor, insular, and anterior cingulate cortices ($p < 0.01$). In response to painful stimuli, FM subjects had greater activity in the contralateral insular cortex ($p < 0.01$). Data from the practice session indicated brain activity in pain-relevant areas for the FM group but not for controls. CONCLUSION: Our results provide further evidence for a physiological explanation for FM pain.
Cox IJ, Puri BK.	Faculty of Medicine, Imaging Sciences	In vivo MR spectroscopy in diagnosis and	Prostaglandins Leukot Essent Fatty Acids. 2004	Magnetic resonance spectroscopy is one of the most important tools for quantitative analysis of chemical composition and structure, and this non-invasive technique is now being applied in vivo to study biochemical processes in those neuropsychiatric disorders that are part of the phospholipid

	Department, Imperial College London, Division of Clinical Sciences, Robert Steiner Magnetic Resonance Unit, Hammersmith Campus, Du Cane Road, London W12 0HS, UK. j.cox@imperial.ac.uk	research of neuropsychiatric disorders.	Apr;70(4):357-60.	spectrum. Interpretation of a clinical magnetic resonance spectrum can provide information about membrane phospholipid turnover, cellular energetics, neuronal function, selected neurotransmitter activity and intracellular pH. Cerebral proton and phosphorus magnetic resonance spectroscopy findings are summarized in relation to schizophrenia, dyslexia and chronic fatigue syndrome.
Crofford LJ, Young EA, Engleberg NC, Korszun A, Brucksch CB, McClure LA, Brown MB, Demitrack MA.	Department of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, MI, USA. crofford@umich.edu	Basal circadian and pulsatile ACTH and cortisol secretion in patients with fibromyalgia and/or chronic fatigue syndrome.	Brain Behav Immun. 2004 Jul;18(4):314-25.	The objective of this study was to evaluate and compare the basal circadian and pulsatile architecture of the HPA axis in groups of patients with FMS, CFS, or both syndromes with individually matched control groups. Forty patients with either FMS (n = 13), FMS and CFS (n = 12), or CFS (n = 15) were matched by age (18-65), sex, and menstrual status to healthy controls. Subjects were excluded if they met criteria for major Axis I psychiatric disorders by structured clinical interview (SCID). Subjects were admitted to the General Clinical Research Center where meals and activities were standardized. Blood was collected from an intravenous line every 10 min over 24 h for analysis of ACTH and cortisol. Samples were evaluable for ACTH in 36 subject pairs and for cortisol in 37 subject pairs. There was a significant delay in the rate of decline from acrophase to nadir for cortisol levels in patients with FMS ($P < .01$). Elevation of cortisol in the late evening quiescent period was evident in half of the FMS patients compared with their control group, while cortisol levels were numerically, but not significantly, lower in the overnight period in patients with CFS compared with their control group. Pulsatility analyses did not reveal statistically significant differences between patient and control groups. We conclude that the pattern of differences for basal circadian architecture of HPA axis hormones differs between patients with FMS and CFS compared to their matched control groups. The abnormalities in FMS patients are consistent with loss of HPA axis resiliency.
de Lange FP, Kalkman JS, Bleijenberg G, Hagoort P, van der Werf SP, van der Meer JW, Toni I.	F.C. Donders Centre for Cognitive Neuroimaging, University of Nijmegen, NL-6500 HB Nijmegen, The Netherlands E-mail: floris.delange@fcdonders.kun.nl	Neural correlates of the chronic fatigue syndrome--an fMRI study.	Brain. 2004 Sep;127(Pt 9):1948-57. Epub 2004 Jul 07.	Chronic fatigue syndrome (CFS) is characterized by a debilitating fatigue of unknown aetiology. Patients who suffer from CFS report a variety of physical complaints as well as neuropsychological complaints. Therefore, it is conceivable that the CNS plays a role in the pathophysiology of CFS. The purpose of this study was to investigate neural correlates of CFS, and specifically whether there exists a linkage between disturbances in the motor system and CFS. We measured behavioural performance and cerebral activity using rapid event-related functional MRI in 16 CFS patients and 16 matched healthy controls while they were engaged in a motor imagery task and a control visual imagery task. CFS patients were considerably slower on performance of both tasks, but the increase in reaction time with increasing task load was similar between the groups. Both groups used largely overlapping neural resources. However, during the motor imagery task, CFS patients evoked stronger responses in visually related structures. Furthermore, there was a marked between-groups difference during

				erroneous performance. In both groups, dorsal anterior cingulate cortex was specifically activated during error trials. Conversely, ventral anterior cingulate cortex was active when healthy controls made an error, but remained inactive when CFS patients made an error. Our results support the notion that CFS may be associated with dysfunctional motor planning. Furthermore, the between-groups differences observed during erroneous performance point to motivational disturbances as a crucial component of CFS.
d'Elia G.	Center for kognitiv psykoterapi i Linkoping. gidelia@telia.com	[Chronic fatigue syndrome in a cognitive perspective. A therapeutic model] [Article in Swedish]	Lakartidningen. 2004 Jan 29;101(5):358-64.	The cognitive approach to the treatment of chronic fatigue syndrome (CSF) is based on a multifactor etiological hypothesis, i.e. inaccurate beliefs and attitudes to the illness interact with pathophysiological processes, ineffective coping behaviours, negative states of mood, social problem, to perpetuate the illness. Patients suffering from CFS are supposed to be hypervigilant to somatic sensations and to interpret them as signs of impending physical catastrophe. The aim of the this paper is to describe the clinical implementation of principles of cognitive therapy in the treatment of CFS. Basic to the treatment approach is a collaborative, listening and empathic attitude, sensitive to the patient's personal beliefs and potential threats to self-esteem. The aim is to develop more useful, functional, formulations of the illness. The patient and the therapist work together to look at how the patient thinks about herself/himself and the illness, detect unhelpful attitudes, thoughts and mental images about the illness, and to make them accessible to Socratic reasoning. Graded behavioural interventions are planned in order to disconfirm unhelpful beliefs and reverse the spiral of tiredness, demoralization and reduced activity. The treatment is structured according to the general principles of cognitive therapy.
Deluca J, Christodoulou C, Diamond BJ, Rosenstein ED, Kramer N, Natelson BH.	Department of Physical Medicine and Rehabilitation, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, New Jersey, USA. Jdeluca@kmrrec.org	Working memory deficits in chronic fatigue syndrome: differentiating between speed and accuracy of information processing.	J Int Neuropsychol Soc. 2004 Jan;10(1):101-9.	To examine the relative influence of speed of information processing versus working memory ability, CFS participants with psychiatric comorbidity (CFS-Psych) and CFS without a psychiatric history (CFS-noPsych) were examined on tests of visual and auditory processing speed and visual and auditory working memory. Compared to healthy controls (HC) and a group of participants with rheumatoid arthritis (RA), the CFS-noPsych group displayed significantly reduced performance on tests of information processing speed, but not on tests of working memory. No significant differences were observed between the CFS-Psych group and any other group in the study. The implications of group heterogeneity on the understanding of cognitive impairment in CFS are discussed.
DiVasta AD, Alexander ME.	Division of Adolescent and Young Adult Medicine, Department of Cardiology, Children's Hospital Boston, Harvard	Fainting freshmen and sinking sophomores: cardiovascular issues of the adolescent.	Curr Opin Pediatr. 2004 Aug;16(4):350-6.	PURPOSE OF REVIEW: Syncope is a common symptom in adolescents. The vast majority of cases are the result of benign neurocardiogenic syncope, without associated risk of sudden death. This paper reviews the mainstays of diagnosis and treatment for syncopal episodes, differentiation of syncope from life-threatening arrhythmia and aborted sudden cardiac death, and the patient populations at highest risk for cardiac symptoms and cardiac disease. RECENT FINDINGS: A detailed history (including past medical history and family history that focus on cardiac disease) combined with dynamic physical examination and electrocardiogram identifies the vast majority of adolescents with significant heart disease. Further diagnostic modalities have limited utility. Reassurance and supportive measures

	Medical School, Boston, Massachusetts 02115, USA. amy.divasta@childrens.harvard.edu			remain the treatment of choice, although drug therapy can sometimes be helpful, even if data are limited. Divergent approaches to the screening of the young competitive athlete exist. Particular attention is required in adolescents and young adults with exercise-associated syncope, eating disorders, chronic fatigue syndrome, or history of congenital heart disease. Their symptoms may be either more serious or challenging to manage. SUMMARY: Syncope in the adolescent patient is very common; true cardiac disease is not. The traditional diagnostic screen of history and physical combined with an electrocardiogram will identify the overwhelming majority of patients with significant disease. Patients with abnormalities on this initial office evaluation, history of cardiac disease, or complicating medical illness may benefit from referral to a cardiologist. Even within this patient subset, many will prove to have benign disease.
Dyer C.		Paediatrician cleared of serious professional misconduct.	BMJ. 2004 May 1;328(7447):1035.	
Dyer C.		Teenager seeks to overturn GMC judgment.(Letter)	BMJ. 2004 Feb 7;328(7435):310.	
Edmonds M, McGuire H, Price J.		Exercise therapy for chronic fatigue syndrome.	Cochrane Database Syst Rev. 2004;(3):CD003200.	BACKGROUND: Chronic fatigue syndrome (CFS) is an illness characterised by persistent medically unexplained fatigue. CFS is a serious health-care problem with a prevalence of up to 3%. Treatment strategies for CFS include psychological, physical and pharmacological interventions. OBJECTIVES: To investigate the relative effectiveness of exercise therapy and control treatments for CFS. SEARCH STRATEGY: CCDANCTR-Studies and CENTRAL were searched using "Chronic Fatigue" and Exercise. The Journal of Chronic Fatigue Syndrome and CFS conferences were handsearched. Experts in the field were contacted. Clinicaltrials.gov and controlled-trials.com were searched. SELECTION CRITERIA: Only Randomised Controlled Trials (RCT) including participants with a clinical diagnosis of CFS and of any age were included. DATA COLLECTION AND ANALYSIS: The full articles of studies identified were inspected by two reviewers (ME and HMG). Continuous measures of outcome were combined using standardised mean differences. An overall effect size was calculated for each outcome with 95% confidence intervals. One sensitivity analysis was undertaken to test the robustness of the results. MAIN RESULTS: Nine studies were identified for possible inclusion in this review, and five of those studies were included. At 12 weeks, those receiving exercise therapy were less fatigued than the control participants (SMD -0.77, 95% CIs -1.26 to -0.28). Physical functioning was significantly improved with exercise therapy group (SMD -0.64, CIs -0.96 to -0.33) but there were more dropouts with exercise therapy (RR 1.73, CIs 0.92 to 3.24). Depression was non-significantly improved in the exercise therapy group compared to the control group at 12 weeks (WMD -0.58, 95% CIs -2.08 to 0.92).Participants receiving exercise therapy were less fatigued than those receiving the antidepressant fluoxetine at 12 weeks (WMD -1.24, 95% CIs -5.31 to 2.83). Participants receiving the combination of the two interventions, exercise + fluoxetine, were less fatigued than those receiving exercise therapy alone at 12 weeks, although again the difference did not reach significance (WMD 3.74, 95% CIs -2.16 to 9.64).When exercise therapy was combined with patient education, those

				receiving the combination were less fatigued than those receiving exercise therapy alone at 12 weeks (WMD 0.70, 95% CIs -1.48 to 2.88). REVIEWERS' CONCLUSIONS: There is encouraging evidence that some patients may benefit from exercise therapy and no evidence that exercise therapy may worsen outcomes on average. However the treatment may be less acceptable to patients than other management approaches, such as rest or pacing. Patients with CFS who are similar to those in these trials should be offered exercise therapy, and their progress monitored Further high quality randomised studies are needed.
Endresen GK.	Revmatologisk avdeling, Rikshospitalet, 0027 Oslo. gerhard.endresen @rikshospitalet.no	[Systemic Mycoplasma blood infection in fibromyalgia and chronic fatigue syndrome][Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Jan 22;124(2):203-5.	
Engstrom JW.	Professor of Neurology, Department of Neurology, University of California, San Francisco, California 94143-0114, USA.	Myasthenia gravis: diagnostic mimics.	Semin Neurol. 2004 Jun;24(2):141-7.	The clinical hallmark of myasthenia gravis (MG) is fluctuating, painless weakness of muscles that most often affect extraocular, lower bulbar, or limb musculature. Predicting the probability of successful treatment for the patient assumes that the physician has made an accurate diagnosis. In this review, the practical differential diagnosis of MG is reviewed from the perspective of conditions (at presentation of symptoms and signs) that may mimic the disorder. The differential diagnosis includes disorders that limit eye movements (with or without associated diplopia), cause false-positive laboratory studies, and mimic MG but have normal eye movements. The differential diagnosis includes disorders that affect the upper brainstem, cranial nerves, neuromuscular junction, muscles, or local orbit anatomy. Nonneurological systemic diseases (i.e., encephalopathy, sepsis) can produce fluctuating ptosis or eye movements that can occasionally be confused with MG. Although MG is considered often in the differential diagnosis of weakness or fatigue symptoms that lack a correlate on neurological examination (subjective fatigue, breakaway weakness, chronic fatigue syndrome), MG is almost never found. Copyright 2004 Thieme Medical Publishers, Inc.
Eriksen HR, Ursin H.	Department of Biological and Medical Psychology, University of Bergen, Jonas Lies vei 91, N-5009 Bergen, Norway.	Subjective health complaints, sensitization, and sustained cognitive activation (stress).	J Psychosom Res. 2004 Apr;56(4):445-8.	INTRODUCTION: This review argues that "subjective health complaints" is a better and neutral term for "unexplained medical symptoms." The most common complaints are musculoskeletal pain, gastrointestinal complaints and "pseudoneurology" (tiredness, sleep problems, fatigue, and mood changes). These complaints are common in the general population, but for some these complaints reach a level that requires care and assistance. THEORETICAL ASSUMPTIONS: We suggest that these complaints are based on sensations from what in most people are normal physiological processes. In some individuals these sensations become intolerable. In some cases it may signal somatic disease, in most cases not. Cases without somatic disease, or with minimal somatic findings, occur under diagnoses like burnout, epidemic fatigue, multiple chemical sensitivity, chronic musculoskeletal pain, chronic low back pain, chronic fatigue syndrome, and fibromyalgia. These complaints are particularly common in individuals with low coping and high levels of helplessness and hopelessness. CONCLUSION: The psychobiological mechanisms for this is suggested to be sensitization in neural loops maintained by sustained attention and arousal.

Famularo G, DE Simone C, Trinchieri V, Mosca	Department of Internal Medicine, San Camillo Hospital, Circonvallazione Gianicolense, 00152 Rome, Italy. gfamularo@scamilloforlanini.rm.it.	Carnitines and its congeners: a metabolic pathway to the regulation of immune response and inflammation. .	Ann N Y Acad Sci. 2004 Nov;1033:132-8.	Carnitine and its congeners may regulate the immune networks, and their influence on functions of immune cells predominantly or exclusively relies on carnitine-dependent energy production from fatty acids. A reduced pool of carnitines has been demonstrated in either serum or tissues, or both, from patients with a wide spectrum of disorders characterized by unregulated or impaired immune responses ranging from sepsis syndrome to systemic sclerosis, infection with human immunodeficiency virus, and chronic fatigue syndrome. Furthermore, experimental studies have consistently reported that the deranged immune responses and the less efficient inflammation towards infectious organisms associated with aging may be enhanced or modulated by treatment with carnitines. There is also evidence that carnitine deprivation could adversely affect the course of the sepsis syndrome, at least in experimental models, and preliminary studies suggest that carnitine deficiency is ultimately implicated in the pathophysiology of endotoxin-mediated multiple organ failure. Several data indicate that carnitine deficiency is a contributing factor to the progression of infection with human immunodeficiency virus, and carnitine therapy in those patients could counteract the unregulated process of lymphocyte apoptosis and improve CD4 counts. Some case reports have suggested the use of carnitine for the treatment of the severe lactic acidosis that complicates in some patients the use of reverse transcriptase inhibitors.
Farmer A, Fowler T, Scourfield J, Thapar A.	MRC Social, Genetic, Developmental Psychiatric Research Centre, Institute of Psychiatry, London, UK. spjuaef@iop.kcl.ac.uk.	Prevalence of chronic disabling fatigue in children and adolescents.	Br J Psychiatry. 2004 Jun;184:477-81.	BACKGROUND: The epidemiology of chronic fatiguing illnesses in young people is poorly understood. AIMS: To estimate the lifetime prevalence of different definitions of chronic fatigue in 8- to 17-year-olds. METHOD: Participants came from two population-based twin series. Parents completed self-report questionnaires that inquired whether either child had ever experienced more than a few days of disabling fatigue. Telephone interviews were undertaken for individuals who had experienced such an episode. RESULTS: Questionnaires were returned by 1468 families (65% response rate) and telephone interviews were undertaken regarding 99 of the 129 subjects (77%) who had experienced fatigue. The lifetime prevalence estimates ranged from 2.34% (95% CI 1.75-2.94) for disabling fatigue lasting 3 months to 1.29% (95% CI 0.87-1.71) for a disorder resembling adult operationally defined chronic fatigue syndrome. CONCLUSIONS: From the age of 11 years, young people have similar rates and types of chronic fatiguing illnesses to adults.
Farney RJ, Lugo A, Jensen RL, Walker JM, Cloward TV.	Intermountain Sleep Disorders Center, LDS Hospital, Salt Lake City, UT 84143, USA. rjfmd@msn.com	Simultaneous use of antidepressant and antihypertensive medications increases likelihood of diagnosis of obstructive sleep apnea syndrome.	Chest. 2004 Apr;125(4):1279-85.	BACKGROUND: Essential hypertension and symptoms of depression such as unexplained fatigue and tiredness are frequently encountered in primary medical care clinics. Although, exhaustive evaluation rarely detects unsuspected underlying disorders, obstructive sleep apnea (OSA) is commonly associated with each of these conditions. We tested the hypothesis that therapy with antihypertensive and antidepressant medications predicts the increased likelihood of OSA. METHODS: We analyzed the computer archive of 212,972 patients for prescriptions for antihypertensive medications, antidepressant medications, and International Classification of Diseases, Ninth Revision codes for OSA. Prevalence, prevalence odds ratio (POR), and confidence intervals (CIs) were calculated correcting for gender and age group. RESULTS: The prevalence rates of OSA were 0.8%, 2.8%, and 3.2% for men and 0.4%, 1.4%, and 1.8% for women aged 20 to 39 years, 40 to 59 years, and >or= 60 years, respectively. Compared to groups of corresponding age and gender who had not received prescriptions for either hypertension or depression, the highest PORs were found in patients receiving medications from both categories: 18.30 (95% CI, 10.69 to 25.66), 5.72 (95% CI, 4.10 to 6.70), and 4.47

				(95% CI, 2.45 to 7.01) for men, and 17.43 (95% CI, 9.54 to 28.67), 7.29 (95% CI, 5.20 to 9.29), and 2.72 (95% CI, 1.48 to 4.73) for women. CONCLUSIONS: We found that the likelihood of having a diagnosis of OSA increases when either antihypertensive or antidepressant medications have been prescribed. The probability is highest in the young and middle-age groups receiving prescriptions for both medications. The possibility of OSA should be considered in any patient with hypertension and depression or unexplained fatigue who is receiving antihypertensive and antidepressant medications.
Gaab J, Engert V, Heitz V, Schad T, Schurmeyer TH, Ehlert U.	Center for Psychobiological and Psychosomatic Research, University of Trier, Germany.	Associations between neuroendocrine responses to the Insulin Tolerance Test and patient characteristics in chronic fatigue syndrome.	J Psychosom Res. 2004 Apr;56(4):419-24.	OBJECTIVE: Subtle dysregulations of the hypothalamic-pituitary-adrenal (HPA) axis have been proposed as an underlying pathophysiological mechanism in chronic fatigue syndrome (CFS). This study attempted to assess the relationship between patient characteristics and HPA axis functioning using a neuroendocrine challenge test. METHOD: A test battery designed to assess different dimensions of CFS was given to 18 CFS patients and 17 controls. To evaluate the integrity of the HPA axis, the Insulin Tolerance Test (ITT), a centrally acting neuroendocrine challenge test, was performed on patients and controls. ACTH, salivary free cortisol and total plasma cortisol levels were assessed as a measure of the HPA axis stress response. Correlations of patient characteristics were calculated with integrated responses for all endocrine parameters. RESULTS: CFS patients had a significantly reduced area under the ACTH response curve (AUC) in the ITT. The AUC was significantly associated with the duration of CFS symptoms (r=-.592, P=.005) and the severity of fatigue symptomatology (r=-.41, P=.045). In addition, duration of CFS was correlated with the severity of fatigue symptoms (r=.38, P=.045). Similar associations were not observed for cortisol parameters. CONCLUSION: It has been postulated that neuroendocrine dysregulations observed in CFS are of an acquired nature. The results of a strong association between the integrated ACTH response and the duration of CFS emphasizes the need to consider factors known to be risk factors for the chronicity of CFS symptoms, such as profound inactivity, deconditioning and sleep abnormalities, as possible candidates for secondary causes of neuroendocrine dysregulations in CFS.
Gallagher AM, Thomas JM, Hamilton WT, White PD.	Centre for Psychiatry and Department of Information Services, Queen Mary School of Medicine and Dentistry, St Bartholomew's Hospital, London EC1A 7BE.	Incidence of fatigue symptoms and diagnoses presenting in UK primary care from 1990 to 2001.	J R Soc Med. 2004 Dec;97(12):571-5.	Little is known about whether the incidence of symptoms of fatigue presented in primary care, and the consequent diagnoses made, change over time. The UK General Practice Research Database was used to investigate the annual incidence of both fatigue symptoms and diagnoses recorded in UK primary care from 1990 to 2001. The overall incidence of all fatigue diagnoses decreased from 87 per 100 000 patients in 1990 to 49 in 2001, a reduction of 44%, while postviral fatigue syndromes decreased from 81% of all fatigue diagnoses in 1990 to 60% in 2001. Chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME) together increased from 9% to 26% of all fatigue diagnoses. The incidence of fibromyalgia increased from less than 1 per 100 000 to 35 per 100 000. In contrast, there was no consistent change in the incidence of all recorded symptoms of fatigue, with an average of 1503 per 100 000, equivalent to 1.5% per year. CFS/ME and fibromyalgia were rarely diagnosed in children and were uncommon in the elderly. All symptoms and diagnoses were more common in females than in males. The overall incidence of fatigue diagnoses in general has fallen, but the incidence rates of the specific diagnoses of CFS/ME and fibromyalgia have risen, against a background of little change in symptom reporting. This is likely to reflect fashions in diagnostic labelling rather than true changes in incidence.
Garralda ME,	Academic Unit of	Impairment and	J Child Psychol	BACKGROUND: Functional impairment is a key feature of chronic fatigue syndrome (CFS) of childhood.

Rangel L.	Child and Adolescent Psychiatry, Imperial College, Faculty of Medicine, London, UK. e.garralda@imperial.ac.uk	coping in children and adolescents with chronic fatigue syndrome: a comparative study with other paediatric disorders.	Psychiatry. 2004 Mar;45(3):543-52.	AIM: To compare impairment, illness attitudes and coping mechanisms in childhood CFS and in other paediatric disorders. METHOD: Participants were 28 children and adolescents with CFS, 30 with juvenile idiopathic arthritis (JIA) and 27 with emotional disorders (ED). The measures used were interviews with children and parents, with detailed enquiry on impairment, including the Functional Disability Inventory (FDI), Illness Attitudes Scales (IAS), and Kidcope to measure coping styles in relation to common problems, illness and disability. RESULTS: Children with CFS reported significantly more illness impairment, especially in school attendance, than those with JIA and ED. They had higher 'worry about illness' scores on the IAS. On the Kidcope they named school issues (work, expectations, attendance) as illness- or disability-related problems more than the other two groups. Fewer CFS participants reported using problem solving as a strategy to cope with illness and disability than with other problems in their lives. More in the CFS than in the JIA group used emotional regulation to cope with illness and disability. Fewer in the CFS than in the ED groups used social withdrawal to cope with illness and self-criticism for disability, but more used resignation to cope with disability. CONCLUSION: Severe illness-related impairment, particularly through school non-attendance, and high levels of illness-related school concerns appear specific to CFS. CFS may also have characteristically high levels of generalised illness worry and particular styles of coping with illness and disability.
Gill AC, Dosen A, Ziegler JB.	Department of General Pediatrics, Sydney Children's Hospital, Sydney, Australia.	Chronic fatigue syndrome in adolescents: a follow-up study. Comment in: Arch Pediatr Adolesc Med. 2004 Mar;158(3):207-8.	Arch Pediatr Adolesc Med. 2004 Mar;158(3):225-9.	OBJECTIVES: To compare the frequency of persistent symptoms up to 8 years after illness onset in adolescents diagnosed as having chronic fatigue syndrome, idiopathic chronic fatigue, and unexplained fatigue for less than 6 months, and to determine if hospital admission is associated with outcome. DESIGN: A cohort study using questionnaire follow-up. SETTING: A tertiary referral hospital. PATIENTS: Consecutive adolescents referred for assessment of persistent fatigue were identified and retrospectively divided into 3 groups according to the diagnostic criteria for chronic fatigue syndrome and idiopathic chronic fatigue. INTERVENTION: A questionnaire was designed and administered by telephone at a mean of 4.57 years after the initial examination. MAIN OUTCOME MEASURE: The persistence of self-reported symptoms was compared with respect to patient group and admission. RESULTS: Outcome data were obtained for 34 (69%) of the 49 eligible subjects. Twenty-five percent of the chronic fatigue syndrome group showed near to complete improvement, 31% showed partial improvement, and 44% showed no improvement. The idiopathic chronic fatigue group had near to complete recovery in 50%, partial in 10%, and no improvement in 40%. Those with unexplained fatigue for less than 6 months had all recovered. There was no difference between the outcome of the subjects admitted to the hospital and those managed as outpatients. CONCLUSIONS: Adolescents with less than 6 months of fatigue have a good outcome. Unexplained fatigue lasting more than 6 months has a similar outcome regardless of the presence of minor criteria for chronic fatigue syndrome.
Glass JM, Lyden AK, Petzke F, Stein P, Whalen G, Ambrose K, Chrousos G, Clauw DJ.	Department of Psychiatry and Institute for Social Research, University of Michigan, Ann Arbor, MI, USA.	The effect of brief exercise cessation on pain, fatigue, and mood symptom development in healthy, fit	J Psychosom Res. 2004 Oct;57(4):391-8.	OBJECTIVE: Abnormalities of the biological stress response (hypothalamic-pituitary-adrenal axis and the autonomic nervous system) have been identified in both fibromyalgia (FM) and chronic fatigue syndrome (CFS). Although these changes have been considered to be partly responsible for symptom expression, we examine an alternative hypothesis that these HPA and autonomic changes can be found in subsets of healthy individuals in the general population who may be at risk of developing these conditions. Exposure to "stressors" (e.g., infections, trauma, etc.) may lead to symptom expression (pain, fatigue, and other somatic symptoms) in part by precipitating lifestyle changes. In

	jglass@umich.edu	individuals.		particular, we focus on the effect of deprivation of routine aerobic exercise on the development of somatic symptoms. METHODS: Eighteen regularly exercising (>/=4 h/week) asymptomatic, healthy adults refrained from physical activity for 1 week. We predicted that a subset of these individuals would develop symptoms of FM/CFS with exercise deprivation, and this manuscript focuses on the baseline HPA axis, immune, and autonomic function measures that may predict the development of symptoms. RESULTS: Eight of the subjects reported a 10% increase in one or more symptoms (pain, fatigue, mood) after 1 week of exercise deprivation. These symptomatic subjects had lower HPA axis (baseline cortisol prior to VO2max testing), immune (NK cell responsiveness to venipuncture), and autonomic function (measured by heart rate variability) at baseline (prior to cessation of exercise) when compared to the subjects who did not develop symptoms. CONCLUSIONS: A subset of subjects developed symptoms of pain, fatigue, or mood changes after exercise deprivation. This cohort was different from the individuals who did not develop symptoms in baseline measures of HPA axis, immune, and autonomic function. We speculate that a subset of healthy individuals who have hypoactive function of the biological stress response systems unknowingly exercise regularly to augment the function of these systems and thus suppress symptoms. These individuals may be at risk for developing chronic multisymptom illnesses (CMIs) (e.g., FM or CFS among others) when a "stressor" leads to lifestyle changes that disrupt regular exercise.
Glise K, Bjorkman A.	Institutet for stressmedicin, Goteborg. kristina.glise@stressmedicin.com	[The burnout syndrome--clinical picture and therapy][Article in Swedish]	Lakartidningen. 2004 Mar 25;101(13):1202-6.	
Gur A, Cevik R, Nas K, Colpan L, Sarac S.	Department of Physical Medicine and Rehabilitation, School of Medicine, Dicle University, Diyarbakir, Turkey. alig@dicle.edu.tr	Cortisol and hypothalamic-pituitary-gonadal axis hormones in follicular-phase women with fibromyalgia and chronic fatigue syndrome and effect of depressive symptoms on these hormones.	Arthritis Res Ther. 2004;6(3):R232-8. Epub 2004 Mar 15.	We investigated abnormalities of the hypothalamic-pituitary-gonadal axis and cortisol concentrations in women with fibromyalgia and chronic fatigue syndrome (CFS) who were in the follicular phase of their menstrual cycle, and whether their scores for depressive symptoms were related to levels of these hormones. A total of 176 subjects participated - 46 healthy volunteers, 68 patients with fibromyalgia, and 62 patients with CFS. We examined concentrations of follicle-stimulating hormone, luteinizing hormone (LH), estradiol, progesterone, prolactin, and cortisol. Depressive symptoms were assessed using the Beck Depression Inventory (BDI). Cortisol levels were significantly lower in patients with fibromyalgia or CFS than in healthy controls ($P < 0.05$); there were no significant differences in other hormone levels between the three groups.Fibromyalgia patients with high BDI scores had significantly lower cortisol levels than controls ($P < 0.05$), and so did CFS patients, regardless of their BDI scores ($P < 0.05$). Among patients without depressive symptoms, cortisol levels were lower in CFS than in fibromyalgia ($P < 0.05$). Our study suggests that in spite of low morning cortisol concentrations, the only abnormalities in hypothalamic-pituitary-gonadal axis hormones among follicular-phase women with fibromyalgia or CFS are those of LH levels in fibromyalgia patients with a low BDI score. Depression may lower cortisol and LH levels, or, alternatively, low morning cortisol may be a biological factor that contributes to depressive symptoms in fibromyalgia. These parameters therefore must be taken into account in future investigations.

Hamlen R.	rhamlen@iximd.com	Lyme borreliosis: perspective of a scientist-patient.	Lancet Infect Dis. 2004 Oct;4(10):603-4. Comment on: Lancet Infect Dis. 2003 Aug;3(8):489-500.	
Hartz AJ, Bentler S, Noyes R, Hoehns J, Logemann C, Sinift S, Butani Y, Wang W, Brake K, Ernst M, Kautzman H. .	University of Iowa, College of Medicine, Department of Family Medicine, Iowa City 52242-1097, USA	Randomized controlled trial of Siberian ginseng for chronic fatigue.	Psychol Med. 2004 Jan;34(1):51-61.	BACKGROUND: Chronic fatigue greatly affects quality of life and is a common reason for consulting a physician. Since conventional therapy is often of limited help, fatigued patients may use herbal treatments. This randomized controlled trial evaluated the effectiveness of Siberian ginseng. METHOD: Subjects were recruited from advertisements in Iowa (82%) and members of chronic fatigue syndrome support groups (18%). Potential subjects were required to have substantial fatigue > or = 6 months with no identifiable cause. The mean change in a fatigue measure was compared for placebo and Siberian ginseng at 1 and 2 months. Comparisons were for all subjects and for subjects with characteristics previously identified in the literature as important for categorizing chronic fatigue. RESULTS: Ninety-six subjects were randomized to treatment groups, and 76 provided information at 2 months of follow-up. Fatigue among subjects assigned to either placebo or Siberian ginseng was substantially reduced during the study, but differences between treatment groups were not statistically significant in the full sample. Fatigue severity and duration had a statistically significant interaction with response to Siberian ginseng at the P < 0.05 level. Treatment was effective at 2 months for 45 subjects with less severe fatigue (P = 0.04 unadjusted for multiple comparisons) and for 41 subjects with fatigue for > or = 5 years (P = 0.09 unadjusted for multiple comparisons). CONCLUSION: Overall efficacy was not demonstrated. However, the findings of possible efficacy for patients with moderate fatigue suggests that further research may be of value.
Hausotter W.		[Appraisal of Lyme borreliosis][Article in German]	Versicherungsmedizin. 2004 Mar 1;56(1):25-9.	Lyme borreliosis is due to infection with a tick-borne spirochete. The variety of signs and symptoms and also the laboratory tests of this multisystem illness often cause great problems in the appraisal of this disease. Frequently indispositions are associated with positive antibody tests for Borrelia burgdorferi. Terms as fibromyalgia or chronic fatigue syndrome are often connected with the diagnosis of Lyme disease. Outdoor workers such as farmers, foresters, hunters, woodcutters and gamekeepers in areas of endemic disease take a great occupational risk of infection with borreliosis. In the German health and social insurance the appraisal of this disease is of great importance. Affected working people can receive financial compensation. Not only serological investigations with the presence of specific antibodies, but also clinical findings must be considered.
Heim C, Bierl C, Nisenbaum R, Wagner D, Reeves WC.	Division of Viral and Rickettsial Diseases, Viral Exanthems and Herpesvirus Branch, National Center for	Regional prevalence of fatiguing illnesses in the United States before and after the terrorist attacks of	Psychosom Med. 2004 Sep-Oct;66(5):672-8.	OBJECTIVE: Stress or emotional traumas are considered risk factors for unexplained fatiguing illnesses. From July to December 2001, the Centers for Disease Control and Prevention conducted a multigeographical pilot study to test the feasibility of a survey to estimate the prevalence of fatiguing illnesses in the United States. We used data obtained during this survey to estimate the effect of the coincidentally occurring terrorist attacks of September 11, 2001, on the regional prevalence of fatiguing illnesses. METHODS: Identified by random-digit dialing, 2,728 households in eight regional strata were interviewed, and 7,317 respondents were screened for severe fatigue of at least 1 month

	Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, USA. cmheim@emory.edu	September 11, 2001.		duration. Identified fatigued people of age 18 to 69 years (N = 440) and a sample of nonfatigued people of the same age range (N = 444) were interviewed in detail concerning fatigue, other symptoms, and medical and psychiatric histories. RESULTS: Weighted prevalence estimates based on interviews performed after the attacks were significantly lower compared with estimates based on interviews performed before the attacks (prolonged fatigue: 5,450 vs. 1,530/100,000, p =.010; chronic fatigue: 18,510 vs. 10,070/100,000, p =.002; chronic fatigue syndrome-like illness: 2,510 vs. 960/100,000, p =.014).CONCLUSION: Our findings suggest decreased regional prevalence of fatiguing illnesses in the aftermath of the terrorist attacks. The causes of this effect are unknown but might involve acute psychological and physiological adaptations that modify the perception or manifestation of fatigue. Future studies should be specifically designed to scrutinize the relationship between stress and fatiguing illnesses and the mediating mechanisms of such a relationship.
Henderson M, Tannock C.	Academic Department of Psychological Medicine, GKT School of Medicine and Institute of Psychiatry, Guys Kings and St. Thomas' Hospital, Weston Education Centre, Cutcombe Road, London SE5 9RJ, UK. m.henderson@iop.kcl.ac.uk	Objective assessment of personality disorder in chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):251-4.	OBJECTIVES: This study aims to objectively assess the prevalence and nature of personality disorders in depressed and nondepressed chronic fatigue syndrome (CFS) patients and compare this to depressed and healthy control groups. METHODS: Sixty-one patients attending a tertiary referral clinic with chronic fatigue syndrome, 40 psychiatric inpatients with depressive disorder and 45 healthy medical students completed the Structured Clinical Interview for DSM-III-R Diagnoses (SCID-II) in addition to providing routine clinical and demographic information. RESULTS: Thirty-nine percent of the CFS group, 73% of the depressed group and 4% of the healthy group were diagnosed with personality disorders. Cluster C disorders were the most common in both the CFS and depressed group. The depressed CFS patients had more Cluster B personality disorders than nondepressed CFS patients. Overall for CFS patients there was no association between mood state and personality disorder. CONCLUSIONS: High levels of personality disorder are found on objective assessment of CFS patients attending a teaching hospital clinic. This cannot be accounted for by comorbid depression.
Horton-Salway M.	Department of Social Sciences, Open University, UK. mkhs2@tutor.open.ac.uk	The local production of knowledge: disease labels, identities and category entitlements in ME support group talk.	Health (London). 2004 Jul;8(3):351-71.	This article uses discursive psychology to analyse how knowledge claims and entitlements are locally produced in an ME support group meeting and a research interview. The article demonstrates how 'expertise' and 'experience' associated with lay and professional membership are locally constituted in the activity of reasoning, arguing and claims making. The analysis shows how expertise and experiential claims are constructed, disclaimed, warranted and undermined in relationship to membership categorization and entitlements to knowledge that are co-constructed in the process of a discussion about disease labels and the nature of the illness as physical or psychological. In a discussion about the definition of contested disease categories, what is 'at stake' for the group members is the entitlement to speak from experience as members who can 'know' their own minds.
Huibers MJ, Bleijenberg G, van Amelsvoort LG, Beurskens AJ, van Schayck CP,	Department of Epidemiology, Maastricht University, P.O. Box 616,	Predictors of outcome in fatigued employees on sick leave Results from	J Psychosom Res. 2004 Nov;57(5):443-449.	OBJECTIVE: The main objective of this study was to identify predictors of fatigue caseness, work resumption and chronic fatigue syndrome (CFS)-like caseness in a sample of fatigued employees on sick leave. METHODS: For 12 months, 151 fatigued employees on sick leave, 44% of whom met research criteria for CFS at baseline, were followed. Measures included fatigue, health aspects, psychological problems, burnout, causal attributions and self-efficacy. Logistic regression analysis was

Bazelmans E, Knottnerus JA.	Maastricht 6200 MD, The Netherlands; Department of Medical Psychology, UMC Nijmegen, The Netherlands; Department of General Practice, Maastricht University, P.O. Box 616, Maastricht 6200 MD, The Netherlands.	a randomised trial.		used to determine associations between predictor variables at baseline and outcome at follow-up. RESULTS: After 12 months, 43% of the patients were no longer fatigue cases, and 62% had resumed work. Recovery from fatigue caseness was predicted by stronger psychological attributions and other perception-related factors, whereas work resumption was predicted by lower age, male sex, CFS-like caseness and less cognitive difficulties. Lower physical functioning scores were predictive of (the development of) CFS-like caseness. CONCLUSION: Recovering from persistent fatigue and work resumption seem to result from different underlying processes and do not necessarily fall together. As many factors associated with outcome in fatigue reflect illness perception, the prevention of persistent fatigue and CFS may partly be achieved by the modification of perception.
Huibers MJ, Beurskens AJ, Van Schayck CP, Bazelmans E, Metsemakers JF, Knottnerus JA, Bleijenberg G.	Department of Epidemiology, Maastricht University, The Netherlands. m.huibers@dmkep.unimaas.nl	Efficacy of cognitive-behavioural therapy by general practitioners for unexplained fatigue among employees: Randomised controlled trial.	Br J Psychiatry. 2004 Mar;184:240-6.	BACKGROUND: Fatigue is a common complaint that may lead to long-term sick leave and work disability. AIMS: To assess the efficacy of cognitive-behavioural therapy by general practitioners for unexplained, persistent fatigue among employees. METHOD: A randomised controlled trial, using a pre-randomisation design in primary care, investigated 151 employees on sick leave with fatigue. Participants in the experimental group were offered five to seven 30 min sessions of cognitive-behavioural therapy by a general practitioner; those in the control group were offered no treatment. Main outcome measures (fatigue severity, self-reported absenteeism, registered absenteeism and clinical recovery) were assessed at 4 months, 8 months and 12 months. RESULTS: At baseline, 44% of the patients already met research criteria for chronic fatigue syndrome. There was no significant difference between the experimental group and the control group on primary or secondary outcomes at any point. CONCLUSIONS: Cognitive-behavioural therapy by general practitioners for unexplained, persistent fatigue did not prove to be an effective intervention. Since these doctors were unable to deliver this therapy effectively under ideal circumstances, it is unlikely that doctors in routine practice would be more successful in doing so.
Huibers MJ, Kant IJ, Knottnerus JA, Bleijenberg G, Swaen GM, Kasl SV.	Department of Epidemiology, Maastricht University, PO Box 616, 6200 MD Maastricht, Netherlands. m.huibers@dmkep.unimaas.nl	Development of the chronic fatigue syndrome in severely fatigued employees: predictors of outcome in the Maastricht cohort study.	J Epidemiol Community Health. 2004 Oct;58(10):877-82.	STUDY OBJECTIVE: To identify risk factors of the development of the chronic fatigue syndrome (CFS), the persistence or recurrence of fatigue, or recovery from fatigue in a large sample of fatigued employees. DESIGN: Analyses were based on the Maastricht cohort study (MCS), a prospective population based cohort study among more than 12 000 employees. Multiple regression models were used to identify predictors of CFS-like caseness (meeting research criteria for CFS), non-CFS fatigue caseness, or no fatigue caseness. SETTING: The working population in the Netherlands. PARTICIPANTS: 1143 employees with medically unexplained fatigue were followed up prospectively for 44 months. MAIN RESULTS: At 44 month follow up, 8% of the employees were CFS-like cases (none of who reported to have received a CFS diagnosis), 40% were non-CFS fatigue cases, and 52% were no longer fatigue cases. Factors that predicted CFS-like caseness compared with non-CFS fatigue caseness were

				high age, exhaustion, female sex, low education, and visits to the general practitioner. Factors that predicted CFS-like caseness compared with no fatigue caseness were fatigue, exhaustion, low education, visits to the GP and occupational physician, and bad self rated health. Factors that predicted non-CFS fatigue caseness compared with no fatigue caseness were fatigue, low self perceived activity, exhaustion, anxious mood, and bad self rated health. CONCLUSIONS: Unexplained fatigue among employees in some instances is a precursor of the development of CFS. The prognostic role of self rated health suggests that prevention and treatment of chronic fatigue should be aimed at changing the perception of health or illness. Less clear is the role of health care seeking or receiving a CFS diagnosis.
Huibers MJ, Kant IJ, Swaen GM, Kasl SV.	Department of Medical, Clinical & Experimental Psychology, Maastricht University, Netherlands. marcus.huibers@hag.unimaas.nl	Prevalence of chronic fatigue syndrome-like caseness in the working population: results from the Maastricht cohort study.	Occup Environ Med. 2004 May;61(5):464-6.	AIM: To determine the prevalence of chronic fatigue syndrome (CFS)-like caseness in the working population. METHODS: Using data from the prospective Maastricht Cohort Study on Fatigue at Work, the prevalence and incidence of CFS-like cases (employees meeting research criteria for CFS) were determined among 5499 employees who responded to the follow up assessment 3 years and 8 months after baseline. RESULTS: Of the 5499 employees, 199 (3.6%) were identified as CFS-like cases. By deleting possible CFS-like cases at baseline, the annual incidence of CFS-like caseness was estimated to be 85 per 10 000. Twenty employees (0.36%) reported having been diagnosed with CFS by a physician. CONCLUSIONS: The prevalence of CFS-like cases (3.6%) was considerably higher than the prevalence of CFS reported in previous studies (0.006-3%). These findings suggest that the CFS-like caseness may be underdetected in the working population and perhaps in other populations as well.
Jason LA, Torres-Harding SR, Jurgens A, Helgerson J.		Comparing the Fukuda et al. Criteria and the Canadian Case Definition for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004; 12(1):37–52.	Fibromyalgia syndrome (FMS) is characterized by widespread pain, fatigue, sleep abnormalities, and distress. Because FMS lacks consistent evidence for tissue abnormalities, recent investigations have focused on central nervous system mechanisms of pain. Abnormal temporal summation of second pain (AWindup@) and central sensitization (CS) have recently been described in FMS patients. Windup (WU) and central sensitization, which rely on central pain mechanisms, occur after prolonged C-nociceptor input and depend on activation of nociceptor specific neurons as well as wide dynamic range neurons in the dorsal horn of the spinal cord. The important role of WU is also supported by its ability to predict the clinical pain intensity of FMS patients. Furthermore, brain-imaging techniques that can detect neuronal activation following nociceptive stimuli have provided additional evidence for abnormal central pain mechanisms in FMS. Most importantly, brain images have corroborated the augmented reported pain experience of FMS patients during experimental pain stimuli. These findings may have important implications for future research as well as the treatment of FMS pain.
Jason LA PhD, Susan R. Torres-Harding PHD, Amber Jurgens BA, Jean Helgerson BA		Article: Comparing the Fukuda et al. Criteria and the Canadian Case Definition for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004 12 (1): 37- 52	Because the pathogenesis of Chronic Fatigue Syndrome (CFS) has yet to be determined, case definitions have relied on clinical observation in classifying signs and symptoms for diagnosis. The selection of diagnostic signs and symptoms has major implications for which individuals are diagnosed with CFS and how seriously the illness is viewed by health care providers, disability insurers and rehabilitation planners, and patients and their families and friends. Diagnostic criteria also have implications for whether research based on varying definitions can be synthesized. The current investigation examined differences between CFS as defined by Fukuda et al. (1994) and a set of criteria that has been proposed for a clinical Canadian Case definition. There were twentythree participants who met the Canadian criteria, 12 in the CFS (Fukuda et al. (7) criteria) group and the 33

				from the chronic fatigue (CF)-psychiatric group. Dependent measures included: work status, psychiatric comorbidity, symptoms, and functional impairment (measured by the Medical Outcomes Study). People meeting the Fukuda et al. and Canadian criteria were compared with people who had a chronically fatiguing illness explained by a psychiatric condition. Statistical tests used included binomial logistic regression and analysis of variance. The Canadian criteria group, in contrast to the Fukuda et al. criteria group, had more variables that statistically significantly differentiated them from the psychiatric comparison group. Overall, there were 17 symptom differences between the Canadian and CF-psychiatric group, but only 7 symptom differences between the CFS and CF-psychiatric group. The findings suggest that both the Canadian and Fukuda et al. case definitions select individuals who are statistically significantly different from psychiatric controls with chronic fatigue, with the Canadian criteria selecting cases with less psychiatric co-morbidity, more physical functional impairment, and more fatigue/weakness, neuropsychiatric, and neurological symptoms.
Jiang SY, Yan JT, Fang M.	Department of Tuina, Yueyang Hospital of Integrated Traditional Chinese and Western Medicine, Shanghai University of Traditional Chinese Medicine, Shanghai 200437, China. jsysy@tom.com	[Progress in research on chronic fatigue syndrome] [Article in Chinese]	Zhong Xi Yi Jie He Xue Bao. 2004 Nov;2(6):459-63.	
Jones JF, Nisenbaum R, Solomon L, Reyes M, Reeves WC.	National Jewish Medical and Research Center, Denver, Colorado, USA.	Chronic fatigue syndrome and other fatiguing illnesses in adolescents: a population-based study.	J Adolesc Health. 2004 Jul;35(1):34-40.	PURPOSE: To estimate the prevalence of chronic fatigue syndrome (CFS) and describe characteristics of other fatiguing illnesses in adolescents (aged 12 through 17 years). METHODS: We conducted a random digit dialing survey of the residents of Wichita, Kansas. Adults identified fatigued adolescents in the household and answered questions relating to the child's health. Selected adolescents were invited to attend a clinic with a parent/guardian. After clinical evaluation they were classified as CFS or another fatigue state as defined in the 1994 CFS definition. Annual telephone interviews and clinical evaluations monitored subjects' fatigue status. Data were analyzed using the Kruskal-Wallis test, the Mantel-Haenszel test, and the exact McNemar test. RESULTS: The survey contacted 34,018 households with 90,316 residents. Of 8586 adolescents, 138 had fatigue for > or =1 month and most (107 or 78%) had chronic fatigue (> or =6 months) at some point during the 3-year follow-up. Twenty-eight had exclusionary diagnoses. Thirty-one were considered to have a CFS-like illness and were invited for clinical evaluation. Eleven agreed to participate and none met the CFS case definition. The baseline weighted prevalence of CFS-like illness was 338 per 100,000. Significant differences existed between parental and adolescents' descriptions of illness. CONCLUSIONS: The prevalence of CFS

				among adolescents was considerably lower than among adults. Evaluation of CFS in adolescents must consider both parent and patient perception of fatigue and other illnesses that might explain the symptom complex.
Kapfhammer HP, Rothenhausler HB.	Universitatsklinik fur Psychiatrie Auenbruggerplatz 31, A-8036 Graz/Osterreich. Hans-Peter.Kapfhammer @klinikum-graz.at	[Chronic fatigue syndrome] [Article in German]	MMW Fortschr Med. 2004 Jul 22;146(29-30):29, 31-3.	The symptoms of fatigue and exhaustion, which are central to chronic fatigue syndrome and neurasthenia, can lay claim to being"psychopathological entities" in their own right. Although ubiquitous, they by no means reflect a homogeneous clinical picture. Chronic fatigue may occur after physical illness, such as viral infections, or be associated with a range of different psychiatric disorders. There is wide overlap with affective, anxiety, somatoform, and personality disorders, and this should be borne in mind when it comes to classifying these symptoms.To investigate the etiopathogenesis, multifactorial models are required. For treatment, adapted cognitive-behavioral therapy, possibly accompanied by an antidepressant, is effective.
Kennedy G, Spence V, Underwood C, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK. g.kirk@dundee.ac.uk	Increased neutrophil apoptosis in chronic fatigue syndrome.	J Clin Pathol. 2004 Aug;57(8):891-3.	BACKGROUND/AIMS: Many patients with chronic fatigue syndrome (CFS) have symptoms that are consistent with an underlying viral or toxic illness. Because increased neutrophil apoptosis occurs in patients with infection, this study examined whether this phenomenon also occurs in patients with CFS. METHODS: Apoptosis was assessed in patients with CFS in conjunction with concentrations of the anti-inflammatory cytokine, transforming growth factor beta1 (TGFbeta1). RESULTS: The 47 patients with CFS had higher numbers of apoptotic neutrophils, lower numbers of viable neutrophils, increased annexin V binding, and increased expression of the death receptor, tumour necrosis factor receptor-I, on their neutrophils than did the 34 healthy controls. Patients with CFS also had raised concentrations of active TGFbeta1 ($p < 0.005$). CONCLUSIONS: These findings provide new evidence that patients with CFS have an underlying detectable abnormality in their immune cells.
Kennedy G, Abbot NC, Spence V, Underwood C, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital & Medical School, Dundee, UK. g.kirk@dundee.ac.uk	The specificity of the CDC-1994 criteria for chronic fatigue syndrome: comparison of health status in three groups of patients who fulfill the criteria.	Ann Epidemiol. 2004 Feb;14(2):95-100.	PURPOSE: The Centers for Disease Control (CDC)-1994 definition of chronic fatigue syndrome (CFS) is very broad, and there have been suggestions that it lacks specificity. To test this, we have compared three groups of patients, all of whom fulfill the criteria but self-report different etiologies. METHODS: Patients with self-reported symptoms which developed sporadically (sCFS, n=48); after Gulf War service (GW, n=24); and following exposure to organophosphate insecticides (OP, n=25) underwent a clinical examination, completed the MOS SF-36 quality of life and Hospital Anxiety and Depression scales, and were assessed for major and minor criteria for CDC-1994 CFS. RESULTS: Significant differences in simple clinical measures and outcome measures were observed between groups. The GW group had significantly more severe physical symptoms-fatigue, muscle and multi-joint pain-than OP or sCFS, and the sCFS group was significantly less impaired than the other two groups in terms of role emotional and mental health. In all three groups, a majority of patients exhibited muscle weakness in the lower limbs, and significant numbers of patients had absent or abnormal reflexes. CONCLUSIONS: Differences in simple, easily performed clinical outcome measurements can be observed between groups of patients, all of whom fulfill the CDC-1994 criteria for CFS. It is likely that their response to treatment may also vary. The specificity of the CFS case definition should be improved to define more homogeneous groups of patients for the purposes of treatment and research.
Kennedy G,	Vascular Diseases	Plasma endothelin-	Rheumatology	

Spence V, Khan F, Belch JJ.	Research Unit, University Department of Medicine, Ninewells Hospital & Medical School, Dundee, UK. g.kirk@dundee.ac.uk	1 levels in chronic fatigue syndrome.	(Oxford). 2004 Feb;43(2):252-3; author reply 253-4.	
Khan F, Kennedy G, Spence VA, Newton DJ, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital and Medical School, Dundee DD1 9SY, Scotland, U.K. f.khan@dundee.ac.uk	Peripheral cholinergic function in humans with chronic fatigue syndrome, Gulf War syndrome and with illness following organophosphate exposure.	Clin Sci (Lond). 2004 Feb;106(2):183-9.	In the present study, we have investigated whether the peripheral cholinergic abnormalities that we have reported previously [Spence, Khan and Belch (2000) Am. J. Med. 108, 736-739] in patients with chronic fatigue syndrome (CFS) are also present in those with Gulf War syndrome (GWS) and agricultural workers exposed to organophosphate pesticides, where cholinesterase inhibition is specifically implicated. We also looked at whether these abnormalities might be due to a reduction in the activity of cholinesterase expressed on the vascular endothelium. We used laser Doppler imaging to measure the forearm skin blood flow responses to iontophoresis of acetylcholine and of methacholine (which is resistant to breakdown by cholinesterase) in patients with CFS, GWS and those with a history of ill health after definite organophosphate exposure, as well as in matched healthy controls. The response to acetylcholine was significantly higher in patients with CFS than in controls (P =0.029, repeated-measures ANOVA), but was normal in those with GWS and those exposed to organophosphates. The methacholine response was higher than the acetylcholine response in all patient groups except for those with CFS, where there was no difference between the responses. Although there are many clinical similarities between these three illnesses, our results indicate peripheral cholinergic abnormalities in the vascular endothelium of only patients with CFS, suggesting that this syndrome has a different aetiology, which might involve inhibition of vascular cholinesterase.
Kreyberg S.		[Chronic/post-viral fatigue syndrome][Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Sep 23;124(18):2382-3.	Seksjon for forebyggende medisin og epidemiologi, Institutt for allmenn- og samfunnsmedisin, Universitetet i Oslo, Postboks 1130 Blindern 0318 Oslo. s.e.kreyberg@medisin.uio.no
Lerner AM, Dworkin HJ, Sayyed T, Chang CH, Fitzgerald JT, Beqaj S, Deeter RG, Goldstein J, Gottipolu P, O'Neill W.	Department of Medicine, William Beaumont Hospital, Royal Oak, Michigan, USA. lerner@cdimed.com	Prevalence of abnormal cardiac wall motion in the cardiomyopathy associated with incomplete multiplication of Epstein-barr Virus and/or cytomegalovirus in patients with	In Vivo. 2004 Jul-Aug;18(4):417-24.	We reported unique incomplete herpesvirus (Epstein-Barr Virus (EBV) and/or nonstructural (HCMV) cytomegalovirus) multiplication in 2 distinct subsets of CFS patients. The CFS subsets were identified by: a) presence of IgM serum antibodies to HCMV nonstructural gene products p52 and CM2 (UL44 and UL57), and/or b) IgM serum antibodies to Epstein-Barr virus viral capsid antigen (EBV, VCA IgM). Diagnostic IgM serum antibodies were found in two independent blinded studies involving 49 CFS patients, but the same antibodies were absent in 170 control patients ($p<0.05$). Abnormal 24 Hr-electrocardiographic monitoring, tachycardias at rest and, in severe chronic cases, abnormal cardiac wall motion (ACWM) were seen in these same CFS patients. We now report a prospective consecutive case control study from 1987--1999 of cardiac dynamics as measured by radionuclide ventriculography in 98 CFS patients from 1987--1999. Controls were patients with various malignancies who were evaluated in protocols requiring radionuclide ventriculography before

		chronic fatigue syndrome.		initiation of cardiotoxic chemotherapeutic agents. The prevalence of abnormal cardiac wall motion (ACWM) at rest in CFS patients was 10 out of 87 patients (11.5%). With stress exercise, 21 patients (24.1%) demonstrated ACWM. Cardiac biopsies in 3 of these CFS patients with ACWM showed a cardiomyopathy. Among the controls, ACWM at rest was present in 4 out of 191 patients (2%) (p=0.0018). A progressive cardiomyopathy caused by incomplete virus multiplication of EBV and/or HCMV in CFS patients is present.
Lerner AM, Beqaj SH, Deeter RG, Fitzgerald JT.	Department of Medicine, William Beaumont Hospital and Wayne State University School of Medicine, Royal Oak, Michigan, USA. lerner@cdimed.com	IgM serum antibodies to Epstein-Barr virus are uniquely present in a subset of patients with the chronic fatigue syndrome.	In Vivo. 2004 Mar-Apr;18(2):101-6.	BACKGROUND: A unique subset of patients with chronic fatigue syndrome (CFS) and IgM serum antibodies to cytomegalovirus (HCMV) non-structural gene products p52 and CM2 (UL 44 and UL 57) has been described. PATIENTS AND METHODS: Fifty-eight CFS patients and 68 non-CFS matched controls were studied. Serum antibodies to EBV viral capsid antigen (VCA) IgM and EBV Early Antigen, diffuse (EA, D) as well HVCMV(V), IgM and IgG; VP (sucrose, density purified V); p52 and CM2 IgM serum antibodies were assayed. RESULTS: Mean age of CFS patients was 44 years (75% women). Control patients were 9 years older (73% women). Serum EBV VCA IgM positive antibody titers were identified in 33 CFS patients (Group A subset EBV VCA IgM 62.3+/-8.3, neg. <20), but were not present in other CFS patients, (Group B subset EBV VCA IgM 6.8+/-0.7) controls (p<0.0001). EBV VCA IgM titers remained positive in CFS patients from Group A for 24-42 months. CONCLUSION: Serum antibody to EBV VCA IgM may be a specific diagnostic test for a second subset of CFS patients.
Liu Z, Wang D, Xue Q, Chen J, Li Y, Bai X, Chang L.	Department of Neurology, Beijing Friendship Hospital, Affiliated Hospital of Capital University of Medical Science, 95 Yong-an Rd, Beijing 100050, China. liuzhandong99@sina.com.cn	Determination of fatty acid levels in erythrocyte membranes of patients with chronic fatigue syndrome.	Nutr Neurosci. 2003 Dec;6(6):389-92.	Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various systems of whole body. The etiology of CFS remains unclear. Literature reported whether the concentrations of the essential fatty acids in red cell membranes of CFS patients were decreased is controversial. In our study, Forty-two patients who fulfilled the diagnostic criteria defined by Centers for Disease Control and Prevention (CDC). Thirty-seven age- and sex-matched controls were selected from healthy medical staffs and volunteers. After lipid analysis, we found that the levels of the arachidonic acid (ARA) and docosahexanoic acid (DHA) were decreased in patients suffered from CFS. However, the levels of the palmitic acid and oleic acid were increased. We speculated that there are two possible mechanisms--one of which is that oxidative stress has led to an excessive oxidation and resulting in the above fatty acids. Alternatively, insufficiency of ingestion of fatty acids might not be the major cause.
Lloyd AR.	Inflammation Research Unit, School of Medical Sciences, University of New South Wales, Kensington, NSW 2052, Australia. a.lloyd@unsw.edu.	To exercise or not to exercise in chronic fatigue syndrome? No longer a question.	Med J Aust. 2004 May 3;180(9):437-8.	

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Looper KJ, Kirmayer LJ.	Department of Psychiatry, Sir Mortimer B. Davis-Jewish General Hospital, 3755 Chemin de la Cote-Ste-Catherine, Montreal, PQ, Canada. karl.looper@mail.mcgill.ca	Perceived stigma in functional somatic syndromes and comparable medical conditions.	J Psychosom Res. 2004 Oct;57(4):373-8.	OBJECTIVE: To determine if patients with functional somatic syndromes (FSS) perceive greater levels of stigma than patients with comparable medical conditions that have a clear medical pathology. METHODS: Patients with chronic fatigue syndrome (CFS), fibromyalgia (FM), or irritable bowel syndrome (IBS) were compared to multiple sclerosis (MS), rheumatoid arthritis (RA), and inflammatory bowel disease (IBS), respectively. RESULTS: There were greater levels of perceived stigma in the combined group of FSS compared to the medical control group. When each FSS was compared to its matched control group, only CFS had a higher level of perceived stigma. These results remained when controlling for other variables relevant to stigma. CONCLUSIONS: The higher level of perceived stigma in CFS may be due to the ambiguity of its status as a medical condition. The absence of this effect in FM and IBS is consistent with a greater level of acceptance of these disorders as medical illnesses.
Lorenzo Gomez MF, Gomez Castro S.	Area de Urologia Femenina de la Clinica San Marcos, Investigadora en el Centro Biosanitario de Investigacion Experimental de la Universidad de Salamanca, Salamanca. mflorenzogo@yahoo.es	[Physiopathologic relationship between interstitial cystitis and rheumatic, autoimmune, and chronic inflammatory diseases][Article in Spanish]	Arch Esp Urol. 2004 Jan-Feb;57(1):25-34.	OBJECTIVES: To evaluate the current knowledge about interstitial cystitis pathophysiology and its relationship with rheumatic, autoimmune and chronic inflammatory diseases. METHODS: Literature search under "interstitial cystitis pathophysiology" either clinical or experimental trials and reports, in Medline, PubMed, Digital Urology Journal and Doctor's Guide, in addition to our own clinical research experience results. RESULTS: Both human and experimental trials show resemblances between interstitial cystitis and rheumatic, autoimmune, and chronic inflammatory diseases on clinical presentations, pathophysiology. Some interstitial cystitis patients show the bladder infiltrated with specific mononuclear cells, high incidence of circulating antinuclear antibodies, good response to anti-inflammatory and/or immunosuppressive therapies. Interstitial cystitis in association with rheumatic, autoimmune and chronic inflammatory diseases is very common. Many patients with systemic lupus erythematosus, Sjogren syndrome and fibromyalgia syndrome show antibodies against urothelium and/or muscle cells and/or other connective tissue components of urinary bladder. Systemic lupus erythematosus and Sjogren syndrome are the autoimmune diseases which bear strongest similarity with interstitial cystitis. Moreover, rheumatoid arthritis, chronic pelvic pain syndrome, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, Evan's syndrome and atopic dermatitis share some pathogenic characteristics. CONCLUSIONS: Nowadays, interstitial cystitis pathophysiology is unknown. Based on clinical presentations, epidemiology, pathology and laboratory findings and treatment response, there is an important correlation among interstitial cystitis and rheumatic, autoimmune and chronic inflammatory diseases. These disorders may share some pathophysiologic mechanisms. Rigorous studies of pathophysiology of these group of diseases are needed to confirm consistently this approach for such conditions.
Luthra A, Wessely S.	King's College School of Medicine, Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK.	Unloading the trunk: neurasthenia, CFS and race.	Soc Sci Med. 2004 Jun;58(11):2363-9.	The aetiologies of both chronic fatigue syndrome (CFS) and its predecessor neurasthenia, have been linked to technological advances in 'developed' countries. This paper discusses how this has led to a form of race thinking within discussions about fatigue which has persisted for more than a century. We review the historical development of this race thinking from neurasthenia to CFS and describe how it is manifested in both the lay- and medical literature. We also review the epidemiological literature on CFS and ethnicity to better understand the relatively low percentage of non-white patients seen in tertiary referral clinics for CFS. The aim of this paper is to act as a starting point for a

				debate on race and CFS.
Mahurin RK, Claypoole KH, Goldberg JH, Arguelles L, Ashton S, Buchwald D.	Department of Radiology, University of Washington, Seattle, WA 98195-6465, USA. mahurin@u.washington.edu	Cognitive processing in monozygotic twins discordant for chronic fatigue syndrome.	Neuropsychology. 2004 Apr;18(2):232-9.	Twenty-one pairs of monozygotic twins discordant for chronic fatigue syndrome (CFS) and 21 matched healthy control (HC) subjects were assessed with 5 untimed tests and 5 timed tests from the computer-based NeuroCognitive Assessment Battery (R. K. Mahurin, 1993). Random effects regression showed no difference between CFS and healthy twins on any of the cognitive tests. Further, the twin groups did not differ from the HC group on any content-dependent measure. In contrast, both sets of twins performed worse than the HC group on all speed-dependent tests except Finger Tapping. Self-rated fatigue and dysphoric mood were only weakly correlated with cognitive performance. These data point toward a shared genetic trait related to information processing that is manifest in the CFS context. The findings have implications for differentiating genetic and acquired vulnerability in the symptomatic expression of the disorder. ((c) 2004 APA, all rights reserved)
Madill PV.		Chronic fatigue syndrome and the cholinergic hypothesis.	JAMA. 2004 Dec 8;292(22):2723; author reply 2723. Comment on: JAMA. 2004 Sep 8;292(10):1195-204.	
Martinez S, Guilleminault C.	Stanford University Sleep Disorders Clinic, Stanford, California 94305, USA.	Periodic leg movements in prepubertal children with sleep disturbance.	Dev Med Child Neurol. 2004 Nov;46(11):765-70.	This study's aims were to determine: (1) prevalence of periodic leg movements (PLMs) in walking prepubertal children consulting a sleep clinic for any sleep disorder; (2) associations between PLMs and other sleep and medical disorders; and (3) the response of other sleep disorders to treatment with the dopamine agonist pramipexol. Clinical evaluation and polysomnography were carried out for a period of 12 months on 252 consecutively seen, prepubertal children with sleep disorders (156 males, 96 females; aged 15mo to 11y, mean 7y 1mo, SD3y 10mo). Sleep disorders unrelated to PLMs were treated, and six children received pramipexol for PLMs. Follow-up included clinical evaluation and polysomnography. Twenty-three per cent of children were diagnosed with PLMs on the basis of polysomnography. The presence of PLMs had usually been unrecognized clinically. The only clinical symptom that could be related to periodic limb movement disorder was a report of leg pains at morning awakening. Only two of 58 children had PLMs without other clinical or polysomnographic findings. Comorbidity seen with PLMs included neuropsychiatric syndromes (n=20), isolated sleep disordered breathing (SDB; n=29), and several other comorbid conditions (n=7). Seven of 11 children seen with attention-deficit-hyperactivity disorder also had PLMs. Surgery for SDB was associated with subsequent cessation of PLMs in 15 of 29 children. Five out of six children with PLMs who received pramipexol were able to tolerate the drug and experienced a complete disappearance of their PLMs. Presence of chronic fatigue, sleepiness, disrupted nocturnal sleep, and difficulties in falling asleep should lead to a systematic search for PLMs that is independent of associated syndromes. Isolated treatment of SDB might help eliminate some, but not all, PLMs.
McCrone P, Ridsdale L, Darbishire L, Seed	Centre for the Economics of Mental Health,	Cost-effectiveness of cognitive behavioural	Psychol Med. 2004 Aug;34(6):991-9.	BACKGROUND: Chronic fatigue is a common condition, frequently presenting in primary care. The aim of this study was to compare the cost-effectiveness of cognitive behavioural therapy (CBT) and graded exercise therapy (GET), and to compare therapy with usual care plus a self-help booklet (BUC).

P.	Health Services Research Department, Institute of Psychiatry, King's College, London, UK. p.mccrone@iop.kcl.ac.uk	therapy, graded exercise and usual care for patients with chronic fatigue in primary care.		METHOD: Patients drawn from general practices in South East England were randomized to CBT or GET. The therapy groups were then compared to a group receiving BUC recruited after the randomized phase. The main outcome measure was clinically significant improvements in fatigue. Cost-effectiveness was assessed using the net-benefit approach and cost-effectiveness acceptability curves. RESULTS: Costs were available for 132 patients, and cost-effectiveness results for 130. Costs were dominated by informal care. There were no significant outcome or cost differences between the therapy groups. The combined therapy group had significantly better outcomes than the standard care group, and costs that were on average 149 pounds higher (a non-significant difference). Therapy would have an 81.9% chance of being cost-effective if society were willing to attach a value of around 500 pounds to each four-point improvement in fatigue. CONCLUSION: The cost-effectiveness of cognitive behavioural therapy and graded exercise were similar unless higher values were placed on outcomes, in which case CBT showed improved cost-effectiveness. The cost of providing therapy is higher than usual GP care plus a self-help booklet, but the outcome is better. The strength of this evidence is limited by the use of a non-randomized comparison. The cost-effectiveness of therapy depends on how much society values reductions in fatigue.
McCully KK, Smith S, Rajaei S, Leigh JS Jr, Natelson BH.	Department of Exercise Science, University of Georgia, Athens, GA 30602, USA. kmccully@coe.uga.edu	Muscle metabolism with blood flow restriction in chronic fatigue syndrome.	J Appl Physiol. 2004 Mar;96(3):871-8. Epub 2003 Oct 24.	The purpose of this study was to determine whether chronic fatigue syndrome (CFS) is associated with reduced blood flow and muscle oxidative metabolism. Patients with CFS according to Centers for Disease Control criteria (n = 19) were compared with normal sedentary subjects (n = 11). Muscle blood flow was measured in the femoral artery with Doppler ultrasound after exercise. Muscle metabolism was measured in the medial gastrocnemius muscle with (31)P-magnetic resonance spectroscopy. Muscle oxygen saturation and blood volume were measured using near-infrared spectroscopy. CFS and controls were not different in hyperemic blood flow or phosphocreatine recovery rate. Cuff pressures of 50, 60, 70, 80, and 90 mmHg were used to partially restrict blood flow during recovery. All pressures reduced blood flow and oxidative metabolism, with 90 mmHg reducing blood flow by 46% and oxidative metabolism by 30.7% in CFS patients. Hyperemic blood flow during partial cuff occlusion was significantly reduced in CFS patients ($P < 0.01$), and recovery of oxygen saturation was slower ($P < 0.05$). No differences were seen in the amount of reduction in metabolism with partially reduced blood flow. In conclusion, CFS patients showed evidence of reduced hyperemic flow and reduced oxygen delivery but no evidence that this impaired muscle metabolism. Thus CFS patients might have altered control of blood flow, but this is unlikely to influence muscle metabolism. Furthermore, abnormalities in muscle metabolism do not appear to be responsible for the CFS symptoms.
Mears CJ, Taylor RR, Jordan KM, Binns HJ; Pediatric Practice Research Group.	Department of Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA.	Sociodemographic and symptom correlates of fatigue in an adolescent primary care sample.	J Adolesc Health. 2004 Dec;35(6):528e.21-6.	PURPOSE: To describe the prevalence of prolonged fatigue, chronic fatigue syndrome (CFS)-like illness, and associated symptom patterns in adolescents attending primary care. METHODS: The design was cross-sectional. A questionnaire designed by the authors assessing fatigue and associated symptoms was administered to 901 adolescents (aged 11-18 years) attending 12 primary care clinics in the Chicago area. Prevalence rates for prolonged fatigue and CFS-like illness were calculated. Univariate comparisons involving sociodemograpic data and fatigue severity were made between adolescents with and without prolonged fatigue, and sociodemographic and symptom predictors of prolonged fatigue were identified using logistic regression analysis. RESULTS: Prolonged fatigue (> or = 1 month)

				occurred at a rate of 8.0% and CFS-like illness occurred at a rate of 4.4%. Adolescents with prolonged fatigue were significantly older and also reported greater fatigue severity than those without fatigue. Findings from logistic regression indicated that, in addition to increasing age, headaches, muscle pains, fever, and fatigue made worse by exercise were significantly associated with prolonged fatigue. CONCLUSIONS: Abnormal fatigue is a disabling and prevalent condition in adolescents in primary care. It is associated with a number of additional symptoms, many of which may have viral origins.
Miike T, Tomoda A, Jhodoi T, Iwatani N, Mabe H.	Department of Child Development, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University Graduate School, 1-1-1 Honjo, Kumamoto 860-8556, Kumamoto, Japan. miketeru@kaiju.medic.kumamoto-u.ac.jp	Learning and memorization impairment in childhood chronic fatigue syndrome manifesting as school phobia in Japan.	Brain Dev. 2004 Oct;26(7):442-7.	For the last 15 years, we have tried to understand the pathophysiology of childhood chronic fatigue syndrome (CCFS) in Japan. In this condition, two major symptoms are important: easy fatigability and disturbed learning and memorization. In CCFS patients we clinically evaluated autonomic nervous system function, circadian rhythm of hormonal secretion (melatonin, cortisol and 3-endorphin), core body temperature, and sleep-wake pattern. Most patients showed autonomic nervous system dysfunction and circadian rhythm disturbances, similar to those observed in jet lag. Radiological imaging studies (SPECT, Xe-CT, and MRS) revealed decreased blood flow in the frontal and thalamic areas, and accumulation of choline in the frontal lobe. We analyzed the relationship between the laboratory data and clinical symptoms in CCFS.
Mourot L, Bouhaddi M, Perrey S, Cappelle S, Henriet MT, Wolf JP, Rouillon JD, Regnard J.	Laboratoire de Physiologie Medecine, Faculte de Medecine, Besancon Cedex, France. mourotlaurent@hotmail.com	Decrease in heart rate variability with overtraining: assessment by the Poincare plot analysis.	Clin Physiol Funct Imaging. 2004 Jan;24(1):10-8.	Numerous symptoms have been associated with the overtraining syndrome (OT), including changes in autonomic function. Heart rate variability (HRV) provides non-invasive data about the autonomic regulation of heart rate in real-life conditions. The aims of the study were to: (i) characterize the HRV profile of seven athletes (OA) diagnosed as suffering of OT, compared with eight healthy sedentary (C) and eight trained (T) subjects during supine rest and 60 degrees upright, and (ii) compare the traditional time- and frequency-domain analysis assessment of HRV with the non-linear Poincare plot analysis. In the latter each R-R interval is plotted as a function of the previous one, and the standard deviations of the instantaneous (SD1) and long-term R-R interval variability are calculated. Total power was higher in T than in C and OA both in supine (1158 +/- 1137, 6092 +/- 3554 and 2970 +/- 2947 ms2 for C, T and OA, respectively) and in upright (640 +/- 499, 1814 +/- 806 and 1092 +/- 712 ms2 for C, T and OA, respectively; P<0.05) positions. In supine position, indicators of parasympathetic activity to the sinus node were higher in T compared with C and OA (high-frequency power: 419.1 +/- 381.2, 1105.3 +/- 781.4 and 463.7 +/- 715.8 ms2 for C, T and OA, respectively; P<0.05; SD1: 29.5 +/- 18.5, 75.2 +/- 17.2 and 37.6 +/- 27.5 for C, T and OA, respectively; P<0.05). OA had a marked predominance of sympathetic activity regardless of the position (LF/HF were 0.47 +/- 0.35, 0.47 +/- 0.50 and 3.96 +/- 5.71 in supine position for C, T and OA, respectively, and 2.09 +/- 2.17, 7.22 +/- 6.82 and 12.04 +/- 10.36 in upright position for C, T and OA, respectively). The changes in HRV indexes

				induced by the upright posture were greater in T than in OA. The shape of the Poincare plots allowed the distinction between the three groups, with wide and narrow shapes in T and OA, respectively, compared with C. As Poincare plot parameters are easy to compute and associated with the 'width' of the scatter gram, they corroborate the traditional time- and frequency-domain analysis. We suggest that they could be used to indicate fatigue and/or prevent OT.
Murphy BE, Abbott FV, Allison CM, Watts C, Ghadirian AM.	Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, Canada H3A 1A1. bev.murphy@mcgill.ca	Elevated levels of some neuroactive progesterone metabolites, particularly isopregnanolone, in women with chronic fatigue syndrome.	Psychoneuroendocrinology. 2004 Feb;29(2):245-68.	Chronic fatigue syndrome (CFS) is a controversial entity whose cause is unknown. In this study we have explored the possibility that progesterone metabolites may be involved. Plasma levels of the progesterone precursor pregnenolone, progesterone itself, and five ring A-reduced metabolites of progesterone were measured in 20 women with CFS and in 13 age-matched controls. To minimize the contribution of the ovary, women were either post-menopausal or in the follicular phase of the menstrual cycle (day 4-8), and progesterone levels were all well within the expected range (< or = 3.5 nmol/l). Mean values for progesterone and all of its metabolites were higher in CFS patients, the most marked being a 2.3-fold elevation in isopregnanolone (3beta,5alpha-tetrahydroprogesterone; p < or = 0.001). Progesterone levels were correlated with those of its metabolites, but even after controlling for progesterone by ANCOVA, isopregnanolone levels were still elevated (p < or = 0.001). These elevated levels of isopregnanolone could not be attributed to medications (antidepressants and anxiolytics). When the CFS patients were divided into two groups according to their Hamilton depression scale ratings, mean (+/-SD) isopregnanolone levels were higher (274+/-160 vs 197+/-119 pmol/l) in the less depressed group (ratings 2-14) than in the more depressed group (ratings 17-28), although this difference did not reach significance. Progesterone levels were negatively correlated with Hamilton depression rating scores (r=-0.56; p<0.01). These results suggest that increases in ring A-reduced progesterone metabolites, particularly isopregnanolone, are associated with CFS, and that the pathophysiology of CFS is unlikely to be due to depression.
Naschitz J, Dreyfuss D, Yeshurun D, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. Naschitz@tx.technion.ac.il	Midodrine treatment for chronic fatigue syndrome.	Postgrad Med J. 2004 Apr;80(942):230-2.	The long term results of midodrine treatment in a patient having debilitating chronic fatigue syndrome (CFS) are reported. Midodrine treatment, directed at the autonomic nervous system, resulted in correction of the dysautonomia followed by improvement of fatigue. This finding is consistent with the hypothesis that dysautonomia plays a major part in the pathophysiology of CFS and that therapies directed at the autonomic nervous system may be effective in the treatment of CFS.
Naschitz JE, Rozenbaum M, Fields M, Isseroff H, Enis S, Babich		Search for disease-specific cardiovascular reactivity patterns	Clin Sci (Lond). 2004 Aug 26 [Epub ahead of print]	Objectives. Aberrations of cardiovascular reactivity (CVR), an expression of autonomic function, lack specificity for a particular disorder. Recently, a CVR pattern particular to chronic fatigue syndrome has been observed. We aimed to develop methodologies for assessment of disease-specific CVR patterns. Subjects. As a prototype, a population of 50 consecutive patients with Familial Mediterranean Fever

JP, Peck S, Rubin Peck E, Gaitini L, Naschitz S, Sabo E, Rosner I.		- Developing the methodology.		(FMF) was studied compared with control populations. Methods. A 10-minute supine-30 minute head-up tilt test with recording the heart rate and blood pressure or the pulse transit time was performed. Five studies were conducted, applying different methods. In each study, statistical analysis identified independent predictors of the CVR in FMF. Based on regression coefficients of these predictors, a linear discriminant score (DS) was computed for every subject. Each study established an equation to assess the CVR, calculate the DS for FMF and determine the sensitivity and specificity of the DS cut-off. Results. In each of the five studies, abnormal CVR was observed in FMF patients. The best accuracy (88% sensitivity and 90.1% specificity for FMF) was obtained by a method based on beat-to-beat heart rate and pulse transit time recordings. Data was processed by fractal and recurrence quantitative analysis with recordings in FMF patients compared with a mixed control population. Conclusions. Identification of disease-specific CVR patterns became possible with methodologies like those described in the present work. In FMF, disease-specific CVR may be explained by the interplay between neuro-endocrine loops specific to FMF with cardiovascular homeostatic mechanisms. Recognition of disease-specific CVR patterns may advance the understanding of homeostatic mechanisms and have implications in clinical practice.
Naschitz JE, Rosner I, Rozenbaum M, Fields M, Isseroff H, Babich JP, Zuckerman E, Elias N, Yeshurun D, Naschitz S, Sabo E.	Departments of Internal Medicine A and Rheumatology, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel. naschitz@tx.technion.ac.il	Patterns of cardiovascular reactivity in disease diagnosis.	QJM. 2004 Mar;97(3):141-51.	BACKGROUND: Aberrations of cardiovascular reactivity (CVR), an expression of autonomic function, occur in a number of clinical conditions, but lack specificity for a particular disorder. Recently, a CVR pattern particular to chronic fatigue syndrome was observed. Aim: To assess whether specific CVR patterns can be described for other clinical conditions. METHODS: Six groups of patients, matched for age and gender, were evaluated with a shortened head-up tilt test: patients with chronic fatigue syndrome (CFS) (n = 20), non-CFS fatigue (F) (n = 15), neurally-mediated syncope (SY) (n = 21), familial Mediterranean fever (FMF) (n = 17), psoriatic arthritis (PSOR) (n = 19) and healthy subjects (H) (n = 20). A 10-min supine phase was followed by recording 600 cardiac cycles on tilt (5-10 min). Beat-to-beat heart rate (HR) and pulse transit time (PTT) were measured. Results were analysed using conventional statistics, recurrence plot analysis and fractal analysis. RESULTS: Multivariate analysis evaluated independent predictors of the CVR in each patient group vs. all other groups. Based on these predictors, equations were determined for a linear discriminant score (DS) for each group. The best sensitivities and specificities of the DS, consistent with disease-related phenotypes of CVR, were noted in the following groups: CFS, 90.0% and 60%; SY, 93.3% and 62.5%; FMF, 90.1% and 75.4%, respectively. DISCUSSION: Pathological disturbances may alter cardiovascular reactivity. Our data support the existence of disease-related CVR phenotypes, with implications for pathogenesis and differential diagnosis.
Naschitz JE, Yeshurun D, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion - Israel	Dysautonomia in chronic fatigue syndrome: facts, hypotheses, implications.	Med Hypotheses. 2004;62(2):203-6.	The diagnosis of chronic fatigue syndrome (CFS) is based on patient history and treatment on cognitive behavior therapy and graded exercise. There is increasing evidence that dysautonomia occurs in CFS manifest primarily as disordered regulation of cardiovascular responses to stress. We impart our experience relating to diagnosis, monitoring, and treatment of CFS based on identification and management of dysautonomia. Recently proposed methods for assessment of the cardiovascular reactivity, the 'hemodynamic instability score' (HIS) and the 'Fractal and Recurrence Analysis-based Score' (FRAS), served for this purpose. On HUTT, a particular dysautonomia is revealed in CFS patients that differ from dysautonomia in several other disorders. This distinct abnormality in CFS can be

	Institute of Technology, PO Box 4940, Haifa 31048, Israel. naschitz@tx.technion.ac.il			identified by HIS >-0.98 (sensitivity 84.5% and specificity 85.1%) and FRAS > +0.22 (sensitivity 70% and specificity 88%). Therefore, the HIS and FRAS may be used, in the appropriate clinical context, to support the diagnosis of CFS, which until now, could only be subjectively inferred. A pilot study suggested that midodrine treatment, directed at the autonomic nervous system in CFS, results first in correction of dysautonomia followed by improvement of fatigue. This finding implies that dysautonomia is pivotal in the pathophysiology CFS, at least in a large part of the patients, and that manipulating the autonomic nervous system may be effective in the treatment of CFS.
Ng BY, Lim CC, Yeoh A, Lee WL.	Department of Behavioral Medicine, Singapore General Hospital, Republic of Singapore. gdmnby@sgh.com.sg	Neuropsychiatric sequelae of Nipah virus encephalitis.	J Neuropsychiatry Clin Neurosci. 2004 Fall;16(4):500-4.	The authors followed nine patients with Nipah virus encephalitis over the course of 24 months. Eight of the nine developed psychiatric features assigned to the encephalitis. Three patients developed major depressive disorder immediately after recovering from the encephalitis, and two developed depression approximately 1 year after the outbreak. Two patients developed personality changes, and two suffered chronic fatigue syndrome. Neuropsychological testing was accomplished in eight of the nine patients. Deficits in attention, verbal, and/or visual memory were substantial in seven of the eight patients tested. Verbal memory was more impaired than visual memory in these patients. Comparison between psychiatric and cognitive impairment and total number of brain lesions showed no discernible trends.
Nijs J PhD, MSc, Garth L. Nicolson PhD		Article: Gulf War Veterans: Evidence for Chromosome Alternations and Their Significance	Journal of Chronic Fatigue Syndrome 2004 12 (1): 79 - 83	
Nijs J, De Meirleir K, Duquet W.	Department of Human Physiology, Vrije Universiteit Brussel, Brussel, Belgium. Jo.Nijs@vub.ac.be	Kinesiophobia in chronic fatigue syndrome: assessment and associations with disability.	Arch Phys Med Rehabil. 2004 Oct;85(10):1586-92.	OBJECTIVES: To investigate aspects of the validity of the total scores of the Tampa Scale for Kinesiophobia (TSK), Dutch Version, which was modified to make it an appropriate questionnaire for the assessment of kinesiophobia (fear of movement) in chronic fatigue syndrome (CFS) patients (the Dutch TSK-CFS), and, using this assessment tool, to examine the associations between kinesiophobia, exercise capacity, and activity limitations and participation restrictions in patients with CFS. DESIGN: Prospective observational studies. SETTING: An outpatient fatigue clinic. PARTICIPANTS: In the first study, 40 patients fulfilling the 1994 US Centers for Disease Control and Prevention (CDC) criteria for CFS were enrolled. The sample of the second study consisted of 51 CDC-defined patients with CSF. INTERVENTIONS: Not applicable.Main outcome measures Study 1: Subjects completed a set of questionnaires; the Utrechtse Coping List (UCL), the Dutch TSK-CFS, and the Dutch Baecke Questionnaire of Habitual Physical Activity. Study 2: All patients completed 2 questionnaires (Chronic Fatigue Syndrome Activities and Participation Questionnaire [CFS-APQ], Dutch TSK-CFS) and performed a maximal exercise stress test on a bicycle ergometer. The heart rate was monitored continuously by use of an electrocardiograph. Metabolic and ventilatory parameters were measured through spirometry. RESULTS: Study 1: The Cronbach alpha coefficient for the individual item scores on the TSK-CFS was .80. The total scores on the Dutch TSK-CFS showed a statistically significant correlation with both the avoidance/abide subscale of the UCL (Spearman rho=.35, P=.029) and the total score of the Baecke Questionnaire (rho=-.45, P=.004). Study 2: The total scores on the Dutch TSK-CFS showed a statistically significant correlation with the total scores on the CFS-APQ (rho=.39,

				P=.004). No statistically significant associations were observed between the exercise capacity parameters and the total scores on the Dutch TSK-CFS. CONCLUSIONS: These results provide evidence for the internal consistency and the convergent and congruent validity of the scores obtained by use of the Dutch TSK-CFS. Kinesiophobia appears to be associated with activity limitations/participation restrictions but not with exercise capacity in patients with CFS.
Nijs J, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy and Chronic Fatigue Clinic, Vrije Universiteit Brussel, Belgium. Jo.Nijs@vub.ac.be	Prediction of peak oxygen uptake in patients fulfilling the 1994 CDC criteria for chronic fatigue syndrome.	Clin Rehabil. 2004 Nov;18(7):785-92.	PURPOSE: To establish an inexpensive, simple method of predicting peak oxygen uptake (VO2peak) in patients fulfilling the 1994 Centers for Disease Control and Prevention (CDC) criteria for chronic fatigue syndrome (CFS). DESIGN: A retrospective observational study. SETTING: An outpatient tertiary care chronic fatigue clinic. SUBJECTS: Two hundred and forty consecutive patients fulfilling the 1994 CDC criteria for CFS. INTERVENTIONS: Heart rate, metabolic and ventilatory parameters were measured continuously during a maximal exercise stress test on a bicycle ergometer. Using the equation peak oxygen uptake = 13.1 x peak workload +284 (used by Mullis et al., Br J Sports Med 1999; 33: 352-56), VO2peak was predicted from the peak workload of a maximal exercise capacity test. Pearson correlation coefficient and linear regression analysis were used to establish the most accurate way to predict VO2peak. RESULTS: Percentage error encountered when comparing actual measured VO2peak with predicted value was 17.3% (+/-10.0). A strong correlation between VO2peak and peak workload was observed ($r= 0.89$, $p < 0.001$). A regression analysis established the relation as VO2peak = 10.47 x peak workload +284.1, where VO2peak is given in ml/min and peak workload in W (error in prediction = 11.0+/-9.5%). CONCLUSIONS: Monitoring of the peak workload during a maximal, graded bicycle ergometric test suffices to predict the VO2peak. When predicting VO2peak the used operational definition for the diagnosis of CFS could be taken into account. Compared with the equation used by Mullis et al., peak workload is multiplied by 10.47 in order to predict peak oxygen uptake in CDC-defined CFS patients.
Nijs J, Vanherberghen K, Duquet W, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy Science, Vrije Universiteit Brussel, Brussels, Belgium. Jo.Nijs@vub.ac.be	Chronic fatigue syndrome: lack of association between pain-related fear of movement and exercise capacity and disability.	Phys Ther. 2004 Aug;84(8):696-705.	BACKGROUND AND PURPOSE: Patients who experience pain, a symptom of chronic fatigue syndrome (CFS), often exhibit kinesiophobia (irrational fear of movement). The purpose of this study was to examine whether pain-related fear of movement is associated with exercise capacity, activity limitations, or participation restrictions in patients with CFS who experience widespread pain. SUBJECTS AND METHODS: Sixty-four subjects met the inclusion criteria. All subjects fulfilled the 1994 Centers for Disease Control and Prevention case definition for CFS and experienced widespread myalgias or arthralgias. The subjects completed the Tampa Scale for Kinesiophobia-Dutch Version (TSK-DV) and the Dutch Chronic Fatigue Syndrome-Activities and Participation Questionnaire (CFS-APQ). They then performed a maximal exercise test on a bicycle ergometer. Heart rate was monitored continuously by use of an electrocardiograph. Ventilatory factors were measured through spirometry. Correlations between the TSK-DV scores and both the exercise capacity data and the CFS-APQ scores were assessed using the Spearman rank correlation coefficient. Using the Mann-Whitney U test, the TSK-DV scores were compared between subjects who performed a maximal exercise stress test and those who did not perform the test. RESULTS: Forty-seven subjects (73.4%) attained a total score of greater than 37 on the TSK-DV, indicating high fear of movement. Neither the exercise capacity data nor the CFS-APQ scores indicated a correlation with the TSK-DV scores (n=64). Subjects who did not perform a maximal exercise capacity test had more fear of movement (median TSK-DV score=43.0,

				interquartile range=10.3) compared with those who did perform a maximal exercise capacity test (median TSK-DV score=38.0, interquartile range=13.2; Mann-Whitney U-test score=322.5, z=-1.974, P=.048), but the correlation analysis was unable to reveal an association between exercise capacity and kinesiophobia in either subgroup. DISCUSSION AND CONCLUSION: These results indicate a lack of correlation between kinesiophobia and exercise capacity, activity limitations, or participation restrictions, at least in patients with CFS who are experiencing widespread muscle or joint pain.
Nijs J, De Meirleir K, Meeus M, McGregor NR, Englebienne P.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy Science, Vrije Universiteit Brussel (VUB), Brussel 1090, Belgium.	Chronic fatigue syndrome: intracellular immune deregulations as a possible etiology for abnormal exercise response.	Med Hypotheses. 2004;62(5):759-65.	The exacerbation of symptoms after exercise differentiates Chronic fatigue syndrome (CFS) from several other fatigue-associated disorders. Research data point to an abnormal response to exercise in patients with CFS compared to healthy sedentary controls, and to an increasing amount of evidence pointing to severe intracellular immune deregulations in CFS patients. This manuscript explores the hypothetical interactions between these two separately reported observations. First, it is explained that the deregulation of the 2-5A synthetase/RNase L pathway may be related to a channelopathy, capable of initiating both intracellular hypomagnesaemia in skeletal muscles and transient hypoglycemia. This might explain muscle weakness and the reduction of maximal oxygen uptake, as typically seen in CFS patients. Second, the activation of the protein kinase R enzyme, a characteristic feature in atleast subsets of CFS patients, might account for the observed excessive nitric oxide (NO) production in patients with CFS. Elevated NO is known to induce vasidilation, which may limit CFS patients to increase blood flow during exercise, and may even cause and enhanced postexercise hypotension. Finally, it is explored how several types of infections, frequently identified in CFS patients, fit into these hypothetical pathophysiological interactions.
Nijs J, De Meirleir K, Wolfs S, Duquet W.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy and Chronic Fatigue Clinic, Vrije Universiteit Brussel (VUB), Belgium. Jo.Nijs@vub.ac.be	Disability evaluation in chronic fatigue syndrome: associations between exercise capacity and activity limitations/participation restrictions.	Clin Rehabil. 2004 Mar;18(2):139-48.	OBJECTIVE: In an attempt to examine whether impairments in cardiorespiratory fitness are associated with daily functioning in patients with chronic fatigue syndrome (CFS), this study addresses the correlations between exercise capacity and activity limitations/participation restrictions. DESIGN: Prospective observational study. SETTING: An outpatient tertiary care, chronic fatigue clinic at the Vrije Universiteit Brussel (VUB), Belgium. SUBJECTS: Seventy-seven patients fulfilling the 1994 Centers for Disease Control and Prevention (CDC) case definition for CFS. INTERVENTIONS: All patients filled in the Chronic Fatigue Syndrome Activities and Participation Questionnaire (CFS-APQ) and performed a maximal exercise stress test on a bicycle ergometer. Heart rate was monitored continuously by use of an electrocardiograph. Metabolic and ventilatory parameters were measured through spirometry. RESULTS: A statistically significant correlation between the score obtained with the CFS-APQ and the body weight-adjusted peak oxygen uptake (Spearman rho = -0.32; p = 0.005), functional aerobic impairment (rho = 0.33; p = 0.004), workload/body weight (rho = -0.30; p = 0.009), exercise duration (rho = -0.30; p = 0.008), and the percentage of target heart rate achieved (rho = -0.33; p = 0.004) was observed. The correlations between the remaining exercise capacity parameters and the scores obtained with the CFS-APQ all indicated a trend towards association (0.01 <p<0.05). CONCLUSIONS: These results suggest a moderate association between exercise capacity and activity limitations/participation restrictions in patients with CFS. The observed correlations lack strength to predict activity limitations/ participation restriction based on exercise capacity parameters. Disability evaluation in CFS should therefore encompass both exercise capacity testing and measurements at the activity/participation dimension.

Nijs J, Nicolson GL.		Gulf War Veterans: Evidence for Chromosome Alternations and Their Significance	Journal of Chronic Fatigue Syndrome 2004; 12(1):79–83.	
Nijs J, Vaes P, McGregor N, Lambrecht L, Van Hoof E, De Meirleir K	Department of Human Physiology, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel (VUB), Belgium, Jo.Nijs@vub.ac.be	Comparison of Activity Limitations/Participation Restrictions Among Fibromyalgia and Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 2004; Mar;11(4):3–18.	Fibromyalgia (FM) and Chronic Fatigue Syndrome (CFS) are related yet overlapping disorders; the current case definitions prohibit a clear-cut differential diagnosis. These diagnostic criteria mainly address the impairment level of the World Health Organization's International Classification of Functioning, Disability and Health. This study aimed at comparing activity limitations and participation restrictions in patients with FM (n = 90) and CFS (n = 47). The Chronic Fatigue Syndrome Activities and Participation Questionnaire (CFS-APQ) was used for assessing functionality in both groups. The convergent validity of the scores obtained with the questionnaire with visual analogue scales for pain, fatigue and concentration was investigated in FM patients, as well as the content validity. No differences in total scores and 25 out of 26 individual items on the CFS-APQ were observed between the 2 groups (independent samples Mann-Whitney U test). This sample of FM patients reported to be more disabled in 'sitting for two hours' as compared to the CFS group (mean scores 3.0 ± 1.0 and 2.3 ± 1.0; P = .004). Four hundred and thirty-seven of the 497 (87.9 %) responses to the request to list difficult activities matched the content of the CFS-APQ. The overall scores of the CFS-APQ correlated statistically significant in respect to visual analogue scales for pain and concentration (Spearman rho for the total scores ranged between .44 and .49). These data question the disease specificity of the CFS-APQ for CFS, but suggests its applicability in 'the Chronic Pain-Fatigue Syndromes'. The present report provides evidence for both the content and convergent validity of the CFS-APQ in FM patients.
Nisenbaum R, Reyes M, Unger ER, Reeves WC.	Viral Exhanthems and Herpesvirus Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases/CDC, 1600 Clifton Road, Mail Stop A-15, Building 6, Room 116, Atlanta, GA 30333, USA. ran7@cdc.gov	Factor analysis of symptoms among subjects with unexplained chronic fatigue: what can we learn about chronic fatigue syndrome?	J Psychosom Res. 2004 Feb;56(2):171-8.	OBJECTIVE: Chronic fatigue syndrome (CFS) case definitions agree that fatigue must be unexplained, debilitating and present for at least 6 months, but they differ over accompanying symptoms. Our objective was to compare the 1994 CFS case-defining symptoms with those identified by factor analysis. METHODS: We surveyed the Wichita population and measured the occurrence of 21 symptoms in 1391 chronically fatigued subjects who did not report fatigue-associated medical or psychiatric conditions. We used factor analyses to identify symptom dimensions of fatigue and cluster analysis to assign subjects to subgroups. RESULTS: Forty-three subjects had CFS. We confirmed three factors: musculoskeletal, infection and cognition-mood-sleep, essentially defined by CFS symptoms. Although factor scores were higher among CFS subjects, CFS and non-CFS distributions overlapped substantially. Three clusters also showed overlap between CFS and non-CFS subjects. CONCLUSION: CFS symptomatology is a multidimensional phenomenon overlapping with other unexplained fatiguing syndromes and this must be considered in CFS research.
Noakes TD.		Physiological factors limiting exercise	Med Sci Sports Exerc. 2004 Jun;36(6):1087.	

		performance in CFS. Comment on: Med Sci Sports Exerc. 2003 Jun;35(6):908-13.		
Ohashi K, Bleijenberg G, van der Werf S, Prins J, Amaral LA, Natelson BH, Yamamoto Y.	Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan. yamamoto@edcom.p.u-tokyo.ac.jp	Decreased fractal correlation in diurnal physical activity in chronic fatigue syndrome.	Methods Inf Med. 2004;43(1):26-9.	OBJECTIVES: Our objectives were to study the temporal correlation of physical activity time series in patients with chronic fatigue syndrome (CFS) during normal daily life and to examine if it could identify the altered physical activity in these patients. METHODS: Fractal scaling exponents of diurnal and nocturnal physical activity time series in 10 CFS patients and 6 healthy control subjects (CON) were calculated by the detrended fluctuation analysis (DFA) and the wavelet transform modulus maxima (WTMM) method. We hypothesized that, due to their illness- and/or fatigue-induced resting episodes, altered physical activity patterns in CFS patients might be observed at the interruption of activity bursts. Thus, we further developed a new method, the wavelet transform negative modulus maxima (WTNMM) method, which could evaluate the temporal correlation at the interruption of activities. We compared the fractal scaling exponents for CFS and CON by each method. RESULTS: Both for CFS and CON, we found the fractal time structures in their diurnal physical activity records for at least up to 35 minutes. No group difference was found in nocturnal activities. The WTNMM method revealed that, in diurnal activities, CFS patients had significantly ($p < 0.01$) smaller fractal scaling exponent (0.87 +/- 0.03) compared to controls (1.01 +/- 0.03). Such a difference was identified neither by the DFA nor WTMM method. CONCLUSIONS: CFS patients had more abrupt interruptions of voluntary physical activity during diurnal periods in normal daily life, probed by the decreased correlation in the negative modulus maxima of the wavelet-transformed activity data, possibly due to their exaggerated fatigue.
Okada T, Tanaka M, Kuratsune H, Watanabe Y, Sadato N.	National Institute for Physiological Sciences, 38 Nishigonaka, Myodaiji, Okazaki, Aichi 444-8585, Japan. tomokada@ibri-kobe.org <tomokada@ibri-kobe.org>	Mechanisms underlying fatigue: a voxel-based morphometric study of chronic fatigue syndrome.	BMC Neurol. 2004 Oct 04;4(1):14.	BACKGROUND: Fatigue is a crucial sensation that triggers rest, yet its underlying neuronal mechanisms remain unclear. Intense long-term fatigue is a symptom of chronic fatigue syndrome, which is used as a model to study the mechanisms underlying fatigue. METHODS: Using magnetic resonance imaging, we conducted voxel-based morphometry of 16 patients and 49 age-matched healthy control subjects. RESULTS: We found that patients with chronic fatigue syndrome had reduced gray-matter volume in the bilateral prefrontal cortex. Within these areas, the volume reduction in the right prefrontal cortex paralleled the severity of the fatigue of the subjects. CONCLUSION: These results are consistent with previous reports of an abnormal distribution of acetyl-L-carnitine uptake, which is one of the biochemical markers of chronic fatigue syndrome, in the prefrontal cortex. Thus, the prefrontal cortex might be an important element of the neural system that regulates sensations of fatigue.
Papanicolaou DA, Amsterdam JD, Levine S, McCann SM, Moore RC, Newbrand CH, Allen G,	Department of Medicine/Endocrinology, Emory University, Atlanta, GA, USA.	Neuroendocrine aspects of chronic fatigue syndrome.	Neuroimmunomodulation. 2004;11(2):65-74.	Chronic fatigue syndrome (CFS) is a serious health concern affecting over 800000 Americans of all ages, races, socioeconomic groups and genders. The etiology and pathophysiology of CFS are unknown, yet studies have suggested an involvement of the neuroendocrine system. A symposium was organized in March 2001 to explore the possibility of an association between neuroendocrine dysfunction and CFS, with special emphasis on the interactions between neuroendocrine dysfunction and other abnormalities noted in the immune and autonomic nervous systems of individuals with CFS.

Nisenbaum R, Pfaff DW, Tsokos GC, Vgontzas AN, Kales A.				This paper represents the consensus of the panel of experts who participated in this meeting. Copyright 2004 S. Karger AG, Basel
Pazderka-Robinson H, Morrison JW, Flor-Henry P.	Clinical Diagnostics and Research Centre, Alberta Hospital Edmonton, Box 307, 17480 Fort Road, Edmonton, Alberta, Canada T5J 2J7. hannah@ualberta.ca	Electrodermal dissociation of chronic fatigue and depression: evidence for distinct physiological mechanisms.	Int J Psychophysiol. 2004 Aug;53(3):171-82.	Chronic fatigue syndrome (CFS) has an estimated prevalence between 0.5% and 3%, yet its diagnosis remains contentious. CFS is characterized by subjective symptoms that can be difficult to verify; moreover, depression is a commonly reported CFS complaint, whereas fatigue is a common symptom of depression. Our primary goal was dissociation of these disorders using psychophysiological methods. As previous research has implicated the autonomic nervous system in CFS, we conducted what we believe to be the first analysis of bilateral electrodermal and skin temperature responses of dextral females in a cross-modal orienting task, to investigate differences between these two patient groups and controls. A multivariate analysis of variance (MANOVA) examining three measures of electrodermal activity revealed prestimulus tonic skin conductance levels (SCLs) were markedly lower for the CFS group, with no difference between controls and depressives. Concurrent skin temperature levels were higher for the CFS group than the other two groups. These findings indicate that, despite overtly similar cognitive and symptom profiles, depression and CFS patients can be differentiated with psychophysiological measures. This study adds to the growing body of evidence demonstrating that CFS and depression have distinct neurobiological profiles, consistent with unique aetiologies. Copyright 2004 Elsevier B.V.
Pearce JM.	Emeritus Consultant Neurologist, Department of Neurology, Hull Royal Infirmary, Hull, UK.	Myofascial Pain, Fibromyalgia or Fibrositis?	Eur Neurol. 2004 Jul 13;52(2):67-72.	The terms myofascial pain, fibromyalgia and fibrositis are critically examined. They constitute diagnostic labels for non-specific musculoskeletal aches and pains. Analysis of the evidence shows that none of these labels is substantiated by hard physical signs or by laboratory evidence of consistent pathological or biochemical abnormality. What is the objective evidence for disorder(s) of muscle, fascia or fibrous tissues, so clearly indicated by these diagnostic names? Alternative terms such as 'regional pain syndrome' or 'chronic pain syndrome' merely redefine the clinical problem without providing a mechanism or basis for diagnosis. Despite different diagnostic criteria, these conditions, along with chronic fatigue syndrome, have many demographic and clinical similarities, most notably tender trigger points. Indeed, the terms are often used interchangeably. There are few differences in the symptoms, physical findings, laboratory tests, functional status, psychosocial features and psychiatric disorders. This paper seeks not to deny the existence of aches and pains, but to critically examine the utility of these terms. The only claimed physical sign is the presence of tender trigger points over muscles or muscle attachments. Research suggests that tender points are a measure of general distress related to pain complaints but separately associated with fatigue and depression. They are present in some normal subjects and are variable in occurrence in time in the same individual. They reflect no demonstrable pathology. It is therefore argued that none of these commonly used diagnoses represent distinct disease entities. A possible but unproven alternative hypothesis is that such symptoms relate to neural pain with both peripheral and central components, and in some instances psychological or wilful embellishment. Copyright 2004 S. Karger AG, Basel
Pendergast DR, Fisher NM,	Department of Physiology,	The distribution of white blood cell fat	J Inherit Metab Dis. 2004;27(1):89-	Fat oxidation is important for maintaining health and for supplying energy for exercise. We have proposed that the predisposition for individual rates of fat oxidation is determined genetically but

Meksawan K, Doubrava M, Vladutiu GD.	University at Buffalo, Buffalo, New York 14214, USA. dpenderg@buffalo.edu	oxidation in health and disease.	99.	may be modulated by acute exercise or exercise training. The purpose of this study was to examine cellular fat oxidation in white blood cells (WBC) using [9,10-3H]palmitic acid. Sedentary controls free of symptoms (SED-C, n=32), were compared with known carnitine palmitoyltransferase (CPT) II-deficient patients (n =2), patients with fatiguing diseases (chronic fatigue syndrome, CFS, n=6; multiple sclerosis, MS, n=31), obesity (OB, n=5), eating disorders (ED, n=16), sedentary individuals prior to and after exercise (SED-Ex, n=12), exercise-trained sedentary individuals (SED-Tr, n=12), and elite runners (ER, n=5). Fat oxidation in WBC for all subjects was normally distributed (mean=0.270 +/- 0.090 nmol/h per 10(9) WBC) and ranged from 0.09 nmol/h per 10(9) WBC in CPT II-deficient patients to 0.59 nmol/h per 10(9) WBC in ER. There were no significant sex or acute exercise effects on WBC fat oxidation. Patients with MS, OB or ED were not different from SED-C; however, in CPT II-deficient patients, fat oxidation was low, while that of CFS patients was high. Exercise training in SED-C resulted in a 16% increase in fat oxidation but in ER it was still 97% higher than in SED-C. We propose that while WBC fat oxidation is not significantly affected by sex or acute exercise, and only by 15-20% with training, genetic factors play a role in determining both high and low fat oxidation in certain groups of individuals. The genetic predisposition for individual rates of fat oxidation may be easily measured using WBC fat oxidation, as has been shown for CPT II-deficient patients and for elite runners. Ranges of WBC fat oxidation that are abnormally low (<20 nmol/h per 10(9) WBC, normal 20-35) or high (>35 nmol/h per 10(9) WBC) are proposed based on genetic factors evaluated in this study.
Perski A.	Stressmottagningen vid Institutet for psykosocial medicin och Karolinska institutet, Stockholm. aleksander.perski@ipm.ki.se	[Rehabilitation of stress-related diseases goes on different phases and is often long-lasting][Article in Swedish]	Lakartidningen. 2004 Apr 1;101(14):1292-4.	
Poteliakhoff A.		Etanercept and methotrexate in rheumatoid arthritis. Comment on: Lancet. 2004 Feb 28;363(9410):675-81.	Lancet. 2004 May 22;363(9422):1734.	
Powell P, Bentall RP, Nye FJ, Edwards RH.	Department of Psychology, University of Manchester, UK.	Patient education to encourage graded exercise in chronic fatigue syndrome. 2-year	Br J Psychiatry. 2004 Feb;184:142-6.	BACKGROUND: An earlier trial demonstrated good outcomes after 1 year for patients with chronic fatigue syndrome (CFS) who received an educational intervention designed to encourage graded activity. AIMS: To determine 2-year outcomes for the same treated patients and the response to treatment of patients formerly in the control condition. METHOD: Patients in the treatment groups (n=114) were followed up at 2 years; 32 patients from the control group were offered the intervention

		follow-up of randomised controlled trial.		after 1 year and were assessed 1 year later. Assessments were the self-rated measures used in the original trial. RESULTS: At 2 years 63 of the treated patients (55%) no longer fulfilled trial criteria for CFS compared with 64 patients (56%) at 1 year. Fourteen of 30 crossover patients (47%) achieved a good outcome at 1 year and seven (23%) no longer fulfilled criteria for CFS. CONCLUSIONS: Benefits of the intervention were maintained at 2 years. Delaying treatment is associated with reduced efficacy and required more intensive therapy.
Price JS, Gardner R Jr, Erickson M.	Odintune Place, Plumpton, East Sussex BN7 3AN, UK. john.price@lycosmail.com	Can depression, anxiety and somatization be understood as appeasement displays?	J Affect Disord. 2004 Apr;79(1-3):1-11.	BACKGROUND: No satisfactory basis in normal function characterizes major depression and its co-morbid disorders. Yet these may represent maladaptive expression of adaptive communicational states exhibited normally in many species. METHODS: We examined the signal value of depressive and anxious mood states, fatigue syndrome and somatoform disorders and found them to resemble appeasement or submission to conspecifics (members of a same species) as studied in other animals. Moreover, applying game theory formulations of conflict resolution and the triune brain theory of MacLean supported the hypothesis. LIMITATIONS: Direct experimental evidence must still test hypotheses that emanate from the presented framework. Conclusions: Implications for this approach include improved understanding and treatment of depression, improved research strategies, and a potential future pathogenesis-focused nosology.
Prins JB, Bos E, Huibers MJ, Servaes P, van der Werf SP, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Medical Centre Nijmegen, Nijmegen, The Netherlands. j.prins@cukz.umcn.nl	Social support and the persistence of complaints in chronic fatigue syndrome.	Psychother Psychosom. 2004 May-Jun;73(3):174-82.	BACKGROUND: Several studies suggested that the surroundings of chronic fatigue syndrome (CFS) patients are of importance in the persistence of complaints. Contrary to what was expected, participation in support groups has not led to clinical improvement. The purpose of the present study was to describe social support in CFS patients as compared with other fatigued and non-fatigued groups. Further, changes in social support and the influence of social support on the course of CFS over a period of more than 1 year were studied in patients with and without treatment. METHODS: Baseline data were assessed in 270 CFS patients, 150 disease-free breast cancer patients, 151 fatigued employees on sick-leave and 108 healthy subjects using the Social Support List and Significant Others Scale. CFS patients were followed in cognitive behaviour therapy (CBT), guided support groups and natural course at 8 and 14 months. RESULTS: CFS patients and fatigued employees reported more negative interactions and insufficiency of supporting interactions than cancer patients and healthy controls. No differences in frequency of supporting interactions were found. Negative interactions decreased significantly after treatment with CBT, but did not change in support groups or natural course. In the natural course, higher fatigue severity at 8 months was predicted by more negative interactions at baseline. CONCLUSIONS: In CFS patients and fatigued employees, social support is worse than in disease-free cancer patients and healthy controls. Lack of social support was identified as a new factor in the model of perpetuating factors of fatigue severity and functional impairment in CFS. Copyright 2004 S. Karger AG, Basel
Puri BK, Holmes J, Hamilton G.	MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College School of	Eicosapentaenoic acid-rich essential fatty acid supplementation in chronic fatigue syndrome	Int J Clin Pract. 2004 Mar;58(3):297-9.	Lateral ventricular enlargement has been reported in chronic fatigue syndrome, while cerebral neurospectroscopy has recently indicated that essential fatty acid treatment may be of value in this condition. An essential fatty acid supplement rich in eicosapentaenoic acid (EPA) was therefore given daily to a female patient with a 6-year history of unremitting symptoms of chronic fatigue syndrome. Cerebral magnetic resonance scanning was carried out at baseline and 16 weeks later. The EPA-rich essential fatty acid supplementation led to a marked clinical improvement in her symptoms of chronic

	Medicine, Hammersmith Hospital, London, UK.	associated with symptom remission and structural brain changes.		fatigue syndrome, starting within 6-8 weeks. Accurate quantification of the lateral ventricular volumes in the baseline and 16-week follow-up registered images of high-resolution magnetic resonance imaging structural scans showed that the treatment was accompanied by a marked reduction in the lateral ventricular volume during this period, from 28,940-23,660 mm3.
Puri BK.	MRI Unit, Imaging Sciences Department, MRC Clinical Sciences Centre, Imperial College School of Medicine, Hammersmith Hospital, Du Cane Road, London W12 0HS, England, UK. basant.puri@csc.mrc.ac.uk	The use of eicosapentaenoic acid in the treatment of chronic fatigue syndrome.	Prostaglandins Leukot Essent Fatty Acids. 2004 Apr;70(4):399-401.	There is evidence that there is an association between chronic fatigue syndrome, a condition of unknown aetiology, and essential fatty acids. This evidence is based on the actions of essential fatty acids, the results of proton neurospectroscopy studies, and essential fatty acid trial data. A series of patients with chronic fatigue syndrome were treated solely with a high-eicosapentaenoic acid-containing essential fatty acid supplement. All showed improvement in their symptomatology within eight to 12 weeks. These results, which are consistent with a recent detailed report of cerebral and clinical changes associated with a high intake of eicosapentaenoic acid, suggest that this n-3 highly unsaturated fatty acid may offer the hope of effective treatment for at least some patients with chronic fatigue syndrome.
Raine R, Sanderson C, Hutchings A, Carter S, Larkin K, Black N.	Health Services Research Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK. rosalind.raine@lshtm.ac.uk	An experimental study of determinants of group judgments in clinical guideline development. Comment in: Lancet. 2004 Jul 31;364(9432):392-3.	Lancet. 2004 Jul 31;364(9432):429-37.	BACKGROUND: Clinical guidelines for improving the quality of care are a familiar part of clinical practice. Formal consensus methods such as the nominal group technique are often used as part of guideline development, but little is known about factors that affect the statements produced by nominal groups, and on their consistency with the research evidence. METHODS: Cognitive behavioural therapy, behavioural therapy, brief psychodynamic interpersonal therapy, and antidepressants for irritable bowel syndrome, chronic fatigue syndrome, and chronic back pain were selected for study. 16 nominal groups in a factorial design allowed comparison of GP-only with mixed groups of GPs and specialists, provision of a literature review with no provision, and ratings made in the context of realistic or ideal levels of health-care resources. Participants rated appropriateness independently, and again after a facilitated meeting. Audiotapes of four group discussions were analysed. FINDINGS: There was agreement with the research evidence for 51% of 192 scenarios. Agreement was more likely if the group was GP-only, if a literature review was provided, or if the evidence was in accordance with clinicians' beliefs. Assumptions about the level of resources available had no impact. Clinical and social cues had mixed effects, irrespective of the research evidence. Qualitative analysis showed the modifying effect of clinical experience and beliefs about research evidence. INTERPRETATION: Guidelines cannot be based on data alone; judgment is unavoidable. The nominal group technique is a method of eliciting and aggregating judgments in a transparent and structured way. It can provide important information on levels of agreement between experts. However, conclusions can be at odds with the published literature. If they are, reasons need to be explicit.
Raine R, Carter S, Sensky T, Black N.	Department of Public Health and	General practitioners'	BMJ. 2004 Jun 5;328(7452):1354-	OBJECTIVES: To compare general practitioners' perceptions of chronic fatigue syndrome and irritable bowel syndrome and to consider the implications of their perceptions for treatment. DESIGN:

	Policy, London School of Hygiene and Tropical Medicine, London WC1E 7HT. rosalind.raine@lshtm.ac.uk	perceptions of chronic fatigue syndrome and beliefs about its management, compared with irritable bowel syndrome: qualitative study. Comment in: BMJ. 2004 Jul 10;329(7457):112-3.	7. Epub 2004 May 28.	Qualitative analysis of transcripts of group discussions. PARTICIPANTS AND SETTING: A randomly selected sample of 46 general practitioners in England. RESULTS: The participants tended to stereotype patients with chronic fatigue syndrome as having certain undesirable traits. This stereotyping was due to the lack of a precise bodily location; the reclassification of the syndrome over time; transgression of social roles, with patients seen as failing to conform to the work ethic and "sick role" and conflict between doctor and patient over causes and management. These factors led to difficulties for many general practitioners in managing patients with chronic fatigue syndrome. For both conditions many participants would not consider referral for mental health interventions, even though the doctors recognised social and psychological factors, because they were not familiar with the interventions or thought them unavailable or unnecessary. CONCLUSIONS: Barriers to the effective clinical management of patients with irritable bowel syndrome and chronic fatigue syndrome are partly due to doctors' beliefs, which result in negative stereotyping of patients with chronic fatigue syndrome and the use of management strategies for both syndromes that may not take into account the best available evidence.
Reeves WC, Lloyd A, Vernon SD, Klimas N, Jason LA, Bleijenberg G, Evengard B, White PD, Nisenbaum R, Unger ER, .	Centers for Disease Control and Prevention, Atlanta, Georgia, United States of America. wcr1@cdc.gov	Identification of ambiguities in the 1994 chronic fatigue syndrome research case definition and recommendations for resolution.	BMC Health Serv Res. 2003 Dec 31;3(1):25.	BACKGROUND: Chronic fatigue syndrome (CFS) is defined by symptoms and disability, has no confirmatory physical signs or characteristic laboratory abnormalities, and the etiology and pathophysiology remain unknown. Difficulties with accurate case ascertainment contribute to this ignorance. METHODS: Experienced investigators from around the world who are involved in CFS research met for a series of three day workshops in 2000, 2001 and 2002 intended to identify the problems in application of the current CFS case definition. The investigators were divided into focus groups and each group was charged with a topic. The investigators in each focus group relied on their own clinical and scientific knowledge, brainstorming within each group and with all investigators when focus group summaries were presented. Relevant literature was selected and reviewed independent of the workshops. The relevant literature was circulated via list-serves and resolved as being relevant by group consensus. Focus group reports were analyzed and compiled into the recommendations presented here. RESULTS: Ambiguities in the current CFS research definition that contribute to inconsistent case identification were identified. Recommendations for use of the definition, standardization of classification instruments and study design issues are presented that are intended to improve the precision of case ascertainment. The International CFS Study Group also identified ambiguities associated with exclusionary and comorbid conditions and reviewed the standardized, internationally applicable instruments used to measure symptoms, fatigue intensity and associated disability. CONCLUSION: This paper provides an approach to guide systematic, and hopefully reproducible, application of the current case definition, so that case ascertainment would be more uniform across sites. Ultimately, an operational CFS case definition will need to be based on empirical studies designed to delineate the possibly distinct biological pathways that result in chronic fatigue.
Reuter K, Harter M.	Freiburg University Medical Center, Department of Psychiatry and Psychotherapy,	The concepts of fatigue and depression in cancer.	Eur J Cancer Care (Engl). 2004 May;13(2):127-34.	REUTER K. & HARTER M. (2004) European Journal of Cancer Care13, 127-134 The concepts of fatigue and depression in cancer A strong association between fatigue and depression in cancer patients has been reported repeatedly in clinical studies. The distinction remains difficult, mainly because of the similar phenomenology of fatigue and depression. It is the aim of this paper to work out similarities and differences in the conception of fatigue and depressive disorders. For that, a differentiation

	Freiburg, Germany.			between depression as emotional distress and depression as clinical syndrome, according to the current classification systems, has to be made. Therefore, the classification of depressive disorders and their criteria is presented in the second section of this paper, especially in view of the diagnosis of depressive disorders in cancer patients. The comparison of the multidimensional fatigue construct and depression shows a strong overlap of symptoms. None of the fatigue symptoms are specific for fatigue, all being elements of depressive syndromes. It is in particular the psychological symptoms of depressive disorders that differentiate between the two concepts. To that end, the question is discussed whether fatigue in its current conceptualization can be defined as a diagnostic entity independent of depressive disorders. Additionally, research approaches are presented from the area of the chronic fatigue syndrome and neurasthenia, which could be adapted to cancer-related fatigue and help to clarify the clinical differences between fatigue and depression. In order to ensure better differential diagnostics in the future, criteria-orientated research in particular is needed.
Reynolds KJ, Vernon SD, Bouchery E, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, U,S,A. wcr1@cdc.gov	The economic impact of chronic fatigue syndrome.	Cost Eff Resour Alloc. 2004 Jun 21;2(1):4.	BACKGROUND: Chronic fatigue syndrome (CFS) is a chronic incapacitating illness that affects between 400,000 and 800,000 Americans. Despite the disabling nature of this illness, scant research has addressed the economic impact of CFS either on those affected or on the national economy. METHODS: We used microsimulation methods to analyze data from a surveillance study of CFS in Wichita, Kansas, and derive estimates of productivity losses due to CFS. RESULTS: We estimated a 37% decline in household productivity and a 54% reduction in labor force productivity among people with CFS. The annual total value of lost productivity in the United States was $9.1 billion, which represents about $20,000 per person with CFS or approximately one-half of the household and labor force productivity of the average person with this syndrome. CONCLUSION: Lost productivity due to CFS was substantial both on an individual basis and relative to national estimates for other major illnesses. CFS resulted in a national productivity loss comparable to such losses from diseases of the digestive, immune and nervous systems, and from skin disorders. The extent of the burden indicates that continued research to determine the cause and potential therapies for CFS could provide substantial benefit both for individual patients and for the nation.
Richardson RD, Engel CC Jr.	VA Puget Sound Healthcare System, Seattle, WA, USA.	Evaluation and management of medically unexplained physical symptoms.	Neurologist. 2004 Jan;10(1):18-30.	BACKGROUND: Medically unexplained physical symptoms (MUPS) and related syndromes are common in medical care and the general population, are associated with extensive morbidity, and have a large impact on functioning. Much of medical practice emphasizes specific pharmacological and surgical intervention for discrete disease states. Medical science, with its emphasis on identifying etiologically meaningful diseases comprised of homogeneous groups of patients, has split MUPS into a number of diagnostic entities or syndromes, each with its own hypothesized pathogenesis. However, research suggests these syndromes may be more similar than different, sharing extensive phenomenological overlap and similar risk factors, treatments, associated morbidities, and prognoses. Examples of syndromes consisting of MUPS include chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivities, somatoform disorders, and 'Gulf War Syndrome.' REVIEW SUMMARY: This paper is a narrative review of the increasing body of evidence suggesting that MUPS and related syndromes are common, disabling, and costly. It emphasizes that MUPS occur along a continuum of symptom count, severity, and duration and may be divided into acute, subacute (or recurrent), and chronic types. Predisposing, precipitating, and perpetuating factors influence the natural history of

				MUPS. CONCLUSIONS: Effective symptom management involves collaborative doctor-patient approaches for identification of problems based on a combination of medical importance and patient readiness to initiate behavioral change, negotiated treatment goals and outcomes, gradual physical activation and exercise prescription. Additionally, efforts should be made to teach and support active rather than passive coping with the symptoms.
Ridsdale L, Darbishire L, Seed PT.	Department of Neurology, Guy's, King's and St Thomas's School of Medicine, London.	Is graded exercise better than cognitive behaviour therapy for fatigue? A UK randomized trial in primary care.	Psychol Med. 2004 Jan;34(1):37-49.	BACKGROUND: Patients frequently present with unexplained fatigue in primary care, but there have been few treatment trials in this context. We aimed to test cognitive behaviour therapy (CBT) and graded exercise therapy (GET) for patients presenting to their family doctor with fatigue. Secondly, we described the outcome for a cohort of patients who presented to the same doctors with fatigue, who received standard care, plus a booklet. METHOD: This was a randomized trial, followed by a prospective cohort study. Twenty-two practices in SE England referred 144 patients aged 16 to 75 years with over 3 months of unexplained fatigue. Self-rated fatigue score, the hospital anxiety and depression rating scale, functional impairment, physical step-test performance and causal attributions were measured. In the trial six sessions of CBT or GET were randomly allocated. RESULTS: In the therapy groups the mean fatigue score decreased by 10 points (95% confidence interval (CI) = -25 to -15), with no significant difference between groups (mean difference = -1.3; CI = -3.9 to 1.3). Fewer patients attended for GET. At outcome one-half of patients had clinically important fatigue in both randomized groups, but patients in the group offered CBT were less anxious. Twenty-seven per cent of the patients met criteria for CFS at baseline. Only 25% of this subgroup recovered, compared to 60% of the subgroup that did not meet criteria for CFS. CONCLUSIONS: Short courses of GET were not superior to CBT for patients consulting with fatigue of over 3 months in primary care. CBT was easier 'to sell'. Low recovery in the CFS subgroup suggests that brief treatment is too short.
Roberts AD, Wessely S, Chalder T, Papadopoulos A, Cleare AJ.	Section of General Hospital Psychiatry, Division of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine and Dentistry, London, UK.	Salivary cortisol response to awakening in chronic fatigue syndrome.	Br J Psychiatry. 2004 Feb;184:136-41.	BACKGROUND: There is accumulating evidence of hypothalamic-pituitary-adrenal (HPA) axis disturbances in chronic fatigue syndrome (CFS). The salivary cortisol response to awakening has been described recently as a non-invasive test of the capacity of the HPA axis to respond to stress. The results of this test correlate closely with those of more invasive dynamic tests reported in the literature; furthermore, it can be undertaken in a naturalistic setting. AIMS: To assess the HPA axis using the salivary cortisol response to awakening in CFS. METHOD: We measured salivary cortisol upon awakening and 10, 20, 30 and 60 min afterwards in 56 patients with CFS and 35 healthy volunteers. RESULTS: Patients had a lower cortisol response to awakening, measured by the area under the curve. CONCLUSIONS: This naturalistic test of the HPA axis response to stress showed impaired HPA axis function in CFS.
Ross SD, Estok RP, Frame D, Stone LR, Ludensky V, Levine CB.	MetaWorks Inc, 10 President's Landing, Medford, MA 02155, USA.	Disability and chronic fatigue syndrome: a focus on function.	Arch Intern Med. 2004 May 24;164(10):1098-107.	BACKGROUND: Evidence was sought in the published literature on how best to measure, monitor, and treat disability in patients with chronic fatigue syndrome (CFS). METHODS: A systematic review was performed of English-language literature published between January 1, 1988, and November 15, 2001. Interventional and observational studies of adults with CFS were eligible if they reported measures of disability and employment. A qualitative synthesis of results relating impairment measures to employment was performed. RESULTS: Of 3840 studies identified, 37 reported employment status and some measure of mental or physical impairment associated with disability. Most patients with CFS in these studies were unemployed. In 22 studies, the employment status of control subjects was also

				available. Only depression seemed to be associated with unemployment in patients with CFS. No other measurable impairment seemed to be consistently associated with disability or work outcomes. Only cognitive behavior therapy, rehabilitation, and exercise therapy interventions were associated with restoring the ability to work. No specific patient characteristics were identified as best predictors of positive employment outcomes. No quantitative syntheses of results were performed. CONCLUSIONS: For questions of disability and employment in CFS, the limitations inherent in the current literature are extensive. Methodologically rigorous, longitudinal, and interventional studies are needed to determine baseline characteristics that are associated with the inability to work and interventions that are effective in restoring the ability to work in the CFS population. Simple and consistent evaluations of functional capacity in patients with CFS are needed.
Roy-Byrne P, Smith WR, Goldberg J, Afari N, Buchwald D.	Department of Psychiatry and Behavioral Science, University of Washington, Seattle, WA, USA.	Post-traumatic stress disorder among patients with chronic pain and chronic fatigue.	Psychol Med. 2004 Feb;34(2):363-8.	BACKGROUND: Fibromyalgia (FM), a chronic pain condition of unknown aetiology often develops following a traumatic event. FM has been associated with post-traumatic stress disorder (PTSD) and major depression disorder (MDD). METHOD: Patients seen in a referral clinic (N=571) were evaluated for FM and chronic fatigue syndrome (CFS) criteria. Patients completed questionnaires, and underwent a physical examination and a structured psychiatric evaluation. Critical components of the diagnostic criteria of FM (tender points and diffuse pain) and CFS (persistent debilitating fatigue and four of eight associated symptoms) were examined for their relationship with PTSD. RESULTS: The prevalence of lifetime PTSD was 20% and lifetime MDD was 42%. Patients who had both tender points and diffuse pain had a higher prevalence of PTSD (OR=3.4, 95% CI 2.0-5.8) compared with those who had neither of these FM criteria. Stratification by MDD and adjustment for sociodemographic factors and chronic fatigue revealed that the association of PTSD with FM criteria was confined to those with MDD. Patients with MDD who met both components of the FM criteria had a three-fold increase in the prevalence of PTSD (95% CI 1.5-7.1); conversely, FM patients without MDD showed no increase in PTSD (OR=1.3, 95% CI 0.5-3.2). The components of the CFS criteria were not significantly associated with PTSD. CONCLUSION: Optimal clinical care for patients with FM should include an assessment of trauma in general, and PTSD in particular. This study highlights the importance of considering co-morbid MDD as an effect modifier in analyses that explore PTSD in patients with FM. PMID: 14982142 [PubMed - in process]
Sackner MA, Gummels EM, Adams JA.	Mt. Sinai Medical Center of Greater Miami, Division of Pulmonary Disease and Critical Care Medicine, Miami Beach, FL 33140, USA. artchive@msn.com	Say NO to fibromyalgia and chronic fatigue syndrome: an alternative and complementary therapy to aerobic exercise.	Med Hypotheses. 2004;63(1):118-23.	Increased shear stress to the endothelium increases activity of endothelial nitric oxide synthase (eNOS) with subsequent release of small quantities (nMol) of nitric oxide (NO) into the circulation. It occurs during moderate aerobic exercise mostly as a result of laminar shear stress and with whole body, periodic acceleration as a result of pulsatile shear stress. The latter is administered by means of a new, non-invasive, passive exercise device. Moderate exercise has long been known to alleviate the symptoms of fibromyalgia and chronic fatigue syndrome and in the current study, whole body, periodic acceleration did as well. Since NO through action of eNOS has potent anti-inflammatory properties mainly by suppressing nuclear factor kappabeta activity, it is hypothesized that both diseases have chronic inflammation as their basis. Whole body periodic acceleration can be applied separately or supplementary to aerobic exercise in the treatment of fibromyalgia and chronic fatigue syndrome.
Schacterle RS,	Department of	A comparison of	Arch Intern Med.	BACKGROUND: Many women with chronic fatigue syndrome (CFS) fear that pregnancy will worsen

Komaroff AL.	Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachasetts 02115, USA.	pregnancies that occur before and after the onset of chronic fatigue syndrome.	2004 Feb 23;164(4):401-4.	their condition, increase the risks of maternal complications of pregnancy, or threaten the health of their offspring. Little empirical evidence, however, has been published on this matter. METHODS: A detailed questionnaire was administered to 86 women regarding 252 pregnancies that occurred before or after the onset of CFS and the outcomes of these pregnancies were observed. RESULTS: During pregnancy, there was no change in CFS symptoms in 29 (41%), an improvement of symptoms in 21 (30%), and a worsening of symptoms in 20 (29%) of 70 subjects. After pregnancy, there was no change in CFS symptoms in 21 (30%), an improvement of symptoms in 14 (20%), and a worsening of symptoms in 35 (20%) of the subjects. The rates of many complications were similar in pregnancies occurring before the onset and in those occurring after the onset of CFS. There was a higher frequency of spontaneous abortions in the pregnancies occurring after, vs before, the onset of CFS (22 [30%] of 73 pregnancies after vs 13 [8%] of 171 before; P<.001), but no differences in the rates of other complications. Developmental delays or learning disabilities were reported more often in the offspring of women who became pregnant after, vs before, the onset of CFS (9 [21%] of 43 children vs 11 [8%] of 139 children; P =.01). CONCLUSIONS: Pregnancy did not consistently worsen the symptoms of CFS. Most maternal and infant outcomes were not systematically worse in pregnancies occurring after the onset of CFS. The higher rates of spontaneous abortions and of developmental delays in offspring that we observed could be explained by maternal age or parity differences, and should be investigated by larger, prospective studies with control populations.
Schacterle RS, Milford EL, Komaroff AL	Division of General Medicine and Primary Care, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, 02115, USA	The Frequency of HLA Class II Antigens in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004; Mar;11(4):33–42.	Chronic fatigue syndrome is a condition characterized by unexplained, persistent fatigue in conjunction with other generalized symptoms. However, the patients as a group are more likely to have objective abnormalities of the immune system than control subjects. We measured the frequency of certain HLA antigens in a representative group of 35 patients. We restricted our analysis to class II molecules as these appear to be more specific predictors of susceptibility to immunologicallybased disorders. The frequency of the HLA-DQ1 antigen was increased in patients compared to general population Caucasian controls. This association between chronic fatigue syndrome and the HLA-DQ1 antigen translates into a relative risk of 3.2. This association has not been reported previously in chronic fatigue syndrome. Differences in the ethnic sub-grouping of patients in this study and in previous studies also could have contributed to the difference between our findings and those of previous investigators. Conversely, this study did not find HLA associations that have been reported by previous studies. The sample size of this study could have led to type II statistical errors and a failure to recognize certain HLA associations as significant.
Schillings ML, Kalkman JS, van der Werf SP, van Engelen BG, Bleijenberg G, Zwarts MJ.	Department of Clinical Neurophysiology, University Medical Centre Nijmegen, Internal postal code 314, P.O. Box 9101, 6500 HB Nijmegen,	Diminished central activation during maximal voluntary contraction in chronic fatigue syndrome.	Clin Neurophysiol. 2004 Nov;115(11):2518-24.	OBJECTIVE: We have investigated whether central activation failure (CAF) is increased during local muscle fatigue in chronic fatigue syndrome (CFS). METHODS: Fourteen female CFS patients and 14 age-matched healthy female controls made a 2 min sustained maximal voluntary contraction (MVC) of the biceps brachii muscle. Before, during, and after sustained MVC, electrical endplate stimulation was applied. Force and 5 channel surface EMG (sEMG) were registered. RESULTS: Although force responses upon stimulation during rest did not differ between patients and controls, MVC was significantly lower in patients. Already at the beginning of sustained MVC, CFS patients showed significantly larger CAF than controls (36.5+/-17.0% and 12.9+/-13.3%, respectively). For all individual patients mean CAF over the first 45 s was higher than 30%, while it was below 30% for all controls.

	Netherlands.			Less peripheral fatigue in patients was demonstrated by the changes in muscle fibre conduction velocity and the differences between force responses before and after contraction. CONCLUSIONS: Central activation is diminished in CFS patients. Possible causes include changed perception, impaired concentration, reduced effort and physiologically defined changes, e.g. in the corticospinal excitability or the concentration of neurotransmitters. As a consequence, demands on the muscle are lower, resulting in less peripheral fatigue. SIGNIFICANCE: CFS patients show reduced central activation during MVC. The underlying pathophysiological processes remain still to be determined.
Scroop GC, Burnet RB.	Lung Function, Royal Adelaide Hospital, North Terrace, Adelaide, SA 5000 gscroop@mail.rah.sa.gov.au.	To exercise or not to exercise in chronic fatigue syndrome?	Med J Aust. 2004 Nov 15;181(10):578-580.	
Severens JL, Prins JB, van der Wilt GJ, van der Meer JW, Bleijenberg G.	Department of Medical Technology Assessment, University Medical Centre Nijmegen, The Netherlands. h.severens@boez.unimaas.nl	Cost-effectiveness of cognitive behaviour therapy for patients with chronic fatigue syndrome.	QJM. 2004 Mar;97(3):153-61.	BACKGROUND: There is some evidence that cognitive behaviour therapy (CBT) is efficacious in chronic fatigue syndrome (CFS), but little data on its cost-effectiveness. DESIGN: Prospective economic analysis alongside a randomized clinical trial. METHODS: CFS patients were randomly assigned to CBT, guided support groups (SG), or the 'natural course' (NC, no protocol-based interventions). Patients were treated for 8 months and followed-up for another 6 months. Costs per patient showing clinically significant improvement, based on the CIS fatigue scale, and costs per quality-adjusted life year, were determined for a time period of 14 months. RESULTS: Data were available for 171 patients at 8 months and for 128 at 14 months. At 8 and 14 months, the percentages of improved patients were 31% and 27% for CBT, 9% and 11% for SG, and 12% and 20% for NC. Mean QALYs gained at 14 months were, for CBT, SG and NC, respectively, 0.0737, -0.0018 and 0.0458. CBT and SG mean treatment costs were euro1490 and euro424. Other medical costs for CBT, SG, and NC, respectively, were euro324, euro623 and euro412 for the first period, and euro232, euro561 and euro378 for the second period. Non-medical costs for these periods for CBT, SG and NC were euro262, euro550, euro427 and euro226, euro439, euro287, respectively. Productivity costs were considerable, but not significantly different between groups. DISCUSSION: CBT was less costly and more effective than SG. Compared to NC, the baseline incremental cost-effectiveness of CBT was euro20 516 per CFS patient showing clinically significant improvement, and euro21 375 per QALY. The bootstrap ratios showed considerable uncertainty regarding the results. Future research should focus on productivity costs, and follow patients prospectively over a longer period.
Shapiro CM.		Chronic fatigue--chronically confusing but growing information.	J Psychosom Res. 2004 Feb;56(2):153-5.	
Shaver JL.	University of Illinois at Chicago,	Fibromyalgia syndrome in	Nurs Clin North Am. 2004	Many more women than men experience the chronically fatiguing condition of fibromyalgia syndrome (FMS), a growing diagnosis in the United States. Estimates are that upwards of 2% to 6% of adults

	College of Nursing, M/C 802, 845 South Damen Avenue, Chicago, IL 60612-7350, USA. jshaver@uic.edu	women.	Mar;39(1):195-204, viii.	have been diagnosed with FMS, and at high societal costs. In this article, common manifestations are described to guide assessment and various lines of research are explored as a basis for under-standing contributing factors and potential treatments for FMS and other chronic disorders, such as chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), and temporomandibular disorders (TMD), and the effectiveness of current treatment options.
Shepherd C.		Patients with chronic fatigue syndrome are being ignored.	BMJ. 2004 Dec 11;329(7479):1405 . Comment on: BMJ. 2004 Oct 23;329(7472):928-9.	
Shin HY, An NH, Cha YJ, Shin EJ, Shin TY, Baek SH, Kim CH, Lyu YS, Lee EJ, Kim HM.	Department of Pharmacology, College of Oriental Medicine, Kyung Hee University, Seoul, South Korea.	Effect of Kuibitang on lipopolysaccharide-induced cytokine production in peripheral blood mononuclear cells of chronic fatigue syndrome patients.	J Ethnopharmacol. 2004 Feb;90(2-3):253-9.	Kuibitang (KBT) is clinically used to treat patients suffering from chronic fatigue syndrome (CFS) in South Korea. However, its effect has not been investigated experimentally. Recent reports have shown that CFS patients display an altered cytokine production. We examined the effect of KBT on lipopolysaccharide (LPS)-induced various cytokines production in peripheral blood mononuclear cells (PBMC) of CFS patients and healthy controls. KBT (1 mg/ml) significantly inhibited LPS-induced tumor necrosis factor-alpha, interleukin-10, and transforming growth factor-beta1 production in PBMC of CFS patients. However, LPS-induced interferon-gamma production was significantly increased by KBT (0.01 mg/ml). These results provide evidence of a novel activity of the KBT that regulate cytokines production related with CFS.
Siemionow V, Fang Y, Calabrese L, Sahgal V, Yue GH.	Department of Biomedical Engineering, The Lerner Research Institute, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA.	Altered central nervous system signal during motor performance in chronic fatigue syndrome.	Clin Neurophysiol. 2004 Oct;115(10):2372-81.	OBJECTIVE: The purpose of this study was to determine whether brain activity of chronic fatigue syndrome (CFS) patients during voluntary motor actions differs from that of healthy individuals. METHODS: Eight CFS patients and 8 age- and gender-matched healthy volunteers performed isometric handgrip contractions at 50% maximal voluntary contraction level. They first performed 50 contractions with a 10 s rest between adjacent trials--'Non-Fatigue' (NFT) task. Subsequently, the same number of contractions was performed with only a 5 s rest between trials--'Fatigue' (FT) task. Fifty-eight channels of surface EEG were recorded simultaneously from the scalp. Spectrum analysis was performed to estimate power of EEG frequency in different tasks. Motor activity-related cortical potential (MRCP) was derived by triggered averaging of EEG signals associated with the muscle contractions. RESULTS: Major findings include: (i) Motor performance of the CFS patients was poorer than the controls. (ii) Relative power of EEG theta frequency band (4-8 Hz) during performing the NFT and FT tasks was significantly greater in the CFS than control group ($P < 0.05$). (iii) The amplitude of MRCP negative potential (NP) for the combined NFT and FT tasks was higher in the CFS than control group ($P < 0.05$) (iv) Within the CFS group, the NP was greater for the FT than NFT task ($P<0.01$), whereas no such difference between the two tasks was found in the control group. CONCLUSIONS: These results clearly show that CFS involves altered central nervous system signals in controlling voluntary muscle activities, especially when the activities induce fatigue. SIGNIFICANCE: Physical activity-induced EEG signal changes may serve as physiological markers for more objective diagnosis of CFS.

Skapinakis P, Lewis G, Mavreas V.	Department of Psychiatry, University of Ioannina, School of Medicine, Greece. pskapin@cc.uoi.gr	Temporal relations between unexplained fatigue and depression: longitudinal data from an international study in primary care.	Psychosom Med. 2004 May-Jun;66(3):330-5.	OBJECTIVE: Unexplained fatigue syndromes, such as chronic fatigue syndrome and neurasthenia, are strongly associated with depression, but the temporal nature of this association is not clear. METHODS: The authors examined this issue by using data from the World Health Organization collaborative study of psychological problems in general health care. Three thousand two hundred one subjects from 15 primary care centers in 14 countries were followed up for 12 months. The Composite International Diagnostic Interview was the main instrument used. Odds ratios and their 95% confidence intervals (CI) were calculated using logistic regression models adjusted for sociodemographic variables, physical morbidity and intercenter variability. RESULTS: Cases of depression were found to have an increased risk of developing a new episode of unexplained fatigue at follow-up with an adjusted odds ratio of 4.15 (95% CI = 2.64-6.54). Similarly, cases of unexplained fatigue were found to have an increased risk of developing a new episode of depression at follow-up with an adjusted odds ratio of 2.76 (95% CI = 1.32-5.78). Further adjustment for subthreshold symptoms at baseline weakened the reported associations, especially between fatigue and development of a new episode of depression, but these remained significant. CONCLUSIONS: The findings support the view that unexplained fatigue and depression might act as independent risk factors for each other.
Skowera A, Cleare A, Blair D, Bevis L, Wessely SC, Peakman M.	Department of Immunology, Guy's, King's & St Thomas's School of Medicine, King's College London, London, UK.	High levels of type 2 cytokine-producing cells in chronic fatigue syndrome.	Clin Exp Immunol. 2004 Feb;135(2):294-302.	The aetiology of chronic fatigue syndrome (CFS) is not known. However, it has been suggested that CFS may be associated with underlying immune activation resulting in a Th2-type response. We measured intracellular production of interferon (IFN)-gamma and interleukin (IL)-2; type 1 cytokines), IL-4 (type 2) and IL-10 (regulatory) by both polyclonally stimulated and non-stimulated CD4 and CD8 lymphocytes from patients with CFS and control subjects by flow cytometry. After polyclonal activation we found evidence of a significant bias towards Th2- and Tc2-type immune responses in CFS compared to controls. In contrast, levels of IFN-gamma, IL-2 and IL-10-producing cells were similar in both study groups. Non-stimulated cultures revealed significantly higher levels of T cells producing IFN-gamma or IL-4 in CFS patients. Concluding, we show evidence for an effector memory cell bias towards type 2 responsiveness in patients with CFS, as well as ongoing type 0 immune activation in unstimulated cultures of peripheral blood cells.
Smith MS.		Adolescent chronic fatigue syndrome. Comment on: Arch Pediatr Adolesc Med. 2004 Mar;158(3):225-9.	Arch Pediatr Adolesc Med. 2004 Mar;158(3):207-8.	
Solomon L, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control	Factors influencing the diagnosis of chronic fatigue syndrome.	Arch Intern Med. 2004 Nov 8;164(20):2241-5.	BACKGROUND: Most of what is believed about chronic fatigue syndrome (CFS) is based on clinic-based studies. These studies may not reflect CFS cases in the population. METHODS: We used data from a population-based study of CFS to identify factors associated with receiving a CFS diagnosis. Wichita, Kan, residents were screened by random-digit dialing. Eligible individuals completed a telephone interview. Respondents meeting CFS criteria were invited for a clinical evaluation to confirm CFS. We analyzed all persons with confirmed CFS. The main outcomes of this study, prevalence and incidence of CFS, are published elsewhere. Herein, we present an exploratory analysis with previous CFS

	and Prevention, Atlanta, GA 30333, USA.			diagnosis as the outcome, predicted by demographic and symptom characteristics. RESULTS: We confirmed CFS in 90 subjects; 14 (16%) had been previously diagnosed as having CFS. Persons in the middle- vs the higher-income group were more likely to have been diagnosed as having CFS (9 [29%] of 31 subjects vs 3 [8%] of 39 subjects; P = .03), as were those with sudden vs gradual fatigue onset (7 [41%] of 17 subjects vs 4 [6%] of 64 subjects; P < .01), those reporting tender lymph nodes (7 [33%] of 21 subjects vs 7 [10%] of 69 subjects; P = .02), and those reporting a sore throat (6 [35%] of 17 subjects vs 8 [11%] of 73 subjects; P = .02). Only 17 (21%) of 81 subjects had sudden fatigue onset, and tender lymph nodes (reported in 21 [23%] of 90 subjects) and a sore throat (reported in 17 [19%] of 90 subjects) were the least common symptoms. CONCLUSION: Most cases of CFS in the population are unrecognized by the medical community; persons diagnosed as having CFS may be different from persons with CFS in the general population.
Spence VA, Khan F, Kennedy G, Abbot NC, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital & Medical School, Dundee DD1 9SY, UK.	Acetylcholine mediated vasodilatation in the microcirculation of patients with chronic fatigue syndrome.	Prostaglandins Leukot Essent Fatty Acids. 2004 Apr;70(4):403-7.	The aetiology of chronic fatigue syndrome (CFS) remains controversial and a number of hypotheses have been put forward to explain it. Research into the condition is hindered by the considerable heterogeneity seen across patients but several reports have highlighted disturbances to cholinergic mechanisms in terms of central nervous system activity, neuromuscular function and autoantibodies to muscarinic cholinergic receptors. This paper examines an altogether separate function for acetylcholine and that is its role as an important and generalized vasodilator. Most diseases are accompanied by a blunted response to acetylcholine but the opposite is true for CFS. Such sensitivity is normally associated with physical training so the finding in CFS is anomalous and may well be relevant to vascular symptoms that characterise many patients. There are several mechanisms that might lead to ACh endothelial sensitivity in CFS patients and various experiments have been designed to unravel the enigma. These are reported here.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport, Qld. 4215, Australia.	Is gulf war syndrome an autoimmune disorder of endogenous neuropeptides, exogenous sandfly maxadilan and molecular mimicry?	Med Hypotheses. 2004;62(5):658-64.	Gulf war syndrome (GWS) remains a contentious diagnosis with conflicting laboratory investigation and lack of a biologically plausible aetiology. This paper discusses the potential role of maxadilan, a potent sandfly vasoactive peptide, in causing autoimmune responses in susceptible individuals through possible molecular mimicry with pituitary adenylate cyclase activating polypeptide (PACAP) and the PAC1R receptor. Gulf war syndrome may share some causative pathology with Chronic Fatigue Syndrome (CFS), a disorder characterised by prolonged fatigue and debility mostly associated with post-infection sequelae although ongoing infection is unproven. Immunological aberration associated with an expanding group of vasoactive neuropeptides in the context of molecular mimicry and inappropriate immunological memory has been recently raised as possible cause of CFS. Vasoactive neuropeptides act as hormones, neurotransmitters, immune modulators and neurotrophes. They are readily catalysed to small peptide fragments. They and their binding sites are immunogenic and are known to be associated with a range of autoimmune conditions. Maxadilan, while not sharing substantial sequence homology with PACAP is a known agonist of the PACAP specific receptor (PAC1R) and therefore emulates these functions. Moreover a specific amino acid sequence peptide deletion within maxadilan converts it to a PACAP receptor antagonist raising the possibility of this substance provoking a CFS like response in humans exposed to it. This paper describes a biologically plausible mechanism for the development of a GWS-like chronic fatigue state based on loss of immunological tolerance to the vasoactive neuropeptide PACAP or its receptor following bites

				of the sandfly Phlebotomus papatasi and injection of the vasodilator peptide maxadilan. Exacerbation of this autoimmune response as a consequence of recent or simultaneous multiple vaccination exposures deserves further investigation. While the possible association between the relatively recently discovered vasoactive neuropeptides and chronic fatigue conditions has only recently been reported in the literature, this paper explores links for further research into GWS and CFS.
Staines DR.	Gold Coast Public Health Unit, 10-12 Young Street, Southport 4215, Qld, Australia.	Is chronic fatigue syndrome an autoimmune disorder of endogenous neuropeptides, exogenous infection and molecular mimicry?	Med Hypotheses. 2004;62(5):646-52.	Chronic fatigue syndrome is a disorder characterised by prolonged fatigue and debility and is mostly associated with post-infection sequelae although ongoing infection is unproven. Immunological aberration is likely and this may prove to be associated with an expanding group of vasoactive neuropeptides in the context of molecular mimicry and inappropriate immunological memory. Vasoactive neuropeptides including vasoactive intestinal peptide (VIP) and pituitary adenylate activating polypeptide (PACAP) belong to the secretin/glucagon superfamily and act as hormones, neurotransmitters, immune modulators and neurotrophes. They are readily catalysed to smaller peptide fragments by antibody hydrolysis. They and their binding sites are immunogenic and are known to be associated with a range of autoimmune conditions. Vasoactive neuropeptides are widely distributed in the body particularly in the central, autonomic and peripheral nervous systems and have been identified in the gut, adrenal gland, reproductive organs, vasculature, blood cells and other tissues. They have a vital role in maintaining vascular flow in organs, and in thermoregulation, memory and concentration. They are co-transmitters for acetylcholine, nitric oxide, endogenous opioids and insulin, are potent immune regulators with primarily anti-inflammatory activity, and have a significant role in protection of the nervous system to toxic assault, promotion of neural development and the maintenance of homeostasis. This paper describes a biologically plausible mechanism for the development of CFS based on loss of immunological tolerance to the vasoactive neuropeptides following infection, significant physical exercise or de novo. It is proposed that release of these substances is accompanied by a loss of tolerance either to them or their receptor binding sites in CFS. Such an occurrence would have predictably serious consequences resulting from compromised function of the key roles these substances perform. All documented symptoms of CFS are explained by vasoactive neuropeptide compromise, namely fatigue and nervous system dysfunction through impaired acetylcholine activity, myalgia through nitric oxide and endogenous opioid dysfunction, chemical sensitivity through peroxynitrite and adenosine dysfunction, and immunological disturbance through changes in immune modulation. Perverse immunological memory established against these substances or their receptors may be the reason for the protracted nature of this condition. The novel status of these substances together with their extremely small concentrations in blood and tissues means that clinical research into them is still in its infancy. A biologically plausible theory of CFS causation associated with vasoactive neuropeptide dysfunction would promote a coherent and systematic approach to research into this and other possibly associated disabling conditions.
Staud R.		Abnormal Pain Processing in Patients with Fibromyalgia	Journal of Chronic Fatigue Syndrome 2004; 12(1):71–77.	Fibromyalgia syndrome (FMS) is characterized by widespread pain, fatigue, sleep abnormalities, and distress. Because FMS lacks consistent evidence for tissue abnormalities, recent investigations have focused on central nervous system mechanisms of pain. Abnormal temporal summation of second pain (AWindup@) and central sensitization (CS) have recently been described in FMS patients. Windup

		Syndrome		(WU) and central sensitization, which rely on central pain mechanisms, occur after prolonged C-nociceptor input and depend on activation of nociceptor specific neurons as well as wide dynamic range neurons in the dorsal horn of the spinal cord. The important role of WU is also supported by its ability to predict the clinical pain intensity of FMS patients. Furthermore, brain-imaging techniques that can detect neuronal activation following nociceptive stimuli have provided additional evidence for abnormal central pain mechanisms in FMS. Most importantly, brain images have corroborated the augmented reported pain experience of FMS patients during experimental pain stimuli. These findings may have important implications for future research as well as the treatment of FMS pain.
Steinau M, Unger ER, Vernon SD, Jones JF, Rajeevan MS.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd., MSG-41, Atlanta, GA 30333, USA.	Differential-display PCR of peripheral blood for biomarker discovery in chronic fatigue syndrome.	J Mol Med. 2004 Nov;82(11):750-5. Epub 2004 Nov.	We used differential-display PCR of peripheral blood mononuclear cells (PBMCs) to search for candidate biomarkers for chronic fatigue syndrome (CFS). PBMCs were collected from a subject with CFS and an age- and sex-matched control before and 24 h after exercise. RNA expression profiles were generated using 46 primer combinations, and the similarity between the individuals was striking. Differentially expressed bands were excised, reamplified, and sequenced, yielding 95 nonredundant sequences, of which 50 matched to known gene transcripts, 38 matched to genes with unknown functions, and 7 had no similarity to any database entry. Most (86%) of the differences between the two subjects were present at baseline. Differential expression of ten genes was verified by real-time reverse-transcription PCR: five (cystatin F, MHC class II, platelet factor 4, fetal brain expressed sequence tag, and perforin) were downregulated, and the remaining five genes (cathepsin B, DNA polymerase epsilon4, novel EST PBMC191MSt, heparanase precursor, and ORF2/L1 element) were upregulated in the subject with CFS. Many of these genes have known functions in defense and immunity, thus supporting prior suggestions of immune dysregulation in the pathogenesis of CFS. Differential-display PCR is a powerful tool for identification of candidate biomarkers. Investigation of these markers in samples from well-designed epidemiological studies of CFS will be required to determine the validity of these candidate biomarkers. The real-time reverse-transcription PCR assays that we developed for assay of these biomarkers will facilitate high-throughput testing of these additional samples.
Stormorken E.		[Harmful psychiatrization] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Jul 1;124(13-14):1826-7; author reply 1827.	
Stormorken E.		[Errors in a textbook on psychiatry] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 May 6;124(9):1277; author reply 1277.	
Stouten B.		Cost-effectiveness of cognitive behaviour therapy for patients with	QJM. 2004 Jun;97(6):379-80.	

		chronic fatigue syndrome.		
Stouten B.		Chronic fatigue syndrome: a clinical and laboratory study with a well-matched control group.	J Intern Med. 2004 Sep;256(3):265-7; author reply 268-9. Comment on: J Intern Med. 1995 May;237(5):499-506.	
Straus SE		Pharmacotherapy of chronic fatigue syndrome: another gallant attempt.	JAMA. 2004 Sep 8;292(10):1234-5. Comment on: JAMA. 2004 Sep 8;292(10):1195-204.	
Suhadolnik RG, Peterson DL, Reichenbach NL, Roen G, Metzger M, McCahan J, O'Brien K, Welsch S, Gabriel J, Gaughan JP, McGregor NR.		Clinical and Biochemical Characteristics Differentiating Chronic Fatique Syndrome from Major Depression and Healthy Control Populations: Relation to Dysfunction and RNase L Pathway	Journal of Chronic Fatigue Syndrome 2004; 12(1):5–35.	Patterns of immune dysfunction have emerged in chronic fatigue syndrome (CFS) that include an immune activation state (evidenced by increased activated T lymphocytes and circulating cytokines) and poor cellular function (low natural killer (NK) cell cytotoxicity and impaired T lymphocyte response to mitogens). Therefore, the aim of the current study was to examine the relationship between clinical and functional characteristics, immune abnormalities and status of the RNase L pathway in CFS compared with healthy control and depression control populations. All study participants were assessed with respect to their general health, functional status, blood count and chemistry, biochemical and immune parameters. The CFS group (N = 66) demonstrated clinical, functional and biochemical abnormalities distinct from the healthy (N = 62) and depression (N = 51) control groups. The CFS group showed marked functional impairment compared with both control groups (P < .001) as measured by the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) (P < .001). The CFS group also showed decreased cognitive performance on a computerized test battery compared to healthy (P < .001) and depression controls (P < .009) and significantly higher 37/80 kDa RNase L ratio (P < .001) compared with both control groups. The odds ratios of a 37/80 kDa RNase L ratio > 2 compared with the CFS patients were 3.9 for the healthy controls (95% confidence limit (CL) 1.0-15.2, P < .05) and 65.8 for the depression controls (95% CL 10.7-406.6, P < .001). The CFS group demonstrated low NK cell cytotoxicity compared to healthy controls (P = .045). The correlation between abnormalities in the RNase L pathway and impaired NKcell function (r = .21, P < .006) suggests that both may be part of the same underlying disease mechanism, at least in this homogeneous population of very disabled CFS patients. Healthy contact-control subjects who had exposure to CFS patients showed a number of characteristics similar to the CFS patients, including an increased mean 37/80 kDa RNase L ratio (P < .04) and prevalence of the 37/80 kDa RNase L ratio > 2 (P < .03). In these contact-control subjects, the 37/80 kDa RNase L ratio was correlated with the interferon-á levels (r = .58, P < .02), suggestive of activation of the interferon pathway. The results of the present study support the cytokine/immune activation model in this well-characterized CFS

				patient group.
Taylor RR, Braveman B, Hammel J.	Department of Occupational Therapy (MC 811), College of Applied Health Sciences, University of Illinois at Chicago, 1919 West Taylor Street, 3rd Floor, Chicago, Illinois 60612-7250, USA. rtaylor@uic.edu	Developing and evaluating community-based services through participatory action research: two case examples.	Am J Occup Ther. 2004 Jan-Feb;58(1):73-82.	Occupational therapy has a strong history of embracing concepts of client empowerment. However there is limited literature in the field on how to achieve empowerment, or on how to extend empowerment to the level of the community and social groups and services within it. This article discusses how concepts and strategies of participatory action research, an extension of empowerment theory, can be used to inform service development and evaluation in occupational therapy. The participatory action research approach is illustrated using two case examples of participatory action research programs for persons with chronic fatigue syndrome and individuals with autoimmune deficiency syndrome (AIDS). A critical analysis of the application of this approach to research and practice is provided. Finally, the paper identifies key principles of participatory action research that can be used to guide occupational therapy services and empower both individuals and communities.
Taylor RR.	University of Illinois at Chicago, Department of Occupational Therapy (MC 811), College of Applied Health Sciences, 1919 West Taylor Street, 3rd Floor, Chicago, Illinois 60612-7250, USA. rtaylor@uic.edu	Quality of life and symptom severity for individuals with chronic fatigue syndrome: findings from a randomized clinical trial.	Am J Occup Ther. 2004 Jan-Feb;58(1):35-43.	OBJECTIVE: Chronic fatigue syndrome is a profoundly disabling condition characterized by severe, unrelenting fatigue and a number of other physical and cognitive symptoms. Currently, there is no cure or widely accepted treatment for chronic fatigue syndrome, and few rehabilitation programs exist to address quality of life issues in chronic fatigue syndrome. In the present randomized clinical trial, the effects of an integrative, consumer-driven rehabilitation program on quality of life and symptom severity for individuals with chronic fatigue syndrome were examined. METHOD: Forty-seven participants were randomly assigned to either an immediate program group (n = 23) or a delayed program control group (n = 24) and assessed with the Chronic Fatigue Syndrome Symptom Rating Scale and the Quality of Life Index before the program, after program participants completed the group phase, and after program participants completed the one-on-one phase. It was hypothesized that the program would lead to improvements in quality of life and an overall reduction in symptom severity. RESULTS: Linear growth models were estimated comparing program and control conditions over time using random-effects regression analyses. Significant condition by time interactions were observed for the main outcomes of symptom severity and overall quality of life. Effect sizes for these interactions involving symptom severity (Cohen's d = 0.71) and overall quality of life (Cohen's d = .66) were moderate. CONCLUSIONS: Findings indicate that consumer driven programs such as this one can have a positive impact on symptom severity and quality of life over time for individuals with chronic fatigue syndrome.
Tomassini V, Pozzilli C, Onesti E, Pasqualetti P, Marinelli F, Pisani A, Fieschi C.	Department of Neurological Sciences, University of Rome "La Sapienza", viale dell' Universita 30, Rome 00185, Italy.	Comparison of the effects of acetyl L-carnitine and amantadine for the treatment of fatigue in multiple sclerosis: results of a pilot, randomised,	J Neurol Sci. 2004 Mar 15;218(1-2):103-8.	Treatment with acetyl L-carnitine (ALCAR) has been shown to improve fatigue in patients with chronic fatigue syndrome, but there have been no trials on the effect of ALCAR for treating fatigue in multiple sclerosis (MS). To compare the efficacy of ALCAR with that of amantadine, one of the drugs most widely used to treat MS-related fatigue, 36 MS patients presenting fatigue were enrolled in a randomised, double-blind, crossover study. Patients were treated for 3 months with either amantadine (100 mg twice daily) or ALCAR (1 g twice daily). After a 3-month washout period, they crossed over to the alternative treatment for 3 months. Patients were rated at baseline and every 3 months according to the Fatigue Severity Scale (FSS), the primary endpoint of the study. Secondary outcome variables were: Fatigue Impact Scale (FIS), Beck Depression Inventory (BDI) and Social

		double-blind, crossover trial.		Experience Checklist (SEC). Six patients withdrew from the study because of adverse reactions (five on amantadine and one on ALCAR). Statistical analysis showed significant effects of ALCAR compared with amantadine for the Fatigue Severity Scale (p = 0.039). There were no significant effects for any of the secondary outcome variables. The results of this study show that ALCAR is better tolerated and more effective than amantadine for the treatment of MS-related fatigue.
Torpy DJ, Bachmann AW, Gartside M, Grice JE, Harris JM, Clifton P, Easteal S, Jackson RV, Whitworth JA.	University of Queensland Department of Medicine, Greenslopes Hospital, Brisbane, Queensland, Australia. dtorpy@mail.rah.sa.gov.au	Association between chronic fatigue syndrome and the corticosteroid-binding globulin gene ALA SER224 polymorphism.	Endocr Res. 2004 Aug;30(3):417-29.	Chronic fatigue syndrome (CFS) is characterized by idiopathic fatigue of greater than 6 months' duration with postexertional exacerbation and many other symptoms. A trend toward relative hypocortisolism is described in CFS. Twin and family studies indicate a substantial genetic etiologic component to CFS. Recently, severe corticosteroid-binding globulin (CBG) gene mutations have been associated with CFS in isolated kindreds. Human leukocyte elastase, an enzyme important in CBG catabolism at inflammatory sites, is reported to be elevated in CFS. We hypothesized that CBG gene polymorphisms may act as a genetic risk factor for CFS. A total of 248 patients with CFS defined by Centers for Disease Control criteria, and 248 controls were recruited. Sequencing and restriction enzyme testing of the CBG gene coding region allowed detection of severe CBG gene mutations and a common exon 3 polymorphism (c.825G-->T, Ala-Ser224). Plasma CBG levels were measured in 125 CFS patients and 198 controls by radioimmunoassay. Total and free (calculated and measured) cortisol levels were ascertained in single samples between 8-10 a.m. The age of onset (mid 30s) and gender ratio (2.2:1, female:male) of the patients were similar to those reported in U.S. epidemiologic studies. A trend toward a preponderance of serine224 homozygosity among the CFS patients was noted, compared with controls (chi2 = 5.31, P = 0.07). Immunoreactive-CBG (IR-CBG) levels were higher in Serine/Alanine (Ser/Ala) than Ala/Ala subjects and higher again in Ser/Ser subjects, this effect was strongest in controls; Ser/Ser: 46.1+/-1.8 (n = 31, P = 0.03) vs. Ser/Ala: 42.4+/-1.0 (n = 56, P = 0.05) vs. Ala/Ala: 40.8+/-1.7 microg/mL (n = 21). Despite higher CBG levels, there was a nonsignificant trend toward lower total and free plasma cortisol in serine allele positive patients, total cortisol: Ser/Ser: 13.3+/-1.4 (n = 34) vs. Ser/Ala: 14.0+/-0.7 (n = 66) vs. Ala/Ala: 15.4+/-1.0 (n = 23). Homozygosity for the serine allele of the CBG gene may predispose to CFS, perhaps due to an effect on hypothalamic-pituitary-adrenal axis function related to altered CBG-cortisol transport function or immune-cortisol interactions.
Tritt K, Nickel M, Mitterlehner F, Nickel C, Forthuber P, Leiberich P, Rother W, Loew T.	Section of Psychosomatic Medicine, University Clinic of the University Regensburg, Regensburg, Germany.	Chronic fatigue and indicators of long-term employment disability in psychosomatic inpatients.	Wien Klin Wochenschr. 2004 Mar 31;116(5-6):182-9.	The major goal of this study was to determine indictors of long-term disability for psychosomatic inpatients with chronic fatigue syndrome. To this end, a cross-sectional study was performed with a random sample of patients (n=1000, response rate: 83.9%) at a psychosomatic inpatient clinic. 51.1% of the patients (n=429) reported intensely persistent exhaustion that had no logical relation to actual exertion. 159 (37.1%) patients in this group were disabled from working and these comprised the main target group of this study. Significantly more patients in the target group worked part time, were disabled for a disproportionately long period of time (50.9% of all were disabled for more than 6 months in the previous year), and felt stressed because of conflicts with their superiors and/or colleagues (in each case, P<0.01). While more frequent psychological comorbidity was not found, they reported physical complaints more often. It was not the patients fit for work who felt more burdened with chronic fatigue, but rather the employment-disabled, who were actually exposed to fewer demands. These patients had, in comparison with those fit to work, a stronger fixation on somatic

				complaints, inadequate perception of physical and psychic sensations, difficulties getting along with other people and in coping with a regular job (in each case, P<0.01). Prospective examination of these indicators could help detect predictor variables for long-term disability in chronic fatigue. Such predictors could contribute to timely social-medical assessment and treatment.
Tryon WW, Jason L, Frankenberry E, Torres-Harding S.	Department of Psychology, Fordham University, 441 East Fordham Road, Bronx, NY 10458-5198, USA. wtryon@fordham.edu	Chronic fatigue syndrome impairs circadian rhythm of activity level.	Physiol Behav. 2004 Oct 15;82(5):849-53.	Some of the symptoms of chronic fatigue syndrome (CFS) are the same as for disrupted circadian rhythm. Activity level is frequently used to study circadian rhythm. Continuous waist activity measurements taken every minute 24 h/day for from 5 to 7 days in 10 controls and from 2 to 7 days in 8 patients with CFS yielded two primary findings: (a) lower daytime activity and (b) less regular activity-rest cycles in persons with CFS than in controls.
Turkington D, Hedwat D, Rider I, Young AH.	Royal Victoria Infirmary, Newcastle upon Tyne, UK.	Recovery from chronic fatigue syndrome with modafinil.	Hum Psychopharmacol. 2004 Jan;19(1):63-4.	PMID: 14716715 [PubMed - in process]
Unger ER, Nisenbaum R, Moldofsky H, Cesta A, Sammut C, Reyes M, Reeves WC.		Sleep assessment in a population-based study of chronic fatigue syndrome.	BMC Neurol. 2004 Apr 19;4(1):6.	Background Chronic fatigue syndrome (CFS) is a disabling condition that affects approximately 800,000 adult Americans. The pathophysiology remains unknown and there are no diagnostic markers or characteristic physical signs or laboratory abnormalities. Most CFS patients complain of unrefreshing sleep and many of the postulated etiologies of CFS affect sleep. Conversely, many sleep disorders present similarly to CFS. Few studies characterizing sleep in unselected CFS subjects have been published and none have been performed in cases identified from population-based studies. Methods. The study included 339 subjects (mean age 45.8 years, 77% female, 94.1% white) identified through telephone screen in a previously described population-based study of CFS in Wichita, Kansas. They completed questionnaires to assess fatigue and wellness and 2 self-administered sleep questionnaires. Scores for five of the six sleep factors (insomnia/hypersomnia, non-restorative sleep, excessive daytime somnolence, sleep apnea, and restlessness) in the Centre for Sleep and Chronobiology's Sleep Assessment Questionnaire(c) (SAQ(c)) were dichotomized based on threshold. The Epworth Sleepiness Scale score was used as a continuous variable. Results. 81.4% of subjects had an abnormality in at least one SAQ(c) sleep factor. Subjects with sleep factor abnormalities had significantly lower wellness scores but statistically unchanged fatigue severity scores compared to those without SAQ(c) abnormality. CFS subjects had significantly increased risk of abnormal scores in the non-restorative (adjusted odds ratio [OR] = 28.1; 95% confidence interval [CI]= 7.4-107.0) and restlessness (OR = 16.0; 95% CI = 4.2-61.6) SAQ(c) factors compared to non-fatigued, but not for factors of sleep apnea or excessive daytime somnolence. This is consistent with studies finding that, while fatigued, CFS subjects are not sleepy. A strong correlation (0.78) of Epworth score was found only for the excessive daytime somnolence factor. Conclusions. SAQ(c) factors describe sleep abnormalities associated with CFS and provide more information than the Epworth score. Validation of these promising results will require formal polysomnographic sleep studies.

van der Meer JW, Lamberts SW, Buchwald D.		Dr Baschetti rides/writes again. Comment on: Eur J Clin Invest. 2003 Dec;33(12):1029-31.	Eur J Clin Invest. 2004 Apr;34(4):317; author reply 318-9.	
Van Engelen BG, Kalkman JS, Schillings ML, Van Der Werf SP, Bleijenberg G, Zwarts MJ.	Neuromusculair Centrum Nijmegen, Instituut voor Neurologie, Universitair Medisch Centrum St Radboud, Postbus 9101, 6500 HB Nijmegen.	[Fatigue in neuromuscular disease] [Article in Dutch]	Ned Tijdschr Geneeskd. 2004 Jul 3;148(27):1336-41.	Chronic fatigue is a symptom of diseases such as cancer, multiple sclerosis, Parkinson's and cerebrovascular disease. Fatigue can also be present in people with no demonstrable somatic disease. If certain criteria are met, chronic-fatigue syndrome may be diagnosed in these cases. Fatigue is a multi-dimensional concept with physiological and psychological dimensions. The 'Short Fatigue Questionnaire' consisting of 4 questions is a tool to measure fatigue with a high degree of reliability and validity. Within the group of neuromuscular disorders, fatigue has been reported by patients with post-polio syndrome, myasthenia gravis, and Guillain-Barre syndrome. The percentage of neuromuscular patients suffering from severe fatigue (64%) is comparable with that of patients with multiple sclerosis, a disease in which fatigue is an acknowledged symptom. Now that reliable psychological and clinical neurophysiological techniques are available, a multidisciplinary approach to fatigue in patients with well-defined neuromuscular disorders may contribute towards the elucidation of the pathophysiological mechanisms of chronic fatigue, with the ultimate goal being to develop methods of treatment for fatigue in neuromuscular patients.
Van Hoof Elke Clin Psych		Article: Cognitive Behavioural Therapy as Cure-All for CFS	Journal of Chronic Fatigue Syndrome 2004 11 (4): 43 - 47	
Van Hoof E, Coomans D, Cluydts R, De Meirleir K.		The Fennell Phase Inventory in a Belgian Sample	Journal of Chronic Fatigue Syndrome 2004; 12(1):53–69.	The present study is a follow-up of the research conducted by Jason, Fennell et al. (1995, 1999, 2000) on a multistage theory for chronic fatigue syndrome (CFS). This multistage model is a very promising method for the evaluation of patients suffering from CFS and could facilitate the appropriate selection of various psychosocial therapies that improve the patient's ability to cope with their illness. Four predictive factors emerged with moderate to excellent reliability. A Spearman's rank correlation revealed positive correlations between our four-factor model and the three-factor model identified by Jason et al. (1999). A correlation matrix between the dimensional psychological investigation and the Fennell Phases revealed characteristics as suggested by previous research. Biological parameters varied over the different phases suggesting an important interaction between body and psyche.
Van Houdenhove B, Egle UT.	Faculty of Medicine, K.U.Leuven, Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Fibromyalgia: a stress disorder? Piecing the biopsychosocial puzzle together.	Psychother Psychosom. 2004 Sep-Oct;73(5):267-75.	Fibromyalgia (FM) is a controversial syndrome, characterised by persistent widespread pain, abnormal pain sensitivity and additional symptoms such as fatigue and sleep disturbance. The syndrome largely overlaps with other functional somatic disorders, particularly chronic fatigue syndrome (CFS). Although the exact aetiology and pathogenesis of FM are still unknown, it has been suggested that stress may play a key role in the syndrome. This article first reviews the function of the stress response system, placing special emphasis on the relationships between adverse life experiences, stress regulation and pain-processing mechanisms, and summarising the evidence for a possible aetiopathogenetic role of stress in FM. Finally, an integrative biopsychosocial model that

				conceptualizes FM as a stress disorder is proposed, and the clinical and research implications of the model are discussed.
Vermeulen RC, Scholte HR.	Research Center Amsterdam, Amsterdam, Netherlands. info@cfscentrumamsterdam.nl	Exploratory open label, randomized study of acetyl- and propionylcarnitine in chronic fatigue syndrome.	Psychosom Med. 2004 Mar-Apr;66(2):276-82.	OBJECTIVES: We compared the effects of acetylcarnitine, propionylcarnitine and both compounds on the symptoms of chronic fatigue syndrome (CFS). METHODS: In an open, randomized fashion we compared 2 g/d acetyl-L-carnitine, 2 g/d propionyl-L-carnitine, and its combination in 3 groups of 30 CFS patients during 24 weeks. Effects were rated by clinical global impression of change. Secondary endpoints were the Multidimensional Fatigue Inventory, McGill Pain Questionnaire, and the Stroop attention concentration test. Scores were assessed 8 weeks before treatment; at randomization; after 8, 16, and 24 weeks of treatment; and 2 weeks later. RESULTS: Clinical global impression of change after treatment showed considerable improvement in 59% of the patients in the acetylcarnitine group and 63% in the propionylcarnitine group, but less in the acetylcarnitine plus propionylcarnitine group (37%). Acetylcarnitine significantly improved mental fatigue (p =.015) and propionylcarnitine improved general fatigue (p =.004). Attention concentration improved in all groups, whereas pain complaints did not decrease in any group. Two weeks after treatment, worsening of fatigue was experienced by 52%, 50%, and 37% in the acetylcarnitine, propionylcarnitine, and combined group, respectively. In the acetylcarnitine group, but not in the other groups, the changes in plasma carnitine levels correlated with clinical improvement. CONCLUSIONS: Acetylcarnitine and propionylcarnitine showed beneficial effect on fatigue and attention concentration. Less improvement was found by the combined treatment. Acetylcarnitine had main effect on mental fatigue and propionylcarnitine on general fatigue.
Vermeulen RC, Scholte HR.	CFS Research Centre Amsterdam, Waalstraat 25-31, 1078 BR Amsterdam, The Netherlands. rcwvermeulen@cfscentrumamsterdam.nl	Chronic fatigue syndrome and sexual dysfunction.	J Psychosom Res. 2004 Feb;56(2):199-201.	OBJECTIVE: The study was undertaken to determine if ambulant female patients with the chronic fatigue syndrome (CFS) report problems with their sexual functioning. METHODS: We studied 35 female CFS patients and 36 healthy female controls. The severity of CFS was measured with a fatigue questionnaire and the presence and severity of sexual dysfunction with a questionnaire about sexual functioning. RESULTS: The mean fatigue score was 24.8 in the CFS patients and 11.9 in the controls (P=.000). No increase in sexual dysfunction was found in the CFS group. The control group showed negative correlations between the score of the fatigue questionnaire and the frequency of "sexual fantasies," "(desire for) sexual contact" and "satisfaction with sex life." Such correlations were absent in the CFS group. CONCLUSION: The satisfaction with sex life was similar in patients and controls. The results suggest that patients and controls have a different perception of fatigue.
Viner R, Gregorowski A, Wine C, Bladen M, Fisher D, Miller M, El Neil S.	Department of Adolescent Medicine, Great Ormond Street Hospital for Children and University College London Hospitals, London, UK. R.Viner@ich.ucl.ac.	Outpatient rehabilitative treatment of chronic fatigue syndrome (CFS/ME).	Arch Dis Child. 2004 Jul;89(7):615-9.	AIMS: To assess the outcome of outpatient multidisciplinary rehabilitative treatment (graded activities/exercise programme, family sessions, and supportive care) compared with supportive care alone for children and adolescents with chronic fatigue syndrome (CFS/ME). METHODS: Fifty six young people (aged 9-17 years) with CFS/ME by standard criteria were followed up for 3-24 months. All subjects received supportive care. Families additionally opted to either enter the rehabilitation programme (supportive care plus graded activities/exercise programme and family sessions) or have no additional treatment. RESULTS: Twenty two (39%) subjects had supportive care alone and 26 (46%) entered the programme. Treatment groups were comparable at baseline in terms of age, severity and duration of illness, Wellness score, and school attendance. At end of follow up, those in the programme group had significantly higher Wellness score and school attendance than those having

	uk			supportive care alone. The programme significantly reduced the overall severity of illness: after the programme, 43% had complete resolution of CFS/ME compared to only 4.5% of those having supportive care alone. The presence of depressed mood and family beliefs about the aetiology of CFS/ME were not significantly associated with outcomes. CONCLUSIONS: Outpatient rehabilitative treatment offers significant potential to improve the prognosis of CFS/ME in childhood and adolescence.
Viner R, Hotopf M.	Department of Paediatrics, Royal Free and University College Medical School, Middlesex Hospital, London W1T 3AA. R.Viner@ich.ucl.ac.uk	Childhood predictors of self reported chronic fatigue syndrome/myalgic encephalomyelitis in adults: national birth cohort study.	BMJ. 2004 Oct 23;329(7472):941. Epub 2004 Oct 06. Comment in: BMJ. 2004 Oct 23;329(7472):928-9.	OBJECTIVE: To study childhood risk factors for chronic fatigue syndrome in adult life. DESIGN: Examination of data from the 1970 British birth cohort. PARTICIPANTS: 16,567 babies born 5-11 April 1970, followed up at 5, 10, 16, and 29-30 years. MAIN OUTCOME MEASURES: Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) identified by self report at age 30 years. Data from childhood from questionnaires given to parents and teachers. Maternal mental health assessed with the malaise inventory. RESULTS: 93 (0.8%, 95% confidence interval 0.7 to 1.0) of 11 261 participants reported ever having CFS/ME, and 48 (0.4%, 0.3 to 0.6) had the condition currently. Higher risk of CFS/ME was associated with having a limiting longstanding condition in childhood (odds ratio 2.3, 1.4 to 3.9), female sex (2.3, 1.4 to 2.6), and high social class in childhood (2.2, 1.4 to 3.5). Higher levels of exercise in childhood were associated with lower risk (0.5, 0.2 to 0.9). Maternal psychological disorder, psychological problems in childhood, birth weight, birth order, atopy, obesity, school absence, academic ability, and parental illness were not associated with risk of CFS/ME. CONCLUSIONS: We identified no association between maternal or child psychological distress, academic ability, parental illness, atopy, or birth order and increasing risk of lifetime CFS/ME. Sedentary behaviour increased the risk.
Vladutiu GD, Natelson BH.	Department of Pediatrics, School of Medicine & Biomedical Sciences, State University of New York at Buffalo, Buffalo, New York, USA. gdv@buffalo.edu	Association of medically unexplained fatigue with ACE insertion/deletion polymorphism in Gulf War veterans.	Muscle Nerve. 2004 Jul;30(1):38-43.	Genes associated with muscle metabolism and physical endurance were evaluated for variants that may contribute to the etiology of medically unexplained severe and chronic fatigue. Subjects included 49 Gulf War veterans and 61 nonveterans with chronic fatigue syndrome (CFS) or idiopathic chronic fatigue (ICF) and 30 veterans and 45 nonveterans who served as healthy controls. Increased risk for CFS/ICF was associated with alterations of the insertion/deletion (I/D) polymorphism in the angiotensin-converting enzyme gene within the Gulf War veteran sample only. The I allele frequency was decreased in affected versus unaffected veterans (0.15 versus 0.48; odds ratio [OR], 5.08; 95% confidence interval [CI], 1.97-13.35; P < 0.0001). Correspondingly, the II genotype was decreased fourfold in affected veterans (0.08 versus 0.35; OR = 5.87; 95% CI: 1.21-28.36; P = 0.02), and the DD genotype was increased twofold (0.78 versus 0.39; OR, 5.4; 95% CI, 1.6-18.4; P = 0.007). Veterans with the DD genotype were eight times more likely to develop CFS/ICF than were those with the II genotype (OR, 8.30; 95% CI, 1.50-56.09; P = 0.009).
Vojdani A, Thrasher JD.	Section of Neuroimmunology, Immunosciences Lab Inc., 8693 Wilshire Boulevard, Suite 200, Beverly Hills,	Cellular and humoral immune abnormalities in Gulf War veterans.	Environ Health Perspect. 2004 Jun;112(8):840-6.	We examined 100 symptomatic Gulf War veterans (patients) and 100 controls for immunologic assays. The veterans and controls were compared for the percentage of T cells (CD3); B cells (CD19); helper:suppressor (CD4:CD8) ratio; natural killer (NK) cell activity; mitogenic response to phytohemagglutin (PHA) and pokeweed mitogen (PWM); level of immune complexes; myelin basic protein (MBP) and striated and smooth muscle autoantibodies; and antibodies against Epstein-Barr virus, cytomegalovirus, herpes simplex virus type 1 (HSV-1), HSV-2, human herpes Type 6 (HHV-6), and Varicella zoster virus (VZV). The percentage of T cells in patients versus controls was not significantly

	CA 90211, USA. drari@msn.com			different, whereas a significantly higher proportion of patients had elevated T cells compared with controls. The percentage of B cells was significantly elevated in the patients versus the controls. The NK cell (NK) activity was significantly decreased in the patients (24.8 +/- 16.5 lytic units) versus the controls (37.3 +/- 26.4 lytic units). The percentage of patients with lower than normal response to PHA and PWM was significantly different from controls. Immune complexes were significantly increased in the patients (53.1 +/- 18.6, mean +/- SD) versus controls (34.6 +/- 14.3). Autoantibody titers directed against MBP and striated or smooth muscle were significantly greater in patients versus controls. Finally, the patients had significantly greater titers of antibodies to the viruses compared with the controls ($p < 0.001$). These immune alterations were detected 2-8 years after participation in the Gulf War. The immune alterations are consistent with exposure to different environmental factors. We conclude that Gulf War syndrome is a multifaceted illness with immune function alterations that may be induced by various factors and are probably associated with chronic fatigue syndrome.
Vos R, Willems D, Houtepen R.	Health Ethics and Philosophy, Department of Health Care Studies, University of Maastricht, Maastricht, The Netherlands. Rein.Vos@ZW.unimaas.nl	Coordinating the norms and values of medical research, medical practice and patient worlds-the ethics of evidence based medicine in orphaned fields of medicine.	J Med Ethics. 2004 Apr;30(2):166-70.	Evidence based medicine is rightly at the core of current medicine. If patients and society put trust in medical professional competency, and on the basis of that competency delegate all kinds of responsibilities to the medical profession, medical professionals had better make sure their competency is state of the art medical science. What goes for the ethics of clinical trials goes for the ethics of medicine as a whole: anything that is scientifically doubtful is, other things being equal, ethically unacceptable. This particularly applies to so called orphaned fields of medicine, those areas where medical research is weak and diverse, where financial incentives are lacking, and where the evidence regarding the aetiology and treatment of disease is much less clear than in laboratory and hospital based medicine. Examples of such orphaned fields are physiotherapy, psychotherapy, medical psychology, and occupational health, which investigate complex syndromes such as RSI, whiplash, chronic low back pain, and chronic fatigue syndrome. It appears that the primary ethical problem in this context is the lack of attention to the orphaned fields. Although we agree that this issue deserves more attention as a matter of potential injustice, we want to argue that, in order to do justice to the interplay of heterogeneous factors that is so typical of the orphaned fields, other ethical models than justice are required. We propose the coordination model as a window through which to view the important ethical issues which relate to the communication and interaction of scientists, health care workers, and patients.
Wallman KE, Morton AR, Goodman C, Grove R, Guilfoyle AM.	School of Human Movement and Exercise Science, University of Western Australia, Stirling Highway, Nedlands, WA 6009, Australia. kwallman@cyllene.uwa.edu.au	Randomised controlled trial of graded exercise in chronic fatigue syndrome.	Med J Aust. 2004 May 3;180(9):444-8.	OBJECTIVE: To investigate whether 12 weeks of graded exercise with pacing would improve specific physiological, psychological and cognitive functions in people with chronic fatigue syndrome (CFS). DESIGN: Randomised controlled trial. SETTING: Human performance laboratory at the University of Western Australia. PARTICIPANTS: 61 patients aged between 16 and 74 years diagnosed with CFS. INTERVENTIONS: Either graded exercise with pacing (32 patients) or relaxation/flexibility therapy (29 patients) performed twice a day over 12 weeks. MAIN OUTCOME MEASURES: Changes in any of the physiological, psychological or cognitive variables assessed. RESULTS: Following the graded exercise intervention, scores were improved for resting systolic blood pressure ($P = 0.018$), work capacity ($W.kg(-1)$) ($P = 0.019$), net blood lactate production ($P = 0.036$), depression ($P = 0.027$) and performance on a modified Stroop Colour Word test ($P = 0.029$). Rating of perceived exertion scores, associated with an exercise test, was lower after graded exercise ($P = 0.013$). No such changes were

				observed in the relaxation/flexibility condition, which served as an attention-placebo control. CONCLUSIONS: Graded exercise was associated with improvements in physical work capacity, as well as in specific psychological and cognitive variables. Improvements may be associated with the abandonment of avoidance behaviours.
Wallman K, Goodman C, Morton A, Grove R, Dawson B	Department of Human Movement, University of Western Australia, Nedlands, Western Australia, Australia	Test-Retest Reliability of the Aerobic Power Index Test in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2004; Mar;11(4):19–32.	Use of maximal aerobic exercise testing in a chronically ill population may not only deter potential subjects from participating in trials, or returning for repeat trials, but may also result in the exacerbation of symptoms related to CFS. The Aerobic Power Index represents a submaximal exercise test that forms the aerobic component of the Trilevel Fitness Profile. This incremental bike test has a predetermined termination point based on a target heart rate (THR) of 75% of age predicted heart rate maximum, making successful completion of the test more likely in chronically ill subjects. The aim of this study was to determine reliability of the Aerobic Power Index in 20 CFS subjects. Results for the 17 subjects who reached THR for both trials, demonstrated high reliability for watts per kilogram and oxygen uptake (ml·kg-1·min-1), as demonstrated by an intraclass correlation coefficient (ICC) of .97 and .91 respectively, while RPE resulted in moderate reliability (ICC = .87). The results of this study indicate that that the Aerobic Power Index is a reliable submaximal test for use in a CFS population.
Wallman KE, Morton AR, Goodman C, Grove R.	School of Human Movement and Exercise Science, The University of Western Australia, Crawely, Western Australia, Australia. kwallman@cyllene.uwa.edu.au	Physiological responses during a submaximal cycle test in chronic fatigue syndrome.	Med Sci Sports Exerc. 2004 Oct;36(10):1682-8.	INTRODUCTION/PURPOSE: Numerous studies have assessed physical function in individuals suffering from chronic fatigue syndrome (CFS) but neglected to match control subjects according to current activity levels, consequently casting doubt on reported results. The purpose of this study was to include current activity levels as one criterion for matching CFS subjects with healthy control subjects in order to more accurately assess physical function in these subjects. METHODS: Thirty-one healthy control subjects were matched to CFS subjects according to age, gender, body mass, height, and current activity levels. Physiological function was assessed weekly over a 4-wk period using a submaximal cycle test. RESULTS: Comparison of absolute physiological results recorded at the end of each incremental work level of the exercise test showed that ratings of perceived effort (RPE) was the only variable that was significantly different between the two groups. Scores for RPE were significantly higher in CFS subjects for each incremental work level assessed. Conversely, results recorded on completion of the exercise test showed that the control group was capable of a greater power output than the CFS group as reflected by significantly higher scores for watts per kilogram ($P < 0.0005$), net lactate production ($P = 0.003$), oxygen uptake (mL x kg(-1) x min(-1); $P < 0.0005$), respiratory exchange ratio ($P = 0.021$), and HR values as a percentage of age predicted HR(max) ($P = 0.001$). End-point RPE scores were again significantly higher in the CFS group ($P < 0.0005$). CONCLUSION: It is proposed that the reduced exercise tolerance in CFS is due to impairment in the mechanisms that constitute effort sense and/or to avoidance behaviors that result in a reluctance by these subject to exercise to full capacity.
Wang XQ, Takahashi T, Zhu SJ, Moriya J, Saegusa S, Yamakawa J, Kusaka K, Itoh T,	Department of General Medicine, Kanazawa Medical University, Ishikawa, Japan.	Effect of Hochu-ekki-to (TJ-41), a Japanese Herbal Medicine, on Daily Activity in a Murine Model of	Evid Based Complement Alternat Med. 2004 Sep 1;1(2):203-206.	We aimed to evaluate the effect of a Japanese herbal medicine, Hochu-ekki-to (TJ-41), on daily activity in a murine model of chronic fatigue syndrome (CFS). CFS was induced by repeated injection of Brucella abortus (BA) antigen every 2 weeks. TJ-41 was orally administered to mice in a dose of 500 mg/kg/day for 1 week before injecting BA and for 4 weeks thereafter. We evaluated daily running activity in mice receiving TJ-41 as compared with that in untreated mice. Survival of both mouse groups was also monitored during the observation period. Body weight (BW), spleen weight (SW),

Kanda T.		Chronic Fatigue Syndrome.		SW/ BW ratio and expression levels of interleukin-10 (IL-10) mRNA in spleen were determined in both groups at the time of sacrifice. The daily activity was significantly higher in the treated group than in the control. Two mice in the untreated group died 2 days after the second injection of BA, whereas no mice in the group treated with TJ-41 died. The SW and SW/BW ratio were significantly lower in the treated mice than in the control. Suppressed IL-10 mRNA levels were observed in the spleens of the mice treated with TJ-41. Our data suggest that Hochu-ekki-to might possess an inhibitory effect on the marked decrease in running activity following BA injection.
Watanabe A.		Various clinical types of Q-fever disease.Comment on: Intern Med. 2004 Jan;43(1):49-54.	Intern Med. 2004 Jan;43(1):1-2.	
Watson NF, Jacobsen C, Goldberg J, Kapur V, Buchwald D.	Department of Neurology, University of Washington, Seattle 98104-2499, USA. nwatson@u.washington.edu	Subjective and objective sleepiness in monozygotic twins discordant for chronic fatigue syndrome.	Sleep. 2004 Aug 1;27(5):973-7.	STUDY OBJECTIVE: To examine the association of chronic fatigue syndrome (CFS) with measures of objective and subjective sleepiness. DESIGN: Monozygotic co-twin control study. SETTING: Academic medical center. PATIENTS AND PARTICIPANTS: Twenty monozygotic twin pairs discordant for CFS. INTERVENTIONS: N/A. MEASUREMENTS AND RESULTS: All twins completed an Epworth Sleepiness Scale (ESS), 4 Stanford Sleepiness Scales (SSS), and underwent a standard 4-nap multiple sleep latency test. We compared the ESS scores, average SSS scores, and average sleep latency in CFS and healthy twins. The CFS twins reported more sleepiness as measured by mean scores on the ESS (10.9 vs 8.2; 95% confidence interval [CI] = 0.3-5.5; P = .03) and the SSS (3.4 versus 2.1; 95% CI = 0.7-1.9; P < .001). The mean sleep latency on the Multiple Sleep Latency Test was not significantly different between the CFS and healthy twins (8.9 vs 10.0 minutes; 95% CI -4.4-1.7; P = .33). Mean SSS scores increased among the CFS twins and decreased among healthy twins from nap 1 to nap 4 (P < .001). The individual ESS scores and mean sleep latencies on the Multiple Sleep Latency Test were negatively correlated for all the twins (Pearson's r = - 0.40; P = .01), with a slightly stronger association among the healthy twins (Pearson's r = -0.42, P = .07) than the CFS twins (Pearson's r = -0.36, P = .15). CONCLUSIONS: CFS twins reported significantly more subjective sleepiness than their healthy co-twins despite similar nonpathologic mean sleep latencies on the Multiple Sleep Latency Test. Patients with CFS may mistake their chronic disabling fatigue for sleepiness.
Weatherley-Jones E, Nicholl JP, Thomas KJ, Parry GJ, McKendrick MW, Green ST, Stanley PJ, Lynch SP.	Medical Care Research Unit, School of Health and Related Research, University of Sheffield, Regent Court, 30 Regent Street, Sheffield S1 4DA, UK.	A randomised, controlled, triple-blind trial of the efficacy of homeopathic treatment for chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):189-97.	OBJECTIVE: There is no management regime for chronic fatigue syndrome (CFS) that has been found to be universally beneficial and no treatment can be considered a "cure". Patients with CFS may use complementary and alternative medicine (CAM). Our aim was to evaluate homeopathic treatment in reducing subjective symptoms of CFS. METHOD: Using a triple-blind design (patient and homeopath blind to group assignment and data analyst blind to group until after initial analyses to reduce the possibility of bias due to data analyst), we randomly assigned patients to homeopathic medicine or identical placebo. One hundred and three patients meeting the Oxford criteria for CFS were recruited from two specialist hospital out patient departments. Patients had monthly consultations with a professional homeopath for 6 months. Main outcome measures were scores on the subscales of the Multidimensional Fatigue Inventory (MFI) and proportions of each group attaining clinically significant

	e.weatherley-jones@sheffield.ac.uk			improvements on each subscale. Secondary outcome measures were the Fatigue Impact Scale (FIS) and the Functional Limitations Profile (FLP). Ninety-two patients completed treatment in the trial (47 homeopathic treatment, 45 placebo). Eighty-six patients returned fully or partially completed posttreatment outcome measures (41 homeopathic treatment group who completed treatment, 2 homeopathic treatment group who did not complete treatment, 38 placebo group who completed treatment, and 5 placebo group who did not complete treatment). RESULTS: Seventeen of 103 patients withdrew from treatment or were lost to follow-up. Patients in the homeopathic medicine group showed significantly more improvement on the MFI general fatigue subscale (one of the primary outcome measures) and the FLP physical subscale but not on other subscales. Although group differences were not statistically significant on four out of the five MFI subscales (the primary outcome measures), more people in the homeopathic medicine group showed clinically significant improvement. More people in the homeopathic medicine group showed clinical improvement on all primary outcomes (relative risk=2.75, P=.09). CONCLUSIONS: There is weak but equivocal evidence that the effects of homeopathic medicine are superior to placebo. Results also suggest that there may be nonspecific benefits from the homeopathic consultation. Further studies are needed to determine whether these differences hold in larger samples.
White PD.		What causes chronic fatigue syndrome?	BMJ. 2004 Oct 23;329(7472):928-9.	
White PD, Thomas JM, Sullivan PF, Buchwald D.	Department of Psychological Medicine, Barts, London and Queen Mary School of Medicine and Dentistry, University of London. p.d.white@qmul.ac.uk	The nosology of sub-acute and chronic fatigue syndromes that follow infectious mononucleosis.	Psychol Med. 2004 Apr;34(3):499-507.	BACKGROUND: A previous principal components analysis of symptoms occurring after infectious mononucleosis suggested that a discrete fatigue syndrome occurs, which is independent of psychiatric disorder. This work has not been replicated and no latent class analysis of subjects has been published. METHOD: We prospectively examined a cohort of 150 American primary care patients 2 and 6 months after the onset of corroborated infectious mononucleosis. A subset of 50 subjects was studied 4 years after onset. We performed principal components analyses of both psychological and somatic symptoms and latent class analyses of subjects. RESULTS: Principal components analyses consistently delineated two fatigue factors at 2 and 6 months and one fatigue factor at 4 years. These factors were separate from a mixed anxiety and depressive factor. A four-class solution for the latent class analyses consisted of most subjects with few symptoms, a few with many symptoms, a group with predominantly mood symptoms and some subjects with fatigue symptoms. CONCLUSIONS: The symptoms of the principal factors with fatigue were similar to those previously described. Both the factors and classes were independent of an equally delineated mood factor and class. These results support the existence of two discrete chronic fatigue syndromes after infectious mononucleosis, one of which is still demonstrable 4 years after onset.
Whitehead L.	Department of Nursing and Midwifery, University of Stirling, Stirling, UK.	Enhancing the quality of hermeneutic research: decision trail.	J Adv Nurs. 2004 Mar;45(5):512-8.	BACKGROUND: Researchers have ethical and professional obligations to produce research of a high standard. The constituents of quality in research appear to differ between authors, leaving readers unsure about which pathway to follow. This can reflect inadequate consideration of the theoretical framework guiding the study. Many papers fail to consider the theoretical underpinnings of the methodology chosen and the link between these and the methods employed. These need to be accessible to readers in order to assess the trustworthiness of the research. AIM: This paper discusses

	lisa.whitehead@stir.ac.uk			the development of trustworthiness in hermeneutic phenomenological research. DISCUSSION: Referring to a study on lived experience of Chronic Fatigue Syndrome/myalgic encephalitis, I describe the decision trail and discuss the strengths and limitations of the choices made throughout the study. CONCLUSION: The methodology focused my approach more fully on the importance of recognizing the influences that I brought to the study and the impact of these in generating the data. It highlighted the fact that the process of setting out my horizon can never be complete, the importance of analysing the data at a macro and micro level, acknowledging the evolution of the data over time, and ensuring that analysis does not move beyond the data and out of the hermeneutic circle. In seeking to make the decision trail clear to others, researchers must distill the philosophical principles of the methodology and set these out in a way that is accessible and open to scrutiny.
Whiteside A, Hansen S, Chaudhuri A.	Departments of Clinical Physics, Institute of Neurological Sciences, South Glasgow University Hospitals NHS Trust, Glasgow, UK.	Exercise lowers pain threshold in chronic fatigue syndrome.	Pain. 2004 Jun;109(3):497-9.	Post-exertional muscle pain is an important reason for disability in patients who are diagnosed to have Chronic Fatigue Syndrome (CFS). We compared changes in pain threshold in five CFS patients with five age and sex matched controls following graded exercise. Pain thresholds, measured in the skin web between thumb and index finger, increased in control subjects with exercise while it decreased in the CFS subjects. Increased perception of pain and/or fatigue after exercise may be indicative of a dysfunction of the central anti-nociceptive mechanism in CFS patients.
Winkler AS, Blair D, Marsden JT, Peters TJ, Wessely S, Cleare AJ.	Department of Medicine, Division of Psychological Medicine, GKT School of Medicine, Institute of Psychiatry, De Crespigny Park, London SE5 9RJ, UK.	Autonomic function and serum erythropoietin levels in chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):179-83.	OBJECTIVE: Given previous findings, we wished to investigate whether there was evidence of autonomic dysfunction in patients with chronic fatigue syndrome, and whether this could be related to reduced erythropoietin levels and altered red blood cell indices. METHODS: We assessed autonomic function and analysed blood parameters (including erythropoietin) in 22 patients with chronic fatigue syndrome who were medication-free and without comorbid depression or anxiety. Results were compared to 23 iron-deficiency anaemia patients and 18 healthy individuals. RESULTS: Autonomic testing in patients with chronic fatigue syndrome yielded a significantly greater increase in heart rate together with a more pronounced systolic blood pressure fall on standing compared to healthy individuals. Heart rate beat-to-beat variation on deep breathing and responses to the Valsalva manoeuvre were normal. Two of 22 patients with chronic fatigue had mild normochromic normocytic anaemia with normal ferritin, vitamin B12 and folate levels. Serum erythropoietin levels were within reference range. CONCLUSION: Some autonomic dysfunction is present in chronic fatigue syndrome (CFS) patients; the explanation remains uncertain, but could relate to cardiovascular deconditioning. There were no major haematological, biochemical or immunological abnormalities in these patients.
Woldehiwet Z	Department of Veterinary Pathology, University of Liverpool, Veterinary Teaching Hospital,	Q fever (coxiellosis): epidemiology and pathogenesis Erratum in: Res Vet Sci. 2004 Dec;77(3):269.	Res Vet Sci. 2004 Oct;77(2):93-100.	

	Leahurst, Neston, Wirral CH64 7TE, UK. zerai@liverpool.ac.uk			
Woolley J, Allen R, Wessely S.	Academic Department of Psychological Medicine, Guy's, King's & St Thomas's School of Medicine and Institute of Psychiatry, 103 Denmark Hill, London SE5 8AF, UK.	Alcohol use in chronic fatigue syndrome.	J Psychosom Res. 2004 Feb;56(2):203-6.	OBJECTIVE: To examine the anecdotal observation that patients with chronic fatigue syndrome develop alcohol intolerance. METHODS: A consecutive case series of 114 patients fulfilling UK criteria for chronic fatigue syndrome referred to a specialist clinic. Self-reported alcohol use pre- and postdiagnosis, fatigue symptoms and comorbidity measures were collected. RESULTS: Two-thirds reduced alcohol intake. The most common reasons were increased tiredness after drinking (67%), increased nausea (33%), exacerbated hangovers (23%) and sleep disturbance (24%). One-third of the subjects also stopped drinking because "it seemed sensible." Some had been advised to avoid alcohol, but the majority (66%) did so on the basis of personal experience. CONCLUSION: Our data supports the anecdotal belief that chronic fatigue syndrome patients reduce or cease alcohol intake. This is associated with greater impairment in employment, leisure and social domains of function, and may hint at psycho-pathophysiological processes in common with other conditions that result in alcohol intolerance.
Wyller VB, Wyller TB.		[Exhaustion--not fatigue] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2004 Nov 4;124(21):2802; author reply 2802.	
Yamamoto S, Ouchi Y, Onoe H, Yoshikawa E, Tsukada H, Takahashi H, Iwase M, Yamaguti K, Kuratsune H, Watanabe Y.	Department of Physiology, Osaka City University Graduate School of Medicine, 1-4-3 Asahimachi, Abeno-ku, Osaka 545-85851Positron Medical Center, Hamamatsu Medical Center, 5000 Hirakuchi, Hamakita, Shizuoka 434-00412Department of Psychology, Tokyo Metropolitan	Reduction of serotonin transporters of patients with chronic fatigue syndrome.	Neuroreport. 2004 Dec 3;15(17):2571-2574.	To assess the involvement of serotonin in the symptoms of chronic fatigue syndrome, we investigated the serotonergic neurotransmitter system of chronic fatigue syndrome patients by the positron emission tomography (PET). Here we show that the density of serotonin transporters (5-HTTs) in the brain, as determined by using a radiotracer, [C](+)McN5652, was significantly reduced in the rostral subdivision of the anterior cingulate as compared with that in normal volunteers. This subdivision is different from that in the dorsal anterior cingulate in which binding potential values of individual patient showed a weak negative correlation with self-reported pain score of the patients. Therefore, an alteration of serotonergic system in the rostral anterior cingulate plays a key role in pathophysiology of chronic fatigue syndrome.

	Institute for Neuroscience, 2-6 Musashidai Fuchu, Tokyo 183-85263Central Research Laboratory, Hamamatsu Photonics KK, 5000 Hirakuchi, Hamakita, Shizuoka 434-86014Psychiatry, Department of Clinical Neuroscience5Department of Hematology and Oncology, Osaka University Graduate School of Medicine, 2-2 Yamadaoka, Suita 565-08716Department of Health Sciences, Faculty of Health Sciences for Welfare, Kansai University of Welfare Sciences, 3-11-1 Asahigaoka, Kashiwara 582-0026, Japan.			
Yoshiuchi K, Quigley KS, Ohashi K, Yamamoto Y, Natelson BH.	Department of Psychiatry, University of Medicine and Dentistry of New Jersey, New Jersey	Use of time-frequency analysis to investigate temporal patterns of cardiac autonomic	Auton Neurosci. 2004 Jun 30;113(1-2):55-62.	Although a number of studies have reported alterations in cardiac autonomic nervous system function in chronic fatigue syndrome (CFS), the results are not consistent across studies. Reasons for these discrepancies include (1) the use of a heterogeneous patient sample that included those with orthostatic postural tachycardia (POTS), a condition with an autonomic changes, and (2) the use of frequency domain techniques which require a stationary signal and averaging data across relatively long epochs. To deal with these shortcomings, we used the smoothed pseudo-Wigner-Ville transform

	Medical School, East Orange, NJ 07018, USA.	response during head-up tilt in chronic fatigue syndrome.		(SPWVT) to analyze heart rate variability (HRV) and blood pressure variability (BPV) during head-up tilt (HUT) by separating CFS patients into those with and without POTS. SPWVT has the advantage of providing instantaneous information about autonomic function under nonstable physiological conditions. We studied 18 CFS patients without POTS, eight CFS patients with POTS and 25 sedentary healthy controls during supine rest and during the first 10 min after HUT. While we found significant effects of postural change in both groups for all autonomic variables, there were significant groupxtime interactions between CFS without POTS and controls for only instant center frequency (ICF) within the low frequency region both from HRV (p=0.02) and from BPV (p=0.01). Although the physiological meaning of ICF still remains unknown, the data suggest that even CFS patients without POTS may have a subtle underlying disturbance in autonomic function.
Zachrisson O, Colque-Navarro P, Gottfries CG, Regland B, Mollby R.	Institute of Clinical Neuroscience, SU/Molndal, 43180 Molndal, Sweden. olof.zachrisson@neuro.gu.se	Immune modulation with a staphylococcal preparation in fibromyalgia/chronic fatigue syndrome: relation between antibody levels and clinical improvement.	Eur J Clin Microbiol Infect Dis. 2004 Feb;23(2):98-105. Epub 2004 Jan 20.	The aims of this study were to evaluate the serological response to treatment with staphylococcal vaccine in fibromyalgia/chronic fatigue syndrome patients and to explore the relationship between serological response and clinical effect. Twenty-eight patients, half of whom served as controls, were recruited from a 6-month randomised trial in which repeated administration of the staphylococcal toxoid vaccine Staphypan Berna (Berna Biotech, Switzerland) was tested against placebo. Antibody status against extracellular toxins/enzymes, cell-wall components, and enterotoxins was evaluated at baseline and at endpoint. The clinical response to treatment was recorded in rating scales. In the group receiving active treatment, significant serological changes were recorded, whereas no significant changes were found in controls. Treatment led to a significantly increased capacity of serum to neutralise alpha-toxin and a significant increase in serum IgG to alpha-toxin and lipase. Furthermore, the increase in these parameters combined paralleled the improvement in clinical outcome. Thus, the greater the serological response, the greater was the clinical effect. In conclusion, this explorative study has shown that repeated administration of the Staphypan Berna vaccine in patients with fibromyalgia/chronic fatigue syndrome causes a serological response to several staphylococcal antigens, particularly to certain extracellular toxins and enzymes. The results further show that this response is related to the clinical outcome of treatment.
Zavestoski S, Brown P, McCormick S, Mayer B, D'Ottavi M, Lucove JC.	Department of Sociology, University of San Francisco, 2130 Fulton Street, San Francisco, CA 94117-1080, USA. smzavestoski@usfca.edu	Patient activism and the struggle for diagnosis: Gulf War illnesses and other medically unexplained physical symptoms in the US.	Soc Sci Med. 2004 Jan;58(1):161-75.	We examine Gulf War illnesses--which include the fatigue, joint pain, dermatitis, headaches, memory loss, blurred vision, diarrhea, and other symptoms reported by Gulf War veterans--in relation to other medically unexplained physical symptoms such as multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. Our intent is to examine the diagnosis negotiations involved in these mysterious diseases, by showing the different forms of legitimacy involved in such interactions. Factors involved in diagnostic legitimacy are: diagnostic legitimacy in the medical community, lay acceptance of the diagnosis, uncertainty in looking for causes, and social mobilization. We conclude by noting that research may not be able to find any cause for these diseases/conditions; hence, it may be necessary to embrace medical uncertainty, and also to accept patient experience in order to facilitate diagnosis, treatment, and recovery process. Such a change can alter patients' expectations and taken-for-granted assumptions about medicine, and perhaps in turn reduce the frequency with which dissatisfied individuals form illness groups that mobilize to challenge what they see as an unresponsive medical system.
[No authors listed]		Handbook of	Aust N Z J	

		chronic fatigue syndrome.	Psychiatry. 2004 Jun;38(6):479-480.	
[No authors listed]		L-carnitine.	Med Lett Drugs Ther. 2004 Nov 22;46(1196):95-6.	Although advertised on the Internet for weight loss, prevention of aging and enhancement of athletic and sexual performance, levocarnitine has only one well-established indication, and that is for treatment of carnitine deficiency. In clinical trials, the drug also seems to have had modest effects in some other conditions, particularly intermittent claudication and recovery after myocardial infarction, but more studies are needed.

2003				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Aaron LA, Buchwald D.	Department of Oral Medicine, University of Washington, 1959 NE Pacific Street, B316, P.O. Box 356370, 98195-6370, Seattle, WA, USA	Chronic diffuse musculoskeletal pain, fibromyalgia and co-morbid unexplained clinical conditions.	Best Pract Res Clin Rheumatol. 2003 Aug;17(4):563-74.	This chapter reviews our current knowledge on the presence of overlapping syndromes in one form of chronic diffuse pain, fibromyalgia. Patients with fibromyalgia often present with signs and symptoms of other unexplained clinical conditions, including chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorders, and multiple chemical sensitivities. The high prevalence, impact on function and opportunities for treatment underscore the need for clinicians and researchers to screen routinely for co-morbid unexplained clinical conditions among persons with fibromyalgia. We, therefore, describe a simple approach to screening for such conditions in accordance with published criteria. Interventions should directly address both fibromyalgia symptoms and co-morbid unexplained clinical conditions, as well as the multiple factors that propagate pain, fatigue and limitations in function.
Afari N, Buchwald D.	Department of Psychiatry, University of Washington, Seattle, USA. afari@u.washington.edu	Chronic fatigue syndrome: a review.	Am J Psychiatry. 2003 Feb;160(2):221-36.	OBJECTIVE: Chronic fatigue syndrome is an illness characterized by disabling fatigue of at least 6 months, accompanied by several other symptoms. This review summarizes the current state of knowledge about chronic fatigue syndrome. METHOD: The case definition, prevalence, clinical presentation, evaluation, and prognosis of chronic fatigue syndrome are discussed. Research on the pathophysiology and treatment of chronic fatigue syndrome is reviewed. RESULTS: Chronic fatigue syndrome is diagnosed on the basis of symptoms. Patients with chronic fatigue syndrome experience significant functional impairment. Pathophysiological abnormalities exist across many domains, suggesting that chronic fatigue syndrome is a heterogeneous condition of complex and multifactorial etiology. Evidence also is beginning to emerge that chronic fatigue syndrome may be familial. Although chronic fatigue syndrome has significant symptom overlap and comorbidity with psychiatric disorders, several lines of research suggest that the illness may be distinct from psychiatric disorders. Patients' perceptions, attributions, and coping skills, however, may help perpetuate the illness. Treatment for chronic fatigue syndrome is symptom-based and includes pharmacological and behavioral strategies. Cognitive behavior therapy and graded exercise can be effective in treating the fatigue and associated symptoms and disability. CONCLUSIONS: Chronic fatigue syndrome is unlikely to be caused or maintained by a single agent. Findings to date suggest that physiological and psychological factors work together to predispose an individual to the illness and to precipitate and perpetuate the illness. The assessment and treatment of chronic fatigue syndrome should be multidimensional and tailored to the needs of the individual patient.
Agadjanyan M, Vasilevko V, Ghochikyan A, Berns P, Kesslak P, Settineri RA, Nicolson GL		Nutritional Supplement (NT Factor™) Restores Mitochondrial Function and Reduces Moderately Severe Fatigue in Aged Subjects	Journal of Chronic Fatigue Syndrome 2003; 11 (3): 23-37	Decreased mitochondrial function is a characteristic of aging and fatigue. Here we determined if mild to moderately severe fatigue in a group of aged subjects (mean age > 60 years), as defined by the validated Piper Fatigue Scale (PFS), can be significantly improved by use of a glycophospholipid dietary supplement, NT Factor™ (NTF). In addition, we determined if mitochondrial function, as defined by transport of the redox dye Rhodamine-123, is reduced in aging subjects with mild to moderately severe fatigue, and if this can be reversed with NTF supplementation in concert with improvement in fatigue scores. Participants with mild to moderately severe fatigue, who fulfilled the entry requirements were admitted to the study

				when their fatigue could not be explained by an obvious clinical condition. Twenty of the respondents (mean age = 68.9 ± 4.18) completed the first part of the study on NTF for 12 weeks, and 16 of these subjects who agreed to discontinue the product also completed a wash-out period for an additional 12 weeks. Fatigue and mitochondrial function were determined every four weeks during the study. There was a time-dependent reduction in overall fatigue in moderately fatigued subjects (P < .001) but not in mildly fatigued subjects. Mitochondrial function at four and eight weeks of NTF use in moderately fatigued subjects increased by 15% and 26.8%, respectively, and restored mitochondrial function to levels similar to those found in young adults. No further increase was noted between 8 and 12 weeks. Post-NTF there was a slow redevelopment of fatigue and a fall in mitochondrial function in moderately fatigued subjects, indicating that continued use of NTF may be necessary to maintain lower fatigue scores and maintain mitochondrial function. The dietary supplement with NTF reduced moderate fatigue and increased mitochondrial function in aged subjects but had no effect upon mild fatigue expression.
Aktan NM.	CFS Cooperative Research Center, New Jersey Medical School, Newark, USA.	Chronic fatigue syndrome. An overview of current concepts.	Adv Nurse Pract. 2003 Dec;11(12):64-6.	
Ambrose K, Lyden AK, Clauw DJ.	Chronic Pain and Fatigue Research Program, University of Michigan, 24 Frank Lloyd Wright Drive, PO Box 385, Ann Arbor, MI 48109-0483, USA. kambrose@med.umich.edu	Applying exercise to the management of fibromyalgia.	Curr Pain Headache Rep. 2003 Oct;7(5):348-54.	Fibromyalgia, chronic fatigue syndrome, and related illnesses fall under the spectrum of chronic multisymptom illnesses (CMI). This constellation of syndromes often is defined by chronic pain, unremitting fatigue, cognitive difficulties, and various other symptoms. In treating these illnesses, pharmacotherapy generally is the mode of choice, with exercise being overlooked often. However, research has shown that exercise is quite beneficial in reducing pain and fatigue in this population and should be included as part of a multimodal therapy regimen. This article reviews the exercise and CMI literature and provides a model for applying these evidence-based guidelines to a clinical population.
Amel Kashipaz MR, Swinden D, Todd I, Powell RJ.	Division of Molecular and Clinical Immunology, School of Clinical Laboratory Sciences, University of Nottingham, Queen's Medical Centre, Nottingham, UK.	Normal production of inflammatory cytokines in chronic fatigue and fibromyalgia syndromes determined by intracellular cytokine staining in short-term cultured blood mononuclear cells.	Clin Exp Immunol. 2003 May;132(2):360-5.	It has been proposed that cytokines play a role in the pathogenesis of chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS). However, different studies have reported conflicting results using enzyme-linked immunosorbent assay or polymerase chain reaction to detect cytokines in these conditions. In the present study, for the first time, the production of inflammatory [interleukin (IL)-1alpha, IL-6, and TNF-alpha] and anti-inflammatory (IL-10) cytokines by CD14+ and CD14- peripheral blood mononuclear cells (PBMC) from chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) patients and sex- and age-matched normal subjects was investigated at the level of individual cells using the technique of intracellular cytokine staining and flow cytometry. Cultures were carried out in the presence of polymyxin B to inhibit the effect of endotoxins on cytokine production by monocytes. The mean intensity of fluorescence (MIF) and percentage of CD14+ (monocytes) and CD14- (lymphocytes) cytokine-

				producing mononuclear cells were comparable in patients and controls in either unstimulated or IFN-gamma-stimulated conditions. Our study indicates that dysregulation of cytokine production by circulating monocytes or non-monocytic cells (lymphocytes) is not a dominant factor in the pathogenesis of CFS/FMS.
Anyanwu E, Campbell AW, Jones J, Ehiri JE, Akpan AI.		The neurological significance of abnormal natural killer cell activity in chronic toxigenic mold exposures.	ScientificWorld Journal. 2003 Nov 13;3(11):1128-37.	Toxigenic mold activities produce metabolites that are either broad-spectrum antibiotics or mycotoxins that are cytotoxic. Indoor environmental exposure to these toxigenic molds leads to adverse health conditions with the main outcome measure of frequent neuroimmunologic and behavioral consequences. One of the immune system disorders found in patients presenting with toxigenic mold exposure is an abnormal natural killer cell activity. This paper presents an overview of the neurological significance of abnormal natural killer cell (NKC) activity in chronic toxigenic mold exposure. A comprehensive review of the literature was carried out to evaluate and assess the conditions under which the immune system could be dysfunctionally interfered with leading to abnormal NKC activity and the involvement of mycotoxins in these processes. The functions, mechanism, the factors that influence NKC activities, and the roles of mycotoxins in NKCs were cited wherever necessary. The major presentations are headache, general debilitating pains, nose bleeding, fevers with body temperatures up to 40C (104F), cough, memory loss, depression, mood swings, sleep disturbances, anxiety, chronic fatigue, vertigo/dizziness, and in some cases, seizures. Although sleep is commonly considered a restorative process that is important for the proper functioning of the immune system, it could be disturbed by mycotoxins. Most likely, mycotoxins exert some rigorous effects on the circadian rhythmic processes resulting in sleep deprivation to which an acute and transient increase in NKC activity is observed. Depression, psychological stress, tissue injuries, malignancies, carcinogenesis, chronic fatigue syndrome, and experimental allergic encephalomyelitis could be induced at very low physiological concentrations by mycotoxin-induced NKC activity. In the light of this review, it is concluded that chronic exposures to toxigenic mold could lead to abnormal NKC activity with a wide range of neurological consequences, some of which were headache, general debilitating pains, fever, cough, memory loss, depression, mood swings, sleep disturbances, anxiety, chronic fatigue, and seizures.
Arcari R, Crombie HD.	Department of Community Medicine and Healthcare, University of Connecticut School of Medicine, Farmington, USA.	Mark Twain and his family's health: Livy Clemens' neurasthenia in the gilded age and chronic fatigue syndrome of today.	Conn Med. 2003 May;67(5):293-6.	Our purpose is to compare and contrast the 19th century diagnosis and disease neurasthenia with the contemporary illness known as Chronic Fatigue Syndrome. The health of Mark Twain's wife, Olivia (Livy) Clemens, will then be discussed and evaluated with respect to these two medical conditions.
Asbring P, Narvanen AL.	Centre for Development of Health Services and the Department of	Ideal versus reality: physicians perspectives on patients with chronic	Soc Sci Med. 2003 Aug;57(4):711-20.	Encountering patients with chronic fatigue syndrome (CFS) or fibromyalgia can cause dilemmas for physicians due to the uncertainty inherent in these illnesses. The aim of this study was to investigate: (1) How physicians in a Swedish sample describe and categorise patients with CFS and fibromyalgia; (2) What the character of CFS and fibromyalgia, with regard to diagnosing,

	Public Health Sciences, Karolinska Institutet, Norrbacka, plan 2/7, 171 76, Stockholm, Sweden	fatigue syndrome (CFS) and fibromyalgia.		treatment and medical knowledge/aetiology, mean to the physicians in encounters with patients; and (3) Which strategies physicians describe that they use in the encounter with these patients. Semi-structured interviews were carried out with 26 physicians, specialists in various fields who all had some experience of either CFS or fibromyalgia. The results suggest that there is a discrepancy between the ideal role of the physician and reality in the everyday work in interaction with these patients. This may lead to the professional role being questioned. Different strategies are developed to handle the encounters with these patients. The results also illuminate the physician's interpretations of patients in moralising terms. Conditions given the status of illness were regarded, for example, as less serious by the physicians than those with disease status. Scepticism was expressed regarding especially CFS, but also fibromyalgia. Moreover, it is shown how the patients are characterised by the physicians as ambitious, active, illness focused, demanding and medicalising. The patient groups in question do not always gain full access to the sick-role, in part as a consequence of the conditions not being defined as diseases.
Assefi NP, Coy TV, Uslan D, Smith WR, Buchwald D.	Department of Medicine, University of Washington, Seattle, Washington, USA.	Financial, occupational, and personal consequences of disability in patients with chronic fatigue syndrome and fibromyalgia compared to other fatiguing conditions.	J Rheumatol. 2003 Apr;30(4):804-8.	OBJECTIVE: To examine the nature and degree of self-reported disability in patients with chronic fatigue syndrome (CFS) and its associated conditions, fibromyalgia (FM) and subsyndromal fatigue (CF), compared with a chronically fatiguing but unrelated medical condition (MED). METHODS: Six hundred and thirty patients evaluated at the University of Washington Chronic Fatigue Clinic were sent questionnaires asking them to identify the financial, occupational, and personal consequences of their fatiguing illness. Thorough medical evaluations had previously applied accepted criteria for defining CFS, FM, and CF. RESULTS: The FM groups (those with and without CFS) were among the least employed. Likewise, the FM and CFS groups, more frequently than the other groups, endorsed loss of material possessions (such as car), loss of job, and loss of support by friends and family, as well as recreational activities as a result of their fatiguing illness. There were no reliable differences between groups in use of disability benefits. CONCLUSION: There is substantial illness-related disability among those evaluated at a specialized chronic fatigue clinic. Those reporting the most pervasive disability met criteria for FM either alone or in conjunction with CFS. Employers and personal relations of patients with chronic fatigue should make a greater effort to accommodate the illness-related limitations of these conditions, especially for those with FM and CFS.
Authier FJ, Sauvat S, Champey J, Drogou I, Coquet M, Gherardi RK.	INSERM E 0011, Faculte de Medecine de Creteil-Paris XII, Creteil, France.	Chronic fatigue syndrome in patients with macrophagic myofasciitis.	Arthritis Rheum. 2003 Feb;48(2):569-70.	
Aylett E, Fawcett TN.	School of Nursing Studies, University of Edinburgh. lizzie@aylett.co.uk	Chronic fatigue syndrome: the nurse's role.	Nurs Stand. 2003 May 14-20;17(35):33-7.	BACKGROUND: Chronic fatigue syndrome (CFS), a disorder of no proven cause, is characterised by extended periods of extreme, debilitating fatigue and related symptoms. This article discusses this distressing disorder and identifies the needs of those who have it. The authors suggest that the nurse could fulfil the role of key professional carer, interacting with the individual with CFS to co-ordinate care and form the pivotal therapeutic relationship. CONCLUSION: CFS remains a chronic illness of uncertain cause and prognosis. For those with CFS, care priorities involve validation, information and advocacy, a therapeutic relationship and co-ordinated care. The

				particular philosophy of care held by nurses makes them potentially ideal co-ordinators of care for those with CFS.
Baschetti R.	Chronic fatigue syndrome and Addison's disease	.	J Pediatr. 2003 Feb;142(2):217; author reply 217-8. Comment on: J Pediatr. 2002 Apr;140(4):412-7	
Baschetti R.		Phantom lymphadenopathy. An association with chronic fatigue syndrome. Comment on: Postgrad Med J. 2003 Jan;79(927):59-60.	Postgrad Med J. 2003 Mar;79(929):185.	
Baschetti R.	Retired Medical Inspector of the Italian State Railways, Fortaleza, Brazil. baschetti@baydenet.com.br	Chronic fatigue syndrome: an endocrine disease off limits for endocrinologists?	Eur J Clin Invest. 2003 Dec;33(12):1029-31.	Endocrinologists were not included in the multidisciplinary working groups that prepared two recent reports on chronic fatigue syndrome, despite its unequalled clinical overlap with Addison's disease, which is a classic endocrine disorder. The failure to include at least one endocrinologist in those panels may explain why in their extensive reports there is not a single word about the 42 clinical features that chronic fatigue syndrome shares with Addison's disease, including all the signs and symptoms listed in the case definition of this syndrome.
Baschetti R.		Fludrocortisone and chronic fatigue syndrome.	N Z Med J. 2003 Aug 8;116(1179):U549.	
Baschetti R.		Assessing chronic fatigue.	QJM. 2003 Jun;96(6):454. Comment on: QJM. 2003 Feb;96(2):133-42.	
Bengtsson IL.	il.bengtsson@telia.com	[Thoughts on burnout: Time to establish "Physicians with borders"?][Article in Swedish	Lakartidningen. 2003 Mar 20;100(12):1060-1. Comment in: Lakartidningen. 2003 Apr 24;100(17):1555.	
Bleijenberg G, Prins J, Severens JL, van		[More care for a limited budget; a	Ned Tijdschr Geneeskd. 2003 Jan	

der Meer JW.		case for a better use of the efficiency criteria] [Article in Dutch]	18;147(3):134; author reply. Comment on: Ned Tijdschr Geneeskd. 2002 Nov 23;146(47):2254-8.	
Bleijenberg G.	Expert Centre for Chronic Fatigue, University Medical Centre Nijmegen, P,O, Box 9101, 6500 HB Nijmegen, The Netherlands. G.Bleijenberg@mailbox.kun.nl	Chronic fatigue and chronic fatigue syndrome in the general population.	Health Qual Life Outcomes. 2003 Oct 6;1(1):52. Epub 2003 Oct 06.	
Blockmans D, Persoons P, Van Houdenhove B, Lejeune M, Bobbaers H.	Department of General Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium. Daniel.Blackmans@uz.kuleuven.ac.be	Combination therapy with hydrocortisone and fludrocortisone does not improve symptoms in chronic fatigue syndrome: a randomized, placebo-controlled, double-blind, crossover study.	Am J Med. 2003 Jun 15;114(9):736-41.	PURPOSE: Chronic fatigue syndrome has been associated with decreased function of the hypothalamic-pituitary-adrenal axis. Although neurally mediated hypotension occurs more frequently in patients with chronic fatigue syndrome than in controls, attempts to alleviate symptoms by administration of hydrocortisone or fludrocortisone have not been successful. The purpose of this study was to investigate the effect of combination therapy (5 mg/d of hydrocortisone and 50 microg/d of 9-alfa-fludrocortisone) on fatigue and well-being in chronic fatigue syndrome. METHODS: We performed a 6-month, randomized, placebo-controlled, double-blind, crossover study in 100 patients who fulfilled the 1994 Centers for Disease Control and Prevention criteria for chronic fatigue syndrome. Between-group differences (placebo minus treatment) were calculated on a 10-point visual analog scale. RESULTS: Eighty patients completed the 3 months of placebo and 3 months of active treatment in a double-blind fashion. There were no differences between treatment and placebo in patient-reported fatigue (mean difference, 0.1; 95% confidence interval [CI]: -0.3 to 0.6) or well-being (mean difference, -0.4; 95% CI: -1.0 to 0.1). There were also no between-group differences in fatigue measured with the Abbreviated Fatigue Questionnaire, the Short Form-36 Mental or Physical Factor scores, or in the Hospital Anxiety and Depression Scale. CONCLUSION: Low-dose combination therapy of hydrocortisone and fludrocortisone was not effective in patients with chronic fatigue syndrome.
Bynum B.	w.bynum@ucl.ac.uk <w.bynum@ucl.ac.uk>	Neurasthenia.	Lancet. 2003 May 17;361(9370):1753.	
Carothers B, Schmidt L, Puri V.		Case reports and review of Postural Orthostatic Tachycardia syndrome (POTS).	J Ky Med Assoc. 2003 Dec;101(12):549-52.	Postural Orthostatic Tachycardia Syndrome (POTS) is a type of orthostatic intolerance that is characterized by excessive tachycardia and decreased cerebral blood flow in the upright position. This can result in significant symptoms of dizziness and light-headedness that can eventually lead to syncope. In this review, we describe two patients with POTS that varied in their degree of symptoms and treatment. One patient was able to be treated as an outpatient, while the other

				required hospitalization and extensive medical therapy. We would like to emphasize with this review that POTS is probably more common than it is diagnosed and is often confused with other conditions, such as chronic fatigue syndrome or functional syncope. It is important to make the correct diagnosis in order to allow appropriate treatment and to improve the quality of life for these patients.
Carruthers BM, Jain AK, De Meirleir KL, Peterson DL, Klimas NG, Lerner AM, Bested AC, Flor-Henry P, Joshi P, Powles ACP, Sherkey JA, van de Sande MI.		Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols	Journal of Chronic Fatigue Syndrome 2003; 11 (1): 7-116	Recent years have brought growing recognition of the need for clinical criteria for myalgic encephalomyelitis (ME), which is also called chronic fatigue syndrome (CFS). An Expert Subcommittee of Health Canada established the Terms of Reference, and selected an Expert Medical Consensus Panel representing treating physicians, teaching faculty and researchers. A Consensus Workshop was held on March 30 to April 1, 2001 to culminate the review process and establish consensus for a clinical working case definition, diagnostic protocols and treatment protocols. We present a systematic clinical working case definition that encourages a diagnosis based on characteristic patterns of symptom clusters, which reflect specific areas of pathogenesis. Diagnostic and treatment protocols, and a short overview of research are given to facilitate a comprehensive and integrated approach to this illness. Throughout this paper, “myalgic encephalomyelitis” and “chronic fatigue syndrome” are used interchangeably and this illness is referred to as “ME/CFS.”
Chalder T, Godfrey E, Ridsdale L, King M, Wessely S.	Department of Psychological Medicine, Guy's, King's and St Thomas's School of Medicine, London.	Predictors of outcome in a fatigued population in primary care following a randomized controlled trial.	Psychol Med. 2003 Feb;33(2):283-7 Comment in: Psychol Med. 2003 Feb;33(2):197-201..	BACKGROUND: The objective of this study was to examine factors that predicted outcome in a chronically fatigued group of patients who were randomized to cognitive behaviour therapy or counselling in primary care. METHOD: Illness perceptions, attributions, fatigue, disability and demographic variables were recorded at assessment and levels of fatigue and disability were measured at 6 months post randomization. Logistic regression was used to examine associations. RESULTS: Factors that predicted a poor outcome (four or more on the fatigue questionnaire) were: poor social adjustment at assessment; the patients self-report that they had never seen the GP for an emotional reason; a physical illness attribution; and, a long perceived future illness duration. CONCLUSIONS: Patients who are more psychologically minded are more likely to improve with psychological treatments in primary care. General practitioners need to assess this before referring to an appropriate therapist.
Chalder T, Goodman R, Wessely S, Hotopf M, Meltzer H.	Department of Psychological Medicine, Guy's, King's, and St Thomas's School of Medicine, London SE5 8AZ. sphatrc@iop.kcl.ac.uk	Epidemiology of chronic fatigue syndrome and self reported myalgic encephalomyelitis in 5-15 year olds: cross sectional study.	BMJ. 2003 Sep 20;327(7416):654-5.	
Chapman S		Copying letters to patients. Copying letters can help	BMJ. 2003 Feb 22;326(7386):449.	

		avoid communications nightmare. Comment on: BMJ. 2002 Dec 7;325(7376):1359.		
Chaudhuri A, Condon BR, Gow JW, Brennan D, Hadley DM.	Department of Neurology, University of Glasgow, South Glasgow University Hospitals NHS Trust, UK. ac54p@udcf.gla.ac.uk	Proton magnetic resonance spectroscopy of basal ganglia in chronic fatigue syndrome.	Neuroreport. 2003 Feb 10;14(2):225-8.	Fatigue is a common symptom of neurological diseases that affect basal ganglia function. We used proton magnetic resonance spectroscopy ((1)H MRS) to study the metabolic functions of the basal ganglia in chronic fatigue syndrome (CFS) to test the hypothesis that fatigue in CFS may have a neurogenic component. (1)H MRS of left basal ganglia was carried out in eight non-psychiatric patients with CFS and their results were compared to age- and sex-matched healthy asymptomatic healthy controls. A highly significant increase in the spectra from choline-containing compounds was seen in the CFS patient group ($p < 0.001$). In the absence of regional structural or inflammatory pathology, increased choline resonance in CFS may be an indicator of higher cell membrane turnover due to gliosis or altered intramembrane signalling.
Chester AC.	Department of Medicine, Georgetown University Medical Center, Washington, DC 20016, USA. achester@foxhallinternists.com	Symptoms of rhinosinusitis in patients with unexplained chronic fatigue or bodily pain: a pilot study.	Arch Intern Med. 2003 Aug 11-25;163(15):1832-6.	BACKGROUND: Recent otolaryngologic studies document significant fatigue and bodily pain (BP) in patients with chronic rhinosinusitis. Studies of general medical patients are lacking. METHODS: A case-control study of 297 consecutive general medical outpatients. RESULTS: Sixty-five patients noted unexplained chronic fatigue (UCF), 33 reported BP, and 26 had both. Compared with 232 patients without UCF, patients with UCF more frequently had the following rhinosinusitis symptoms: facial pressure (odds ratio [OR], 9.7; 95% confidence interval [CI], 5.2-18.2), heavy-headedness (OR, 21.9; 95% CI, 10.9-44.0), nasal obstruction (OR, 4.3; 95% CI, 2.3-7.9), frontal headache (OR, 13.6; 95% CI, 6.5-28.5), postnasal drip (OR, 2.8; 95% CI, 1.6-5.0), sore throat (OR, 3.1; 95% CI, 1.5-6.6), and tender cervical lymph nodes (OR, 9.2; 95% CI, 4.3-19.7). A similar predominance of rhinosinusitis symptoms was noted in patients with BP and in 15 patients with UCF who had chronic fatigue syndrome. No increased prevalence of pollen allergy was noted in association with UCF, BP, or chronic fatigue syndrome. Gastrointestinal, sleep, and psychiatric problems were similar between patients with UCF and 38 patients with explained fatigue. Rhinosinusitis symptoms, however, were more common in UCF. CONCLUSIONS: There is an increased prevalence of rhinosinusitis symptoms but not pollen allergy among general medical outpatients with UCF, BP, or both. Rhinosinusitis symptoms are at least as common as gastrointestinal complaints, sleep disturbance, and psychiatric problems (previously well documented complaints associated with UCF and BP). Rhinosinusitis symptoms, furthermore, are more common in UCF than in fatigue explained by a physical or mental illness.
Chia JK, Chia A.		Diverse etiologies for chronic fatigue syndrome.	Clin Infect Dis. 2003 Mar 1;36(5):671-2; author reply 672-3. Comment on: Clin Infect Dis. 2002 Sep 1;35(5):518-25.	

Chiaravalloti ND, Christodoulou C, Demaree HA, DeLuca J.	Kessler Medical Rehabilitation Research and Education Corporation, West Orange, NJ 07052, USA.	Differentiating simple versus complex processing speed: influence on new learning and memory performance.	J Clin Exp Neuropsychol. 2003 Jun;25(4):489-501.	The current study was designed to examine how the construct of human information processing speed is conceptualized and measured, while also examining the influence of information processing speed on higher cognitive processes (i.e., learning). A mixed medical sample of 92 subjects participated in this study. Subjects underwent a broad-based neuropsychological evaluation, including measures of verbal and visuospatial new learning, spatial and verbal working memory, simple reaction time, choice reaction time, and information processing speed. Principal components factor analysis with varimax rotation resulted in a three-factor solution, comprised of: (1) simple speed/reaction time, (2) complex information processing and new learning, and (3) working memory. Notably, this factor solution identified 2 distinct forms of processing speed--simple and complex information processing speeds. In contrast to the abundance of literature grouping these two constructs together under one term (i.e., processing speed), these results indicate simple and complex speed to be distinct constructs assessed with different neuropsychological instruments. While the expected relationship between complex information processing capacities and working memory abilities was evident in this study, information processing speed also showed a significant relationship with new learning ability. The implications of this intriguing relationship are discussed.
Ciccone DS, Busichio K, Vickroy M, Natelson BH.	Department of Psychiatry, UMDNJ-New Jersey Medical School, 07107, Newark, NJ, USA	Psychiatric morbidity in the chronic fatigue syndrome. Are patients with personality disorder more physically impaired?	J Psychosom Res. 2003 May;54(5):445-52.	OBJECTIVE: The long-term consequences of chronic fatigue syndrome (CFS) include substantial impairment in physical functioning and high levels of work disability. In the absence of a medical explanation for this impairment, some have speculated that it may be due to comorbid psychiatric illness or personality disorder. We addressed this possibility by comparing the functional status of three CFS groups: no psychiatric diagnosis, psychiatric illness only, psychiatric illness and personality disorder. A second aim of the study was to determine whether a continuous measure of psychological distress could provide a better account of impairment than psychiatric diagnosis. METHOD: The study sample consisted of 84 consecutive female referrals with CFS. All participants satisfied the case definition and completed an assessment protocol consisting of: physical examination, psychiatric interview and self-report questionnaires. RESULTS: Psychiatric illness, either alone or in combination with a comorbid personality disorder, was not associated with physical impairment or disability in female participants. A regression model of physical functioning found that psychological distress accounted for 6% and symptom severity for 41% of the variance (P=.06 and <.01, respectively). In the case of disability, the corresponding percentages were 2% and 18% (NS and P<.01, respectively). The modest effects of psychological distress could not be attributed to symptom severity. CONCLUSIONS: Although psychiatric illness and personality disorder was prevalent, neither could explain the effects of CFS on physical functioning and disability. As yet, there is no psychological or medical explanation for the behavioral consequences of CFS.
Ciccone DS, Natelson BH.	Departments of Psychiatry (D.S.C) and Neuroscience (B.H.N.), University of Medicine and	Comorbid illness in women with chronic fatigue syndrome: a test of the single syndrome	Psychosom Med. 2003 Mar-Apr;65(2):268-75.	OBJECTIVE: Evidence of comorbidity among unexplained illness syndromes raises the possibility that all are variants of a single functional disorder, leading some to suggest that separate case definitions for chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivity (MCS) may be unnecessary. Our objective was to determine whether discrete diagnostic labels provide useful information about physical functioning, symptom severity, and

	Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey.	hypothesis.		risk of psychiatric illness. METHODS: The sample consisted of 163 consecutive female referrals with CFS enrolled at a tertiary clinic. Each participant was retrospectively assigned to one of four groups: CFS only, CFS/FM, CFS/MCS, and CFS/FM/MCS. At enrollment, participants gave their history, underwent a physical examination and a standardized psychiatric interview (Diagnostic Interview Schedule), and answered self-report questionnaires. RESULTS: Additional unexplained syndromes were prevalent: 37% met criteria for FM, and 33% met criteria for MCS. With the exception of FM-related pain and disability, there were few differences between the CFS only and CFS with comorbid illness groups. Patients with additional illness were more likely to have major depression and a higher risk of psychiatric morbidity compared with patients in the CFS only group ($p < .01$). Rates of lifetime depression increased from 27.4% in the CFS only group to 52.3% in the CFS/FM group, 45.2% in the CFS/MCS group, and 69.2% in the CFS/FM/MCS group. CONCLUSIONS: The prevalence of comorbid illness in the present CFS sample and the failure to find widespread differences in symptom severity can be seen as support for the single syndrome hypothesis. On the other hand, the existence of discrete syndromes could not be ruled out because of reliable differences between CFS and CFS/FM. Increasing comorbidity was associated with a corresponding increase in risk of major depression.
Clarke JN, James S.	Department of Sociology and Anthropology, Wilfrid Laurier University, Waterloo, N2L 3C5 ON, Canada. jclarke@wlu.ca	The radicalized self: the impact on the self of the contested nature of the diagnosis of chronic fatigue syndrome.	Soc Sci Med. 2003 Oct;57(8):1387-95.	Chronic fatigue syndrome (CFS) is a relatively new disease that is difficult to diagnose. It is also a contested disease immersed in dispute about whether it is a physical or psychiatric reality. Sufferers often claim to experience not only the physical challenges of the disease, and these can be extensive, but also, initially, the anomie of suffering from a condition whose very reality is debated both in the medical and in the wider communities. Theories of self in illness emphasize how people who are diagnosed as chronically ill work hard as they seek to maintain previous, or to develop supernormal, selves. Such goals are cast in a critical light by Foucault's notion of the technologies of self in the context of circulating neo-liberal discourses. As people with CFS, lacking an uncontested medical diagnosis, search for meaningful self-identities, they resist previously available discourses to take up an alternative discourse, one that we call radicalized selves. This paper raises questions about the constraints and liberties, power and powerlessness associated with a clear and undisputed medical diagnosis. It suggests a model of the self in chronic illness that considers not only changes in body and biography but also the availability of an uncontested diagnosis.
Cleare AJ.	Section of Neurobiology of Mood Disorders, Division of Psychological Medicine, The Institute of Psychiatry, London SE5 8AZ, United Kingdom.	The neuroendocrinology of chronic fatigue syndrome.	Endocr Rev. 2003 Apr;24(2):236-52.	Chronic fatigue syndrome (CFS) is a common and disabling problem; although most likely of biopsychosocial origin, the nature of the pathophysiological components remains unclear. There has been a wealth of interest in the endocrinology of this condition, which will be reviewed in this article. Most studied has been the hypothalamic-pituitary-adrenal (HPA) axis; although the quality of many studies is poor, the overall balance of evidence points to reduced cortisol output in at least some patients, with some evidence that this is linked to symptom production or persistence. There is evidence for heightened negative feedback and glucocorticoid receptor function and for impaired ACTH and cortisol responses to a variety of challenges. However, there is no evidence for a specific or uniform dysfunction of the HPA axis. Given the many factors that may impinge on the HPA axis in CFS, such as inactivity, sleep disturbance, psychiatric comorbidity,

				medication, and ongoing stress, it seems likely that HPA axis disturbance is heterogeneous and of multifactorial etiology in CFS. Studies assessing GH, dehydroepiandrostenedione and its sulfate, melatonin, leptin, and neuroendocrine-monoamine interactions are also reviewed. There is some evidence from these studies to suggest alterations of dehydroepiandrostenedione sulfate function and abnormal serotonin function in CFS, but whether these changes are of functional importance remains unclear. To obtain a clearer assessment of the etiological and pathophysiological relevance of endocrine changes in CFS, it is suggested that more prospective cohort studies be undertaken in groups at high risk for CFS, that patients with CFS are followed up into recovery, and that multidimensional assessments are undertaken to unravel the influence of the various confounding factors on the observed endocrine changes in CFS.
Colby J.		ME and children.	Prof Nurse. 2003 Jun;18(10):544.	
Cook DB, Nagelkirk PR, Peckerman A, Poluri A, Lamanca JJ, Natelson BH.	1Center for the Study of War-Related Illnesses, VA NJ Health Care, East Orange, NJ; 2Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey - New Jersey Medical School, Newark, NJ; and.	Perceived Exertion in Fatiguing Illness: Gulf War Veterans with Chronic Fatigue Syndrome.	Med Sci Sports Exerc. 2003 Apr;35(4):569-574.	COOK, D. B., P. R. NAGELKIRK, A. PECKERMAN, A. POLURI, J. J. LAMANCA, and B. H. NATELSON. Perceived Exertion in Fatiguing Illness: Gulf War Veterans with Chronic Fatigue Syndrome. Med. Sci. Sports Exerc., Vol. 35, No. 4, pp. 569-574, 2003.PURPOSEIt has been reported that ratings of perceived exertion (RPE) are elevated in chronic fatigue syndrome (CFS). We have challenged this notion by examining perceived exertion in civilian females with CFS and expressing the data relative to exercise capacity (%[OV0312]O(2max)). The purpose of the present investigation was to further examine RPE during exercise in a unique population of CFS patients, Gulf veterans (GV).METHODSThirty-four GV (N = 15 CFS, 42 +/- 8 yr; N = 19 healthy, 43 +/- 5 yr) performed a maximal exercise test on a cycle ergometer. After a 3-min warm-up, exercise intensity increased by 30 W every minute until exhaustion. RPE were obtained during the last 15 s of each minute using Borg's CR-10 scale.RESULTSWith the exception of peak [OV0312]E, there were no significant differences in any peak exercise variables. Repeated measures ANOVA revealed significantly higher RPE at each power output examined ($F(1,32) = 16.4$, $P < 0.001$). Group differences in RPE remained significant when analyzed relative to peak [OV0312]O(2) ($F(1,32) = 7.2$, $P = 0.01$). Both group main effects and the interaction were eliminated when self-reported fatigue symptoms were controlled for in the analyses. Power functions for RPE as a function of relative oxygen consumption were not different between groups and were significantly greater than a linear value of 1.0 (1.6 +/- 0.3 for both groups, $P < 0.02$).CONCLUSIONSOur results show that RPE are greater in GV with CFS regardless of whether the data were expressed in terms of absolute or relative exercise intensity. However, self-reported fatigue associated with CFS eliminated the group differences. These results suggest that GV with CFS were unique compared with their civilian counterparts. Future research aimed at determining the influence of preexisting fatigue on RPE during exercise is warranted.
Cook DB, Nagelkirk PR, Peckerman A, Poluri A, Lamanca JJ, Natelson BH.	1Center for the Study of War-Related Illnesses, VA NJ Health Care, East Orange, NJ; 2Chronic	Perceived Exertion in Fatiguing Illness: Civilians with Chronic Fatigue Syndrome.	Med Sci Sports Exerc. 2003 Apr;35(4):563-568.	COOK, D. B., P. R. NAGELKIRK, A. PECKERMAN, A. POLURI, J. J. LAMANCA, and B. H. NATELSON. Perceived Exertion in Fatiguing Illness: Civilians with Chronic Fatigue Syndrome. Med. Sci. Sports Exerc., Vol. 35, No. 4, pp. 563-568, 2003.PURPOSEIt has been reported that ratings of perceived exertion (RPE) are elevated in chronic fatigue syndrome (CFS). However, methodological limitations have rendered this conclusion suspect. The purpose of the present investigation was

	Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey - New Jersey Medical School, Newark, NJ; and.			to examine RPE during exercise in civilians with CFS by comparing subjects at both absolute exercise stage and relative oxygen consumption reference criteria.METHODSA sample of 39 civilian females (N = 19 CFS, 34 +/- 7 yr; N = 20 healthy controls, 33 +/- 7 yr) underwent a maximal exercise test on a treadmill. RPE were obtained during the last 15 s of each 3-min stage using Borg's 6-20 scale.RESULTSThere were no significant differences in peak [OV0312]O(2), RER, or RPE. However, controls exercised longer (20.0 +/- 1.1 vs 15.9 +/- 1.1 min, P = 0.01, healthy vs CFS) and had higher peak HR (183 +/- 3 vs 174 +/- 2 bpm, P = 0.03, healthy vs CFS). Civilians with CFS reported higher RPE at stages 3 through 5 compared with controls (F(3,111)= 3.6,P = 0.017). Preexercise fatigue ratings were not a significant predictor of perceived exertion during exercise. There were no group differences (F(1,37)= 1.9,P = 0.17) when RPE were expressed relative to peak [OV0312]O(2).CONCLUSIONSOur results show that RPE are greater in civilians with CFS when the data are expressed in terms of absolute exercise intensity. However, by examining RPE relative to a common maximum (i.e., peak [OV0312]O(2)) no differences were observed. The findings of the present investigation challenge the notion that RPE are dysregulated in CFS.
Covelli V, Pellegrino NM, Jirillo E.	Division of Neurology, Azienda Policlinico, Bari, Italy. nm.pellegrino@midim.uniba.it	A point of view: The need to identify an antigen in psyconeuroimmunological disorders.	Curr Pharm Des. 2003;9(24):1951-5.	Several lines of evidence support a mutual relationship between the nervous system and the immune system. Therefore, it is not surprising that some neuropsychiatric disorders are also characterized by immune abnormalities. In patients with phobic disorders and in patients with migraine without aura some common immune abnormalities have been detected and, in particular, natural immunity deficits, exaggerated release of proinflammatory cytokines and circulating bacterial endotoxins have been found. In other neurological disease, some etiologic factors have been detected as in the case of Guillain-Barre syndrome in which molecular mimicry between Campylobacter jejuni endotoxin and GM1 ganglioside may cause an acute inflammatory polyneuropathy. On the other hand, attempts to identify an antigen have been made in patients with Alzheimer's disease and schizophrenia. Finally, the chronic fatigue syndrome, an old illness in search for an antigen, risk factors and precipitating agents have been described but evidence for a specific antigen is still lacking.
Creswell C, Chalder T.	Sub-Department of Clinical Health Psychology, University College London, UK. c.creswell@ucl.ac.uk	The relationship between illness attributions and attributional style in Chronic Fatigue Syndrome.	Br J Clin Psychol. 2003 Mar;42(Pt 1):101-4.	OBJECTIVE: To examine the relationship between illness attributions and general attributional style in Chronic Fatigue Syndrome (CFS). METHOD: Participants with CFS answered questions on their explanation for their illness and completed the Attributional Style Questionnaire (parallel form). RESULTS: Of the participants, 58.3% attributed their illness to predominantly physical factors. A significant relationship was found between the presence of a self-serving attributional style and illness attributions. CONCLUSION: Illness attributions were associated with an individual's general attributional style. It is suggested that illness attributions may be less important with regards prognosis than, for example, other variables which influence a person's general view of the world.
Dalakas MC.		Enteroviruses in chronic fatigue syndrome: "now you see them, now you don't".	J Neurol Neurosurg Psychiatry. 2003 Oct;74(10):1361-2. Comment on: J Neurol Neurosurg	

			Psychiatry. 2003 Oct;74(10):1382-6.	
Darbishire L, Ridsdale L, Seed PT.	Department of General Practice, Guy's, King's College and St Thomas's School of Medicine, London. lucy.darbishire.ac.uk	Distinguishing patients with chronic fatigue from those with chronic fatigue syndrome: a diagnostic study in UK primary care.	Br J Gen Pract. 2003 Jun;53(491):441-5.	BACKGROUND: Chronic fatigue syndrome (CFS) has been defined, but many more patients consult in primary care with chronic fatigue that does not meet the criteria for CFS. General practitioners (GPs) do not generally use the CFS diagnosis, and have some doubt about the validity of CFS as an illness. AIM: To describe the proportion of patients consulting their GP for fatigue that met the criteria for CFS, and to describe the social, psychological, and physical differences between patients with CFS and those with non-CFS chronic fatigue in primary care. DESIGN OF STUDY: Baseline data from a trial of complex interventions for fatigue in primary care. SETTING: Twenty-two general practices located in London and the South Thames region of the United Kingdom recruited patients to the study between 1999 and 2001. METHOD: One hundred and forty-one patients who presented to their GP with unexplained fatigue lasting six months or more as a main symptom were recruited, and the Centers for Disease Control (CDC) case definition was applied to classify CFS. RESULTS: Approximately two-thirds (69%) of patients had chronic fatigue and not CFS. The duration of fatigue (32 months) and perceived control over fatigue were similar between groups; however, fatigue, functioning, associated symptoms, and psychological distress were more severe in the patients in the CFS group, who also consulted their GP significantly more frequently, were twice as likely to be depressed, and more than twice as likely to be unemployed. About half (CFS = 50%; chronic fatigue = 55%) in each group attributed their fatigue to mainly psychological causes. CONCLUSIONS: In primary care, CFS is a more severe illness than chronic fatigue, but non-CFS chronic fatigue is associated with significant fatigue and is reported at least twice as often. That half of patients, irrespective of CFS status, attribute their fatigue to psychological causes, more than is observed in secondary care, indicates an openness to the psychological therapies provided in that setting. More evidence on the natural history of chronic fatigue and CFS in primary care is required, as are trials of complex interventions. The results may help determine the usefulness of differentiating between chronic fatigue and CFS.
Davey NJ, Puri BK, Catley M, Main J, Nowicky AV, Zaman R.	Department of Sensorimotor Systems, Division of Neuroscience and Psychological Medicine, Imperial College Faculty of Medicine, Charing Cross Hospital, London W6 8RF, UK.	Deficit in motor performance correlates with changed corticospinal excitability in patients with chronic fatigue syndrome.	Int J Clin Pract. 2003 May;57(4):262-4.	Chronic fatigue syndrome (CFS) is characterised by fatigue and musculosketetal pain, the severity of which is variable. Simple reaction times (SRTs) and movement times (SMTs) are slowed in CFS. Our objective is to correlate the day-to-day changes in symptomatology with any change in SRT, SMT or corticospinal excitability. Ten CFS patients were tested on two occasions up to two years apart. Motor evoked potentials (MEPs) to transcranial magnetic stimulation (TMS) of the motor cortex were recorded from the thenar muscles. Threshold TMS strength to evoke MEPs was measured to index corticospinal excitability. SRTs and SMTs were measured. The percentage change in both SRTs and SMTs between the two test sessions correlated with the percentage change in corticospinal excitability assessed according to threshold TMS intensity required to produce MEPs. This study provides evidence that changing motor deficits in CFS have a neurophysiological basis. The slowness of SRTs supports the notion of a deficit in motor preparatory areas of the brain.

De Meirleir K, McGregor N.		Chronic Fatigue Syndrome Guidelines	Journal of Chronic Fatigue Syndrome 2003; 11 (1): 1	
Diaz-Mitoma F, Turgonyi E, Kumar A, Lim W, Larocque L, Hyde BM		Clinical Improvement in Chronic Fatigue Syndrome Is Associated with Enhanced Natural Killer Cell-Mediated Cytotoxicity: The Results of a Pilot Study with Isoprinosine	Journal of Chronic Fatigue Syndrome 2003; 11 (2): 71	Chronic fatigue syndrome is associated with systemic and cognitive symptoms and with several immune abnormalities. The clinical impact of Isoprinosine® was evaluated in sixteen CFS patients, followed for 28 weeks in a single-blind, placebo controlled trial. Patients were also monitored for various immune parameters. Improvement based on clinical staging was observed in six of ten treated patients (6)0%). Clinically improved patients showed significantly enhanced natural killer (NK) cell activity, which correlated with the duration of Isoprinosine treatment ($p < 0.03$). Treatment with Isoprinosine resulted in significantly increased numbers of CD4+ T helper cells ($p < 0.03$). Treatment with Isoprinosine for 12 weeks did not appreciably influence the in vitro production of IFN-?, IL-1?, IL-10 or IL-12. However, IL-12 was significantly increased at week 28 ($p < 0.02$) in patients who improved after treatment with Isoprinosine. These results suggest that taking Isoprinosine may benefit a subgroup of patients with CFS, and this clinical improvement is associated with enhanced NK cell function and IL-12 levels. Further trials to evaluate the use of Isoprinosine in the treatment of CFS patients are warranted.
Douche-Aourik F, Berlier W, Feasson L, Bourlet T, Harrath R, Omar S, Grattard F, Denis C, Pozzetto B.	Laboratory of Bacteriology-Virology (GIMAP), Faculte de Medecine Jacques Lisfranc, Saint-Etienne, France.	Detection of enterovirus in human skeletal muscle from patients with chronic inflammatory muscle disease or fibromyalgia and healthy subjects.	J Med Virol. 2003 Dec;71(4):540-7.	Enterovirus RNA has been found previously in specimens of muscle biopsy from patients with idiopathic dilated cardiomyopathy, chronic inflammatory muscle diseases, and fibromyalgia or chronic fatigue syndrome (fibromyalgia/chronic fatigue syndrome). These results suggest that skeletal muscle may host enteroviral persistent infection. To test this hypothesis, we investigated by reverse transcription-polymerase chain reaction (RT-PCR) assay the presence of enterovirus in skeletal muscle of patients with chronic inflammatory muscle diseases or fibromyalgia/chronic fatigue syndrome, and also of healthy subjects. Three of 15 (20%) patients with chronic inflammatory muscle diseases, 4 of 30 (13%) patients with fibromyalgia/chronic fatigue syndrome, and none of 29 healthy subjects was found positive. The presence of VP-1 enteroviral capsid protein was assessed by an immunostaining technique using the 5-D8/1 monoclonal antibody; no biopsy muscle from any patient or healthy subject was found positive. The presence of viral RNA in some muscle biopsies from patients exhibiting muscle disease, together with the absence of VP-1 protein, is in favor of a persistent infection involving defective viral replication. Copyright 2003 Wiley-Liss, Inc.
Duclos P.	Department of Vaccines and Biologicals, Health Technology and Pharmaceuticals, World Health Organization, Geneva, 20 Avenue Appia, CH-1211 Geneva 27,	Safety of immunisation and adverse events following vaccination against hepatitis B.	Expert Opin Drug Saf. 2003 May;2(3):225-31.	Hepatitis B vaccines (HBVs) are composed of highly purified preparations of hepatitis B virus surface antigen (HBsAg). An adjuvant, either aluminium phosphate or aluminium hydroxide, is added to the vaccines, which are sometimes preserved with thiomersal. In placebo-controlled studies, common side effects other than local reactions were reported no more frequently among vaccine recipients than among individuals receiving a placebo. A number of controversial adverse events have, however, been purported to be associated with HBVs, including rheumatoid arthritis (RA), diabetes, demyelinating diseases (e.g., multiple sclerosis [MS]), chronic fatigue syndrome, and more recently, lymphoblastic leukaemia. In addition, the safety of the thiomersal and aluminium contained in the vaccine has also been under close scrutiny. These issues have been reviewed by a number of country-specific or international independent review committees

	Switzerland. duclosp@who.int			such as that of the US Institute of Medicine (IOM) and the World Health Organization's (WHO) Global Advisory Committee on Vaccine Safety (GACVS). Upon review of the scientific evidence, none of the serious allegations have so far been confirmed. On the contrary, scientific evidence has accumulated to disprove many of the allegations. In particular, the IOM committee has concluded that the evidence favoured rejection of a causal relationship between HBV administered to adults and incident MS or MS relapse. Whilst it is important to continue monitoring some of the safety issues, there is no evidence to suggest that the WHO should consider altering its recommendation that all countries should have universal infant and/or adolescent immunisation programmes. The risks of hepatitis B vaccination are only theoretical in comparison with clear benefits in terms of cirrhosis and cancer prevention, and the HBV remains one with an excellent safety profile.
Eidelman D.	Ramat Hasharon, Israel	Chronic fatigue syndrome - medical fact or artifact.	Med Hypotheses. 2003 Jun;60(6):840-2.	Despite extensive investigation, the enigma of Chronic Fatigue Syndrome (CFS) continues to confound medical researchers. It is suggested that this may be due to two impediments inherent in their overall approach to the problem. Firstly, although fatigue is central to CFS, medical scientists appear not to understand what fatigue itself really is, nor what is its purpose or mode of function. A functional definition of fatigue is suggested to help resolve this. Secondly, physicians and other researchers - psychologists and alternative medicine practitioners - fail to observe an elementary and fundamental procedure of clinical medicine, namely, that of properly examining their patients before making a diagnosis or providing treatment. The notion of the 'black hole' of medicine is introduced. Recognizing the existence of these impediments is considered a self-evident precondition for further significant progress being made in this field.
Endresen GK.	Department of Rheumatology, The National Hospital, University of Oslo, Forskningsvn. 2-Block B, 0027, Oslo, Norway. gerhard.endresen@rikshospitalet.no	Mycoplasma blood infection in chronic fatigue and fibromyalgia syndromes.	Rheumatol Int. 2003 Sep;23(5):211-5. Epub 2003 Jul 16.	Chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) are characterised by a lack of consistent laboratory and clinical abnormalities. Although they are distinguishable as separate syndromes based on established criteria, a great number of patients are diagnosed with both. In studies using polymerase chain reaction methods, mycoplasma blood infection has been detected in about 50% of patients with CFS and/or FMS, including patients with Gulf War illnesses and symptoms that overlap with one or both syndromes. Such infection is detected in only about 10% of healthy individuals, significantly less than in patients. Most patients with CFS/FMS who have mycoplasma infection appear to recover and reach their pre-illness state after long-term antibiotic therapy with doxycycline, and the infection can not be detected after recovery. By means of causation and therapy, mycoplasma blood infection may permit a further subclassification of CFS and FMS. It is not clear whether mycoplasmas are associated with CFS/FMS as causal agents, cofactors, or opportunistic infections in patients with immune disturbances. Whether mycoplasma infection can be detected in about 50% of all patient populations with CFS and/or FMS is yet to be determined.
Englebienne P.		RNase L in Health and Disease–What Did We Learn Recently?	Journal of Chronic Fatigue Syndrome 2003; 11 (2): 97	The 29,59-oligoadenylate-dependent ribonuclease L (RNase L) is central to the innate cellular defense mechanism induced by type I interferons during intracellular infection. The protein, activated by 29,59-oligoadenylates, precludes the replication of the infectious agent by cleaving single-stranded RNA and, along with the double-stranded RNA-dependent protein kinase, its spreading by inducing the cell to undergo suicide (apoptosis). In absence of infection, the protein

				remains dormant. Recent evidence indicates however that the protein is activated in absence of infection and may play a role in cell differentiation, immune activation, and to act as a tumor-suppressor. A deregulation in this pathway has been documented in immune cells of chronic fatigue syndrome patients which involves the presence of a catalytically active truncated RNase L. This protein escapes the normal regulation which implies the development of a cascade of unwanted cellular events. The present article reviews our current understanding of this deregulation, enlightens its relevance in the pathological process and proposes new targets for therapeutic development.
Englebienne P, Verhas M, Herst CV, De Meirleir K.	University of Brussels (ULB/VUB), and RED Laboratories, N.V., Brussels, Belgium	Type I interferons induce proteins susceptible to act as thyroid receptor (TR) corepressors and to signal the TR for destruction by the proteasome: possible etiology for unexplained chronic fatigue.	Med Hypotheses. 2003 Feb;60(2):175-80.	In some patients complaining of chronic fatigue such as those suffering from the chronic fatigue syndrome (CFS), no underlying physical cause can be clearly identified and they typically present a normal thyroid function. Several studies indicate a dysregulation in the type I interferons (IFN-alpha/beta) pathway in CFS resulting in a sustained upregulation of 2('),5(')-oligoadenylate synthetases (2-5OAS). Likewise, patients treated with IFN-alpha/beta usually complain of severe fatigue as a limiting side effect. Beside the 2-5OAS, IFN-alpha/beta induce also the expression of three closely related proteins of unknown function termed the 2-5OAS-like (2-5OASL) proteins. The amino acid sequences of the 2-5OASL proteins display 96% identity with the partial sequence of the thyroid receptor interacting protein (TRIP) 14, further contain two typical thyroid hormone receptor (TR) coregulator domains and feature two ubiquitin C-terminal domains. From these observations, we raise the hypothesis that the 2-5OASL proteins are TRIPs capable of, respectively, repressing TR transactivation and/or signaling the receptor for destruction by the proteasome. Such molecular mechanisms could explain the development of a clinical hypothyroid state in presence of a normal thyroid function.
Evengard B, Jonzon E, Sandberg A, Theorell T, Lindh G.	Departments of Laboratory Medicine and Medicine, Karolinska Institute at Huddinge University Hospital and National Institute for Psychosocial Factors and Health, Stockholm, Sweden.	Differences between patients with chronic fatigue syndrome and with chronic fatigue at an infectious disease clinic in Stockholm, Sweden.	Psychiatry Clin Neurosci. 2003 Aug;57(4):361-8.	Background data were collected from patients presenting with fatigue at the clinic of infectious diseases at Huddinge University Hospital, Stockholm. The main purpose was to look for differences as to demographic and functional status for patients fulfilling criteria for chronic fatigue syndrome (CFS) and chronic fatigue (CF). A cross-sectional questionnaire survey was performed using a variety of instruments. A thorough medical investigation was performed. No difference was found as to social situation, occupation and illness attributions for patients in the two categories. Patients with CFS reported in general a higher degree of 'sickness' with more self-reported somatic symptoms, more self-reported functional impairment and more absence from work. A higher degree of psychiatric comorbidity was observed in CF than in CFS patients. A majority of CFS patients (80%) had an acute infectious onset compared to 43% in the CF group. Presently used criteria might, according to findings presented here, define two different patient categories in a population characterized by severe, prolonged fatigue. Because CFS patients (compared to patients with CF) have more somatic symptoms, more often report an infectious, sudden onset and have less psychiatric comorbidity, and CF patients seem to have more of an emotional, burn-out-like component one could speculate about the existence of different pathogenetic backgrounds behind the two diagnoses.
Fasih T, Pickin M, Cuschieri RJ.	Department of Vascular Surgery and	Non-vascular claudication: a	Int J Clin Pract. 2003 Mar;57(2):87-9.	This is a prospective study of patients referred to our department with symptoms of claudication unlikely to be of vascular origin. After clinical assessment these patients were referred to an

	Orthopaedic Medicine, Doncaster Royal Infirmary, Doncaster, Yorkshire.	clinical conundrum.		orthopaedic physician. Of 1070 patients referred, 33 patients were diagnosed with a non-vascular problem. Of these, 21 were cases of spinal stenosis with or without nerve root irritation, seven had a combination of spinal pathology and peripheral vascular disease, and five were diagnosed with intervertebral disc prolapse (n=3), diabetic neuropathy (n=1) and chronic fatigue syndrome (n=1). The prognosis for patients with non-vascular claudication in respect of the development of premature vascular events is likely to be different from vascular claudicants and they should be counselled appropriately. Furthermore, the potentially less favourable outcome following reconstruction must be clearly explained to patients with a non-vascular contribution to their symptoms before any therapeutic vascular intervention. Failure to do this is likely to have significant medicolegal implications.
Fisher L, Chalder T.	Guy's, King's and St. Thomas' School of Medicine, Chronic Fatigue Syndrome Research Unit, King's Denmark Hill Campus, New Medical School Building, SE5 9PJ, London, UK	Childhood experiences of illness and parenting in adults with Chronic Fatigue Syndrome.	J Psychosom Res. 2003 May;54(5):439-43.	OBJECTIVE: There are many similarities between chronic fatigue syndrome (CFS), the somatoform disorders and problems otherwise known as "medically unexplained symptoms." There is some evidence to suggest that a combination of inadequate parenting and early illness experience may predispose the individual to develop medically unexplained symptoms in adult life. The aim of this investigation was to compare the contributions of childhood experiences of illness and parenting in adults with CFS with a fracture clinic control group. METHOD: A retrospective case control design was used. Thirty patients with a diagnosis of CFS and 30 patients attending a fracture clinic in an inner London teaching hospital completed questionnaires measuring parental care and protection and were interviewed about childhood experiences of illness. RESULTS: There were no differences in childhood experience of illness in the two groups. However, logistic regression revealed that maternal overprotection and depression were associated with the diagnosis of CFS. CONCLUSION: The findings may represent risk factors for the development of CFS in adult life. It is possible that maternal overprotection in particular is related to the formation of belief systems about avoiding activity that operate to adversely influence behaviour in patients with CFS.
Fulle S, Belia S, Vecchiet J, Morabito C, Vecchiet L, Fano G.	Laboratorio Interuniversitario di Miologia, Universita 'G. d'Annunzio', Nuovo Polo Didattico, 66013 Chieti Scalo, Italy. s.fulle@unich.it	Modification of the functional capacity of sarcoplasmic reticulum membranes in patients suffering from chronic fatigue syndrome.	Neuromuscul Disord. 2003 Aug;13(6):479-84.	In chronic fatigue syndrome, several reported alterations may be related to specific oxidative modifications in muscle. Since sarcoplasmic reticulum membranes are the basic structures involved in excitation-contraction coupling and the thiol groups of Ca(2+) channels of SR terminal cisternae are specific targets for reactive oxygen species, it is possible that excitation-contraction coupling is involved in this pathology. We investigated the possibility that abnormalities in this compartment are involved in the pathogenesis of chronic fatigue syndrome and consequently responsible for characteristic fatigue. The data presented here support this hypothesis and indicate that the sarcolemmal conduction system and some aspects of Ca(2+) transport are negatively influenced in chronic fatigue syndrome. In fact, both deregulation of pump activities (Na(+)/K(+) and Ca(2+)-ATPase) and alteration in the opening status of ryanodine channels may result from increased membrane fluidity involving sarcoplasmic reticulum membranes.]
Gaab J, Huster D, Peisen R, Engert V, Heitz V, Schad T, Schurmeyer T,	Center for Psychobiological and Psychosomatic Research, University	Assessment of cortisol response with low-dose and high-dose ACTH in	Psychosomatics. 2003 Mar-Apr;44(2):113-9.	A reduced secretion of cortisol has been proposed as a possible explanation of the symptoms in chronic fatigue syndrome. However, the evidence of hypocortisolism in chronic fatigue syndrome is conflicting. In order to simultaneously assess possible alterations in adrenocortical sensitivity and secretory adrenal reserve, the authors administered both low-dose and high-dose ACTH to a

Ehlert U.	of Trier, Germany. jgaab@klipsy.unizh.ch	patients with chronic fatigue syndrome and healthy comparison subjects.		group of 18 chronic fatigue syndrome patients and 18 age- and gender-matched healthy comparison subjects. No response differences for salivary and plasma cortisol were detectable after administration of either low-dose or high-dose ACTH, indicating that primary adrenal insufficiency is unlikely to play a significant role in the etiology of chronic fatigue syndrome.
Garrison RL, Breeding PC.	3306 Montavesta Drive, Lexington, KY 40502, USA.	A metabolic basis for fibromyalgia and its related disorders: the possible role of resistance to thyroid hormone.	Med Hypotheses. 2003 Aug;61(2):182-9.	It has long been recognized that the symptom complex of fibromyalgia can be seen with hypothyroidism. Hypothyroidism may been categorized, like diabetes, into type I (hormone deficient) and type II (hormone resistant). Most cases of fibromyalgia fall into the latter category. The syndrome is reversible with treatment, and is usually of late onset. It is likely more often acquired than due to mutated receptors. Now that there is evidence to support the hypothesis that fibromyalgia may be due to thyroid hormone resistance, four major questions appear addressable. First, can a simple biomarker be found to help diagnose it? Second, what other syndromes similar to Fibromyalgia may share a thyroid-resistant nature? Third, in non-genetic cases, how is resistance acquired? Fourth, what other methods of treatment become available through this new understanding? Preliminary evidence suggests that serum hyaluronic acid is a simple, inexpensive, sensitive, and specific test that identifies fibromyalgia. Overlapping symptom complexes suggest that chronic fatigue syndrome, Gulf war syndrome, premenstrual syndrome, post traumatic stress disorder, breast implant silicone sensitivity syndrome, bipolar affective disorder, systemic candidiasis, myofascial pain syndrome, and idiopathic environmental intolerance are similar enough to fibromyalgia to merit investigation for possible thyroid resistance. Acquired resistance may be due most often to a recently recognized chronic consumptive coagulopathy, which itself may be most often associated with chronic infections with mycoplasmids and related microbes or parasites. Other precipitants of thyroid resistance may use this or other paths as well. In addition to experimentally proven treatment with supraphysiologic doses of thyroid hormone, the thyroid-resistant disorders might be treatable with anti-hypercoagulant, anti-infective, insulin-sensitizing, and hyaluronolytic strategies.
Georgiades E, Behan WM, Kilduff LP, Hadjicharalambous M, Mackie EE, Wilson J, Ward SA, Pitsiladis YP.		Chronic fatigue syndrome: new evidence for a central fatigue disorder.	Clin Sci (Lond). 2003 Apr 23 [Epub ahead of print].	Considerable evidence points towards a prominent role for central neural (CNS) mechanisms in the pathogenesis of chronic fatigue syndrome (CFS), a disorder characterised chiefly by persistent, often debilitating, fatigue. We wished to characterise circulating profiles of putative amino acid modulators of CNS serotoninergic and dopaminergic function in CFS patients at rest, during symptom-limited exercise and subsequent recovery. Twelve CFS patients and eleven age- and sex-matched sedentary controls, with similar physical activity histories, underwent ramp-incremental exercise to the limit of tolerance. Plasma amino acid concentrations, oxygen uptake (Vo 2) and ratings of perceived exertion (RPE) were measured at rest, during exercise and recovery. Peak oxygen uptake (Vo 2peak) was significantly lower in the CFS patients, compared to controls. RPE in the patients was higher at all measured time points, including rest, relative to controls. Levels of free tryptophan [free Trp];the rate-limiting serotoninergic precursor, were significantly higher in CFS patients at exhaustion and recovery, whereas concentrations of branched-chain and large-neutral amino acids (BCAA and LNAA, respectively) were lower in patients at exhaustion and, for [LNAA], also during recovery. Consequently, the [free Trp] : [BCAA] and [free Trp] : [LNAA] ratios were significantly higher in CFS patients, except at rest. On

				the other hand, levels of tyrosine, the rate-limiting dopaminergic precursor, were significantly lower at all time points in the patients. The significant differences observed in a number of key putative CNS serotoninergic and dopaminergic modulators, coupled with the exacerbated effort perception, provide further evidence for a potentially significant role of CNS mechanisms in CFS pathogenesis.
Gherardi RK.	Groupe Nerf-Muscle, Departement de Pathologie, Hopital Henri Mondor, Creteil. romain.gherardi@hmn.ap-hop-paris.fr	[Lessons from macrophagic myofasciitis: towards definition of a vaccine adjuvant-related syndrome] [Article in French]	Rev Neurol (Paris). 2003 Feb;159(2):162-4.	Macrophagic myofasciitis is a condition first reported in 1998, which cause remained obscure until 2001. Over 200 definite cases have been identified in France, and isolated cases have been recorded in other countries. The condition manifests by diffuse myalgias and chronic fatigue, forming a syndrome that meets both Center for Disease Control and Oxford criteria for the so-called chronic fatigue syndrome in about half of patients. One third of patients develop an autoimmune disease, such as multiple sclerosis. Even in the absence of overt autoimmune disease they commonly show subtle signs of chronic immune stimulation, and most of them are of the HLADRB1*01 group, a phenotype at risk to develop polymyalgia rheumatica and rheumatoid arthritis. Macrophagic myofasciitis is characterized by a stereotyped and immunologically active lesion at deltoid muscle biopsy. Electron microscopy, microanalytical studies, experimental procedures, and an epidemiological study recently demonstrated that the lesion is due to persistence for years at site of injection of an aluminum adjuvant used in vaccines against hepatitis B virus, hepatitis A virus, and tetanus toxoid. Aluminum hydroxide is known to potently stimulate the immune system and to shift immune responses towards a Th-2 profile. It is plausible that persistent systemic immune activation that fails to switch off represents the pathophysiologic basis of chronic fatigue syndrome associated with macrophagic myofasciitis, similarly to what happens in patients with post-infectious chronic fatigue and possibly idiopathic chronic fatigue syndrome. Therefore, the WHO recommended an epidemiological survey, currently conducted by the French agency AFSSAPS, aimed at substantiating the possible link between the focal macrophagic myofasciitis lesion (or previous immunization with aluminium-containing vaccines) and systemic symptoms. Interestingly, special emphasis has been put on Th-2 biased immune responses as a possible explanation of chronic fatigue and associated manifestations known as the Gulf war syndrome. Results concerning macrophagic myofasciitis may well open new avenues for etiologic investigation of this syndrome. Indeed, both type and structure of symptoms are strikingly similar in Gulf war veterans and patients with macrophagic myofasciitis. Multiple vaccinations performed over a short period of time in the Persian gulf area have been recognized as the main risk factor for Gulf War syndrome. Moreover, the war vaccine against anthrax, which is administered in a 6-shot regimen and seems to be crucially involved, is adjuvanted by aluminium hydroxide and, possibly, squalene, another Th-2 adjuvant. If safety concerns about long-term effects of aluminium hydroxide are confirmed it will become mandatory to propose novel and alternative vaccine adjuvants to rescue vaccine-based strategies and the enormous benefit for public health they provide worldwide.
Ghosh AK, Ghosh K.		The head-up tilt test for diagnosing chronic fatigue	QJM. 2003 May;96(5):379-80. Comment on: QJM.	

		syndrome.	2003 Feb;96(2):133-42.	
Gottfries CG, Regland B, Zachrisson O, Walinder J.	Institutionen for klinisk neurovetenskap, Goteborgs universitet.	[Sick listing--"disaster" or incompetence in statistics and diagnostics?] [Article in Swedish]	Lakartidningen. 2003 May 22;100(21):1912-4.	
Granvik M, Hallberg H.	Centrum for klinisk forskning, Falun. mats.granvik@ltdalarna.se	[Marianne, 40 years old, a fictive patient with burnout symptoms. Sick listed by general practitioners, but was not the physician-patient dialogue neglected?] [Article in Swedish	Lakartidningen. 2003 Mar 20;100(12):1036-8, 1041.	
Gusev EI, Demina TL, Boiko AN, Khachanova NV.		[Certain problems of therapy with beta-interferon preparations] [Article in Russian]	Zh Nevrol Psikhiatr Im S S Korsakova. 2003;Spec No 2:98-102.	The latest data on clinical effects of beta-interferon-1b (betaferon) in different clinical types of multile sclerosis (MS) are discussed in this review. All local and systemic side effects of this treatment are discussed as well as possible influence of neutralizing antibodies (NAB) on clinical efficacy of this treatment. Moderate and easily treated side effects as well as the absence of significant evidence for modulation of positive clinical effects of beta-interferons by NAT allow one to consider this medicine as one of the basic methods of MS treatment.
Hanley NR, Van de Kar LD.	Department of Pharmacology, Center for Serotonin Disorders Research, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois 60153, USA.	Serotonin and the neuroendocrine regulation of the hypothalamic--pituitary-adrenal axis in health and disease.	Vitam Horm. 2003;66:189-255.	Serotonin (5-hydroxytryptamine, 5-HT)-containing neurons in the midbrain directly innervate corticotropin-releasing hormone (CRH)-containing cells located in paraventricular nucleus of the hypothalamus. Serotonergic inputs into the paraventricular nucleus mediate the release of CRH, leading to the release of adrenocorticotropin, which triggers glucocorticoid secretion from the adrenal cortex. 5-HT1A and 5-HT2A receptors are the main receptors mediating the serotonergic stimulation of the hypothalamic-pituitary-adrenal axis. In turn, both CRH and glucocorticoids have multiple and complex effects on the serotonergic neurons. Therefore, these two systems are interwoven and communicate closely. The intimate relationship between serotonin and the hypothalamic-pituitary-adrenal axis is of great importance in normal physiology such as circadian rhythm and stress, as well as pathophysiological disorders such as depression, anxiety, eating disorders, and chronic fatigue.
Hartz AJ, Bentler SE, Brake KA, Kelly MW.	Department of Family Medicine, University of Iowa College of Medicine, Iowa City 52242-	The effectiveness of citalopram for idiopathic chronic fatigue.	J Clin Psychiatry. 2003 Aug;64(8):927-35.	BACKGROUND: Chronic fatigue greatly affects quality of life and is a common reason for physician visits. Patients with chronic fatigue are often treated with antidepressants. METHOD: Prior to enrollment, all subjects had substantial fatigue for 6 months or more that was not explained by depression, organic illness, or lifestyle behaviors. Patients already taking an antidepressant were excluded from the study. Two designs were used. (1) Thirty-one subjects were given placebo for 1

	1097, USA. arthur-hartz@uiowa.edu.			week and then citalopram, 20 to 40 mg/day, for 2 months. Statistical testing evaluated whether fatigue (measured with the Rand Vitality Index) was reduced after citalopram was started. (2) Fatigue changes for subjects taking citalopram were compared with fatigue changes after 1 month and 2 months for 76 similar subjects taking an ineffective treatment. RESULTS: In design 1, fatigue for subjects taking citalopram was significantly and substantially reduced when subjects were switched from placebo to citalopram, p <.05. Benefits at 2 months were greatest for subjects who had fatigue less than 5 years, p <.01, and women, p <.01. In design 2, fatigue scores for subjects taking citalopram were not significantly better than the comparison group for all subjects but were significantly better at 2 months for subjects with less severe fatigue at baseline, p =.005, and for women, p =.08. Depression scores were not significantly better for citalopram subjects overall (p >.10) but were for certain subgroups. For all subjects, citalopram was associated with greater decrease in headaches and muscle aches at 1 month, p <.01. CONCLUSION: Citalopram may improve fatigue and symptoms associated with fatigue for some patients.
Hatcher S, House A.	Academic Unit of Psychiatry and Behavioural Sciences, School of Medicine, University of Leeds.	Life events, difficulties and dilemmas in the onset of chronic fatigue syndrome: a case-control study.	Psychol Med. 2003 Oct;33(7):1185-92.	BACKGROUND: The role of stress in the onset of chronic fatigue syndrome is unclear. Our objectives in this study were first, to determine the relation between the onset of chronic fatigue syndrome and stressful life events and difficulties. Secondly, we examined the role of a particular type of problem, dilemmas, in the onset of chronic fatigue syndrome. METHOD: We used a case-control design with 64 consecutive referrals from an Infectious Diseases/ Liaison Psychiatry Fatigue clinic and 64 age- and sex-matched controls from a general practice population control group in Leeds. We had two main outcome measures; the odds ratios of the risk of developing chronic fatigue syndrome after experiencing a severe life event, severe difficulties or both in the year and 3 months preceding onset; and the proportion of subjects in each group who experienced a dilemma prior to onset. RESULTS: Patients with chronic fatigue syndrome were more likely to experience severe events and difficulties in the 3 months (OR = 9, 95% CI 3.2 to 25.1) and year (OR = 4.3, 95% CI 1.8 to 10.2) prior to onset of their illness than population controls. In the 3 months prior to onset 19 of the 64 patients (30%) experienced a dilemma compared to none of the controls. CONCLUSIONS: Chronic fatigue syndrome is associated with stressful events and difficulties prior to onset. Those events and difficulties characterized as being dilemmas seem to be particularly important.
Hatchette TF, Hayes M, Merry H, Schlech WF, Marrie TJ.	Queen Elizabeth II Health Sciences Centre, Dalhousie University, Halifax, Nova Scotia, Canada.	The effect of C. burnetii infection on the quality of life of patients following an outbreak of Q fever.	Epidemiol Infect. 2003 Jun;130(3):491-5.	Sixty-six cases of Q fever were diagnosed in people affiliated with a goat-farming co-operative in rural Newfoundland in the spring of 1999. Follow-up studies which included administration of the Short Form 36 Health Survey (SF-36) were conducted 3 and 27 months after the initial outbreak to prospectively follow the effects of acute Q fever on the quality of life of the participants. Twenty-seven months after the outbreak 51% of those who had Q fever reported persistent symptoms including seven participants whose symptoms had initially resolved 3 months after the outbreak. Individuals with Q fever had significantly lower scores on five of the eight scales in the SF-36 and lower scores in the mental and physical summary scales compared to uninfected controls. Although this supports the hypothesis of a 'post Q fever fatigue syndrome' (QFFS), further study is warranted.

Helbig KJ, Heatley SL, Harris RJ, Mullighan CG, Bardy PG, Marmion BP.	Q Fever Research Group, IMVS, Adelaide, South Australia. kjhelbig@hotmail.com	Variation in immune response genes and chronic Q fever. Concepts: preliminary test with post-Q fever fatigue syndrome.	Genes Immun. 2003 Jan;4(1):82-5.	Acute primary Q fever is followed by various chronic sequelae. These include subacute Q fever endocarditis, granulomatous reactions in various organs or a prolonged debilitating post-infection fatigue syndrome (QFS). The causative organism, Coxiella burnetii, persists after an initial infection. The differing chronic outcomes may reflect variations within cytokine and accessory immune control genes which affect regulation of the level of persistence. As a preliminary test of the concept we have genotyped QFS patients and controls for gene variants spanning 15 genes and also examined HLA-B and DR frequencies. QFS patients exhibited a significantly increased frequency of HLA-DR-11 compared with controls and also significant differences in allelic variant frequencies within the NRAMP, and IFNgamma genes. These results indicate a possible genetic role in the expression of overt chronic Q fever. Further studies will be undertaken to increase sample sizes, to survey other forms of chronic Q fever and to examine Q fever patients who have recovered without sequelae.
Henningsen P, Zimmermann T, Sattel H.	Department of Psychosomatic Medicine, University of Heidelberg, Heidelberg, Germany. Peter_henningsen@med.uni-heidelberg.de	Medically unexplained physical symptoms, anxiety, and depression: a meta-analytic review.	Psychosom Med. 2003 Jul-Aug;65(4):528-33.	OBJECTIVE: Our objective was to review and compare, with meta-analytic methods, observational studies on the association of medically unexplained physical symptoms, anxiety, and depression with special emphasis on healthy and organically ill control groups and on different types of symptoms, measures, and illness behavior. METHODS: A search of MEDLINE and PsycLIT/PsycINFO for abstracts from 1980 to April 2001 was performed; principal investigators in the field were contacted and article reference lists were used to retrieve additional relevant articles. Two hundred forty-four studies were included on the basis of consensus ratings if they fulfilled seven of eight inclusion criteria pertaining to diagnostic accuracy and statistical appropriateness. Five hundred twenty-two studies were deferred or excluded. We focused specifically on the four functional somatic syndromes for which there were sufficient numbers for meta-analytic integration: irritable bowel syndrome (IBS), nonulcer dyspepsia (NUD), fibromyalgia (FM), and chronic fatigue syndrome (CFS). Data were extracted independently by two authors according to a prespecified coding manual with up to 70 parameters per study. RESULTS: Effect sizes for the association of the four functional somatic syndromes with depression and anxiety were of moderate magnitude but were highly significant statistically when compared with healthy persons and controls with medical disorders of known organic pathology. Moreover, this association was significant whether depression was measured with or without somatic items. Chronic fatigue syndrome is characterized by higher scores of depression, fibromyalgia by lower scores of anxiety than irritable bowel syndrome. Consulting behavior and severity of somatization is related to higher levels of anxiety and depression. CONCLUSIONS: Meta-analytic integration confirms that the four functional somatic syndromes (IBS, NUD, FM, CFS) are related to (but not fully dependent on) depression and anxiety. At present, there is only limited meta-analytic evidence for the same sort of association for medically unexplained physical symptoms in general. In view of the relative independence from depression and anxiety, classification and treatment of these symptoms and syndromes as "common mental disorders" does not seem fully appropriate.
Hiltebeitel C, Squires J, Waller DA.		Neuropsychological profiles in Chronic	Arch Clin Neuropsychol.	

		Fatigue Syndrome.	1989;4(2):139-40.	
Hofmann SG.	Department of Psychology, Boston University, Massachusetts, USA.	Review: cognitive behavioural interventions may be effective for chronic fatigue syndrome and chronic back pain..	Evid Based Ment Health. 2003 May;6(2):55. Comment on: BMJ. 2002 Nov 9;325(7372):1082	
Hokama Y, Uto GA, Palafox NA, Enlander D, Jordan E, Cocchetto A.	Department of Pathology, University of Hawaii-Manoa, Honolulu, Hawaii.	Chronic phase lipids in sera of chronic fatigue syndrome (CFS), chronic ciguatera fish poisoning (CCFP), hepatitis B, and cancer with antigenic epitope resembling ciguatoxin, as assessed with MAb-CTX.	J Clin Lab Anal. 2003;17(4):132-9.	Clinical reports and descriptions of chronic fatigue syndrome (CFS) and chronic ciguatera fish poisoning (CCFP) show great similarities in clinical symptomology. These similarities in the literature suggested the exploration of lipids in sera of CFS, CCFP, and other diseases with the membrane immunobead assay (MIA), which is typically used for screening ciguateric ocean fish. Sera from patients with other diseases, including hepatitis B, cancer, and diabetes, were included to assess the degree of specificity involved. Sera were treated with acetone in a ratio of 1 part serum to 4 parts acetone. The suspension was centrifuged, and the acetone layer was evaporated. The residue was weighed and redissolved in 1.0 mL methanol and tested by the MIA, undiluted and titered to 1:160. The undiluted acetone fraction of the 37 normal showed +/- activity to +activity with 16 no titer, 15 with 1:5 titer and two with 1:10 titer, and four with >/=1:40 titers. One hundred fifteen CFS sera showed 1 with 1+ and 114 with 2+ activity in the undiluted samples, 1 with 1:10 titer, 3 with 1:20 titer, 31 with 1:40 titer, 50 with 1:80 titer, and 30 with 160 titer. Thus 95.6% of the samples had >/=1:40 titer. Eight hepatitis B sera samples had >/=1:40 titers. Four CCFP samples had >/=1:40 titers. Three of 16 cancer samples had 1:40 titer. These data are summarized in Fig. 1. As shown in Table 1, a significant increase (P<0.001) in the chronic phase lipids (CPLs) was shown relative to the normal group. A preliminary chemical study in C18 octadecylsilyl columns showed all fractions (100% chloroform, 9:1 chloroform : methanol, 1:1 chloroform : methanol, and 100% methanol) to contain lipids reactive to MAb-CTX with different intensities. Prostaglandins were shown in 100% methanol fraction. Competitive MIA with crude fish ciguatoxin and CFS with synthetic JKLM ciguatoxin epitope suggested similarities in structure with ciguatoxin. This was compatible with the neuroblastoma assay demonstrated in the C(18) column fractions 9:1 and 1:1, chloroform : methanol solvents. J. Clin. Lab. Anal. 17:132-139, 2003. Copyright 2003 John Wiley & Sons, Ltd.
Huibers MJ, Beurskens AJ, Prins JB, Kant IJ, Bazelmans E, Van Schayck CP, Knottnerus JA, Bleijenberg G.	Department of Epidemiology, Maastricht University, Netherlands. marcus.huibers@hag.unimaas.nl	Fatigue, burnout, and chronic fatigue syndrome among employees on sick leave: do attributions make the difference?	Occup Environ Med. 2003 Jun;60 Suppl 1:i26-31.	BACKGROUND: Persistent fatigue among employees, burnout, and chronic fatigue syndrome (CFS) are three fatigue conditions that share some characteristics in theory. However, these conditions have not been compared in empirical research, despite conceptual similarities. METHODS: This cross sectional study aimed to investigate relations between persistent fatigue, burnout, and CFS by describing the clinical features of a sample of 151 fatigued employees on sick leave. Using validated instruments, subgroups based on research criteria for CFS and burnout within the sample of fatigued employees and a reference group of 97 diagnosed CFS patients were compared. Analyses of covariance were performed. RESULTS: A total of 66 (43.7%) fatigued employees met research criteria for CFS (except symptom criteria) and 76 (50.3%) met research

				criteria for burnout. "CFS-like employees" (fatigued employees who met CFS criteria) reported stronger somatic attributions than "non-CFS-like employees". Burnt out CFS-like employees were more depressed and distressed than CFS-like employees who were not burnt out. Burnout cases among the non-CFS-like employees had stronger psychological attributions than fatigued employees who were not burnt out. Compared to diagnosed CFS patients, CFS-like employees merely had a shorter duration of fatigue complaints. Burnt out CFS-like employees had stronger psychological attributions and were more distressed than CFS patients. CONCLUSIONS: Fatigued employees shared many important characteristics with CFS patients, regardless of burnout status, and many fatigued employees met CFS criteria and/or burnout criteria. Differences however concerned the causal attributions that were made. This raises questions about the role of causal attributions: are they modified by fatigue complaints or do they determine illness outcome?
Hyams KC.	Department of Veterans Affairs, Office of Public Health and Environmental Hazards, Washington, DC, USA	The investigation of chronic fatigue syndrome: a case-study of the limitations of inductive inferences and non-falsifiable hypotheses in medical research.	Med Hypotheses. 2003 May;60(5):760-6.	Karl Popper's argument that deductive logic and falsifiable hypotheses are necessary for the growth of scientific knowledge has been controversial. One approach to assess the relevance of his ideas to medical science has been to evaluate examples of successful research. Another approach is to analyze an unsuccessful investigation. The inconclusive search for a unique 'chronic fatigue syndrome' offers a well-documented case-study for this analysis. Over the past 130 years, numerous studies have provided clinical and epidemiological data, which have supported competing hypotheses about the etiology of chronic fatigue. However, few hypotheses have been refuted because it has not been possible to establish objective standards of inquiry for a subjective symptom like fatigue. As a result, intensive research efforts have not converged on correct explanations by eliminating erroneous ideas. This unsuccessful investigation illustrates how non-falsifiable hypotheses are insufficient to advance medical knowledge, even when there is an abundance of empirical data.
Ikuta K, Yamada T, Shimomura T, Kuratsune H, Kawahara R, Ikawa S, Ohnishi E, Sokawa Y, Fukushi H, Hirai K, Watanabe Y, Kurata T, Kitani T, Sairenji T.	Division of Biosignaling, Department of Biomedical Sciences, Faculty of Medicine, School of Life Science, Tottori University, Yonago 683-8503, Japan.	Diagnostic evaluation of 2', 5'-oligoadenylate synthetase activities and antibodies against Epstein-Barr virus and Coxiella burnetii in patients with chronic fatigue syndrome in Japan.	Microbes Infect. 2003 Oct;5(12):1096-102.	To investigate the association of viral infections with chronic fatigue syndrome (CFS), we assayed 2', 5'-oligoadenylate synthetase (2-5AS) activities in peripheral blood mononuclear cells from CFS patients in Japan. These patients were diagnosed in two hospitals, H1 and H2, located in different areas of the country. The activities were detected in 19 (86%) and 7 (32%) of each of the 22 patients in H1 and H2, respectively, while they were detected in only four (11%) out of the 38 healthy controls. IFN-alpha was similarly detected in a few CFS patients and healthy controls. We also assayed the antibody titers against Epstein-Barr virus (EBV) and Coxiella burnetii in these patients. The EBV anti-EA-IgG antibodies were detected in two (9%) and seven (32%) of each of the 22 patients in H1 and H2, respectively. Anti-C. burnetii IgG antibodies were detected in six (27%) out of 22 patients in H1 but not in 22 patients in H2, while they were detected in one (11%) of the nine healthy controls. Some CFS patients may be associated with EBV or C. burnetii infection. There were some statistical correlations between the 2-5AS activities and antibody titers of EA-IgG ($P < 0.05$, Student's t-test) but not to the antibody titers of C. burnetii. The up-regulation of 2-5AS activities suggests immunological dysfunctions with some virus infections in the CFS patients. Our results indicate that 2-5AS activities are useful for a diagnostic marker of CFS and for exploring the complicated pathogenesis of CFS.
Jason LA, Helgerson	Center for	Variability in	Eval Health Prof.	Chronic fatigue syndrome (CFS) is an illness that involves severe, prolonged exhaustion as well as

J, Torres-Harding SR, Carrico AW, Taylor RR.	Community Research, DePaul University, 990 W. Fullerton Ave., Chicago, IL 60614, USA.	diagnostic criteria for chronic fatigue syndrome may result in substantial differences in patterns of symptoms and disability.	2003 Mar;26(1):3-22.	neurologic, immunologic, and endocrine system pathology. Because the pathogenesis of CFS has yet to be determined, case definitions have relied on clinical observation in classifying signs and symptoms for diagnosis. The current investigation examined differences between CFS as defined by Fukuda and colleagues and a set of criteria that has been stipulated for myalgic encephalomyelitis (ME). Dependent measures included psychiatric comorbidity, symptom frequency, symptom severity, and functional impairment. The ME and Fukuda et al. (1994) CFS criteria were compared with a group having chronic fatigue due to psychiatric reasons. Significant differences occurred primarily with neurologic, neuropsychiatric, fatigue/weakness, and rheumatological symptoms. These findings suggest that it might be inappropriate to synthesize results from studies of this illness that use different definitions to select study populations.
Jason LA, Taylor RR, Kennedy CL, Jordan KM, Song S, Johnson D, Torres-Harding S.	Center for Community Research, DePaul University, Chicago, IL 60614, USA. ljason@wppost.depaul.edu	Chronic fatigue syndrome: symptom subtypes in a community based sample.	Women Health. 2003;37(1):1-13.	Most studies of Chronic Fatigue Syndrome (CFS) have been based on patients recruited from primary or tertiary care settings. Patients from such settings might not be typical of patients in the general population. The present investigation involved examining individuals with CFS from a community-based study. A random sample of 18,675 respondents in Chicago were first interviewed by telephone. A group of individuals with chronic fatigue accompanied by at least four Fukuda et al. (1994) symptoms associated with CFS were given medical and psychiatric examinations. From this sample, a physician review group diagnosed individuals with CFS. Those diagnosed with CFS were subclassified based on frequency of symptoms. Important differences emerged on measures of sociodemographics and disability. The implications of these findings and others are discussed.
Jeffcott LB, Dobson J, Roberts C, Slater J, Henson F.		Equine referrals for two ongoing studies. Letter	Vet Rec. 2003 Feb 15;152(7):216.	
Jones JF, Nisenbaum R, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Road, Mail Stop A15, Atlanta, GA 30333. jaj9@cdc.gov	Medication Use by Persons with Chronic Fatigue Syndrome: Results of a Randomized Telephone Survey in Wichita, Kansas.	Health Qual Life Outcomes. 2003 Dec 2;1(1):74. Epub 2003 Dec 02.	BACKGROUND: Chronic fatigue syndrome (CFS) is characterized by profound fatigue, which substantially interferes with daily activities, and a characteristic symptom complex. Patients use a variety of prescribed and self-administered medications, vitamins, and supplements for relief of their symptoms. The objective of this study was to describe utilization of medications and supplements by persons with CFS and non-fatigued individuals representative of the general population of Wichita, Kansas. METHODS: We used a random-digit dialing telephone survey to identify persons with CFS in the general population of Wichita, Kansas. Subjects who on the basis of telephone interview met the CFS case definition, and randomly selected non-fatigued controls, were invited for a clinic evaluation that included self-reported use of medications and supplements. Sex-adjusted odds ratios and 95% confidence interval were estimated to measure the association between CFS and use of various drug categories. RESULTS: We clinically evaluated and classified 90 subjects as CFS during the study and also collected clinical data on 63 who never described fatigue. Subjects with CFS reported using 316 different drugs compared to 157 reported by non-fatigued controls. CFS subjects were more likely to use any drug category than controls (p = 0.0009). Pain relievers and vitamins/supplements were the two most common agents listed by both groups. In addition CFS persons were more likely to use pain relievers, hormones, antidepressants, benzodiazepines, gastro-intestinal, and central nervous system

				medications (Sex-adjusted odds ratios range = 2.97 - 12.78). CONCLUSION: Although the reasons for increased use of these agents were not elucidated, the data indicated the CFS patients' need for symptom relief.
Kagawa FT, Wehner JH, Mohindra V.	Santa Clara Valley Medical Center, San Jose, CA 95128, USA. Frank.Kagawa@hhs.co.santa-clara.ca.us	Q fever as a biological weapon.	Semin Respir Infect. 2003 Sep;18(3):183-95.	Q fever is a bacterial zoonosis caused by Coxiella burnetii, a unique intracellular coccobacillus, adapted to live within the phagolysosomes of macrophages and monocytes. It is highly infectious, with as little as one organism needed to cause clinical infection, making it an attractive organism for use in biowarfare. Despite its high infectivity, it has low virulence, and most patients undergo only asymptomatic seroconversion. Acute clinical manifestations are a nonspecific febrile illness, pneumonia, hepatitis, and neurologic abnormalities ranging from headache to meningoencephalitis. Chronic Q fever can result in endocarditis, hepatitis, or a chronic fatigue syndrome. Diagnosis usually is made by serology because culture of the highly contagious organism is potentially hazardous. Tetracyclines are the antibiotics of choice. When individualized therapy is possible, a 14- to 21-day course of doxycycline usually is used. In a mass casualty situation, a 5- to 7-day course of doxycycline is recommended, both for therapy and prophylaxis. For chronic infections such as endocarditis, 18 months of doxycycline supplemented with hydroxychloroquine is currently the best therapy.
Kakumanu SS, Mende CN, Lehman EB, Hughes K, Craig TJ.	Division of Biology and Medicine, Brown Medical School, Brown University, Providence, RI, USA.	Effect of topical nasal corticosteroids on patients with chronic fatigue syndrome and rhinitis.	J Am Osteopath Assoc. 2003 Sep;103(9):423-7.	BACKGROUND: Chronic fatigue syndrome (CFS) is a disabling illness of persistent fatigue. Recent studies have shown that patients with CFS have an increased prevalence of nonallergic rhinitis. Inflammation of the nasal passages due to allergic rhinitis can cause nasal congestion resulting in an increased number of sleep disturbances and daytime fatigue. While topical nasal corticosteroids have been shown to alleviate nasal obstruction effectively in patients with rhinitis who do not have CFS, it is unknown whether topical nasal corticosteroids will reduce CFS symptoms. STUDY OBJECTIVE: The purpose of this study is to determine whether topical nasal corticosteroids will reduce daytime sleepiness in patients with CFS and rhinitis. METHODS: Twenty-eight of 31 subjects with rhinitis and a diagnosis of CFS completed the double-blind, randomized, placebo-controlled trial. Two subjects failed screening, and 3 subjects withdrew from the study prior to its completion. Subjects were randomized according to Balaam's crossover design, and one of the following interventions was used for each group in the study: 8-week treatment with a topical nasal corticosteroid, 8-week treatment with a placebo saline spray, 4-week treatment with a topical nasal corticosteroid followed by a 4-week treatment with a placebo saline spray, or a 4-week treatment with a placebo saline spray followed by a 4-week treatment with a topical nasal corticosteroid. Data focusing on rhinitis symptoms, severity of chronic fatigue symptoms, and quality of life were gathered at biweekly office visits and with daily diaries. RESULTS: The results indicated that daytime sleepiness was reduced when patients with rhinitis and CFS were treated with topical nasal corticosteroids. The severity of associated CFS symptoms, specifically fatigue, muscle pain, postexertional fatigue, and daily activity, did not improve with treatment. CONCLUSION: Treating the symptoms of rhinitis in patients with CFS does not appear to alleviate daytime fatigue or associated nasal, musculoskeletal, or cognitive complaints. Therefore, it is unlikely that aggressive treatment of such symptoms with topical nasal corticosteroids will provide significant benefit to patients with CFS who do not have allergic

				rhinitis. These results indicate that the nonallergic rhinitis seen in patients with CFS may arise from a mechanism other than chronic inflammation.
Karper WB, Stasik SC.	University of North Carolina at Greensboro, PO Box 26170, Greensboro, NC 27402, USA. wbkarper@uncg.edu	A successful, long-term exercise program for women with fibromyalgia syndrome and chronic fatigue and immune dysfunction syndrome.	Clin Nurse Spec. 2003 Sep;17(5):243-8.	This article describes an ongoing, long-term clinical exercise program for women with fibromyalgia syndrome (FMS), some of whom also have chronic fatigue and immune dysfunction syndrome (CFIDS). The recorded outcomes from the most recent year of the program also are reported. Participants engaged in sessions lasting 50-70 minutes, 5 days per week; each session involved aerobic activity, resistance training, and other dynamic exercise. One group was in the program for 3 years and another group was in the program for 2 years. Program outcomes for the year (comparing beginning and end-of-year results) are presented for both groups on physical fitness, psychosocial, and FMS/CFIDS symptoms. The outcomes support that all of the women appear to have benefited from the program in numerous ways, suggesting that the program works. Also, those outcomes are in agreement with past research reported in this journal. Implications for clinical nurse specialists working with FMS/CFIDS patients are discussed.
Kang HK, Natelson BH, Mahan CM, Lee KY, Murphy FM.	Veterans Health Administration, Department of Veterans Affairs, Washington, DC, USA. han.kang@mail.va.gov	Post-traumatic stress disorder and chronic fatigue syndrome-like illness among Gulf War veterans: a population-based survey of 30,000 veterans.	Am J Epidemiol. 2003 Jan 15;157(2):141-8.	The authors estimated the prevalence of post-traumatic stress disorder (PTSD) and illness resembling chronic fatigue syndrome (CFS) in the entire population of Gulf War and non-Gulf-War veterans. They also evaluated the relation between the extent of deployment-related stress and the risk of either PTSD or CFS. In 1995-1997, the authors conducted a health survey in which these two symptom-based medical diagnoses in a population-based sample of 15,000 Gulf War veterans representing four military branches and three unit components (active, reserve, and National Guard) were compared with those of 15,000 non-Gulf veteran controls. Gulf War veterans, compared with non-Gulf veteran controls, reported significantly higher rates of PTSD (adjusted odds ratio = 3.1, 95% confidence interval: 2.7, 3.4) and CFS (adjusted odds ratio = 4.8, 95% confidence interval: 3.9, 5.9). The prevalence of PTSD increased monotonically across six levels of deployment-related stress intensity (test for trend: $p < 0.01$), while the prevalence of CFS rose only at the low end of the stress spectrum. While deployment-related stress could account for the higher risks of both PTSD and CFS, additional factor(s) unique to the Gulf environment may have contributed to the risk of CFS among Gulf War veterans.
Kawamura Y, Kihara M, Nishimoto K, Taki M.	Department of Neurology, Kawamura Hospital, Gifu, Japan	Efficacy of a half dose of oral pyridostigmine in the treatment of chronic fatigue syndrome: three case reports.	Pathophysiology. 2003 May;9(3):189-194.	Chronic fatigue syndrome (CFS) is characterized by persistent mental and physical fatigue for at least 6 months. Its pathophysiology is unknown and there is no proven effective treatment. We describe three cases who fulfill the criteria of CFS, in whom a defect of neuromuscular transmission and dysautonomia are present and who respond to acetylcholine-esterase inhibition. Case 1: 18-year-old female with a 3-year history of CFS. Response of compound-muscle-action potential, recorded using surface recording electrode, over left abductor pollicis brevis muscle, to repetitive nerve stimulation (RNS) at a rate of 10 Hz showed a 42% incremental response. Composite autonomic scoring system (CASS) showed mild cholinergic impairment (cardiovagal score: 1; sudomotor score: 2). Serological tests for Epstein-Barr virus (EBV) revealed positive antiviral capsid antigens (anti-VCA) immunoglobulins G (IgG). Oral pyridostigmine therapy (30 mg) resulted in marked improvement in symptoms. Case 2: 28-year-old female with 10-year history of CFS. RNS, using identical protocol, showed a 60% incremental response over the same muscle. CASS showed mild cholinergic impairment (cardiovagal score: 1; sudomotor

				score: 2) and this patient was also positive for EBV. This patient responded dramatically to 10-mg pyridostigmine. Case 3: 29-year-old female with a history of CFS for longer than 15 years. Repetitive stimulation, using identical paradigm to left abductor pollicis brevis muscle, showed a 42% incremental response. CASS showed mildly cholinergic impairment (cardiovagal score: 2; sudomotor score: 1). EBV antibody titers were positive. Patient responded to 30-mg pyridostigmine with an improvement in her fatigue. These three cases generate the hypothesis that the fatigue in some patients with clinical CFS might be due to a combination of mild neuromuscular transmission defect combined with cholinergic dysautonomia. Support for this thesis derives from the improvement with cholinesterase inhibition.
Kerr JR, Cunniffe VS, Kelleher P, Bernstein RM, Bruce IN.	Department of Microbiology, Royal Brompton Hospital, Imperial College London, Sydney St, London SW3 6NP, United Kingdom. j.kerr@imperial.ac.uk	Successful intravenous immunoglobulin therapy in 3 cases of parvovirus B19-associated chronic fatigue syndrome.	Clin Infect Dis. 2003 May 1;36(9):e100-6. Epub 2003 Apr 22.	Three cases of chronic fatigue syndrome (CFS) that followed acute parvovirus B19 infection were treated with a 5-day course of intravenous immunoglobulin (IVIG; 400 mg/kg per day), the only specific treatment for parvovirus B19 infection. We examined the influence of IVIG treatment on the production of cytokines and chemokines in individuals with CFS due to parvovirus B19. IVIG therapy led to clearance of parvovirus B19 viremia, resolution of symptoms, and improvement in physical and functional ability in all patients, as well as resolution of cytokine dysregulation.
Kerr JR, Tyrrell DA.	Department of Microbiology, Royal Brompton Hospital, National Heart & Lung Institute, Imperial College London, UK. j.kerr@imperial.ac.uk	Cytokines in parvovirus B19 infection as an aid to understanding chronic fatigue syndrome.	Curr Pain Headache Rep. 2003 Oct;7(5):333-41.	Human parvovirus B19 infection has been associated with various clinical manifestations of a rheumatic nature such as arthritis, fatigue, and chronic fatigue syndrome (CFS), which can persist for years after the acute phase. The authors have demonstrated recently that acute B19 infection is accompanied by raised circulating levels of IL-1b, IL-6, TNF-a, and IFN-g and that raised circulating levels of TNF-a and IFN-g persist and are accompanied by MCP-1 in those patients who develop CFS. A resolution of clinical symptoms and cytokine dysregulation after intravenous immunoglobulin (IVIG) therapy, which is the only specific treatment for parvovirus B19 infection, also has been reported. Although CFS may be caused by various microbial and other triggers, that triggered by B19 virus is clinically indistinguishable from idiopathic CFS and exhibits similar cytokine abnormalities and may represent an accessible model for the study of CFS.
Khan F, Kennedy G, Spence VA, Newton DJ, Belch JJ.		Peripheral cholinergic function in humans with chronic fatigue syndrome, gulf war syndrome, and with illness following organophosphate exposure.	Clin Sci (Lond). 2003 Sep 23 [Epub ahead of print].	We investigated whether the peripheral cholinergic abnormalities we previously reported in patients with chronic fatigue syndrome (CFS) are also present in those with Gulf War syndrome (GWS) and agricultural workers exposed to organophosphate pesticides, where cholinesterase inhibition is specifically implicated. We also looked at whether these abnormalities might be due to a reduction in the activity of cholinesterase expressed on the vascular endothelium. We used laser Doppler imaging to measure the forearm skin blood flow responses to iontophoresis of acetylcholine and of methacholine (which is resistant to breakdown by cholinesterase) in patients with CFS, GWS, and those with a history of ill health after definite organophosphate exposure, as well as in matched, healthy controls. The response to acetylcholine was significantly higher in patients with CFS than in controls ($P = 0.029$, repeated-measures analysis of variance), but was normal in those with GWS and those exposed to organophosphates. The methacholine response was higher than the acetylcholine response in all patient groups except for CFS, where there was

				no difference between the responses. Although there are many clinical similarities between these three illnesses, our results indicate peripheral cholinergic abnormalities in the vascular endothelium of only patients with CFS, suggesting that this syndrome has a different aetiology, which might involve inhibition of vascular cholinesterase.
Khan F, Spence V, Kennedy G, Belch JJ.	Vascular Diseases Research Unit, University Department of Medicine, Ninewells Hospital and Medical School, Dundee, UK. f.khan@dundee.ac.uk.	Prolonged acetylcholine-induced vasodilatation in the peripheral microcirculation of patients with chronic fatigue syndrome.	Clin Physiol Funct Imaging. 2003 Sep;23(5):282-5.	Although the aetiology of chronic fatigue syndrome (CFS) is unknown, there have been a number of reports of blood flow abnormalities within the cerebral circulation and systemic blood pressure defects manifesting as orthostatic intolerance. Neither of these phenomena has been explained adequately, but recent reports have linked cerebral hypoperfusion to abnormalities in cholinergic metabolism. Our group has previously reported enhanced skin vasodilatation in response to cumulative doses of transdermally applied acetylcholine (ACh), implying an alteration of peripheral cholinergic function. To investigate this further, we studied the time course of ACh-induced vasodilatation following a single dose of ACh in 30 patients with CFS and 30 age- and gender-matched healthy control subjects. No differences in peak blood flow was seen between patients and controls, but the time taken for the ACh response to recover to baseline was significantly longer in the CFS patients than in control subjects. The time taken to decay to 75% of the peak response in patients and controls was 13.7 +/- 11.3 versus 8.9 +/- 3.7 min (P = 0.03), respectively, and time taken to decay to 50% of the peak response was 24.5 +/- 18.8 versus 15.1 +/- 8.9 min (P = 0.03), respectively. Prolongation of ACh-induced vasodilatation is suggestive of a disturbance to cholinergic pathways, perhaps within the vascular endothelium of patients with CFS, and might be related to some of the unusual vascular symptoms, such as hypotension and orthostatic intolerance, which are characteristic of the condition.
Kurup RK, Kurup PA.	Department of Neurology, Medical College Hospital, Trivandrum, Kerala, India.	Hypothalamic digoxin, cerebral chemical dominance and myalgic encephalomyelitis.	Int J Neurosci. 2003 May;113(5):683-701.	The isoprenoid pathway was assessed in 15 patients with chronic fatigue syndrome. The pathway was also assessed in individuals with differing hemispheric dominance to assess whether hemispheric dominance had any correlation with these disease states. The isoprenoid metabolites--digoxin, dolichol, and ubiquinone--RBC membrane Na+-K+ ATPase activity, serum magnesium and tyrosine/tryptophan catabolic patterns were assessed. The free-radical metabolism, glycoconjugate metabolism, and RBC membrane composition was also assessed. Membrane Na+-K+ ATPase activity and serum magnesium levels were decreased while HMG CoA reductase activity and serum digoxin levels were increased in myalgic encephalomyelitis (ME). There were increased levels of tryptophan catabolites--nicotine, strychnine, quinolinic acid, and serotonin--and decreased levels of tyrosine catabolites--dopamine, noradrenaline, and morphine in ME. There was an increase in dolichol levels, carbohydrate residues of glycoproteins, glycolipids, total/individual GAG fractions, and lysosomal enzymes in ME. Reduced levels of ubiquinone, reduced glutathione, and free-radical scavenging enzymes, as well as increased lipid peroxidation products and nitric oxide, were noticed in ME. The biochemical patterns in ME correlated with those obtained in right hemi spheric chemical dominance. The role of hypothalamic digoxin and neurotransmitter induced immune activation, altered glycoconjugate metabolism, and resultant defective viral antigen presentation, NMDA excitotoxicity and cognitive dysfunction, and mitochondrial dysfunction related myalgia in the pathogenesis of ME is stressed. ME occurs in individuals with right hemispheric chemical dominance.

Lane RJ, Soteriou BA, Zhang H, Archard LC.	Division of Clinical Neurosciences and Psychological Medicine, Imperial College, London SW7, UK. r.lane@imperial.ac.uk	Enterovirus related metabolic myopathy: a postviral fatigue syndrome.	J Neurol Neurosurg Psychiatry. 2003 Oct;74(10):1382-6. Comment in: J Neurol Neurosurg Psychiatry. 2003 Oct;74(10):1361-2.	OBJECTIVE: To detect and characterise enterovirus RNA in skeletal muscle from patients with chronic fatigue syndrome (CFS) and to compare efficiency of muscle energy metabolism in enterovirus positive and negative CFS patients. METHODS: Quadriceps muscle biopsy samples from 48 patients with CFS were processed to detect enterovirus RNA by two stage, reverse transcription, nested polymerase chain reaction (RT-NPCR), using enterovirus group specific primer sets. Direct nucleotide sequencing of PCR products was used to characterise the enterovirus. Controls were 29 subjects with normal muscles. On the day of biopsy, each CFS patient undertook a subanaerobic threshold exercise test (SATET). Venous plasma lactate was measured immediately before and after exercise, and 30 minutes after testing. An abnormal lactate response to exercise (SATET+) was defined as an exercise test in which plasma lactate exceeded the upper 99% confidence limits for normal sedentary controls at two or more time points. RESULTS: Muscle biopsy samples from 20.8% of the CFS patients were positive for enterovirus sequences by RT-NPCR, while all the 29 control samples were negative; 58.3% of the CFS patients had a SATET+ response. Nine of the 10 enterovirus positive cases were among the 28 SATET+ patients (32.1%), compared with only one (5%) of the 20 SATET- patients. PCR products were most closely related to coxsackie B virus. CONCLUSIONS: There is an association between abnormal lactate response to exercise, reflecting impaired muscle energy metabolism, and the presence of enterovirus sequences in muscle in a proportion of CFS patients.
Lashley FR.	College of Nursing, Rutgers, The State University of New Jersey, Newark, NJ 07102, USA. lashley@nightingale.rutgers.edu	A review of sleep in selected immune and autoimmune disorders.	Holist Nurs Pract. 2003 Mar-Apr;17(2):65-80.	Evidence for the reciprocal role of the immune system in sleep is growing. Sleep disturbances are believed to be both a cause and a consequence of various immune and autoimmune conditions.
Le Bon O, Minner P, Van Moorsel C, Hoffmann G, Gallego S, Lambrecht L, Pelc I, Linkowski P.	Department of Psychiatry, CHU Brugmann S48, Place Van Gehuchten 4, 1020 Brussels, Belgium. lebono@ulb.ac.be	First-night effect in the chronic fatigue syndrome.	Psychiatry Res. 2003 Sep 30;120(2):191-9.	Since the magnitude of the first-night effect has been shown to be a function of medical conditions and of settings in which polysomnographies are performed, it is essential to evaluate the habituation phenomenon in each case in order to determine the optimal recording methodology. A first-night effect was evidenced in certain cases of chronic fatigue syndrome, but not in others. To clarify this issue, a large group of patients with chronic fatigue syndrome who had no primary sleep disorders were selected and recorded for two consecutive nights in a hospital sleep unit. Several parameters, frequently associated with the first-night effect, were found to be influenced by the recording methodology: Total Sleep Time, Sleep Efficiency, Sleep Efficiency minus Sleep Onset, Sleep Onset Latency, Wake Time, Slow Wave Sleep, Rapid Eye Movement Sleep, Rapid Eye Movement Sleep Latency and Number of Sleep Cycles. Bland and Altman plots determined that the difference scores between the nights included a systematic bias linked to the order of recordings (first-night effect). Factorial analysis grouped the difference scores into three factors. No significant difference was observed between patients with generalized anxiety comorbidity and those with no psychiatric comorbidity, or between those with and without psychiatric comorbidity. Chronic fatigue syndrome must thus be added on the

				list of conditions where a clinically significant habituation effect takes place.
Lim BR, Tan SY, Zheng YP, Lin KM, Park BC, Turk AA.	Fuller Theological Seminary, Graduate School of Psychology, Pasadena, California, USA. blim@fuller.edu	Psychosocial factors in chronic fatigue syndrome among Chinese Americans: a longitudinal community-based study.	Transcult Psychiatry. 2003 Sep;40(3):429-41.	Chronic fatigue syndrome (CFS) is a relatively new condition of unknown etiology. Research suggests that psychosocial factors such as perceived social support, life stress, and acculturation may significantly influence individuals who are prone to CFS. For 57 Chinese American individuals initially diagnosed with CFS, those who recovered after one year reported lower levels of life stress than those who did not recover. Effects of changes in perceived social support also appeared to be mediated by life stress.
Logan AC, Venket Rao A, Irani D.	CFS-FM Integrative Care Centre, Toronto, Canada	Chronic fatigue syndrome: lactic acid bacteria may be of therapeutic value.	Med Hypotheses. 2003 Jun;60(6):915-23.	Chronic fatigue syndrome (CFS) is complex illness with unknown aetiology. Recent research shows that patients with CFS have marked alterations in microbial flora, including lowered levels of bifidobacteria and small intestinal bacterial overgrowth (SIBO). Research also indicates that CFS patients are under increased oxidative stress, have a type 2 helper cell dominate cytokine profile, frequently report allergies, have altered essential fatty acid (EFA) status and may have malabsorption of certain micronutrients. Lactic acid bacteria (LAB) have the potential to influence the immune system in CFS patients by supporting T helper cell 1 driven cellular immunity and may decrease allergies. In addition LAB are strong antioxidants, may improve EFA status, can enhance absorption of micronutrients by protecting the intestinal epithelial barrier, and have been used to treat SIBO. It is our contention that LAB may have a therapeutic role in the treatment of CFS.
Lyall M, Peakman M, Wessely S.	Department of Psychological Medicine, Guy's, King's and St. Thomas' School of Medicine, 103 Denmark Hill, London SE5 8AZ, UK.	A systematic review and critical evaluation of the immunology of chronic fatigue syndrome.	J Psychosom Res. 2003 Aug;55(2):79-90.	OBJECTIVE: Immune dysfunction in patients with chronic fatigue syndrome (CFS) has been widely but inconsistently reported. Traditional reviews of the literature have produced a variety of conclusions. We present the results of the first systematic review of the subject. METHODS: EMBASE, MEDLINE and PSYCHINFO databases were searched, and leading researchers in the field were contacted. Inclusion criteria were applied, and studies were then divided into groups based on the quality of their methodology. Study results were collated and described. RESULTS: Studies ranged widely in quality. There was an inverse association between study quality and finding low levels of natural killer cells, suggesting that the association may be related to study methodology. On the other hand, reports of abnormalities in T cells and cytokine levels were not related to study quality. CONCLUSIONS: The conclusions of this systematic review differ from a recent traditional narrative review of the immunology of CFS. No consistent pattern of immunological abnormalities is identified.
Madariaga MG, Rezai K, Trenholme GM, Weinstein RA.	Division of Infectious Disease, Cook County Hospital, Chicago and the Section of Infectious Diseases, Rush-Presbyterian-St Luke's Medical Center, Chicago, IL	Q fever: a biological weapon in your backyard.	Lancet Infect Dis. 2003 Nov;3(11):709-21.	Coxiella burnetii, which causes Q fever, is a highly infectious agent that is widespread among livestock around the world. Although the culture process for coxiella is laborious, large amounts of infectious material can be produced. If used as an aerosolised biological weapon, coxiella may not cause high mortality, but could provoke acute disabling disease. In its late course, Q fever can be complicated by fatal (eg, endocarditis) or debilitating (eg, chronic fatigue syndrome) disorders. The diagnosis of Q fever might be delayed because of non-specific and protean presentations. Effective antibiotic treatment is available for the acute form of disease but not for the chronic complications. Vaccination and chemoprophylaxis in selected individuals may be used in the event of bioterrorism.

	60612, USA. migmad@worldnet.att.net			
Matano S, Kinoshita H, Tanigawa K, Terahata S, Sugimoto T.	Department of Hematology, Tonami General Hospital, Tonami, Toyama.	Acute parvovirus B19 infection mimicking chronic fatigue syndrome.	Intern Med. 2003 Sep;42(9):903-5.	A Japanese woman developed prolonged fatigue, neck and shoulder pain, headache, pyrexia, insomnia, anorexia, lymphadenopathy, and diarrhea for two months. She had experienced various stressors before these symptoms developed. Serological test demonstrated that she had acute parvovirus B19 infection. Major depressive disorder was also diagnosed by a psychiatrist. Her symptoms disappeared after administration of selective serotonin reuptake inhibitors and oriental herbs, although human parvovirus B19 viral genome has been present in her serum for nine months. These findings suggest that parvovirus B19 causes clinical features similar to those of chronic fatigue syndrome in cases who have prior life stressors.
McCrone P, Darbishire L, Ridsdale L, Seed P.	Centre for the Economics of Mental Health, Health Services Research Department, Institute of Psychiatry, King's College, London.	The economic cost of chronic fatigue and chronic fatigue syndrome in UK primary care.	Psychol Med. 2003 Feb;33(2):253-61. Comment in: Psychol Med. 2003 Feb;33(2):197-201	BACKGROUND: Chronic fatigue and chronic fatigue syndrome are most often encountered in primary care settings. Given the disabling nature of chronic fatigue it may have a substantial impact on service use and costs as well as on employment. This study estimates this impact. METHOD: Patients presenting to general practitioners with unexplained chronic fatigue were recruited to the study. Service use over a 3 month period was measured and lost employment recorded. These data were used to estimate economic costs. Patients with chronic fatigue syndrome were compared to patients with only chronic fatigue using a multiple regression model with sample differences controlled. RESULTS: The mean total cost of services and lost employment across the sample was Pound Sterling1906 for the 3-month period with formal services accounting for 9.3% of this figure. Service use was higher for patients with chronic fatigue syndrome compared to those with chronic fatigue alone. Total 3-month costs were on average higher for chronic fatigue syndrome (Pound Sterling3515 v. Pound Sterling1176) but when sample differences were taken account of the mean difference was reduced to Pound Sterling1406 (P = 0.086). Over 90% of the cost was accounted for by care provided by friends and family members and by lost employment. Patients with dependants had significantly higher costs than those with none and costs were also significantly higher for greater levels of functional impairment. CONCLUSION: Chronic fatigue imposes substantial economic costs on society, mainly in the form of informal care and lost employment. Treatments need to be developed which recognize these impacts.
McCully KK, Smith S, Rajaei S, Leigh Jr JS, Natelson BH.	Exercise Science, University of Georgia, Athens, GA, USA.	Muscle metabolism with blood flow restriction in chronic fatigue syndrome.	J Appl Physiol. 2003 Oct 24 [Epub ahead of print].	The purpose of this study was to determine if chronic fatigue syndrome (CFS) is associated with reduced blood flow and muscle oxidative metabolism. Patients with CFS according to CDC criteria (n=19) were compared to normal sedentary subjects (n = 11). Muscle blood flow was measured in the femoral artery with Doppler ultrasound after exercise. Muscle metabolism was measured in the medial gastrocnemius muscle using 31P magnetic resonance spectroscopy (MRS). Muscle oxygen saturation and blood volume were measured using near-infrared spectroscopy. CFS and controls were not different in hyperemic blood flow or phosphocreatine recovery rate. Cuff pressures of 50,60,70,80,and 90 mmHg were used to partially restrict blood flow during recovery. All pressures reduced blood flow and oxidative metabolism, with 90 mmHg reducing blood flow by 46% and oxidative metabolism by 30.7% in CFS patients. Hyperemic blood flow during partial

				cuff occlusion was significantly reduced in CFS patients (P < 0.01), and recovery of oxygen saturation was slower (P < 0.05). No differences were seen in the amount of reduction in metabolism with partially reduced blood flow. In conclusion, CFS patients showed evidence of reduced hyperemic flow and reduced oxygen delivery, but no evidence that this impaired muscle metabolism. Thus, CFS patients might have altered control of blood flow, but this is unlikely to influence muscle metabolism. Further, abnormalities in muscle metabolism do not appear to be responsible for the CFS symptoms.
McCully KK, Smith S, Rajaei S, Leigh Jr JS, Natelson BH.	Department of Exercise Science, University of Georgia, 300 River Road, Athens GA 30602, U.S.A.	Blood flow and muscle metabolism in chronic fatigue syndrome.	Clin Sci (Lond). 2003 Jun;104(6):641-7.	The purpose of this study was to determine if chronic fatigue syndrome (CFS) is associated with reduced blood flow and oxidative delivery to skeletal muscle. Patients with CFS according to CDC (Center for Disease Control) criteria (n =19) were compared with normal sedentary subjects (n =11). Muscle blood flow was measured with Doppler ultrasound after cuff ischaemia and exercise. Muscle oxygen delivery was measured as the rate of post-exercise and post-ischaemic oxygen-haem resaturation. Oxygen-haem resaturation was measured in the medial gastrocnemius muscle using continuous wavelength near-IR spectroscopy. Muscle metabolism was measured using (31)P magnetic resonance spectroscopy. CFS patients and controls were not different in the peak blood flow after cuff ischaemia, the rate of recovery of phosphocreatine after submaximal exercise, and the rate of recovery of oxygen saturation after cuff ischaemia. In conclusion, CFS patients showed no deficit in blood flow or oxidative metabolism. This suggests that CFS symptoms do not require abnormal peripheral function.
Moss-Morris R, Chalder T.	Health Psychology, The Faculty of Medical and Health Sciences, The University of Auckland, Private Bag 92 019, Auckland, New Zealand. r.moss-morris@auckland.ac.nz	Illness perceptions and levels of disability in patients with chronic fatigue syndrome and rheumatoid arthritis.	J Psychosom Res. 2003 Oct;55(4):305-8.	OBJECTIVE: To investigate the strength of chronic fatigue syndrome (CFS) patients' negative illness perceptions by comparing illness perceptions and self-reported disability in patients with CFS and rheumatoid arthritis (RA). METHODS: Seventy-four RA patients and 49 CFS patients completed the Illness Perception Questionnaire-Revised and the 36-item Short-Form Health Survey. RESULTS: When compared to the RA group, the CFS group attributed a wider range of everyday somatic symptoms to their illness, perceived the consequences of their illness to be more profound and were more likely to attribute their illness to a virus or immune system dysfunction. Both groups reported equivalent levels of physical disability but the CFS group reported significantly higher levels of role and social disability. CONCLUSION: Although the symptoms of CFS are largely medically unexplained, CFS patients have more negative views about their symptoms and the impact that these have had on their lives than do patients with a clearly defined and potentially disabling medical condition. The data support the cognitive behavioural models of CFS that emphasise the importance of patients' illness perceptions in perpetuating this disorder.
Moss-Morris R, Petrie KJ.	Department of Health Psychology, The University of Auckland, New Zealand.	Experimental evidence for interpretive but not attention biases towards somatic information in patients with chronic	Br J Health Psychol. 2003 May;8(Pt 2):195-208.	OBJECTIVE: This study tested whether CFS patients have an attentional information processing bias for illness-related information and a tendency to interpret ambiguous information in a somatic fashion. DESIGN: 25 patients meeting research criteria for a diagnosis of CFS were compared to 24 healthy matched controls on a modified Stroop task and an ambiguous cues task. METHOD: In the modified Stroop task, participants colour named a series of somatic, depressed and neutral words in order to ascertain whether the somatic words were more distracting to the CFS patients than the depressed and neutral words when compared to controls. In the

		fatigue syndrome.		ambiguous cues task, participants were presented with a tape-recorded list of 30 words including 15 ambiguous illness words (e.g., vein/vain) and 15 unambiguous words. For each word, they were asked to write down the first word that came into their head. A somatic bias score was obtained for each subject by summing the number of somatic responses to the ambiguous word cues. RESULTS: Although CFS patients were significantly slower in colour naming all of the Stroop word categories than controls, there was no evidence for illness or depressed words creating greater interference than neutral words. However, on the ambiguous cues task, CFS patients made significantly more somatic interpretations than controls and this bias was significantly associated with the extent to which they currently reported symptoms. CONCLUSION: CFS patients have an interpretive bias for somatic information which may play a part in the maintenance of the disorder by heightening patients' experience of physical symptoms and helping to maintain their negative illness schemas. Although patients did not show an attentional bias in this study, this may be related to the methodology employed.
Murdoch JC.	School of Primary, Aboriginal and Rural Health Care, Rural Clinical School, University of Western Australia. cmurdoch@rcs.uwa.edu.au	Chronic fatigue syndrome. The patient centred clinical method--a guide for the perplexed.	Aust Fam Physician. 2003 Nov;32(11):883-7.	BACKGROUND: Chronic fatigue states are common in general practice and over the past 20 years there has been considerable worldwide consensus developed on the criteria for chronic fatigue syndrome (CFS) also commonly known as myalgic encephalomyelitis (ME). Chronic fatigue syndrome is an illness characterised by the new onset of disabling fatigue, accompanied by cognitive, musculoskeletal and sleep symptoms. There are no specific diagnostic tests or biological markers and the diagnosis is made by ruling out other causes of fatigue. The pathophysiology of CFS is still unclear. OBJECTIVE: This article discusses the application of the patient centred clinical method to the diagnosis and treatment of CFS. DISCUSSION: There is no new breakthrough in the diagnosis or management of CFS in spite of much research and controversy. There is considerable evidence that the best place to manage CFS is in primary care under the care of the patient's own general practitioner, but it has been suggested that doctors feel unable to deal with the problem. The patient centred clinical method offers a constructive guide to management. The author considers that the best hope for sufferers is self management guided by a supportive and helpful health professional, preferably the patient's own GP.
Murphy BE, Abbott FV, Allison CM, Watts C, Ghadirian AM.	Department of Psychiatry, McGill University, 1033 Pine Avenue West, Montreal, Canada H3A 1A1. bev.murphy@mcgill.ca	Elevated levels of some neuroactive progesterone metabolites, particularly isopregnanolone, in women with chronic fatigue syndrome.	Psychoneuroendocrinology. 2004 Feb;29(2):245-68.	Chronic fatigue syndrome (CFS) is a controversial entity whose cause is unknown. In this study we have explored the possibility that progesterone metabolites may be involved. Plasma levels of the progesterone precursor pregnenolone, progesterone itself, and five ring A-reduced metabolites of progesterone were measured in 20 women with CFS and in 13 age-matched controls. To minimize the contribution of the ovary, women were either post-menopausal or in the follicular phase of the menstrual cycle (day 4-8), and progesterone levels were all well within the expected range (< or = 3.5 nmol/l). Mean values for progesterone and all of its metabolites were higher in CFS patients, the most marked being a 2.3-fold elevation in isopregnanolone (3beta,5alpha-tetrahydroprogesterone; p < or = 0.001). Progesterone levels were correlated with those of its metabolites, but even after controlling for progesterone by ANCOVA, isopregnanolone levels were still elevated (p < or = 0.001). These elevated levels of isopregnanolone could not be attributed to medications (antidepressants and anxiolytics). When the CFS patients were divided into two groups according to their Hamilton depression scale ratings, mean (+/-SD)

				isopregnanolone levels were higher (274+/-160 vs 197+/-119 pmol/l) in the less depressed group (ratings 2-14) than in the more depressed group (ratings 17-28), although this difference did not reach significance. Progesterone levels were negatively correlated with Hamilton depression rating scores (r=-0.56; p<0.01). These results suggest that increases in ring A-reduced progesterone metabolites, particularly isopregnanolone, are associated with CFS, and that the pathophysiology of CFS is unlikely to be due to depression.
Nagelkirk PR, Cook DB, Peckerman A, Kesil W, Sakowski T, Natelson BH, LaManca JJ.	Center for the Study of War-Related Illnesses, Veterans Affairs New Jersey Health Care, East Orange, NJ, USA.	Aerobic capacity of Gulf War veterans with chronic fatigue syndrome.	Mil Med. 2003 Sep;168(9):750-5.	A large overlap exists between the diagnosis of chronic fatigue syndrome (CFS) and the unexplained symptoms reported by many Gulf War veterans (GV). Previous investigations have reported reduced aerobic capacity in civilians with CFS. The present investigation examined metabolic responses to maximal exercise in GVs with CFS compared with healthy GVs. Cardiorespiratory and metabolic responses were recorded during a maximal exercise test on a cycle ergometer. The groups were not different in any demographic category (p > 0.05) or self-reported physical activity (p > 0.05). No differences were observed between groups for maximal oxygen uptake (28.9 +/- 6.7 mL/kg/min for CFS vs. 30.8 +/- 7.1 mL/kg/min for controls; p = 0.39), heart rate (155.8 +/- 16.1 bpm for CFS vs. 163.3 +/- 14.9 bpm for controls; p = 0.17), exercise time (9.6 +/- 1.5 minutes for CFS vs. 10.2 +/- 1.4 minutes for controls; p = 0.26), or workload achieved (208 +/- 36.7 W for CFS vs. 224 +/- 42.9 W for controls; p = 0.25). Likewise, no differences were observed at submaximal intensities (p > 0.05). Compared with healthy controls, GVs who report multiple medically unexplained symptoms and meet criteria for CFS do not show a decreased exercise capacity. Thus, it does not appear that the pathology of the GVs with CFS includes a deficiency with mobilizing the cardiopulmonary system for strenuous physical effort.
Narita M, Nishigami N, Narita N, Yamaguti K, Okado N, Watanabe Y, Kuratsune H.	Institute of Basic Medical Sciences, University of Tsukuba, Tennoudai 1-1-1, Tsukuba, Ibaraki 305-8575, Japan.	Association between serotonin transporter gene polymorphism and chronic fatigue syndrome.	Biochem Biophys Res Commun. 2003 Nov 14;311(2):264-6.	Interaction between the hypothalamo-pituitary-adrenal axis and the serotonergic system is thought to be disrupted in chronic fatigue syndrome (CFS) patients. We examined a serotonin transporter (5-HTT) gene promoter polymorphism, which affects the transcriptional efficiency of 5-HTT, in 78 CFS patients using PCR amplification of the blood genomic DNA. A significant increase of longer (L and XL) alleic variants was found in the CFS patients compared to the controls both by the genotype-wise and the allele-wise analyses (both p<0.05, by chi(2) test and Fisher's exact test). Attenuated concentration of extracellular serotonin due to longer variants may cause higher susceptibility to CFS.
Naschitz JE, Sabo E, Dreyfuss D, Yeshurun D, Rosner I.	Department of Internal Medicine A, Bnai Zion Medical Center, Technion Faculty of Medicine, Haifa, Israel. Naschitz@tx.technion.ac.il	The head-up tilt test in the diagnosis and management of chronic fatigue syndrome.	Isr Med Assoc J. 2003 Nov;5(11):807-11.	
Naschitz JE, Rosner I, Rozenbaum M, Musafia-Priselac R,		Successful treatment of chronic fatigue syndrome with	Clin Exp Rheumatol. 2003 May-Jun;21(3):416-7.	

Sabo E, Gaitini L, Eldar S, Zukerman E, Yeshurun D.		midodrine: a pilot study.		
Naschitz JE, Itzhak R, Shaviv N, Khorshidi I, Sundick S, Isseroff H, Fields M, Priselac RM, Yeshurun D, Sabo E.	Department of Internal Medicine A, Bnai-Zion Medical Center and Bruce Rappaport Faculty of Medicine, Haifa 31048, Israel. Naschitz@tx.technion.ac.il	Assessment of cardiovascular reactivity by fractal and recurrence quantification analysis of heart rate and pulse transit time.	J Hum Hypertens. 2003 Feb;17(2):111-8.	Methods used for the assessment of cardiovascular reactivity are flawed by nonlinear dynamics of the cardiovascular responses to stimuli. In an attempt to address this issue, we utilized a short postural challenge, recorded beat-to-beat heart rate (HR) and pulse transit time (PTT), assessed the data by fractal and recurrence quantification analysis, and processed the obtained variables by multivariate statistics. A 10-min supine phase of the head-up tilt test was followed by recording 600 cardiac cycles on tilt, that is, 5-10 min. Three groups of patients were studied, each including 20 subjects matched for age and gender--healthy subjects, patients with essential hypertension (HT), and patients with chronic fatigue syndrome (CFS). The latter group was studied on account of the well-known dysautonomia of CFS patients, which served as contrast against the cardiovascular reactivity of the healthy population. A total of 52 variables of the HR and PTT were determined in each subject. The multivariate model identified the best predictors for the assessment of reactivity of healthy subjects vs CFS. Based on these predictors, the "Fractal & Recurrence Analysis-based Score" (FRAS) was calculated: FRAS=76.2+0.04*HR-supine-DET -12.9*HR-tilt-R/L -0.31*HR-tilt-s.d. -19.27*PTT-tilt-R/L -9.42*PTT-tilt-WAVE. The median values and IQR of FRAS in the groups were: healthy=-1.85 (IQR 1.89), hypertensives=+0.52 (IQR 5.78), and CFS=-24.2 (5.34) (HT vs healthy subjects: P=0.0036; HT vs CFS: P<0.0001). Since the FRAS differed significantly between the three groups, it appears likely that the FRAS may recognize phenotypes of cardiovascular reactivity.
Naschitz JE, Rosner I, Rozenbaum M, Musafia-Priselac R, Sabo E, Gaitini L, Eldar S, Zukerman E, Yeshurun D.		Successful treatment of chronic fatigue syndrome with midodrine: a pilot study. (letter)	Clin Exp Rheumatol. 2003 May-Jun;21(3):416-7.	
Naschitz JE, Rosner I, Rozenbaum M, Naschitz S, Musafia-Priselac R, Shaviv N, Fields M, Isseroff H, Zuckerman E, Yeshurun D, Sabo E.	Department of Internal Medicine A, Bnai Zion Medical Center, Haifa, Israel. Naschitz@tx.technion.ac.il	The head-up tilt test with haemodynamic instability score in diagnosing chronic fatigue syndrome.	QJM. 2003 Feb;96(2):133-42. Comment in: QJM. 2003 Jun;96(6):454. QJM. 2003 May;96(5):379-80.	BACKGROUND: Studying patients with chronic fatigue syndrome (CFS), we have developed a method that uses a head-up tilt test (HUTT) to estimate BP and HR instability during tilt, expressed as a 'haemodynamic instability score' (HIS). Aim: To assess HIS sensitivity and specificity in the diagnosis of CFS. DESIGN:Prospective controlled study. METHODS: Patients with CFS (n=40), non-CFS chronic fatigue (n=73), fibromyalgia (n=41), neurally mediated syncope (n=58), generalized anxiety disorder (n=28), familial Mediterranean fever (n=50), arterial hypertension (n=28), and healthy subjects (n=59) were evaluated with a standardized head-up tilt test (HUTT). The HIS was calculated from blood pressure (BP) and heart rate (HR) changes during the HUTT. RESULTS: The tilt was prematurely terminated in 22% of CFS patients when postural symptoms occurred and the HIS could not be calculated. In the remainder, the median(IQR) HIS values were: CFS +2.14(4.67), non-CFS fatigue -3.98(5.35), fibromyalgia -2.81(2.62), syncope -3.7(4.36), generalized anxiety disorder -0.21(6.05), healthy controls -2.66(3.14), FMF -5.09(6.41), hypertensives -5.35(2.74) (p<0.0001 vs. CFS in all groups, except for anxiety disorder, p=NS). The

				sensitivity for CFS at HIS >-0.98 cut-off was 90.3% and the overall specificity was 84.5%. DISCUSSION: There is a particular dysautonomia in CFS that differs from dysautonomia in other disorders, characterized by HIS >-0.98. The HIS can reinforce the clinician's diagnosis by providing objective criteria for the assessment of CFS, which until now, could only be subjectively inferred.
Nelsen DA Jr..	Differential diagnosis for chronic fatigue syndrome		Am Fam Physician. 2003 Jan 15;67(2):252; author reply 252. Comment on: Am Fam Physician. 2002 Mar 15;65(6):1083-90.	
Neri S, Pistone G, Saraceno B, Pennisi G, Luca S, Malaguarnera M.	Department of Senescence, Urological and Neurological Sciences, University of Catania, Catania, Italy.	L-carnitine decreases severity and type of fatigue induced by interferon-alpha in the treatment of patients with hepatitis C.	Neuropsychobiology. 2003;47(2):94-7.	BACKGROUND: Hepatitis C virus (HCV) is one of the major agents of chronic hepatitis and liver disease worldwide. Infection with HCV leads to chronic hepatitis in about 80% of the cases. The most used treatment is based on interferon (IFN)-alpha, which is effective in less than 50% of patients; however, a high proportion of responders may relapse after interferon withdrawal. Fatigue is a common complaint in patients with liver disease. The aim of our study was to evaluate the efficacy of carnitine on IFN-induced fatigue in subjects with chronic hepatitis C. PATIENTS AND METHODS: We studied 50 patients (30 males and 20 females) with chronic hepatitis C. Chronic hepatitis was diagnosed by determination of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels (at least 2-fold upper normal values for 1 year). Our study series was divided into two groups and matched as to number, age, sex, as well as grade and duration of disease. Group 1, composed of 25 patients, was treated with leucocytic IFN-alpha at a dosage of 3 million IU thrice a week; group 2 (25 patients) was treated with the same protocol as group 1, but was also administered carnitine 2 g per os daily. Patients' response was evaluated on the basis of serum levels of AST and ALT as well as liver functions; fatigue was evaluated by Wessely and Powell scores. All patients studied were tested before treatment and then 1, 3 and 6 months after the beginning of IFN administration. RESULTS: The difference of physical fatigue between the two groups after 1 month of therapy was significant ($p < 0.01$) for patients treated with carnitine. This significance continued at the end of month 3 ($p < 0.01$). With reference to mental fatigue, the comparison between the two groups showed a significant difference for group 2 after 1 month ($p < 0.01$). Finally, with respect to the fatigue severity, the comparison between the two groups showed that after 1 and 3 months of therapy, fatigue was significantly less severe in group 2 than group 1 ($p < 0.0005$). CONCLUSIONS: If we take into account baseline values of mental and physical fatigue as well as the severity of this symptom in our study series, one observes that therapy with IFN alone induces fatigue in the majority of cases after 1 and 3 months, while at month 6, the values decrease. In contrast, patients treated with IFN + carnitine show a marked and early significant reduction of fatigue levels. These data suggest that the greater energetic substrate utilised by group 2 patients may in some way provide a better response of the patients to this side-effect. Abnormalities of neurotransmission concerning serotonine seem involved in the genesis of depression and fatigue. In addition,

				depression and fatigue commonly occur together, and the former is the most commonly observed symptom in patients with chronic fatigue syndrome. Copyright 2003 S. Karger AG, Basel
Nicolson GL, Gan R, Haier J.	The Institute for Molecular Medicine, Huntington Beach, California 92649, USA. gnicolson@immed.org	Multiple co-infections (Mycoplasma, Chlamydia, human herpes virus-6) in blood of chronic fatigue syndrome patients: association with signs and symptoms.	APMIS. 2003 May;111(5):557-66.	Previously we and others found that a majority of chronic fatigue syndrome (CFS) patients showed evidence of systemic mycoplasmal infections, and their blood tested positive using a polymerase chain reaction assay for at least one of the four following Mycoplasma species: M. fermentans, M. hominis, M. pneumoniae or M. penetrans. Consistent with previous results, patients in the current study (n=200) showed a high prevalence (overall 52%) of mycoplasmal infections. Using forensic polymerase chain reaction we also examined whether these same patients showed evidence of infections with Chlamydia pneumoniae (overall 7.5% positive) and/or active human herpes virus-6 (HHV-6, overall 30.5% positive). Since the presence of one or more infections may predispose patients to other infections, we examined the prevalence of C. pneumoniae and HHV-6 active infections in mycoplasma-positive and -negative patients. Unexpectedly, we found that the incidence of C. pneumoniae or HHV-6 was similar in Mycoplasma-positive and -negative patients, and the converse was also found in active HHV-6-positive and -negative patients. Control subjects (n=100) had low rates of mycoplasmal (6%), active HHV-6 (9%) or chlamydial (1%) infections, and there were no co-infections in control subjects. Differences in bacterial and/or viral infections in CFS patients compared to control subjects were significant. Severity and incidence of patients' signs and symptoms were compared within the above groups. Although there was a tendency for patients with multiple infections to have more severe signs and symptoms ($p<0.01$), the only significant differences found were in the incidence and severity of certain signs and symptoms in patients with multiple co-infections of any type compared to the other groups ($p<0.01$). There was no correlation between the type of co-infection and severity of signs and symptoms. The results indicate that a large subset of CFS patients show evidence of bacterial and/or viral infection(s), and these infections may contribute to the severity of signs and symptoms found in these patients.
Nicolson GL, Nasralla MY, De Meirleir K, Gan R, Haier J		Evidence for Bacterial (Mycoplasma, Chlamydia) and Viral (HHV-6) Co-Infections in Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 2003; 11 (2): 7	Using the blood of 100 CFS patients and forensic polymerase chain reaction we have found that a majority of Chronic Fatigue Syndrome (CFS) patients show evidence of multiple, systemic bacterial and viral infections (OR = 18.0, 95%CL 8.5-37.9, $P < 0.001$) that could play an important role in CFS morbidity. CFS patients had a high prevalence (5)1%) of one of four Mycoplasma species (OR = 13.8, 95%CL 5.8-32.9, $P < 0.001$) and often showed evidence of co-infections with different Mycoplasma species, Chlamydia pneumoniae (OR = 8.6, 95%CL 1.0-71.1, $P < 0.01$) and/or active Human Herpes Virus-6 (HHV-6) (OR = 4.5, 95%CL 2.0-10.2, $P < 0.001$). We found that 8% of the CFS patients showed evidence of C. pneumoniae and 31% of active HHV-6 infections. Since the presence of one or more chronic systemic infections may predispose patients to other infections, we examined the prevalence of C. pneumoniae and active HHV-6 infections in mycoplasma-positive and-negative patients. The incidence of C. pneumoniae or HHV-6 was similar in mycoplasma-positive and-negative patients, suggesting that such infections occur independently in CFS patients. Also, the incidence of C. pneumoniae in active HHV-6-positive and-negative patients was similar. Control subjects (n = 100) had low rates of mycoplasma (6)%), active HHV-6 (9)%) or Chlamydia (1)%) infections, and there were no co-

				infections in control subjects. Differences in bacterial and/or viral infections in CFS patients compared to control subjects were significant. The results indicate that a relatively large subset of CFS patients show evidence of bacterial and viral co-infections.
Nicolson GL, Nasralla MY, Nicolson NL, Haier J		High Prevalence of Mycoplasma Infections in Symptomatic (Chronic Fatigue Syndrome) Family Members of Mycoplasma-Positive Gulf War Illness Patients	Journal of Chronic Fatigue Syndrome 2003; 11 (2): 21	Immediate family members of veterans diagnosed with Gulf War Illnesses (GWI) often complain of fatiguing illnesses, and upon analysis they report similar signs and symptoms as their veteran family members. Since a relatively common finding in Gulf War illness patients is a bacterial infection due to Mycoplasma spp., we examined military families (1)49 patients: 42 veterans, 40 spouses, 32 other relatives and 35 children with at least one family complaint of illness) selected from a group of 110 veterans with Gulf War illness who tested positive (~41%) for at least one of four Mycoplasma spp.: M. fermentans, M. hominis, M. pneumoniae or M. genitalium. Consistent with previous results, over 80% of Gulf War illness patients who were positive for blood mycoplasma infections had only one Mycoplasma spp. (Odds ratio = 9.0, 95%CL 3.3-24.3, P < .0.001), in particular M. fermentans (Odds ratio = 17.9, 95%CL 4.1-78.1, P < .0.001). In healthy control subjects the incidence of mycoplasma infection was ~8.5% and none were found to have multiple mycoplasma species (Multiple species Odds ratio >25, Chi^2 = 8.1, P < .0.004). In 107 family members of mycoplasma-positive Gulf War illness patients there were 57 patients (5)3%) that had essentially the same signs and symptoms as the veterans and were diagnosed with Chronic Fatigue Syndrome (CFS) and/or Fibromyalgia Syndrome. Most of these CFS patients also had mycoplasma infections compared to the few non-symptomatic family members (Odds ratio = 16.9, 95%CL 6.0-47.6, P < .0.001), and the most common species found was M. fermentans (Odds ratio = 40.3, 95%CL 8.7-186.4, P < .0.001). In contrast, in the few non-symptomatic family members that tested mycoplasma-positive, the Mycoplasma spp. were often different from the species found in the Gulf War illness patients. The results suggest that a subset of Gulf War illness patients have mycoplasma infections, possibly obtained as contaminants from multiple vaccines given during deployment, and these infections can be transmitted to immediate family members who subsequently display similar signs and symptoms and are diagnosed with CFS and/or Fibromyalgia Syndrome.
Nicolson GL, Berns P, Nasralla MY, Haier J, Nicolson NL, Nass M.		Gulf War Illnesses: Chemical, Biological and Radiological Exposures Resulting in Chronic Fatiguing Illnesses Can Be Identified and Treated	Journal of Chronic Fatigue Syndrome 2003; 11 (1): 135	Gulf War illnesses involve multiple, complex chronic signs and symptoms that loosely fit the clinical criteria for Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME) and/or Fibromyalgia Syndrome (FMS). Most Gulf War illness patients had multiple exposures: (a) complex chemical mixtures, including organophosphate pesticides, anti-nerve agents, carbamates and possibly nerve and blister agents, (b) radiological sources, subjecting patients to both heavy metal and radiation effects, and (c) biological sources, including bacteria and toxins and the effects of multiple vaccines. Chemically exposed patients may benefit by removing offending chemicals and depleting toxic chemicals from the patient's system and other symptomatic treatments. Patients with systemic infections, including mycoplasma and other chronic bacterial infections, can be treated with antibiotics and additional nutritional supplementation. Some patients may have their illness linked to radiological exposures, and a minority to battlefield stress. The vaccines are a prime suspect for immune dysfunction and chronic infections. The multiple, complex exposures resulted in poorly defined chronic illnesses, but subsets of Gulf War

				illness can be identified and effectively treated using appropriate procedures.
Nijs J, Demanet C, McGregor NR, De Becker P, Verhas M, Englebienne P, De Meirleir K.		Monitoring a Hypothetical Channelopathy in Chronic Fatigue Syndrome: Preliminary Observations	Journal of Chronic Fatigue Syndrome 2003; 11 (1): 117	This study was aimed at monitoring of a previously suggested channelopathy in Chronic Fatigue Syndrome, and at searching for possible explanations by means of immune system characteristics. Twenty-seven CFS patients and 20 age and sex matched healthy volunteers were recruited. RNase L-ratio, percent of the norm of whole body potassium content, serum electrolytes (sodium, calcium and potassium), immune cells, blood cell count and erythrocyte sedimentation rate were determined. More than fifty percent of our patients presented with abnormal whole body potassium content. Eight patients had increased, while six had depleted potassium content. Discriminant function analysis revealed that the CFS patients and control subjects could be differentiated on immunophenotyping with the predominant cell differences being the increase in CD19+ CD5+ (mature B-) cells and the decrease in CD32 CD16+ CD56+ (NK) cells in both the percentage and count distributions. The fall in NK-cells was very strongly associated with increases in the RNase L-ratio and falls in serum calcium levels. In addition, four patients with low serum calcium levels showed lower whole body potassium levels. In conclusion, these observations suggest a channelopathy in a subset of CFS patients, probably induced by the deregulated 2-5A RNase L antiviral pathway.
Nijs J.		Cellular Immunity and Markers of Viral Infection in Monozygotic Twins Discordant for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2003; 11 (2)	
Nijs J, De Becker P, De Meirleir K, Demanet C, Vincken W, Schuermans D, McGregor N.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy, Academic Hospital, Vrije Universiteit Brussel, Belgium. Jo.Nijs@vub.ac.be	Associations between bronchial hyperresponsiveness and immune cell parameters in patients with chronic fatigue syndrome.	Chest. 2003 Apr;123(4):998-1007.	STUDY OBJECTIVE: To examine whether bronchial hyperresponsiveness (BHR) in patients with chronic fatigue syndrome (CFS) is caused by immune system abnormalities. DESIGN: Prospective comparative study. SETTING: A university-based outpatient clinic (Vrije Universiteit; Brussels, Belgium). PARTICIPANTS: One hundred thirty-seven CFS patients and 27 healthy volunteers. MEASUREMENTS: Pulmonary function testing, histamine bronchoprovocation test, immunophenotyping, and ribonuclease (RNase) latent determination. RESULTS: Seventy-three of 137 patients presented with BHR, of whom 64 had normal results of the histamine bronchoprovocation test. No significant differences were found in age or sex characteristics between the groups. There were no differences in the RNase L ratio, total lung capacity, or FEV(1)/FVC ratio between CFS patients with or without BHR. The group of patients in whom BHR was present (BHR+) differs most significantly from the control group with eight differences in the immunophenotype profile in the cell count analysis and seven differences in the percentage distribution profile. The group of patients in whom no BHR was detected (BHR-) only differed from the control subjects in CD25+ count and in the percentage of CD25+ cells. We observed a significant increase in cytotoxic T-cell count and in the percentage of BHR+ patients compared to BHR- patients, which is consistent with the significant reduction in percentage naive T cells. CONCLUSIONS: These results refute any association between the cleaving of 80 kd RNase L and

				BHR. Immunophenotyping of our sample confirmed earlier reports on (chronic) immune activation in patients with CFS, compared to healthy control subjects. BHR+ CFS patients have more evidence of immune activation compared to BHR- patients. Inflammation and the consequent IgE-mediated activation of mast cells and eosinophils, as seen in asthma patients, is unlikely to be responsible for the presence of BHR in patients with CFS.
Nijs J, De Meirleir K, Englebienne P, McGregor N.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussel, Belgium	Chronic fatigue syndrome: a risk factor for osteopenia?	Med Hypotheses. 2003 Jan;60(1):65-8.	No data documenting a possible depletion of bone mineral density in patients with chronic fatigue syndrome (CFS) are currently available. However, recent pathophysiological observations in CFS patients may have deleterious consequences on bone density. Firstly, the deregulation of the 2,5A synthetase RNase L antiviral pathway and its associated channelopathy, implicates increased demands for calcium and consequent increased calcium-re-absorption from the skeletal system. Secondly, Mycoplasma fermentans which has been frequently associated with CFS, produces a lipopeptide, named 2-kDa macrophage-activating lipopeptide (MALP-2), which stimulates macrophages. MALP-2 has been shown to enhance bone resorption in a dose-dependent manner, at least in part by stimulating the formation of prostaglandins. Thirdly, decreased levels of insulin-like growth factor I (IGF-I) have been reported in CFS-patients. IGF-I is critical to the proliferation of osteoblasts. Consequently, depleted levels of IGF-I may shift the balance between osteoclastic and osteoblastic activity towards bone resorption.
Nijs J, Vaes P, McGregor N, Van Hoof E, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Belgium. Jo.Nijs@vub.ac.be	Psychometric properties of the Dutch Chronic Fatigue Syndrome--Activities and Participation Questionnaire (CFS-APQ).	Phys Ther. 2003 May;83(5):444-54.	BACKGROUND AND PURPOSE: The Chronic Fatigue Syndrome-Activities and Participation Questionnaire (CFS-APQ) is a recently developed disease-specific assessment tool for monitoring activity limitations and participation restrictions in patients with chronic fatigue syndrome (CFS). In this study, the convergent validity, content validity, and test-retest reliability of data obtained with the Dutch-language version of the questionnaire were examined. SUBJECTS AND METHODS: One hundred eleven consecutive patients with CFS were enrolled, of whom 47 fulfilled all inclusion criteria. The subjects were first asked to rate their pain, fatigue, and ability to concentrate using 3 visual analog scales, to list at least 5 activities that had become difficult to perform due to their complaints, and to complete the CFS-APQ. Furthermore, subjects were asked to complete a modified version of the CFS-APQ at home and return it to the investigators. The content of the questionnaire was reviewed using the World Health Organization's International Classification of Impairments, Disability and Health (ICIDH) beta II draft. Spearman rank correlation coefficients (R) were used for the convergent validity analysis, and intraclass correlation coefficients were computed for the assessment of the test-retest data. RESULTS: Overall scores on the CFS-APQ correlated with the scores from the visual analog scales for pain (R=.51, P<.001) and fatigue (R=.50, P<.001). The majority of the responses (157 out of 183 answers [85.8%]) to the request to "list difficult activities" matched the content of the CFS-APQ. Using the ICIDH beta II draft, 21 out of 26 questions were found to address activities, and the remaining 5 questions measured the participation level. The Cronbach alpha coefficient was.94, and intraclass correlation coefficients for test-retest reliability of the overall scores were >or= .95 (P<.001). DISCUSSION AND CONCLUSION: The results substantiate the convergent validity, content validity, and reliability of the CFS-APQ scores for patients with CFS.
Nijs J		Melatonin	Journal of Chronic	

		Treatment and Phototherapy in Patients with Chronic Fatigue Syndrome CRITICAL REVIEW AND COMMENT	Fatigue Syndrome 2003; 11 (3): 69-72	
Nijs J		Altered Central Pain Processing in Fibromyalgia	Journal of Chronic Fatigue Syndrome 2003; 11 (3): 72	
Nijs J, De Meirleir K, Coomans D, De Becker P, Nicolson GL		Deregulation of the 2,5A Synthetase RNase L Antiviral Pathway by Mycoplasma spp. in Subsets of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2003; 11 (2): 37	The deregulation of the 2,5A synthetase RNase L antiviral pathway and the prevalence of Mycoplasma spp. in subsets of Chronic Fatigue Syndrome (CFS) have been separately reported in the scientific literature. We hypothesised that a co-morbid pathophysiological mechanism involving infection by Mycoplasma spp. and the deregulation of the 2,5A synthetase/RNase L antiviral pathway may exist in CFS. Therefore, 186 consecutive CFS patients were enrolled. Mycoplasma detection was performed using forensic polymerase chain reaction. For RNase L determination, a radioactive probe was used to label 2,5A binding proteins in unfractionated peripheral blood mononuclear cell extracts. Mycoplasma-infected CFS patients presented with significantly elevated RNase L-ratio, compared to non-infected age- and sex-matched patients (p = 0.016). These results suggest that mycoplasma infections may cause deregulation of the 2,5A synthetase RNase L antiviral pathway in patients with CFS
Nijs J, Coomans D, Nicolson GL, De Becker P, Christian D, De Meirleir K		Immunophenotyping Predictive of Mycoplasma Infection in Patients with Chronic Fatigue Syndrome?	Journal of Chronic Fatigue Syndrome 2003; 11 (2): 51	An impaired immune system and opportunistic infections are considered important characteristics in the pathophysiology of Chronic Fatigue Syndrome (CFS). Using immunofluorescence we examined healthy subjects (N = 35) and two subsets of CFS patients: those without evidence of Mycoplasma (N = 55) and those with evidence of a Mycoplasma infection in their blood (N = 131). Using monoclonal antibodies and forensic polymerase chain reaction for detection of M. hominis, M. fermentans, M. pneumoniae and M. penetrans we examined leukocytes in peripheral blood samples. Both patients groups presented with significantly elevated CD25+ (activated) cells as compared to healthy volunteers. CFS patients without evidence of mycoplasma infection(s) had increased amounts of CD5+ B-cells. Stepwise discriminant analysis indicated the number of activated cells, number of memory CD4+ cells and percentage of suppressor T-cells (lower in Mycoplasma + patients as compared to Mycoplasma2 patients) as the discriminant variables. A classification tree, for predicting the presence of Mycoplasma species in CFS patients, was constructed. Taken together, these data confirm earlier reports on immune activation among CFS patients, but this does not appear to be specific for Mycoplasma-infected CFS patients.
Nisenbaum R, Jones JF, Unger ER, Reyes M, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases,	A population-based study of the clinical course of chronic fatigue syndrome.	Health Qual Life Outcomes. 2003 Oct 3;1(1):49. Epub 2003 Oct 03.	BACKGROUND: Chronic fatigue syndrome (CFS) presents a challenge for patients, health care providers, and health insurance groups because of its incapacitating nature, unknown cause, and poorly understood prognosis. We conducted a longitudinal population-based study to characterize the clinical course of CFS. METHODS: Sixty-five CFS subjects were identified from a

	Centers for Disease Control and Prevention, Atlanta, Georgia, USA. ran7@cdc.gov			random-digit-dialing survey of Wichita, Kansas residents and followed for up to 3 years. We evaluated changes in CFS classification (partial or total remission, alternative medical or psychiatric diagnoses), CFS case-defining criteria, wellness scores, hours of activities and sleep, and treatments used to reduce fatigue. Associations between risk factors and outcomes were determined by use of logistic regression and generalized estimating equations models. RESULTS: Only 20%-33% of the subjects were classified as having CFS at follow-up, 56.9% ever experienced partial or total remission, 10% sustained total remission, and 23.1% received alternative diagnoses, of which 20% were sleep disorders. Higher fatigue severity scores and total number of symptoms were negatively associated with ever remitting. Duration of illness leq; 2 years was positively associated with sustained remission. Unrefreshing sleep persisted in at least 79% of the subjects across all periods but, as with most of the CFS symptoms, tended to be less frequent over time. The number of activities affected by fatigue decreased over time, while wellness scores increased. At any follow-up, more than 35% of subjects reporting reduced fatigue used complementary and alternative medicine therapies, and of those subjects, at least 50% thought these therapies were responsible for reducing their fatigue. CONCLUSIONS: The clinical course of CFS was characterized by an intermittent pattern of relapse and remission. Remission rates documented by our population-based study were similar to those reported in clinical studies. Shorter illness duration was a significant predictor of sustained remission, and thus early detection of CFS is of utmost importance. The persistence of sleep complaints and identification of sleep disorders suggest that CFS subjects be evaluated for sleep disturbances, which could be treated.
Olson LG, Ambrogetti A, Sutherland DC.	Department of Respiratory and Sleep Medicine, John Hunter Hospital, Faculty of Medicine, University of Newcastle, Australia. lolson@mail.newcastle.edu.au	A pilot randomized controlled trial of dexamphetamine in patients with chronic fatigue syndrome.	Psychosomatics. 2003 Jan-Feb;44(1):38-43.	This study determined whether dexamphetamine improved symptoms and quality of life in patients with chronic fatigue syndrome. The setting was a specialized clinic within a tertiary referral hospital. This was a 6-week parallel-group, placebo-controlled trial with random allocation. There was a 2-week dose-adjustment phase and a 4-week stable treatment period. Outcome measures were the Fatigue Severity Scale, the Medical Outcomes Study 36-item Short-Form Health Survey, and two patient-determined outcomes. Ten patients were randomly assigned to dexamphetamine, and 10 were assigned to placebo. Fatigue Severity Scale scores improved in nine of 10 dexamphetamine and four of 10 placebo patients. The change in mean score was statistically significant. There were large but statistically nonsignificant changes in scores for the Short-Form Health Survey domains vitality and physical functioning. Dexamphetamine may be useful in the management of chronic fatigue syndrome; a larger and longer trial is justified by these results.
Patel MX, Smith DG, Chalder T, Wessely S.	Institute of Psychiatry and GKT School of Medicine, De Crespigny Park, London SE5 8AF, UK.	Chronic fatigue syndrome in children: a cross sectional survey.	Arch Dis Child. 2003 Oct;88(10):894-8.	BACKGROUND: Chronic fatigue syndrome (CFS) in children is a controversial diagnosis with unclear aetiology, ill defined but likely increasing incidence, and debatable clinical management options. However these children experience real and considerable suffering. Appropriate research in this clinical population is sparse and usually occurs in tertiary referral units. METHODS: Cross sectional survey of 36 children attending a GP specialist interest clinic in southeast England. RESULTS: Patient sociodemographics and clinical morbidity were largely comparable to the literature from tertiary referral research centres. Some prognostic indicators

				for adults did not readily transfer to this younger age group, although several children had a positive family psychiatric history. Receiving treatment was associated with increased school attendance, but one third of subjects obtained no qualifications. Return to normal health or significant overall improvement was reported by 29/36 subjects. CONCLUSIONS: The outcomes in this setting are favourable and comparable to those seen in a controlled setting; this study supports the concept that the prognosis for CFS in children and adolescents is generally good. However, the impact of the illness is significant and this is perhaps most evident in terms of education. Current methods of reporting educational outcomes in the literature are varied and merit development of standardised tools.
Peckerman A, Dahl K, Chemitiganti R, LaManca JJ, Ottenweller JE, Natelson BH.	VA Medical Center, East Orange, NJ 07018, USA. apeckerm@njneuromed.org	Effects of posttraumatic stress disorder on cardiovascular stress responses in Gulf War veterans with fatiguing illness.	Auton Neurosci. 2003 Oct 31;108(1-2):63-72.	Abnormal cardiovascular stress responses have been reported in Gulf War veterans with chronic fatigue. However, many of these veterans also suffer from posttraumatic stress disorder (PTSD), which could potentially explain the reported abnormalities. To test this hypothesis, 55 Gulf veterans (GVs) with chronic fatigue syndrome (CFS) or idiopathic chronic fatigue (ICF) were stratified into groups with (N=16) and without (N=39) comorbid PTSD, and were compared to healthy Gulf veterans (N=47) on cardiovascular responses to a series of stressors. The CFS/ICF with PTSD group had lower blood pressure responses to speech and arithmetic tasks, and more precipitous declines and slower recoveries in blood pressure after standing up than the controls. Similar trends in the CF/ICF group without PTSD were not significant, however. Both CFS/ICF groups had blunted increases in peripheral vascular resistance during mental tasks. However, only the veterans with comorbid PTSD had diminished cardiac output responses to the mental stressors and excessive vasodilatory responses to standing. Symptoms of posttraumatic stress were significant predictors of hypotensive postural responses, but only in veterans reporting a significant exposure to wartime stress. We conclude that comorbid PTSD contributes to dysregulation of cardiovascular responses to mental and postural stressors in Gulf veterans with medically unexplained fatiguing illness, and may provide a physiological basis for increased somatic complaints in Gulf veterans with symptoms of posttraumatic stress.
Peckerman A, LaManca JJ, Qureishi B, Dahl KA, Golfetti R, Yamamoto Y, Natelson BH.	VA Medical Center, War-Related Illness and Injury Study Center, East Orange, New Jersey 07018, USA. apeckerm@njneuromed.org	Baroreceptor reflex and integrative stress responses in chronic fatigue syndrome.	Psychosom Med. 2003 Sep-Oct;65(5):889-95.	OBJECTIVE: Altered cardiovascular responses to mental and postural stressors have been reported in chronic fatigue syndrome (CFS). This study examined whether those findings may involve changes in baroreceptor reflex functioning. METHODS: Chronotropic baroreceptor reflex (by sequential analysis) and cardiovascular stress responses were recorded during postural (5-minute of active standing) and cognitive (speech task) stress testing in patients with CFS grouped into cases with severe (N = 21) or less severe (N = 22) illness, and in 29 matched control subjects. RESULTS: Patients with CFS had a greater decline in baroreceptor reflex sensitivity (BRS) during standing, although only those with severe CFS were significantly different from the controls. Systolic blood pressure declined during standing in the control group but was maintained in the CFS patients. In contrast, the patients with less severe CFS had blunted increases in blood pressure during the speech task, which could not, however, be explained by inadequate inhibition of the baroreceptor reflex, with all groups showing an appropriate reduction in BRS during the task. CONCLUSIONS: These results indicate that in CFS, deficiencies in orthostatic regulation, but not in centrally mediated stress responses, may involve the baroreceptor reflex.

				This study also suggests that classifying patients with CFS on illness severity may discriminate between patients with abnormalities in peripheral vs. central mechanisms of cardiovascular stress responses.
Peckerman A, LaManca JJ, Dahl KA, Chemitiganti R, Qureishi B, Natelson BH.	Department of Neurosciences, CFS Cooperative Research Center, University of Medicine and Dentistry of New Jersey, Newark, NJ, USA. apeckerm@njneuromed.org	Abnormal impedance cardiography predicts symptom severity in chronic fatigue syndrome.	Am J Med Sci. 2003 Aug;326(2):55-60.	BACKGROUND: Findings indicative of a problem with circulation have been reported in patients with chronic fatigue syndrome (CFS). We examined this possibility by measuring the patient's cardiac output and assessing its relation to presenting symptoms. METHODS: Impedance cardiography and symptom data were collected from 38 patients with CFS grouped into cases with severe (n = 18) and less severe (n = 20) illness and compared with those from 27 matched, sedentary control subjects. RESULTS: The patients with severe CFS had significantly lower stroke volume and cardiac output than the controls and less ill patients. Postexertional fatigue and flu-like symptoms of infection differentiated the patients with severe CFS from those with less severe CFS (88.5% concordance) and were predictive (R2 = 0.46, P < 0.0002) of lower cardiac output. In contrast, neuropsychiatric symptoms showed no specific association with cardiac output. CONCLUSIONS: These results provide a preliminary indication of reduced circulation in patients with severe CFS. Further research is needed to confirm this finding and to define its clinical implications and pathogenetic mechanisms.
Pinching AJ.	Barts and the London, Queen Mary's School of Medicine and Dentistry.	AIDS and CFS/ME: a tale of two syndromes.	Clin Med. 2003 Jan-Feb;3(1):78-82.	Both HIV/AIDS and chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) presented major challenges for medicine, science and society. This article explores what could have impeded investigation of--and specifically pharmaceutical engagement with--CFS/ME, in contrast to the impressive achievements seen in HIV/AIDS. It explores the obstruction of mind-body dualism in a historical context, and examines some of the possible obstacles to pharmaceutical enquiry. Nothing of real substance is identified that would justify the lack of investment and interest in solutions for patients with CFS/ME.
Planz O, Rziha HJ, Stitz L.	Institut fur Immunologie, Bundesforschungsanstalt fur Viruskrankheiten der Tiere, Tubingen. oliver.planz@tue.bfav.de	Genetic relationship of Borna disease virus isolates.	Virus Genes. 2003 Jan;26(1):25-30.	The infection of humans with Boma disease virus (BDV) is still a matter of debate. In a recent publication, we described a BDV (RW98) isolated from the blood of a psychiatric patient. The RNA of this virus differed more than 5% from that of the widely used strain He/80, which was supposed to represent our laboratory virus. Here, we show that the virus used in our laboratory was not He/80 and, furthermore, that RW98 has sequence identity to the laboratory strain. We also present data that BDV-specific nucleic acid detected in blood of the donor of the presumed RW98 isolate and one other patient differs from all known BDV-p24 sequences, arguing for the existence of BDV sequences in man.
Poteliakhoff A.		Adrenal insufficiency.	Lancet. 2003 Aug 16;362(9383):580. Comment on: Lancet. 2003 May 31;361(9372):1881-93.	
Powell R, Ren J, Lewith G, Barclay W, Holgate S, Almond J.	Southampton University Hospital, Southhampton, UK.	Identification of novel expressed sequences, up-	Clin Exp Allergy. 2003 Oct;33(10):1450-6.	BACKGROUND: Chronic fatigue syndrome (CFS) is an increasing medical phenomenon of unknown aetiology leading to high levels of chronic morbidity. Of the many hypotheses that purport to explain this disease, immune system activation, as a central feature, has remained

	rmp2@soton.ac.uk	regulated in the leucocytes of chronic fatigue syndrome patients.		prominent but unsubstantiated. Supporting this, a number of important cytokines have previously been shown to be over-expressed in disease subjects. The diagnosis of CFS is highly problematic since no biological markers specific to this disease have been identified. The discovery of genes relating to this condition is an important goal in seeking to correctly categorize and understand this complex syndrome. OBJECTIVE: The aim of this study was to screen for changes in gene expression in the lymphocytes of CFS patients. METHODS: 'Differential Display' is a method for comparing mRNA populations for the induction or suppression of genes. In this technique, mRNA populations from control and test subjects can be 'displayed' by gel electrophoresis and screened for differing banding patterns. These differences are indicative of altered gene expression between samples, and the genes that correspond to these bands can be cloned and identified. Differential display has been used to compare expression levels between four control subjects and seven CFS patients. RESULTS: Twelve short expressed sequence tags have been identified that were over-expressed in lymphocytes from CFS patients. Two of these correspond to cathepsin C and MAIL1 - genes known to be upregulated in activated lymphocytes. The expression level of seven of the differentially displayed sequences have been verified by quantifying relative level of these transcripts using TAQman quantitative PCR. CONCLUSION: Taken as a whole, the identification of novel gene tags up-regulated in CFS patients adds weight to the idea that CFS is a disease characterized by subtle changes in the immune system.
Prins JB, Elving LD, Koning H, Bleijenberg G, van der Meer JW.	Department of Medical Psychology, University Medical Centre St Radboud, PO Box 9101, 6500 HB Nijmegen, The Netherlands. j.prins@cukz.umcn.nl	Diagnosing chronic fatigue syndrome: comparison of a protocol and computerised questionnaires.	Neth J Med. 2003 Apr;61(4):120-6.	BACKGROUND: In the context of outpatient care and within the framework of scientific research, guidelines and measuring instruments have been developed to help improve CFS diagnostics. The purpose of this study was to measure the agreement between the evaluations of chronically fatigued patients by physicians using a CFS protocol and by researchers using computerised questionnaires. METHODS: The sample consisted of 516 patients referred to an internal medicine outpatient clinic with complaints of chronic fatigue. Retrospectively the medical records and the computerised questionnaires were checked separately and compared to see whether the criteria for diagnosis of CFS had been met. In addition, the reasons for not diagnosing CFS were evaluated. RESULTS: Agreement between the physicians' and the researchers' evaluations was 84%. Disagreement mostly concerned severity of fatigue and functional impairment, or premorbid exclusion criteria. A physical cause for the chronic fatigue was only found in 3% of the cases. CONCLUSIONS: For physicians, questionnaire assessment may be complementary to the CFS protocol in optimising the process of diagnosing CFS.
Rains JC, Penzien DB.	Center for Sleep Evaluation, Elliot Hospital, One Elliot Way, Manchester, NH 03102, USA. jrains@elliot-hs.org	Sleep and chronic pain: challenges to the alpha-EEG sleep pattern as a pain specific sleep anomaly.	J Psychosom Res. 2003 Jan;54(1):77-83.	OBJECTIVE: The alpha-EEG sleep anomaly has been associated with chronic benign pain syndromes. Although controversial, the anomaly is believed by some to be an important biologic correlate of certain otherwise poorly explained painful conditions (e.g., fibromyalgia and chronic fatigue syndrome). To shed further light on this phenomenon, this study compared the sleep and psychological characteristics of chronic pain patients who exhibited the alpha-EEG sleep anomaly with pain-free psychiatric and medical patients who also were found to exhibit the alpha-EEG anomaly. METHODS: The alpha-EEG sleep was identified in the polysomnographic records of 5% of over 1000 consecutive sleep patients. Objective sleep parameters, daytime sleepiness and psychological characteristics (Minnesota Multiphasic Personality Inventory [MMPI] scores) of

				patients exhibiting this anomaly were examined. RESULTS: The alpha-EEG anomaly was identified in only 5% of the total patient sample. Patients with the alpha-EEG anomaly could be further classified into three diagnostic subgroups: chronic pain, psychiatric and other medical/sleep disorders, The subgroups were compared on sleep parameters and psychological characteristics. Less than 40% of the patients exhibiting the alpha-EEG anomaly experienced chronic pain. Chronic pain patients evidenced disturbed sleep patterns and psychological characteristics that were for the most part similar to those observed in some pain-free medical and psychiatric patients. Only the medical subgroup exhibited objective daytime sleepiness. The alpha-EEG sleep disturbance was not accounted for by psychological characteristics. CONCLUSIONS: These findings challenge the notion that alpha-EEG sleep is of direct etiological significance in producing the pain complaint among patients with chronic pain since the alpha-EEG sleep was not a sufficient condition for pain. Copyright 2003 Elsevier Science Inc.
Rangel L, Garralda ME, Hall A, Woodham S.	Academic Unit of Child and Adolescent Psychiatry, Faculty of Medicine, Imperial College at St Mary's Campus, London.	Psychiatric adjustment in chronic fatigue syndrome of childhood and in juvenile idiopathic arthritis.	Psychol Med. 2003 Feb;33(2):289-97. Comment in: Psychol Med. 2003 Feb;33(2):197-201.	BACKGROUND: High rates of psychopathology and of personality problems have been reported in children and adolescents with chronic fatigue syndrome (CFS). It is not clear whether this is consequent on the experience of chronic physical ill health. We compare psychiatric adjustment in children with CFS and in children suffering from another chronic physical disorder (juvenile idiopathic arthritis or JIA). METHOD: Our sample consisted of 28 children with CFS and 30 with JIA attending tertiary paediatric centres (age range, 11 to 18 years, mean 15, S.D. 2.3). In order to assess psychiatric status and functioning, we used the K-SADS psychiatric interviews, CGAS and Harter Self-Esteem Questionnaire with child subjects; behavioural questionnaires (CBCL) and child personality assessment interviews (PAS) with parent informants. RESULTS: Psychiatric disorders in the year prior to interview had been present significantly more commonly in the CFS group (72% v. 34% in JIA) and were more impairing to them (CGAS scores of 45 v. 77). Most common diagnoses in both groups were depressive and anxiety disorders. Personality problems were also significantly more frequent in CFS subjects (48% disorder and 26% difficulty v. 11% and 11% in JIA). There were few differences between the two groups in self-esteem. CONCLUSIONS: Psychopathology and personality problems are common in children and adolescents with severe forms of CFS and cannot be explained strictly through the experience of chronic physical illness.
Razumovsky AY, DeBusk K, Calkins H, Snader S, Lucas KE, Vyas P, Hanley DF, Rowe PC.	Departments of Anesthesiology/Critical Care Medicine, Neurology, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA. arazumov@surgicalmonitoring.net	Cerebral and systemic hemodynamics changes during upright tilt in chronic fatigue syndrome.	J Neuroimaging. 2003 Jan;13(1):57-67.	BACKGROUND AND PURPOSE: During head-up tilt (HUT), patients with chronic fatigue syndrome (CFS) have higher rates of neurally mediated hypotension (NMH) and postural tachycardia syndrome (POTS) than healthy controls. The authors studied whether patients with CFS were also more likely to have abnormal cerebral blood flow velocity (CBFV) compared with controls in response to orthostatic stress. METHODS: Transcranial Doppler monitoring of middle cerebral artery (MCA) CBFV was performed during 3-stage HUT prospectively in 26 patients with CFS and 23 healthy controls. At the same time, continuous monitoring of arterial blood pressure (BP), heart rate (HR), endtidal CO2 (ET-CO2) were performed. Results are reported as mean +/- SD. RESULTS: NMH developed in 21 patients with CFS and in 14 controls (P = .22). POTS was present in 9 CFS patients and 7 controls (P = .76). Supine HR was higher in CFS patients, but all other hemodynamics and CBFV measures were similar at baseline. The median time to hypotension did not differ, but the median time to onset of orthostatic symptoms was shorter in those with CFS (P

				< .001). The CBFV did not differ between groups in the supine posture, at 1 or 5 minutes after upright tilt, at 5 or 1 minute before the end of the test, or at termination of the test. Mean CBFV fell at termination of tilt testing in those with CFS and controls. ET-CO2 was lower at termination of the test in those with CFS versus controls (P = .002). CONCLUSIONS: The results of this study are not consistent with the hypothesis that patients with CFS have a distinctive pattern of MCA CBFV changes in response to orthostatic stress.
Reid S, Chalder T, Cleare A, Hotopf M, Wessely S.	St Mary's Hospital, London, UK.	Chronic fatigue syndrome.	Clin Evid. 2003 Jun;(9):1172-85.	
Renan MJ.	Division of Medical Microbiology, Health Sciences Faculty, University of Cape Town, South Africa.	Is hypercortisolaemia a factor in chronic fatigue syndrome?	Horm Metab Res. 2003 Apr;35(4):201-3.	
Reyes M, Nisenbaum R, Hoaglin DC, Unger ER, Emmons C, Randall B, Stewart JA, Abbey S, Jones JF, Gantz N, Minden S, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Public Health Service, US Department of Health and Human Services, Atlanta, GA 30333, USA.	Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas.	Arch Intern Med. 2003 Jul 14;163(13):1530-6.	BACKGROUND: Chronic fatigue syndrome (CFS) is a debilitating illness with no known cause or effective therapy. Population-based epidemiologic data on CFS prevalence and incidence are critical to put CFS in a realistic context for public health officials and others responsible for allocating resources and for practicing physicians when examining and caring for patients. METHODS: We conducted a random digit-dialing survey and clinical examination to estimate the prevalence of CFS in the general population of Wichita, Kan, and a 1-year follow-up telephone interview and clinical examination to estimate the incidence of CFS. The survey included 33 997 households representing 90 316 residents. This report focuses on 7162 respondents aged 18 to 69 years. Fatigued (n = 3528) and randomly selected nonfatigued (n = 3634) respondents completed telephone questionnaires concerning fatigue, other symptoms, and medical history. The clinical examination included the Diagnostic Interview Schedule for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, laboratory testing, and a physical examination. RESULTS: The overall weighted point prevalence of CFS, adjusted for nonresponse, was 235 per 100,000 persons (95% confidence interval, 142-327 per 100,000 persons). The prevalence of CFS was higher among women, 373 per 100,000 persons (95% confidence interval, 210-536 per 100,000 persons), than among men, 83 per 100,000 persons (95% confidence interval, 15-150 per 100,000 persons). Among subjects nonfatigued and fatigued for less than 6 months, the 1-year incidence of CFS was 180 per 100,000 persons (95% confidence interval, 0-466 per 100,000 persons). CONCLUSIONS: Chronic fatigue syndrome constitutes a major public health problem. Longitudinal follow-up of this cohort will be used to further evaluate the natural history of this illness.
Sabin TD.	Department of Neurology, Tufts University School of Medicine and New	An approach to chronic fatigue syndrome in adults.	Neurolog. 2003 Jan;9(1):28-34.	BACKGROUND: The neurologist is often asked to evaluate patients with a chief complaint of fatigue. Many neurologists do not believe in the pathologically based disease known as chronic fatigue syndrome, yet as a group, neurologists are well suited to guide the diagnostic work up of such patients to pinpoint treatable disorders in the realm of neurology, general medicine, and

	England Medical Center, Boston, Massachusetts. E-mail: tsabin@lifespan.org			psychiatry. REVIEW SUMMARY: Every patient should be carefully evaluated for certain medical, psychiatric, and neurologic disease that can cause fatigue as the most prominent symptom. This is most pressing because new work in virology, immunology, and imaging holds promise but still does not provide any diagnostic test or a mechanism for the production of these symptoms. Only a few treatments meet with even modest success in CFS. The goal of this paper is to provide the clinical neurologist with a framework for the investigation and management of this challenging group of patients. CONCLUSIONS: Neurologists are typically also trained in psychiatry and general medicine, and this is a strong position to evaluate the patient with fatigue. Because no presently available test can make the diagnosis of CFS, the assessment is vital to seek out more treatable illnesses.
Schaefer KM.	Department of Nursing, Temple University-CAHP, Philadelphia, Pa 19140, USA. karen.schaefer@temple.edu	Sleep disturbances linked to fibromyalgia.	Holist Nurs Pract. 2003 May-Jun;17(3):120-7.	Fibromyalgia (FM) is a chronic muscle disorder characterized by muscle aches and pain of varying intensities. Sleep disturbances have been recognized as one of the probable causes of this disorder. Pharmacological and nonpharmacological approaches are often used to manage the symptoms of sleep disturbances. This article provides a brief background on FM, discusses the physiology of sleep, reviews the current literature on sleep disturbances associated with FM, provides insight to interventions that might be beneficial given the data available, and recommends ongoing research.
Schmaling KB, Lewis DH, Fiedelak JI, Mahurin R, Buchwald DS. University of Washington, Seattle.	College of Health Sciences (K.B.S.), University of Texas, El Paso, Texas, and the Departments of Psychiatry and Behavioral Sciences (K.B.S., R.M.), Radiology (D.H.L.), and Medicine (J.I.F., D.S.B.),	Single-photon emission computerized tomography and neurocognitive function in patients with chronic fatigue syndrome.	Psychosom Med. 2003 Jan-Feb;65(1):129-36.	OBJECTIVE: The purposes of this study were to compare functional imaging under control and experimental conditions among patients with chronic fatigue syndrome (CFS) and healthy persons and to examine perceived and objective performance on a test of attention and working memory previously found to be difficult for persons with CFS. METHODS: Single-photon emission computerized tomography scans were completed on 15 subjects with CFS and 15 healthy persons twice: at rest and when performing the Paced Auditory Serial Addition Test (PASAT). RESULTS: No group differences were found for performance on the PASAT despite CFS subjects' perceptions of exerting more mental effort to perform the task than healthy subjects. Inspection of the aggregate scans by group and task suggested a pattern of diffuse regional cerebral blood flow among subjects with CFS in comparison with the more focal pattern of regional cerebral blood flow seen among healthy subjects. Between-group region-of-interest analysis revealed that although CFS subjects showed less perfusion in the anterior cingulate region, the change in CFS subjects' activation of the left anterior cingulate region during the PASAT was greater than that observed for healthy subjects. The differences were not attributable to lesser effort by the subjects with CFS, confounding effects of mood perturbation, or to poorer performance on the experimental task. CONCLUSIONS: Further research regarding CFS subjects' diffuse cerebral perfusion and its relationship to inefficient neuropsychological performance is warranted.
Schmaling KB, Fiedelak JI, Katon WJ, Bader JO, Buchwald DS.	Office of the Provost, University of Texas at El Paso, El Paso, TX 79968, USA. schmaling@utep.edu	Prospective study of the prognosis of unexplained chronic fatigue in a clinic-based cohort.	Psychosom Med. 2003 Nov-Dec;65(6):1047-54.	OBJECTIVES: To determine prospective changes in clinical status related to chronic fatigue over an 18-month period, and to test demographic and clinical predictors of outcome. METHODS: A cohort of 100 patients with unexplained chronic fatigue (UCF), which encompasses both chronic fatigue syndrome (CFS) and idiopathic chronic fatigue (ICF), completed questionnaire measures and medical and psychiatric evaluations on four occasions, each six months apart. RESULTS: Approximately 21% of the sample did not meet criteria for either CFS or ICF at their last research

				appointment 1.5 years after their index visit. Vitality increased over time, and physical functioning tended to improve, but UCF symptoms did not decrease significantly. Less education, being unemployed, worse mental health, more use of sedating and antidepressant medications, and more somatic attributions for their symptoms were associated with worsening symptom severity over time. Older age, current depression, and more somatic attributions predicted worsening physical functioning. Better mental health, less use of sedating medications, and fewer somatic attributions for illness were significant predictors of increases in vitality. CONCLUSIONS: Demographic and clinical variables predict outcomes over time among a cohort of patients with unexplained chronic fatigue.
Shapiro B.	barbarashapiro@earthlink.net	Building bridges between body and mind: The analysis of an adolescent with paralyzing chronic pain.	Int J Psychoanal. 2003 Jun;84(Pt 3):547-61.	This paper describes the evaluation, initial psychotherapy and subsequent psychoanalysis of an adolescent who presented with a severe psychosomatic process involving total body pain and profound fatigue. The author details the complex and multifaceted nature of the psychosomatic process as it unfolded in the treatment. The psychosomatic problem was not a single entity, but rather was comprised of diverse interwoven elements such as somatization, conversion on pre-oedipal and oedipal levels, conflicts over aggression, sexuality, identity, masochism, secondary gain, anaclitic depression, internalized self-other interactions with a depressed mother and transgenerational transmission of trauma. The author uses the case material to discuss technical approaches to problems that often arise in the analytic treatment of patients with complicated chronic pain and fatigue as the primary complaints. Such approaches include respecting the mind-body split as a primary defense, speaking the language of the body along with the language of the mind and developing the verbal sphere around the non-verbal symptoms. The author emphasizes that complicated chronic pain problems are common and can be helped by psychoanalysis as long as the unique and complex features are understood and reflected in the technical approach.
Shee CD.	Department of Medicine, Queen Mary's Sidcup NHS Trust, Kent, UK. charles.shee@qms-tr.sthames.nhs.uk	Phantom lymphadenopathy. An association with chronic fatigue syndrome.	Postgrad Med J. 2003 Jan;79(927):59-60. Comment in: Postgrad Med J. 2003 Mar;79(929):185.	Ten patients with self diagnosed enlarged lymph glands were referred to a general medicine outpatient clinic and careful examination did not confirm lymphadenopathy. All patients also complained of severe chronic fatigue associated with aches and miscellaneous somatic symptoms, and fulfilled criteria for diagnosis of chronic fatigue syndrome (CFS). Phantom lymphadenopathy may be a symptom in some people with CFS, and possible reasons for this are discussed.
Shin HY, Shin CH, Shin TY, Lee EJ, Kim HM.	Department of Pharmacology, College of Oriental Medicine, Kyung Hee University, Dongdaemun-Gu, Seoul, South Korea.	Effect of bojungikki-tang on lipopolysaccharide-induced cytokine production from peripheral blood mononuclear cells of chronic fatigue syndrome patients.	Immunopharmacol Immunotoxicol. 2003 Nov;25(4):491-501.	Bojungikki-tang (BIT) has been widely used to treat patients suffering from chronic fatigue syndrome (CFS). However, its effect has not been yet investigated experimentally. Based upon the clinical presentation of CFS, we hypothesized that cytokines may play a role in the pathogenesis of the disease. We studied the effect of BIT on lipopolysaccharide (LPS)-induced various cytokines production in peripheral blood mononuclear cells (PBMC) of CFS patients. Bojungikki-tang (1 mg/mL) significantly inhibited LPS-induced tumor necrosis factor (TNF)-alpha, interleukin (IL)-6, IL-10, transforming growth factor (TGF)-beta1 production by 63.55% +/- 0.19%, 55.06% +/- 0.27%, 48.23% +/- 0.48%, 54.09% +/- 0.76%, respectively ($P < 0.05$). Bojungikki-tang showed a slightly lower inhibitory effect of LPS-induced Interferon (IFN)-gamma production. These results suggest that BIT may be useful in treating fatigue associated with chronic diseases.

Shor S		Pathogenesis of Chronic Fatigue Syndrome, a Multisystem Hypothesis	Journal of Chronic Fatigue Syndrome 2003; 11 (3): 51-69	Fatigue is a very common complaint with a number of meanings. If the fatigue lasts for more than 6 months, it fulfills the definition of "chronic." The Center for Disease Control (CDC) has established specific criteria for the diagnosis of CFS. This is characterized by a persistent or relapsing debilitating fatigue for at least 6 months in the absence of a medical diagnosis that would otherwise explain the clinical presentation. CFS represents a heterogeneous group of patients that manifest symptom complexes with varying degrees of fatigue, limited exertional reserve and cognitive dysfunction. This treatise explores the pathogenesis of CFS as it relates to a complex multidimensional systemic process and offers a hypothesis for the disease processes. In particular, an up-regulated immune system, affecting mitochondrial dysfunction is described. These pathophysiologic mechanisms impact and in turn are being impacted by the neuroendocrine system and the HPA axis. In addition, the cardiovascular system involving blood pressure and heart rate anomalies along with neurocognitive pathology is characterized.
Siegmeth W.	Ludwig-Boltzmann-Forschungsstelle fur Epidemiologie rheumatischer Erkrankungen, Rheuma-Sonderkrankenanstalt der No. Gebietskrankenkasse, Baden. rska-med@noegkk.sozvers.at	[Article in German]	Wien Med Wochenschr. 2003;153(13-14):309-13.	Nowadays, fibromyalgia syndrome (FMS) should be diagnosed according to established criteria in order to differentiate it from other specified or unspecified pain conditions. Various underlying reasons for pain exist and possible correlations with FMS should be thoroughly discussed with the patient. Recent pathophysiological examinations suggest that fibromyalgia syndrome may constitute a disorder of the central nervous system, especially of the hypothalamus-hypophysis-axis, and/or of the autonomous nervous system and of pain regulating nerves. The most common co-morbidity comprises sleep disturbances. The patients' complaints usually prevail over a long period of time. There is a variety of trigger factors for the development of fibromyalgia syndrome, which leads to the suggestion that a number of fibromyalgia-syndrome subgroups exist. A genetic disposition is a topic of ongoing discussion. Treatment of fibromyalgia syndrome should be multidisciplinary. Drug therapy is often disappointing. Extensive patient information, therapeutic devotion and means of physical therapy seem to be more efficient, providing a multitude of therapeutic options. Both fibromyalgia syndrome and chronic fatigue syndrome have to be accepted as medical entities, treated efficiently and studied scientifically. By these means, patients suffering from fibromyalgia syndrome, will not be lost to non-established forms of therapy.
Siessmeier T, Nix WA, Hardt J, Schreckenberger M, Egle UT, Bartenstein P.	Department of Nuclear Medicine, Johannes Gutenberg University, Mainz, Germany. siessmeier@nuklear.klinik.uni-mainz.de	Observer independent analysis of cerebral glucose metabolism in patients with chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry. 2003 Jul;74(7):922-8.	OBJECTIVES: To evaluate cerebral glucose metabolism, assessed by 18-fluorodeoxyglucose positron emission tomography (FDG-PET), in patients with chronic fatigue syndrome (CFS), using an observer independent analytical approach; and to characterise any observed alterations by correlating them with neuropsychological deficits. METHODS: 26 patients (13 female, 13 male) were examined. They all fulfilled the CDC diagnostic criteria for CFS. Their ages ranged from 26 to 61 years (mean (SD) age, 43 (9.3) years). They underwent extensive psychometric testing including the hospital anxiety and depression scale (HADS) and the short form 36 item health questionnaire (SF-36). Brain FDG-PET was done in all the subjects. After stereotactic normalisation, single subject comparisons with an age and sex matched normal database (n = 18) and a group comparison between the patients and normal controls were undertaken, along with additional correlation analyses between brain metabolism and psychometric test scores. RESULTS: 12 of the 26 patients showed no significant decrease in FDG uptake compared with the

				controls. Of the remaining 14, 12 showed hypometabolism bilaterally in the cingulate gyrus and the adjacent mesial cortical areas. Five of these 12 patients also had decreased metabolism in the orbitofrontal cortex. The two remaining patients had hypometabolism in the cuneus/praecuneus. Correlation analyses showed significant correlations between some test scores (anxiety, depression, health related quality of life) but not fatigue and regional reductions in glucose metabolism. CONCLUSIONS: Although abnormalities in FDG-PET were only detectable in approximately half the CFS patients examined, and no specific pattern for CFS could be identified, PET may provide valuable information in helping to separate CFS patients into subpopulations with and without apparent alterations in the central nervous system.
Skapinakis P, Lewis G, Mavreas V.	Department of Psychiatry, University of Bristol, Cotham Hill, UK. p.skapinakis@bristol.ac.uk	Unexplained fatigue syndromes in a multinational primary care sample: specificity of definition and prevalence and distinctiveness from depression and generalized anxiety.	Am J Psychiatry. 2003 Apr;160(4):785-7.	OBJECTIVE: The authors investigated whether narrow definitions of unexplained fatigue syndromes that require additional minor somatic symptoms are more strongly associated with psychiatric morbidity than wider ones. METHOD: This was a secondary analysis of the World Health Organization Collaborative Project on Psychological Problems in General Health Care. A total of 5,438 primary care patients from 14 countries were assessed with the Composite International Diagnostic Interview. RESULTS: The prevalence of fatigue syndromes fell from 7.99 to 1.69 as somatic criteria were added. Patients with depression or anxiety were more likely to report unexplained fatigue, but this association was stronger for definitions of unexplained fatigue with more somatic criteria. CONCLUSIONS: Definitions of unexplained fatigue syndromes that require more somatic criteria selected more patients with psychiatric disorders in this culturally diverse sample. These findings might have implications for the revision of existing international diagnostic criteria for neurasthenia or chronic fatigue syndrome.
Skapinakis P, Lewis G, Mavreas V.	Department of Psychiatry, University of Bristol, Cotham Hill.	One-year outcome of unexplained fatigue syndromes in primary care: results from an international study.	Psychol Med. 2003 Jul;33(5):857-66.	BACKGROUND: Outcome studies of chronic fatigue, neurasthenia and other unexplained fatigue syndromes are few and have been carried out in developed Western countries. This paper aimed to study the outcome of unexplained fatigue syndromes in an international primary care sample and to identify risk factors for persistence. METHOD: We used data from the WHO collaborative study of psychological problems in general health care, in which 3201 primary care attenders from 14 countries were followed-up for 12 months. The assessment included a modified version of the Composite International Diagnostic Interview. RESULTS: Unexplained fatigue persisted in one-fifth to one-third of the subjects depending on the definition of fatigue. From the factors studied only severity of fatigue and psychiatric morbidity at baseline were associated with persistence 12 months later. Outcome did not differ between countries of different stages of economic development. CONCLUSIONS: The prognosis of fatigue syndromes in international primary care is relatively good. The study underlines the importance of psychological factors in influencing short-term prognosis.
Smirnova IV, Pall ML.	Department of Medicine, Division of Nephrology, New York Medical College, Valhalla, NY, USA.	Elevated levels of protein carbonyls in sera of chronic fatigue syndrome patients.	Mol Cell Biochem. 2003 Jun;248(1-2):93-5.	Protein carbonyl levels, a measure of protein oxidation, were found to be significantly elevated ($p < 0.0005$) in the sera of chronic fatigue syndrome (CFS) patients vs. controls. In contrast, the total protein levels in sera CFS patients were unchanged from those of controls. The elevated protein carbonyl levels confirm earlier reports suggesting that oxidative stress is associated with chronic fatigue syndrome and are consistent with a prediction of the elevated nitric oxide/peroxynitrite theory of chronic fatigue syndrome and related conditions.

Smith MS, Martin-Herz SP, Womack WM, Marsigan JL.	Children's Hospital & Regional Medical Center, Department of Pediatrics, University of Washington, Seattle 98105, USA. mark.smith@seattlechildrens.org	Comparative study of anxiety, depression, somatization, functional disability, and illness attribution in adolescents with chronic fatigue or migraine.	Pediatrics. 2003 Apr;111(4 Pt 1):e376-81.	OBJECTIVE: To compare adolescents with migraine, unexplained profound chronic fatigue of >6 months duration, and normal school controls on measures of anxiety, depression, somatization, functional disability, and illness attribution. METHODS: Adolescents referred to Children's Hospital and Regional Medical Center for behavioral treatment of migraine (n = 179) or evaluation of chronic fatigue (n = 97) were compared with a group of healthy controls of similar age and sex from a middle school (n = 32). Subjects completed the Spielberger State-Trait Anxiety Inventory-Trait Form, the Children's Depression Inventory, the Childhood Somatization Inventory, and estimated the number of school days missed in the past 6 months because of illness. Migraine and fatigued subjects completed an illness attribution questionnaire. RESULTS: Subjects in the 3 groups were 56% to 70% female and ranged from 11 years old to 18 years old with a mean age of 14.0 +/- 2.0. Forty-six of the 97 chronically fatigued adolescents met 1994 Centers for Disease Control and Prevention (CDC) criteria for chronic fatigue syndrome (CDC-CFS), while 51 had idiopathic chronic fatigue syndrome (I-CFS) that did not meet full CDC criteria. Adolescents with migraine had significantly higher anxiety scores than those with I-CFS or controls and higher somatization scores than controls. Adolescents with CDC-CFS had significantly higher anxiety scores than those with I-CFS or controls, and higher depression and somatization scores than all other groups. There were significant differences between all groups for school days missed with CDC-CFS more than I-CFS more than migraine more than controls. Parents of adolescents with unexplained I-CFS had significantly lower attribution scores relating illness to possible psychological or stress factors than parents of adolescents with CDC-CFS or migraine. CONCLUSIONS: Adolescents referred to an academic center for evaluation of unexplained chronic fatigue had greater rates of school absenteeism than adolescents with migraine or healthy controls. Those meeting CDC-CFS criteria had higher anxiety scores than controls and higher depression and somatization scores than migraineurs or controls. Parents of adolescents with I-CFS were less likely to endorse psychological factors as possibly contributing to their symptoms than parents of adolescents with CDC-CFS or migraine.
Smith S, Sullivan K.	University of Queensland, Australia; Karen Sullivan, Queensland University of Technology, Australia, ssmith@psy.uq.edu.a	Examining the influence of biological and psychological factors on cognitive performance in chronic fatigue syndrome: a randomized, double-blind, placebo-controlled, crossover study.	Int J Behav Med. 2003;10(2):162-73.	The pathophysiology of chronic fatigue syndrome (CFS) remains unclear; however, both biological and psychological factors have been implicated in establishing or maintaining this condition. People with CFS report significant and disabling cognitive difficulties such as impaired concentration that in some cases are exacerbated by exposure to chemical triggers. The aim of this study was to determine if neuropsychological deficits in CFS are triggered by exposure to chemicals, or perceptions about the properties of these substances. Participants were 36 people with a primary diagnosis of CFS, defined according to Centers for Disease Control (CDC) criteria. A randomized, double-blind, placebo-controlled, crossover design was used, with objective assessment of neuropsychological function and participant rating of substance type, before and after exposure to placebo or chemical trigger. Results showed decrements in neuropsychological tests scores on three out of four outcome measures when participants rated the substance they had been exposed to as "chemical." No change in performance was found based on actual substance type. These results suggest that cognitive attributions about exposure substances in people with CFS may be associated with worse performance on neuropsychological tasks. In

				addition, these findings suggest that psychological interventions aimed at modifying substance-related cognitions may reduce some symptoms of CFS.
Solomon L, Nisenbaum R, Reyes M, Papanicolaou DA, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA. wcr1@cdc.gov	Functional status of persons with chronic fatigue syndrome in the Wichita, Kansas, population.	Health Qual Life Outcomes. 2003 Oct 3;1(1):48. Epub 2003 Oct 03.	BACKGROUND: Scant research has adequately addressed the impact of chronic fatigue syndrome on patients' daily activities and quality of life. Enumerating specific problems related to quality of life in chronic fatigue syndrome patients can help us to better understand and manage this illness. This study addresses issues of functional status in persons with chronic fatigue syndrome and other fatiguing illnesses in a population based sample, which can be generalized to all persons with chronic fatigue. METHODS: We conducted a random telephone survey in Wichita, Kansas to identify persons with chronic fatigue syndrome and other fatiguing illnesses. Respondents reporting severe fatigue of at least 1 month's duration and randomly selected non-fatigued respondents were asked to participate in a detailed telephone interview. Participants were asked about symptoms, medical and psychiatric illnesses, and about physical, social, and recreational functioning. Those meeting the 1994 chronic fatigue syndrome case definition, as determined on the basis of their telephone responses, were invited for clinical evaluation to confirm a diagnosis of chronic fatigue syndrome. For this analysis, we evaluated unemployment due to fatigue, number of hours per week spent on work, chores, and other activities (currently and prior to the onset of fatigue), and energy level. RESULTS: There was no difference between persons with chronic fatigue syndrome and persons with a chronic fatigue syndrome-like illness that could be explained by a medical or psychiatric condition for any of the outcomes we measured except for unemployment due to fatigue (15% vs. 40%, P <.01). Persons with chronic fatigue syndrome and other fatiguing illnesses had substantially less energy and spent less time on hobbies, schooling, or volunteer work than did non-fatigued controls (P <.01). CONCLUSIONS: Persons with chronic fatigue syndrome are as impaired as persons whose fatigue could be explained by a medical or psychiatric condition, and they have less energy than non-fatigued controls.
Sorensen B, Streib JE, Strand M, Make B, Giclas PC, Fleshner M, Jones JF.	Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO, USA.	Complement activation in a model of chronic fatigue syndrome.	J Allergy Clin Immunol. 2003 Aug;112(2):397-403.	BACKGROUND: A need exists to identify biological markers in chronic fatigue syndrome (CFS). OBJECTIVE: To use an exercise and/or allergen challenge to induce the symptoms of CFS and to identify a biological marker that correlates with these symptoms. METHODS: Patients with CFS (n = 32) and age-matched, normal control patients (n = 29) exercised for 20 minutes on a stationary bike at 70% of their predicted max work load (Watts). Patients from each group with positive skin test results were also challenged with intranasally administered relevant allergens. Symptoms were recorded for 2 weeks before and 1 week after each challenge, using 3 different instruments. Blood samples were taken before, and 0, 1, 6, and 24 hours after challenges. Levels of complement split products, cell-associated cytokines, and eosinophilic cationic protein were measured. Mean preexercise and postexercise symptom scores were evaluated for each group. RESULTS: Exercise challenge induced significant increases of the complement split product C4a, but not C3a or C5a, at 6 hours after exercise only in the CFS group (P <.01), regardless of allergy status. Mean symptom scores were significantly increased after exercise through the use of a daily diary (P <.03) and a weekly diary (P <.01) for the CFS group only. Mean scores for the

				Multidimensional Fatigue Inventory categories "reduced activity" and "mental fatigue" were significantly increased in the CFS group only (P <.04 and P <.02, respectively). CONCLUSIONS: Exercise challenge may be a valuable tool in the development of diagnostic criteria and tests for CFS. Establishment of a role for complement activation products as markers or participants in production of illness require further study.
Stenager EN, Svendsen MA, Stenager E.	Syddansk Universitet, Institut for Sundhedstjenesteforskning, Den Sociale Ankestyrelse, Kobenhavn.	[Disability retirement pension for patients with syndrome diagnoses. A registry study on the basis of data from the Social Appeal Board] [Article in Danish]	Ugeskr Laeger. 2003 Jan 27;165(5):469-74.	INTRODUCTION: Since the early 1990s, disability retirement pension may be granted on the basis of a syndrome diagnosis. Before the pension can be granted, local public authorities collect information on health and social matters and report to The Social Appeal Board. In 1998, a new diagnostic tool was introduced based on the International Statistical Classification of Diseases and Related Health Problems (ICD-10) diagnoses. The information available in The Social Appeal Board has made it possible to study the social consequences of a syndrome diagnosis. The purpose of the study was: 1) To estimate the incidence of patients granted disability retirement pension with the diagnoses whiplash, fibromyalgia, chronic pain disorder, chronic fatigue syndromee, chronic strain syndromee, and pelvic syndromee. 2) To estimate changes in the level of pension granted to patients with syndromee diagnosis. 3) To compare differences between patients with syndromee diagnosis granted disability retirement pension to patients with other diagnoses on the following parameters: sex, civil status, income when applying for pension, and attempts of rehabilitation. 4) To estimate comorbidity of psychiatric diagnosis in patients with syndromee diagnosis. MATERIAL AND METHODS: A register study of data on pension reported to The National Social Appeal Board in the period July 1st 1998 to December 31st, 2000. RESULTS: Of all patients granted pension in the period 8.3 per cent had a syndromee diagnosis, 11 per cent of the women and 5 per cent of the men. Both the relative and the absolute number of patients with syndromee diagnosis granted a pension were increasing. Comorbidity of psychiatric disorders was 3 per cent in the group with syndromee diagnosis. More patients with syndromee diagnosis than with other diagnoses had received sickness benefits and rehabilitation when pension was granted. DISCUSSION: The large number of patients with syndromee diagnosis granted pension calls for multidisciplinary prophylactic and treatment initiatives in order to reduce the number of patients in need of public support. The results are discussed in view of the new Pension's Act which will become effective as from January 1st, 2003.
Stewart CC, Cookfair DL, Hovey KM, Wende KE, Bell DS, Warner CL.	Laboratory of Flow Cytometry, Roswell Park Cancer Institute, Buffalo, New York.	Predictive immunophenotypes: Disease-related profile in chronic fatigue syndrome.	Cytometry. 2003 May;53B(1):26-33.	BACKGROUND: There is a growing body of evidence supporting the theory that problems with immune function play an important role in chronic fatigue syndrome (CFS). METHODS: We studied 90 CFS cases and 50 healthy controls from two different areas of upstate New York to determine whether there were differences in the absolute number and pattern of natural killer (NK) and cytotoxic T-cell phenotypes between CFS cases and healthy controls in the two regions. One group was from a small town where a cluster of cases existed; the other was from a large metropolitan area where there was not a known cluster. RESULTS: The number of CD56+CD3+CD8+ and CD56+CD3+CD8- cells in cases from the two areas were both significantly elevated over that of controls from the metropolitan area (P < 0.03). The number of CD56+CD3-CD8+ and CD56+CD3-CD8- cells was significantly reduced in the two case groups compared to that of controls from the metropolitan area (P = 0.04). However, controls who were from the

				same town as the cluster cases had numbers of CD56+CD3+CD8+, CD56+CD3+CD8-, and CD56+CD3-CD8- cells that were more like that of cases than controls. Only the number of CD56+CD3-CD8+ cells (an NK cell subset) was significantly different in cases versus controls from the cluster area (P = 0.022). CONCLUSIONS: These data suggest that differences in controls from cluster and noncluster areas may be responsible for some of the inconsistencies in results from other studies. Furthermore, they suggest the possibility that NK cell function may play an important role in preventing the development of CFS in individuals who live in a community where a cluster of cases have been identified. Cytometry Part B (Clin. Cytometry) 53B:26-33, 2003. Copyright 2003 Wiley-Liss, Inc.
Sullivan PF, Kovalenko P, York TP, Prescott CA, Kendler KS.	Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University, Richmond, VA 23298-0126, USA.	Fatigue in a community sample of twins.	Psychol Med. 2003 Feb;33(2):263-81. Comment in: Psychol Med. 2003 Feb;33(2):197-201	BACKGROUND: Fatigue is a complex symptom associated with many physiological, psychological and pathological processes. Its correlates and typology remain inadequately understood. METHOD: These data were from two large, longitudinal twin studies. Trained interviewers enquired as to the presence of a > or = 5 day period in the previous year of fatigue or tiredness that interfered with daily activities. A range of potential correlates was assessed in a structured interview: demography; health beliefs; the presence of nine physical disorders; mood, anxiety and addictive disorders; neuroticism and extraversion; recollections of parental rearing; and nine stressful life events. Statistical analyses included logistic regression, CART, MARS, latent class analysis and univariate twin modelling. RESULTS: Data were available for interfering fatigue (IF) on 7740 individual twins (prevalence 9.9% in the previous year). IF was significantly associated with 42 of 52 correlates (most strongly with major depression, generalized anxiety disorder, reported major health problems and neuroticism). Multivariate analyses demonstrated that IF is a highly complex construct with different sets of correlates in its subtypes. There were two broad clusters of correlates of IF: (a) major depression, generalized anxiety disorder and neuroticism; and (b) beliefs of ill health coexisting with alcoholism and stressful life events. Twin analyses were consistent with aetiological heterogeneity--genetic effects may be particularly important in women and shared environmental effects in men. CONCLUSIONS: IF is a complex and common human symptom that is highly heterogeneous. More precise understanding of the determinants of IF may lead to a fuller understanding of more extreme conditions like chronic fatigue syndrome.
Szyndler JE, Towns S, Hoffman RC, Bennett DL.	Department of Adolescent Medicine, Children's Hospital at Westmead, Locked Bag 4001, Westmead NSW 2145, Australia.	Clinical assessment, management and outcomes of a group of adolescents presenting with complex medico-psychosocial conditions.	Ann Acad Med Singapore. 2003 Jan;32(1):51-7.	BACKGROUND: Adolescents with complex medico-psychosocial presentations are often seen as a management challenge. The Medical Family Therapy model provides a useful framework for working with these patients in the context of a multidisciplinary approach to treatment. MATERIALS AND METHODS: A retrospective case analysis of 38 patients referred over a two-year period to the Department of Adolescent Medicine was carried out. These patients met DSM-IV criteria for somatoform disorder or had a diagnosis of chronic fatigue syndrome (CFS). Duration of symptomatology, diagnosis, the presence of psychiatric conditions in the young person and their immediate family and the type and duration of the intervention were examined in relation to outcome. Two case presentations illustrate the complexity of the assessment and treatment process. RESULTS: Clinicians rated 47% of patients who engaged with the service as improved. There was no relationship between diagnosis, length of intervention and outcome. No significant

				differences emerged between the group of young people diagnosed with CFS and those with somatoform disorders in terms of outcome. Nine patients presented with symptoms which were similar or identical to those of one of their parents. Physical illness was more likely to be reported as a precipitating factor in the CFS group. Poor school attendance and psychiatric morbidity were linked to poor outcome. CONCLUSIONS: A comprehensive evaluation of presenting symptomatology and focussed intervention with measurable outcomes are important aspects of the clinical approach to complex medico-psychosocial conditions in adolescents. Families' beliefs about the presenting symptomatology and experiences of illness should be explored.
Tahmaz N, Soutar A, Cherrie JW.	Department of Environmental and Occupational Medicine, University of Aberdeen, Foresterhill Road, Aberdeen AB25 2ZP.	Chronic Fatigue and Organophosphate Pesticides in Sheep Farming: A Retrospective Study Amongst People Reporting to a UK Pharmacovigilance Scheme.	Ann Occup Hyg. 2003 Jun;47(4):261-7.	The Department of Health has recently published a report from the CFS/ME Working Group which concluded that chronic fatigue syndrome (CFS) should be recognized as a chronic illness. Symptoms consistent with CFS are often reported by people who consider their health has been affected by exposure to pesticides, but the Working Group concluded that this type of exposure is not a common trigger for the syndrome. The Veterinary Medicines Directorate (VMD) collects self-assessed reports of ill health in humans associated with veterinary medicines under their Suspected Adverse Reaction Surveillance Scheme. The reporters have mainly been sheep farmers. These reports were used to investigate the possible relationship between chronic fatigue (CF) and exposure to organophosphate pesticides in sheep farming. The overall aim of the study was to investigate a possible association between exposure to organophosphates and the development of CF amongst people who consider their health has been affected by pesticides in sheep farming. The hypothesis investigated was that repeated exposure to organophosphate pesticides in sheep dip may increase the probability of developing CF. A group of mostly sheep farmers who had reported to the VMD surveillance scheme were identified. We planned to use a retrospective case-control study design but the initial symptoms reports were not sufficiently reliable to enable this. The study population was asked to complete two questionnaires. The first questionnaire was designed to identify the history of exposure of subjects to organophosphate pesticides, and their exposure was then reconstructed using a metric specifically developed for this purpose. The second questionnaire collected detailed information to identify whether the subjects had CF when they originally reported to the VMD and at the time of the survey. The questionnaire was sent to a total of 206 subjects, of whom 28 had moved home. A total of 37% of the remaining 178 subjects participated. There was a high prevalence of CF amongst those who completed the questionnaire and this has generally persisted since the subjects reported to the VMD. Higher CF scores were associated with higher exposure to organophosphate pesticides. CF is very common amongst those who consider their health was affected by pesticides and we have shown there is limited evidence of an association between exposure to organophosphates and CF. Further research is needed to investigate the cause of this syndrome amongst farmers exposed to pesticides.
Taillefer SS, Kirmayer LJ, Robbins JM, Lasry JC.	Department of Psychology, Universite de Montreal, Montreal,	Correlates of illness worry in chronic fatigue syndrome.	J Psychosom Res. 2003 Apr;54(4):331-7.	BACKGROUND: Anxiety about illness leading to restriction of activity and physical deconditioning has been hypothesized to contribute to the chronicity of fatigue. Pathological symptom attributions, personality traits, and depression have all been hypothesized to contribute to illness worry. METHODS: We compared 45 chronic fatigue syndrome (CFS) and 40 multiple sclerosis

	Quebec, Canada			(MS) outpatients using a battery of psychometric instruments comprising the 12-item Illness Worry scale, the Symptom Interpretation Questionnaire (SIQ), the NEO Five-Factor Inventory (NEO-FFI), and a modified version of the SCL-90R Depression scale. RESULTS: There was no difference between the two diagnostic groups on neuroticism, depressive symptoms, as well as the three scales of the SIQ. On the illness worry index, the CFS group had significantly higher scores than the MS group. This difference was due to items tapping vulnerability to illness and the perception that others are not taking their illness seriously. Somatic attributional style, neuroticism, depressive symptoms, and age were all significant predictors of illness worry in both CFS and MS patients. CONCLUSIONS: Somatic attributions, neuroticism, and depression all contribute to illness worry in chronic illness. However, these factors do not account for the higher levels of illness worry in CFS as opposed to MS, which may be due to other specific cognitive and social interactional processes.
Tanaka S, Kuratsune H, Hidaka Y, Hakariya Y, Tatsumi KI, Takano T, Kanakura Y, Amino N.	Department of Laboratory Medicine, Osaka University Graduate School of Medicine (D2), Suita-shi, Osaka 565-0871, Japan. tanaka@labo.med.osaka-u.ac.jp	Autoantibodies against muscarinic cholinergic receptor in chronic fatigue syndrome.	Int J Mol Med. 2003 Aug;12(2):225-30.	The disturbance of the central nervous system and immunological abnormalities have been suggested in patients with chronic fatigue syndrome (CFS). We focused on immunological abnormalities against neurotransmitter receptors in CFS. Using a sensitive radioligand assay, we examined serum autoantibodies to recombinant human muscarinic cholinergic receptor 1 (CHRM1), mu-opioid receptor (OPRM1), 5-hydroxytryptamine receptor 1A (HTR1A), and dopamine receptor D2 (DRD2) in patients with CFS (n=60) and results were compared with those in patients with autoimmune disease (n=33) and in healthy controls (n=30). The mean anti-CHRM1 antibody index was significantly higher in patients with CFS ($p<0.0001$) and autoimmune disease ($p<0.05$) than that in healthy controls, and positive reaction was found in 53.3% of patients with CFS. Anti-OPRM1 antibodies, anti-HTR1A antibodies, and anti-DRD2 antibodies were found in 15.2, 1.7, and 5.0% of patients with CFS, respectively. Anti-nuclear antibodies were found in 56.7% (34/60) of patients with CFS, but anti-nuclear antibody titers did not correlate with the activities of the above four autoantibodies. The patients with positive autoantibodies to CHRM1 had a significantly higher mean score (1.81) of 'feeling of muscle weakness' than negative patients (1.18) among CFS patients ($p<0.01$). Higher scores on 'painful node', 'forgetfulness', and 'difficulty thinking' were also found in CFS patients with anti-CHRM1 antibodies but did not reach statistical significance. In conclusion, autoantibodies to CHRM1 were detected in a large number of CFS patients and were related to CFS symptoms. Our findings suggested that subgroups of CFS are associated with autoimmune abnormalities of CHRM1.
Tarello W.	Clinica Veterinaria Airone of Nus, Aosta, Italy. wtarello@yahoo.it	Immunological anomalies and thrombocytopenia in 117 dogs and cats diagnosed with chronic fatigue syndrome (CFS).	Acta Vet Hung. 2003;51(1):61-72.	Retrospective analysis of immune dysfunctions found in 55 dogs and 62 cats diagnosed with Chronic Fatigue Syndrome (CFS), revealed leukopenia in 11% of dogs (n = 6) and 22.5% of cats (n = 14), lymphopenia in 14.5% of dogs (n = 8) and 10% of cats (n = 6), hypogammaglobulinaemia in 9% of dogs (n = 5) and 13% of cats (n = 8) and thrombocytopenia in 20% of dogs (n = 11) and 68% of cats (n = 42). All patients had creatine kinase enzyme levels above the normal range (CK = 5-100 IU/L) and carried micrococcus-like organisms on erythrocytes. Blood cultures proved positive for Staphylococcus spp. in 16 cases. After low-dosage arsenic-based therapy (thiacetarsamide sodium) all animals experienced complete clinical remission. Subsequent controls demonstrated immune restoration in 4 representative FIV-FeLV negative cats, previously diagnosed with CFS

				associated with leukopenia, lymphopenia, hypogammaglobulinaemia and thrombocytopenia. The main conclusion is that a CFS-like disease in dogs and cats, characterised by the common hallmarks of high CK levels, absence of known causes of chronic fatigue in animals and presence of micrococcus-like organisms in the blood, can be associated with humoral and/or cellular immune deficiencies in 9-22.5% of cases and with thrombocytopenia in 20-68% of cases. Considerations are made on the possible role of micrococci in the aetiology of the condition and on the similarities with CFS in humans.
Terr AI.	Department of Medicine, University of California San Francisco Medical School, 450 Sutter Street, #2534, San Francisco, CA 94108, USA. abbaterrmed@attglobal.net	Environmental sensitivity.	Immunol Allergy Clin North Am. 2003 May;23(2):311-28.	The concept of environmental sensitivity is popular among a small group of physicians who believe that exposure to low levels of numerous environmental chemicals can cause a disease with numerous symptoms but no objective physical or laboratory abnormalities. The condition lacks a clear definition. Numerous theories that have been offered to explain the condition encompass immunotoxic, allergic, autoimmune, neurotoxic, cytotoxic, metabolic, behavioral, psychiatric, iatrogenic, and sociologic mechanisms. Environmental sensitivity has many features in common with other controversial syndromes, such as the chronic fatigue syndrome. Patients with environmental sensitivity frequently are subjected to unproven and unnecessary diagnostic tests and therapeutic modalities. In spite of the lack of physical illness and absence of pathology, patients often experience extreme disability, because their symptoms are triggered by common environmental exposures. The phenomenon of environmental sensitivity needs to be evaluated critically using scientifically sound methods. The practice of clinical ecology encompasses the practices of environmental sensitivity and its theories. Most methods of diagnosis and treatment have been disproved, and the concepts underlying these theories are not scientific. Alternative means of diagnosis and management are presented.
The GK, Prins J, Bleijenberg G, van der Meer JW.	University Medical Centre Nijmegen, Department of Internal Medicine, PO Box 9101, 6500 HB Nijmegen, The Netherlands. g.the@aig.umcn.nl	The effect of granisetron, a 5-HT3 receptor antagonist, in the treatment of chronic fatigue syndrome patients--a pilot study.	Neth J Med. 2003 Sep;61(9):285-9.	OBJECTIVE: To explore the effect of granisetron, a 5-HT3 antagonist, on fatigue and functional impairment in patients with chronic fatigue syndrome (CFS). METHODS: Five female patients were eligible to receive oral granisetron for one month (1 mg a day for the first two weeks and 2 mg a day for the second two weeks). The patients had to be between 18 and 65 years of age and suffering from CFS according to the CDC criteria. The effect was assessed by pre- and post-testing, using validated instruments designed to assess the different dimensions of CFS. Treatment response was also evaluated by visual analogue scales (VAS) for fatigue. Analysis was based on intention to treat. RESULTS: Treatment with granisetron resulted in significant improvement in fatigue severity and functional impairment. Activity level showed no significant increase. CONCLUSION: The promising results of this study have encouraged us to perform a placebo-controlled, double-blind study to evaluate the efficacy of 5-HT3 receptor antagonists in the treatment of CFS.
Tiersky LA, Matheis RJ, Deluca J, Lange G, Natelson BH.	Fairleigh Dickinson University, School of Psychology, Williams Hall (T-WH1-01), 1000 River Road, Teaneck, NJ 07666,	Functional status, neuropsychological functioning, and mood in chronic fatigue syndrome (CFS): relationship to	J Nerv Ment Dis. 2003 May;191(5):324-31.	Individuals with chronic fatigue syndrome (CFS) face chronic physical debilitation, reduced neuropsychological functioning, and changes in emotional well-being that significantly detract from quality of life. The role of psychiatric disturbance in reducing quality of life in CFS remains unclear. In the current investigation, the role of psychiatric status in reducing health-related quality of life in CFS was examined. Four subject groups were compared on measures of functional well-being, mood, and neuropsychological status: individuals with CFS and no history

	USA.	psychiatric disorder.		of psychiatric illness, individuals who had current symptoms of psychiatric illness that began after their CFS diagnosis, individuals who had current symptoms of psychiatric illness that began before their CFS diagnosis, and a healthy sedentary control group. Overall, it was found that individuals with CFS suffer from profound physical impairment. Concurrent psychiatric illness, however, did not adversely affect physical functional capacity. Physical functional capacity was not worse in individuals with a concurrent psychiatric illness. As expected, concurrent psychiatric illness was found to reduce emotional well-being. Moreover, individuals with a psychiatric illness that predated the onset of CFS suffered the greatest emotional distress. Thus, an individual's psychiatric history should be considered when attempting to understand the factors maintaining disability in CFS.
Tiev KP, Demettre E, Ercolano P, Bastide L, Lebleu B, Cabane J.	Service de Medecine Interne, Hopital Saint Antoine, 75571 Paris Cedex 12. UMR 5124 CNRS, Universite Montpellier 2, 34293 Montpellier Cedex 5, France.	RNase L Levels in Peripheral Blood Mononuclear Cells: 37-Kilodalton/83-Kilodalton Isoform Ratio Is a Potential Test for Chronic Fatigue Syndrome.	Clin Diagn Lab Immunol. 2003 Mar;10(2):315-6.	Chronic fatigue syndrome (CFS) is a disorder characterized by debilitating fatigue associated with immunological abnormalities. The etiology remains unclear. A low-molecular-mass (37 kDa) isoform of RNase L has been described in peripheral blood mononuclear cell (PBMC) extracts, and the ratio of two isoforms of RNase L (37 kDa/83 kDa) has been proposed as a potential biochemical marker of CFS. In a prospective case-control study, we tested whether the RNase L 37-kDa/83-kDa ratio could discriminate a SFC population. We compared the ratio of RNase L isoforms in PBMCs from 11 patients with CFS (6 women and 5 men; mean age +/- standard deviation, 43.2 +/- 13.8 years) and PBMCs from 14 healthy well-matched volunteers (10 women and 4 men; age, 39.1 +/- 11.6 years). A ratio of RNase L of 0.4 used as a threshold allowed diagnosis of CFS with high sensitivity (91%; 95% confidence interval [CI], 57 to 99%) and specificity (71%; 95% CI, 41 to 90%). The positive and negative prognostic values were 71% (95% CI, 41 to 90%) and 91% (95% CI, 57 to 99%), respectively. In the absence of acute infection or chronic inflammation, a high RNase L ratio could distinguish CFS patients from healthy volunteers. Additional large studies and follow-up studies are required to confirm the stability of this high ratio of RNase L isoforms in a CFS group.
van Gelder T, Smits P.		Pilot studies: one swallow does not make a summer...	Neth J Med. 2003 Sep;61(9):270-2.	What should we expect from pilot studies, done in small series of patients? In the literature there are many examples of small studies with very promising results, that in subsequent larger or better controlled studies proved to be much less promising, or even disastrous. In some instances the initial favourable outcome was due to selection bias. In others the use of nonvalidated methods of measuring outcome made the reproducibility of promising observations problematic. However, we have to start somewhere. In ths issue The et al. report favourable results of granisetron treatment in four out of five patients with chronic fatigue syndrome. A prospective, randomised, placebo-controlled, double-blind clinical trial with granisetron in patients with chronic fatigue syndrome is now ongoing.
Van Hoof E, Cluydts R, De Meirleir K.	Department of Human Physiology, Vrije Universiteit Brussel, Brussel, Belgium	Atypical depression as a secondary symptom in chronic fatigue syndrome.	Med Hypotheses. 2003 Jul;61(1):52-5.	Chronic fatigue syndrome (CFS) has gained prominence since 1988 and a substantial amount of research has been done in this domain. However, it is still regarded as a controversial condition. Moreover, most of the symptoms of CFS itself are non-specific, occurring in many illnesses; some of the symptoms are also common in depression. Indeed, an area of continued controversy and debate involves the diagnostic overlap between CFS and psychiatric disorders. Through anecdotal evidence, atypical depression appears to be common in CFS. Recent developments in

				psychobiology underscore the role of the acute phase response and its associated sickness behavior in affective disorders. Thus, we hypothesize that atypical depression is sickness behavior rather than an affective disorder as shown by anecdotal evidence in CFS.
Van Hoof E, De Meirleir K, Cluydts R, Coomans D		The Symptoms and Psychiatric Status of the Bijlmermeer Plane Crash Disaster: Similarities with Chronic Fatigue Syndrome and Gulf War Syndrome	Journal of Chronic Fatigue Syndrome 2003; 11 (3): 3-23	On October 4, 1992, the El Al Boeing crashed in the residential quarter 'Bijlmermeer' in Amsterdam (The Netherlands). In the years after the plane crash, local residents and assistance personnel began reporting a variety of unusual symptoms not unlike those reported by patients with chronic fatigue syndrome (CFS) and Gulf War Syndrome (GWS). The aim of this study was to define the symptom constellations reported by the patients and assess the possible causes of the illness. Standardized psychological questionnaires (MMPI-II, SCL-90, KPS and a complaints checklist) were used to screen for psychological changes and to describe the symptoms reported by the patients. Differences between local residents and assistance personnel, gender differences, Mycoplasma-infected and Mycoplasma non-infected patients were monitored. The major symptoms reported were extreme fatigue, non-restorative sleep, concentration-problems, memory problems and muscle and joint pains. There were no changes in the SCL-90 responses that indicated any alteration of psychological distress. Assessment using the MMPI-II revealed a profile typically seen in chronic physical illness and assessment of the Harris-Lingoes scales revealed no elevations in pathogenic scales. Twelve subjects (67%) had a positive Mycoplasma PCR response. Victims of the Bijlmermeer plane crash disaster had increases in symptoms similar to patients with Gulf War Syndrome and CFS and no evidence of somatoform disorder, anxiety or depression. Similar to patients with Gulf War Syndrome and CFS, a deregulation of the immune-competence through a combination of toxic material exposure and psychological stressors associated with increased opportunistic infections may be the most likely etiological hypothesis.
Van Hoof, Elke Danny Coomans Pascale De Becker Romain Meeusen Raymond Cluydts Kenny De Meirleir		Hyperbaric Therapy in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2003; 11 (3): 37-51	The aim of this study was to determine if hyperbaric oxygen treatment (HBOT) could be used as adjunctive therapy and if HBOT could increase the quality of life in such a way that the functional status would improve in patients with an infection. A randomized, controlled trial was conducted on 15 Mycoplasma sp. infected CFS (CDC 1994) patients and 14 CFS (CDC 1994) patients with no evidence of a Mycoplasma infection were enrolled in a convenience randomization sample from our referral clinic. No statistical differences were found by use of univariate repeated measures although Bodily Pain as measured by the SF-36 seems to decrease after hyperbaric therapy (Greenhouse-Geisser: p = .010). Trends were found using paired t-testing for Mycoplasma infected CFS patients. The general perceived fatigue seemed to decrease after hyperbaric therapy (General Fatigue: p = .06). Directly after one week of hyperbaric therapy general fatigue improved (p = .03) but there was a reduction of activity (reduced activity: p = .05) and general perceived health (general health: p = .04). One month later the physical role increased (Role-Physical: p = .07). Although more data is required to make firm conclusions, trends were found. Reduced fatigue, increased levels of activity and an improved reaction time improved significantly their quality of life and therefore, enhanced also their functional status and thus could be used as an adjunctive therapy.
Van Houdenhove B.		Chronic fatigue syndrome,	Psychosomatics. 2003 Mar-	

		fibromyalgia, and complex regional pain syndrome type I.	Apr;44(2):173-4.	
Van Houdenhove B.		Response to Brimacombe et al., birth order and its association with the onset of chronic fatigue syndrome.	Hum Biol. 2003 Jun;75(3):411; author reply 413. Comment on: Hum Biol. 2002 Aug;74(4):615-20.	
van Hout MS, Wekking EM, Berg IJ, Deelman BG.	Medical Spectrum Twente Hospital, Enschede, The Netherlands. MSEvanHout@ziekenhuis-mst.nl	Psychological treatment of patients with chronic toxic encephalopathy: lessons from studies of chronic fatigue and whiplash.	Psychother Psychosom. 2003 Sep-Oct;72(5):235-44.	BACKGROUND: Chronic toxic encephalopathy (CTE), which can result from long-term exposure to organic solvents, is characterized by problems of attention and memory, fatigue and affective symptoms. There is little experience with (neuro)psychological treatment in this patient group. We reviewed treatment outcome studies of CTE and comparable syndromes, namely, chronic whiplash-associated disorder (WAD) and chronic fatigue syndrome (CFS), with a view to providing recommendations for the psychological treatment of patients with CTE. METHODS: PubMed and PsychLIT were systematically searched and reference lists of retrieved articles were studied. The articles were classified according to study design and level of evidence. RESULTS: The studies of CFS provided high-level evidence for the effectiveness of cognitive-behavior therapy (CBT) in challenging dysfunctional cognitions regarding the effectiveness of rest and in stimulating graded activity. The studies of WAD were methodologically weaker, and most evaluated a combination of CBT and graded activity training. There was some evidence that changing fatigue- or pain-related behaviors may result in cognitive improvement. Two uncontrolled studies of CTE evaluated cognitive rehabilitation techniques but yielded inconsistent findings. CONCLUSIONS: CBT techniques focusing on changing illness attributions and on stimulating graded activity might be useful for patients with CTE, diminishing fatigue-related problems of concentration and memory. Future studies should evaluate whether cognitive deficits of CTE patients as a result of neurotoxic effects of exposure should be treated by cognitive rehabilitation. Copyright 2003 S. Karger AG, Basel
Vanness JM, Snell CR, Strayer DR, Dempsey L 4th, Stevens SR.	University of the Pacific, Department of Sport Sciences, Stockton, CA 95211, USA. mvanness@uop.edu	Subclassifying chronic fatigue syndrome through exercise testing.	Med Sci Sports Exerc. 2003 Jun;35(6):908-13.	PURPOSE: The purpose of this study was to examine physiological responses of persons with chronic fatigue syndrome (CFS) to a graded exercise test. METHODS: Cardiopulmonary exercise tests were performed on 189 patients diagnosed with CFS. Based on values for peak oxygen consumption, patients were assigned to one of four impairment categories (none, mild, moderate, and severe), using American Medical Association (AMA) guidelines. A one-way MANOVA was used to determine differences between impairment categories for the dependent variables of age, body mass index, percentage of predicted [OV0312]O(2), resting and peak heart rates, resting and peak systolic blood pressure, respiratory quotient (RQ), and rating of perceived exertion. RESULTS: Significant differences were found between each impairment level for percentage of predicted [OV0312]O(2) and peak heart rate. Peak systolic blood pressure values for the "moderate," and "severe" groups differed significantly from each other and both other

				groups. The more impaired groups had lower values. The no impairment group had a significantly higher peak RQ than each of the other impairment levels (all P < 0.001). Peak [OV0312]O(2) values were less than predicted for all groups. Compared with the males, the women achieved actual values for peak [OV0312]O(2) that were closer to their predicted values. CONCLUSION: Despite a common diagnosis, the functional capacity of CFS patients varies greatly. Stratifying patients by function allows for a more meaningful interpretation of the responses to exercise and may enable differential diagnosis between subsets of CFS patients.
Vecchiet J, Cipollone F, Falasca K, Mezzetti A, Pizzigallo E, Bucciarelli T, De Laurentis S, Affaitati G, De Cesare D, Giamberardino MA.	Department of Medicine and Science of Aging, G. D'Annunzio University of Chieti, Italy.	Relationship between musculoskeletal symptoms and blood markers of oxidative stress in patients with chronic fatigue syndrome.	Neurosci Lett. 2003 Jan 2;335(3):151-4.	In 21 patients with chronic fatigue syndrome (CFS) versus 20 normal subjects, we investigated the oxidant/antioxidant balance and its correlation with muscle symptoms. Patients versus controls showed significantly: lower Lag Phase and Vitamin E (Vit E) concentrations in plasma and low-density lipoproteins (LDL), higher LDL thiobarbituric acid reactive substances (TBARS), higher fatigue and lower muscle pain thresholds to electrical stimulation. A significant direct linear correlation was found between fatigue and TBARS, thresholds and Lag Phase, thresholds and Vit E in plasma and LDL. A significant inverse linear correlation was found between fatigue and Lag Phase, fatigue and Vit E, thresholds and TBARS. Increased oxidative stress and decreased antioxidant defenses are related to the extent of symptomatology in CFS, suggesting that antioxidant supplementation might relieve muscle symptoms in the syndrome.
Velanovich V.	Division of General Surgery, Henry Ford Hospital, Detroit, Michigan 48202-2689, USA. vvelanol@hfhs.org	The effect of chronic pain syndromes and psychoemotional disorders on symptomatic and quality-of-life outcomes of antireflux surgery.	J Gastrointest Surg. 2003 Jan;7(1):53-8.	Psychoemotional disorders (PED) and chronic pain syndromes (CPS) are common problems. Many patients with these disorders also suffer from gastroesophageal reflux disease (GERD). It is unclear how PED/CPS affect outcomes of antireflux surgery; therefore, the purpose of this study was to determine if PED/CPS adversely affects the results of surgical therapy for GERD. All patients referred for surgical therapy for GERD completed both the GERD-HRQL symptom severity instrument and the SF-36 generic quality-of-life instrument prior to surgery. To be candidates for surgery, patients must have symptomatic GERD and objective evidence of pathologic reflux by upper endoscopy, esophageal manometry and 24-hour pH monitoring. Patients underwent either laparoscopic or open Nissen or Toupet fundoplication. Six to 24 months postoperatively, patients were evaluated for satisfaction and quality-of-life. Ninety-three percent of control patients compared to 25% of PED/CPS patients were satisfied with surgery (P < 0.001). Dissatisfaction in PED/CPS patients was generally due to persistent or new somatic complaints. Median total GERD-HRQL scores improved for both groups, although postoperative scores were worse in the PED/CPS group. PED/CPS patients had significantly worse SF-36 scores both preoperatively and postoperatively compared to control patients. SF-36 scores improved in four of eight domains in control patients and none in the PED/CPS patients. In conclusion, PED/CPS patients are generally dissatisfied with antireflux surgery. Although some patients do benefit from surgery, careful patient selection is required. Copyright 2003 The Society for Surgery of the Alimentary Tract, Inc.
Vermeulen RC, Scholte HR.	Chronic Pain and Fatigue Research Centre, Waalstraat 25, 1078 BR	Rupture of silicone gel breast implants and symptoms of pain and fatigue.	J Rheumatol. 2003 Oct;30(10):2263-7.	OBJECTIVE: To compare symptoms of women with silicone gel breast implants and women with chronic fatigue syndrome (CFS), and to study the effect of rupture of the silicone implant. METHODS: Five hundred readers of the Dutch silicone breast implant support group magazine were asked to respond if they had been informed by the surgeon about the silicone implant

	Amsterdam, The Netherlands. rcwvermeulen@cfsccentrumamsterdam.nl			status at operation, and to answer questions about symptoms of CFS. Their complaints were compared with those of 100 female patients with CFS and 40 female controls. RESULTS: The questionnaires were returned by 319 women. Of these, 227 had symptoms of debilitating chronic fatigue. The patterns of symptoms differed from those in patients with CFS. An analysis of the relation between integrity of the implants and the symptoms could be carried out in 176 women, and 74% of these latter women reported ruptured implants. Significantly more women with ruptured implants than those with intact implants had debilitating chronic fatigue (75% vs 51%), postexertional malaise > 24 h (77% vs 51%), impaired short term memory (58% vs 38%), and multi-joint pain (77% vs 60%). CONCLUSION: Women with silicone breast implants often report severe pain and chronic fatigue. Rupture of the implant is associated with an increase in symptoms of pain and chronic fatigue.
Vernon SD, Shukla SK, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA Clinical Research Center, Marshfield Clinic Research Foundation, 1000 North Oak Avenue, Marshfield, WI 54449-5790, USA.	Absence of Mycoplasma species DNA in chronic fatigue syndrome.	J Med Microbiol. 2003 Nov;52(11):1027-1028.	
Watkins P.		Changing perceptions of disease.	Clin Med. 2003 Jan-Feb;3(1):5-6.	
Watson NF, Kapur V, Arguelles LM, Goldberg J, Schmidt DF, Armitage R, Buchwald D.	Department of Neurology and Sleep Disorders Center, University of Washington, Seattle 98104-2499, USA. nwatson@u.washington.edu	Comparison of subjective and objective measures of insomnia in monozygotic twins discordant for chronic fatigue syndrome.	Sleep. 2003 May 1;26(3):324-8.	STUDY OBJECTIVES: To examine the objective and subjective measures of insomnia in chronic fatigue syndrome (CFS). DESIGN: Monozygotic co-twin control study. SETTING: Academic medical center. PATIENTS OR PARTICIPANTS: Twenty-two pairs of monozygotic twins where 1 member of the pair had CFS and the other did not. INTERVENTIONS: N/A. MEASUREMENTS AND RESULTS: Twenty-two CFS-discordant twin pairs completed a Sleep Disorders Questionnaire, overnight polysomnography, and a postpolysomnography sleep survey. Mean and percent differences in the sleep measures were compared between the CFS and healthy twins using matched-pair methods of analysis. Compared with their healthy co-twins, the CFS twins more frequently endorsed 8 subjective measures of insomnia and poor sleep (all p < or = 0.05). However, the CFS and healthy twins did not differ in objective polysomnographic measures of insomnia, including sleep latency, total sleep time, sleep efficiency, arousal number, arousal index, hypnogram

				awakenings, rapid eye movement (REM)-sleep latency, and percent stages 1, 2, and 3-4 (delta). Percent stage REM sleep was increased in the CFS twins compared with the healthy twins (27.7% vs. 24.4%, p < or = 0.05). On the postpolysomnography survey, CFS twins reported that they had slept fewer hours (6.2 vs. 6.7; p < or = 0.05), and were less well rested (p < or = 0.001) compared to their co-twins. CONCLUSIONS: CFS patients had worse subjective sleep than their co-twins despite little objective data supporting this discrepancy, suggesting they suffer from an element of sleep-state misperception. The higher percentage of REM sleep in the CFS twins implies that REM sleep may play a role in this illness.
Weinbacher BS.		[Persistent fatigue despite sufficient sleep] [Article in German]	Schweiz Rundsch Med Prax. 2003 Feb 19;92(8):356-9.	Medizinische Universitatspoliklinik, Departement Innere Medizin, Kantonsspital Basel.
Westropp JL, Welk KA, Buffington CA.	Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Ohio State University, Columbus 43210-1089, USA.	Small adrenal glands in cats with feline interstitial cystitis.	J Urol. 2003 Dec;170(6 Pt 1):2494-7.	PURPOSE: We documented the uncoupling of sympathetic nervous system activity from the hypothalamic-pituitary-adrenal axis in cats with feline interstitial cystitis (FIC). Altered hypothalamic-pituitary-adrenal activity was recently suggested in some humans with interstitial cystitis (IC) but to our knowledge no information exists on adrenal gland size and histopathology in this disease. To investigate further adrenal function in cats with FIC we determined cortisol responses to 125 microg synthetic adrenocorticotropic hormone (ACTH) as well as adrenal size and histology. MATERIALS AND METHODS: ACTH stimulation studies were performed in 11 healthy cats and 20 with FIC. Adrenal glands obtained at autopsy in 8 healthy cats and 13 with FIC were weighed, measured and examined histologically. RESULTS: Cats with FIC had significantly decreased responses to ACTH (2-way repeated measures ANOVA p <0.05). Mean weight +/- SD (58 +/- 50 vs 241 +/- 60 mg) and volume (264 +/- 72 vs 410 +/- 115 mm3) of adrenal glands were significantly smaller in cats with FIC than in healthy cats (p <0.05). CONCLUSIONS: These results suggest that cats with FIC may have mild primary adrenal insufficiency. Decreased adrenal size has been observed in patients with chronic fatigue syndrome, which can be a co-morbid condition in some patients with IC. If these abnormalities are confirmed in humans with IC, hormone replacement therapy may be indicated in select patients.
Whistler T, Unger ER, Nisenbaum R, Vernon SD.	Viral Exanthems and Herpes Virus Branch, Division of Viral and Rickettsial Diseases, National Centre for Infectious Diseases, Centres for Disease Control and Prevention, 1600 Clifton Rd, Atlanta, Georgia. sdv2@cdc.gov	Integration of gene expression, clinical, and epidemiologic data to characterize Chronic Fatigue Syndrome.	J Transl Med. 2003 Dec 1;1(1):10. Epub 2003 Dec 01.	BACKGROUND: Chronic fatigue syndrome (CFS) has no diagnostic clinical signs or diagnostic laboratory abnormalities and it is unclear if it represents a single illness. The CFS research case definition recommends stratifying subjects by co-morbid conditions, fatigue level and duration, or functional impairment. But to date, this analysis approach has not yielded any further insight into CFS pathogenesis. This study used the integration of peripheral blood gene expression results with epidemiologic and clinical data to determine whether CFS is a single or heterogeneous illness. RESULTS: CFS subjects were grouped by several clinical and epidemiological variables thought to be important in defining the illness. Statistical tests and cluster analysis were used to distinguish CFS subjects and identify differentially expressed genes. These genes were identified only when CFS subjects were grouped according to illness onset and the majority of genes were involved in pathways of purine and pyrimidine metabolism, glycolysis, oxidative phosphorylation, and glucose metabolism. CONCLUSION: These results provide a

				physiologic basis that suggests CFS is a heterogeneous illness. The differentially expressed genes imply fundamental metabolic perturbations that will be further investigated and illustrates the power of microarray technology for furthering our understanding CFS.
White PD..	Costs, correlates and consequences of fatigue in children and adults		Psychol Med. 2003 Feb;33(2):197-201. Comment on: Psychol Med. 2003 Feb;33(2):253-61. Psychol Med. 2003 Feb;33(2):263-81. Psychol Med. 2003 Feb;33(2):283-7. Psychol Med. 2003 Feb;33(2):289-97.	
Whitehead J, Matsushita T.	Medical and Pharmaceutical Statistics Research Unit, The University of Reading, Reading, UK. j.r.whitehead@reading.ac.uk	Stopping clinical trials because of treatment ineffectiveness: a comparison of a futility design with a method of stochastic curtailment.	Stat Med. 2003 Mar 15;22(5):677-87.	This paper introduces a simple futility design that allows a comparative clinical trial to be stopped due to lack of effect at any of a series of planned interim analyses. Stopping due to apparent benefit is not permitted. The design is for use when any positive claim should be based on the maximum sample size, for example to allow subgroup analyses or the evaluation of safety or secondary efficacy responses. A final frequentist analysis can be performed that is valid for the type of design employed. Here the design is described and its properties are presented. Its advantages and disadvantages relative to the use of stochastic curtailment are discussed. Copyright 2003 John Wiley & Sons, Ltd.
Wiesmuller GA, Ebel H, Hornberg C, Kwan O, Friel J.	Institute of Hygiene and Environmental Medicine, University Hospital Aachen, Aachen, Germany.	Are syndromes in environmental medicine variants of somatoform disorders?	Med Hypotheses. 2003 Oct;61(4):419-30.	To date, relatively little is known about the etiology, pathophysiology, diagnosis, therapy, prevention and prognosis of environment-related syndromes like multiple chemical sensitivity (MCS), idiopathic environmental intolerance (IEI), sick building syndrome (SBS), chronic fatigue syndrome (CFS), candida syndrome (CS) and burnout syndrome (BS). Part of the reason is that these syndromes have not been clearly defined and classified in scientific categories distinct from each other, and that they show clinical similarities to classified somatoform disorders. Furthermore, there are at least three possible explanations for the existence of these syndromes: (1) The syndromes may result from the interaction of environmental factors, individual susceptibility and psychological factors (i.e., how they are perceived and seen by the patient); (2) they may reflect socially and culturally accepted methods of expressing distress; and/or (3) they may be iatrogenic. Despite all the uncertainties in evaluation of environmental syndromes, physicians have the duty to take the affected person's problems seriously. A comprehensive systematic classification which better accounts for these complex clinical manifestations is long overdue. Until these syndromes are well defined, the terms used for them should definitely not be applied to connote a specific disease process.
Yamamoto Y, LaManca JJ, Natelson BH.	Department of Neurosciences, New Jersey Medical	A measure of heart rate variability is sensitive to	Exp Biol Med (Maywood). 2003 Feb;228(2):167-74.	The use of symptoms generated by head up tilt (HUT) is not a useful tool in identifying chronic fatigue syndrome (CFS). We investigated whether heart rate variability (HRV) assessed early during HUT might be useful. A sample of 46 female subjects (24 with CFS and 22 sedentary, age-

	School, East Orange, New Jersey 07018-1095, USA.	orthostatic challenge in women with chronic fatigue syndrome.		matched healthy controls; CON) who had exhibited no difference in time to syncope during tilt was examined for HRV responses to 10 min of 70 degrees HUT after 5 min of baseline in the supine position. HRV data were analyzed by the method of coarse graining spectral analysis. Variables compared between groups included mean and standard deviation (SD(RRI)) of RR intervals (RRI), amplitudes of low- (A(LF); 0.04-0.15 Hz) and high-frequency (A(HF); >0.15 Hz) harmonic as well as aperiodic, fractal (A(FR); 1/f(beta)) spectral components, the spectral exponent beta, and the difference in these values between baseline and HUT for each subject. In the supine baseline, only mean RRI was significantly ($P < 0.01$) lower in CFS than in CON. During HUT, however, mean RRI ($P < 0.01$), SD(RRI) ($P < 0.01$), A(HF) ($P < 0.05$), and A(FR) ($P < 0.01$) were significantly lower in CFS than in CON. When the difference in values between baseline and HUT for each subject was examined, only the difference for A(FR) (deltaA(FR)) was significantly ($P < 0.01$) lower in CFS than in CON, suggesting that A(FR)is a disease-specific response of HRV to HUT. When a cut-off level was set to deltaA(FR) = -2.7 msec, the sensitivity and the specificity in differentiating CFS from controls were 90% and 72%, respectively. The data suggest that a decrease in aperiodic fractal component of HRV in response to HUT can be used to differentiate patients with CFS from CON.
Zavestoski S, Brown P, McCormick S, Mayer B, D'Ottavi M, Lucove JC.	Department of Sociology, University of San Francisco, 2130 Fulton Street, 94117-1080, San Francisco, CA, USA	Patient activism and the struggle for diagnosis: Gulf War illnesses and other medically unexplained physical symptoms in the US.	Soc Sci Med. 2004 Jan;58(1):161-75.	We examine Gulf War illnesses-which include the fatigue, joint pain, dermatitis, headaches, memory loss, blurred vision, diarrhea, and other symptoms reported by Gulf War veterans-in relation to other medically unexplained physical symptoms such as multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. Our intent is to examine the diagnosis negotiations involved in these mysterious diseases, by showing the different forms of legitimacy involved in such interactions. Factors involved in diagnostic legitimacy are: diagnostic legitimacy in the medical community, lay acceptance of the diagnosis, uncertainty in looking for causes, and social mobilization. We conclude by noting that research may not be able to find any cause for these diseases/conditions; hence, it may be necessary to embrace medical uncertainty, and also to accept patient experience in order to facilitate diagnosis, treatment, and recovery process. Such a change can alter patients' expectations and taken-for-granted assumptions about medicine, and perhaps in turn reduce the frequency with which dissatisfied individuals form illness groups that mobilize to challenge what they see as an unresponsive medical system.
[No authors listed]		[Article in Russian]	Vestn Oftalmol. 2003 Mar-Apr;119(2):45-7.	218 patients were examined and the chronic fatigue syndrome (CFS) was diagnosed in them on the basis of clinical-and-immunologic data. 126 somatically healthy persons of the same age and sex were in the control group. Vascular pathology of the vision organ was found in 153 (70.2%) persons, and dystrophic pathology was found in 115 (52.8%) persons. A combination of vascular and dystrophic pathologies of the vision organ was diagnosed in 46 (21.1%) patients. The detection of vision pathology in the CFS patients essentially exceeded the morbidity of similar pathology in the controls. No reliable differences of refraction anomalies were found between the CFS patients and the controls.

2002				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
[No authors listed]		Cognitive behavioral therapy and exercise for chronic fatigue syndrome.	J Pain Palliat Care Pharmacother. 2002;16(3):110-1.	
Aaron LA, Arguelles LM, Ashton S, Belcourt M, Herrell R, Goldberg J, Smith WR, Buchwald D.	Department of Oral Medicine, University of Washington, Seattle, Washington 98195, USA. laaron@u.washington.edu	Health and functional status of twins with chronic regional and widespread pain.	J Rheumatol. 2002 Nov;29(11):2426-34. Erratum in: J Rheumatol. 2002 Dec;29(12):2667. Buchwald Dedra [corrected to Buchwald Debra]	OBJECTIVE: To examine the independent effects of chronic regional and widespread pain syndromes on health and functional status after accounting for comorbid chronic fatigue using a co-twin control design. METHODS: We identified 95 twin pairs discordant for pain in which one twin had chronic regional or widespread pain and the other denied chronic pain. Demographic data, functional and psychological status, health behaviors, and symptoms based on the 1994 criteria for chronic fatigue syndrome (CFS) were assessed by questionnaire. Psychiatric diagnoses were based on structured interview. Random effects regression modeling estimated associations between chronic regional and widespread pain and each health measure with and without adjustment for CFS. RESULTS: Significant differences ($p </= 0.05$) were found within twin pairs discordant for chronic regional and widespread pain, for general health perception, and physical and mental health functioning as measured by summary scores from the Short Form-36. In addition, differences were observed within pain discordant pairs in psychological distress as measured by the General Health Questionnaire as well as the number of psychiatric diagnoses. Adjustment for CFS eliminated the association between chronic pain and mental health, but the association between chronic pain and poor general health, physical functioning, and sleep quality persisted ($p </= 0.01$). Only the intra-pair difference in physical functioning distinguished twins with regional vs widespread pain ($p </= 0.05$). CONCLUSION: Both chronic regional and widespread pain exact debilitating effects on perceived general health, physical functioning, and sleep quality independent of CFS. However, the psychological and psychiatric influence of chronic pain appears closely tied to CFS. Research should examine the additive role of CFS-like illnesses in patients with chronic pain, and its influence on treatment and outcome.
Akid M.		Myalgic encephalomyelitis. Gold standard care.	Nurs Times. 2002 Jan 24-30;98(4):10-1.	
Alijotas J, Alegre J, Fernandez-Sola J, Cots JM, Panisello J, Peri JM, Pujol R; Grupo de Trabajo del Sindrome de Fatiga Cronico de Catalunya.	Unitat d'Atencio Hospitalaria, Area Sanitaria, Servei Catala de Salut, Universitat de Barcelona, Spain. 16297jar@comb.es	[Consensus report on the diagnosis and treatment of chronique fatigue syndrome in Catalonia] [Article in Spanish]	Med Clin (Barc). 2002 Jan 26;118(2):73-6.	
Allanson J, Bass C, Wade DT.	Heberden Rehabilitation Unit,	Characteristics of patients with	J Neurol Neurosurg Psychiatry. 2002	This study audited 25 patients (21 female) from Oxfordshire who had been referred to either the liaison psychiatry or the neurological disability service between 1992 and 1998, reported a

	Amersham Hospital, Amersham, Buckinghamshire HP7 0JD, UK. allanson@doctors.org.uk	persistent severe disability and medically unexplained neurological symptoms: a pilot study.	Sep;73(3):307-9.	Barthel activities of daily living index score < 20 or a global assessment of functioning score of < or = 30, and had no pathology to explain their neurological disability. Levels of motor impairment, disability, mood, and cognitive status were assessed using standardised scales, and all patients were assigned a psychiatric diagnosis according to the International classification of diseases, 10th revision. Of the 25 patients, 13 had a motor conversion disorder, 8 had diverse somatoform disorders, and 3 had chronic fatigue syndrome. Nine had extensive previous contact with psychiatric services and 11 had experienced physical or sexual abuse. In 6 patients cessation of repeated self harm was closely associated with the onset of wheelchair use. Seven were receiving treatment for depression. The commonest putative diagnoses were multiple sclerosis (6) and epilepsy (5). Twelve were unable to walk and 20 owned a wheelchair but only 3 had formal care packages. The mean (SD) Barthel score was 14.1 (3.3) and the mean (SD) Frenchay activity index score was 12.9 (7.5). All were unemployed and receiving a disability living allowance, and some had benefits of up to pound 1815 a month. This small but significant group of disabled patients had a variety of psychiatric and neurological diagnoses and used considerable health care resources.
Anderson LS, Beverly WT, Corey LA, Murrelle L.	Virginia Institute for Psychiatric and Behavioral Genetics, Department of Human Genetics, Virginia Commonwealth University, Richmond, VA 23298-0003, USA. lsanders@hsc.vcu.edu	The Mid-Atlantic Twin Registry.	Twin Res. 2002 Oct;5(5):449-55.	The Mid-Atlantic Twin Registry (MATR) is a population-based registry of twin pairs ascertained from birth records and school system records of Virginia, North Carolina, and South Carolina. The MATR was formed in 1997 with the merging of the Virginia and North Carolina Twin Registries, and it expanded to include South Carolina when access to twin birth records in that state was granted in 1998. Registered twins ("participants") number more than 51,000, with approximately 46,000 of these individuals representing complete pairs. Roughly two-thirds of MATR participants are over age 18, with a mean age of approximately 35 years. These participants have primarily been drawn from the more than 170,000 identical and fraternal twin pairs born in the three states between 1913 and 2000. Twins and their family members have participated in numerous research projects, ranging from general health surveys to studies on specific health topics such as cardiovascular disease; depression and anxiety; seizures; behavioral development; pregnancy complications; conduct disorder; drug use, abuse, and dependence; cleft lip/palate; obesity; and chronic fatigue syndrome. The MATR has established a privacy policy and strict standard operating procedures to protect the confidentiality of participant data. The MATR considers a limited number of qualified requests per year from investigators interested in recruiting MATR participants into their research studies.
Anon		Information from your family doctor. Chronic fatigue syndrome: how to help yourself.	Am Fam Physician. 2002 Mar 15;65(6):1095.	
Anon		Endometriosis sufferers risk other diseases. Surveys explore etiology,	AWHONN Lifelines. 2002 Dec;6(6):502-4.	

		long-term effects in women.		
Anon		Systematic review of the current literature related to disability and Chronic Fatigue Syndrome.	Evid Rep Technol Assess (Summ). 2002 Dec;(66):1-3.	
Arnold MC, Papanicolaou DA, O'Grady JA, Lotsikas A, Dale JK, Straus SE, Grafman J.	National Institute of Neurological Disorders and Stroke, National Institute of Child Health and Human Development and National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892-1440, USA.	Using an interleukin-6 challenge to evaluate neuropsychological performance in chronic fatigue syndrome.	Psychol Med. 2002 Aug;32(6):1075-89.	BACKGROUND: Individuals with acute infections experience a range of symptoms including fatigue, malaise, muscle aches, and difficulties with concentration and memory that are usually self-limited. This cluster of symptoms is otherwise, similar to those that characterize chronic fatigue syndrome (CFS). The goal of the present study was to evaluate the cognitive and psychological functioning of CFS patients and normal controls (NCs) when they both were experiencing acute influenza-like symptoms. To induce influenza-like symptoms, we administered interleukin-6 (IL-6), a cytokine that temporarily activates the acute phase immunological and endocrine responses. METHODS: Nineteen patients who met the 1994 International CFS Study Group Criteria and ten normal controls (NCs) completed routine clinical evaluations, neuropsychological tests of short-term memory, selective attention, and executive control, and self-ratings of somatic symptoms and psychological mood before, shortly following, and 1 day after IL-6 administration. RESULTS: CFS patients consistently reported more somatic symptoms, even when both groups perceived that they were ill. Both groups somatic symptoms increased during the IL-6 challenge, but the CFS patients symptoms increased more rapidly than controls. In general, the CFS patients performed similarly to NCs on the cognitive measures before, during, and after the IL-6. In contrast to predictions, IL-6 provocation did not impair the cognitive performance of either CFS patients or NCs. CONCLUSIONS: The IL-6 provocation exacerbated the patients self-reported symptoms but did not reveal notable cognitive impairments between patients and controls during cytokine-induced acute influenza-like symptoms.
Asbring P, Narvanen AL.	Centre for Development of Health Services, Department of Public Health Sciences at Karolinska Institutet in Stockholm, Sweden.	Women's experiences of stigma in relation to chronic fatigue syndrome and fibromyalgia.	Qual Health Res. 2002 Feb;12(2):148-60. Comment in: Evid Based Ment Health. 2002 Nov;5(4):127.	Chronic fatigue syndrome and fibromyalgia are characterized by being difficult to diagnose and having an elusive etiology and no clear-cut treatment strategy. The question of whether these illnesses are stigmatizing was investigated through interviews with 25 women with these illnesses. The women experienced stigmatization primarily before receiving a diagnosis, and the diffuse symptomatology associated with the illnesses were significant for stigmatization. Stigma consisted of questioning the veracity, morality, and accuracy of patient symptom descriptions and of psychologizing symptoms. Coping with stigma was also explored and found to comprise both withdrawal and approach strategies, depending on the individual's circumstances and goals.
Ax S, Gregg VH, Jones D.	School of Health, Liverpool John Moores University, 79 Tithebarn Street, Liverpool L2 2ER,	Caring for a relative with chronic fatigue syndrome: difficulties, cognition and acceptance over	J R Soc Health. 2002 Mar;122(1):35-42.	The present study explored the difficulties experienced by carers of chronic fatigue syndrome (CFS) sufferers, their cognitions, and their efforts to accept the illness. Semi-structured interviews were conducted with 17 carers to study these issues, retrospectively, over three stages: before the diagnosis of CFS, shortly after the diagnosis, and at present. Surprisingly, the results suggested that carers, several of them absent from home during the day, felt that their lives were

	England. heasax@yahoo.com	time.		only minimally constrained by the illness. Nevertheless, all carers reported specific coping efforts to manage both the illness and their own distress, and indicated that they learned to accept the illness over time. However, acceptance appeared to be a form of resignation rather than a positive appreciation of the illness. In light of the uncertainties surrounding the origin of CFS and carers' apparent confusion, the results obtained in the present study are significant in that they increase our understanding of CFS carers' quality of life, their efforts to cope with the illness, and the physical and emotional help they may provide to the sufferer. Such information can be usefully employed in the increasing development of counselling interventions and instrumental support networks that involve both sufferers and their carers.
Ayres JG, Wildman M, Groves J, Ment J, Smith EG, Beattie JM.	Department of Respiratory Medicine, Birmingham Heartlands Hospital, Birmingham, UK. ayresj@heartsol.wmids.nhs.uk	Long-term follow-up of patients from the 1989 Q fever outbreak: no evidence of excess cardiac disease in those with fatigue.	QJM. 2002 Aug;95(8):539-46. Comment in: QJM. 2002 Aug;95(8):491-2.	BACKGROUND: In 1989, an outbreak of Q fever (C. burnetii infection) with 147 confirmed cases occurred in Solihull, West Midlands. Three patients developed cardiomyopathy in the subsequent 10 years. The cohort has been followed up with respect to the development of fatigue and, in this instance, cardiac effects after the original infection. AIM: To determine whether persisting fatigue after Q fever represented sub-clinical cardiomyopathy. DESIGN: Prospective follow-up study. METHODS: All traceable subjects from the original outbreak, and community age-, sex- and smoking-matched controls, were studied. Questionnaires for idiopathic fatigue, 12-lead ECG, echocardiography, spirometry and shuttle walk distance were undertaken, and a subset with CDC-defined chronic fatigue syndrome had gated cardiac scans. RESULTS: Of the original cohort, 19 had died, three had emigrated and 10 were untraceable. Of the remaining 115, 108 responded to a mailed questionnaire and 87 were investigated further, of whom 85 provided complete data. Two developed aortic valve vegetations, one of whom died. Chronic fatigue syndrome was found in 20% of cases and 5.3% of controls (including those with co-morbidities), falling to 8.2% and 0 when excluding those with co-morbidities. There were no significant differences in ECG and echocardiographic investigations or shuttle-walk distance between those with fatigue and those without. Six of the seven patients with CFS had gated cardiac scans: all were within normal limits. CONCLUSIONS: These findings do not support the existence of a sub-clinical cardiomyopathy in the patients in this cohort who suffer from fatigue after acute Q fever, although endocarditis can occur after acute infection.
Bagnall AM, Whiting P, Richardson R, Sowden AJ.	NHS Centre for Reviews and Dissemination, University of York, York YO10 5DD, UK. amb13@york.ac.uk	Interventions for the treatment and management of chronic fatigue syndrome/myalgic encephalomyelitis.	Qual Saf Health Care. 2002 Sep;11(3):284-8.	
Bagnall AM, Whiting P, Richardson R, Sowden AJ.	NHS Centre for Reviews and Dissemination, University of York, York YO10 5DD, UK.	Interventions for the treatment and management of chronic fatigue syndrome/myalgic encephalomyelitis.	Qual Saf Health Care. 2002 Sep;11(3):284-8.	The research evidence on the effectiveness of interventions for the treatment and management of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) published in a recent issue of Effective Health Care is reviewed.

Bailly L	Chronic fatigue syndrome or neurasthenia		Br J Psychiatry. 2002 Oct;181:350-1. Comment on: Br J Psychiatry. 2002 Jul;181:56-61.	.
Barbier D		[Demedicalization of hysteria] [Article in French]	Soins Psychiatr. 2002 Jul;(221):34.	
Barron DF, Cohen BA, Geraghty MT, Violand R, Rowe PC.	Department of Pediatrics, and the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, 21287, USA.	Joint hypermobility is more common in children with chronic fatigue syndrome than in healthy controls.	J Pediatr. 2002 Sep;141(3):421-5.	OBJECTIVE: To determine whether children with chronic fatigue syndrome (CFS) have a higher prevalence of joint hypermobility than gender-matched controls.Study design: Matched case-control study comparing the Beighton joint hypermobility scores in 58 consecutive children with CFS (incident cases) with 58 otherwise healthy controls referred to a dermatology clinic for evaluation of common skin problems. A second group of 58 patients previously diagnosed with CFS (prevalent cases) was matched by gender to the incident cases to evaluate temporal changes in referral patterns. RESULTS: Of the 58 patients in each group, 71% were female. The median Beighton scores were higher in incident CFS cases than in healthy controls (4 vs 1, P <.001). More incident CFS cases had Beighton scores >/=4 (consistent with joint hypermobility), 60% versus 24%, P <.0001. Incident and prevalent CFS cases had similar Beighton scores. The odds ratio for hypermobility in all patients with CFS versus healthy controls was 3.5 (P <.001; 95% CI, 1.6-7.5). CONCLUSIONS: Joint hypermobility is more common in patients with CFS than in otherwise healthy children with common skin disorders. The etiologic significance of the observed association remains to be defined.
Baschetti R.	Chronic unexplained fatigue		Postgrad Med J. 2002 Dec;78(926):763; author reply 763. Comment on: Postgrad Med J. 2002 Aug;78(922):445-6.	
Beard DD.	Chronic fatigue syndrome clinical practice guidelines: psychological factors.		Med J Aust. 2002 Nov 4;177(9):526; author reply 526-7. Comment on: Med J Aust. 2002 Jul 1;177(1):51-2	
Beck-Friis J.	j.beck-friis@telia.com	[Diagnosis of depressive disorder and so-called exhaustion	Lakartidningen. 2002 Feb 7;99(6):512-7.	Depressive disorders can be recognized by the loss of self-esteem; this contrasts with mourning and neurasthenic reactions, in which self-esteem remains intact. Just as depression can result from the gradual reduction and eventual loss of self-esteem, mourning and neurasthenic reactions can evolve into true depressive states. "Exhaustion depression", a new diagnostic

		depression. Self-esteem--a central concept] [Article in Swedish]		category connected to "burnout" situations, should be applied only when criteria for depressive disorder are fulfilled, including loss of self-esteem. When these criteria are lacking we should refer only to an exhaustion state provoked by stress. Neurotic mechanisms may represent a special class of relevant stress factors, but are not seen in manifest neurasthenic reactions and exhaustion depression.
Bentall RP, Powell P, Nye FJ, Edwards RH.	Department of Psychology, University of Manchester, Coupland I Building, Oxford Road, Manchester M13 9PL, UK.	Predictors of response to treatment for chronic fatigue syndrome.	Br J Psychiatry. 2002 Sep;181:248-52.	BACKGROUND: Controlled trials have shown that psychological interventions designed to encourage graded exercise can facilitate recovery from chronic fatigue syndrome. AIMS: To identify predictors of response to psychological treatment for chronic fatigue syndrome. METHOD: Of 114 patients assigned to equally effective treatment conditions in a randomised, controlled trial, 95 completed follow-up assessments. Relationships between variables measured prior to randomisation and changes in physical functioning and subjective handicap at 1 year were evaluated by multiple regression. RESULTS: Poor outcome was predicted by membership of a self-help group, being in receipt of sickness benefit at the start of treatment, and dysphoria as measured by the Hospital Anxiety and Depression scale. Severity of symptoms and duration of illness were not predictors of response. CONCLUSIONS: Poor outcome in the psychological treatment of chronic fatigue syndrome is predicted by variables that indicate resistance to accepting the therapeutic rationale, poor motivation to treatment adherence or secondary gains from illness.
Berner I, Gaubitz M, Jackisch C, Pfleiderer B.	Institute for Clinical Radiology, Universitat Munster, Albert-Schweitzer-Street 33, D-48129 Munster, Germany.	Comparative examination of complaints of patients with breast-cancer with and without silicone implants.	Eur J Obstet Gynecol Reprod Biol. 2002 Apr 10;102(1):61-6.	OBJECTIVE: To measure the relationship between silicone breast implants and various symptoms using a control group. STUDY DESIGN: A matched-pair-analysis of 96 women with breast-cancer (32 with silicone implants (K I); 64 without implants (K II)) was performed with help of a standardized questionnaire in respect to 50 single criteria. The condition of implants was monitored by MR-imaging. RESULTS: Athralgias and myalgias were not significantly more frequent in K I. Only six symptoms were reported significantly more often in patients with implants. Positive correlation with implant rupture was given only for the numb feeling/tingling sensation in extremities (P=0.02). There was no correlation between silicone implants and the symptoms of the "chronic-fatigue syndrome" nor any other described silicone-induced disease. CONCLUSIONS: According to our analysis many of the symptoms examined here are present in middle-aged women regardless of silicone implants and underlying disease.
Bourrillon A, Arsan A.	Service de pediatrie generale, hopital Robert Debre, 48, boulevard Serurier, 75019 Paris, France. antoine.bourrillon@rdb.ap-hop-paris.fr	[Childhood fatigue] [Article in French]	Arch Pediatr. 2002 May;9 Suppl 2:203s-207s.	
Brage S.	Utredningsavdelingen Rikstrygdeverket 0241 Oslo. brage@ryggnett.no	[Utilization of national insurance in connection with functional somatic	Tidsskr Nor Laegeforen. 2002 May 30;122(14):1397-	BACKGROUND: Functional somatic disorders are often seen in medical practice. This study describes their financial consequences for the national insurance scheme. MATERIAL AND METHODS: National Insurance Administration data for the year 2000 were collected on sickness leave and disability pensions for fibromyalgia, whiplash injuries, chronic fatigue syndrome,

		disorders] [Article in Norwegian]	401.	dissociative and somatoform disorders, functional gastrointestinal disorders, chronic pelvic pain, and non-cardiac chest pain. RESULTS: Functional somatic disorders caused 2.9% of all sick leave among employees. Most of these were caused by fatigue/exhaustion or fibromyalgia. 6.3% of all new disability pensioners had a functional disorder, two thirds of them fibromyalgia. Functional disorders were more frequent in women, and in the 25-59 age group. INTERPRETATION: Functional disorders, fibromyalgia especially, are a great concern for the national insurance system. More focus on individual functioning rather than the disorder might contribute to better follow-up for these patients.
Brimacombe M, Helmer DA, Natelson BH.		Birth order and its association with the onset of chronic fatigue syndrome.	Hum Biol. 2002 Aug;74(4):615-20.	Chronic fatigue syndrome (CFS) is a medically unexplained illness that is diagnosed on the basis of a clinical case definition; so it probably is an illness with multiple causes producing the same clinical picture. One way of dealing with this heterogeneity is to stratify patients based on illness onset. We hypothesized that either the whole group of CFS patients or that group which developed CFS gradually would show a relation with birth order, while patients who developed CFS suddenly, probably due to a viral illness, would not show such a relation. We hypothesized the birth order effect in the gradual onset group because those patients have more psychological problems, and birth order effects have been shown for psychological characteristics. We compared birth order in our CFS patients to that in a comparison group derived from U.S. demographic data. We found a tendency that did not reach formal statistical significance for a birth order effect in the gradual onset group, but not in either the sudden onset or combined total group. However, the birth order effect we found was due to relatively increased rates of CFS in second-born children; prior birth order studies of personality characteristics have found such effects to be skewed toward first-born children. Thus, our data do support a birth order effect in a subset of patients with CFS. The results of this study should encourage a larger multicenter study to further explore and understand this relation.
Brimacombe M, Zhang Q, Lange G, Natelson BH.	Department of Preventive Medicine, University of Medicine and Dentistry - New Jersey Medical School, Newark, NJ 070718, USA.	Immunological variables mediate cognitive dysfunction in gulf war veterans but not civilians with chronic fatigue syndrome.	Neuroimmunomodulation. 2002-2003;10(2):93-100.	We explored the relationship between a set of immunological variables and a set of cognitive and functional status measures and a diagnosis of chronic fatigue syndrome (CFS) in civilians and veterans using various regression and factor analytic methods. Our approach emphasized the extraction of a few distinct factors in order to limit statistical problems associated with doing large numbers of multiple comparisons. This approach led to our finding cytokine data grouping into type 1 and type 2 clusters. A type 2 cluster plus a T and B cell factor predicted CFS caseness for Gulf War veterans but not for civilians with CFS. When a cognitive variable, reaction time, was added into the model, both immunological factors lost statistical significance; this indicates that the cognitive variable reaction time moderated the effects of the immunological factors in predicting patient status. We did a similar analysis on the roles of the immunological and cognitive variables in functional status using SF-36 data. Higher levels of these same two immunological factors predicted poorer general health as well as poorer physical and social functioning in Gulf War veterans but not in civilians with CFS. When the reaction time factor was added, only the lymphocyte factor remained significant. This implies that lymphocytes are directly related to functional status in Gulf War veterans with CFS, but the Th2 factor produces its effect on functional status via changes in cognitive abilities. Copyright 2002 S. Karger AG, Basel

Bron D.	Service d'Hematologie, Institut Jules Bordet, U.L.B.	[Fatigue and quality of life in cancer patients] [Article in French]	Rev Med Brux. 2002 Sep;23(4):A294-8.	Fatigue is the most frequent adverse event encountered in cancer patients and often underestimated by oncologists. This fatigue results in a deterioration of the quality of life physically, psychologically and socio-professionally. We have to distinguish various degrees of fatigue and identify "acute" fatigue from "chronic" fatigue. The acute fatigue appears normal after a physical or psychological effort and requires less than a week of rest to recover; the impact on quality of life is thus minimal. Chronic fatigue is more insidious; the causes are multiple. The patient feels that this fatigue is abnormal and disproportionate. It last several weeks and has a severe impact on the quality of life. Somatic mechanisms of fatigue related to the tumour and/or treatment are: vitaminic or proteic deficiencies due to malnutrition, accumulation of toxic metabolites, infections and septicemia, the abuse of sleeping tablets or antalgics, insomnias, immobilisation, organic insufficiencies or ionic disturbances. Anemia--observed in more than 50% of the cancerous patients--deserves a particular attention. The causes of this anemia are also multiple. It is obvious that anemia interferes with quality of life of the patient, decreases his physical performances and leads to a lack of motivation or energy. Patients with an hemoglobin level higher than 12 g/dl describe significantly less complaints and a higher physical and functional well being. To better assess the treatment of fatigue, it is important to first evaluate if the cause is organic, psychologic or mixed. Among the somatic causes, nutritious deficiencies, pain and anemia, . all these complications can be treated with appropriate medications. This fatigue is often recognized by the patient as a progression of the tumour or as a treatment failure. Therefore, it is important to inform the patients of the possibility of that adverse event so that it does not generate additional stress and anxiety during the treatment.
Brouwers FM, Van Der Werf S, Bleijenberg G, Van Der Zee L, Van Der Meer JW.	Departments of. General Internal Medicine and. Medical Psychology, University Medical Center Nijmegen, The Netherlands.	The effect of a polynutrient supplement on fatigue and physical activity of patients with chronic fatigue syndrome: a double-blind randomized controlled trial.	QJM. 2002 Oct;95(10):677-83.	BACKGROUND:The efficacy of dietary supplements in chronic fatigue syndrome (CFS) is uncertain, with conflicting evidence. Aim: To assess the effect of a polynutrient supplement on fatigue and physical activity of patients with CFS. DESIGN:Prospective randomized placebo-controlled, double-blind trial. METHODS:Fifty-three patients (16 males, 37 females) fulfilling the CDC criteria of CFS. The entry criteria were a score on the Checklist Individual Strength subscale fatigue severity (CIS fatigue) >or=40 and a weighted sum score of >or=750 for the eight subscales of the Sickness Impact Profile (SIP8) and no use of nutritional supplements in the 4 weeks prior to entry. The exclusion criteria were pregnancy and lactose intolerance. The intervention-a polynutrient supplement containing several vitamins, minerals and (co)enzymes, or placebo, twice daily for 10 weeks-was preceded by 2 weeks of baseline measurements. Outcome measurements took place in week 9 and 10 of the intervention. Five participants dropped out (4 supplement, 1 placebo). The main outcome measures were CIS fatigue score, number of CDC symptoms and SIP8 score. Efficacy analyses were performed on an intention-to-treat basis. RESULTS:No significant differences were found between the placebo and the treated group on any of the outcome measures: CIS fatigue +2.16 (95%CI -4.3 to +4.39, p=0.984); CDC symptoms +0.42 (95%CI -0.61 to +1.46, p=0.417); SIP8 +182 (95%CI -165 to +529, p=0.297). No patient reported full recovery. DISCUSSION:The findings do not support the use of a broad-spectrum nutritional supplement in treating CFS-related symptoms.
Brunet JL, Fatoohi F,	Service des Maladies	[Role of pathological	Allerg Immunol	Chronic fatigue syndrome or benign myalgic encephalomyelitis has been extensively described

Liaudet AP, Cozon GJ.	Infectieuses, Hopital de la Croix-Rousse, Lyon, France.	delayed-type hypersensitivity in chronic fatigue syndrome: importance of the evaluation of lymphocyte activation by flow cytometry and the measurement of urinary neopterin] [Article in French]	(Paris). 2002 Feb;34(2):38-44.	and investigated. Although numerous immunological abnormalities have been linked with the syndrome, none have been found to be specific. This article describes the detection of delayed-type hypersensitive responses to certain common environmental antigens in almost fifty per cent of patients with this syndrome. Such hypersensitivity can be detected by the intradermal administration of antigens derived from commensal organisms like the yeast Candida albicans, and then monitoring for a systemic reaction over the following six to forty eight hours. This approach can be consolidated by performing lymphocyte activation tests in parallel and measuring in vitro T-cell activation by Candida albicans antigens by three-colour flow cytometry based on CD3, CD4 and either CD69 or CD25. Another useful parameter is the kinetics of neopterin excretion in the urine over the course of the skin test. The results showed that the intensity of the DTH response correlated with the number of T-cells activated in vitro. Various factors have been implicated in the fatigue of many patients, notably lack of sleep. However, it remains difficult to establish causality in either one direction or the other. This work is in the spirit of a multifactorial approach to the group of conditions referred to as "chronic fatigue syndrome".
Candy B, Chalder T, Cleare AJ, Wessely S, White PD, Hotopf M.	Department of Psychological Medicine, Guy's, King's and St. Thomas' School of Medicine, London.	Recovery from infectious mononucleosis: a case for more than symptomatic therapy? A systematic review.	Br J Gen Pract. 2002 Oct;52(483):844-51.	Infectious mononucleosis is usually an acute, transiently incapacitating condition, but for some sufferers it precipitates chronic illness. It is unclear which patients are at risk of a prolonged state of illness following onset of infectious mononucleosis and if there are any useful preventive measures that would facilitate recovery. The aim of this study was to review all cohort studies and intervention trials that provide information on: (a) the longitudinal course of ill health subsequent to the onset of infectious mononucleosis; (b) the relationship between psychosocial and clinical factors and recovery rate; and (c) the effect of interventions on recovery. A systematic review was conducted, based on a search of the PSYCHINFO, MEDLINE, EMBASE and CINHAL databases up to October 2001, and ISI Science and Social Sciences Citation Indices up to 22 November 2001. Eight papers were identified that gave data on illness following onset of infectious mononucleosis. The best evidence concluded that there is a distinct fatigue syndrome after infectious mononucleosis. Eight papers explored risk factors for prolonged illness following acute infectious mononucleosis. Results varied on the association of acute illness characteristics and psychological features with prolonged ill health. Poor physical functioning, namely lengthy convalescence and being less fit or active, consistently predicted chronic ill health. Three trials reported on interventions that aimed to shorten the time taken to resolve symptoms after uncomplicated infectious mononucleosis. None of the drug trials found any evidence that drug therapy shortens recovery time. The trial that compared the effect of activity with imposed bed rest, found that those patients allowed out of bed as soon as they felt able reported a quicker recovery. More information is needed on the course of ill health subsequent to the onset of infectious mononucleosis. Certain risk factors associated with delay may be amenable to a simple intervention in primary care.
Cavanaugh RM Jr.	Department of Pediatrics, SUNY Upstate Medical	Evaluating adolescents with fatigue: ever get	Pediatr Rev. 2002 Oct;23(10):337-48.	

	University, Syracuse, NY, USA.	tired of it?		
Chalder T, Tong J, Deary V.	Academic Department of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine, 103 Denmark Hill, London SE5 8AZ, UK. t.chalder@iop.kcl.ac.uk	Family cognitive behaviour therapy for chronic fatigue syndrome: an uncontrolled study.	Arch Dis Child. 2002 Feb;86(2):95-7.	AIM: To examine the efficacy of family focused cognitive behaviour therapy for 11-18 year olds with chronic fatigue syndrome. METHODS: Twenty three patients were offered family focused cognitive behaviour therapy. The main outcome was a fatigue score of less than 4 and attendance at school 75% of the time. RESULTS: Twenty patients completed treatment. Eighteen had completed all measures at six months follow up; 15 of these (83%) improved according to our predetermined criterion. Substantial improvements in social adjustment, depression, and fear were noted. CONCLUSIONS: Family focused cognitive behaviour therapy was effective in improving functioning and reducing fatigue in 11-18 year olds. Gains were maintained at six months follow up.
Chaudhuri A.	Chronic fatigue syndrome and myalgic encephalomyelitis.		Lancet. 2002 May 11;359(9318):1698-9. Comment on: Lancet. 2002 Jan 12;359(9301):97-8.	
Cheng JS, Nash J, Meyer GA.	Section of Spinal Surgery, Vanderbilt University Medical Center, Nashville, Tennessee.	Chiari type I malformation revisited: diagnosis and treatment.	Neurolog. 2002 Nov;8(6):357-62.	BACKGROUND: Chiari type I malformations (Chiari I) are congenital deformities where caudal migration of the cerebellar tonsils through the foramen magnum compresses the cerebellum and cervicomedullary junction (lower brainstem and upper cervical spinal cord). Associations with chronic fatigue syndrome, fibromyalgia, orthostatic intolerance, and other neurologic syndromes have been proposed along with the current plethora of known symptoms of this disease process. In advanced cases, Chiari I malformations can lead to significant neurologic deficit and be the cause of permanent nervous system damage. REVIEW SUMMARY: This article focuses on the clinical diagnosistreatment of patients with Chiari I, including a discussion on the possible mechanisms of Chiari I with a review of present diagnostic tests, indications for treatment, and appraisal of surgical outcome. CONCLUSIONS: Future radiological advances and research will undoubtedly be directed to better understanding of the pathology of the Chiari malformation and more effective medical and surgical treatment.
Clark C, Buchwald D, MacIntyre A, Sharpe M, Wessely S.	Action for ME, 4 Dean's Court, St Paul's Churchyard, EC4V 5AA, London, UK. chris@afme.org.uk	Chronic fatigue syndrome: a step towards agreement.	Lancet. 2002 Jan 12;359(9301):97-8. Erratum in: Lancet 2002 Apr 13;359(9314):1352. Lancet 2002 May 25;359(9320):1866.	
Clark C.		Chronic fatigue syndrome.	Br J Gen Pract. 2002 Jul;52(480):586-7.	
Cogan E.	Service de Medecine	[Chronic fatigue	Rev Med Brux. 2002	Chronic fatigue is a very common symptom in primary care medicine. Psychiatric causes

	Interne, Hopital Erasme, U.L.B.	syndrome: the point of view of the internist] [Article in French]	Sep;23(4):A399-406.	represent more than 80% of the cases. After excluding all known causes of fatigue, 30% of the patients remain without a specific diagnosis and suffered from idiopathic chronic fatigue. The chronic fatigue syndrome (CFS) which represents a very small subset of these patients is a heterogeneous disorder characterized by fatigue, neuropsychiatric symptoms, and various other somatic complaints. The cause remains underdetermined and most of the treatments are ineffective. Antidepressants drugs may be helpful. A supportive approach, cognitive behavioural therapy and graded exercise seem so far the only evidence-based therapeutic approach.
Colby J.	Chronic fatigue syndrome and myalgic encephalomyelitis.		Lancet. 2002 May 11;359(9318):1698. Comment on: Lancet. 2002 Jan 12;359(9301):97-8.	
Craig T, Kakumanu S.	Department of Medicine, Pennsylvania State University College of Medicine, Hershey 17033, USA. tcraig@psu.edu	Chronic fatigue syndrome: evaluation and treatment.	Am Fam Physician. 2002 Mar 15;65(6):1083-90. Comment in: Am Fam Physician. 2002 Nov 15;66(10):1838-9; author reply 1839. Am Fam Physician. 2003 Jan 15;67(2):252; author reply 252.	Severe fatigue is a common complaint among patients. Often, the fatigue is transient or can be attributed to a definable organic illness. Some patients present with persistent and disabling fatigue, but show no abnormalities on physical examination or screening laboratory tests. In these cases, the diagnosis of chronic fatigue syndrome (CFS) should be considered. CFS is characterized by debilitating fatigue with associated myalgias, tender lymph nodes, arthralgias, chills, feverish feelings, and postexertional malaise. Diagnosis of CFS is primarily by exclusion with no definitive laboratory test or physical findings. Medical research continues to examine the many possible etiologic agents for CFS (infectious, immunologic, neurologic, and psychiatric), but the answer remains elusive. It is known that CFS is a heterogeneous disorder possibly involving an interaction of biologic systems. Similarities with fibromyalgia exist and concomitant illnesses include irritable bowel syndrome, depression, and headaches. Therefore, treatment of CFS may be variable and should be tailored to each patient. Therapy should include exercise, diet, good sleep hygiene, antidepressants, and other medications, depending on the patient's presentation.
Creswell C, Chalder T.	Sub-Department of Clinical Health Psychology, University College London, Gower Street, London WC1E 6BT, UK. c.creswell@ucl.ac.uk	Underlying self-esteem in chronic fatigue syndrome.	J Psychosom Res. 2002 Sep;53(3):755-61.	OBJECTIVE: It has been suggested that people with chronic fatigue syndrome (CFS) have low self-esteem; however, this is not necessarily apparent when self-esteem is measured overtly. This study is the first to investigate underlying self-esteem using information-processing measures and overtly administered measures of self-esteem with this population. METHODS: The study comprised 68 participants (24 CFS, 24 healthy volunteers, and 20 chronic illness volunteers). A Self-Statements Questionnaire (SSQ) and an Emotional Stroop Test (EST) using neutral, positive, and negative trait words were administered. RESULTS: Participants with CFS reported lower self-esteem than the two comparison groups on overt measures. Overt responses, however, did not fully account for the full extent of the interference effect from the negative word Stroop compared to the positive word Stroop. CONCLUSION: In contrast to previous studies, participants with CFS reported lower levels of self-esteem on overt measures than two comparison groups. It is suggested, however, that the extent to which participants reported low self-esteem did not fully reflect their underlying low self-esteem and that this may result from the use of rigidly held defence mechanisms. Further use of information-processing measures, in contrast to relying only on self-report measures, is advocated for future research. Copyright 2002 Elsevier Science Inc.

Cullen W, Kearney Y, Bury G.	Department of General Practice, University College Dublin, Ireland. walter.cullen@ucd.ie	Prevalence of fatigue in general practice.	Ir J Med Sci. 2002 Jan-Mar;171(1):10-2.	BACKGROUND: Fatigue is an important symptom in general practice due to its association with physical, psychological and social problems. AIM: To determine the prevalence of fatigue as an unsolicited symptom during general practice consultations. METHODS: A random sample of GPs practising in Ireland was invited to provide data on consultations held over one day. Data were recorded on the presence of fatigue as a main or supporting symptom, social and demographic characteristics. RESULTS: Data were recorded by 89 GPs on 1,428 consultations. The prevalence of fatigue was 25%. It was the main reason for attending the doctor in 6.5% and a secondary reason in 19%. Sixty-two per cent of patients were female and 48% were eligible for free GP services. The mean age was 47.1 years. The presence of fatigue was associated with: attending a female GP, being female, attending a GP who had been qualified for fewer years and attending the GP frequently. CONCLUSION: The prevalence of fatigue reported in this study is over three times higher than that reported in earlier work. Doctor characteristics appear to be as important as patient characteristics in determining fatigue.
De Becker P, McGregor N, De Meirleir K.		Possible Triggers and Mode of Onset of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2002; 10(2): 3 - 18	To identify the possible triggering events of CFS, we collected data on 1546 CFS patients and 309 excluded fatigued patients. Using extensive present and past medical history and lab reports as close as possible to the date of onset, an attempt was made to identify the agents that could play a role in the disease process. Significant differences were found between the events at onset, between the Fukuda or Holmes definitions and a sudden as distinct from a gradual onset. We further found a series of subgroups of events that occurred at onset of CFS. Each of these onset event clusters was associated with an infectious event, blood transfusion or hepatitis B vaccination. In a large percentage of our study group an infectious event was combined with a non-infectious event. In summary, we can conclude that a number of different stressors and consequent immunological and neuroendocrinological changes can contribute to the onset of CFS.
De Meirleir K, Suhadolnik RJ, Lebleu B, Englebienne P.	Antiviral pathway activation in chronic fatigue syndrome and acute infection.		Clin Infect Dis. 2002 May 15;34(10):1420-1; author reply 1421-2. Comment on: Clin Infect Dis. 2001 Dec 15;33(12):2080-1.	
De Sanctis V, Mangiagli A, Campisi S, Raiola G.	UO di Pediatria ed Adolscentologia, Arcispedale S. Anna, Ferrara, Italy.	[Chronic fatigue syndrome in adolescent] [Article in Italian]	Minerva Pediatr. 2002 Dec;54(6):631-7.	Fatigue is defined as a subjective sensation of tiredness or weariness that occurs at rest. The perception of fatigue among 12-15 years-old Italian adolescents in a school survey was about 70%. Generally the symptoms are reported after a viral illness or an infection. In adolescents with persistent or severe fatigue a selected screening evaluation to look for an underlying organic disorder is warranted. A practical diagnostic approach is given and a brief description of chronic fatigue syndrome is reported according to CDC revised diagnostic criteria published in 1997.
Demettre E, Bastide L, D'Haese A, De Smet K, De Meirleir K, Tiev KP,	UMR 5124 CNRS, Universite Montpellier 2, 34293 Montpellier, France.	Ribonuclease L proteolysis in peripheral blood mononuclear cells of	J Biol Chem. 2002 Sep 20;277(38):35746-51. Epub 2002 Jul 12.	A 37-kDa binding polypeptide accumulates in peripheral blood mononuclear cell (PBMC) extracts from chronic fatigue syndrome (CFS) patients and is being considered as a potential diagnostic marker (De Meirleir, K., Bisbal, C., Campine, I., De Becker, P., Salehzada, T., Demettre, E., and Lebleu, B. (2000) Am. J. Med. 108, 99-105). We establish here that this low molecular weight 2-

Englebienne P, Lebleu B.		chronic fatigue syndrome patients.		5A-binding polypeptide is a truncated form of the native 2-5A-dependent ribonuclease L (RNase L), generated by an increased proteolytic activity in CFS PBMC extracts. RNase L proteolysis in CFS PBMC extracts can be mimicked in a model system in which recombinant RNase L is treated with human leukocyte elastase. RNase L proteolysis leads to the accumulation of two major fragments with molecular masses of 37 and 30 kDa. The 37-kDa fragment includes the 2-5A binding site and the N-terminal end of native RNase L. The 30-kDa fragment includes the catalytic site in the C-terminal part of RNase L. Interestingly, RNase L remains active and 2-5A-dependent when degraded into its 30- and 37-kDa fragments by proteases of CFS PBMC extract or by purified human leukocyte elastase. The 2-5A-dependent nuclease activity of the truncated RNase L could result from the association of these digestion products, as suggested in pull down experiments.
Di Gallo A.	Kinder- und Jugendpsychiatrische Universitatsklinik und -poliklinik Basel. alain.di-gallo@unibas.ch	[Symptom or illness? The exhausting life of an adolescent with chronic fatigue syndrome] [Article in German]	Z Kinder Jugendpsychiatr Psychother. 2002 May;30(2):135-40.	This case report presents the assessment of a 16-year old boy with chronic fatigue syndrome (CFS). Questions on the etiology, dynamics, diagnostics and treatment of this complex condition are briefly discussed.
Ducobu J.	Service de Medecine Interne, C.H.U. Tivoli, U.L.B.	[Chronic fatigue: introduction] [Article in French	Rev Med Brux. 2002 Sep;23(4):A279-82.	Chronic fatigue is frequent in primary care practice. After exclusion of medical causes, psychosocial factors and chronic fatigue syndrome (CFS) must be searched. The differential diagnosis is long and difficult, but it depends more of good clinical evaluation than of extensive laboratory investigation.
Durlach J, Pages N, Bac P, Bara M, Guiet-Bara A, Agrapart C.	SDRM, Universite Pierre et Marie Curie Paris V, F-75252 Paris, France. Jean.Durlach@wanadoo.fr	Chronopathological forms of magnesium depletion with hypofunction or with hyperfunction of the biological clock.	Magnes Res. 2002 Dec;15(3-4):263-8.	The main mechanisms of the chronopathological forms of magnesium depletion associate a low Mg intake with various dysregulating biorhythms. The differentiation between forms with hyperfunction and forms with hypofunction of the biological clock is seminal and the main marker is the production of melatonin (MT). The clinical forms of the various patterns of the chronopathological forms of Mg depletion may be central or peripheral. The clinical forms with hyperfunction of the biological clock (marker: increase in MT) may associate diverse expressions of nervous hypoexcitability: depression (i.e. Seasonal affective disease); cephalalgias nocturnal, without photophobia (i.e. cluster headaches); dyssomnia LASPS (advanced sleep phase syndrome) particularly]; asthenia and myalgias (i.e. fibromyalgia, chronic fatigue syndrome). The main comorbidity is found with depressive states. The therapy relies on classical bright light phototherapy, sometimes associated with psychoanaleptics. The clinical forms with hypofunction of biological clock (marker: decrease in MT) may associate various signs of nervous hyperexcitability (HEN): anxiety (from generalized anxiety to panic attacks); cephalalgias diurnal with photophobia (mainly migraine); dyssomnia [DSPS (delayed sleep phase syndrome) particularly, jet lag, night work disorders, age related insomnia, sometimes with inappropriate behaviour; photogenic epilepsia, generalized or focal; some clinical forms of chronic fatigue syndrome and fibromyalgia. The main comorbidity is between migraine and epilepsia. The treatment relies on the diverse forms of darkness therapy, possibly with the help of some psycholeptics: anxiolytics and anticonvulsants. The indications of chromatotherapy remain to be validated.

Durlach J, Pages N, Bac P, Bara M, Guiet-Bara A.	SDRM, Univ P et M Curie, Paris VI, France. Jean.Durlach@wanadoo.fr	Biorhythms and possible central regulation of magnesium status, phototherapy, darkness therapy and chronopathological forms of magnesium depletion.	Magnes Res. 2002 Mar;15(1-2):49-66.	Biological clock and magnesium status are linked. Central magnesium regulation may be hypothetized. Balanced magnesium status is requested to obtain efficiency of suprachiasmatic nuclei and of pineal gland. Conventional bright light therapy appears as a speedy and efficient antidepressant medication useful for the treatment of various types of depression, and of non migrainous headaches also. Although decrease in melatonin production seems accessory, increases of serotonergy and perhaps of Reactive Oxygen Species constitute the main mechanisms of action. Chromatotherapy emphazizes the effects of short exposure to specific colors. Although the increased production of melatonin constitutes the best marker of darkness, it is only an accessory mechanism of its action. The psycholeptic sedative effects of darkness, like those of magnesium, rely on direct membraneous and oxidant actions, neural mediated effects (i.e. stimulation of inhibitory neuromodulators such as GABA and taurine), and on antagonism of neuroactive gases (CO and NO). Darkness therapyper se, partial substitutive therapy with melatonin and with their mimicking agents (Mg, L-Tryptophan,Taurine) apply to all the chronopathological forms of magnesium depletion with decreased production of melatonin: sleep disorders, migraine, chronic fatigue syndrome, fibromyalgia, some forms of asthma and of sudden infant death syndrome. Further research should assess the importance of the chronopathological forms of magnesium depletion in the physiopathology of these disorders.
Dyer C.		Doctor accused of "interfering" in girl's treatment is cleared by GMC.	BMJ. 2002 Sep 28;325(7366):673.	
Eaton L.		Recognising chronic fatigue is key to improving outcomes.	BMJ. 2002 Jan 19;324(7330):131. Comment in: BMJ. 2002 Jan 19;324(7330):124-5.	
Eaton L.		Chronic fatigue report delayed as row breaks out over content.	BMJ. 2002 Jan 5;324(7328):7.	
Egg R, Hogl B, Glatzl S, Beer R, Berger T.	Department of Neurology, University Hospital Innsbruck, Austria.	Autonomic instability, as measured by pupillary unrest, is not associated with multiple sclerosis fatigue severity.	Mult Scler. 2002 May;8(3):256-60.	Multiple sclerosis (MS) fatigue is one of the most common symptoms in MS, but its pathophysiology is still not understood Sympathovagal imbalance was suggested as a reason for fatigue in chronic fatigue syndrome. We examined the role of an imbalance in the central autonomic nervous system (ANS) as a cause of MS fatigue in 51 MS patients and a control group of 22 healthy volunteers. Fatigue was assessed with the revised MS Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale (MFIS). Depression was evaluated with the Beck Depression Inventory (BDI). Disintegration of the central ANS expressed by pupillary fatigue waves was measured with pupillography and documented in the pupillary unrest index (PUI). All subjects had less than five points on the seven-point Stanford Sleepiness Scale and were therefore not sleepy. MS patients had significant higher mean FSS scores (p=0.001) and mean

				MFIS scores (p=0.003) than our control group. Mean BDI scores were significant higher (p=0.001) in the MS group, but were in the lowest score range (0-10 points) in both groups. Surprisingly, we found a statistically significant inverse correlation between PUI values and either FSS scores (p=0.001; r=-0.521) or MFIS scores (p=0.002; r=-0.423) in the MS group, but not in healthy participants. We therefore conclude that autonomic instability, as measured by pupillary unrest is not associated with MS fatigue severity.
Endicott NA.		Chronic Fatigue Syndrome in Psychiatric Patients: Exposure to Potentially Toxic Substances	Journal of Chronic Fatigue Syndrome 2002; 10 (1): 37 - 53	Several investigators have suggested that environmental chemicals or "pollutants" play a significant role in the pathogenesis of chronic fatigue syndrome (CFS). This study compares the reported exposures to environmental chemicals and other potentially toxic environmental factors of psychiatric patients with CFS and two sets of controls fom the same practice who did not meet the criteria for CFS. All comparisons found the CFS patients reported significantly more exposures to potentially toxic substances than any of the control groups. The extensive scientific literature on chemical intolerance and sensitization to generally non-toxic levels of potentially toxic substances, and its possible relevance to the investigation of CFS, is discussed.
Engel CC Jr, Adkins JA, Cowan DN.	Deployment Health Clinical Center, Walter Reed Army Medical Center, Washington, DC, USA. cengel@usuhs.mil	Caring for medically unexplained physical symptoms after toxic environmental exposures: effects of contested causation.	Environ Health Perspect. 2002 Aug;110 Suppl 4:641-7.	Medically unexplained physical symptoms (MUPS) are persistent idiopathic symptoms that drive patients to seek medical care. MUPS syndromes include chronic fatigue syndrome, fibromyalgia syndrome, and multiple chemical sensitivities. When MUPS occur after an environmental exposure or injury, an adversarial social context that we call "contested causation" may ensue. Contested causation may occur publicly and involve media controversy, scientific disagreement, political debate, and legal struggles. This adversarial social context may diminish the effectiveness of the provider-patient relationship. Contested causation also may occur privately, when disagreement over the causes of MUPS takes place in the patient-provider context. These patient-provider disagreements over causation often occur because of the enigmatic nature of MUPS. We suggest that a context of contested causation may have serious negative effects on healthcare for individuals with MUPS. Context plays a larger role in MUPS care than it does for most medical care because of the uncertain nature of MUPS, the reliance of standard MUPS therapies on a potentially tenuous patient-provider partnership, and the clinical need to rely routinely on subjective MUPS assessments that often yield discordant patient and provider conclusions. Contested causation may erode patient-provider trust, test the provider's self-assurance and capacity to share power with the patient, and raise problematic issues of compensation, reparation, and blame. These issues may distract patients and providers from therapeutic goals. In occupational and military settings, the adverse impact of contested causation on the patient-provider partnership may diminish therapeutic effectiveness to a greater degree than it does in other medical settings. Contested causation therefore raises questions regarding generalizability of standard therapies for MUPS and related syndromes to these settings. Future research is needed to learn whether intuitively sensible and evidence-based MUPS therapies benefit occupational and military medical patients who are afforded care in the context of contested causation.
Evengard B, Klimas N.	Department of Immunology,	Chronic fatigue syndrome: probable	Drugs. 2002;62(17):2433-	Chronic fatigue syndrome (CFS) belongs in the medically unexplained illnesses. It affects approximately 0.2-0.7% of the population in Western countries. It is characterised by unexplained

	Microbiology and Pathology, Karolinska Institutet at Huddinge University Hospital, Stockholm, Sweden. birgitta.evengard@infect.hs.sll.se	pathogenesis and possible treatments.	46.	fatigue, lasting 6 months or more, impairment of neurocognitive functions and quality of sleep, and of somatic symptoms, such as recurrent sore throat, muscle aches, arthralgias, headache and postexertional malaise. No link between infections and CFS has been clearly established but the immune system is activated, there are aberrations in several hypothalamic-pituitary axes and involvement of other parts of the central nervous system. No specific treatment has been found. Cognitive behavioural therapy is established to be of value to improve quality of life. More effective treatment should result, as advances in biomedical as well as psychological research continue.
Farquhar WB, Hunt BE, Taylor JA, Darling SE, Freeman R.	Center for Autonomic and Peripheral Nerve Disorders, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215, USA.	Blood volume and its relation to peak O(2) consumption and physical activity in patients with chronic fatigue.	Am J Physiol Heart Circ Physiol. 2002 Jan;282(1):H66-71.	Individuals with chronic fatigue syndrome (CFS) experience a number of somatic complaints including severe, disabling fatigue, and exercise intolerance. We hypothesized that hypovolemia, through its interaction with central hemodynamics, would contribute to the exercise intolerance associated with this disorder. We examined blood volume, peak aerobic power, habitual physical activity, fatigue level, and their interrelations to understand the physiological basis of this disorder. Seventeen patients who met the Centers for Disease Control criteria for CFS and 17 age-matched controls participated in the study. Blood volume was assessed using a single bolus injection of Evans blue dye. Peak oxygen consumption was measured during exercise on an upright cycle ergometer. Supine cardiac output and stroke volumes were measured using CO(2) rebreathing. Questionnaires were used to assess habitual physical activity and fatigue. Patients displayed a trend for a 9% lower blood volume (58.3 +/- 2.1 vs. 64.2 +/- 2.5 ml/kg, P = 0.084) and had a 35% lower peak oxygen consumption (22.0 +/- 1.2 vs. 33.6 +/- 1.9 ml/kg, P < 0.001). These two variables were highly related within the patients (r = 0.835, P < 0.001) and the controls (r = 0.850, P < 0.001). Peak ventilation and habitual physical activity were significantly lower in the patients. Fatigue level was not related to any of the measured physiological parameters within the CFS group. In conclusion, individuals with CFS have a significantly lower peak oxygen consumption and an insignificant trend toward lower blood volume compared with controls. These variables were highly related in both subject groups, indicating that blood volume is a strong physiological correlate of peak oxygen consumption in patients with CFS.
Ferreira AC, de Marchena E.		Grading autonomic dysfunction in chronic fatigue syndrome.	Semin Arthritis Rheum. 2002 Dec;32(3):137-8 Comment on: Semin Arthritis Rheum. 2002 Dec;32(3):141-8.	Review Review, Tutorial
Fisher M, Krilov LR, Ovadia M.	Division of Adolescent Medicine, Division of Pediatric Infectious Diseases, Division of Pediatric Cardiology,	Chronic fatigue syndrome and eating disorders: concurrence or coincidence?	Int J Adolesc Med Health. 2002 Oct-Dec;14(4):307-16.	In this report we present four patients who were found to have both an eating disorder and the chronic fatigue syndrome (CFS). Two of the patients presented for evaluation of an eating disorder and also had CFS, while two of the patients presented for evaluation of CFS and also had an eating disorder. In all four patients the eating disorder preceded the CFS. We consider the question of whether the occurrence of these two disorders in the same patients is merely a coincidence; whether an eating disorder can act as a precipitant for CFS, perhaps through the

	North Shore University Hospital, North Shore-Long Island Jewish Health System, Manhasset, NY, USA. Fisher@nshs.edu			exacerbation of an underlying vascular instability; and whether overlapping etiologies may predispose some adolescents to develop both disorders. We also discuss similarities (including diagnostic dilemmas, cultural influences, psychological correlates, demographic similarities, perceptual biases, and cardiovascular effects) encountered in the management of both of these disorders.
Fitzpatrick M.	fitz@easynet.co.uk	Myalgic encephalomyelitis--the dangers of Cartesian fundamentalism.	Br J Gen Pract. 2002 May;52(478):432-3.	
Fortune DG, Richards HL, Main CJ, Griffiths CE.	Dermatology Centre, University of Manchester School of Medicine, Hope Hospital, Salford, UK.	Patients' strategies for coping with psoriasis.	Clin Exp Dermatol. 2002 May;27(3):177-84.	There is a paucity of research on the types of strategies that patients with psoriasis use to cope with the impact of their condition. By contrast there are a number of studies assessing coping by patients with nondermatological disease. The purpose of the present study was to examine strategies for coping in patients with psoriasis and investigate whether they differ as compared with normal controls and patients with other major medical diseases. Two hundred and fifty patients with a definite dermatologist-confirmed diagnosis of psoriasis participated in this cross-sectional study. Patients were assessed by psoriasis area severity index and all patients completed the COPE questionnaire and psoriasis disability index. Sixty healthy, control participants completed the COPE questionnaire for comparison purposes. Mean COPE scores from patients with psoriasis were also compared with published COPE scores from other medical diseases. The coping strategies most frequently used by patients with psoriasis were acceptance, planning, active coping and positive reinterpretation. The least frequently used were alcohol and nonprescription drugs, religion, and denial of their condition. Despite reporting greater disability, patients with severe psoriasis did not significantly differ from those with mild/moderate disease in their use of particular forms of coping strategies. Patients with psoriasis as a whole tended to use significantly less active coping strategies, planning, positive reinterpretation and humour when compared with normal controls. There was marked similarity in the frequency of use of particular coping strategies between patients with psoriasis and patients with other medical conditions. Similar types of coping strategies are utilized by patients regardless of whether their illness is visible (psoriasis) invisible (chronic fatigue syndrome, atrial fibrillation), has significant physical impairment (spinal cord injury), or is life-threatening (cancer, and myocardial infarction). It appears that illness brings with it a generic form of coping that may require shaping to fit the individual demands of diseases such as psoriasis.
Freeman R.		The chronic fatigue syndrome is a disease of the autonomic nervous system. Sometimes.	Clin Auton Res. 2002 Aug;12(4):231-3.	

Frey DR.	.	Chronic fatigue syndrome and depression	Am Fam Physician. 2002 Nov 15;66(10):1838-9; author reply 1839. Comment on: Am Fam Physician. 2002 Mar 15;65(6):1083-90.	
Friedberg F.	Department of Psychiatry and Behavioral Science, Putnam Hall/South Campus, State University of New York at Stony Brook, PO Box 616, Stony Brook, NY 11794-8790, USA. fred.friedberg@stonybrook.edu	Does graded activity increase activity? A case study of chronic fatigue syndrome.	J Behav Ther Exp Psychiatry. 2002 Sep-Dec;33(3-4):203-15.	The reliance on self-report outcome measures in clinical trials of graded activity-oriented cognitive-behavior therapy in chronic fatigue syndrome (CFS) makes it difficult to draw definitive conclusions about actual behavioral change. The participant in this case study was a 52-year-old married male with CFS who was working full-time. Outcome measures included a step counter to objectively measure physical activity as well as a daily diary measure of exercise activity and in vivo ratings of perceived energy, fatigue, and affect. The following psychometric instruments were also used: the CFS Symptom Inventory, the SF-36, the Beck Depression Inventory, and the Beck Anxiety Inventory. The 26-session graded activity intervention involved gradual increases in physical activity. From baseline to treatment termination, the patient's self-reported increase in walk time from 0 to 155 min a week contrasted with a surprising 10.6% decrease in mean weekly step counts. The final follow-up assessment revealed a "much improved" global rating, substantial increases in patient-recorded walk time and weight lifting intensity, yet a relatively modest increment in weekly step counts. It appeared that improvement was associated with mood-enhancing, stress-reducing activities that were substituted for stress-exacerbating activities. Copyright 2003 Elsevier Science Ltd.
Gaab J, Huster D, Peisen R, Engert V, Heitz V, Schad T, Schurmeyer TH, Ehlert U.	Center for Psychobiological and Psychosomatic Research, University of Trier, Trier, Germany. jgaab@klipsy.unizh.ch	Hypothalamic-pituitary-adrenal axis reactivity in chronic fatigue syndrome and health under psychological, physiological, and pharmacological stimulation.	Psychosom Med. 2002 Nov-Dec;64(6):951-62.	OBJECTIVES: Subtle alterations of the hypothalamic-pituitary-adrenal (HPA) axis in chronic fatigue syndrome (CFS) have been proposed as a shared pathway linking numerous etiological and perpetuating processes with symptoms and observed physiological abnormalities. Because the HPA axis is involved in the adaptive responses to stress and CFS patients experience a worsening of symptoms after physical and psychological stress, we tested HPA axis functioning with three centrally acting stress tests. METHODS: We used two procedures mimicking real-life stressors and compared them with a standardized pharmacological neuroendocrine challenge test. CFS patients were compared with healthy control subjects regarding their cardiovascular and endocrine reactivity in a psychosocial stress test and a standardized exercise test, and their endocrine response in the insulin tolerance test (ITT). RESULTS: Controlling for possible confounding variables, we found significantly lower ACTH response levels in the psychosocial stress test and the exercise test, and significantly lower ACTH responses in the ITT, with no differences in plasma total cortisol responses. Also, salivary-free cortisol responses did not differ between the groups in the psychosocial stress test and the exercise test but were significantly higher for the CFS patients in the ITT. In all tests CFS patients had significantly reduced baseline ACTH levels. CONCLUSIONS: These results suggest that CFS patients are capable of mounting a sufficient cortisol response under different types of stress but that on a central level subtle

				dysregulations of the HPA axis exist.
Gaab J, Huster D, Peisen R, Engert V, Schad T, Schurmeyer TH, Ehlert U.	Center for Psychobiological and Psychosomatic Research, University of Trier, Trier, Germany. jgaab@klipsy.unizh.ch	Low-dose dexamethasone suppression test in chronic fatigue syndrome and health.	Psychosom Med. 2002 Mar-Apr;64(2):311-8.	OBJECTIVE: Subtle dysregulations of the hypothalamus-pituitary-adrenal axis in chronic fatigue syndrome have been described. The aim of this study was to examine the negative feedback regulations of the hypothalamus-pituitary-adrenal axis in chronic fatigue syndrome. METHODS: In 21 patients with chronic fatigue syndrome and 21 healthy control subjects, awakening and circadian salivary free cortisol profiles were assessed over 2 consecutive days and compared with awakening and circadian salivary free cortisol profiles after administration of 0.5 mg of dexamethasone at 11:00 PM the previous day. RESULTS: Patients with chronic fatigue syndrome had normal salivary free cortisol profiles but showed enhanced and prolonged suppression of salivary free cortisol after the administration of 0.5 mg of dexamethasone in comparison to the control subjects. CONCLUSIONS: Enhanced negative feedback of the hypothalamus-pituitary-adrenal axis could be a plausible explanation for the previously described alterations in hypothalamus-pituitary-adrenal axis functioning in chronic fatigue syndrome. Because similar changes have been described in stress-related disorders, a putative role of stress in the pathogenesis of the enhanced feedback is possible.
Gaby AR.		Intravenous nutrient therapy: the "Myers' cocktail".	Altern Med Rev. 2002 Oct;7(5):389-403.	Building on the work of the late John Myers, MD, the author has used an intravenous vitamin-and-mineral formula for the treatment of a wide range of clinical conditions. The modified "Myers' cocktail," which consists of magnesium, calcium, B vitamins, and vitamin C, has been found to be effective against acute asthma attacks, migraines, fatigue (including chronic fatigue syndrome), fibromyalgia, acute muscle spasm, upper respiratory tract infections, chronic sinusitis, seasonal allergic rhinitis, cardiovascular disease, and other disorders. This paper presents a rationale for the therapeutic use of intravenous nutrients, reviews the relevant published clinical research, describes the author's clinical experiences, and discusses potential side effects and precautions.
Gaines S.		Finding Amy Peterson. An olympic speed skater battles with chronic fatigue syndrome.	Minn Med. 2002 Jun;85(6):24-6.	
Garralda ME, Rangel L.	Academic Unit of Child and Adolescent Psychiatry, Imperial College School of Medicine, London, UK. e.garralda@ic.ac.uk	Annotation: Chronic Fatigue Syndrome in children and adolescents.	J Child Psychol Psychiatry. 2002 Feb;43(2):169-76.	BACKGROUND: Over the past two decades Chronic Fatigue Syndrome (CFS) of childhood has gained increasing prominence. A number of clinical reports and case-control studies have examined the nature of the disorder, its associations, response to treatment and outcome. METHOD: A review of publications on childhood CFS was undertaken and reference to work on adult CFS made. Most studies on childhood CFS have been on markedly affected children attending specialist pediatric clinics and very little is known about the condition as it presents in the community or to general medical services. RESULTS: The main symptom is fatigue in association with a variety of physical symptoms and with marked and prolonged functional impairment. CFS is commonly reported as being brought on by acute infections. Co-morbid psychiatric (usually mood) disorders are present in at least a half. Personality problems and health attitudes have been described as possible predisposing and maintaining factors. Clinical

				reports indicate that family work focused on engagement and on a rehabilitation programme (including graded increasing activity and treatment of psychiatric co-morbidity) can help even the more severely impaired children. Recovery may be expected in over two-thirds. CONCLUSIONS: CFS presents as a distinct, markedly impairing disorder of childhood. In its severe form, it is often associated with mood disorders. Further research into milder forms and into the efficacy of different treatment interventions is specially needed.
Geraghty J.	dr.geraghty@virgin.net	Homeopathic treatment of Chronic Fatigue Syndrome: three case studies using Jan Scholten's methodology.	Homeopathy. 2002 Apr;91(2):99-105.	This paper explores the treatment of Chronic Fatigue Syndrome following a viral infection in young people. The methodology is based on that of Dr Jan Scholten, Holland, who has systematically described the homeopathic themes of all elements in the periodic table. Three case studies are presented, Cobaltum Phosphoricum, Calcium Phosphoricum and Cadmium Phosphoricum were prescribed. The common themes and the differentiating features of these Phosphate salts are described in detail to show how the homeopathic similimum is found and cure achieved.
Gerrity TR, Bates J, Bell DS, Chrousos G, Furst G, Hedrick T, Hurwitz B, Kula RW, Levine SM, Moore RC, Schondorf R.	Georgetown University Medical Center, Washington, DC, USA.	Chronic fatigue syndrome: what role does the autonomic nervous system play in the pathophysiology of this complex illness?	Neuroimmunomodulation. 2002-2003;10(3):134-41.	Chronic fatigue syndrome (CFS) is a serious health concern affecting over 800000 Americans of all ages, races and socioeconomic groups and both genders. The etiology and pathophysiology of CFS are unknown, yet studies have suggested an involvement of the autonomic nervous system (ANS). A symposium was organized in December 2000 to explore the possibility of an association between ANS dysfunction and CFS, with special emphasis on the interactions between ANS dysfunction and other abnormalities noted in the immune and endocrine systems of individuals with CFS. This paper represents the consensus of the panel of experts who participated in this meeting. Copyright 2002 S. Karger AG, Basel
Girault V.		[Chronic fatigue syndrome, an unappreciated syndrome] [Article in French]	Presse Med. 2002 Mar 30;31(12):531.	
Goldberger AL.		Chronic fatigue syndrome and hidden happenings of the heartbeat.	Clin Auton Res. 2002 Aug;12(4):228-30. Comment on: Clin Auton Res. 2002 Aug;12(4):264-72.	
Goldstein DS, Robertson D, Esler M, Straus SE, Eisenhofer G.	Clinical Neurocardiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Building 10, Room	Dysautonomias: clinical disorders of the autonomic nervous system.	Ann Intern Med. 2002 Nov 5;137(9):753-63.	The term dysautonomia refers to a change in autonomic nervous system function that adversely affects health. The changes range from transient, occasional episodes of neurally mediated hypotension to progressive neurodegenerative diseases; from disorders in which altered autonomic function plays a primary pathophysiologic role to disorders in which it worsens an independent pathologic state; and from mechanistically straightforward to mysterious and controversial entities. In chronic autonomic failure (pure autonomic failure, multiple system atrophy, or autonomic failure in Parkinson disease), orthostatic hypotension reflects sympathetic neurocirculatory failure from sympathetic denervation or deranged reflexive regulation of sympathetic outflows. Chronic orthostatic intolerance associated with postural tachycardia can

	6N252, 10 Center Drive MSC-1620, Bethesda, MD 20892-1620, USA.			arise from cardiac sympathetic activation after "patchy" autonomic impairment or blood volume depletion or, as highlighted in this discussion, from a primary abnormality that augments delivery of the sympathetic neurotransmitter norepinephrine to its receptors in the heart. Increased sympathetic nerve traffic to the heart and kidneys seems to occur as essential hypertension develops. Acute panic can evoke coronary spasm that is associated with sympathoneural and adrenomedullary excitation. In congestive heart failure, compensatory cardiac sympathetic activation may chronically worsen myocardial function, which rationalizes treatment with beta-adrenoceptor blockers. A high frequency of positive results on tilt-table testing has confirmed an association between the chronic fatigue syndrome and orthostatic intolerance; however, treatment with the salt-retaining steroid fludrocortisone, which is usually beneficial in primary chronic autonomic failure, does not seem to be beneficial in the chronic fatigue syndrome. Dysautonomias are an important subject in clinical neurocardiology.
Goudsmit E.	Chronic fatigue syndrome/ME	Comment on: Br J Gen Pract. 2002 Sep;52(482):763; author reply 763-4.	Br J Gen Pract. 2002 Dec;52(485):1023-4.	
Goudsmit E.	Chronic fatigue syndrome/myalgic encephalitis.		Br J Gen Pract. 2002 Sep;52(482):763; author reply 763-4. Comment in: Br J Gen Pract. 2002 Dec;52(485):1023-4.	
Graffelman AW, Neven AK, Nagelkerken L, Petri H, Springer MP.		Subjective Sleep Quality and Depressive Symptoms in Patients with the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2002; 10(2): 19 - 28	Objectives: To evaluate subjective quality of sleep and depressive symptoms of patients with chronic fatigue syndrome (CFS). Methods: Adult patients, who met the criteria for CFS, were recruited by general practitioners in the Leiden area, The Netherlands. Age and sex-matched controls were recruited. Questionnaires were handed out to 59 patients and 56 controls. Results: CFS patients had a significant higher mean score than controls on the Groningen Sleep Quality Score (GSQS) and the Zung-index, i.e., worse sleep and depression scores. In the multivariate logistic regression model, the GSQS had an OR of 1.35 per unit score (CI: 1.07-1.70), and the Zung-index had an OR of 1.21 per unit score (CI: 1.10-1.33). Conclusions: In our study, CFS patients report more subjective sleep impairment and depressive symptoms than controls but these factors appear to be independent. The fact that only a minority of the CFS patients have depressive symptoms suggests it is unlikely that depression is the cause of CFS.
Gray GC, Reed RJ, Kaiser KS, Smith TC, Gastanaga VM.	Department of Defense Center for Deployment Health Research, Naval Health Research Center, San Diego, CA, USA. gregory-	Self-reported symptoms and medical conditions among 11,868 Gulf War-era veterans: the Seabee Health Study.	Am J Epidemiol. 2002 Jun 1;155(11):1033-44.	US Navy Seabees have been among the most symptomatic Gulf War veterans. Beginning in May 1997, the authors mailed Gulf War-era Seabees a health survey in serial mailings. As of July 1, 1999, 68.6% of 17,559 Seabees contacted had returned the questionnaire. Compared with other Seabees, Gulf War Seabees reported poorer general health, a higher prevalence of all 33 medical problems assessed, more cognition difficulties, and a higher prevalence of four physician-diagnosed multisymptom conditions: chronic fatigue syndrome, posttraumatic stress disorder, multiple chemical sensitivity, and irritable bowel syndrome. Because the four multisymptom

	gray@uiowa.edu			conditions were highly associated with one another, the authors aggregated them into a working case definition of Gulf War illness. Among the 3,831 (22% cases) Gulf War Seabee participants, multivariable modeling revealed that female, Reserve, and enlisted personnel and participants belonging to either of two particular Seabee units were most likely to meet the case definition. Twelve of 34 self-reported Gulf War exposures were mildly associated with meeting the definition of Gulf War illness, with exposure to fumes from munitions having the highest odds ratio (odds ratio = 1.9, 95% confidence interval: 1.5, 2.4). While these data do not implicate a specific etiologic exposure, they demonstrate a strong association and a high prevalence of self-reported multisymptom conditions in a large group of symptomatic Gulf War veterans.
Green B.	University of Liverpool, UK. ben@priory.com	Focus on amisulpride.	Curr Med Res Opin. 2002;18(3):113-7.	Amisulpride is a second-generation antipsychotic, a substituted benzamide. It appears to be an effective agent in treating schizophrenia for what are characterised as positive and negative symptoms. The recommended doses are between 400 mg/day and 800 mg/day. Amisulpride demonstrates a good global safety profile, particularly when compared with first-generation antipsychotics, such as haloperidol. There are interesting studies that point towards amisulpride's antidepressant effect in dysthymia speculative on possible roles in affective psychoses and chronic fatigue syndrome.
Gupta A.	Robinson College, University of Cambridge, Cambridge CB3 9AN, UK. ashok@harleystressclinic.com	Unconscious amygdalar fear conditioning in a subset of chronic fatigue syndrome patients.	Med Hypotheses. 2002 Dec;59(6):727-35.	Here, a novel hypothesis for chronic fatigue syndrome (CFS) is proposed. CFS may be a neurophysiological disorder focussing on the amygdala. During a 'traumatic' neurological event often involving acute psychological stress combined with a viral infection or other chemical or physiological stressor, a conditioned network or 'cell assembly' may be created in the amygdala. The unconscious amygdala may become conditioned to be chronically sensitised to negative symptoms arising from the body. Negative signals from the viscera or physiological, chemical and dietary stressors, become conditioned stimuli and the conditioned response is a chronic sympathetic outpouring from the amygdala via various brain pathways including the hypothalamus. This cell assembly then produces the CFS vicious circle, where an unconscious negative reaction to symptoms causes immune reactivation/dysfunction, chronic sympathetic stimulation, leading to sympathetic dysfunction, mental and physical exhaustion, and a host of other distressing symptoms and secondary complications. And these are exactly the symptoms that the amygdala and associated limbic structures are trained to monitor and respond to, perpetuating a vicious circle. Recovery from CFS may involve projections from the medial prefrontal cortex to the amygdala, to control the amygdala's expressions. I shall firstly discuss predisposing, precipitating, and perpetuating factors involved in the possible etiology of chronic fatigue syndrome (CFS), followed by the patient's experience of the illness. Finally, I shall look at a suggested explanation for the symptoms of CFS. Copyright 2002 Elsevier Science Ltd.
Hakimi R.		[Comment on W. Hausotter: Modern illness from the critical viewpoint] [Article in German]	Versicherungsmedizin. 2002 Sep 1;54(3):149-50; author reply 150. Comment on: Versicherungsmedizi	

			n. 2001 Dec 1;53(4):177-81.	
Hampshire M.		Could it be ME?	Nurs Stand. 2002 May 15-21;16(35):14-5.	
Harrison S, Smith A, Sykes R.		Residential Rehabilitation Courses in the Self-Directed Management of Chronic Fatigue Syndrome: A Preliminary Evaluation	Journal of Chronic Fatigue Syndrome 2002; 10(2): 59 - 65	Residential rehabilitation courses in self-directed illness management offer a potentially useful patient-centered and multidiscipliary therapeutic option for Chronic Fatigue Syndrome. A retrospective survey of the data from the courses run by Westcare UK between 1995 and 1998 was undertaken to give a preliminary evaluation of outcomes and acceptability. The outcome results, for 49 participants, show improvements, at 12 months, on the Fatigue and Emotional Distress subscales of the PFRS. (Fatigue: before course: mean 3.66, s.d. 1.14; 12 months later: mean 3.11, s.d. 1.57; $F(1,48) = 11.10$ $p < 0.005$. Emotional distress: before course: mean 2.53, s.d. 1.46; 12 months later: mean 2.04, s.d. 1.39; $F(1,48) = 5.96$ $p < 0.01$.) Participants also reported a high level of general satisfaction with the course: 89.4% gave a rating of five or six, out of six. These results describe both longand short-term benefits, and support the continued use of these courses and the implementation of a further more rigorous study.
Hartocollis P.		'Actual neurosis' and psychosomatic medicine: the vicissitudes of an enigmatic concept.	Int J Psychoanal. 2002 Dec;83(Pt 6):1361-73.	Out of the concept of neurasthenia, the main non-psychotic diagnosis of nineteenth-century psychiatry besides hysteria, and on the basis of psychophysiological problems of his own, self-diagnosed as neurasthenia, Freud developed the notion of 'actual neurosis', a 'contentless psychic state' manifested by various somatic symptoms and a depressive mood, which he attributed to a chemical factor associated with aberrant sexual practices and in particular masturbation. Rejected by post-Freudian analysts as such along with the diagnosis of neurasthenia, the concept of 'actual neurosis' has survived under various theoretical schemes that seek to explain psychosomatic illness and somatisation, in general, with its concomitant poverty of affects and dearth of fantasy life. In more recent years, the concept of 'actual neurosis' has resurfaced under the label of chronic fatigue syndrome, a medical entity thought to be an immunological deficiency, while in psychoanalysis Freud's idea of a contentless mental state has been replaced by that of unconscious fantasy and symbolisation at a pre-genital or pre-verbal level.
Hatcher S.		Review: cognitive behavioural therapy and graded exercise show the most promise for chronic fatigue syndrome	Evid Based Ment Health. 2002 May;5(2):54. Comment on: JAMA. 2001 Sep 19;286(11):1360-8.	University of Auckland, Auckland, New Zealand.
Heilig M, Oreland L, Ekman R, Akerstedt T, Nygren A.	Huddinge Universitetssjukhus.	[The brain behind stress and fatigue depression] [Article in Swedish]	Lakartidningen. 2002 May 30;99(22):2515-8.	
Herrell R, Goldberg	Division of	Chronic fatigue and	Qual Life Res. 2002	Chronic fatigue syndrome (CFS) and the symptom of chronic fatigue may be accompanied by

J, Hartman S, Belcourt M, Schmaling K, Buchwald D.	Epidemiology-Biostatistics, University of Illinois at Chicago, USA.	chronic fatigue syndrome: a co-twin control study of functional status.	Aug;11(5):463-71.	substantial functional disability. A volunteer sample of twins discordant for fatigue was identified from throughout the US. Fatigued twins were classified using three increasingly stringent definitions: (1) > or = 6 months of fatigue (119 pairs); (2) CFS-like illness based on self-report of the Centers for Disease Control and Prevention CFS research definition criteria (74 pairs); and (3) CFS assessed by clinical examination (22 pairs). Twins with chronic fatigue were compared with their unaffected co-twins on the eight standard scales and two physical and mental component summary scales from the medical outcomes study short-form health survey (SF-36). Substantial impairment was observed for fatigued twins across all levels of fatigue, while scores in the healthy twins were similar to US population values. Mean scores among fatigued twins on the physical and mental component summary scales were below 97 and 77%, respectively, of the US population scores. Diminished functional status was found across increasingly stringent classifications of fatigue and was associated with a dramatic decrement in physical functioning. The symptom of fatigue has a pronounced impact on functional status, especially in the domain of physical functioning.
Hickie IB.	Chronic fatigue syndrome clinical practice guidelines: psychological factors.	.	Med J Aust. 2002 Nov 4;177(9):526; author reply 526-7. Comment on: Med J Aust. 2002 Jul 1;177(1):51-2	
Hoffman DB.	Department of Rheumatic and Immunologic Diseases, Cleveland Clinic Foundation, Cleveland, USA.	Chronic fatigue syndrome. Symptom relief is primary goal.	Adv Nurse Pract. 2002 Mar;10(3):97-100.	
Hoffman R.	Hematology-Oncology Section, University of Illinois-Chicago College of Medicine, Chicago, IL 60607, USA.	Quality of life issues in patients with essential thrombocythemia and polycythemia vera.	Semin Oncol. 2002 Jun;29(3 Suppl 10):3-9.	Essential thrombocythemia and polycythemia vera are both chronic progressive myeloproliferative disorders of insidious onset. If the excessive production of red cells and/or platelets is controlled, patients with these disorders may have prolonged survival. However, the clinical course of these patients can be complicated by a variety of events, including thrombotic episodes, bleeding episodes, arthropathies, pruritis, weakness, weight loss, neurologic impairment, erythromelalgia, fever, abdominal pain, and the life-threatening consequences of progression to myelofibrosis and/or acute leukemia. Effective control of hematopoiesis by phlebotomy or a variety of therapeutic agents has resulted in a reduction or elimination of many of these clinical events, but has not altered the evolution to myelofibrosis or acute leukemia. Use of each of these therapeutic strategies is also associated with a range of adverse events. Monitoring overall survival or a reduction in the frequency of clinical events has previously served as a means of assessing the results of these therapeutic interventions. Quality-of-life instruments have not been applied in a systematic fashion to the evaluation of outcomes in patients with these chronic myeloproliferative disorders. Quality-of-life assessments evaluate not only the

				state of well-being of a patient that results from an assessment of the individual's ability to perform everyday activities, which are reflective of physical, psychological, and social well-being, but also patient satisfaction with the control of disease and/or treatment-related symptoms. Quality-of-life instruments have been used to assess the clinical course of patients suffering from a variety of disorders, ranging from cancer to renal failure to chronic fatigue syndrome. Information about quality-of-life outcomes can contribute to the evaluation of variations in dose and timing of administration of therapeutic agents. It is possible that the side effects of a particular therapy may outweigh the disease regression achieved with a particular therapy. In the future, quality-of-life instruments may prove useful in prospectively evaluating therapeutic end points in patients with essential thrombocythemia and polycythemia vera. Copyright 2002, Elsevier Science (USA). All rights reserved.
Hundertmark JD.	Chronic fatigue syndrome clinical practice guidelines: psychological factors.		Med J Aust. 2002 Nov 4;177(9):525-7; author reply 526-7. Comment on: Med J Aust. 2002 Jul 1;177(1):51-2	
Ikuta K, Ibrahim MS, Kobayashi T, Tomonaga K.	Department of Virology, Research Institute for Microbial Diseases, Osaka University, Suita, Osaka 565-0871, Japan. ikuta@biken.osaka-u.ac.jp	Borna disease virus and infection in humans.	Front Biosci. 2002 Feb 1;7:d470-95.	Borna disease virus (BDV) is a nonsegmented, negative-, single-stranded, highly neurotropic RNA virus with noncytolytic replication in the central nervous system. This virus causes neurological and behavioral disturbances primarily in horses and sheep, in addition to a variety of other vertebrate animal species and in laboratory animal models. BDV is now gaining much of the research attention, because the disturbances seen in animals resemble those of neuropsychiatric disorders in humans. These observations raise the possibility that BDV infection may be associated with certain human disorders. Serological and molecular studies on many samples from human patients with a variety of psychiatric disorders have been performed. Some reported the presence and elevated levels of serum antibodies to BDV. Others reported the presence of BDV-RNAs or BDV-antigens in the peripheral blood samples as well as in autopsied brains. Taken together these data support the possibility of human infection with BDV. On the contrary, others reported the complete absence of such BDV-markers from their samples, supporting the absence of a link between BDV infection and psychiatric disorders as well as excluding it as a human pathogen. Thus, BDV infection in humans is highly controversial. Further investigations are required to answer the question whether BDV is a human pathogen and moreover, to elucidate the possible role, if any, of BDV in the pathogeneses of these disorders.
Jackson E.	Shaw Heath Health Centre, Stockport, Cheshire. libb.jackson@ntlworld.com	An overview of chronic fatigue syndrome.	Nurs Stand. 2002 Dec 11-17;17(13):45-53; quiz 54-5.	This article provides an overview of the condition known as chronic fatigue syndrome, or myalgic encephalomyelitis. The author describes common symptoms and their treatment, and discusses a model of patient care, piloted in the community, which includes elements of a range of therapeutic strategies.
Jason LA, Taylor RR, Kennedy CL, Jordan	Department of Psychology, DePaul	A factor analysis of chronic fatigue	Soc Psychiatry Psychiatr Epidemiol.	BACKGROUND: This study examined characteristics of fatigue in individuals with chronic fatigue from a community-based study. Most studies of chronic fatigue have been based on patients

K, Huang CF, Torres-Harding S, Song S, Johnson D.	University, Chicago, IL 60614, USA. ljason@wppost.depaul.edu	symptoms in a community-based sample.	2002 Apr;37(4):183-9.	recruited from primary or tertiary care settings. Samples such as these might not be representative of patients within the general population. The purpose of this study was to determine the factor structure of participants' symptoms in a random community sample of individuals with chronic fatigue. METHOD: A random sample of 18,675 respondents in Chicago received a brief telephone questionnaire designed to identify individuals with chronic fatigue. A group of 780 (4.2%) with chronic fatigue received further interview via telephone questionnaire involving characteristics of their fatigue. The analyses for this study were based on those people identified with having chronic fatigue. A factor analysis was conducted on responses to questionnaire items, and a four-factor solution emerged. Mean factor scores were derived and analyzed in relation to sociodemographic characteristics and sample subgroups. RESULTS: The four factors were labeled: Lack of Energy, Physical Exertion, Cognitive Functioning, and Fatigue and Rest. CONCLUSIONS: Results indicated that individuals with chronic fatigue have symptoms that can be differentiated into theoretically distinct factors.
Jason LA, Taylor RR, Plioplys S, Stepanek Z, Shlaes J.	Center for Community Research, DePaul University, Chicago, Illinois 60614, USA. ljason@wppost.depaul.edu	Evaluating attributions for an illness based upon the name: chronic fatigue syndrome, myalgic encephalopathy and Florence Nightingale disease.	Am J Community Psychol. 2002 Feb;30(1):133-48.	In recent years, considerable discussion has occurred about stigma surrounding the name given to an illness currently known as chronic fatigue syndrome (CFS). Although patients and medical personnel have expressed varying opinions on this issue, no studies have evaluated how beliefs about the illness change based upon the type of name used for diagnostic purposes. Proposals have been put forth to rename the illness with an eponym (a famous patient's or researcher's name) or with a less trivial sounding, more medically based type of name. In this study, attributions about CFS were measured in three groups of medical trainees. All groups read the same case study of a person with classic symptoms of chronic fatigue syndrome, with the only difference being in the type of name given. Trainees then were asked to provide attributions about certain aspects of the illness, including its cause, severity, and prognosis. Results suggested that, across name conditions, most trainees appeared to consider the symptom complex of CFS a serious illness resulting in poor quality of life. In addition, findings indicated that the name, chronic fatigue syndrome, may be regarded less seriously than the Myalgic Encephalopathy name with respect to some important aspects of the illness. In this study, specialty of medical trainee also played a role in how the illness was perceived.
Jason LA, Torres-Harding SR, Carrico AW, Taylor RR.	DePaul University, Center for Community Research, 990 West Fullerton Road, Chicago, IL 60614, USA. Ljason@depaul.edu	Symptom occurrence in persons with chronic fatigue syndrome.	Biol Psychol. 2002 Feb;59(1):15-27.	This investigation compared differences in the occurrence of symptoms in participants with CFS, melancholic depression, and no fatigue (controls). The following Fukuda et al. [Ann. Intern. Med. 121 (1994) 953] criteria symptoms differentiated the CFS group from controls, but did not differentiate the melancholic depression group from controls: headaches, lymph node pain, sore throat, joint pain, and muscle pain. In addition, participants with CFS uniquely differed from controls in the occurrence of muscle weakness at multiple sites as well as in the occurrence of various cardiopulmonary, neurological, and other symptoms not currently included in the current case definition. Implications of these findings are discussed.
Jones NL, Heigenhauser GJ.		VO2max and lactate production are not normal in all patients with chronic fatigue.	Med Sci Sports Exerc. 2002 Jul;34(7):1215; author reply 1215-6.	

Katz BZ.	Department of Pediatrics, Northwestern University Feinberg, School of Medicine, Chicago, IL, USA. bkatz@northwestern.edu	Update on chronic fatigue syndrome and Epstein-Barr virus.	Pediatr Ann. 2002 Nov;31(11):741-4.	
Kerr JR, Bracewell J, Laing I, Mattey DL, Bernstein RM, Bruce IN, Tyrrell DA.	Department of Microbiology, Royal Brompton Hospital, National Heart and Lung Institute, Imperial College School of Medicine, London, UK. j.kerr@ic.ac.uk	Chronic fatigue syndrome and arthralgia following parvovirus B19 infection.	J Rheumatol. 2002 Mar;29(3):595-602.	OBJECTIVE: To determine the incidence of arthralgia and fatigue complicating B19 infection, along with associated B19 markers and autoantibodies. METHODS: We studied patients with acute B19 infection (n = 51), patients followed from the time of acute B19 infection (mean 22.5 mo) (n = 39), and healthy controls (n = 50). Clinical details were collected using a questionnaire and blood was tested for B19 markers and autoantibodies. RESULTS: Acute B19 arthralgia occurred in 31 patients and was associated with female sex ($p = 0.007$) and age > 20 years ($p = 0.02$). Acute B19 fatigue occurred in 8 patients and was not significantly associated with any marker. At followup, symptoms consisted of arthralgia (n = 5), arthralgia and fatigue (n = 6), fatigue (n = 7), lymphadenopathy (n = 1), and purpura due to thrombocytopenia (n = 2). Chronic B19 arthralgia was associated with persistent B19 viremia ($p = 0.029$). Comparison of the B19 followup group with the controls revealed a significantly increased prevalence of arthralgia ($p = 0.0002$), fatigue ($p < 0.0001$), and all other markers. Chronic B19 arthralgia was associated with both acute B19 arthralgia ($p = 0.0168$) and positive ANA at acute infection ($p = 0.0043$). Chronic B19 fatigue was associated with acute B19 fatigue ($p = 0.011$). Five patients fulfilled the Centers for Disease Control criteria for a diagnosis of chronic fatigue syndrome (CFS) and one of these was negative for serum anti-B19 IgG at followup by both Western blot and immunofluorescence. However, there was no characteristic pattern of B19 markers/autoantibodies in patients with B19 associated chronic fatigue. CONCLUSION: CFS may follow acute parvovirus B19 infection; however, attribution of a case of CFS to B19 infection may be extremely difficult in the absence of serological confirmation of acute infection at fatigue onset.
Kinsella P	Psychological Medicine, Queens Medical Centre, Nottingham, UK.	Review: behavioural interventions show the most promise for chronic fatigue syndrome.	Evid Based Nurs. 2002 Apr;5(2):46. Comment on: JAMA. 2001 Sep 19;286(11):1360-8.	
Kipen HM, Fiedler N.	Environmental and Occupational Health Sciences Institute, University of Medicine and Dentistry-Robert Wood Johnson	The role of environmental factors in medically unexplained symptoms and related syndromes: conference summary	Environ Health Perspect. 2002 Aug;110 Suppl 4:591-5.	This monograph of peer-reviewed articles is based on presentations at the conference "Environmental Factors in Medically Unexplained Physical Symptoms and Related Syndromes" held 10-12 January 2001 in Piscataway, New Jersey, USA. The purpose of the conference was to determine research priorities for elucidating the role of environmental factors in medically unexplained symptoms and symptom syndromes. These include conditions such as chronic fatigue syndrome, multiple chemical sensitivities, sick building syndrome, Gulf War illness, and the like. Approximately 1 1/2 days were devoted to plenary talks and 1 day was devoted to break-

	Medical School, Piscataway, New Jersey 08854, USA. kipen@eohsi.rutgers.edu	and recommendations.		out sessions to discuss epidemiologic, psychosocial, and experimental research. Recommendations were made for a series of epidemiologic, psychosocial, and experimental research approaches, with acknowledgment that nosology issues are clearly fundamental to advancing understanding of these conditions.
Kipen HM, Fiedler N.	Environmental and Occupational Health Sciences Institute--Occupational Health Division, University of Medicine and Dentistry of New Jersey--Robert Wood Johnson Medical School, Piscataway, New Jersey 08854, USA. kipen@eohsi.rutgers.edu	Environmental factors in medically unexplained symptoms and related syndromes: the evidence and the challenge.	Environ Health Perspect. 2002 Aug;110 Suppl 4:597-9.	Symptoms, and especially those without clear underlying medical explanations, account for a large percentage of clinical encounters. Many unexplained symptoms have been organized by patients and practitioners into syndromes such as chronic fatigue syndrome, multiple chemical sensitivity, sick building syndrome, Gulf War syndrome, and the like. All these syndromes are defined solely on the basis of symptoms rather than by medical signs. Some of the above-described conditions overlap strongly with explained conditions such as asthma. The relationship of such symptoms and syndromes to environmental exposure is often sharply debated, as is the distinction between the various syndromes. This leads to problems of what type of research should be conducted and who should conduct it. It is time to develop a comprehensive research agenda to sort out nomenclature, epidemiology, and environmental causation for these conditions, moving toward comprehensive and effective public health and clinical approaches.
Kisely SR.	Primary Care Mental Health Center, University of Western Australia, Fremantle, WA, Australia. stephenk@cyllene.uwa.edu.au	Treatments for chronic fatigue syndrome and the Internet: a systematic survey of what your patients are reading.	Aust N Z J Psychiatry. 2002 Apr;36(2):240-5.	OBJECTIVE: To evaluate the type, quality, and focus of patient information on the treatment of chronic fatigue syndrome on the Internet using simple search techniques. DESIGN: The search phrase 'chronic fatigue syndrome' was entered into nine common Internet search engines. The 25 most highly ranked pages identified by each of the nine search engines were analysed using a standardized pro forma. The following outcome measures were used: balance of content, consistency of content with evidence-based practice, declared authorship with credentials, information sources including the presence of references, the declaration of any potential conflict of interest, and the need to clarify information with an appropriate health professional. RESULTS: Two hundred and twenty-five websites were reviewed during a 2-week period in September 2000. A further 15 sites (6.3%) were inaccessible. Agreement between websites and systematic reviews of treatment for chronic fatigue syndrome ranged from 4 to 68%, the greatest agreement being for recommendations for graded exercise and the avoidance of prolonged rest. Most sites (64%) had a named author. Only a quarter to a third contained a declaration of interest, advised readers to clarify information with an appropriate health professional, or avoided inaccurate statements. CONCLUSIONS: The Internet contains a great deal of information on chronic fatigue syndrome that is neither balanced nor consistent with evidence-based practice. Doctors individually, and as a profession, should provide guidance on which Internet sites to trust.
Kmietowicz Z.		Cognitive behaviour therapy and exercise are the only effective treatments for	BMJ. 2002 Jun 1;324(7349):1298.	

		chronic fatigue, says study.		
Kobayashi H, Demura S.	Fukui National College of Technology.	[Relationship between chronic fatigue and subjective symptoms of fatigue with performance status (P.S.) and subjective fatigue scale for young adults (SFS-Y)] [Article in Japanese	Nippon Koshu Eisei Zasshi. 2002 Oct;49(10):1062-9.	OBJECTIVE: Today, fatigue complaints in adolescence are regarded as an issue for young adults as they may progress to the chronic fatigue syndrome. The purpose of this study was to examine the relationships between chronic fatigue based on self-reported performance states (P.S.) and subjective symptoms of fatigue assessed with a fatigue scale for young adults (SFS-Y). METHOD: The SFS-Y consisted of 24 item questions represonting 6 sub-scales, for difficulty in concentrated thinking, languor, reduced activation, reduced motivation, drowsiness and feeling of physical disintegration. The SFS-Y and for assessing fatigue symptoms and P.S. for chronic fatigue were administered to 548 male and female students aged 15-18 yr and to 608 male students aged 16-18 yr, respectively. Discriminant analysis and a logistic analysis model were employed to define the relevance of subjective symptoms of fatigue to chronic fatigue. RESULTS: It was determined that the SFS-Y can discliminate P.S. with high probability (74.0-81.4%), with accuracy beyond a fixed level. In particular, the correlation with "difficulty in concentrated thinking" was high. CONCLUSION: It was judged that the SFS-Y is effective as an index for discrimination of chronic fatigue in young adults with a particularly high relationship between "difficulty in centrated thinking" and chronic fatigue.
Koelle DM, Barcy S, Huang ML, Ashley RL, Corey L, Zeh J, Ashton S, Buchwald D.	Department of Laboratory Medicine, University of Washington, Seattle, WA, USA. dedra@u.washington.edu	Markers of viral infection in monozygotic twins discordant for chronic fatigue syndrome.	Clin Infect Dis. 2002 Sep 1;35(5):518-25. Epub 2002 Jul 31. Comment in: Clin Infect Dis. 2003 Mar 1;36(5):671-2; author reply 672-3.	To estimate the prevalence of viruses associated with chronic fatigue syndrome (CFS) and to control for genetic and environmental factors, we conducted a co-twin control study of 22 monozygotic twin pairs, of which one twin met criteria for CFS and the other twin was healthy. Levels of antibodies to human herpesvirus (HHV)-8, cytomegalovirus, herpes simplex virus 1 and 2, and hepatitis C virus were measured. Polymerase chain reaction (PCR) assays for viral DNA were performed on peripheral blood mononuclear cell specimens to detect infection with HHV-6, HHV-7, HHV-8, cytomegalovirus, Epstein-Barr virus, herpes simplex virus, varicella zoster virus, JC virus, BK virus, and parvovirus B19. To detect lytic infection, plasma was tested by PCR for HHV-6, HHV-8, cytomegalovirus, and Epstein-Barr virus DNA, and saliva was examined for HHV-8 DNA. For all assays, results did not differ between the group of twins with CFS and the healthy twins.
Kowal K, Schacterele RS, Schur PH, Komaroff AL, DuBuske LM.	Department of Allergology and Internal Disease, University Medical School, Bialystok, Poland.	Prevalence of allergen-specific IgE among patients with chronic fatigue syndrome.	Allergy Asthma Proc. 2002 Jan-Feb;23(1):35-9.	The prevalence of atopy among patients having chronic fatigue syndrome (CFS) has been reported to be as high as 80% in published surveys of patients with this syndrome. However, many of the reports relied on self-assessment by patients for the presence of atopy or solely used total immunoglobulin E (IgE) levels to assess the likelihood of atopy. To more critically assess the presence of atopy among patients with CFS, testing was done for total IgE and allergen-specific IgE using the Pharmacia CAP system including 20 common allergens: trees (birch/oak/ash), grass (rye/blue), weeds (common/giant ragweed), molds (Penicillium/Aspergillus/Alternaria), dust mites (Dermatophagoides pteronyssinus/Dermatophagoides farinae), animal dander (cat/dog), and foods (egg white/milk/wheat/corn/peanut/shrimp). Testing of 50 patients having documented CFS indicated that 78% had total IgE < 100 IU/mL, among whom 26% had a positive test for allergen-specific IgE of class I or greater for one or more allergens. Among the 22% of CFS patients having a total IgE > 100 IU/mL, 73% had a positive test for allergen-specific IgE for one or more allergens. The most commonly positive allergens were dust mites (24-26%), whereas molds

				(0-6%) and foods (0-4%) were rarely positive. The overall frequency of positive results for the presence of allergen-specific IgE among CFS patients was 36%, not significantly different from the normal prevalence of these antibodies in the general population (20-35%). This assessment of the prevalence of allergen-specific IgE antibodies in patients with CFS fails to support a potential association between CFS and atopy.
Krueger GR, Brandt ME, Wang G, Berthold F, Buja LM.	Department of Pathology & Laboratory Medicine, University of Texas-Houston Medical School, 77030, USA. Gerhard.Krueger@uth.tmc.edu	A computational analysis of Canale-Smith syndrome: chronic lymphadenopathy simulating malignant lymphoma.	Anticancer Res. 2002 Jul-Aug;22(4):2365-71.	OBJECTIVE: The objective of this study was to simulate changes in the human T cell system representing Canale-Smith syndrome using a dynamic computer model of T cell development and comparing with available human data. STUDY DESIGN: Physiological stepwise maturation and function of T lymphocytes in the computer model is altered by introducing functional disturbances following lymphotropic virus infection. In the present model, acute and chronic persistent infection with the human herpesvirus-6 (HHV-6) was simulated, and ensuing changes in T cell populations were compared with those measured in human patients. RESULTS: Using our computer model we previously found that simulated acute HHV-6 infection produced T cell computer data, which resembled an infectious mononucleosis-like disease in patients. Simulated chronic persistent infection, instead, resulted in variable cell changes comparing well to patients with chronic fatigue syndrome. In one setting, however, persistent immature lymphocytosis was observed similar to what initial has been described in this journal as Canale-Smith syndrome. CONCLUSION: Using a computer model developed by us we were able to produce simulations that resemble the immune system features of Canale-Smith syndrome. Further understanding of these simulation results may possibly guide future investigations into this disorder.
Kuratsune H, Yamaguti K, Lindh G, Evengard B, Hagberg G, Matsumura K, Iwase M, Onoe H, Takahashi M, Machii T, Kanakura Y, Kitani T, Langstrom B, Watanabe Y.	Department of Molecular Medicine, Hematology and Oncology, Osaka University Graduate School of Medicine, C9, 2-2 Yamada-oka, Suita, Osaka 565-0871, Japan. kura@bldon.med.osaka-u.ac.jp	Brain regions involved in fatigue sensation: reduced acetylcarnitine uptake into the brain.	Neuroimage. 2002 Nov;17(3):1256-65.	Fatigue is an indispensable sense for ordering rest. However, the neuronal and molecular mechanisms of fatigue remain unclear. Chronic fatigue syndrome (CFS) with long-lasting fatigue sensation seems to be a good model for studying these mechanisms underlying fatigue sensation. Recently, we found that most patients with CFS showed a low level of serum acetylcarnitine, which well correlated with the rating score of fatigue, and that a considerable amount of acetyl moiety of serum acetylcarnitine is taken up into the brain. Here we show by metabolite analysis of the mouse brain that an acetyl moiety taken up into the brain through acetylcarnitine is mainly utilized for the biosynthesis of glutamate. When we studied the cerebral uptake of acetylcarnitine by using [2-(11)C]acetyl-L-carnitine in 8 patients with CFS and in 8 normal age- and sex-matched controls, a significant decrease was found in several regions of the brains of the patient group, namely, in the prefrontal (Brodmann's area 9/46d) and temporal (BA21 and 41) cortices, anterior cingulate (BA24 and 33), and cerebellum. These findings suggest that the levels of biosynthesis of neurotransmitters through acetylcarnitine might be reduced in some brain regions of chronic fatigue patients and that this abnormality might be one of the keys to unveiling the mechanisms of the chronic fatigue sensation.
Lacour M, Zunder T, Dettenkofer M, Schonbeck S, Ludtke R, Scheidt C.	Institute of Environmental Medicine and Hospital Epidemiology,	An interdisciplinary therapeutic approach for dealing with patients attributing chronic	Int J Hyg Environ Health. 2002 Feb;204(5-6):339-46.	Nonspecific symptoms and a general feeling of ill health that is difficult to objectify are the commonest health problems with which patients present to an Environmental Medicine Outpatient Department (OPD). Of this group, a great proportion meets the classification criteria for Chronic Fatigue Syndrome (CFS) or Functional Memory Disorders in association with Idiopathic Chronic Fatigue (FMD-ICF). This is a longitudinal study of the OPD of Environmental

	Freiburg University Hospital, Hugstetter Strasse 55, D-79106 Freiburg, Germany. mlac@iuk3.ukl.uni-freiburg.de	fatigue and functional memory disorders to environmental poisoning--a pilot study.		Medicine, Freiburg University Hospital, Germany, to determine the feasibility and impact of an interdisciplinary therapeutic approach (self-help program, acupuncture, psychosomatic support by group interventions) in 8 patients with CFS, FMD-ICF, or CFS in association with self-reported Multiple Chemical Sensitivities (sr-MCS). The intervention took into consideration the patients' need for treatment of physical aspects of their disease. This is an important step to motivate patients into required psychosomatic support. Although none of the patients was willing to accept psychosomatic support or psychotherapy at study outset, acceptance of psychosomatic group interventions was high during the study course. Additionally five patients started with personal counseling at the Psychosomatic Clinic, and, without feeling stigmatized, 4 patients started with specific psychotherapy. The patients' quality of life showed no increase after four months, but, as shown by the Sum-Score of SF-36, it had improved significantly at the end of the study, which covered eight months' treatment (p = 0.015). Two follow-up investigations showed that this improvement probably persisted in part (mainly in the dimensions mental health, social function, physical role function, and vitality). In conclusion our interdisciplinary therapeutic approach indicates successful treatment of patients attributing CFS, CFS/sr-MCS, and FMD-ICF to environmental poisoning. We now plan to conduct a randomized controlled trial in the future.
Larkins RG, Molesworth SR.	.	Chronic fatigue syndrome clinical practice guidelines	Med J Aust. 2002 Jul 1;177(1):51-2. Comment in: Med J Aust. 2002 Nov 4;177(9):525-7; author reply 526-7.	
Lehman AM, Lehman DR, Hemphill KJ, Mandel DR, Cooper LM.	Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada	Illness experience, depression, and anxiety in chronic fatigue syndrome.	J Psychosom Res. 2002 Jun;52(6):461-5.	OBJECTIVE: Given the high rate of psychiatric comorbidity with chronic fatigue syndrome (CFS), we considered two possible correlates of anxiety and depression: lack of illness legitimization and beliefs about limiting physical activity. METHOD: A total of 105 people diagnosed with CFS reported on their experiences with medical professionals and their beliefs about recovery and completed the depression and anxiety subscales of the Brief Symptom Inventory. RESULTS: Those who said that their physician did not legitimize their illness (36%) had higher depression and anxiety scores (P's<.05) than their counterparts. Those who believed that limiting their physical exertion was the path to recovery (55%) had lower depression and anxiety scores (P's<.01) than their counterparts. CONCLUSION: Lack of illness legitimization ranked high as a source of dissatisfaction for CFS patients, and it may aggravate psychiatric morbidity. Many CFS patients believed that staying within what they felt to be their physical limits would improve their condition. This belief, and possibly an accompanying sense of control over their symptoms, may alleviate psychiatric morbidity.
Lerner AM, Beqaj SH, Deeter RG, Dworkin HJ, Zervos M, Chang CH, Fitzgerald JT,	School of Medicine, Wayne State University, Detroit, MI, USA. lerner@cdimed.com	A six-month trial of valacyclovir in the Epstein-Barr virus subset of chronic fatigue syndrome:	Drugs Today (Barc). 2002 Aug;38(8):549-61.	This study was designed to determine safety and efficacy of a 6-month trial of valacyclovir in single-virus Epstein-Barr virus (EBV) persistent infection. Phase I of this study used four specific criteria to define a subset of patients with chronic fatigue syndrome (CFS). In the second phase, myocardial dynamics were measured by MUGA rest/stress radionuclide ventriculographic (RVG) examinations pre- and posttreatment with valacyclovir. In phase I, a trial was performed in 19

Goldstein J, O'Neill W.		improvement in left ventricular function.		consecutive CFS patients with the following diagnostic conditions: patients met criteria for diagnosis of CFS; they had had CFS for less than 1 year. They demonstrated repetitively abnormal oscillating T waves (ischemic or flat) at 24-h Holter monitoring; and they had elevated serum IgM antibody titers to EBV viral capsid antigen and/or total diffuse early antigen as measured by the enzyme-linked immunosorbent assay method. The treatment group comprised 10 CFS patients with no serum antibodies to human cytomegalovirus, but the control group (nine CFS patients) had, additionally, high titers of serum antibodies (IgG) to conformational structural antigens of human cytomegalovirus. Both the parallel treatment and control CFS groups received valacyclovir 1.0-1.5 gm q.6.h. for 6 months. This valacyclovir dose achieved serum acyclovir C(max) of > 7 microm and high antiviral activity versus EBV (IC(50) of 4.4-13.3 m). In phase II, six additional CFS patients met the same four criteria as the 19 CFS patients in phase I. They had, however, been ill for a mean of 55.8 months. Thus, 25 CFS patients comprise this study. The studies were carried out at a single outpatient practice in Birmingham, MI, U.S.A. Before initiating valacyclovir, and after 6 months of treatment, clinical and laboratory observations were made. The CFS Energy Index point score (Table I) was used to record each CFS patient's functional capacity at baseline and after 1, 3 and 6 months of valacyclovir. Energy Index point scores, as well as EBV and human cytomegalovirus serum antibody titers were assessed. In the second phase, left ventricular dynamics were repeated after 6 months of treatment with valacyclovir. We concluded that the 16 CFS patients (included in both phases of this study) with EBV-persistent infection (EBV single-virus subset) are improved after 6 months of continuous pharmacokinetic dosing with valacyclovir. Nine CFS patients with EBV/human cytomegalovirus co-infection did not benefit from 6 months of similar treatment. Valacyclovir is not an effective anti-human cytomegalovirus antiviral drug. Unimproved CFS patients with co-infections EBV and human cytomegalovirus may require combined treatment with valacyclovir and another drug more active against human cytomegalovirus. This preliminary trial, with a small number of patients, may be critical to an appropriately designed larger, double-blind, placebo-controlled trial. Copyright 2002 Prous Science
Lerner MA, Beqaj SH, Deeter RG, Fitzgerald JT.	Department of Medicine, William Beaumont Hospital, Wayne State University School of Medicine, Royal Oak, Michigan, USA. lerner@cdimed.com	IgM serum antibodies to human cytomegalovirus nonstructural gene products p52 and CM2(UL44 and UL57) are uniquely present in a subset of patients with chronic fatigue syndrome.	In Vivo. 2002 May-Jun;16(3):153-9.	Human cytomegalovirus (HCMV) IgM serum antibodies to two nonstructural gene products UL44 and UL57 (p52 and CM2) were assayed in patients with the diagnosis of the chronic fatigue syndrome (CFS) according to criteria established by the US Centers for Disease Control and Prevention. A subset of 16 CFS patients demonstrated HCMV IgG, but no HCMV IgM serum antibodies to conformational structural HCMV antigens (designated, V). By convention, these findings are interpreted to indicate only a remote HCMV infection. However, HCMV IgM p52 and CM2 antibodies were uniquely present in these 16 CFS patients. Other CFS patients with similar HCMV (V) IgG antibodies (18 patients), non-fatigued HCMV (V) IgG-positive control patients (18 patients), random HCMV (V) IgG-positive control patients from a clinical laboratory (26 patients), and non-fatigued HCMV (V) IgG-negative control patients (15 patients) did not have HCMV, IgM p52 or CM2 serum antibodies ($p < 0.05$). Control HCMV (V) IgG-positive patients had no serum IgM HCMV (V) antibodies to conventional structural HCMV (V) antigen. Thus, 77 various control patients did not contain IgM p52 or CM2 serum antibodies. The presence of IgM p52 and/or CM2

				HCMV serum antibodies in this subset of CSF-specific patients may detect incomplete HCMV multiplication in which a part of the HCMV protein-coding content of the HCMV genome is processed, but remains unassembled. These findings suggest that the presence of HCMV IgM p52 and CM2 serum antibodies may be a specific diagnostic test for the diagnosis of a subset of CFS patients. Further, these data suggest an etiologic relationship for HCMV infection in this group of CFS patients.
Lim A, Lubitz L.	Department of Paediatrics, Austin and Repatriation Medical Centre, Melbourne, Victoria, Australia.	Chronic fatigue syndrome: successful outcome of an intensive inpatient programme.	J Paediatr Child Health. 2002 Jun;38(3):295-9.	OBJECTIVE: To study the outcome of adolescents with chronic fatigue syndrome (CFS) following an intensive multi-disciplinary inpatient programme. METHODS: A follow-up questionnaire was distributed to all 57 adolescents who had completed the CFS inpatient programme at the Austin and Repatriation Medical Centre. RESULTS: Forty-two adolescents (74%) returned follow-up questionnaires. Immediately following the programme and up to five years after the programme, the majority of participants had returned to school and were functioning better in terms of physical activity and social interactions as compared with before the programme. Before the programme, 94% of adolescents were attending school half-time or less. Up to 5 years after the programme, 78% of adolescents were attending school full-time or with occasional absences only. CONCLUSIONS: A multidisciplinary inpatient programme for CFS was successful in helping to rehabilitate this group of adolescents who were significantly incapacitated prior to entering the inpatient programme.
Lindal E, Stefansson JG, Bergmann S.	Department of Psychiatry, Landspitalinn University Hospital, IS-101 Reykjavik, Iceland. elindal@landspitali.is	The prevalence of chronic fatigue syndrome in Iceland - a national comparison by gender drawing on four different criteria.	Nord J Psychiatry. 2002;56(4):273-7.	The study was carried out to estimate the prevalence of chronic fatigue syndrome (CFS) in Iceland. No previous prevalence studies known to us have been undertaken in Iceland or in Scandinavia. A 95-item custom-made questionnaire was sent to 4000 randomly selected people. The response rate was 63%. The questionnaire was constructed to include questions on all the items found in the four most common criteria for diagnosing CFS; the criteria being Australian, British and American. Results show very different prevalences according to the criteria used. The prevalence ranged from 0 to 4.9%, with the most established criteria yielding a prevalence of 1.4%. Re-test validity of the questionnaire was good, the following results are based on the selection criteria by Fukuda et al. (Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A, et al. The chronic fatigue syndrome: a comprehensive approach to its definition and study. Ann Int Med 1994;121:953-9). Women were in a majority (78%); their mean age was 44, they were fully employed and worked long hours. They believed that the onset of their symptoms was stress related. The type of work was unskilled in the majority of cases. A significant proportion of the males felt a constant buzzing in their ears ($P < 0.05$). Food suppliants were used daily by significantly more women than men ($P < 0.01$). Men had more frequently phobic symptoms ($P < 0.001$) than did women. Differences were found in the prevalence of phobia and panic ($P < 0.001$) between women in the CFS group compared to healthy ones. A positive correlation was found in the prevalence of phobia between women in the CFS group and those with Iceland Disease.
Linder R, Dinser R, Wagner M, Krueger GR, Hoffmann A.	Institute of Medical Informatics, Medical University of Lubeck, Ratzeburger Allee	Generation of classification criteria for chronic fatigue syndrome using an	In Vivo. 2002 Jan-Feb;16(1):37-43.	OBJECTIVE: The definition of chronic fatigue syndrome (CFS) is still disputed and no validated classification criteria have been published. Artificial neural networks (ANN) are computer-based models that can help to evaluate complex correlations. We examined the utility of ANN and other conventional methods in generating classification criteria for CFS compared to other diseases

	160, 23538 Lubeck, Germany. linder@medinf.mu-luebeck.de	artificial neural network and traditional criteria set.		with prominent fatigue, systemic lupus erythematosus (SLE) and fibromyalgia syndrome (FMA). PATIENTS AND METHODS: Ninety-nine case patients with CFS, 41 patients with SLE and 58 with FMA were recruited from a generalist outpatient population. Clinical symptoms were documented with help of a predefined questionnaire. The patients were randomly divided into two groups. One group (n = 158) served to derive classification criteria sets by two-fold cross-validation, using a) unweighted application of criteria, b) regression coefficients, c) regression tree analysis, and d) artificial neural networks in parallel. These criteria were validated with the second group (n = 40). RESULTS: Classification criteria developed by ANN were found to have a sensitivity of 95% and a specificity of 85%. ANN achieved a higher accuracy than any of the other methods. CONCLUSION: We present validated criteria for the classification of CFS versus SLE and FMA, comparing different classification approaches. The most accurate criteria were derived with the help of ANN. We therefore recommend the use of ANN for the classification of syndromes with complex interrelated symptoms like CFS.
Lindh U, Hudecek R, Danersund A, Eriksson S, Lindvall A.	Department of Oncology, Radiology and Clinical Immunology, Rudbeck Laboratory, SE-751 85 Uppsala, Sweden. Ulf.Lindh@bms.uu.se	Removal of dental amalgam and other metal alloys supported by antioxidant therapy alleviates symptoms and improves quality of life in patients with amalgam-associated ill health.	Neuroendocrinol Lett. 2002 Oct-Dec;23(5-6):459-82.	OBJECTIVES: The purpose of this study was to evaluate treatment of patients suffering from chronic ill health with a multitude of symptoms associated with metal exposure from dental amalgam and other metal alloys. SETTING AND DESIGN: We included 796 patients in a retrospective study using a questionnaire about symptom changes, changes in quality of life as a consequence of treatment and assessment of care taking. METHODS: Treatment of the patients by removal of offending dental metals and concomitant antioxidant therapy was implemented according to the Uppsala model based on a close co-operation between physicians and dentists. RESULTS: More than 70% of the responders, remaining after exclusion of those who had not begun or completed removal, reported substantial recovery and increased quality of life. Comparison with similar studies showed accordance of the main results. Plasma concentrations of mercury before and after treatment supported the metal exposure to be causative for the ill health. MAIN FINDINGS: Treatment according to the Uppsala model proved to be adequate for more than 70% of the patients. Patients with a high probability to respond successfully to current therapy might be detected by symptom profiles before treatment. CONCLUSIONS: The hypothesis that metal exposure from dental amalgam can cause ill health in a susceptible part of the exposed population was supported. Further research is warranted to develop laboratory tests to support identification of the group of patients responding to current therapy as well as to find out causes of problems in the group with no or negative results.
Loder C, Allawi J, Horrobin DF.		Treatment of multiple sclerosis with lofepramine, L-phenylalanine and vitamin B(12): mechanism of action and clinical importance: roles of the locus coeruleus	Med Hypotheses. 2002 Nov;59(5):594-602.	In a randomized, placebo-controlled double-blind trial a combination of lofepramine, phenylalanine and vitamin B(12) was found to be effective in relieving the symptoms of multiple sclerosis (MS). The effect occurred within 2-4 weeks, and improved all types of symptoms in all types of MS. The combination was also effective in relieving symptoms in patients with chronic pain and chronic fatigue. We hypothesize that the action of this combined therapy may relate to activation of the noradrenergic locus coeruleus/lateral tegmentum (LC/LT) system which has the potential to influence the functioning of large areas of the brain and spinal cord.

		and central noradrenergic systems.		
Logan AC, Beaulne TM.	Integrative Care Centre, 3600 Ellesmere Road, Unit 4, Toronto, ON M1C 4Y8, Canada.	The treatment of small intestinal bacterial overgrowth with enteric-coated peppermint oil: a case report.	Altern Med Rev. 2002 Oct;7(5):410-7. Comment in: Altern Med Rev. 2003 Feb;8(1):3; author reply 4-5.	Recent investigations have shown that bacterial overgrowth of the small intestine is associated with a number of functional somatic disorders, including irritable bowel syndrome (IBS), fibromyalgia, and chronic fatigue syndrome. A number of controlled studies have shown that enteric-coated peppermint oil (ECPO) is of benefit in the treatment of IBS. However, despite evidence of strong antimicrobial activity, ECPO has not been specifically investigated for an effect on small intestinal bacterial overgrowth (SIBO). A case report of a patient with SIBO who showed marked subjective improvement in IBS-like symptoms and significant reductions in hydrogen production after treatment with ECPO is presented. While further investigation is necessary, the results in this case suggest one of the mechanisms by which ECPO improves IBS symptoms is antimicrobial activity in the small intestine.
Loge JH, Hem E.		[Article in Norwegian]	Tidsskr Nor Laegeforen. 2002 May 30;122(14):1352.	
Looper KJ, Kirmayer LJ.	Division of Social and Transcultural Psychiatry, McGill University, Montreal, Quebec, Canada. karl.looper@mcgill.ca	Behavioral medicine approaches to somatoform disorders.	J Consult Clin Psychol. 2002 Jun;70(3):810-27.	This article reviews the research evidence for the efficacy of cognitive-behavioral therapy (CBT) for somatoform disorders. Randomized controlled studies support the efficacy of individual CBT for the treatment of hypochondriasis, body dysmorphic disorder (BDD), and undifferentiated somatoform disorders including medically unexplained symptoms, chronic fatigue syndrome, and noncardiac chest pain, and group CBT for the treatment of BDD and somatization disorder. On the basis of this review of the existing research and a theoretical model of the processes involved in somatoform disorders, the authors offer suggestions for future research and effective treatment.
Lundin A.	Rehabiliteringsmedicinska kliniken, Danderyds sjukhus, Stockholm. Anders.lundin@reh.ds.sll.se	[Chronic fatigue syndrome is a condition still without medical explanation] [Article in Swedish]	Lakartidningen. 2002 Aug 22;99(34):3280-1. Comment on: Lakartidningen. 2002 Aug 22;99(34):3282-7.	
Marmion BP, Harris RJ, Storm PA, Semendric L.	Q fever: still a mysterious disease.		QJM. 2002 Dec;95(12):832-3. Comment on: QJM. 2002 Aug;95(8):491-2.	
Marx JJ.	. Prevention of organ failure in hereditary haemochromatosis		Neth J Med. 2002 Dec;60(11):419-22. Comment on: Neth J Med. 2002	In this editorial the dominant sites of organ manifestations in hereditary haemochromatosis are discussed as well as conditions that can occur as a result of iron-mediated manifestations: liver disease, diabetes mellitus, arthritis, and cardiomyopathy. The incidences of these organ manifestations and their well-known typical symptomatology are mentioned, in order to

			Dec;60(11):429-33.	investigate hereditary haemochromatosis as a possible (missed?) cause of the chronic fatigue syndrome. In particular the limitations of most studies about the prevalence of hereditary haemochromatosis in patients with the chronic fatigue syndrome are clearly summarised.
Masuda A, Munemoto T, Yamanaka T, Takei M, Tei C.	First Department of Internal Medicine, Faculty of Medicine, Kagoshima University, 8-35-1, Sakuragaoka, Kagoshima 890-8520, Japan.	Psychosocial characteristics and immunological functions in patients with postinfectious chronic fatigue syndrome and noninfectious chronic fatigue syndrome.	J Behav Med. 2002 Oct;25(5):477-85.	Differences between patients with postinfectious chronic fatigue syndrome (CFS, n = 16) and noninfectious CFS (n = 20) were clarified. The noninfectious CFS group had problems in family and developmental history, and had chronic stresses. Members of the postinfectious CFS group were social extroverts while those in the noninfectious CFS group was neurotic and introspective. Natural killer cell activity was suppressed in both groups. These findings suggest that the postinfectious CFS group and the noninfectious CFS group differed in their pathogenesis until the onset of CFS. The latter group should be considered as a variant of psychiatric disorder and treated accordingly.
Masuda A, Nakayama T, Yamanaka T, Koga Y, Tei C.	First Department of Internal Medicine, Faculty of Medicine, Kagoshima University, 8-35-1, Sakuragaoka, Kagoshima 890-8520, Japan.	The prognosis after multidisciplinary treatment for patients with postinfectious chronic fatigue syndrome and noninfectious chronic fatigue syndrome.	J Behav Med. 2002 Oct;25(5):487-97.	The prognosis after multidisciplinary treatment for patients with postinfectious chronic fatigue syndrome (CFS, n = 9) and noninfectious CFS (n = 9) was clarified. After treatment, natural killer (NK) cell activity increased in the postinfectious CFS group but did not recover to within normal range in the noninfectious CFS group. In the postinfectious CFS group, physical and mental symptoms improved, and 8 patients returned to work. In the noninfectious CFS group, symptoms did not improve, and only 3 patients returned to work. The prognosis of postinfectious CFS group was better than that of noninfectious CFS group. Classification of CFS patients into postinfectious and noninfectious groups is useful for choosing the appropriate treatment in order to obtain better prognosis.
Maxhall U.		[Are muscular and articular pains more than functional diseases?] [Article in Norwegian]	Tidsskr Nor Laegeforen. 2002 Nov 30;122(29):2818.	
McCauley LA, Joos SK, Barkhuizen A, Shuell T, Tyree WA, Bourdette DN.	Center for Research on Occupational and Environmental Toxicology, Oregon Health & Science University Portland, Oregon 97201, USA. mccauley@ohsu.edu	Chronic fatigue in a population-based study of Gulf War veterans.	Arch Environ Health. 2002 Jul-Aug;57(4):340-8.	Fatigue has been associated with illness in veterans of the Gulf War; however, few studies have confirmed self-reported fatigue by using clinical evaluation, and symptomatic veterans have not been evaluated with established criteria for Chronic Fatigue Syndrome (CFS). The authors describe the frequency and clinical characteristics of CFS in a sample of veterans residing in the northwestern United States. The sample was selected randomly from U.S. Department of Defense databases of troops deployed to southwest Asia during the Gulf War. The selected individuals were invited to participate in a clinical case-control study of unexplained illness. Of 799 survey respondents eligible for clinical evaluation, 178 had fatigue symptoms. Of the 130 veterans who were evaluated clinically, 103 had unexplained fatigue, and 44 veterans met the 1994 U.S. Centers for Disease Control criteria for CFS. In this population, the authors estimated a minimum prevalence of any unexplained fatigue to be 5.1%, and of CFS to be 2.2%. The estimated prevalence was greater among females than among males. Cases were similar to

				healthy controls, as determined by laboratory tests and physical findings. In comparison to several clinical studies of CFS patients, the authors of this study found a lower proportion of veterans who reported a sudden onset of symptoms (19%) vs. a gradual onset (50%). Although it has previously been suggested that veterans of the Gulf War suffer from higher rates of chronic fatigue than the general population, the study results described herein--on the basis of clinical examination of a population-based sample of veterans-actually indicate that an increased rate may indeed exist. Gulf War veterans with unexplained fatigue should be encouraged to seek treatment so that the impact of these symptoms on overall quality of life can be reduced.
McCue P, Scholey AB, Herman C, Wesnes KA.	Human Cognitive Neuroscience Unit, University of Northumbria, Newcastle upon Tyne, UK.	Validation of a telephone cognitive assessment test battery for use in chronic fatigue syndrome.	J Telemed Telecare. 2002;8(6):337-43.	We compared a computerized version of the Cognitive Drug Research (CDR) cognitive assessment test battery and a completely automated telephone version of the same battery. These assessed aspects of attention, working memory and long-term memory. Both methods were used to assess the cognitive performance of a cohort of 30 people with confirmed chronic fatigue syndrome (CFS) and a group of 30 healthy controls matched for age and education. The CFS group had significantly slower reaction times on all four cognitive measures on both the computerized and telephone tests. The mood data followed similar patterns inthe computer and telephone assessments. The results from both forms of the test battery confirmed the pattern and severity of cognitive impairment in CFS. Furthermore, the two methods of testing were similarly sensitive in detecting cognitive deficits. The incapacitating nature of CFS may cause problems for researchers if the restrictions to mobility affect the representativeness of the study group. The findings of the present study support the use of a fully automated telephone cognitive testing system for detecting deficits in CFS.
Merz S.	susanne@merz.as	[Chronic fatigue syndrome. More and more differential diagnoses suggest a new view of this syndrome] [Article in Swedish]	Lakartidningen. 2002 Aug 22;99(34):3282-7.	The diagnosis of chronic fatigue syndrome (CFS) requires a number of symptoms beyond chronic fatigue, according to the criteria developed in 1994 by the US Centers for Disease Control (CDC) International CFS Study Group. CFS is thus no synonym for chronic fatigue but rather an unusual syndrome afflicting no more than 0.1% of the population. Several CFS definitions have been developed over the years, and it is common for investigators to erroneously compare studies based on different definitions, which nevertheless all use the term CFS. Much of our "understanding" of CFS does not apply to the small group of patients who fulfill the current (1994) CDC definition (above). Recent studies have shown that a number of somatic diseases can present with CFS symptoms and thus be misdiagnosed as CFS. This review presents a list of such differential diagnoses, mainly chronic infections, endocrine diseases, and allergies. In view of these differential diagnoses (1) investigation and therapy must be individualized, and (2) we should offer rehabilitation where different specialists work as a coordinated team.
Merz S.	susanne@merz.as	[Research on chronic fatigue syndrome face to face with a paradigm shift] [Article in Swedish]	Lakartidningen. 2002 Aug 29;99(35):3438-40.	
Metzger FA, Denney DR.	Department of Psychology,	Perception of cognitive	Ann Behav Med. 2002	This study examined discrepancies between perceived and actual performance by patients with chronic fatigue syndrome (CFS) confronted with a challenging cognitive task. Before and after

	University of Kansas, Lawrence 66045-7556.	performance in patients with chronic fatigue syndrome.	Spring;24(2):106-12.	completing a modified version of the Stroop task, 40 patients and 40 healthy control participants estimated their own performance and the performance that would normally be achieved by someone of equal age and education level. After correcting for differences between the groups in depression, we found no differences in actual performance on the Stroop. However, patients with CFS consistently underestimated their performance relative to normal performance. This difference was observed for both depressed and nondepressed subgroups of patients, persisted after adjusting the results for depression, and correlated with patients' ratings of the mental effort and fatigue evoked by the task. The results are discussed in light of cognitive models of CFS that suggest the setting of impossibly high standards of personal performance may contribute to the dynamism of this disease.
Michalsen A, Weidenhammer W, Melchart D, Langhorst J, Saha J, Dobos G.	Abteilung fur Innere Medizin V, Naturheilkunde und Integrative Medizin, Kliniken Essen Mitte, Essen.	[Short-term therapeutic fasting in the treatment of chronic pain and fatigue syndromes--well-being and side effects with and without mineral supplements] [Article in German]	Forsch Komplementarmed Klass Naturheilkd. 2002 Aug;9(4):221-7.	BACKGROUND: Fasting followed by vegetarian diet has shown to be an effective treatment for rheumatoid arthritis, moreover fasting is frequently used as an adjunctive treatment in chronic pain and stress/exhaustion syndromes. Data on well-being and the frequency of side effects during fasting are mostly retrospective. Mineral supplements are frequently used in order to compensate for fasting-induced tissue acidosis and to reduce side effects. There are only limited data that support this practice. OBJECTIVE: To study the effects of oral mineral supplements on common side effects and well-being during short-term fasting. PATIENTS AND METHODS: 209 consecutive inpatients with chronic pain/exhaustion syndromes were recruited. In a controlled non-randomised study design all patients underwent fasting (250 kcal; 3 l fluid intake/day) over 7 days, in study phase 1 without (n = 103) and in study phase 2 with (n = 106) concomitant prescription of standardised oral mineral supplements (3 x 2 to 3 x 3 Bullrich's Vital). Weight, blood pressure and urinary pH were recorded daily. Well-being and mood as well as common side effects (i.e. fatigue, hunger, heart burn, headache) were assessed with standardised self-reports. RESULTS: Baseline characteristics of the 209 patients (mean age 54.7 +/- 10.5 years; 83.3% female) were balanced. Both groups showed a fasting-induced decrease of blood pressure, a slight decrease in mood and well-being on days 3 and 4 with consecutive increase and moderate hunger, i.e. in the evening. Side effects and general tolerability of fasting as well as well-being and mood were not different between the groups. There were no serious side effects in both groups. CONCLUSIONS: Short-term fasting in inpatients with pain and stress syndromes is safe and well tolerated, concomitant mineral supplements have no additive benefit. Copyright 2002 S. Karger GmbH, Freiburg
Miller RG.	Department of Neurology, California Pacific Medical Center, San Francisco, California 94115, USA.	Role of fatigue in limiting physical activities in humans with neuromuscular diseases.	Am J Phys Med Rehabil. 2002 Nov;81(11 Suppl):S99-107.	New methods of examining both central and peripheral fatigue are now available. A broader understanding of the mechanisms of fatigue in healthy human subjects has begun to emerge. The mechanisms of fatigue in patients with various neuromuscular diseases are even more complex than in healthy persons. Examples of both central and peripheral fatigue in various neuromuscular diseases and other disorders are presented, including metabolic myopathy, chronic fatigue syndrome, postpolio syndrome, and amyotrophic lateral sclerosis.
Morriss RK, Robson MJ, Deakin JF.	Department of Psychiatry, University of	Neuropsychological performance and noradrenaline	Psychopharmacology (Berl). 2002 Sep;163(2):166-73.	RATIONALE: Subjective and objective impairments in neuropsychological function have been reported in chronic fatigue syndrome (CFS) patients under conditions of high arousal. These impairments may reflect impaired central noradrenaline function such as impaired post-synaptic

	Liverpool, Royal Liverpool Hospital, Prescot Street, Liverpool L69 3GA, UK. r.k.morris@liverpool.ac.uk	function in chronic fatigue syndrome under conditions of high arousal.	Epub 2002 Jul 30.	alpha-2 adrenoceptor function. OBJECTIVES: To determine whether high-dose clonidine has greater agonist effects at central post-synaptic alpha-2 receptors in CFS patients than controls under conditions of high arousal. As a result clonidine may reverse neuropsychological deficits underlying symptoms of poor concentration and memory. METHODS: High-dose clonidine (2.5 mg/kg) and placebo challenge tests were given in random order to ten medication-free CFS patients without anxiety disorders, depressive disorders or migraine and ten matched healthy controls under the same stressors (timed neuropsychological testing, venous sampling, intravenous drug administration). Growth hormone, cortisol, blood pressure, pulse rate, visual analogue scales of subjective neuropsychological performance and the performance on several tests from a computerised neuropsychological battery were measured. RESULTS: In CFS patients versus controls, clonidine enhanced both growth hormone (P = 0.028) and cortisol release (P = 0.021) and increased speed in the initial stage of a planning task (P = 0.023). There were no other differences between CFS patients and controls on hormonal, physiological, symptomatic or neuropsychological measures. CONCLUSIONS: Under conditions of high arousal, CFS patients may display supersensitive central post-synaptic alpha-2 adrenoceptor function associated with the release of cortisol and growth hormone and initial thinking time in planning tasks.
Naranch K, Park YJ, Repka-Ramirez MS, Velarde A, Clauw D, Baraniuk JN.	Chronic Pain and Fatigue Research Center, Division of Rheumatology, Immunology and Allergy, Georgetown University, Washington, DC 20007-2097, USA.	A tender sinus does not always mean rhinosinusitis.	Otolaryngol Head Neck Surg. 2002 Nov;127(5):387-97.	BACKGROUND: Sinus tenderness has not been quantitatively assessed. OBJECTIVE: We sought to compare sinus and systemic tenderness in rhinosinusitis, allergic rhinitis, and chronic fatigue syndrome (CFS), and healthy (non-CFS) groups. METHODS: Cutaneous pressures (kg/cm(2)) causing pain at 5 sinus and 18 systemic sites were measured in acute and chronic rhinosinusitis, active allergic rhinitis, healthy non-CFS/no rhinosinusitis, and CFS subjects. RESULTS: Sinus thresholds differed significantly (P </= 10(-11), ANOVA) between non-CFS/no rhinosinusitis (1.59 +/- 0.14 kg/cm(2), mean +/- 95% CI, n = 117), allergic rhinitis (1.19 +/- 0.31, n = 30), exacerbations of chronic rhinosinusitis (1.25 +/- 0.26, n = 25), non-CFS/chronic rhinosinusitis (1.23 +/- 0.27, n = 23), acute rhinosinusitis (1.10 +/- 0.20, n = 22), CFS/no rhinosinusitis (0.98 +/- 0.15, n = 70), and CFS/chronic rhinosinusitis (0.78 +/- 0.12, n = 56). Systemic pressure thresholds were lower for CFS (1.46 +/- 0.15) than for non-CFS (2.67 +/- 0.22, P </= 10(-11)). CONCLUSIONS: The lower sinus thresholds of rhinosinusitis groups validated the sign of sinus tenderness. Sinus and systemic thresholds were both 44% lower in CFS than in non-CFS subjects, suggesting that systemic hyperalgesia contributed to CFS sinus tenderness and "rhinosinusitis" complaints.
Naranch K, Repka-Ramirez SM, Park Y-J, Velarde A, Finnegan R, Murray J, Pheiffer A, Hwang E, Clauw D, Baraniuk JN.		Differences in Baseline Nasal Secretions Between Chronic Fatigue Syndrome (CFS) and Control Subjects	Journal of Chronic Fatigue Syndrome 2002; 10 (1): 3 - 15	Objective: To assess potential mechanism(s) for the rhinitis found in Chronic Fatigue Syndrome (CFS) subjects. Methods: The concentration of mucus constituents were measured in basal nasal lavage fluids of 103 CFS and 92 non-CFS control subjects. Subjects were further characterized by their Rhinitis Score and allergy skin test results into nonallergic and allergic rhinitis, atopic, and negative subgroups to determine if differences were related to atopy. Other questionnaires of irritant sensitivity and medicine use were completed. Results: Mucin polysaccaride (p = 0.043, ANOVA), free hemoglobin (p = 0.0044), mucin/total protein (p = 0.039) and hemoglobin/total protein (p = 0.043) were much higher in CFS than controls. CFS subjects with positive Rhinitis Scores (p = 0.023) or skin tests (p = 0.047) had higher mucin levels than those with negative values. For all subjects, inceased mucin was correlated with total protein (Pearson's r2 = 0.188)

				and inhaled corticosteroid use (r2 = 0.082) and elevated Tobacco Scores (r2 = 0.061). Other correlations with demographic, medication, or questionnaire responses gave r2 < 0.05. Conclusions: CFS subjects have a higher level of complaints in many systems including the nose. They appear to have an irritant (nonallergic) rhinitis with increased mucin production and mucosal friability (epistaxis of hemoglobin). Nasal and systemic drugs do not explain these significant baseline changes.
Naschitz JE, Sabo E, Naschitz S, Rosner I, Rozenbaum M, Madelain F, Hillel I, Priselac RM, Gaitini L, Eldar S, Zukerman E, Yeshurun D.	Departments of Internal Medicine A, Rheumatology, Anesthesiology, and Surgery, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.	Hemodynamics instability score in chronic fatigue syndrome and in non-chronic fatigue syndrome.	Semin Arthritis Rheum. 2002 Dec;32(3):141-8 Comment in: Semin Arthritis Rheum. 2002 Dec;32(3):137-8.	OBJECTIVE: In studying patients with chronic fatigue syndrome (CFS) we developed a method that confers numerical expression to the degree of blood pressure and heart rate lability, ie, the 'hemodynamic instability score' (HIS). The HIS in CFS patients differed significantly from healthy subjects. The present investigation compares the HIS in CFS, non-CFS chronic fatigue and patients with recurrent syncope. METHODS: Patients with CFS (n = 21), non-CFS chronic fatigue (n = 24), syncope of unknown cause (n = 44), and their age and sex-matched healthy controls (n = 21) were evaluated with a standardized head-up tilt test (HUTT). Abnormal reactions (endpoints) on HUTT were classified 'clinical outcomes' (cardioinhibitory or vasodepressor reaction, orthostatic hypotension, postural tachycardia syndrome) and 'HIS endpoint', i.e. HIS >-0.98. RESULTS: The highest incidence of endpoints was noted in patients with CFS (79%), followed by patients with syncope of unknown cause (46%), non-CFS chronic fatigue (35%), and healthy subjects (14%). Presyncope or syncope during tilt occurred in 38% of CFS patients, 21% of patients with non-CFS chronic fatigue, and 43% of patients with recurrent syncope. The average HIS values were: CFS = +2.02 (SD 4.07), non-CFS chronic fatigue = -2.89 (SD 3.64), syncope = -3.2 (SD 3.0), healthy = -2.48 (4.07). The odds ratios for CFS patients to have HIS >-0.98 was 8.8 compared with non-CFS chronic fatigue patients, 14.6 compared with recurrent syncope patients, and 34.8 compared with healthy subjects. CONCLUSION: The cardiovascular reactivity in patients with CFS has certain features in common with the reactivity in patients with recurrent syncope or non-CFS chronic fatigue, such as the frequent occurrence of vasodepressor reaction, cardioinhibitory reaction, and postural tachycardia syndrome. Apart from to these shared responses, the large majority of CFS patients exhibit a particular abnormality which is characterized by HIS values >-0.98. Thus, HIS >-0.98 lends objective criteria to the assessment of CFS. Copyright 2002, Elsevier Science (USA). All rights reserved.
Naschitz JE, Sabo E, Naschitz S, Rosner I, Rozenbaum M, Priselac RM, Gaitini L, Zukerman E, Yeshurun D.	Department of Internal Medicine A, Bnai Zion Medical Center, Haifa 31048, P. O. Box 4940, Israel. naschitz@tx.technion.ac.il	Fractal analysis and recurrence quantification analysis of heart rate and pulse transit time for diagnosing chronic fatigue syndrome.	Clin Auton Res. 2002 Aug;12(4):264-72. Comment in: Clin Auton Res. 2002 Aug;12(4):228-30.	This study aimed to develop a method to distinguish between the cardiovascular reactivity in chronic fatigue syndrome (CFS) and other patient populations. Patients with CFS (n = 23), familial Mediterranean fever (n = 15), psoriatic arthritis (n = 10), generalized anxiety disorder (n = 12), neurally mediated syncope (n = 20), and healthy subjects (n = 20) were evaluated with a shortened head-up tilt test (HUTT). A 10-minute supine phase of the HUTT was followed by recording 600 cardiac cycles on tilt, i. e., 5 to 10 minutes. Beat-to-beat heart rate (HR) and pulse transit time (PTT) were acquisitioned. Data were processed by recurrence plot and fractal analysis. Fifty-two variables were calculated in each subject. On multivariate analysis, the best predictors of CFS were HR-tilt-R/L, PTT-tilt-R/L, HR-supine-DET, PTT-tilt-WAVE, and HR-tilt-SD. Based on these predictors, the 'Fractal & Recurrence Analysis-based Score' (FRAS) was calculated: FRAS = 76.2 + 0.04*HR-supine-DET - 12.9*HR-tilt-R/L - 0.31*HR-tilt-SD - 19.27*PTT-tilt-R/L - 9.42*

				PTT-tilt-WAVE. The best cut-off differentiating CFS from the control population was FRAS = + 0.22. FRAS > + 0.22 was associated with CFS (sensitivity 70 % and specificity 88 %). The cardiovascular reactivity received mathematical expression with the aid of the FRAS. The shortened HUTT was well tolerated. The FRAS provides objective criteria which could become valuable in the assessment of CFS.
Nash J, Cheng JS, Meyer GA, Remler BF.	Medical College of Wisconsin, Milwaukee, Wis., USA.	Chiari type I malformation: overview of diagnosis and treatment.	WMJ. 2002;101(8):35-40.	Chiari Type I malformation (Chiari I) is a congenital hindbrain anomaly characterized by downward displacement of the cerebellar tonsils through the foramen magnum. This can lead to compression of cerebellar components, the lower brainstem, and the upper cervical spinal cord. In turn, a variety of neurological deficits and permanent nervous system damage may evolve. This review article discusses the etiology, diagnosis, and treatment of patients with Chiari I malformation. Its protean manifestations cause significant overlap with multiple sclerosis, chronic fatigue syndrome, and numerous other conditions. Accordingly, the diagnosis of Chiari I is difficult to establish by clinical evaluation alone. Demonstration of the characteristic hindbrain abnormalities, however, is easily accomplished with magnetic resonance imaging. Neuroimaging should therefore be considered in patients with cerebellar, brainstem, and cervical cord dysfunction. Surgical treatment is indicated in symptomatic patients with radiographic evidence of hindbrain abnormalities. Posterior fossa decompression has also been performed in patients with fibromyalgia and chronic fatigue syndrome based solely on overlapping symptoms with Chiari I. This practice remains controversial. Appraisal of surgical outcome requires postoperative neuroimaging and long-term patient follow-up to assess the permanency of improvement. Preliminary study results of the impact of surgical technique on patient outcome are reported. Ongoing research is devoted to a better understanding of the pathophysiology of Chiari I malformation and the development of more effective medical and surgical treatments.
Natelson BH, Haghighi MH, Ponzio NM.	Departments of Neurosciences, University of Medicine and Dentistry-New Jersey Medical School, Newark, New Jersey 07018 USA. bhm@njneuromed.org	Evidence for the presence of immune dysfunction in chronic fatigue syndrome.	Clin Diagn Lab Immunol. 2002 Jul;9(4):747-52.	
Natelson BH, Lange G.	Department of Neurosciences, Chronic Fatigue Syndrome Cooperative Research Center, UMDNJ, Newark,	A status report on chronic fatigue syndrome.	Environ Health Perspect. 2002 Aug;110 Suppl 4:673-7.	Medical history has shown that clinical disease entities or syndromes are composed of many subgroups--each with its own cause and pathogenesis. Although we cannot be sure, we expect the same outcome for chronic fatigue syndrome (CFS), a medically unexplained condition characterized by disabling fatigue accompanied by infectious, rheumatological, and neuropsychiatric symptoms. Although the ailment clearly can occur after severe infection, no convincing data exist to support an infectious (or immunologic) process in disease maintenance. Instead, data point to several possible pathophysiological processes: a covert encephalopathy,

	USA. bhn@njneuromed.org			impaired physiological capability to respond to physical and mental stressors, and psychological factors related to concerns about effort exacerbating symptoms. Each of these is under intense investigation. In addition, some data do exist to indicate that environmental agents also can elicit a state of chronic fatigue. We expect data to accumulate to support the belief that CFS has multiple causes.
Nijs J, Nicolson GL, De Becker P, Coomans D, De Meirleir K.	Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, KRO Gebouw-1, Laarbeeklaan 101, 1090 Brussel, Belgium. jo.nijs@vub.ac.be	High prevalence of Mycoplasma infections among European chronic fatigue syndrome patients. Examination of four Mycoplasma species in blood of chronic fatigue syndrome patients.	FEMS Immunol Med Microbiol. 2002 Nov 15;34(3):209-14.	Prevalence of Mycoplasma species infections in chronic fatigue syndrome (CFS) has been extensively reported in the scientific literature. However, all previous reports highlighted the presence of Mycoplasmas in American patients. In this prospective study, the presence of Mycoplasma fermentans, M. penetrans, M. pneumoniae and M. hominis in the blood of 261 European CFS patients and 36 healthy volunteers was examined using forensic polymerase chain reaction. One hundred and seventy-nine (68.6%) patients were infected by at least one species of Mycoplasma, compared to two out of 36 (5.6%) in the control sample (P<0.001). Among Mycoplasma-infected patients, M. hominis was the most frequently observed infection (n=96; 36.8% of the overall sample), followed by M. pneumoniae and M. fermentans infections (equal frequencies; n=67; 25.7%). M. penetrans infections were not found. Multiple mycoplasmal infections were detected in 45 patients (17.2%). Compared to American CFS patients (M. pneumoniae>M. hominis>M. penetrans), a slightly different pattern of mycoplasmal infections was found in European CFS patients (M. hominis>M. pneumoniae, M. fermentansz.Gt;M. penetrans).
Nijs J, Vaes P, Van Hoof E, De Becker P, McGregor N, De Meirleir K.		Activity Limitations and Participation Restrictions in Patients with Chronic Fatigue Syndrome-Construction of a Disease Specific Questionnaire	Journal of Chronic Fatigue Syndrome Volume 2002; 10 (3/4): 3 - 23	Review of the literature indicated the lack of disease specific measures for assessing activity limitations and participation restriction in patients with Chronic Fatigue Syndrome. Retrospective analysis of Karnofsky Performance Status questionnaires and Activities of Daily Living questionnaires (a Dutch version of the Barthel index, modified for CFS) of 141 subjects was performed to create a new questionnaire. Data analysis resulted in the following item selection, based on most frequently reported activity limitations and participation restriction; cleaning, washing dishes and returning them to cupboard, iron, do the wash, gardening, replace light bulb, walking, climb one flight of stairs, stand one hour, sit two hours, doing groceries, thirty minutes of computer work, carrying heavy objects, write a full page letter, use a screwdriver, hammer a nail, make one bed, reading, social activities, doing sports, studying, driving a car, going to school/working, preparing meals and caring for a child. These data were used to create the CFS-Activities and Participation Questionnaire (CFS-APQ). The reliability and different aspects of validity of this new measure still need to be established.
Ohashi K, Yamamoto Y, Natelson BH.	Educational Physiology Laboratory, Graduate School of Education, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo	Activity rhythm degrades after strenuous exercise in chronic fatigue syndrome.	Physiol Behav. 2002 Sep;77(1):39-44.	Post-exertional exacerbation of symptoms is one of the major characteristics of chronic fatigue syndrome (CFS). In this study, we evaluated the hypothesis that disturbances in circadian chronobiological regulation may play a role in generating this phenomenon. We recorded physical activity for 6-day periods in 16 women (10 CFS and 6 sedentary healthy controls, CON) before and after performing a maximal treadmill test. We calculated activity rhythms by computing autocorrelation coefficients by cutting 1 day apart from the data as a template and sliding it sequentially through each of the other days; all of 6 days were used as the templates. The peak value of autocorrelation coefficient (R) and the time between peak R's (circadian

	113-0033, Japan.			period, CP) were calculated. CFS patients had a lengthening (P < .05) of mean circadian period (MCP) that was longer than 24 h (P < .05), while MCP in CON remained unchanged. No difference was found in the standard error of each subject's MCP (circadian period variability, CPV) before and after exercise for both groups. We interpret this increase in circadian rest-activity period seen in CFS patients following exercise to indicate that exhaustive exercise interferes with normal entrainment to 24-h zeitgeber(s). This effect may be associated in part with the common patient complaint of symptom worsening following exertion. Copyright 2002 Elsevier Science Inc.
Palaniappan R, Sirimanna T.	Royal National Throat Nose and Ear Hospital, Gray's Inn Road, London WC1X 8EE, UK. rudipal@hotmail.com	Peripheral vestibular dysfunction in chronic fatigue syndrome.	Int J Pediatr Otorhinolaryngol. 2002 May 31;64(1):69-72.	OBJECTIVE: To report left-sided peripheral vestibular failure as the cause of dizziness in a 12-year-old boy diagnosed as having chronic fatigue syndrome (CFS). DESIGN: Retrospective case report with review of literature and discussion. SETTING: Tertiary children's hospital. CONCLUSION: We recommend proper vestibular assessment for CFS patients presenting with dizziness, as effective treatment for peripheral vestibular disorder exists in the form of balance rehabilitation exercises.
Pall ML.	Chronic fatigue syndrome/myalgic encephalitis.		Br J Gen Pract. 2002 Sep;52(482):762; author reply 763-4. Comment on: Br J Gen Pract. 2002 May;52(478):355-6.	
Pall ML.		Levels of Nitric Oxide Synthase Product Citrulline Are Elevated in Sera of Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome Volume 2002; 10 (3/4): 37 - 41	Serum levels of citrulline, a product of nitric oxide synthase activity, were measured in 36 CFS patients and 16 controls to determine whether synthase activity may be elevated in CFS patients. Serum citrulline levels were found to be significantly elevated in CFS patients and, in addition, there was a trend towards higher levels in CFS patients with stronger symptoms. These results provide support for the view that nitric oxide synthase activity tends to be elevated in CFS patients, thus supporting a prediction of the elevated nitric oxide/peroxynitrite theory of CFS etiology.
Panerai AE, Vecchiet J, Panzeri P, Meroni P, Scarone S, Pizzigallo E, Giamberardino MA, Sacerdote P.	Department of Pharmacology, Istituto di Ricerca e Cura a Carattere Scientifico, University of Milan, Italy.	Peripheral blood mononuclear cell beta-endorphin concentration is decreased in chronic fatigue syndrome and fibromyalgia but not in depression: preliminary report.	Clin J Pain. 2002 Jul-Aug;18(4):270-3.	OBJECTIVE: The aim of this study was to examine the possible role of the immune system in the pathophysiology of chronic fatigue syndrome and fibromyalgia syndrome and in the differential diagnosis of depression by investigating changes in peripheral blood mononuclear cell levels of beta-endorphin, an endogenous opioid known to be involved in regulation of the immune system function. DESIGN: Beta-endorphin concentrations were measured by radioimmunoassay in peripheral blood mononuclear cells from healthy controls (n = 8) and patients with chronic fatigue syndrome (n = 17), fibromyalgia syndrome (n = 5), or depression (n = 10). RESULTS: Beta-endorphin concentrations were significantly lower in patients with chronic fatigue syndrome or fibromyalgia syndrome than in normal subjects and depressed patients ($p < 0.001$ and $p < 0.01$, respectively). They were significantly higher in depressed patients than in controls ($p < 0.01$). CONCLUSIONS: Evaluation of peripheral blood mononuclear cell beta-endorphin concentrations could represent a diagnostic tool for chronic fatigue syndrome and fibromyalgia and help with differential diagnosis of these syndromes versus depression. The results obtained are also

				consistent with the hypothesis that the immune system is activated in both chronic fatigue syndrome and fibromyalgia syndrome.
Pastel RH.	Radiation Pathophysiology and Toxicology Department, Armed Forces Radiobiology Research Institute, 8901 Wisconsin Avenue, Bethesda, MD 20889-5603, USA.	Radiophobia: long-term psychological consequences of Chernobyl.	Mil Med. 2002 Feb;167(2 Suppl):134-6.	The primary health effect of Chernobyl has been widespread psychological distress in liquidators (workers brought in for cleanup), evacuees, residents of contaminated areas, and residents of adjacent noncontaminated areas. Several psychoneurological syndromes characterized by multiple unexplained physical symptoms including fatigue, sleep and mood disturbances, impaired memory and concentration, and muscle and/or joint pain have been reported in the Russian literature. These syndromes, which resemble chronic fatigue syndrome and fibromyalgia, are probably not due to direct effects of radiation because they do not appear to be dose related to radiation exposure and because they occur in areas of both high and low contamination.
Patarca-Montero R, Fletcher MA.		The Paul-Bunnell Heterophile Antibody Determinant in Epstein-Barr Virus-Associated Disease	Journal of Chronic Fatigue Syndrome Volume 2002; 10 (3/4): 51 - 86	Reactivation of latent herpes viruses (notably EpsteinBarr virus, human herpesvirus-6) is commonly seen in chronic fatigue syndrome and it is believed to contribute to symptom perpetuation. EpsteinBarr virus (EBV), which was first isolated by Epstein, Barr and Achong (1964) from a cultured Burkitt's lymphoma lymphoblast cell line, is the etiological agent for infectious mononucleosis (IM), polyclonal and oligoclonal lymphomas associated with primary and acquired immunodeficiencies, and the complications of X-linked lymphoproliferative syndrome (XLP) (Cantani and Mastrantoni, 1989; Englund, 1988; Ernberg et al., 1990; Jones and Straus, 1987; Okano et al., 1988; Purtilo, 1987; Purtilo et al., 1981; Rowe et al., 1986; Saemundsen et al., 1981) and nasopharyngeal cancer (Pearson et al., 1984). Furthermore, people who have had IM have higher rates of subsequent development of malignant lymphoproliferative disorders (Abo et al., 1982; Snydman et al., 1982) and Hodgkin's disease (Green et al., 1979; Mueller, 1987; Poppema et al., 1985; Weiss et al., 1989), while patients with XLP have a higher incidence of non-Hodgkin's malignant lymphoma (Harrington et al., 1987). The precise role of EBV in these diseases or in CFS is not well understood. Nonetheless, it is known that EBV infection triggers the formation of heterophile antibodies that, for many decades, have formed the basis for serologic diagnosis of IM. In this review, we discuss the discovery, species variation, and structure of the erythrocyte membrane-associated Paul-Bunnell (PB) heterophile antibody determinant, its implications to IM diagnosis, and its potential contribution to defective immune surveillance, such as that seen in chronic fatigue syndrome.
Patarca-Montero R, Fletcher MA.		Effects of Benzalkonium Salts on G-protein-Mediated Processes and Surface Membranes: Relevance to Microbial- and Chemical-Induced	Journal of Chronic Fatigue Syndrome Volume 2002; 10 (3/4): 87 - 168	Benzalkonium salts comprise a group of positively charged surface-active alkylamine biocides with the general formula alkyldimethylbenzylammonium chloride or bromide. They interact with guanine nucleotide triphosphate-binding proteins (G proteins), thereby affecting signal transduction in a variety of cell types and processes. The present report reviews the known and potential basic science research and clinical applications and manifestations of benzalkonium salts. Benzalkonium salts have antiproliferative effects on a variety of cells (including T cells) through G-protein-dependent pathways, affect cytokine gene expression (downregulate tumor necrosis factor expression), and are also effective bactericidal, fungicidal, and virucidal agents with multisite (direct and immunologically-mediated) inhibitory activity against many pathogens,

		Diseases		including the human immunodeficiency virus (HIV), papillomavirus, and herpesviruses. Therefore, benzalkonium salts not only appear to be effective as disinfectants and spermicides but may also prove useful in the prevention and treatment of several diseases, particularly those linked to viruses and originating at the skin or mucosal surface. The untoward effects of benzalkonium salts are also discussed as a paradigm for chemical-induced diseases.
Patarca-Montero R.		Cytolytic Cells and Their Function	Journal of Chronic Fatigue Syndrome 2002; 10(2): 29 - 58	Cytolytic cells play an important role in cellular immunity and their function is compromised in a subgroup of patients with chronic fatigue syndrome. This review summarizes historical, methodological, clinical, therapeutic, and basic immunology aspects of cytolytic cells.
Pedersen NL, Lichtenstein P, Svedberg P.	Department of Medical Epidemiology, Karolinska Institutet, Stockholm, Sweden. Nancy.Pedersen@mep.ki.se	The Swedish Twin Registry in the third millennium.	Twin Res. 2002 Oct;5(5):427-32.	Since the Swedish Twin Registry was first established in the late 1950s to study the importance of smoking and alcohol consumption on cancer and cardiovascular diseases, it has been expanded and updated on several occasions. The focus has similarly broadened to most common complex diseases. The content of the database is described, ongoing projects based on the registry are summarized, and we review some of the principal findings on aging, cancer and cardiovascular disease that have come from the registry. Ongoing efforts and future plans for the STR are discussed. Among others, we plan blood collection and genotyping to study the genetic bases of complex diseases, a first contact ever with the cohorts born after 1958, and in-depth studies of selected diseases, such as Parkinson's disease and chronic fatigue syndrome.
Peres MF, Zukerman E, Young WB, Silberstein SD.	Sao Paulo Headache Centre and Albert Einstein Hospital Sao Paulo, Brazil. marioperes@yahoo.com	Fatigue in chronic migraine patients.	Cephalalgia. 2002 Nov;22(9):720-4.	Fatigue is a common symptom frequently reported in many disorders including headaches, but little is known about its nature. The objective was to determine the prevalence of fatigue in chronic migraine (CM) patients, to define its subtypes and its relationship with other conditions comorbid with CM. Sixty-three CM patients were analysed. The Fatigue Severity Scale (FSS), the Chalder fatigue scale and the CDC diagnostic criteria for chronic fatigue syndrome (CFS) were used. Fifty-three (84.1%) patients had FSS scores greater than 27. Forty-two (66.7%) patients met the CDC criteria for CFS. Thirty-two patients (50.8%) met the modified CDC criteria (without headache). Beck depression scores correlated with FSS, mental and physical fatigue scores. Trait anxiety scores also correlated with fatigue scales. Women had higher FSS scores than men, $P < 0.05$. Physical fatigue was associated with fibromyalgia, $P < 0.05$. Fatigue as a symptom and CFS as a disorder are both common in CM patients. Therapeutic interventions include a graded aerobic exercise program, cognitive behavioural therapy and antidepressants. Identification of fatigue and its subtypes in headache disorders and recognition of headaches in CFS patients has implications for the pathophysiology, diagnosis and treatment of these disorders.
Perski A, Grossi G, Evengard B, Blomkvist V, Yilbar B, Orth-Gomer K.	Stressmottagningen, Institutet for psykosocial miljomedicin, Stockholm.	[Emotional exhaustion common among women in the public sector] [Article in Swedish]	Lakartidningen. 2002 May 2;99(18):2047-52.	This cross-sectional investigation aimed at assessing levels of emotional exhaustion among female employees within the Swedish public sector. Other aims were to study the associations between self-rated emotional exhaustion and psychosocial factors at work, as well as findings from medical examinations. Data was collected by means of questionnaires including the Maslach Burnout Inventory, among 183 women working in geriatric care and 143 employees at the National Social Insurance Office. We found high proportions of emotional exhaustion in both samples (geriatric care = 34%; Social Insurance Office = 26%). Participants with high scores for emotional exhaustion reported more job-strain, less social support at work and more somatic, emotional and cognitive complaints than those with low or intermediate scores. Medical

				examinations performed on 19 participants with low scores and 41 with high scores for emotional exhaustion revealed significantly more findings among participants with high emotional exhaustion, particularly fatigue, sleep disturbances and cognitive impairment. There were no group differences in terms of depression or other findings. This study shows that individuals at risk for stress-related disorders may be identified using simple questionnaires. Early interventions for stress in the workplace may prevent incapacitating conditions among a great proportion of women working in the public sector.
Pollack S.	Institute of Allergy Immunology and AIDS, Rambam Medical Center, Technion Faculty of Medicine, Haifa, Israel. pollack@rambam.health.gov.il	Chronic fatigue syndrome and immune dysfunction: cause or effect?	Isr Med Assoc J. 2002 Nov;4(11 Suppl):883-5.	
Price EJ, Venables PJ. Department of Rheumatology, Princess Margaret Hospital, Okus Road, Swindon SN1 4JU, UK.		Dry eyes and mouth syndrome--a subgroup of patients presenting with sicca symptoms.	Rheumatology (Oxford). 2002 Apr;41(4):416-22.	OBJECTIVE: To evaluate the characteristics of patients presenting with symptoms suggestive of Sjogren's syndrome (SS) but failing to satisfy diagnostic criteria. METHODS: Clinical, serological and histological data were collected on 34 patients presenting with dry eyes and/or mouth who did not satisfy the Vitali criteria for the diagnosis of SS. They were compared with 136 patients with primary SS, 38 patients with secondary SS, and 13 patients without SS. Questionnaires on symptoms from each group were compared with 43 healthy controls. RESULTS: The 34 patients who did not satisfy the diagnostic criteria for SS or any other connective tissue disease were designated dry eyes and mouth syndrome (DEMS). Their demography including age was similar to that of a primary SS group and there was no more atrophy seen on their biopsies compared with SS and non-SS controls. They scored highly on visual analogue scales of symptoms but had few objective signs. All were negative for anti-Ro and anti-La although the prevalence of antinuclear antibodies (19%) was increased compared with a normal population. There was no excess of SS-associated tissue types. CONCLUSION: There was no evidence that age, salivary gland atrophy or subclinical SS accounted for the symptoms in DEMS. Most of the patients fitted into a spectrum of disease which tended more towards fibromyalgia and/or chronic fatigue syndrome.
Prins JB, Bleijenberg G, van der Meer JW.	Chronic fatigue syndrome and myalgic encephalomyelitis.		Lancet. 2002 May 11;359(9318):1699. Comment on: Lancet. 2002 Jan 12;359(9301):97-8.	
Puri BK, Counsell SJ, Zaman R, Main J, Collins AG, Hajnal JV, Davey NJ.	MRI Unit, MRC Clinical Sciences Centre, Imperial College School of	Relative increase in choline in the occipital cortex in chronic fatigue	Acta Psychiatr Scand. 2002 Sep;106(3):224-6.	OBJECTIVE: To test the hypothesis that chronic fatigue syndrome (CFS) is associated with altered cerebral metabolites in the frontal and occipital cortices. METHOD: Cerebral proton magnetic resonance spectroscopy (1H MRS) was carried out in eight CFS patients and eight age- and sex-matched healthy control subjects. Spectra were obtained from 20 x 20 x 20 mm3 voxels in the

	Medicine, Hammersmith Hospital, London, UK. basant.puri@csc.mrc.ac.uk	syndrome.		dominant motor and occipital cortices using a point-resolved spectroscopy pulse sequence. RESULTS: The mean ratio of choline (Cho) to creatine (Cr) in the occipital cortex in CFS (0.97) was significantly higher than in the controls (0.76; P=0.008). No other metabolite ratios were significantly different between the two groups in either the frontal or occipital cortex. In addition, there was a loss of the normal spatial variation of Cho in CFS. CONCLUSION: Our results suggest that there may be an abnormality of phospholipid metabolism in the brain in CFS.
Quan N, Herkenham M.	Department of Oral Biology, Ohio State University, Columbus 43210, USA. quan.14@osu.edu	Connecting cytokines and brain: a review of current issues.	Histol Histopathol. 2002 Jan;17(1):273-88.	Cytokines have been a multi-disciplinary research focus for over 2 decades. To date, there have been more than 15,000 articles published concerning the relationship between cytokines and the central nervous system (CNS). Over half of these articles have been published in the last 5 years. From such vast number of studies, two major topics emerge as the critical issues: 1) how do cytokines modulate the functions of the CNS? 2) what is the role of cytokines in the pathogenesis of neurological diseases? Thus far, it has been clearly established that cytokines can alter the functions of the CNS in specific manners, invoking CNS-controlled autonomic, neuroendocrine, and behavioral responses. Induced expression of cytokines has also been found in the CNS during brain injury and infection, contributing to the immunological processes at this "immunologically privileged" site. Furthermore, increasing evidence points to the potential involvement of cytokines in the induction and modulation of an array of neurological diseases ranging from Alzheimer's disease to chronic fatigue syndrome. Despite such progress, however, substantial obstacles remain for both the basic understanding and the potential clinical exploitation of how cytokines interact with CNS. In this review, we will attempt to synopsize the current theories and evidence regarding the answers to the above-mentioned critical questions. These issues will be reviewed not only in isolation, as most of the original reports focused on only one of the questions, but also in parallel such that inter-issue insights may be gained.
Raine R, Haines A, Sensky T, Hutchings A, Larkin K, Black N.	Department of Public Health and Policy, London School of Hygiene and Tropical Medicine, London WC1E 7HT. rosalind.raine@lshtm.ac.uk	Systematic review of mental health interventions for patients with common somatic symptoms: can research evidence from secondary care be extrapolated to primary care?	BMJ. 2002 Nov 9;325(7372):1082. Comment in: Evid Based Ment Health. 2003 May;6(2):55	OBJECTIVES: To determine the strength of evidence for the effectiveness of mental health interventions for patients with three common somatic conditions (chronic fatigue syndrome, irritable bowel syndrome, and chronic back pain). To assess whether results obtained in secondary care can be extrapolated to primary care and suggest how future trials should be designed to provide more rigorous evidence. DESIGN: Systematic review. DATA SOURCES: Five electronic databases, key texts, references in the articles identified, and citations from expert clinicians. STUDY SELECTION: Randomised controlled trials including participants with one of the three conditions for which no physical cause could be found. Two reviewers screened sources and independently extracted data and assessed quality. RESULTS: Sixty one studies were identified; 20 were classified as primary care and 41 as secondary care. For some interventions, such as brief psychodynamic interpersonal therapy, little research was identified. However, results of meta-analyses and of randomised controlled trials suggest that cognitive behaviour therapy and behaviour therapy are effective for chronic back pain and chronic fatigue syndrome and that antidepressants are effective for irritable bowel syndrome. Cognitive behaviour therapy and behaviour therapy were effective in both primary and secondary care in patients with back pain, although the evidence is more consistent and the effect size larger for secondary care. Antidepressants seem effective in irritable bowel syndrome in both settings but ineffective in

				chronic fatigue syndrome. CONCLUSIONS: Treatment seems to be more effective in patients in secondary care than in primary care. This may be because secondary care patients have more severe disease, they receive a different treatment regimen, or the intervention is more closely supervised. However, conclusions of effectiveness should be considered in the light of the methodological weaknesses of the studies. Large pragmatic trials are needed of interventions delivered in primary care by appropriately trained primary care staff.
Rainer JP.	Midtown Psychological Associates, Valdosta, GA 31601, USA.	Bent but not broken: an introduction to the issue on chronic illness.	J Clin Psychol. 2002 Nov;58(11):1347-50.	What is the difference between sackcloth and ashes and chronic illness? You can always take a shower and change shirts. Copyright 2002 Wiley Periodicals, Inc.
Reid S, Chalder T, Cleare A, Hotopf M, Wessely S.	St Mary's Hospital, London, UK.	Chronic fatigue syndrome.	Clin Evid. 2002 Dec;(8):1075-88.	
Reid S, Chalder T, Cleare A, Hotopf M, Wessely S.	Guy's, King's and St Thomas' School of Medicine, Institute of Psychiatry, London, UK.	Chronic fatigue syndrome.	Clin Evid. 2002 Jun;(7):966-78.	
Repka-Ramirez S, Naranch K, Park YJ, Clauw D, Baraniuk JN.	Division of Rheumatology, Immunology, and Allergy, Center for Chronic Pain and Fatigue Research, Georgetown University, 3800 Reservoir Road, N.W., Washington, D.C. 20007-2197, USA.	Cytokines in nasal lavage fluids from acute sinusitis, allergic rhinitis, and chronic fatigue syndrome subjects.	Allergy Asthma Proc. 2002 May-Jun;23(3):185-90.	The aim of this study was to compare the degree of inflammation present in acute sinusitis, allergic rhinitis, chronic Fatigue Syndrome (CFS), and non-CFS control subjects by measuring cytokine concentrations in nasal lavage fluids. The concentrations of total protein (TP; Lowry assay), nerve growth factor (NGF), tumor necrosis factor (TNF) alpha, and interleukin (IL)-8 were measured by ELISA in nasal lavage fluids from acute sinusitis (n = 13), active allergic rhinitis (n = 16), CFS (n = 95), and non-CFS (n = 89) subjects. CFS and non-CFS groups were subdivided further using allergy skin test and rhinitis score results. Acute sinusitis subjects had significantly higher TP ($p = 0.011$, ANOVA), TNF-alpha ($p = 0.00071$), and IL-8 ($p = 0.0000027$) concentrations and IL-8/TP ratios ($p = 0.0030$) than the other three patient groups. There were no differences based on skin test or rhinitis score severity within either the CFS or non-CFS groups. The mucopurulent discharge of acute sinusitis contained significantly higher TNF-alpha and IL-8. Neutrophils were a likely source for these cytokines. There were no differences between CFS and non-CFS subjects, making it unlikely that the rhinitis of CFS has an inflammatory component.
Richardson A.		The symptoms and management of myalgic encephalomyelitis.	Nurs Times. 2002 May 7-13;98(19):32-5.	Myalgic encephalomyelitis (ME), which is also known as chronic fatigue syndrome, is a chronic, debilitating illness with varying symptoms and patterns of progression. Research has yet to establish its aetiology and pathogenesis, and there is no cure. A number of management strategies have proved effective, but these should always be tailored to the individual patient. Although no drug treatment has been developed specifically for ME, therapies used to manage the same symptoms in other conditions can provide some relief. Treatment and management should be planned in partnership with the patient.
Richardson J.		Myalgic Enchephalomyelitis:	Journal of Chronic Fatigue Syndrome	

		Guidelines for Doctors	2002; 10 (1): 65 - 80	
Richardson J.		Toxins and Immunity in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome Volume 2002; 10 (3/4): 43 - 50	In this paper, Dr. Richardson illustrates links between exposure, absorption and effects of viruses, bacteria, and inorganic toxins, and their toll on the immune system, as potential causes of chronic symptomatology as seen in chronic fatigue syndrome.
Romans S, Belaise C, Martin J, Morris E, Raffi A.	Department of Psychological Medicine, Dunedin School of Medicine, Dunedin, New Zealand. sarah.romans@stonebow.otago.ac.nz	Childhood abuse and later medical disorders in women. An epidemiological study.	Psychother Psychosom. 2002 May-Jun;71(3):141-50.	BACKGROUND: There have been many studies documenting adverse psychiatric consequences for people who have experienced childhood and adult sexual and physical abuse. These include posttraumatic stress disorder, anxiety, depression, substance abuse, eating disorders and probably some personality disorders or trait abnormalities. Much less is known about the links between abuse and physical/psychosomatic conditions in adult life. Hints of causal links are evident in the literature discussing headache, lower back pain, pelvic pain and irritable bowel syndrome. These studies are not definitive as they use clinic-based samples. METHODS: This study used interview data with a random community sample of New Zealand women, half of whom reported childhood sexual abuse and half who did not. Details about childhood physical abuse and adult abuse were also collected in a two-phase study. RESULTS: Complex relationships were found, as abuses tended to co-occur. Seven of 18 potentially relevant medical conditions emerged as significantly increased in women with one or more types of abuse. These were chronic fatigue, bladder problems, headache including migraine, asthma, diabetes and heart problems. Several of these associations with abuse are previously unreported. CONCLUSIONS: In this random community sample, a number of chronic physical conditions were found more often in women who reported different types of sexual and physical abuse, both in childhood and in adult life. The causal relationships cannot be studied in a cross-sectional retrospective design, but immature coping strategies and increased rates of dissociation appeared important only in chronic fatigue and headache, suggesting that these are not part of the causal pathway between abuse experiences and the other later physical health problems. This finding and the low co-occurrence of the identified physical conditions suggest relative specificity rather than a general vulnerability to psychosomatic conditions in women who have suffered abuses. Each condition may require separate further study. Copyright 2002 S. Karger AG, Basel
Rosendal B.		[Chronic fatigue belongs to the emotional life's domains]	Lakartidningen. 2002 Sep 5;99(36):3542. Comment on: Lakartidningen. 2002 Aug 22;99(34):3280-1. Lakartidningen. 2002 Aug 22;99(34):3282-7. Article in Swedish]	
Rowe PC.		Orthostatic intolerance and	J Pediatr. 2002 Apr;140(4):387-9.	

		chronic fatigue syndrome: new light on an old problem.	Comment on: J Pediatr. 2002 Apr;140(4):404-11.	
Roy-Byrne P, Afari N, Ashton S, Fischer M, Goldberg J, Buchwald D.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA 98104, USA.	Chronic fatigue and anxiety/depression: a twin study.	Br J Psychiatry. 2002 Jan;180:29-34.	BACKGROUND: Up to three-quarters of patients with fatigue syndromes have comorbid mood or anxiety disorders, suggesting that chronic fatigue is a forme fruste of anxiety or depressive states. AIMS: To establish whether the association of chronic fatigue with psychological distress is causal or due to a common genetic or environmental factor. METHOD: 69 monozygotic (MZ) and 31 dizygotic (DZ) female twin pairs, with only one co-twin reporting at least 6 months of fatigue, completed questions on fatigue, the General Health Questionnaire (GHQ) and a structured psychiatric interview. We examined the effects of three progressively more stringent definitions of chronic fatigue on four GHQ sub-scales. RESULTS: Fatigued MZ and DZ twins by all definitions were significantly more depressed, anxious, somatically preoccupied and socially dysfunctional than their non-fatigued co-twins. Intrapair differences were similar in DZ and MZ twins, but non-significant differences were observed for the somatic symptoms and anxiety/insomnia sub-scales. CONCLUSIONS: In this sample, chronic fatigue and psychological distress are strongly associated without evidence for genetic covariation, implying that the association is environmental, or due to overlapping definitions. Any genetic covariation missed is likely to involve anxiety rather than depression.
Sabath DE, Barcy S, Koelle DM, Zeh J, Ashton S, Buchwald D.	Department of Laboratory Medicine, Chronic Fatigue Syndrome Cooperative Research Center, University of Washington, Seattle, Washington 98195-7110, USA. dsabath@u.washington.edu	Cellular immunity in monozygotic twins discordant for chronic fatigue syndrome.	J Infect Dis. 2002 Mar 15;185(6):828-32. Epub 2002 Feb 28.	Studies elsewhere have suggested that immune dysfunction may be common in patients with chronic fatigue syndrome (CFS). The objective of this study was to assess the nature and extent of abnormalities in lymphocyte cell surface markers and NK cell activity in patients with CFS while controlling for genetic factors. A co-twin control study of immune system parameters was conducted for 22 pairs of monozygotic twins discordant for CFS and 9 healthy pairs of twins. The CFS twins had greater numbers of CD62L(+) T cells in several T cell subsets, although these differences did not achieve statistical significance. Significantly greater variability was noted in twins discordant for CFS than in the concordant healthy twins for 20 of 48 variables examined. The monozygotic co-twin control design is of unique value because of its ability to control for genetic influences on CFS; however, additional studies will be required to further assess immune dysregulation in this illness.
Sargent C, Scroop GC, Nemeth PM, Burnet RB, Buckley JD.	Exercise Physiology Research Unit, Department of Physiology, University of Adelaide, South Australia 5005, Australia.	Maximal oxygen uptake and lactate metabolism are normal in chronic fatigue syndrome.	Med Sci Sports Exerc. 2002 Jan;34(1):51-6. Comment in: Med Sci Sports Exerc. 2002 Oct;34(10):1691-2; author reply 1692-3.	PURPOSE: Previous studies in chronic fatigue syndrome (CFS) have reported reductions in maximal oxygen uptake (VO(2max)), yet often the testing procedures have not followed accepted guidelines, and gender data have been pooled. The present study was undertaken to reevaluate exercise capacity in CFS patients by using "gold standard" maximal exercise testing methodology and stratifying results on a gender basis. METHODS: Sixteen male and 17 female CFS patients and their gender-, age-, and mass-matched sedentary controls performed incremental exercise to volitional exhaustion on a stationary cycle ergometer while selected cardiorespiratory and metabolic variables were measured. RESULTS: VO(2max) in male CFS patients was not different from control values (CFS: 40.5 +/- 6.7; controls: 43.3 +/- 8.6; mL x kg(-1) x min(-1)) and was 96.3 +/- 17.9% of the age-predicted value, indicating no functional aerobic impairment (3.7 +/- 17.9%).

				In female CFS patients, VO(2max) was lower than control values (CFS: 30.0 +/- 4.7; controls: 34.2 +/- 5.6; mL x kg(-1) x min(-1), P = 0.002), but controls were higher than the age-predicted value (112.6 +/- 15.4%, P = 0.008) whereas the CFS patients were 101.2 +/- 20.4%, indicating no functional aerobic impairment (-1.2 +/- 20.4%). Maximal heart rate (HR(max)) in male CFS patients was lower than their matched controls (CFS: 184 +/- 10; controls: 192 +/- 12; beats x min(-1); P = 0.016) but was 99.1 +/- 5.5% of their age-predicted value. In female CFS patients, HR(max) was not different from controls (CFS: 183 +/- 11; controls: 186 +/- 10; beats x min(-1)) and was 98.9 +/- 5.1% of the age-predicted value. The VO(2) at the lactate threshold (LT) in each gender group, whether expressed in mL x kg(-1) x min(-1) or as a percentage of VO(2max), was not different between CFS patients and controls. CONCLUSIONS: In contrast to most previous reports, the present study found that VO(2max), HR(max), and the LT in CFS patients of both genders were not different from the values expected in healthy sedentary individuals of a similar age.
Schafer ML.	Klinikum der Philipps-Universitat Marburg, Klinik fur Psychiatrie und Psychotherapie, Germany.	[On the history of the concept neurasthenia and its modern variants chronic-fatigue-syndrome, fibromyalgia and multiple chemical sensitivities] [Article in German	Fortschr Neurol Psychiatr. 2002 Nov;70(11):570-82.	This article deals with the history of the terminological and nosological development of the concept neurasthenia introduced in 1869 by George Miller Beard and in particular with its reappearance in western medicine in the 1980 s. Beginning with its predecessors in antiquity and continuing with hypochondria, which became a fashionable disease in the 18 th century, the concept neurasthenia reached a high point and world-wide medical acceptance at the end of the 19 th/beginning of the 20 th century. However, between the 1930 s and 1960 s it declined in popularity and gradually disappeared until finally it only had a rudimentary nosological role in the term "pseudoneurasthenia". In the countries of the Far East, on the contrary, the concept of neurasthenia has been in continual use since its importation in the first decades of the last century. In the 1980 s, when an interest in the symptoms of chronic fatigue was reawakened in western medicine, the concept neurasthenia reappeared, this time to define the particular form of a neurotic disorder. Parallel to these developments increasing importance was attached to clinical descriptions of illnesses which on account of their similarity to the symptoms of neurasthenia could be termed modern variants of the concept neurasthenia. These are "Chronic-Fatigue-Syndrome", "Fibromyalgia" and "Multiple Chemical Sensitivities" which have more or less adopted the organic inheritance of Beard's former concept of neurasthenia, despite the fact that so far the question of organicity could not be decisively answered in a single case. In order to clarify possible influences on the development of the concept neurasthenia and its variants, the theories and ideas of E. Shorter, medical historian at the University of Toronto, are discussed in the final part of the article, whereby the particular cultural background in each case has a decisive influence on the manifestation of the psychosomatic symptoms.
Senna G, Gani F, Leo G, Schiappoli M.	Unita Operativa di Allergologia, Ospedale Civile Maggiore, Verona. gianenrico.senna@mail.azosp.vr.it	[Alternative tests in the diagnosis of food allergies] [Article in Italian]	Recenti Prog Med. 2002 May;93(5):327-34.	In the last years an increase of allergic diseases has been observed whose prevalence is about 20-30% in general population of western countries. However there is a risk of an over diagnosis of allergic diseases as many different diseases (migraine, chronic urticaria, chronic inflammatory bowel diseases, chronic-fatigue syndrome etc.) are considered due to food allergy or intolerance. In many patients the diagnosis is based on the results of alternative diagnostic tests such as the cytotoxic test, the provocation/neutralization sublingual or subcutaneous test, the heart-ear

				reflex test, the kinesiology, the biorisonance, the electro-acupuncture, and the hair analysis, or on immunological tests (immunocomplex or specific food IgG). We reviewed the scientific evidences of these tests (specificity, sensibility, rationale, reproducibility). According to most studies none of them had to be recommended as useful for the diagnosis of food allergy or intolerance. Physicians should alert patients about the risk of an indiscriminate use of these test in the diagnosis of food allergy. In fact the use of an incorrect diet could be dangerous, particularly in childhood, as recently shown.
Servaes P, Prins J, Verhagen S, Bleijenberg G.	Netherlands Fatigue Research Group, Department of Medical Psychology (118), University Medical Centre Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. p.servaes@cksmps.azn.nl	Fatigue after breast cancer and in chronic fatigue syndrome: similarities and differences.	J Psychosom Res. 2002 Jun;52(6):453-9.	OBJECTIVE: Fatigue is investigated in 57 severely fatigued disease-free breast cancer patients and in 57 gender- and age-matched patients with chronic fatigue syndrome (CFS) using multidimensional and multimethod assessment. A comparison between these groups of patients is important to determine whether a cognitive behavioural intervention to reduce fatigue in CFS patients would be appropriate as well for severely fatigued disease-free breast cancer patients. METHODS: Measurement included computerised questionnaires and a standardised neuropsychological test. Furthermore, patients filled out a daily Self-Observation List (SOL) and wore an actometer during a period of 12 days. RESULTS: In comparison to severely fatigued disease-free breast cancer patients, CFS patients score more problematic with regard to the level of fatigue, functional impairment, physical activity, pain and self-efficacy. However, a subgroup of severely fatigued disease-free breast cancer patients reports the same amount of problems as CFS patients with regard to psychological well-being, sleep and concentration. Finally, CFS patients and severely fatigued breast cancer patients score equal on measures of social support. CONCLUSION: There seem to be some similarities but also many differences between severely fatigued breast cancer survivors and females with CFS. Therefore, cognitive behaviour therapy (CBT) to reduce fatigue after treatment for cancer should also differ in certain aspects from cognitive behaviour therapy as it has been developed for patients with CFS.
Setness PA, Mettner J.		Patient notes: chronic fatigue syndrome.	Postgrad Med. 2002 Apr;111(4):137-8.	
Shapiro CM, Moller HJ.	Department of Psychiatry, University of Toronto & University Health Network, Canada. colin.shapiro@uhn.on.ca	Chronic fatigue: listen and measure.	J Psychosom Res. 2002 Jun;52(6):427-36.	
Sharpe M.	University of Edinburgh. michael.sharpe@ed.ac.uk	The report of the Chief Medical Officer's CFS/ME working group: what does it say and will it	Clin Med. 2002 Sep-Oct;2(5):427-9. Comment in: Clin Med. 2002 Sep-Oct;2(5):389-90.	Chronic fatigue syndrome (CFS) sometimes known as myalgic encephalomyelitis or encephalopathy (ME) has long been a controversial topic. This year has seen the publication of a report from an independent working party set up by the UK Chief Medical Officer (CMO) to make recommendations for the management of the condition. The report makes a number of general recommendations about the provision of appropriate care and services. The more controversial

		help?		issues of what to call the illness, the nature of the illness and what treatment should be recommended are all addressed, but in the form of compromise rather than resolution. To the extent that this report is a step towards highlighting the needs not only of patients with CFS but the larger group of patients with symptom-defined conditions, it is to be welcomed. As a guide to management it raises as many questions as it answers. Much remains to be resolved before guidance that is both evidence based and acceptable to all parties is achieved.
Sharpe M.	University of Edinburgh, EH10 5HF, Scotland, Edinburgh, UK.	The English Chief Medical Officer's Working Parties' report on the management of CFS/ME: significant breakthrough or unsatisfactory compromise?	J Psychosom Res. 2002 Jun;52(6):437-8.	
Shenker NG, Blake DR.	Royal National Hospital for Rheumatic Diseases, Bath. mpxns@bath.ac.uk	Understanding pain: the enigma of pain and suffering.	Clin Med. 2002 Nov-Dec;2(6):574-7.	
Shephard RJ.	Faculty of Physical Education and Health, Department of Public Health Sciences, Faculty of Medicine, University of Toronto, Toronto, Canada. royjshep@shaw.ca	Cytokine responses to physical activity, with particular reference to IL-6: sources, actions, and clinical implications.	Crit Rev Immunol. 2002;22(3):165-82.	The present review examines the cytokine response to acute exercise stress, with particular emphasis on the balance between proinflammatory and anti-inflammatory mechanisms, and the release of IL-6. Prolonged endurance exercise induces a sequenced release of pro- and anti-inflammatory cytokines, and IL-6 plays a dominant role. The magnitude of this response bears a general relationship to the intensity of effort, but the duration of activity and many environmental factors also modulate cytokine release. Although many types of cells are capable of producing cytokines, the main source of the exercise-induced IL-6 production appears to be the exercising muscle. The primary function of the additional IL-6 may be to regulate the supply of carbohydrate as muscle reserves of glycogen become depleted. There is also a delayed release of cytokines following eccentric exercise that is related to the repair of muscle injury. Since the production of cytokines is greater with endurance than with resistance exercise, it seems unlikely that they play an important role in the hypertrophy of muscle and bone. More research is needed on a number of important clinical issues where the exercise-induced release of cytokines may have relevance. Exercise-induced cytokine secretion has the potential to provide a simple model of sepsis. Preliminary observations suggest it may also modulate the risk of type 2 diabetes mellitus. Cytokine concentrations are increased in chronic fatigue syndrome, although it is less dear that the cytokine secretion is responsible for fatigue in humans. Exercise-induced modulations in cytokine secretion may contribute to allergies, bronchospasm, and upper respiratory infections in the endurance athlete. Further, the cytokine cascade is involved in the process of atherogenesis, and exercise-induced changes in cytokine production may expose

				latent HIV to chemotherapeutic agents.
Shepherd C.		Editorial on CFS was biased, inaccurate, and misleading.	BMJ. 2002 Apr 13;324(7342):914.	
Shetzline SE, Martinand-Mari C, Reichenbach NL, Buletic Z, Lebleu B, Pfleiderer W, Charubala R, De Meirleir K, De Becker P, Peterson DL, Herst CV, Englebienne P, Suhadolnik RJ.	Department of Biochemistry and the Fels Institute for Cancer Research and Molecular Biology, Temple University School of Medicine, Philadelphia, PA 19140, USA.	Structural and functional features of the 37-kDa 2-5A-dependent RNase L in chronic fatigue syndrome.	J Interferon Cytokine Res. 2002 Apr;22(4):443-56.	A 2',5'-oligoadenylate (2-5A)-dependent 37-kDa form of RNase L has been reported in extracts of peripheral blood mononuclear cells (PBMC) from individuals with chronic fatigue syndrome (CFS). In the current study, analytic gel permeation FPLC, azido photoaffinity labeling, two-dimensional (2-D) gel electrophoresis, and matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) have been used to examine the biochemical relationship between the 80-kDa RNase L in healthy control PBMC and the 37-kDa RNase L in PBMC from individuals with CFS. Like the 80-kDa RNase L, the 37-kDa RNase L is present as a catalytically inactive heterodimer complex with the RNase L inhibitor (RLI). Formation of a 37-kDa RNase L-RLI complex indicates that the 37-kDa RNase L is structurally similar to the 80-kDa RNase L at the N-terminus, which contains the 2-5A binding domain. The enzymatically active monomer form of 37-kDa RNase L resolved by 2-D gel electrophoresis has a pI of 6.1. RT-PCR and Southern blot analyses demonstrated that the 37-kDa RNase L is not formed by alternative splicing. In-gel tryptic digestion of the 37-kDa RNase L that was excised from 2-D gels and subsequent MALDI-MS analysis identified three peptide masses that are identical to three predicted peptide masses in the 80-kDa RNase L. The electrophoretic mobility of 2-5A azido photolabeled/immunoprecipitated 37-kDa RNase L was the same under reducing and nonreducing conditions. The results presented show that the 37-kDa form of RNase L in PBMC shares structural and functional features with the native 80-kDa RNase L, in particular in the 2-5A binding and catalytic domains.
Short K, McCabe M, Tooley G.	School of Psychology, Deakin University, 221 Burwood Highway, Victoria 3125, Burwood, Australia.	Cognitive functioning in chronic fatigue syndrome and the role of depression, anxiety, and fatigue.	J Psychosom Res. 2002 Jun;52(6):475-83.	OBJECTIVE: This study was designed to investigate the role of depression, anxiety, and fatigue in Chronic Fatigue Syndrome (CFS) sufferers' objective and subjective cognitive performance. METHODS: Twenty-three CFS sufferers and 23 healthy control participants were compared on objective and subjective assessments of cognitive performance. Depression, anxiety, and fatigue were also evaluated. RESULTS: CFS sufferers did not demonstrate any impairment in objective cognitive functioning compared to the control group, and objective performance was not related to their higher levels of depression or their level of fatigue. Depression scores only accounted for a small amount of the variance in CFS sufferers' lower subjective assessment of their cognitive performance compared to control participants. There were no differences between the groups on anxiety scores. CONCLUSION: The results are discussed in terms of the heterogeneity of the CFS population and the complex interaction of symptomatological factors that characterise CFS.
Sigal LH, Hassett AL.	Division of Rheumatology and Connective Tissue Research, Department of Medicine, Lyme Disease Center,	Contributions of societal and geographical environments to "chronic Lyme disease": the psychopathogenesis	Environ Health Perspect. 2002 Aug;110 Suppl 4:607-11. Comment in: Environ Health Perspect. 2003 Feb;111(2):A76;	Lyme disease is a relatively well-described infectious disease with multisystem manifestations. Because of confusion over conflicting reports, anxiety related to vulnerability to disease, and sensationalized and inaccurate lay media coverage, a new syndrome, "chronic Lyme disease," has become established. Chronic Lyme disease is the most recent in a continuing series of "medically unexplained symptoms" syndromes. These syndromes, such as fibromyalgia, chronic fatigue syndrome, and multiple chemical sensitivity, meet the need for a societally and morally acceptable explanation for ill-defined symptoms in the absence of objective physical and

	University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, New Brunswick, New Jersey 08903-0019, USA. sigallh@umdnj.edu	and aporology of a new "medically unexplained symptoms" syndrome.	author reply A77. Environ Health Perspect. 2003 Feb;111(2):A77; author reply A77.	laboratory findings. We describe factors involved in the psychopathogenesis of chronic Lyme disease and focus on the confusion and insecurity these patients feel, which gives rise to an inability to adequately formulate and articulate their health concerns and to deal adequately with their medical needs, a state of disorganization termed aporia.
Silver A, Haeney M, Vijayadurai P, Wilks D, Pattrick M, Main CJ.	Department of Psychological Medicine, John Radcliffe Hospital, Headington, Oxford, UK. amysilver@appleonline.net	The role of fear of physical movement and activity in chronic fatigue syndrome.	J Psychosom Res. 2002 Jun;52(6):485-93.	OBJECTIVE: To examine beliefs in relation to avoidance of activity in chronic fatigue syndrome (CFS) patients. METHODS: The first phase consisted of modifying an existing chronic pain measure of kinesiophobia-fear of physical movement and activity-and validating it on the CFS population [Tampa Scale of Kinesiophobia-Fatigue (TSK-F); n=129; test-retest: r=.89, P<.001; alpha=.68]. Subscales of Illness Beliefs (alpha=.78) and Beliefs about Activity (alpha=.70) were identified. The second phase consisted of evaluating whether behavioural persistence was predicted by the TSK-F (n=33). Participants were asked to ride an exercise bike for as long as they felt able. RESULTS: Analyses indicated that behavioural persistence did not correlate with maximal heart rate or resting heart rate, level of tiredness, symptom severity, illness identity or emotional distress. However, the TSK-F did correlate highly with distance travelled and added a significant 15% of the variance in distance after adjustments for gender and physical functioning (PF). The TSK-F Beliefs about Activity subscale appears to be the predictive factor, explaining 12% of the variance in excise performance or rather 12% of the avoidance of exercise. CONCLUSION: Beliefs about Activity appear to be an important variable in predicting behaviour and avoidance of exercise. As avoidance has been suggested as a key to the maintenance of symptoms, disability and distress in CFS patients, this research has important theoretical, clinical and research implications.
Silver DS, Wallace DJ.	Division of Rheumatology, Cedars-Sinai Medical Center, UCLA School of Medicine, Los Angeles, CA 90048, USA. davids@omcresearch.org	The management of fibromyalgia-associated syndromes.	Rheum Dis Clin North Am. 2002 May;28(2):405-17.	Most of the six million Americans with fibromyalgia have at least one associated syndrome which mandates specialized attention in addition to traditional therapeutic approaches. These include localized procedures, regional blocks, antiinflammatory or antimicrobial regimens, attention to non soft tissue sources of psychosocial distress, and classes of medicines not usually prescribed for fibromyalgia. The successful treatment of fibromyalgia-associated syndromes improves the symptoms, quality of life, and prognosis of fibromyalgia.
Sinaii N, Cleary SD, Ballweg ML, Nieman LK, Stratton P.	Pediatric and Reproductive Endocrinology Branch, National Institute of Child	High rates of autoimmune and endocrine disorders, fibromyalgia, chronic fatigue syndrome	Hum Reprod. 2002 Oct;17(10):2715-24.	BACKGROUND: Women with endometriosis may also have associated disorders related to autoimmune dysregulation or pain. This study examined whether the prevalence of autoimmune, chronic pain and fatigue and atopic disorders is higher in women with endometriosis than in the general female population. METHODS AND RESULTS: A cross-sectional survey was conducted in 1998 by the Endometriosis Association of 3680 USA members with surgically diagnosed

	Health and Human Development, NIH, 10 Center Drive, Building 10, Room 9D42, MSC 1583, Bethesda, MD 20892-1583, USA. sinaiin@mail.nih.gov	and atopic diseases among women with endometriosis: a survey analysis.		endometriosis. Almost all responders had pain (99%), and many reported infertility (41%). Compared with published rates in the general USA female population, women with endometriosis had higher rates of hypothyroidism (9.6 versus 1.5%, P < 0.0001), fibromyalgia (5.9 versus 3.4%, P < 0.0001), chronic fatigue syndrome (4.6 versus 0.03%, P < 0.0001), rheumatoid arthritis (1.8 versus 1.2%, P = 0.001), systemic lupus erythematosus (0.8 versus 0.04%, P < 0.0001), Sjogren's syndrome (0.6 versus 0.03%, P < 0.0001) and multiple sclerosis (0.5 versus 0.07%, P < 0.0001), but not hyperthyroidism or diabetes. Allergies and asthma were more common among women with endometriosis alone (61%, P < 0.001 and 12%, P < 0.001 respectively) and highest in those with fibromyalgia or chronic fatigue syndrome (88%, P < 0.001 and 25%, P < 0.001 respectively) than in the USA female population (18%, P < 0.001 and 5%, P < 0.001 respectively). CONCLUSIONS: Hypothyroidism, fibromyalgia, chronic fatigue syndrome, autoimmune diseases, allergies and asthma are all significantly more common in women with endometriosis than in women in the general USA population.
Singh A, Garg V, Gupta S, Kulkarni SK.	Pharmacology Division, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh 160 014, India.	Role of antioxidants in chronic fatigue syndrome in mice.	Indian J Exp Biol. 2002 Nov;40(11):1240-4.	The present study was carried out using mice model of chronic fatigue syndrome (CFS) in which mice were forced to swim everyday for 7 days for a 6 min session. There was a significant increase in despair behavior (immobility period) in saline treated mice on successive days. Treatment with potent antioxidants carvedilol (5 mg/kg, i.p.) and melatonin (10 mg/kg, i.p.) produced a significant reduction in immobility period. Similar results were observed with herbal products St. John's Wort (Hypericum perforatum L) (10 mg/kg, p.o.) and GS-02 (20 mg/kg, p.o.). Fluoxetine, a selective serotonin reuptake inhibitor produced a significant effect only on first and second day of its treatment. Biochemical analysis revealed that chronic swim test significantly increased lipid peroxidation and catalase levels in whole brains of mice. There was a decrease in the levels of super oxide dismutase (SOD) and glutathione reductase (GSH) in the brain. Administration of carvedilol, melatonin, GS-02 and St. John's Wort restored the levels of lipid peroxidation and glutathione. The enzymes SOD and catalase were also restored. Fluoxetine affected the biochemical variables not to the same extent as other treatments. The findings of the present study suggest that oxidative stress might play a significant role in the pathophysiology of CFS. Thus antioxidants and herbal products like St. Johns wort and GS-02 could be useful in the treatment of CFS.
Skowera A, Stewart E, Davis ET, Cleare AJ, Unwin C, Hull L, Ismail K, Hossain G, Wessely SC, Peakman M.	Department of Immunology, Guy's, King's & St Thomas' School of Medicine, King's College London, London, UK.	Antinuclear autoantibodies (ANA) in Gulf War-related illness and chronic fatigue syndrome (CFS) patients.	Clin Exp Immunol. 2002 Aug;129(2):354-8.	It is established that veterans of the 1991 Gulf War have an increased frequency of experiencing multiple symptoms. The underlying mechanism of these ailments is unclear, although they do not correspond to any clearly defined syndrome. The most common symptoms overlap with those of chronic fatigue syndrome (CFS). CFS was recently associated with a novel subtype of antinuclear autoantibody (ANA) that reacts with nuclear envelope (NE) antigens. NE autoantibodies are not known to be linked with any distinct clinical condition, but have been observed in patients with unusual mixed chronic autoimmune disorders and connective tissue diseases. In this study we examined whether NE ANAs are a feature of patients with CFS and symptomatic Gulf War veterans (sGWV). We studied the prevalence of ANA in 130 sGWV, 90 well Gulf War veterans (wGWV), 128 symptomatic Bosnia and Era veterans (sBEV), 100 CFS patients, and 111 healthy control subjects matching for age and sex. We found no significant difference in the prevalence of

				ANAs between any of the groups. None of the patients/or veterans we studied had ANA of the NE type. Our results show that multisymptom illness due to CFS or related to Gulf War service is not associated with antinuclear autoimmunity.
Slavkin HC.	School of Dentistry, University of Southern California Los Angeles, California, USA.	Distinguishing Mars from Venus: emergence of gender biology differences in oral health and systemic disease.	Compend Contin Educ Dent. 2002 Oct;23(10 Suppl):29-31.	We are learning to appreciate and understand that men and women have different genes and gene products (proteins), biochemistry and physiology, body weights and distribution of fats, and a few different tissues and organs. In such comparisons, we discover that women have a different prevalence for many oral and systemic diseases and disorders, and often illustrate differences in responses to disease mechanisms as well as to drug therapy and treatments. For example, consider the milestones of development, such as puberty or menopause, the unique differences in the prevalence of autoimmune diseases and disorders (Sjogren's syndrome, Hashimoto's disease), differences in the onset and progression of osteoporosis and osteoarthritis, differences in response to radiation and chemotherapy, and the differences in chronic facial pain, chronic fatigue syndrome, and fibromyalgia. This article highlights many opportunities to enhance the quality of oral health care for women.
Smith RC.	Michigan State University, East Lansing, USA.	Review: behavioral interventions show the most promise for the chronic fatigue syndrome.	ACP J Club. 2002 Mar-Apr;136(2):61. Comment on: JAMA. 2001 Sep 19;286(11):1360-8.	
Smits MG, Van Rooy R, Nagtegaal JE.		Influence of Melatonin on Quality of Life in Patients with Chronic Fatigue and Late Melatonin Onset	Journal of Chronic Fatigue Syndrome Volume 2002; 10 (3/4): 25 - 32	Medical Outcome Study Short Form-36 (MOS SF-36) qualities of life scores were studied in 38 chronic fatigue patients with late melatonin onset before and after treatment with melatonin. Before start of the treatment, quality of life was assessed twice. Pre-treatment scores were compared with each other and with the scores of 43 patients with Delayed Sleep Phase Syndrome and of 1063 healthy subjects. Melatonin, 5 mg, was taken orally, 5 hours before baseline salivary endogenous dim light melatonin onset. After mean (SD) treatment of 13.7 (0.8) weeks, quality of life scores "physical functioning," "energy/vitality," "bodily pain," and "general health perception" improved (p values, respectively, 0.017, 0.002, 0.002 and 0.009). In the pre-treatment period (mean [SD] interval: 6.5 [0.6] weeks) "social functioning" and "general health perception" improved (p = 0.013 and 0.010, respectively). In the chronic fatigue patients the quality of life scores did not differ from those of the Delayed Sleep Phase Syndrome patients, except for "physical functioning," "energy/vitality" and "general health perception." These were significantly lower. All chronic fatigue patient's scores were significantly lower than those of the healthy subjects except for "health transition."
Snell CR, Vanness JM, Strayer DR, Stevens SR.	Department of Sport Sciences, University of the Pacific, 3601 Pacific Avenue, Stockton, CA 95211-0197, USA.	Physical performance and prediction of 2-5A synthetase/RNase L antiviral pathway activity in patients with chronic fatigue	In Vivo. 2002 Mar-Apr;16(2):107-9.	The elevated RNase L enzyme activity observed in some Chronic Fatigue Syndrome (CFS) patients may be linked to the low exercise tolerance and functional impairment that typify this disease. The purpose of this investigation was to determine if specific indicators of physical performance can predict abnormal RNase L activity in CFS patients. Seventy-three CFS patients performed a graded exercise test to voluntary exhaustion. Forty-six patients had elevated RNase L levels. This measure was employed as the dependent variable in a discriminant function analysis, with peak V02, exercise duration and Karnofsky Performance Scores (KPS) serving as the independent

		syndrome.		variables. All three variables entered the single significant function ($p < 0.001$). The elevated RNase L group had a lower peak V02 and duration than the normal group, but a higher KPS. The results suggest that both exercise testing and the RNase L biomarker have potential to aid in the diagnosis of CFS.
Stalfors S, Wahl I.		[Fatigue syndrome--a new name of a well-known psychological crisis reaction] [Article in Swedish]	Lakartidningen. 2002 Feb 7;99(6):554.	
Stanley I, Salmon P, Peters S.	Doctors and social epidemics: the problem of persistent unexplained physical symptoms, including chronic fatigue		Br J Gen Pract. 2002 May;52(478):355-6. Comment in: Br J Gen Pract. 2002 Sep;52(482):762-3;	
Steere AC.	Harvard Medical School and Comprehensive Arthritis Center, Massachusetts General Hospital, Boston, MA 02129, USA. ASteere@partners.org	A 58-year-old man with a diagnosis of chronic lyme disease.	JAMA. 2002 Aug 28;288(8):1002-10.	
Straus SE.		Caring for patients with chronic fatigue syndrome. Conclusions in CMO's report are shaped by anecdote not evidence.	BMJ. 2002 Jan 19;324(7330):124-5. Comment on: BMJ. 2002 Jan 19;324(7330):131.	
Sullivan PF, Smith W, Buchwald D.	Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University,	Latent class analysis of symptoms associated with chronic fatigue syndrome and fibromyalgia.	Psychol Med. 2002 Jul;32(5):881-8.	BACKGROUND: Chronic fatigue syndrome and fibromyalgia continue to be perplexing conditions of unknown validity. Aetiological and symptomatic heterogeneity is likely and the distinctiveness of these disorders remains unclear. Our aims were to investigate empirically symptomatic heterogeneity in chronic fatigue syndrome and fibromyalgia. METHODS: Latent class analysis was applied to data from 646 patients who met accepted criteria for chronic fatigue syndrome and/or fibromyalgia who were systematically evaluated at a specialist fatigue clinic. Thirty-two

	Richmond 23298-0126, USA.			symptoms commonly found in chronic fatigue syndrome and fibromyalgia were entered into the latent class analysis. RESULTS: We chose to interpret a four class solution. The classes appeared to differ in a graded fashion (rather than qualitatively) for symptom endorsements, pre-morbid characteristics, and co-morbidity with panic disorder and major depression. CONCLUSIONS: These results were unexpected given the usual assumption of the distinctiveness of chronic fatigue syndrome and fibromyalgia. These results support a conceptualization of chronic fatigue syndrome and fibromyalgia as being characterized by greater similarities than differences.
Sundbom E, Henningsson M, Holm U, Soderbergh S, Evengard B.	Department of Psychology, Umea University, Sweden. elisabet.sundbom@psy.umu.se	Possible influence of defenses and negative life events on patients with chronic fatigue syndrome: a pilot study.	Psychol Rep. 2002 Dec;91(3 Pt 1):963-78.	13 patients with a diagnosis of chronic fatigue syndrome and two contrast groups of conversion disorder patients (n = 19) and healthy controls (n = 13) were assessed using the projective perceptual Defense Mechanism Test to investigate if specific defense patterns are associated with chronic fatigue syndrome. Another objective was to assess the possible influence of perceived negative life events prior the onset of the illness. The overall results showed significant differences in defensive strategies among groups represented by two significant dimensions in a Partial Least Squares analysis. Compared to the contrast groups the patients with chronic fatigue syndrome were distinguished by a defense pattern of different distortions of aggressive affect, induced by an interpersonal anxiety-provoking stimulus picture with short exposures. Their responses suggested the conversion group was characterized by a nonemotionally adapted pattern and specific constellations of defenses, associated with interior reality orientation compared to the patients with chronic fatigue syndrome and the healthy controls. Rated retrospectively, the group with chronic fatigue syndrome reported significantly more negative life events prior to the onset of their illness than healthy controls. For instance, 5 of the 13 patients reported sexual assault or physical battery as children or teenagers compared to none of the healthy controls. A significant association was found between defense pattern and frequency of reported negative life events. However, these retrospective reports might be confounded to some extent by the experience of the patients' illness; for example, the reports may be interpreted in terms of present negative affect.
Swinkels DW, Aalbers N, Elving LD, Bleijenberg G, Swanink CM, van der Meer JW.	Department of Clinical Chemistry 564, University Medical Centre St Radboud, PO Box 9101, 6500 HB Nijmegen, The Netherlands. D.Swinkels@CKCL.azn.nl	Primary haemochromatosis: a missed cause of chronic fatigue syndrome?	Neth J Med. 2002 Dec;60(11):429-33. Comment in: Neth J Med. 2002 Dec;60(11):419-22.	OBJECTIVE: To determine whether patients previously diagnosed as chronic fatigue syndrome (CFS) actually have primary haemochomatosis (PH). METHODS: The setting was a Dutch referral centre. Transferrin saturation (TS) was retrospectively evaluated in banked blood samples of 88 patients diagnosed as CFS. Patients with elevated TS values were asked to provide a new overnight fasting blood sample for a second determination of TS and measurement of serum ferritin. The DNA was investigated for mutations in the HFE gene when one of these iron parameters was elevated. RESULTS: For 19 out of 88 patients with CFS an elevated TS was found. A new blood sample was obtained from 11 of these 19: six had increased TS and two had elevated serum ferritin values. These eight patients were neither C282Y homozygotes nor compound C282Y-H63D heterozygotes. In the eight cases where no new blood samples could be obtained, the TS was > 50% for two of the five men and < 45% for the three female patients. CONCLUSION: In a group of 88 CFS patients we could exclude PH in all but two of them (prevalence 2.3%; 95% confidence interval 0-5.5%). In our population of CFS patients PH is not more common than in a control population of northern European descent (prevalence 0.25-

				0.50%).
Sykes R.	Chronic fatigue syndrome/myalgic encephalitis.		Br J Gen Pract. 2002 Sep;52(482):762-3; author reply 763-4. Comment on: Br J Gen Pract. 2002 May;52(478):355-6.	
Taillefer SS, Kirmayer LJ, Robbins JM, Lasry JC.	Department of Psychology, Universite de Montreal, Canada.	Psychological correlates of functional status in chronic fatigue syndrome.	J Psychosom Res. 2002 Dec;53(6):1097-106.	BACKGROUND: The present study was designed to test a cognitive model of impairment in chronic fatigue syndrome (CFS) in which disability is a function of severity of fatigue and depressive symptoms, generalized somatic symptom attributions and generalized illness worry. METHODS: We compared 45 CFS and 40 multiple sclerosis (MS) outpatients on measures of functional ability, fatigue severity, depressive symptoms, somatic symptom attribution and illness worry. RESULTS: The results confirmed previous findings of lower levels of functional status and greater fatigue among CFS patients compared to a group of patients with MS. Fatigue severity was found to be a significant predictor of physical functioning but not of psychosocial functioning in both groups. In CFS, when level of fatigue was controlled, making more somatic attributions was associated with worse physical functioning, and both illness worry and depressive symptoms were associated with worse psychosocial functioning. CONCLUSIONS: Our findings support the role of depression and illness cognitions in disability in CFS sufferers. Different cognitive factors account for physical and psychosocial disability in CFS and MS. The SF-36 may be sensitive to symptom attributions, suggesting caution in its interpretation when used with patients with ill-defined medical conditions.
Tamizi far B, Tamizi B.	Department of Research, Isfahan University of Medical Sciences, Shahrekord, Isfahan, Iran. babak360@yahoo.com	Treatment of chronic fatigue syndrome by dietary supplementation with omega-3 fatty acids--a good idea?	Med Hypotheses. 2002 Mar;58(3):249-50.	Minor alterations of immune, neuroendocrine, and autonomic function may be associated with the chronic fatigue syndrome. omega-3 fatty acids decrease the production of putative mediators of inflammation, including interleukin-1, and tumor necrosis factor. Since interleukin-1 and tumor necrosis factor are the principal polypeptide mediators of immunoregulation, reduced production of these cytokines by dietary supplementation with omega-3, may be a possible mechanism for the treatment of chronic fatigue syndrome. Copyright 2002, Elsevier Science Ltd. All rights reserved.
Tan EM, Sugiura K, Gupta S.	W.M. Keck Autoimmune Disease Center, The Scripps Research Institute, La Jolla, California 92037, USA.	The case definition of chronic fatigue syndrome.	J Clin Immunol. 2002 Jan;22(1):8-12.	The 1994 case definition of chronic fatigue syndrome is widely used not only for diagnosis but also for clinical and laboratory-based observations of this clinical entity. The criteria for the 1994 case definition are based primarily on symptoms and not on physical signs or chemical or immunological tests. This situation has resulted in conflicting clinical and laboratory observations that in all likelihood is due to different populations of patients being studied in different centers. Based on some of the recent publications, there appears to be an emerging picture of this disease entity that we propose could be used to subgroup chronic fatigue syndrome into four different subclasses. These subclasses would consist of chronic fatigue with primarily nervous system disorders such as impaired memory or concentration and headache, chronic fatigue with primarily endocrine system disorders such as unrefreshing sleep and postexertional malaise,

				chronic fatigue with musculoskeletal system disorders such as muscle pain and joint pain, and chronic fatigue with immune system/infectious disorders such as sore throat and tender lymph nodes. It is suggested that if clinical and laboratory-based studies on chronic fatigue syndrome were conducted on more homogeneous subgroups of patients, the data from one center to the other might not be as conflicting and more insights can be shed on the nature of this clinical condition.
Tanaka H, Matsushima R, Tamai H, Kajimoto Y.	Department of Pediatrics, Osaka Medical College, Takatsuki-shi, Japan.	Impaired postural cerebral hemodynamics in young patients with chronic fatigue with and without orthostatic intolerance.	J Pediatr. 2002 Apr;140(4):412-7. Comment in: J Pediatr. 2002 Apr;140(4):387-9. J Pediatr. 2003 Feb;142(2):217; author reply 217-8.	OBJECTIVES: To measure postural changes in cerebral hemodynamics in young patients with chronic fatigue with and without orthostatic intolerance. STUDY DESIGN: We studied 28 patients (age, 10 to 22 years) and 20 healthy control subjects (age, 6 to 27 years). Cerebral oxygenated hemoglobin (oxy-Hb) and deoxygenated Hb were noninvasively and continuously measured with near infrared spectroscopy during active standing. Beat-to-beat arterial pressure was monitored by Finapres. RESULTS: Orthostatic intolerance determined by cardiovascular responses to standing was observed in 16 of 28 patients: instantaneous orthostatic hypotension in 8, delayed orthostatic hypotension in 2, and postural orthostatic tachycardia in 6. A rapid recovery of oxy-Hb by near infrared spectroscopy at the onset of active standing was not found in 15 of 16 patients with chronic fatigue and orthostatic intolerance and in 6 of 12 patients with chronic fatigue without orthostatic intolerance but only in 2 of 20 control subjects. Thirteen of 16 patients with orthostatic intolerance showed prolonged reduction in oxy-Hb during standing. CONCLUSIONS: Impaired cerebral hemodynamics in patients with chronic fatigue syndrome and postural orthostatic tachycardia suggest a link between impaired cerebral oxygenation and chronic fatigue. However, this cannot explain the symptoms in patients meeting the criteria of chronic fatigue without orthostatic intolerance.
Taylor RR, Jason LA, Curie CJ.	Department of Psychology, DePaul University, 2219 North Kenmore Avenue, Chicago, IL 60614, USA.	Prognosis of chronic fatigue in a community-based sample.	Psychosom Med. 2002 Mar-Apr;64(2):319-27.	OBJECTIVE: This study examined predictors of fatigue severity and predictors of continued chronic fatigue status at wave 2 follow-up within a random, community-based sample of individuals previously evaluated in a wave 1 prevalence study of chronic fatigue and chronic fatigue syndrome that originally took place between 1995 and 1997. METHODS: Wave 1 data were from a larger community-based prevalence study of chronic fatigue syndrome. In the present study, a second wave of data were collected by randomly selecting a sample of participants from the wave 1 sample of 18,675 adults and readministering a telephone screening questionnaire designed to assess symptoms of chronic fatigue syndrome. RESULTS: Findings revealed that wave 1 fatigue severity was a predictor of fatigue severity at wave 2 in the overall sample of individuals with and without chronic fatigue. In the smaller sample of individuals with chronic fatigue, wave 1 fatigue severity, worsening of fatigue with physical exertion, and feeling worse for 24 hours or more after exercise significantly predicted continued chronic fatigue status (vs. improvement) at wave 2 follow-up. CONCLUSIONS: These findings underscore the prognostic validity of postexertional malaise in predicting long-term chronic fatigue and also highlight the importance of using population-based, representative random samples when attempting to identify long-term predictors of chronic fatigue at follow-up.
Taylor RR, Jason LA.	Department of Psychology, DePaul	Chronic fatigue, abuse-related	Soc Sci Med. 2002 Jul;55(2):247-56.	The relationship between sexual and physical abuse history and negative health effects has been well-documented in medical facility samples. Few studies have examined the role of abuse

	University, Chicago, IL 60614, USA. rtaylor@wppost.depaul.edu	traumatization, and psychiatric disorders in a community-based sample.		history and its relationship with chronic fatigue and psychiatric disorders in a diverse, randomly selected community-based sample. The present study compared rates of different types of abuse events in individuals with chronic fatigue and non-symptomatic controls. Relationships between specific types of abuse and psychiatric disorders commonly associated with chronic fatigue were also explored. A stratified random sample of 18,675 adults residing in ethnically and socioeconomically diverse neighborhoods in Chicago first completed a telephone screening questionnaire. A control group and a group of individuals with chronic fatigue symptomatology were identified and administered a semi-structured psychiatric interview assessing DSM-IV Axis I psychiatric disorders and a sexual and physical abuse history questionnaire. Controlling for sociodemographic differences, fatigue outcome was significantly predicted by childhood sexual abuse and the total number of different childhood abuse events. Within the chronic fatigue group, diagnosis of posttraumatic stress disorder (PTSD) was significantly predicted by childhood sexual abuse, childhood death threat, the total number of childhood abuse events, and lifetime abuse events. Sexual abuse during adolescence or adulthood significantly predicted other anxiety disorders among individuals with chronic fatigue. These findings suggest that a history of abuse, particularly during childhood, may play a role in the development and perpetuation of a wide range of disorders involving chronic fatigue. Among individuals with chronic fatigue, PTSD and other anxiety disorders appear to demonstrate the strongest association with abuse history. The implications of these findings are discussed.
Thorn A.	Karolinska Institutet, Department of Public Health Sciences, Stockholm, Sweden. ake.thorn@nll.se	Methodologic aspects of the study of modern-age diseases: the example of sick-building syndrome.	Int J Occup Environ Health. 2002 Oct-Dec;8(4):363-70.	In recent decades, variously identified nebulous disorders such as sick-building syndrome, electrical hypersensitivity, and chronic fatigue syndrome, characterized by combinations of nonspecific symptoms and absence of demonstrable signs have appeared. Their similar nonspecific etiologic attributions have given rise to generic names such as "modern-age disease" and "symptom-based conditions." The lack of demonstrable biological correlates as well as the vagueness of the etiologic attributions makes modern-age diseases unusually problematic to study with epidemiologic methods, potentially leading to serious biases. Case studies of sick-building syndrome demonstrate that qualitative methods can help to elucidate the dynamic processes involved in syndrome development.
Timmers HJ, Wieling W, Soetekouw PM, Bleijenberg G, Van Der Meer JW, Lenders JW.	Department of General Internal Medicine, University Medical Center St. Radboud, P. O. Box 9101, 6500 HB Nijmegen, The Netherlands.	Hemodynamic and neurohumoral responses to head-up tilt in patients with chronic fatigue syndrome.	Clin Auton Res. 2002 Aug;12(4):273-80.	BACKGROUND: Data on the prevalence of orthostatic intolerance (OI) in patients with chronic fatigue syndrome (CFS) are limited and controversial. We tested the hypothesis that a majority of CFS patients exhibit OI during head-up tilt. METHODS: Hemodynamic and neurohumoral responses to 40 minutes of head-up tilt were studied in 36 CFS patients and 36 healthy controls. Changes in stroke volume, cardiac output and peripheral vascular resistance were estimated from finger arterial pressure waveform analysis (Modelflow). Blood samples were drawn before and at the end of head-up tilt for measurement of plasma catecholamines. RESULTS: At baseline, supine heart rate was higher in CFS patients (CFS: 66.4 +/- 8.4 bpm; controls: 57.4 +/- 6.6 bpm; $p < 0.001$) as was the plasma epinephrine level (CFS: 0.11 +/- 0.07 nmol/l; controls: 0.08 +/- 0.07 nmol/l: $p = 0.015$). An abnormal blood pressure and/or heart rate response to head-up tilt was seen in 10 (27.8 %) CFS patients (6 presyncope, 2 postural tachycardia, 2 tachycardia and presyncope) and 6 (16.7 %, $p = 0.26$) controls (5 presyncope, 1 tachycardia, 2 tachycardia and presyncope). Head-up

				tilt-negative CFS patients showed a larger decrease in stroke volume during tilt (-46.9 +/- 10.6) than head-up tilt-negative controls (-40.3 +/- 13.6 %, p = 0.008). Plasma catecholamine responses to head-up tilt did not differ between these groups. CONCLUSION: Head-up tilt evokes postural tachycardia or (pre)syncope in a minority of CFS patients. The observations in head-up tilt-negative CFS patients of a higher heart rate at baseline together with a marked decrease in stroke volume in response to head-up tilt may point to deconditioning.
Torres-Harding SR, Jason LA, Cane V, Carrico A, Taylor RR.	DePaul University, USA. storres@depaul.edu	Physicians' diagnoses of psychiatric disorders for people with chronic fatigue syndrome.	Int J Psychiatry Med. 2002;32(2):109-24.	OBJECTIVE: To examine rates of psychiatric diagnoses given by patients' primary or regular physicians to persons with chronic fatigue syndrome (CFS), persons with psychiatrically explained fatigue, and a control group. Physicians' psychiatric diagnosis and participants' self-reported psychiatric diagnoses were compared to lifetime psychiatric diagnoses as measured by a structured psychiatric interview. METHOD: Participants were recruited as part of a community-based epidemiology study of chronic fatigue syndrome. Medical records of 23 persons with chronic fatigue syndrome, 25 persons with psychiatrically explained chronic fatigue, and 19 persons without chronic fatigue (controls) were examined to determine whether their physician had given a diagnosis of mood, anxiety, somatoform, or psychotic disorder. Lifetime psychiatric status was measured using the Structured Clinical Interview for the DSM-IV (SCID). Participants' self reports of specific psychiatric disorders were assessed as part of a detailed medical questionnaire. RESULTS: Physicians' diagnosis of a psychiatric illness when at least one psychiatric disorder was present ranged from 40 percent in the psychiatrically explained group, 50 percent in the control group, and 64.3 percent in the CFS group. Participants in the psychiatrically explained group were more accurate than physicians in reporting the presence of a psychiatric disorder, and in accurately reporting the presence of a mood or anxiety disorder. CONCLUSIONS: The present investigation found underrecognition of psychiatric illness by physicians, with relatively little misdiagnosis of psychiatric illness. Physicians had particular difficulty assessing psychiatric disorder in those patients whose chronic fatigue was fully explained by a psychiatric disorder. Results emphasized the importance of using participant self report as a screening for psychiatric disorder.
Tournier JN, Drouet E, Jouan A.	Departement de biologie des agents transmissibles, Centre de recherches du service de sante des armees, 24, avenue des maquis du Gresivaudan, BP 87, F38702 La Tronche. j.tournier@eudoramail.com	[The Gulf war syndrome] [Article in French]	Presse Med. 2002 Jan 12;31(1 Pt 1):3-9.	SPARSE DATA: The Gulf war syndrome remains a little know entity since its first appearance 10 years ago. The objective of our work was to synthesize the data published on the subject in the scientific literature. We analysed the results of American and English epidemiological surveys, from which it was difficult to distinguish the existence of a univocal syndrome. IMPRECISE DEFINITION: It is difficult to give a clear clinical definition of the syndrome, the signs of which fluctuate depending on the studies. Chronic fatigue is frequently associated with the Gulf war syndrome, although some studies have described electrophysiological neurological lesions. NUMEROUS HYPOTHESES: The role of stress, vaccinations and their adjuvants, exposition to neurotoxic substances and weak uranium have been incriminated. We propose that multiple factors be integrated in the research for the genesis of this atypic syndrome.
Tudor-Thomas W,	Dorset ME Support	Myalgic	Health Serv J. 2002	

Richards S.	Group.	encephalomyelitis. Talking to ME.	Mar 28;112(5798):31.	
van der Werf SP, de Vree B, Alberts M, van der Meer JW, Bleijenberg G; Netherlands Fatigue Research Group Nijmegen.	Department of Medical Psychology, University Medical Centre, Post Box 9101, 6500 HB Nijmegen, The Netherlands. s.vanderwerf@cksmps.azn.nl	Natural course and predicting self-reported improvement in patients with chronic fatigue syndrome with a relatively short illness duration.	J Psychosom Res. 2002 Sep;53(3):749-53.	OBJECTIVE: To describe the course of fatigue in chronic fatigue syndrome (CFS) patients with a relatively short duration of complaints and to test which psychosocial factors predict spontaneous improvement 1 year later. METHODS: Seventy-nine patients with a complaint duration of less than 2 years were tested at baseline and 78 of the same group at 1-year follow-up. During this time period, no systematic intervention took place. Self-reported improvement and fatigue severity were the main outcome measures. RESULTS: Forty-six percent (95% confidence intervals, 95CI = 35-58%) of the patients with a short illness duration reported to be improved. This was a significantly (chi(2) = 20.3, P < .001) higher percentage compared to the 20% (95CI = 15-26%) self-reported improvement in a previously published natural-course study among 246 CFS patients with a longer illness duration. Persistence of complaints after 1-year follow-up was associated with high baseline levels of experienced concentration problems, less strong psychosocial causal explanations for the complaints, and higher levels of the experienced lack of social support. Baseline fatigue severity predicted fatigue severity at follow-up. CONCLUSION: The results showed that CFS patients with a relatively short duration of complaints had a more favourable outcome compared to patients with a long illness duration. The data also indicated that complete recovery only occurred in patients with a complaint duration of less than 15 months. This finding has important implications, since it suggests that after such a time period spontaneous recovery hardly occurs. Copyright 2002 Elsevier Science Inc.
van der Werf SP, de Vree B, van Der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Medical Center Nijmegen, the Netherlands. S.vanderWerf@cksmps.AZN.NL	The relations among body consciousness, somatic symptom report, and information processing speed in chronic fatigue syndrome.	Neuropsychiatry Neuropsychol Behav Neurol. 2002 Mar;15(1):2-9.	OBJECTIVE: The aim of this study was to assess the potential influence of body consciousness and levels of somatic symptom report upon information processing speed in patients with chronic fatigue syndrome (CFS). BACKGROUND: According to a model of a fixed information processing capacity, it was predicted that in a group of patients with CFS, high body consciousness in combination with a high report of somatic symptoms would affect information-processing speed negatively. METHODS: Information- and motor-processing speed were simultaneously measured with a simple- and a choice-reaction time task, whereas cognitive complaints were rated with two questionnaires. The hypothesized influence of private body consciousness and somatic symptom report upon information-processing speed was tested in a model. A symptom-validity test was used to screen for possible illness behavior. RESULTS: Private body consciousness was directly related to information-processing speed and somatic symptom report. Somatic symptom report was related to both test performance and memory and concentration complaints. CONCLUSIONS: Levels of private body consciousness directly affected somatic symptom report and information-processing speed. This finding supports the role of attentive processes in CFS, and offers, besides possible cerebral dysfunction, an alternative explanation for slowing of information processing in CFS.
Van Heck GL, De Vries J.		Quality of Life of Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2002; 10 (1): 17 - 35	The purpose of this study was to compare quality of life between patients with Chronic Fatigue Syndrome (CFS; n = 73) and healthy controls (n = 147), using a broad and generic quality of life assessment instrument, the World Health Organization Quality of Life assessment (WHOQOL-100). Partricipants were assessed on the WHOQOL-100, a self-assessment instrument designed

				for quantifying 24 facets relating to quality of life. These facets are groups into six larger domains: physical health, psychological health, level of independence, social relationships, environment, and spirituality. The WHOQOL-100 also includes one facet examining the overall quality of life and general health perceptions. Analyses revealed that the CFS group reported significantly lower levels of quality of life than the control group on overall quality of life and general health perceptions and on 22 out of the 24 facets of quality of life. Compared to earlier studies that used health-status scales or rather limited quality of life measures, this study generated a more complete picture of the problems of patients with CFS. The results suggest that the impact of CFS on the patients' lives is very profound. CFS has a quality-of-life burden that affects a wide range of factors inherent to quality of life. Questions that must be addressed by future research are considered.
Van Houdenhove B, Neerinckx E, Onghena P, Vingerhoets A, Lysens R, Vertommen H.	Faculty of Medicine, K.U. Leuven, Leuven, Belgium. Boudewijn.VanHoudenhove@uz.kuleuven.ac.be	Daily hassles reported by chronic fatigue syndrome and fibromyalgia patients in tertiary care: a controlled quantitative and qualitative study.	Psychother Psychosom. 2002 Jul-Aug;71(4):207-13.	BACKGROUND: This study aimed at providing insight in the frequency, emotional impact and nature of daily hassles, experienced by patients suffering from chronic fatigue syndrome (CFS) and/or fibromyalgia (FM), compared with patients with a chronic organic disease. METHODS: One hundred and seventy-seven CFS/FM patients, 26 multiple sclerosis (MS) and 26 rheumatoid arthritis (RA) patients were investigated within 2-6 months after diagnosis. All patients completed a self-report questionnaire assessing daily hassles and associated distress, a visual analogue scale assessing fatigue and pain and a depression and anxiety questionnaire. RESULTS: CFS/FM patients show a higher frequency of hassles, higher emotional impact and higher fatigue, pain, depression and anxiety levels compared with MS/RA patients. Three hassle themes dominate in the CFS/FM group: dissatisfaction with oneself, insecurity and a lack of social recognition. In contrast, hassles reported by MS/RA patients show a much larger diversity and are not focused on person-dependent problems. CONCLUSIONS: Patients recently diagnosed as suffering from CFS and/or FM are highly preoccupied and distressed by daily hassles that have a severe impact on their self-image, as well as their personal, social and professional functioning. An optimal therapeutic approach of CFS and FM should take account of this heavy psychosocial burden, which might refer to core themes of these patients' illness experience. Copyright 2002 S. Karger AG, Basel
Van Houdenhove B.		Listening to CFS: why we should pay more attention to the story of the patient.	J Psychosom Res. 2002 Jun;52(6):495-9.	
Vernon SD, Shukla SK, Conradt J, Unger ER, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA. svernon@cdc.gov	Analysis of 16S rRNA gene sequences and circulating cell-free DNA from plasma of chronic fatigue syndrome and non-fatigued subjects.	BMC Microbiol. 2002 Dec 23;2(1):39.	BACKGROUND: The association of an infectious agent with chronic fatigue syndrome (CFS) has been difficult and is further complicated by the lack of a known lesion or diseased tissue. Cell-free plasma DNA could serve as a sentinel of infection and disease occurring throughout the body. This type of systemic sample coupled with broad-range amplification of bacterial sequences was used to determine whether a bacterial pathogen was associated with CFS. Plasma DNA from 34 CFS and 55 non-fatigued subjects was assessed to determine plasma DNA concentration and the presence of bacterial 16S ribosomal DNA (rDNA) sequences. RESULTS: DNA was isolated from 81 (91%) of 89 plasma samples. The 55 non-fatigued subjects had higher plasma DNA concentrations than those with CFS (average 151 versus 91 ng) and more CFS subjects (6/34, 18%) had no

				detectable plasma DNA than non-fatigued subjects (2/55, 4%), but these differences were not significant. Bacterial sequences were detected in 23 (26%) of 89. Only 4 (14%) CFS subjects had 16S rDNA sequences amplified from plasma compared with 17 (32%) of the non-fatigued (P = 0.03). All but 1 of the 23 16S rDNA amplicon-positive subjects had five or more unique sequences present. CONCLUSIONS: CFS subjects had slightly lower concentrations or no detectable plasma DNA than non-fatigued subjects. There was a diverse array of 16S rDNA sequences in plasma DNA from both CFS and non-fatigued subjects. There were no unique, previously uncharacterized or predominant 16S rDNA sequences in either CFS or non-fatigued subjects.
Vernon SD, Unger ER, Dimulescu IM, Rajeevan M, Reeves WC.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333, USA.	Utility of the blood for gene expression profiling and biomarker discovery in chronic fatigue syndrome.	Dis Markers. 2002;18(4):193-9.	Chronic fatigue syndrome (CFS) is a debilitating illness lacking consistent anatomic lesions and eluding conventional laboratory diagnosis. Demonstration of the utility of the blood for gene expression profiling and biomarker discovery would have implications into the pathophysiology of CFS. The objective of this study was to determine if gene expression profiles of peripheral blood mononuclear cells (PMBCs) could distinguish between subjects with CFS and healthy controls. Total RNA from PBMCs of five CFS cases and seventeen controls was labeled and hybridized to 1764 genes on filter arrays. Gene intensity values were analyzed by various classification algorithms and nonparametric statistical methods. The classification algorithms grouped the majority of the CFS cases together, and distinguished them from the healthy controls. Eight genes were differentially expressed in both an age-matched case-control analysis and when comparing all CFS cases to all controls. Several of the diffrentially expressed genes are associated with immunologic functions (e.g., CMRF35 antigen, IL-8, HD protein) and implicate immune dysfunction in the pathophysiology of CFS. These results successfully demonstrate the utility of the blood for gene expression profiling to distinguish subjects with CFS from healthy controls and for identifying genes that could serve as CFS biomarkers.
Veyssier-Belot C.		[First scientific conference on chronic fatigue syndrome and fibromyalgia, Lyon, January 25, 2002] [Article in French]	Rev Med Interne. 2002 Jul;23(7):577-80.	Service de medecine interne, centre hospitalier general Poissy-Saint-Germain-en-Laye, 20, rue Armangis, 78100 Saint-Germain-en-Laye, France.
Walach H, Bosch H, Haraldsson E, Marx A, Tomasson H, Wiesendanger H, Lewith G.	Institute of Environmental Medicine and Hospital Epidemiology, University Hospital Freiburg, Germany. walach@ukl.uni-freiburg.de	Efficacy of distant healing--a proposal for a four-armed randomized study (EUHEALS).	Forsch Komplementarmed Klass Naturheilkd. 2002 Jun;9(3):168-76.	BACKGROUND: Distant healing as a treatment modality is frequently used by patients and healers. Some preliminary evidence suggests possible effects. Since patients suffering from multiple chemical sensitivity and chronic fatigue syndrome have only few effective treatment options, distant healing will be offered as a treatment within a formal trial of distant healing. DESIGN AND METHOD: A four-armed randomized trial will include 400 patients with self-attributed, environmental problems who fulfil the diagnostic criteria of severe idiopathic chronic fatigue, chronic fatigue syndrome or multiple chemical sensitivity. Patients will be recruited by specialized general practitioners and environmental clinics. They will be treated by healers distributed all over Europe, coming from various healing traditions and nationalities. Each patient will be treated by 3 healers. Healers will have no contact with the patients and will only be

				provided with the patient's Christian name and a photograph. The patients will be randomized to one of 4 groups in a 2 x 2 factorial design. They will either receive (distant) healing or not, and either know or not know this decision. Thereby the effects of expectation and of time can be disentangled from the specific effects of healing. OUTCOME MEASURE: Primary outcome measure will be the mental health summary scale of the MOS SF-36. The measure will be taken at the beginning and at the end of a 6- month treating or waiting period, respectively. A variety of moderator variables will be considered to evaluate which of these may be predictive of outcome. Copyright 2002 S. Karger GmbH, Freiburg
Weetman AP.	University of Shieffield Clinical Sciences Centre, Northern General Hospital, UK. k.f.watson@sheffield.ac.uk	Thyroxine treatment in biochemically euthyroid but clinically hypothyroid individuals.	Clin Endocrinol (Oxf). 2002 Jul;57(1):25-7.	
Wessely S.	Women experienced chronic fatigue syndrome and fibromyalgia as stigmatising.	Comment on: Qual Health Res. 2002 Feb;12(2):148-60.	Evid Based Ment Health. 2002 Nov;5(4):127.	Guy's, King's and St Thomas's School of Medicine and Institute of Psychiatry, London, UK.
White PD, Fulcher KY.	Chronic fatigue syndrome, deconditioning, and graded exercise therapy.		Med Sci Sports Exerc. 2002 Oct;34(10):1691-2; author reply 1692-3. Comment on: Med Sci Sports Exerc. 2002 Jan;34(1):51-6.	
White PD, Pinching AJ, Rakib A, Castle M, Hedge B, Priebe S.	Department of Psychological Medicine, Barts and the London, Queen Mary's School of Medicine and Dentistry, University of London, London EC1A 7BE, UK. p.d.white@qmul.ac.uk	A comparison of patients with chronic fatigue syndrome attending separate fatigue clinics based in immunology and psychiatry.	J R Soc Med. 2002 Sep;95(9):440-4.	Hospital clinics for patients with chronic unexplained fatigue are held in departments of various disciplines. This causes difficulties for referrers in choosing the appropriate clinic and for researchers in generalizing findings from one type of clinic to others. We randomly selected 37 outpatients attending an immunology fatigue clinic and 36 outpatients attending a psychiatry fatigue clinic, all of whom had chronic fatigue syndrome. We compared demographic factors, symptoms, disability, quality of life, psychological distress and illness attributions. The patients from the two clinics were closely similar in their specific symptoms, disability, quality of life, psychological distress and previous attendance to mental health professionals. Psychological distress was high and equal in the two samples. The proportion of men was greater among patients attending the immunology clinic. In a post-hoc analysis, 64% of immunology attenders attributed their fatigue to physical factors, compared with 31% of psychiatry clinic attenders (chi(2)=6.35, 1 d.f., P=0.01). These findings suggest that research data from one type of chronic fatigue clinic can be generalized to others. Clinically similar patients are referred to different

				clinics, and the choice of clinic may be influenced by the patients' illness beliefs. The high levels of emotional distress suggest that psychosocial management is as important as physical management in hospital outpatients with chronic fatigue syndrome, irrespective of its aetiology.
White PD.	Discomfort of patient power. Power sharing is not a takeover bid.		BMJ. 2002 May 18;324(7347):1214. Comment on: BMJ. 2002 Mar 2;324(7336):497-8.	
White PD.		Chronic unexplained fatigue	Postgrad Med J. 2002 Aug;78(922):445-6. Comment in: Postgrad Med J. 2002 Dec;78(926):763; author reply 763.	
Whitehead L, Campion P.		Can General Practitioners Manage Chronic Fatigue Syndrome? A Controlled Trial	Journal of Chronic Fatigue Syndrome 2002; 10 (1): 55 - 64	Background: Chronic Fatigue Syndrome/Myalgic Encephalomyeltis (CFS/ME) is now recognised as a condition that results in substantial disability with a prevalence of around 0.6%. Aim: The study aimed to test the hypotheses that general practitioners could (a) diagnose and (b) treat patients with the Chronic Fatigue Syndrome (CFS). Method: All practices in two health authorities were contacted with a 35% uptake. Fifty percent of practices then entered a patient into the study. Practices were randomised to either intervention or control groups, and were encouraged to recruit patients. It was intended that the intervention practices would introduce a form of brief cognitive behavioural therapy. Control practices were invited to manage their patients as usual, which often included referral to secondary care. Results: The study suffered from both poor recruitment and high drop out. However, we were able to show that this intervention had no effect on the illness of the patients enrolled, and that patients with CFS remained highly disabled over the 12 month study period, whatever their treatment. Conclusion: The study suggests that general practitioners in this study were unable to effectively treat the condition. This accords with the Royal Colleges' report (1996), that the only evidence for effective treatment thus far has come from specialist units. The study suggests that general practitioners are unable to provide a management programme of this nature, and possibly effective treatment programmes for CFS in primary care.
Whitehead WE, Palsson O, Jones KR.	Division of Digestive Diseases and Center for Functional Gastrointestinal and Motility Disorders, University of North Carolina, Chapel Hill,	Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications?	Gastroenterology. 2002 Apr;122(4):1140-56.	BACKGROUND & AIMS: Comorbid or extraintestinal symptoms occur frequently with irritable bowel syndrome and account for up to three fourths of excess health care visits. This challenges the assumption that irritable bowel is a distinct disorder. The aims of this study were to (1) assess comorbidity in 3 areas: gastrointestinal disorders, psychiatric disorders, and nongastrointestinal somatic disorders; and (2) evaluate explanatory hypotheses. METHODS: The scientific literature since 1966 in all languages cited in Medline was systematically reviewed. RESULTS: Comorbidity with other functional gastrointestinal disorders is high and may be caused by shared

	North Carolina 27599, USA. Whitehd@unch.unc.edu			pathophysiological mechanisms such as visceral hypersensitivity. Psychiatric disorders, especially major depression, anxiety, and somatoform disorders, occur in up to 94%. The nongastrointestinal nonpsychiatric disorders with the best-documented association are fibromyalgia (median of 49% have IBS), chronic fatigue syndrome (51%), temporomandibular joint disorder (64%), and chronic pelvic pain (50%). CONCLUSIONS: Multivariate statistical analyses suggest that these are distinct disorders and not manifestations of a common somatization disorder, but their strong comorbidity suggests a common feature important to their expression, which is most likely psychological. Some models explain the comorbidity of irritable bowel with other disorders by suggesting that each disorder is the manifestation of varying combinations of interacting physiological and psychological factors. An alternative hypothesis is that the irritable bowel diagnosis is applied to a heterogeneous group of patients, some of whom have a predominantly psychological etiology, whereas others have a predominantly biological etiology, and that the presence of multiple comorbid disorders is a marker for psychological influences on etiology.
Wikland B, Sandberg PO.[		[Benefits of cytological thyroid gland examination using needle biopsy in chronic fatigue] Article in Swedish]	Lakartidningen. 2002 Nov 21;99(47):4778.	
Wildman MJ, Ayres JG.	. Q fever: still a mysterious disease		QJM. 2002 Dec;95(12):833-4. Comment on: QJM. 2002 Aug;95(8):491-2.	
Wildman MJ, Smith EG, Groves J, Beattie JM, Caul EO, Ayres JG.	Department of Respiratory Medicine, Birmingham Heartlands Hospital, UK.	Chronic fatigue following infection by Coxiella burnetii (Q fever): ten-year follow-up of the 1989 UK outbreak cohort.	QJM. 2002 Aug;95(8):527-38. Comment in: QJM. 2002 Aug;95(8):491-2.	BACKGROUND: Some patients exposed to Q fever (Coxiella burnetii infection) may develop chronic fatigue. AIM: To determine whether subjects involved in the West Midlands Q fever outbreak of 1989 had increased fatigue, compared to non-exposed controls, 10 years after exposure. DESIGN: Matched cohort study comparing cases to age-, sex- and smoking-history-matched controls not exposed to Q fever. METHODS: A postal questionnaire was sent to subjects at home, followed by further assessment in hospital, including a physical examination and blood tests. RESULTS: Of 108 Q-exposed subjects, 70 (64.8%) had fatigue, 37 idiopathic chronic fatigue (ICF) (34.3%), vs. 29/80 (36.3%) and 12 (15.0%), respectively, in controls. In 77 matched pairs, fatigue was commoner in Q-exposed subjects than in controls: 50 (64.9%) vs. 27 (35.1%), p<0.0001. ICF was found in 25 (32.5%) of Q-exposed patients and 11(14.3%) of controls (p=0.01). There were 36 (46.8%) GHQ cases in Q-exposed subjects, vs. 18 (23.4%) controls (p=0.004). A matched analysis of those more intensively studied showed fatigue in 48 (66.7%) Q-exposed patients and 25 (34.7%) controls, (p<0.0001), ICF in 25 (34.7%) Q-exposed and 10 (13.9%) controls (p=0.004), and chronic fatigue syndrome (CFS) in 14 (19.4%) Q-exposed patients and three (4.2%) controls (p=0.003). Thirty-four (47.2%) Q-exposed patients were GHQ cases

				compared to 17 (23.6%) controls (p=0.004). DISCUSSION: Subjects who were exposed to Coxiella in 1989 had more fatigue than did controls, and some fulfilled the criteria for CFS. Whether this is due to ongoing antigen persistence or to the psychological effects of prolonged medical follow-up is uncertain.
Wilhelmsen I.	Institute of Medicine, University of Bergen, Norway. Ingvard.Wilhelmsen @med.uib.no	Somatization, sensitization, and functional dyspepsia.	Scand J Psychol. 2002 Apr;43(2):177-80.	Functional dysepsia (FD) is defined as persistent or recurrent pain or discomfort centered in the upper abdomen without evidence of organic disease likely to explain the symptoms. Visceral hypersensitivity, motor dysfunction, and impaired gastric accommodation are found in some patients with FD, and psychological factors like chronic stress, attention and perception bias are also likely to play a part in the symptom formation. There is considerable overlap of non-specific symptoms like fatigue, headache, abdominal discomfort, muscle pain, and sleep disturbance in patients with different functional disorders, in this article exemplified by FD, fibromyalgia, and chronic fatigue syndrome. This overlap of symptoms indicates a common underlying sensitization process, leading to somatization.
Williams G, Waterhouse J, Mugarza J, Minors D, Hayden K.	Diabetes and Endocrinology Research Group, Department of Medicine, University Hospital Aintree, Liverpool, UK. gareth@liv.ac.uk	Therapy of circadian rhythm disorders in chronic fatigue syndrome: no symptomatic improvement with melatonin or phototherapy.	Eur J Clin Invest. 2002 Nov;32(11):831-7.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) show evidence of circadian rhythm disturbances. We aimed to determine whether CFS symptoms were alleviated by melatonin and bright-light phototherapy, which have been shown to improve circadian rhythm disorders and fatigue in jet-lag and shift workers. DESIGN: Thirty patients with unexplained fatigue for > 6 months were initially assessed using placebo and then received melatonin (5 mg in the evening) and phototherapy (2500 Lux for 1 h in the morning), each for 12 weeks in random order separated by a washout period. Principal symptoms of CFS were measured by visual analogue scales, the Shortform (SF-36) Health Survey, Mental Fatigue Inventory and Hospital Anxiety and Depression Scale. We also determined the circadian rhythm of body temperature, timing of the onset of melatonin secretion, and the relationship between these. RESULTS: Neither intervention showed any significant effect on any of the principal symptoms or on general measures of physical or mental health. Compared with placebo, neither body temperature rhythm nor onset of melatonin secretion was significantly altered by either treatment, except for a slight advance of temperature phase (0.8 h; P = 0.04) with phototherapy. CONCLUSION: Melatonin and bright-light phototherapy appear ineffective in CFS. Both treatments are being prescribed for CFS sufferers by medical and alternative practitioners. Their unregulated use should be prohibited unless, or until, clear benefits are convincingly demonstrated.
Wolf C, Barth A	Klinische Abteilung fur Arbeitsmedizin, Universitatsklinik fur Innere Medizin 4, Wahringer Gurtel 18-20, 1090 Wien/Osterreich. christian.wolf@univie.ac.at	[Somatoform disorders without findings--modern syndromes] [Article in German]	Internist (Berl). 2002 Jul;43(7):833-4, 837-9.	
Working Group of		Chronic fatigue	Med J Aust. 2002	

the Royal Australasian College of Physicians.		syndrome. Clinical practice guidelines--2002.	May 6;176 Suppl:S23-56.	
Youssefi M, Linkowski P.	Service de Psychiatrie, Hopital Erasme, U.L.B.	[Chronic fatigue syndrome: psychiatric perspectives] [Article in French]	Rev Med Brux. 2002 Sep;23(4):A299-304.	Chronic fatigue syndrome (CFS) is a common illness of unknown etiology and pathogenesis characterized by severe disabling fatigue and a variety of musculoskeletal, neurocognitive, mood symptoms and sleep disorders lasting at least six months. A significant proportion of patients fulfilling operative criteria for a diagnosis of CFS will also meet criteria for a psychiatric disorder such as depression, somatization or anxiety disorders. Premorbid lifestyle may play a predisposing, and/or perpetuating role in CFS. Some patients improve with time but most remain functionally impaired for several years. A variety of interventions have been used in the treatment and management of CFS. Interventions which have shown promising results include cognitive behavioural therapy and graded exercise therapy. Antidepressants can be useful particularly in the case of comorbid affective disorders. Development of good therapeutic doctor-patient alliance with empathic care is central to the effective management of CFS. In this article we overview the nature and definition of CFS. The prevalence, the prognosis and the psychopathological issues are presented. The management of this controversial syndrome is discussed.
Yunus MB.	Section of Rheumatology, University of Illinois College of Medicine at Peoria, 1 Illini Dr, PO Box 1649, Peoria, IL 61656, USA. yunus@uic.edu	Gender differences in fibromyalgia and other related syndromes.	J Gend Specif Med. 2002 Mar-Apr;5(2):42-7.	Fibromyalgia syndrome is characterized by widespread musculoskeletal pain, fatigue, poor sleep, and tenderness on palpation at multiple sites called tender points. It occurs mostly among women; only about 10% of patients are men. Two recent studies showed that women had significantly more common fatigue, morning fatigue, "hurt all over," a greater total number of symptoms, as well as a greater number of tender points. Gender differences have also been reported in other related syndromes such as tension headache, migraine, irritable bowel syndrome, chronic fatigue syndrome, and temporomandibular disorder. Although the mechanisms of gender differences in these illnesses are not fully understood, they are likely to involve an interaction between biology, psychology, and sociocultural factors.
Zachrisson O, Regland B, Jahreskog M, Jonsson M, Kron M, Gottfries CG.	Psychiatry Section, Institute of Clinical Neuroscience, Goteborg University, Goteborg, Sweden. olof.zachrisson@neuro.gu.se	Treatment with staphylococcus toxoid in fibromyalgia/chronic fatigue syndrome--a randomised controlled trial.	Eur J Pain. 2002;6(6):455-66.	We have previously conducted a small treatment study on staphylococcus toxoid in fibromyalgia (FM) and chronic fatigue syndrome (CFS). The aim of the present study was to further assess the efficacy of the staphylococcus toxoid preparation Staphypan Berna (SB) during 6 months in FM/CFS patients. One hundred consecutively referred patients fulfilling the ACR criteria for FM and the 1994 CDC criteria for CFS were randomised to receive active drug or placebo. Treatment included weekly injections containing 0.1 ml, 0.2 ml, 0.3 ml, 0.4 ml, 0.6 ml, 0.8 ml, 0.9 ml, and 1.0 ml SB or coloured sterile water, followed by booster doses given 4-weekly until endpoint. Main outcome measures were the proportion of responders according to global ratings and the proportion of patients with a symptom reduction of > or =50% on a 15-item subscale derived from the comprehensive psychopathological rating scale (CPRS). The treatment was well tolerated. Intention-to-treat analysis showed 32/49 (65%) responders in the SB group compared to 9/49 (18%) in the placebo group (P<0.001). Sixteen patients (33%) in the SB group reduced their CPRS scores by at least 50% compared to five patients (10%) in the placebo group (P< 0.01). Mean change score on the CPRS (95% confidence interval) was 10.0 (6.7-13.3) in the SB group

				and 3.9 (1.1-6.6) in the placebo group (P<0.01). An increase in CPRS symptoms at withdrawal was noted in the SB group. In conclusion, treatment with staphylococcus toxoid injections over 6 months led to significant improvement in patients with FM and CFS. Maintenance treatment is required to prevent relapse.
Zachrisson O, Regland B, Jahreskog M, Kron M, Gottfries CG.	Psychiatry Section, Institute of Clinical Neuroscience, Goteborg University, Goteborg, Sweden. olof.zachrisson@neuro.gu.se	A rating scale for fibromyalgia and chronic fatigue syndrome (the FibroFatigue scale).	J Psychosom Res. 2002 Jun;52(6):501-9.	OBJECTIVE: To construct an observer's rating scale sensitive to change for measuring severity and treatment outcome in fibromyalgia (FM) and chronic fatigue syndrome (CFS) patients. METHODS: A selection of items from the Comprehensive Psychopathological Rating Scale (CPRS) were repeatedly rated and used as outcome measure of a 24-week treatment study. In the study 100 women, fulfilling the criteria for both FM and CFS, received intermittent injections of a staphylococcus toxoid or placebo. Nine CPRS-items with high baseline incidence (cutoff 70%) were extracted and validated against global ratings and the Fibromyalgia Impact Questionnaire (FIQ). The fibromyalgia and chronic fatigue syndrome rating scale (the FibroFatigue scale) was thereafter formed based upon the extracted items and three supplemented ones. The interrater reliability was tested in 27 consecutive patients of both sexes. RESULTS: The FibroFatigue scale is an observer's rating scale with 12 items measuring pain, muscular tension, fatigue, concentration difficulties, failing memory, irritability, sadness, sleep disturbances, and autonomic disturbances (items derived from the CPRS) and irritable bowel, headache, and subjective experience of infection (new items). There was a statistically significant correlation between the CPRS-extracted items and global ratings as well as with the FIQ. The interrater reliability of the new scale was excellent (correlation coefficient.98), irrespective of the patients' gender. CONCLUSION: The FibroFatigue scale seems to be a reliable and valid measuring instrument with capacity to monitor symptom severity and change during treatment of FM/CFS patients.
Zeman K, Lewandowicz-Uszynska A.	Zaklad Immunologii Klinicznej Instytutu Centrum Zdrowia Matki Polki i Zaklad Immunologii Klinicznej WAM w lodzi. zeman@achilles.wam.lodz.pl		Postepy Hig Med Dosw. 2002;56 Suppl:91-102. [Article in Polish]	The research connects usefulness of intravenous preparates of immunoglobulins in patients with secondary immunodeficiencies. Basing on the data of literature there was discussed the using IVIG in patients with HIV infection and with the chronic fatigue syndrome. There was also discussed the matt of using IVIG after multiorgans traumas, burns and operations with high risk complications.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Aaron LA, Buchwald D.	Department of Medicine, Division of Internal Medicine, Harborview Medical Center, 325 Ninth Avenue, Box 359780, Seattle, WA 98104, USA. laaron@u.washington.edu	A review of the evidence for overlap among unexplained clinical conditions.	Ann Intern Med. 2001 May 1;134(9 Pt 2):868-81.	PURPOSE: Unexplained clinical conditions share features, including symptoms (fatigue, pain), disability out of proportion to physical examination findings, inconsistent demonstration of laboratory abnormalities, and an association with "stress" and psychosocial factors. This literature review examines the nature and extent of the overlap among these unexplained clinical conditions and the limitations of previous research. DATA SOURCES: English-language articles were identified by a search of the MEDLINE database from 1966 to January 2001 by using individual syndromes and their hallmark symptoms as search terms. STUDY SELECTION: Studies that assessed patients with at least one unexplained clinical condition and that included information on symptoms, overlap with other unexplained clinical conditions, or physiologic markers. Conditions examined were the chronic fatigue syndrome, fibromyalgia, the irritable bowel syndrome, multiple chemical sensitivity, temporomandibular disorder, tension headache, interstitial cystitis, and the postconcussion syndrome. DATA EXTRACTION: Information on authorship, patient and control groups, eligibility criteria, case definitions, study methods, and major findings. DATA SYNTHESIS: Many similarities were apparent in case definition and symptoms, and the proportion of patients with one unexplained clinical condition meeting criteria for a second unexplained condition was striking. Tender points on physical examination and decreased pain threshold and tolerance were the most frequent and consistent objective findings. A major shortcoming of all proposed explanatory models is their inability to account for the occurrence of unexplained clinical conditions in many affected patients. CONCLUSIONS: Overlap between unexplained clinical conditions is substantial. Most studies are limited by methodologic problems, such as case definition and the selection and recruitment of case-patients and controls.
Aaron LA, Buchwald D.	Department of Medicine, Harborview Medical Center, 325 Ninth Avenue, Box 359780, Seattle, WA 98104, USA. laaron@u.washington.edu.	Fibromyalgia and other unexplained clinical conditions.	Curr Rheumatol Rep. 2001 Apr;3(2):116-22.	Several unexplained clinical conditions frequently coexist with fibromyalgia; these include chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorder, tension and migraine headaches, and others. However, only recently have studies directly compared the physiological parameters of these conditions (eg, fibromyalgia vs irritable bowel syndrome) to elucidate underlying pathogenic mechanisms. This review summarizes data from comparative studies and discusses their implications for future research.
Aaron LA, Herrell R, Ashton S, Belcourt M, Schmaling K, Goldberg J, Buchwald D.	Division of General Internal Medicine, Department of Medicine, University of Washington, Seattle, WA 98104, USA.	Comorbid clinical conditions in chronic fatigue: a co-twin control study.	J Gen Intern Med. 2001 Jan;16(1):24-31.	OBJECTIVES: Chronically fatiguing illness, defined as fatigue for at least 6 months, has been associated with various physical health conditions. Our objective was to determine whether there is a significant relationship between chronically fatiguing illness and 10 clinical conditions that frequently appear to be associated with fatigue, adjusting for the potentially confounding effects of psychiatric illness. DESIGN: A co-twin control study controlling for genetic and many environmental factors by comparing chronically fatigued twins with their nonfatigued co-twins. SETTING: A nationally distributed volunteer twin

	laaron@u.washington.edu			registry. PARTICIPANTS: The study included 127 twin pairs in which one member of the pair experienced fatigue of at least 6 months' duration and the co-twin was healthy and denied chronic fatigue. Fatigued twins were classified into 3 levels using increasingly stringent diagnostic criteria. MEASUREMENTS AND MAIN RESULTS: Twins reported on a history of fibromyalgia, irritable bowel syndrome, multiple chemical sensitivities, temporomandibular disorder, interstitial cystitis, postconcussion syndrome, tension headache, chronic low back pain, chronic pelvic pain (women), and chronic nonbacterial prostatitis (men). The prevalence of these comorbid clinical conditions was significantly higher in the fatigued twins compared to their nonfatigued co-twins. Most notably, compared to their nonfatigued co-twins, the chronically fatigued twins had higher rates of fibromyalgia (> 70% vs < 10%) and irritable bowel syndrome (> 50% vs < 5%). The strongest associations were observed between chronic fatigue and fibromyalgia (odds ratios > 20), irritable bowel syndrome, chronic pelvic pain, multiple chemical sensitivities, and temporomandibular disorder (all with odds ratios > or = 4). Regression analysis suggested that the number of comorbid clinical conditions associated with chronic fatigue could not be attributed solely to psychiatric illness. CONCLUSIONS: Chronically fatiguing illnesses were associated with high rates of many other clinical conditions. Thus, patients with chronic fatigue may present a complex clinical picture that poses diagnostic and management challenges. Nonetheless, clinicians should assess such patients for the presence of comorbid clinical conditions. Future research should provide a better understanding of the temporal relationship of the onset of fatigue and these conditions, and develop strategies for early intervention.
Addington AM, Gallo JJ, Ford DE, Eaton WW.	Department of Mental Hygiene, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD 21205, USA.	Epidemiology of unexplained fatigue and major depression in the community: the Baltimore ECA follow-up, 1981-1994.	Psychol Med. 2001 Aug;31(6):1037-44.	BACKGROUND: Fatigue is a common, non-specific, subjective symptom associated with several medical and psychiatric illnesses. The purpose of this investigation was to explore further the epidemiology of unexplained fatigue in the general population and the relationship between fatigue and depression. METHODS: The design was a prospective population-based study. Subjects included community-dwelling adults who were participants of the Baltimore sample of the Epidemiologic Catchment Area Program in 1981 and who were reinterviewed 13 years later. Lay interviewers using the Diagnostic Interview Schedule interviewed subjects. RESULTS: Number of somatization symptoms and history of a dysphoric episode at baseline were the two strongest predictors of both new onset of fatigue as well as recurrent/chronic fatigue over the 13-year follow-up interval. In addition, individuals who reported a history of unexplained fatigue at baseline as well as during the follow-up, were at markedly increased risk for new onset major depression as compared to those who never reported such fatigue, (RR = 28.4, 95% CI) (11.7, 68.0). Similarly, respondents who developed new fatigue or had remitted fatigue after 1981 were also at increased risk for developing major depression. CONCLUSIONS: Somatization was the strongest predictor of both new and chronic fatigue with unknown cause. In addition, fatigue was both predictive and a consequence of the depression syndrome.
Akagi H, Klimes I,	Leeds General	Cognitive behavioral	Gen Hosp Psychiatry.	Cognitive behavior therapy (CBT) has been shown to be effective in recent randomized

Bass C.	Infirmary, Leeds, UK.	therapy for chronic fatigue syndrome in a general hospital--feasible and effective.	2001 Sep-Oct;23(5):254-60.	controlled trials for chronic fatigue syndrome (CFS). We examined the effectiveness of CBT in a general hospital setting in a retrospective questionnaire follow-up study of 94 patients offered CBT by liaison psychiatry services. The questionnaire response rate was 61%. Eighteen percent had returned to normal functioning at follow-up. For the group as a whole, there was a significant improvement in the functional and social impairment and the number of frequently experienced symptoms. Those in work or study at follow-up was 53% (29% pretreatment), and 65% of patients mentioned occupational stress as a contributory factor in their illness. There was a significant reduction in the frequency of attendance at primary care in the year after the end of CBT. We conclude that cognitive behavioral therapy is an acceptable treatment for most patients and can be used in a general hospital outpatient setting by a variety of trained therapists. However, a proportion of patients do not benefit and remain significantly disabled by the condition.
Altemus M, Dale JK, Michelson D, Demitrack MA, Gold PW, Straus SE.	Weill Medical College, Cornell University, Box 244, 1300 York Avenue, New York, NY 10021, USA. maltemus@mail.med.cornell.edu	Abnormalities in response to vasopressin infusion in chronic fatigue syndrome.	Psychoneuroendocrinology. 2001 Feb;26(2):175-88.	Several neuroendocrine studies have suggested hypoactivation of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome. One possible determinant of this neuroendocrine abnormality, as well as the primary symptom of fatigue, is reduced hypothalamic secretion of corticotropin-releasing hormone (CRH). Because CRH and vasopressin secreted from the hypothalamus act synergistically at the pituitary to activate ACTH secretion, the ACTH response to peripheral infusion of vasopressin can provide an indirect measure of hypothalamic CRH secretion. We measured the ACTH and cortisol response to a one hour infusion of arginine vasopressin in 19 patients with chronic fatigue syndrome and 19 age and sex matched healthy volunteers. Patients with chronic fatigue syndrome had a reduced ACTH response to the vasopressin infusion and a more rapid cortisol response to the infusion. These results provide further evidence of reduced hypothalamic CRH secretion in patients with chronic fatigue syndrome.
Anderberg UM.	Centrum for miljorelaterad ohalsa och stress (CEOS), institutionen for folkhalso- och vardvetenskap, enheten for socialmedicin, Uppsala universitet, Akademiska sjukhuset, Uppsala. ullamaria.anderberg@socmed.uu.se	[Stress-related syndromes--contemporary illnesses] [Article in Swedish]	Lakartidningen. 2001 Dec 19;98(51-52):5860-3.	There are many indications that distress within the family as well as at work are strong predictors for developing stress-related disorders. The relatively new diagnoses burnout, chronic fatigue syndrome and fibromyalgia syndrome probably represent different ways of reacting to an overwhelming situation. The boundary between these diseases, on the one hand, and depression, heart disease or infarction on the other is often diffuse, and the new diagnoses may well delineate preliminary stages of more serious diseases such as angina pectoris or myocardial infarction. There is evidence that also other causes of death may be related to stress. These circumstances reflect not only considerable suffering on the part of individuals, but also a substantial economic burden for society.
Anon		DHEA. Monograph.	Altern Med Rev. 2001 Jun;6(3):314-8.	Dehydroepiandrosterone (DHEA) is a steroid hormone secreted primarily by the adrenal glands and to a lesser extent by the brain, skin, testes, and ovaries. It is the most abundant circulating steroid in humans and can be converted into other hormones, including

				estrogen and testosterone. It has been characterized as a pleiotropic "buffer hormone," with receptor sites in the liver, kidney, and testes, and has a key role in a wide range of physiological responses. Circulating levels of DHEA decline with age and a relationship has been suggested between lower DHEA levels and heart disease, cancer, diabetes, obesity, chronic fatigue syndrome, AIDS, and Alzheimer's disease. Other research suggests that autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and multiple sclerosis might be associated with declining DHEA levels.
Anon		Bibliography. Current world literature. Nonarticular rheumatism, sports-related injuries, and related conditions.	Curr Opin Rheumatol. 2001 Mar;13(2):B30-41.	
Anon		Defining and managing chronic fatigue syndrome.	Evid Rep Technol Assess (Summ). 2001 Sep;(42):1-4.	
Asbring P.	Centre for Development of Health Services, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden. pia.asbring@smd.sll.se	Chronic illness -- a disruption in life: identity-transformation among women with chronic fatigue syndrome and fibromyalgia.	J Adv Nurs. 2001 May;34(3):312-9.	BACKGROUND: People with chronic illnesses often suffer from identity-loss. Empirical research concerning patients with chronic fatigue syndrome (CFS) or fibromyalgia has not, however, adequately addressed the consequences of these illnesses for identity. AIM: The aim of this article is to describe how women with CFS and fibromyalgia create new concepts of identity after the onset of illness, and how they come to terms with their newly arisen identities. I aim to illuminate the biographical work done by these individuals, which includes a re-evaluation of their former identity and life. This process is illustrated by the following themes: An earlier identity partly lost and Coming to terms with a new identity. METHOD: The study is based on interviews with 25 women in Sweden, 12 with the diagnosis of CFS and 13 diagnosed with fibromyalgia. A grounded theory orientated approach was used when collecting and analysing the data. FINDINGS: The main findings are that: (1) the illnesses can involve a radical disruption in the women's biography that has profound consequences for their identity, particularly in relation to work and social life, (2) biographical disruptions are partial rather than total, calling for different degrees of identity transformation, (3) many of the women also experience illness gains in relation to the new identity. CONCLUSIONS: Thus, the biographical disruption and illness experience comprised both losses and illness gains that had consequences for identity.
Ax S, Gregg VH, Jones D.	Liverpool John Moores University. heasax@yahoo.com	Coping and illness cognitions: chronic fatigue syndrome.	Clin Psychol Rev. 2001 Mar;21(2):161-82.	The chronic fatigue syndrome (CFS) is described, and research on coping with this illness reviewed and analysed. CFS is a severely disabling illness of unknown etiology, which has occurred in epidemic forms all over the world. However, the number of sufferers has dramatically increased over previous years. The heterogeneous symptomatology of CFS was reviewed, and diagnostic criteria were discussed. The difficulty in establishing causality was emphasized. An interaction of factors appears most likely to be associated with illness onset and maintenance. As the mediating factor could be sufferers' coping behavior, the

				existing coping literature was reviewed. There might be an association between coping and physical and psychological well-being. Finally, recommendations are made for longitudinal research on coping and coping effectiveness, and for the development of therapeutic interventions.
Banks J, Prior L.	Cardiff University School of Social Sciences, Cardiff CF10 3WT, UK.	Doing things with illness. The micro politics of the CFS clinic.	Soc Sci Med. 2001 Jan;52(1):11-23.	This paper focuses on lay and professional ideas about the nature of chronic fatigue syndrome (CFS), and in particular, the ways in which understandings of the disorder are developed in a clinical setting. Our data are drawn from observations of consultations between sufferers and physicians in a UK medical out-patients clinic. We treat the clinic as a political field. That is to say, as an arena in which 'problems' (about the management of illness) are constituted, and alternative approaches and solutions to such problems are pressed. We note that in the realms of symptoms, aetiology and treatment evaluation, lay people in the CFS clinic have quite distinct ideas about what their problems are and how they might be analysed and managed--ideas that are often in conflict with those of medical professionals. Thus, lay sufferers, for example, operate within a different conceptual terrain from that of many professional experts. They are more likely to refer to a disease (myalgic encephalomyelitis or ME), rather than a syndrome. They call upon different kinds of hypotheses to explain their symptoms. They hold to conflicting ideas about the order of causal sequences, and they give emphasis to different kinds of phenomena in their accounts of illness. As a consequence, clinical consultations can often take on the form of a political contest between physician and patient to define the true and real nature of the patient's disorder--a micro political struggle in which neurological symptoms can be re-framed as psychiatric symptoms, and psychiatric symptoms as neurological. In short, a contest in which the demarcation lines between mind and body are continually assessed and re-defined, and the tenets of 'biomedicine' are constantly challenged.
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Baschetti R.		Cognitive behaviour therapy and chronic fatigue syndrome.	Br J Gen Pract. 2001 Apr;51(465):316-7. Comment on: Br J Gen Pract. 2001 Jan;51(462):19-24.	
Baschetti R.		Orthostatic hypotension and chronic fatigue syndrome.	JAMA. 2001 Mar 21;285(11):1441-2; author reply 1443. Comment on: JAMA. 1996 Feb 7;275(5):359; author reply 360.	

Baschetti R.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):240; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Bass C.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1889. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
Bateman C.		Unscrupulous get fat on yuppie flu.	S Afr Med J. 2001 Jan;91(1):24-5.	
Bazelmans E, Bleijenberg G, Van Der Meer JW, Folgering H.	Department of Medical Psychology, University of Nijmegen, The Netherlands.	Is physical deconditioning a perpetuating factor in chronic fatigue syndrome? A controlled study on maximal exercise performance and relations with fatigue, impairment and physical activity.	Psychol Med. 2001 Jan;31(1):107-14.	BACKGROUND: Chronic fatigue syndrome (CFS) patients often complain that physical exertion produces an increase of complaints, leading to a greater need for rest and more time spent in bed. It has been suggested that this is due to a bad physical fitness and that physical deconditioning is a perpetuating factor in CFS. Until now, studies on physical deconditioning in CFS have shown inconsistent results. METHODS: Twenty CFS patients and 20 matched neighbourhood controls performed a maximal exercise test with incremental load. Heart rate, blood pressure, respiratory tidal volume, O2 saturation, O2 consumption, CO2 production, and blood-gas values of arterialized capillary blood were measured. Physical fitness was quantified as the difference between the actual and predicted ratios of maximal workload versus increase of heart rate. Fatigue, impairment and physical activity were assessed to study its relationship with physical fitness. RESULTS: There were no statistically significant differences in physical fitness between CFS patients and their controls. Nine CFS patients had a better fitness than their control. A negative relationship between physical fitness and fatigue was found in both groups. For CFS patients a negative correlation between fitness and impairment and a positive correlation between fitness and physical activity was found as well. Finally, it was found that more CFS patients than controls did not achieve a physiological limitation at maximal exercise. CONCLUSIONS: Physical deconditioning does not seem a perpetuating factor in CFS.
Bell DS, Jordan K, Robinson M.	Primary Care Pediatrics, Lyndonville, New York, USA.	Thirteen-year follow-up of children and adolescents with chronic fatigue syndrome.	Pediatrics. 2001 May;107(5):994-8.	OBJECTIVE: To describe the educational, social, and symptomatic outcome of children and adolescents with chronic fatigue syndrome 13 years after illness onset. METHODS: Between January 1984 and December 1987, 46 children and adolescents developed an illness suggestive of chronic fatigue syndrome. Follow-up questionnaires were obtained from 35 participants an average of 13 years after illness onset. Data were obtained concerning subsequent medical diagnoses, amount of school missed, presence and severity of current symptoms, and subjective assessment of degree of illness resolution. RESULTS: Of the 35 participants, 24 were female (68.6%) and 11 were male (31.4%). Average age at illness onset was 12.1 years. Eight participants (22.9%) had an acute onset

				of symptoms, 27 (77.1%) had a gradual onset. No participant received an alternative medical diagnosis that could have explained the symptom complex between illness onset and follow-up. Thirteen participants (37.1%) considered themselves resolved of illness at follow-up; 15 participants (42.9%) considered themselves well but not resolved; 4 (11.4%) considered themselves chronically ill; and 3 (8.6%) considered themselves more ill than during the early years of illness. Correlation with the Medical Outcomes Study Short Form Health Survey was good for current level of symptoms and degree of recovery. Eight participants (22.9%) missed >2 years of school, and 5 of these were still ill at follow-up. Amount of school missed correlated with both illness severity at follow-up and perceived social impact of the illness. CONCLUSIONS: These data demonstrate the presence of an illness consistent with the current definition of chronic fatigue syndrome. Eighty percent of children and adolescents affected had a satisfactory outcome from their fatiguing illness, although the majority of these participants had mild to moderate persisting symptoms. Twenty percent of participants remain ill with significant symptoms and activity limitation 13 years after illness onset. Chronic fatigue syndrome in children and adolescents may result in persistent somatic symptoms and disability in a minority of those affected.
Bell IR, Baldwin CM, Stoltz E, Walsh BT, Schwartz GER.		Concomitant Environmental Chemical Intolerance Modifies the Neurobehavioral Presentation of Women with Fibromyalgia	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 3	Background: This study compared personality, dietary, and psychophysiological characteristics of 3 groups of women: fibromyalgia (FM) with illness from low levels of environmental chemicals (chemical intolerance, CI), FM alone without CI, and normal controls. CI may be a marker for enhanced central nervous system response amplification (sensitization) in limbic and mesolimbic pathways, which play a role in hedonic responses to food and drugs and in pain. Method: Fibromyalgic women with (FM/CI, n = 11) and without CI (FM, n = 10) and normals (NORM, n = 10) participated in the study. Measures included psychological trait questionnaires, a food frequency questionnaire, a taste test for hedonic and sweetness ratings of different sucrose concentrations, pain self-ratings, and resting spectral electroencephalographic alpha over midline sites, averaged over four separate days. Results: FM with CI had the highest scores on the Harm Avoidance dimension of the Tridimensional Personality Questionnaire, Carbohydrate Addicts Test, Limbic Symptom sensory and behavior subscales, and SCL-90-R somatization and obsessiveness subscales. FM groups both had the highest mean pain ratings for 21 tender point sites. Groups did not differ for macronutrient intake or for sweetness and hedonic ratings for sucrose. The combined FM groups had greater EEG alpha activity towards posterior midline sites than did normals. Conclusion: The pattern of findings may reflect impaired serotonergic function and/or elevated dopaminergic receptor activation by endogenous and/or exogenous agents. The data could have implications for pharmacological and dietary interventions in different subsets of FM patients.
Bested AC, Saunders PR, Logan AC.	Environmental Health Clinic, Sunnybrook and Women's College, Health	Chronic fatigue syndrome: neurological findings may be related to	Med Hypotheses. 2001 Aug;57(2):231-7.	Despite volumes of international research, the etiology of chronic fatigue syndrome (CFS) remains elusive. There is, however, considerable evidence that CFS is a disorder involving the central nervous system (CNS). It is our hypothesis that altered permeability of the blood-brain barrier (BBB) may contribute to ongoing signs and symptoms found in CFS. To

	Sciences Centre, Toronto, Canada.	blood--brain barrier permeability.		support this hypothesis we have examined agents that can increase the blood-brain barrier permeability (BBBP) and those that may be involved in CFS. The factors which can compromise the normal BBBP in CFS include viruses, cytokines, 5-hydroxytryptamine, peroxynitrite, nitric oxide, stress, glutathione depletion, essential fatty acid deficiency, and N-methyl-D-aspartate overactivity. It is possible that breakdown of normal BBBP leads to CNS cellular dysfunction and disruptions of neuronal transmission in CFS. Abnormal changes in BBBP have been linked to a number of disorders involving the CNS; based on review of the literature we conclude that the BBB integrity in CFS warrants investigation. Copyright 2001 Harcourt Publishers Ltd.
Binder LM, Storzbach D, Campbell KA, Rohlman DS, Anger WK; Members of the Portland Environmental Hazards Research Center.	Oregon Health Sciences University, Portland, USA. Larry_Binder@email.msn.com	Neurobehavioral deficits associated with chronic fatigue syndrome in veterans with Gulf War unexplained illnesses.	J Int Neuropsychol Soc. 2001 Nov;7(7):835-9.	Gulf War unexplained illnesses (GWUI) are a heterogeneous collection of symptoms of unknown origin known to be more common among veterans of the Gulf War than among nonveterans. In the present study we focused on one of these unexplained illnesses. We tested the hypothesis that in a sample of Persian Gulf War veterans chronic fatigue syndrome (CFS) was associated with cognitive deficits on computerized cognitive testing after controlling for the effects of premorbid cognitive differences. We obtained Armed Forces Qualification Test (AFQT) data acquired around the date of induction into the military on 94 veterans of the Gulf War, 32 with CFS and 62 healthy controls. Controls performed better than participants diagnosed with CFS on the AFQT. Cognitive deficits were associated with CFS on 3 of 8 variables after the effect of premorbid AFQT scores was removed with ANCOVA.
Bourdette DN, McCauley LA, Barkhuizen A, Johnston W, Wynn M, Joos SK, Storzbach D, Shuell T, Sticker D.	Portland Veterans Affairs Medical Center, Department of Neurology, Mailcode P-3-NEURO, 3710 SW US Veteran's Hospital Road, Portland, OR 97201, USA. Dennis.Bourdette@med.va.gov	Symptom factor analysis, clinical findings, and functional status in a population-based case control study of Gulf War unexplained illness.	J Occup Environ Med. 2001 Dec;43(12):1026-40.	Few epidemiological studies have been conducted that have incorporated clinical evaluations of Gulf War veterans with unexplained health symptoms and healthy controls. We conducted a mail survey of 2022 Gulf War veterans residing in the northwest United States and clinical examinations on a subset of 443 responders who seemed to have unexplained health symptoms or were healthy. Few clinical differences were found between cases and controls. The most frequent unexplained symptoms were cognitive/psychological, but significant overlap existed with musculoskeletal and fatigue symptoms. Over half of the veterans with unexplained musculoskeletal pain met the criteria for fibromyalgia, and a significant portion of the veterans with unexplained fatigue met the criteria for chronic fatigue syndrome. Similarities were found in the clinical interpretation of unexplained illness in this population and statistical factor analysis performed by this study group and others.
Brewer JH, Berg D.		Hypercoaguable State Associated with Active Human Herpesvirus-6 (HHV-6) Viremia in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 111	Objectives: A subset of patients with Chronic Fatigue Syndrome (CFS) have been found to be hypercoaguable in small previous studies. We wanted to analyze the incidence of a hypercoaguable state and assess hereditary hypercoaguable risk factors in a group of patients with known CFS and HHV-6 viremia. Methods: Thirty patients diagnosed with CFS that had at least one prior positive blood culture for active HHV-6 by rapid culture method were studied. A hypercoaguable panel was obtained to assess activation of coagulation. Two or more positive tests were determined to represent activation of coagulation. Hereditary thrombosis risk panels were also performed which included eight different

				genetic tests to assess hereditary abnormalities. Results: Twenty-four of thirty (80%) patients had a hypercoaguable state, thus activation of coagulation. Twenty-five of thirty (83%) of patients had a hereditary abnormality. Conclusions: CFS patients with active HHV-6 infection (viremia) have activation of coagulation and are hypercoaguable. Hereditary thrombosis risk factors are very prevalent in these patients. These hereditary abnormalities increase the hypercoaguable tendencies. The hypercoaguable state associated with active HHV-6 infection may be a significant contributing factor to the symptoms seen in CFS patients.
Brunet JL, Liaudet AP, Later R, Peyramond D, Cozon GJ.	Infectious Diseases Department-Hopital de la Croix-Rousse-69317 Lyon, France.	Delayed-type hypersensitivity and chronic fatigue syndrome: the usefulness of assessing T-cell activation by flow cytometry--preliminary study.	Allerg Immunol (Paris). 2001 Apr;33(4):166-72.	Chronic fatigue syndrome or benign myalgic encephalomyelitis has been extensively described and investigated. Although numerous immunological abnormalities have been linked with the syndrome, none have been found to be specific. This article describes the detection of delayed-type hypersensitive responses to certain common environmental antigens in almost fifty per cent of patients with this syndrome. Such hypersensitivity can be detected by the intradermal administration of antigens derived from commensal organisms like the yeast Candida albicans albicans, and then monitoring for a systemic reaction over the following six to forty-eight hours. This approach can be consolidated by performing lymphocyte activation tests in parallel and measuring in vitro T-cell activation by Candida albicans albicans antigens by three-colour flow cytometry based on CD3, CD4 and either CD69 or CD25. Another useful parameter is the kinetics of neopterin excretion in the urine over the course of the skin test. The results showed that the intensity of the DTH response correlated with the number of T-cells activated in vitro. Various factors have been implicated in the fatigue of many patients, notably lack of sleep. However, it remains difficult to establish causality in either one direction or the other. This work is in the spirit of a multifactorial approach to the group of conditions referred to as "chronic fatigue syndrome".
Buchwald D, Herrell R, Ashton S, Belcourt M, Schmaling K, Sullivan P, Neale M, Goldberg J.	Department of Medicine, University of Washington, Seattle, WA, USA. dedra@u.washington.edu	A twin study of chronic fatigue.	Psychosom Med. 2001 Nov-Dec;63(6):936-43.	OBJECTIVE: The etiology of chronic fatigue syndrome is unknown, but genetic influences may be important in its expression. Our objective was to assess the role of genetic and environmental factors in unexplained chronic fatigue. METHODS: A classic twin study was conducted using 146 female-female twin pairs, of whom at least one member reported > or =6 months of fatigue. After completing questionnaires on symptoms, zygosity, physical health, and a psychiatric interview, twins were classified using three increasingly stringent definitions: 1) chronic fatigue for > or =6 months, 2) chronic fatigue not explained by exclusionary medical conditions, and 3) idiopathic chronic fatigue not explained by medical or psychiatric exclusionary criteria of the chronic fatigue syndrome case definition. Concordance rates in monozygotic and dizygotic twins were calculated for each fatigue definition along with estimates of the relative magnitude of genetic and environmental influences on chronic fatigue. RESULTS: The concordance rate was higher in monozygotic than dizygotic twins for each definition of chronic fatigue. For idiopathic chronic fatigue, the concordance rates were 55% in monozygotic and 19% in dizygotic twins (p =.042). The estimated heritability in liability was 19% (95% confidence interval = 0-56) for chronic

				fatigue > or =6 months, 30% (95% confidence interval = 0-81) for chronic fatigue not explained by medical conditions, and 51% (95% confidence interval = 7-96) for idiopathic chronic fatigue. CONCLUSIONS: These results provide evidence supporting the familial aggregation of fatigue and suggest that genes may play a role in the etiology of chronic fatigue syndrome.
Buskila D, Press J.	Rheumatic Disease Unit and Department of Medicine 'B', Soroka Medical Centre and Ben-Gurion University, Beer-Sheva, 84101, Israel.	Neuroendocrine mechanisms in fibromyalgia-chronic fatigue.	Best Pract Res Clin Rheumatol. 2001 Dec;15(5):747-58.	Fibromyalgia and chronic fatigue syndrome are poorly understood disorders that share similar demographic and clinical characteristics. Because of the clinical similarities between both disorders it was suggested that they share a common pathophysiological mechanism, namely, central nervous system dysfunction. This chapter presents data demonstrating neurohormonal abnormalities, abnormal pain processing and autonomic nervous system dysfunction in fibromyalgia and chronic fatigue syndrome. The possible contribution of the central nervous system dysfunction to the development and symptomatology of these conditions is discussed. The chapter concludes by reviewing the effect of current treatments and emerging therapeutic modalities in fibromyalgia and chronic fatigue syndrome. Copyright 2001 Harcourt Publishers Ltd.
Buskila D.	Ben Gurion University of the Negev, Faculty of Health Sciences, Soroka Medical Center, Beer Sheva, Israel.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol. 2001 Mar;13(2):117-27.	The prevalence of chronic widespread pain in the general population in Israel was comparable with reports from the USA, UK, and Canada. Comorbidity with fibromyalgia (FM) resulted in somatic hyperalgesia in patients with irritable bowel syndrome. One sixth of the subjects with chronic widespread pain in the general population were also found to have a mental disorder. Mechanisms involved in referred pain, temporal summation, muscle hyperalgesia, and muscle pain at rest were attenuated by the N-methyl-D-aspartate (NMDA) antagonist, ketamine, in FM patients. Delayed corticotropin release, after interleukin-6 administration, in FM was shown to be consistent with a defect in hypothalamic corticotropin-releasing hormone neural function. The basal autonomic state of FM patients was characterized by increased sympathetic and decreased parasympathetic systems tones. The severity of functional impairment as assessed by the Medical Outcome Survey Short Form (SF-36) discriminated between patients with widespread pain alone and FM patients. Chronic fatigue syndrome (CFS) occurred in about 0.42% of a random community-based sample of 28,673 adults in Chicago, Illinois. A significant clinical overlap between CFS and FM was reported. Cytokine dysregulation was not found to be a singular or dominant factor in the pathogenesis of CFS. A favorable outcome of CFS in children was reported; two thirds recovered and resumed normal activities. No major therapeutic trials in FM and CFS were reported over the past year.
Butler JA, Chalder T, Wessely S.	Department of Psychological Medicine, Maudsley Hospital, London.	Causal attributions for somatic sensations in patients with chronic fatigue syndrome and their partners.	Psychol Med. 2001 Jan;31(1):97-105.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) often make somatic attributions for their illness which has been associated with poor outcome. A tendency to make somatic attributions in general may be a vulnerability factor for the development of CFS. METHODS: This cross-sectional study based on self-report questionnaire data aimed to investigate the type of attributions for symptoms made by patients with CFS and to compare this to attributions made by their partners. It was hypothesized that patients with CFS would make more somatic attributions for their own symptoms than control subjects

				and that partners of patients with CFS would make more somatic attributions for their ill relative's symptoms but would be similar to controls regarding their own symptoms. Fifty patients with CFS were compared to 50 controls from a fracture clinic in the same hospital and 46 relatives living with the patients with CFS. A modified Symptom Interpretation Questionnaire was used to assess causal attributions. RESULTS: CFS patients were more likely to make somatic attributions for their symptoms. The relatives of patients with CFS made significantly more somatic attributions for symptoms in their ill relative. However, they were like the fracture clinic controls in terms of making predominantly normalizing attributions for their own symptoms. CONCLUSIONS: The data support modification of existing cognitive behavioural treatments for CFS to investigate whether addressing partners' attributions for patients' symptoms improves recovery in the patient. Furthermore, a tendency to make somatic attributions for symptoms may be a vulnerability factor for the development of CFS.
Caserta MT, Mock DJ, Dewhurst S.	Department of Pediatrics, University of Rochester Medical Center, Rochester, NY 14642, USA.	Human herpesvirus 6.	Clin Infect Dis. 2001 Sep 15;33(6):829-33. Epub 2001 Aug 10.	The development of techniques for the culture of lymphoid cells and the isolation of viruses that infect these cells led to the discovery of human herpesvirus (HHV) 6 in 1986. At the time, HHV-6 was the first new human herpesvirus to be discovered in roughly a quarter of a century, and its isolation marked the beginning of an era of discovery in herpesvirology, with the identification of HHV-7 and HHV-8 (Kaposi's sarcoma-associated herpesvirus) during the following decade. Like most human herpesviruses, HHV-6 is ubiquitous and capable of establishing a lifelong, latent infection of its host. HHV-6 is particularly efficient at infecting infants and young children, and primary infection with the virus is associated with roseola infantum (exanthem subitum) and, most commonly, an undifferentiated febrile illness. Viral reactivation in the immunocompromised host has been linked to a variety of diseases, including encephalitis, and HHV-6 has been tentatively associated with multiple sclerosis. This article discusses the major properties of HHV-6, its association with human disease, and the pathobiological significance of viral reactivation.
Chaudhuri A.		Patient education to encourage graded exercise in chronic fatigue syndrome. Trial has too many shortcomings.	BMJ. 2001 Jun 23;322(7301):1545-6. Comment on: BMJ. 2001 Feb 17;322(7283):387-90.	
Chaudhuri A.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):238; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Clauw DJ.	Georgetown Chronic Pain and Fatigue	Potential mechanisms in chemical	Ann N Y Acad Sci. 2001 Mar;933:235-	The symptom of chemical intolerance may occur in isolation, but often occurs in conjunction with other chronic symptoms such as pain, fatigue, memory disturbances, etc.

	Research Center, Department of Medicine, Georgetown University Medical Center, Washington, District of Columbia 20007, USA.	intolerance and related conditions.	53.	This frequent clustering of symptoms in individuals has led to the definition of several chronic multisymptom syndromes, such as multiple chemical sensitivity, fibromyalgia, chronic fatigue syndrome, and Gulf War illnesses. The aggregate research into these syndromes has suggested some unifying mechanisms that contribute to symptomatology. Multiple lines of evidence suggest that there is aberrant function of numerous efferent neural pathways, such as the autonomic nervous system and hypothalamic-pituitary axes, in subsets of individuals with these conditions. There is perhaps the greatest evidence for abnormal sensory processing in these syndromes, with a low "unpleasantness threshold" for multiple types of sensory stimuli. Psychological and behavioral factors are known to play a significant role in initiating or perpetuating symptoms in some persons with these illnesses. In the field of pain research, the interrelationship between physiologic and psychologic factors in symptom expression has been well studied. Using both established and novel methodologies, studies have suggested that psychologic factors such as hypervigilance and expectancy are playing a relatively minor role in most individuals with fibromyalgia and that clear evidence exists of physiologic amplification of sensory stimuli. These studies need to be extended to more sensory tasks and to larger numbers of subjects with related conditions. It is of note, though, that existing data on this spectrum of illnesses would suggest that there may be greater psychologic contributions to symptomatology if an illness is defined in part by behavior (e.g., avoidance of chemical exposures) rather than on the basis of symptoms alone.
Claypoole K, Mahurin R, Fischer ME, Goldberg J, Schmaling KB, Schoene RB, Ashton S, Buchwald D.	Departments of Psychiatry and Behavioral Sciences, University of Washington, Seattle, Washington, USA.	Cognitive compromise following exercise in monozygotic twins discordant for chronic fatigue syndrome: fact or artifact?	Appl Neuropsychol. 2001;8(1):31-40.	This study examined the effects of exhaustive exercise on cognitive functioning among 21 monozygotic twin pairs discordant for chronic fatigue syndrome (CFS). The co-twin control design adjusts for genetic and family environmental factors not generally accounted for in more traditional research designs of neuropsychological function. Participants pedaled a cycle ergometer to exhaustion; maximum oxygen output capacity (VO2max) as well as perceived exertion were recorded. Neuropsychological tests of brief attention and concentration, speed of visual motor information processing, verbal learning and recognition memory, and word and category fluency were administered with alternate forms to participants pre- and postexercise. The preexercise neuropsychological test performance of CFS twins tended to be slightly below that of the healthy twin controls on all measures. However, twins with CFS did not demonstrate differential decrements in neuropsychological functioning after exercise relative to their healthy co-twins. Because exercise does not appear to diminish cognitive function, rehabilitative treatment approaches incorporating exercise are not contraindicated in CFS.
Cleare AJ, Blair D, Chambers S, Wessely S.	Department of Psychological Medicine, Guy's King's and St. Thomas' School of Medicine and the	Urinary free cortisol in chronic fatigue syndrome.	Am J Psychiatry. 2001 Apr;158(4):641-3.	OBJECTIVE: The authors measured 24-hour urinary free cortisol in a group of well-characterized patients with chronic fatigue syndrome. METHOD: They obtained 24-hour urine collections from 121 consecutive clinic patients with chronic fatigue syndrome and 64 comparison subjects without the syndrome. RESULTS: Urinary free cortisol was significantly lower in the subjects with chronic fatigue syndrome regardless of the presence or absence of current or past comorbid psychiatric illness. Lower levels of urinary free

	Institute of Psychiatry, 103 Denmark Hill, London SE5 8AZ, UK. a.cleare@iop.kcl.ac.uk			cortisol were not related to medication use, sleep disturbance, or disability levels. CONCLUSIONS: There is mild hypocortisolism in chronic fatigue syndrome. Whether a primary feature or secondary to other factors, hypocortisolism may be one factor contributing to the symptoms of chronic fatigue syndrome.
Cleare AJ, Miell J, Heap E, Sookdeo S, Young L, Malhi GS, O'Keane V.	Department of Psychological Medicine, Institute of Psychiatry and Guy's, King's and St Thomas' School of Medicine, London SE5 8AZ, United Kingdom. a.cleare@iop.kcl.ac.uk	Hypothalamo-pituitary-adrenal axis dysfunction in chronic fatigue syndrome, and the effects of low-dose hydrocortisone therapy.	J Clin Endocrinol Metab. 2001 Aug;86(8):3545-54.	These neuroendocrine studies were part of a series of studies testing the hypotheses that 1) there may be reduced activity of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome and 2) low-dose augmentation with hydrocortisone therapy would improve the core symptoms. We measured ACTH and cortisol responses to human CRH, the insulin stress test, and D-fenfluramine in 37 medication-free patients with CDC-defined chronic fatigue syndrome but no comorbid psychiatric disorders and 28 healthy controls. We also measured 24-h urinary free cortisol in both groups. All patients (n = 37) had a pituitary challenge test (human CRH) and a hypothalamic challenge test [either the insulin stress test (n = 16) or D-fenfluramine (n = 21)]. Baseline cortisol concentrations were significantly raised in the chronic fatigue syndrome group for the human CRH test only. Baseline ACTH concentrations did not differ between groups for any test. ACTH responses to human CRH, the insulin stress test, and D- fenfluramine were similar for patient and control groups. Cortisol responses to the insulin stress test did not differ between groups, but there was a trend for cortisol responses both to human CRH and D-fenfluramine to be lower in the chronic fatigue syndrome group. These differences were significant when ACTH responses were controlled. Urinary free cortisol levels were lower in the chronic fatigue syndrome group compared with the healthy group. These results indicate that ACTH responses to pituitary and hypothalamic challenges are intact in chronic fatigue syndrome and do not support previous findings of reduced central responses in hypothalamic-pituitary-adrenal axis function or the hypothesis of abnormal CRH secretion in chronic fatigue syndrome. These data further suggest that the hypocortisolism found in chronic fatigue syndrome may be secondary to reduced adrenal gland output. Thirty-two patients were treated with a low-dose hydrocortisone regime in a double-blind, placebo-controlled cross-over design, with 28 days on each treatment. They underwent repeated 24-h urinary free cortisol collections, a human CRH test, and an insulin stress test after both active and placebo arms of treatment. Looking at all subjects, 24-h urinary free cortisol was higher after active compared with placebo treatments, but 0900-h cortisol levels and the ACTH and cortisol responses to human CRH and the insulin stress test did not differ. However, a differential effect was seen in those patients who responded to active treatment (defined as a reduction in fatigue score to the median population level or less). In this group, there was a significant increase in the cortisol response to human CRH, which reversed the previously observed blunted responses seen in these patients. We conclude that the improvement in fatigue seen in some patients with chronic fatigue syndrome during hydrocortisone treatment is accompanied by a reversal of the blunted

				cortisol responses to human CRH.
Cleare AJ, O'Keane V, Miell J.	Department of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine, 103 Denmark Hill, London SE3 8AF, UK. a.cleare@iop.kcl.ac.uk	Plasma leptin in chronic fatigue syndrome and a placebo-controlled study of the effects of low-dose hydrocortisone on leptin secretion.	Clin Endocrinol (Oxf). 2001 Jul;55(1):113-9.	OBJECTIVE: Previous studies have suggested that chronic fatigue syndrome (CFS) is associated with changes in appetite and weight, and also with mild hypocortisolism. Because both of these features may be related to leptin metabolism, we undertook a study of leptin in CFS. DESIGN: (i) A comparison of morning leptin concentration in patients with CFS and controls and (ii) a randomized, placebo-controlled crossover study of the effects of hydrocortisone on leptin levels in CFS. PATIENTS: Thirty-two medication free patients with CFS but not comorbid depression or anxiety. Thirty-two age, gender, weight, body mass index and menstrual cycle matched volunteer subjects acted as controls. MEASUREMENTS: We measured basal 0900 h plasma leptin levels in patients and controls. All 32 patients were taking part in a randomized, placebo-controlled crossover trial of low dose (5 or 10 mg) hydrocortisone as a potential therapy for CFS. We measured plasma leptin after 28 days treatment with hydrocortisone and after 28 days treatment with placebo. RESULTS: At baseline, there was no significant difference in plasma leptin between patients [mean 13.8, median 7.4, interquartile range (IQR) 18.0 ng/ml] and controls (mean 10.2, median 5.5, IQR 11.3 ng/ml). Hydrocortisone treatment, for both doses combined, caused a significant increase in leptin levels compared to placebo. When the two doses were analysed separately, only 10 mg was associated with a significant effect on leptin levels. We also compared the hydrocortisone induced increase in leptin between those who were deemed treatment-responders and those deemed nonresponders. Responders showed a significantly greater hydrocortisone-induced rise in leptin than nonresponders. This association between a clinical response to hydrocortisone and a greater rise in leptin levels may indicate a greater biological effect of hydrocortisone in these subjects, perhaps due to increased glucocorticoid receptor sensitivity, which may be present in some patients with CFS. CONCLUSIONS: We conclude that, while we found no evidence of alterations in leptin levels in CFS, low dose hydrocortisone therapy caused increases in plasma leptin levels, with this biological response being more marked in those CFS subjects who showed a positive therapeutic response to hydrocortisone therapy. Increases in plasma leptin levels following low dose hydrocortisone therapy may be a marker of pretreatment physiological hypocortisolism and of response to therapy.
Cleare AJ.	Guy's, King's and St Thomas' School of Medicine, Institute of Psychiatry, Division of Psychological Medicine, London, UK. a.cleare@iop.kcl.ac.uk	Regulatory disturbance of energy.	Adv Psychosom Med. 2001;22:17-34.	
Cochran John W.		Effect of Modafinil on	Journal of Chronic	Fatigue is a common symptom of a variety of neurological illnesses, such as Alzheimer's

		Fatigue Associated with Neurological Illnesses	Fatigue Syndrome 2001; 8(2): 65	disease, chronic fatigue syndrome, multiple sclerosis, Parkinson's disease, and stroke. Fatigue severely impairs productivity, performance, social functioning, and quality of life. Modafinil (PROVIGIL®) has been shown to significantly improve fatigue associated with multiple sclerosis and depression. Here, a retrospective review of the medical charts of 25 patients treated with modafinil for fatigue associated with various neurological illnesses was conducted. Modafinil was effective for the treatment of fatigue in 21 of 25 patients (84%), and was well tolerated. Therefore, modafinil appears to be a potentially attractive candidate for the treatment of fatigue associated with neurological disorders.
Coetzer P, Lockyer I, Schorn D, Boshoff L.	Sanlam, Bellville, Republic of South Africa.	Assessing impairment and disability for syndromes presenting with chronic fatigue.	J Insur Med. 2001;33(2):170-82.	Many disability claims are based on the subjective symptom of fatigue, which can be caused by a wide spectrum of diagnoses including fibromyalgia, chronic fatigue syndrome and cardiopulmonary diseases. Chronic pain is very often a compounding problem. It is vital for every insurer to have fair and objective criteria to distinguish between invalid claims and those with merit. This review article proposes objective tools and parameters to achieve this goal.
Cohen H, Neumann L, Kotler M, Buskila D.	Anxiety and Stress Research Unit, Ministry of Health Mental Health Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel. hagitc@bgumail.bgu.ac.il	Autonomic nervous system derangement in fibromyalgia syndrome and related disorders.	Isr Med Assoc J. 2001 Oct;3(10):755-60.	Fibromyalgia syndrome is a chronic, painful musculoskeletal disorder of unknown etiology and/or pathophysiology. During the last decade many studies have suggested autonomic nervous system involvement in this syndrome, although contradictory results have been reported. This review focuses on studies of the autonomic nervous system in fibromyalgia syndrome and related disorders, such as chronic fatigue syndrome and irritable bowel syndrome on the one hand and anxiety disorder on the other, and highlights techniques of dynamic assessment of heart rate variability. It raises the potentially important prognostic implications of protracted autonomic dysfunction in patient populations with fibromyalgia and related disorders, especially for cardiovascular morbidity and mortality.
Cook DB, Lange G, DeLuca J, Natelson BH.	Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark, NJ 07103, USA.	Relationship of brain MRI abnormalities and physical functional status in chronic fatigue syndrome.	Int J Neurosci. 2001 Mar;107(1-2):1-6.	Chronic Fatigue Syndrome (CFS) is an unexplained illness that is characterized by severe fatigue. Some have suggested that CFS is a "functional somatic syndrome" in which symptoms of fatigue are inappropriately attributed to a serious illness. However, brain magnetic resonance imaging (MRI) data suggest that there may be an organic abnormality associated with CFS. To understand further the significance of brain MRI abnormalities, we examined the relationship between MRI identified brain abnormalities and self-reported physical functional status in 48 subjects with CFS who underwent brain MR imaging and completed the Medical Outcomes Study SF-36. Brain MR images were examined for the presence of abnormalities based on 5 general categories previously shown to be sensitive to differentiating CFS patients from healthy controls. There were significant negative relationships between the presence of brain abnormalities and both the physical functioning (PF) (rho=-.31, p=.03), and physical component summary PCS (rho=-.32, p=.03) subscales of the SF-36. CFS patients with MRI identified brain abnormalities scored significantly lower on both PF (t(1,46) =2.3, p=.026) and the PCS (t(1,41) =2.4, p=.02) than CFS subjects without an identified brain abnormality. When adjusted for age differences

				only the PF analysis remained significant. However, the effect sizes for both analyses were large indicating meaningful differences in perceived functional status between the groups. These results demonstrate that the presence of brain abnormalities in CFS are significantly related to subjective reports of physical function and that CFS subjects with MRI brain abnormalities report being more physically impaired than those patients without brain abnormalities.
Cordingley L, Wearden A, Appleby L, Fisher L.	School of Psychiatry and Behavioural Sciences, University of Manchester, Room 704, Stopford Building, Oxford Road, M13 9PT, Manchester, UK. lis.cordingley@man.ac.uk	The Family Response Questionnaire: a new scale to assess the responses of family members to people with chronic fatigue syndrome.	J Psychosom Res. 2001 Aug;51(2):417-24.	OBJECTIVE: Family responses to patients with chronic fatigue syndrome (CFS) may influence the course of the disorder and family members themselves are likely to be adversely affected. However, the beliefs and responses of relatives of CFS patients have been under-researched. The aim of this study was to produce an easy-to-administer questionnaire to assess the responses of family members to people with CFS. METHODS: Seventy-eight people, all close relatives of (physician-diagnosed) CFS sufferers, completed the first version of the Family Response Questionnaire (FRQ). RESULTS: Examination of the correlation matrix and a cluster analysis of the items support four scales rather than the original five. The four response scales were labelled: sympathetic-empathic, active engagement, rejecting-hostile, and concern with self. Measures of test-retest and internal reliability were high. Participants found the items both comprehensible and relevant to their experiences of living with people with CFS. CONCLUSION: The new version of the FRQ will be useful in further examination of the responses of CFS on individuals and their families.
Coutts R, Weatherby R, Davie A.	School of Exercise Science and Sport Management, Southern Cross University, P.O. Box 157, New South Wales 2480, Lismore, Australia.rcoutts@scu.edu.au	The use of a symptom "self-report" inventory to evaluate the acceptability and efficacy of a walking program for patients suffering with chronic fatigue syndrome.	J Psychosom Res. 2001 Aug;51(2):425-9.	OBJECTIVES: The purpose of this research was to evaluate the effectiveness of the modality of walking as a management strategy for patients suffering with chronic fatigue syndrome (CFS). METHODS: Six males and fourteen females with medically diagnosed CFS (CDC, 1994), completed a 12-week walking program. Prior to starting the program subjects underwent an incremental walking exercise test to predetermine their walking intensity. The SCL-90-R symptom "self-report" questionnaire was administered prior to, and at the completion of, the walking program. RESULTS: At the completion of the 12 weeks of walking, changes in four of the nine SCL-90-R dimensions were significant (somatisation, paranoid ideation, phobic anxiety, and psychoticism). Also significant were the changes in the combination indices, the Global Indices of Distress (GID) and the Positive Symptom Total (PST). CONCLUSION: This group of CFS subjects, by way of "self-report", indicated the possibility of an exercise-induced decrease in psychological stress. The walking intervention may have evoked positive changes in their well-being and, furthermore, provided no evidence of any exacerbation in their symptoms.
Creswell C, Chalder T.	Sub-Department of Clinical Health Psychology, University College London, Gower Street, WC1E 6BT,	Defensive coping styles in chronic fatigue syndrome.	J Psychosom Res. 2001 Oct;51(4):607-10.	OBJECTIVE: The cognitive-behavioral model of chronic fatigue syndrome (CFS) proposes that rigidly held beliefs act to defend individuals against low self-esteem. This study is the first to investigate the prevalence of a potential mechanism, the Defensive High Anxious coping style, among individuals with CFS. METHODS: The study comprised 68 participants (24 CFS; 24 healthy volunteers; 20 chronic illness volunteers). Participants completed the Bendig short form of the Taylor Manifest Anxiety Scale (B-MAS) and the Marlowe-Crowne

	London, UK. c.creswell@ucl.ac.uk			Social Desirability Scale (MC) in order to ascertain the distribution of participants in each group within the four coping styles defined by Weinberger et al. [J. Abnorm. Psychol. 88 (1979) 369]. RESULTS: A greater number of participants in the CFS group (46%) were classified as Defensive High Anxious compared to the two comparison groups [chi(2)(2)=8.84, P=.012]. CONCLUSION: This study provides support for the existence of defensive coping mechanisms as described by the cognitive-behavioral model of CFS. Furthermore, it has been suggested that this particular coping style may impinge directly on physical well being through similar mechanisms as identified in CFS, and further research linking these areas of research is warranted.
Csef H.	Arbeitsbereich Psychosomatische Medizin und Psychotherapie, Medizinische Poliklinik, der Universitat, Klinikstrasse 8, 97070 Wurzburg.	[Chronic fatigue] [Article in German]	Internist (Berl). 2001 Nov;42(11):1495-502, 1504; quiz 1504-7.	
Curt GA.	National Cancer Institute, National Institutes of Health, Clinical Center, Oncology Program, Building 10, Room 12N214, 9000 Rockville Pike, Bethesda, Maryland 20892, USA.	[Fatigue syndrome caused by malignant tumor. An increasing priority in patient care] [Article in Italian	Recenti Prog Med. 2001 Jun;92(6):408-12.	As oncologists have become more effective in alleviating pain, nausea and depression, fatigue has emerged as the most important symptom suffered by cancer patients. Indeed, the current literature suggests that fatigue is currently the most important untreated symptom in cancer medicine. In recent surveys of patients and their caregivers, fatigue is more important for the quality of life than pain, nausea or depression. Yet these same surveys confirm that oncologists underestimate the importance of cancer related fatigue. This may be partly because patients often do not fully share the full nature of their concerns. When patients do raise the issue of fatigue, the physicians' recommendations are often non specific. However, recent research has shown that fatigue is not inevitable and untreatable, but a symptom amenable to differential diagnosis and specific intervention. Like pain, fatigue is intrinsically a subjective problem where the doctor relies on the patient's reporting. Weakness, exhaustion, lethargy and asthenia are all used as functional descriptions of fatigue. While these are descriptive terms, clinical research in the measurement and alleviation of fatigue requires reproducible measurement tools. Several studies already exist and have begun to explore this important area of symptom management.
Custaud MA.	Laboratoire de physiologie de l'environnement (Pr C. Gharib) EA 645 Faculte de medecine Lyon-Grange Blanche	[Don't forget the gravity] [Article in French]	Rev Prat. 2001 Oct 15;51(16):1745-7.	

	8, avenue Rockefeller 69373 Lyon. Claude.Gharib@univ-lyon1.fr			
Daly E, Komaroff AL, Bloomingdale K, Wilson S, Albert MS.	Department of Psychiatry, Massachusetts General Hospital, 149 13th Street, Charlestown, MA 02129, USA. albert@psych.mgh.harvard.edu	Neuropsychological function in patients with chronic fatigue syndrome, multiple sclerosis, and depression.	Appl Neuropsychol. 2001;8(1):12-22.	Patients with chronic fatigue syndrome (CFS), multiple sclerosis (MS), and major depression were compared with controls and with each other on a neuropsychological battery that included standard neuropsychological tests and a computerized set of tasks that spanned the same areas of ability. A total of 101 participants were examined, including 29 participants with CFS, 24 with MS, 23 with major depressive disorder, and 25 healthy controls. There were significant differences among the groups in 3 out of 5 cognitive domains: memory, language, and spatial ability. Assessment of psychiatric symptoms indicated that all 3 patient groups had a higher prevalence of depression than the controls. A total measure of psychiatric symptomatology also differentiated the patients from the controls. After covarying the cognitive test scores by a measure of depression, the patient groups continued to differ from controls primarily in the area of memory. The findings support the view that the cognitive deficits found in CFS cannot be attributed solely to the presence of depressive symptomatology in the patients.
Davey NJ, Puri BK, Nowicky AV, Main J, Zaman R.	Department of Sensimotor Systems, Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, Fullham Palace Road, W6 8RF, London, UK. n.davey@ic.ac.uk	Voluntary motor function in patients with chronic fatigue syndrome.	J Psychosom Res. 2001 Jan;50(1):17-20.	INTRODUCTION: The pathogenesis of chronic fatigue syndrome (CFS) remains unknown. In particular, little is known of the involvement of the motor cortex and corticospinal system. METHODS: Transcranial magnetic stimulation (TMS) was used to assess corticospinal function in terms of latency and threshold of motor-evoked potentials (MEPs) in thenar muscles. Reaction times and speed of movement were assessed using button presses in response to auditory tones. RESULTS: Patients had higher (P<.05) self-assessed indices of fatigue (7/10) than for pain (5/10), anxiety (4/10) or depression (3/10). Mean (+/-S.E.M.) simple reaction times (SRTs) were longer (P<.05) in the patients (275+/-19 ms) than in the controls (219+/-9 ms); choice reaction times (CRTs) were not significantly longer in the patients. Movement times, once a reaction task had been initiated, were longer (P<.05) in the patients in both SRTs (patients, 248+/-13 ms; controls, 174+/-9 ms) and CRTs (patients, 269+/-13 ms; controls, 206+/-12 ms). There was no difference (P>.05) in threshold or latency of MEPs in hand muscles between the patients (threshold, 54.5+/-2.2% maximum stimulator output [% MSO]; latency 22+/-0.3 ms) and controls (threshold 54.6+/-3.6% MSO; latency 22.9+/-0.5 ms). Regression analysis showed no correlation (P>.05) of SRTs with either threshold for MEPs or fatigue index. CONCLUSION: Corticospinal conduction times and excitability were within the normal range despite a slower performance time for motor tasks and an increased feeling of fatigue. This suggests that the feeling of fatigue and the slowness of movement seen in CFS are manifest outside the corticospinal system.
De Becker P, McGregor N, De Meirleir K.	VUB, Vakgroep Interne Geneeskunde, KRO gebouw niv.-1, Laarbeeklaan 101,	A definition-based analysis of symptoms in a large cohort of patients with chronic	J Intern Med. 2001 Sep;250(3):234-40.	OBJECTIVE: The Holmes and Fukuda criteria are widely used criteria all over the world, yet a specific European study regarding chronic fatigue syndrome (CFS) patient symptomatology has not been conducted so far. This study was performed to answer the need to assess the homogeneity of a large CFS population in relationship to the Fukuda or

	1090 Brussels, Belgium. pdbeck@minf.vub.ac.be	fatigue syndrome.		Holmes definitions and to assess the importance of a symptom severity scale. DESIGN: Multivariate analyses were performed to assess the symptom presentation within a fatigued population and the differences between the Fukuda and Holmes definitions compared with an excluded chronic fatigued group in a large cohort of fatigued patients. SETTING: An outpatient tertiary care setting fatigue clinic in Brussels. MAIN OUTCOME MEASURES: Prevalence and severity of symptoms and signs in a CFS population and in a chronic fatigued population. SUBJECTS AND METHODS: A total of 2073 consecutive patients with major complaints of prolonged fatigue participated in this study. Multivariate analyses were performed to assess the symptom presentation and severity and the differences between the Fukuda and Holmes definitions. RESULTS: Of the 2073 patients complaining of chronic fatigue (CF), 1578 CFS patients fulfilled the Fukuda criteria (100% of CFS group) and 951 (60.3% of the CFS group) fulfilled the Holmes criteria. Discriminant function analysis revealed that the Fukuda and Holmes definitions can be differentiated by symptom severity and prevalence. The Holmes definition was more strongly associated than the Fukuda definition with the symptoms that differentiated the CFS patients from the patients that did not comply with the CFS definitions. The inclusion of 10 additional symptoms was found to improve the sensitivity/specificity and accuracy for selection of CFS patients. CONCLUSIONS: The CFS patients fulfilling the Holmes criteria have an increased symptom prevalence and severity of many symptoms. Patients fulfilling the Fukuda criteria were less severely affected patients which leads to an increase in clinical heterogeneity. Addition of certain symptoms and removal of others would strengthen the ability to select CFS patients.
De Toni T, Calvillo M.	Istituto G. Gaslini, Dipartimento di Pediatria, Centro di Adolescentologia, Universita degli Studi, Genova, Italy.	[Adolescents and the problem of a chronic disease] [Article in Italian]	Minerva Pediatr. 2001 Oct;53(5):383-9.	
De Vries M, Soetekouw PM, Van Der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Medical Centre St Radboud, Nijmegen, The Netherlands.	Natural course of symptoms in Cambodia veterans: a follow-up study.	Psychol Med. 2001 Feb;31(2):331-8.	BACKGROUND: Dutch (ex-)servicemen were deployed in the 1992-3-peace operation UNTAC in Cambodia. Since their return, they have voiced concerns about the health consequences of their service and they have reported symptoms such as fatigue and cognitive problems. The natural course of symptoms in Dutch Cambodia veterans was evaluated in a prospective study. METHODS: At 18-months follow-up, a questionnaire was sent to 354 veterans who met a set case definition for symptoms in Cambodia veterans or who had sub-threshold scores. Initial measurement of fatigue severity, psychological well-being, depression, post-traumatic stress disorder, trait-anxiety, self-efficacy and causal attributions, was used to evaluate predictors for self-reported improvement and low levels of fatigue at follow-up. RESULTS: At follow-up, 19% of the respondents reported complete recovery, 20% felt much better, 57% had the same complaints and 4% had become worse compared with their initial assessment. Self-reported improvement and less severe fatigue

				at follow-up were predicted by less severe fatigue at initial assessment and more perceived control over symptoms. CONCLUSIONS: Self-reported improvement was reported in a considerable percentage of Cambodia veterans, whereas another substantial percentage of Cambodia veterans continued to suffer with severe levels of fatigue and related symptoms. Predictors of improvement in Cambodia veterans and patients with chronic fatigue syndrome show similarities and also seem to bear importance for Gulf War veterans.
Deale A, Husain K, Chalder T, Wessely S.	Academic Department of Psychological Medicine, Guy's, King's, and St. Thomas's School of Medicine, London, UK. a.deale@iop.kcl.ac.uk	Long-term outcome of cognitive behavior therapy versus relaxation therapy for chronic fatigue syndrome: a 5-year follow-up study.	Am J Psychiatry. 2001 Dec;158(12):2038-42.	OBJECTIVE: This study evaluated the long-term outcome of cognitive behavior therapy versus relaxation therapy for patients with chronic fatigue syndrome. METHOD: Sixty patients who participated in a randomized controlled trial of cognitive behavior therapy versus relaxation therapy for chronic fatigue syndrome were invited to complete self-rated measures and participate in a 5-year follow-up interview with an assessor who was blind to treatment type. RESULTS: Fifty-three patients (88%) participated in the follow-up study: 25 received cognitive behavior therapy and 28 received relaxation therapy. A total of 68% of the patients who received cognitive behavior therapy and 36% who received relaxation therapy rated themselves as "much improved" or "very much improved" at the 5-year follow-up. Significantly more patients receiving cognitive behavior therapy, in relation to those in relaxation therapy, met criteria for complete recovery, were free of relapse, and experienced symptoms that had steadily improved or were consistently mild or absent since treatment ended. Similar proportions were employed, but patients in the cognitive behavior therapy group worked significantly more mean hours per week. Few patients crossed the threshold for "normal" fatigue, despite achieving a good outcome on other measures. Cognitive behavior therapy was positively evaluated and was still used by over 80% of the patients. CONCLUSIONS: Cognitive behavior therapy for chronic fatigue syndrome can produce some lasting benefits but is not a cure. Once therapy ends, some patients have difficulty making further improvements. In the future, attention should be directed toward ensuring that gains are maintained and extended after regular treatment ends.
Deale A, Wessely S.	Academic Department of Psychological Medicine, Guy's, King's and St Thomas's School of Medicine, Kings College, University of London, UK. alicia.deale@kcl.ac.uk	Patients' perceptions of medical care in chronic fatigue syndrome.	Soc Sci Med. 2001 Jun;52(12):1859-64.	This study investigated perceptions of medical care among patients with chronic fatigue syndrome (CFS) referred to a specialist clinic. Sixty-eight patients completed a questionnaire survey on their overall satisfaction with medical care received since the onset of their illness, and their views on specific aspects of care. Two-thirds of patients were dissatisfied with the quality of medical care received. Dissatisfied patients were significantly more likely to describe delay, dispute or confusion over diagnosis; to have received and rejected a psychiatric diagnosis; to perceive doctors as dismissive, skeptical or not knowledgeable about CFS and to feel that the advice given was inadequate or conflicting. Satisfied patients were significantly more likely to perceive doctors as caring, supportive and interested in their illness; to state that they did not expect their doctors to cure CFS and to perceive their GP or hospital doctor as the source of greatest help during their illness. Many patients were critical of the paucity of treatment, but this was not

				associated with overall satisfaction. The findings suggest that medical care was evaluated less on the ability of doctors to treat CFS, and more on their interpersonal and informational skills. Dissatisfaction with these factors is likely to impede the development of a therapeutic doctor-patient alliance, which is central to the effective management of CFS. The findings suggest a need for better communication and better education of doctors in the diagnosis and management of CFS.
Dendy C, Cooper M, Sharpe M.	Isis Education Centre, Warneford Hospital, Oxford, UK.	Interpretation of symptoms in chronic fatigue syndrome.	Behav Res Ther. 2001 Nov;39(11):1369-80.	Chronic fatigue syndrome (CFS) is an illness characterised by fatigue and other symptoms. Both psychological and biological aetiological factors have been proposed, but the disorder is of uncertain origin. The aetiology of the symptoms is therefore ambiguous. It has been suggested (a) that patients with CFS tend to interpret their symptoms as indicating physical illness and (b) they tend not to interpret these symptoms in terms of negative emotion. In order to test these hypotheses we developed a self-report questionnaire to assess the interpretation of symptoms in patients with CFS. It was administered to patients with CFS, patients with depression, patients with multiple sclerosis (MS), and normal controls. Preliminary results suggest that the measure has acceptable psychometric properties. Patients with CFS were more likely than either depressed patients or normal controls to interpret symptoms (characteristic of CFS) in terms of physical illness, but did not differ in this from the MS patients. When compared with all three other groups (including the MS patients), the patients with CFS were least likely to interpret symptoms in terms of negative emotional states. The theoretical and clinical implications of the findings are discussed.
DiClementi JD, Schmaling KB, Jones JF.	Department of Psychology, University of Colorado at Denver, Denver, CO, USA. diclemej@ipfw.edu	Information processing in chronic fatigue syndrome: a preliminary investigation of suggestibility.	J Psychosom Res. 2001 Nov;51(5):679-86.	This study examines the effects of certain types of information processing on the subjective experience of cognitive deficits in persons with chronic fatigue syndrome (CFS). Two groups of participants, persons with CFS and a group of healthy controls, were administered a symptom inventory and measures of intellectual functioning, memory, automatic processing, and suggestibility. The groups differed significantly on number and severity of reported symptoms and on measures of global suggestibility and automatic processing, but not on measures of intellectual functioning and memory. Suggestibility was related to number and severity of reported symptoms, as well as the inability to inhibit the automatic processing of information. Implications of these findings are discussed, as well as directions for future research and treatment of symptoms associated with CFS.
Dinan TG, Scott LV, Thakore J, Naesdal J, Keeling PW.	Department of Pharmacology and Therapeutics, University College Cork, The Cork Clinic, Western Road, Cork, Ireland. tdinan@indigo.ie	Impact of cortisol on buspirone stimulated prolactin release: a double-blind placebo-controlled study.	Psychoneuroendocrinology. 2001 Oct;26(7):751-6.	Buspirone is known to stimulate prolactin release. Clinical studies (e.g. in chronic fatigue syndrome) suggest that the response may be influenced by baseline cortisol levels. We conducted a double-blind placebo-controlled study to examine the relationship between the prolactin response to buspirone challenge and baseline cortisol level. Fifty healthy volunteers took part in the study. Buspirone was found to consistently elevate PRL levels above those seen following placebo administration. The PRL response as measured by area under the curve was highly correlated with the baseline cortisol level.
Dobbs BM, Dobbs	Department of	Working memory	J Int Neuropsychol	Cognitive impairments are among the most frequently reported and least investigated

AR, Kiss I.	Psychology, University of Alberta, Edmonton, Canada. bdobbs@ualberta.ca	deficits associated with chronic fatigue syndrome.	Soc. 2001 Mar;7(3):285-93.	components of the chronic fatigue syndrome (CFS). As part of a multifaceted study of the CFS, the present study investigated the cognitive functioning of chronic fatigue patients. The performance of 20 CFS patients was compared to that of controls (N = 20) on 4 tests of working memory (WM). Digit Span Forward was used to assess the storage capacity of WM. Multiple aspects of central executive functioning were assessed using several standard measures: Digit Span Backward, and Trails A and Trails B. More recently developed measures of WM were used to assess control of processing under temporal demands (working memory task) and resistance to interference (a sustained attention task). Deficits were restricted to more demanding tasks, requiring resistance to interference and efficient switching between processing routines. The overall results clearly implicate deficits in the control aspects of central executive function in CFS.
Edwards R, Suresh R, Lynch S, Clarkson P, Stanley P.	Division of Psychiatry and Behavioural Sciences, University of Leeds, LS9 7TF, Leeds, UK.	Illness perceptions and mood in chronic fatigue syndrome.	J Psychosom Res. 2001 Feb;50(2):65-8.	BACKGROUND: Individual beliefs and cognitions may affect adjustment to chronic fatigue syndrome (CFS) and illness perceptions, in particular, have been reported to correlate with both disability and psychological adjustment to CFS in self-diagnosed cases. OBJECTIVES: The aim of the present study was to examine these relationships in a clinic sample of CFS patients assessed by both a physician and psychiatrist. METHOD: A sample of 173 patients referred to a multidisciplinary CFS clinic and fulfilling current operational criteria for CFS [Ann Intern Med 121 (1994) 953; J R Soc Med 84 (1991) 118.] were randomly selected from the clinic database and surveyed with the Hospital Anxiety and Depression scale, Fatigue Questionnaire and Illness Perceptions Questionnaire [J Psychosom Res 37 (1993) 147; Psychol Health 11 (1996) 431; Acta Psychiatr Scand 67 (1983) 361.]. RESULTS: A total of 126 patients responded (73% response rate). The illness perception components studied were consequences (of illness), illness identity, causes (of illness), the ability to control/cure the illness and (expected) timeline of the illness. These components accounted for 15%, 28% and 30% of the variance in levels of fatigue, depression and anxiety, respectively. Two of the illness perception components (consequences and illness identity) were stronger predictors of fatigue score than mood scores. CONCLUSIONS: These findings confirmed in a clinical sample that illness perceptions are associated with variation in both disability and psychological adjustment in CFS. Illness perceptions may have an important and long-lasting effect on adaptation to CFS, and it is necessary to have a greater understanding of their role in order to tailor effective interventions for the condition.
Ehlert U, Gaab J, Heinrichs M.	Department of Clinical Psychology, University of Zurich, Zurichbergstrasse 43, CH-8044, Zurich, Switzerland. ehlertu@klipsy.unizh.ch	Psychoneuroendocrinological contributions to the etiology of depression, posttraumatic stress disorder, and stress-related bodily disorders: the role of the hypothalamus-	Biol Psychol. 2001 Jul-Aug;57(1-3):141-52.	Following the assumption that stressors play an important part in the etiology and maintenance of psychiatric disorders, it is necessary to evaluate parameters reflecting stress-related physiological reactions. Results from these examinations may help to deepen the insight into the etiology of psychiatric disorders and to elucidate diagnostic uncertainties. One of the best-known stress-related endocrine reactions is the hormonal release of the hypothalamic-pituitary-adrenal (HPA) axis. Dysregulations of this axis are associated with several psychiatric disorders. Profound hyperactivity of the HPA-axis has been found in melancholic depression, alcoholism, and eating disorders. In contrast, posttraumatic stress disorder, stress-related bodily disorders like idiopathic pain

		pituitary-adrenal axis.		syndromes, and chronic fatigue syndrome seem to be associated with diminished HPA activity (lowered activity of the adrenal gland). Hypotheses referring to (a) the psychophysiological meaning and (b) the development of these alterations are discussed.
Englebienne P, Herst CV, Smet K, D'Haese A, De Meirleir K.		Interactions Between RNase L Ankyrin-Like Domain and ABC Transporters as a Possible Origin for Pain, Ion Transport, CNS and Immune Disorders of Chronic Fatigue Immune Dysfunction Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 83	Low molecular weight (LMW) ribonuclease L (RNase L) forms have been identified in peripheral blood mononuclear cells (PBMC) of patients with chronic fatigue immune dysfunction syndrome (CFIDS). Data from our laboratory indicate that these LMW RNase L proteins are produced by proteolytic cleavage of the native monomeric enzyme and we have identified calpain as one of the possible proteases involved. Using human recombinant RNase L (r-hRNase L) His-tagged at the N-terminus, we show here at the one hand that both calpain and PBMC extracts from CFIDS patients cleave the protein in fragments of identical sizes containing ankyrin-like repeat sequences. At the other hand, the activity of RNase L is modulated by its interaction with a specific inhibitor (RLI), a member of the ATP binding cassette (ABC) superfamily. RLI interacts with the ankyrin domain of RNase L, which results in a blockade of the 2N,5N-oligoadenylate (2-5A)-binding site of the enzyme. We show that RLI contains a small ankyrin-interacting peptide cluster through which it interacts with the first two ?-hairpin coils of the RNase L ankyrin domain. A similarity search performed at the NCBI using RLI aminoacid sequence as the entry allowed to identify several other ABC transporter proteins sharing significant identities with RLI, including the ankyrin-interacting peptide. Taken together, these results show that upon pathological cleavage of RNase L, fragments containing the ankyrin domain are released, which could be capable of interacting with selected members of the human ABC superfamily, preventing their interaction with the normal cognate ankyrin protein and hence impairing their proper cellular function. This interaction constitutes a common physiological mechanism explaining numerous and currently unexplained symptoms experienced by patients with CFIDS, which are otherwise totally unrelated.
Estroff SE.	Department of Social Medicine, University of North Carolina at Chapel Hill, USA.	Transformations and reformulations: chronicity and identity in politics, policy, and phenomenology.	Med Anthropol. 2001;19(4):411-3. Comment on: Med Anthropol. 2001;19(4):299-317	
Ferguson E, Cassaday HJ.	School of Psychology, University of Nottingham, Nottingham, NG7 2RD, UK. eamonn.ferguson@nottingham.ac.uk	Theoretical accounts of Gulf War Syndrome: from environmental toxins to psychoneuroimmunology and neurodegeneration.	Behav Neurol. 2001-2002;13(3-4):133-47.	Non-specific illness includes a wide variety of symptoms: behavioural (e.g., reduced food and water intake), cognitive (e.g., memory and concentration problems) and physiological (e.g., fever). This paper reviews evidence suggesting that such symptoms can be explained more parsimoniously as a single symptom cluster than as a set of separate illnesses such as Gulf War Syndrome (GWS) and chronic fatigue syndrome (CFS). This superordinate syndrome could have its biological basis in the activity of pro-inflammatory cytokines (in particular interleukin-1: IL-1), that give rise to what has become known as the 'sickness response'. It is further argued that the persistence of non-specific illness in chronic conditions like GWS may be (in part) attributable to a bio-associative mechanism (Ferguson

				and Cassaday, 1999). In the case of GWS, physiological challenges could have produced a non-specific sickness response that became associated with smells (e.g., petrol), coincidentally experienced in the Persian Gulf. On returning to the home environment, these same smells would act as associative triggers for the maintenance of (conditioned) sickness responses. Such associative mechanisms could be mediated through the hypothalamus and limbic system via vagal nerve innervation and would provide an explanation for the persistence of a set of symptoms (e.g., fever) that should normally be short lived and self-limiting. We also present evidence that the pattern of symptoms produced by the pro-inflammatory cytokines reflects a shift in immune system functioning towards a (T-helper-1) Th1 profile. This position contrasts with other immunological accounts of GWS that suggest that the immune system demonstrates a shift to a Th2 (allergy) profile. Evidence pertaining to these two contrasting positions is reviewed.
Ferrada-Noli M.	Folkhalsovetenskap med inriktning mot epidemiologi, Hogskolan i Gavle. mferrada-noli@hms.harvard.edu	[Occupational stress, suicide and fatigue depression] [Article in Swedish]	Lakartidningen. 2001 Jun 27;98(26-27):3158-60.	
Fiedler N, Kipen HM.	UMDNJ-Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Piscataway, New Jersey 08854, USA. nfiedler@eohsi.rutgers.edu	Controlled exposures to volatile organic compounds in sensitive groups.	Ann N Y Acad Sci. 2001 Mar;933:24-37.	Sensitivities to chemicals are characterized by symptoms in multiple organ systems in response to low-level chemical exposures. This paper reviews studies of controlled exposures to odorants and to mixtures of volatile organic compounds. Sensitive subgroups include subjects who met Cullen's 1987 criteria for multiple chemical sensitivity (MCS), Gulf War veterans with chronic fatigue syndrome and chemical sensitivity (CFS/CS), and subjects with specific self-reported sensitivities to methyl terbutyl ether (MTBE) in gasoline (MTBE-sensitive). All studies include comparison of age- and sex-matched healthy controls. Studies of olfaction did not support unusual sensitivity, defined as lower odor thresholds, among MCS subjects; however, a dose-response pattern of symptoms was observed in response to suprathreshold concentrations of phenyl ethyl alcohol. In blinded, controlled exposures to clean air, gasoline, gasoline/11% MTBE, and gasoline/15% MTBE, a threshold effect was observed with MTBE-sensitive subjects reporting significantly increased symptoms to gasoline/15% MTBE exposure. Autonomic arousal (heart and respiration rate; end-tidal CO2) in response to odor of chemical mixtures may mediate symptoms for subjects with generalized chemical sensitivities, but not for those whose sensitivities are confined to specific chemicals. For example, Gulf War veterans with CFS/CS experienced reduced end-tidal CO2 when exposed to diesel fumes, while exposure to MTBE did not produce any psychophysiologic changes in MTBE-sensitive subjects. Controlled olfactory and exposure studies reveal that significant responses can be observed in chemically sensitive subjects even when de-adaptation has not occurred. However, these studies suggest that symptoms are not necessarily accompanied by changes in physiologic arousal.

				Subject characteristics play a critical role in outcomes.
Forton DM, Allsop JM, Main J, Foster GR, Thomas HC, Taylor-Robinson SD.		Evidence for a cerebral effect of the hepatitis C virus.	Lancet. 2001 Jul 7;358(9275):38-9.	Patients with hepatitis C virus (HCV) infection frequently complain of symptoms akin to the chronic fatigue syndrome and score worse on health-related quality of life indices than matched controls. We address the hypothesis that HCV itself affects cerebral function. Using proton magnetic-resonance spectroscopy we have shown elevations in basal ganglia and white matter choline/creatine ratios in patients with histologically-mild hepatitis C, compared with healthy volunteers and patients with hepatitis B. This elevation is unrelated to hepatic encephalopathy or a history of intravenous drug abuse, and suggests that a biological process underlies the extrahepatic symptoms in chronic HCV infection.
Francis C.		Take ME seriously.	Nurs Stand. 2001 Jan 10-16;15(17):22.	
Frankish H.		Some evidence cognitive therapy and exercise benefit chronic fatigue.	Lancet. 2001 Sep 22;358(9286):989.	
Friedberg F, Jason LA.	Department of Psychiatry and Behavioral Science, State University of New York at Stony Brook, USA. ffriedbe@ct1.nai.net	Chronic fatigue syndrome and fibromyalgia: clinical assessment and treatment.	J Clin Psychol. 2001 Apr;57(4):433-55.	Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are closely related illnesses of uncertain etiology. This article reviews the research literature on these biobehavioral conditions, with an emphasis on explanatory models, clinical evaluation of comorbid psychiatric disorders, assessment of stress factors, pharmacologic and alternative therapies, and cognitive-behavioral treatment studies. Furthermore, clinical protocols suitable for professional practice are presented based on an integration of the authors' clinical observations with published data. The article concludes with the recognition that mental health professionals can offer substantial help to these patients. Copyright 2001 John Wiley & Sons, Inc.
Friedman TC, Echeverry D, Poland RE.		Orthostatic hypotension and chronic fatigue syndrome.	JAMA. 2001 Mar 21;285(11):1442; author reply 1443. Comment on: JAMA. 1995 Sep 27;274(12):961-7. JAMA. 2001 Jan 3;285(1):52-9.	
Fuentes K, Hunter MA, Strauss E, Hultsch DF.	Department of Psychology, University of Victoria, Victoria, BC, Canada. kfuentes@uvic.ca	Intraindividual variability in cognitive performance in persons with chronic fatigue syndrome.	Clin Neuropsychol. 2001 May;15(2):210-27.	Studies of cognitive performance among persons with chronic fatigue syndrome (CFS) have yielded inconsistent results. We sought to contribute to findings in this area by examining intraindividual variability as well as level of performance in cognitive functioning. A battery of cognitive measures was administered to 14 CFS patients and 16 healthy individuals on 10 weekly occasions. Analyses comparing the two groups in terms of level of performance defined by latency and accuracy scores revealed that the CFS patients were slower but not less accurate than healthy persons. The CFS group showed greater intraindividual variability (as measured by intraindividual standard deviations and coefficients of variation)

				than the healthy group, although the results varied by task and time frame. Intraindividual variability was found to be stable across time and correlated across tasks at each testing occasion. Intraindividual variability also uniquely differentiated the groups. The present findings support the proposition that intraindividual variability is a meaningful indicator of cognitive functioning in CFS patients.
Gantz NM, Coldsmith EE.	Division of Infectious Diseases, Department of Medicine, Pinnacle Health System, Harrisburg, PA 17110, USA. ngantz@pinnaclehealth.org [corrected]	Chronic fatigue syndrome and fibromyalgia resources on the world wide web: a descriptive journey.	Clin Infect Dis. 2001 Mar 15;32(6):938-48. Epub 2001 Mar 09.	A wealth of information on chronic fatigue syndrome (CFS) and fibromyalgia is available on the World Wide Web for health care providers and patients. These illnesses have overlapping features, and their etiologies remain unknown. Multiple Web sites were reviewed, and selected sites providing useful information were identified. Sites were classified according to their content and target audience and were judged according to suggested standards of Internet publishing. Fifty-eight sites were classified into groups as follows: comprehensive and research Web sites for CFS and fibromyalgia, meetings, clinical trials, literature search services, bibliographies, journal, and CFS and fibromyalgia Web sites for the patient.
Garland EM, Robertson D.	Autonomic Dysfunction Center, Department of Medicine, Vanderbilt University, Nashville, Tennessee, USA.	Chiari I malformation as a cause of orthostatic intolerance symptoms: a media myth?	Am J Med. 2001 Nov;111(7):546-52.	There is much interest in a putative relationship between Chiari I malformation and symptoms of orthostatic intolerance. It has been reported at scientific meetings that a number of patients with chronic fatigue syndrome or fibromyalgia have Chiari I malformation, or hindbrain compression in the absence of Chiari, and that they experience improvement after decompression surgery. Many of these patients have symptoms of orthostatic intolerance. A connection between Chiari I malformation and these conditions has been discussed in newspaper articles and on national television programs. Patients have also had access to much information on this topic via the Internet. Unfortunately, the Chiari I malformation and orthostatic intolerance connection is almost entirely unsupported by peer-reviewed literature. The purpose of this article is to provide an objective review of the available information.
Garralda ME, Rangel L.		Childhood chronic fatigue syndrome.	Am J Psychiatry. 2001 Jul;158(7):1161.	
Gartner BC, Fischinger JM, Roemer K, Mak M, Fleurent B, Mueller-Lantzsch N.	Department of Virology, University of Homburg/Saar, Kirrbergerstr. Haus 47, D-66421 Hombury Saar, Germany.	Evaluation of a recombinant line blot for diagnosis of Epstein-Barr Virus compared with ELISA, using immunofluorescence as reference method.	J Virol Methods. 2001 Apr;93(1-2):89-96.	A commercial line blot using recombinant antigens was compared with a commercial ELISA and 'in-house' IFA (reference test). Two panels were evaluated: Panel A was selected to distinguish between primary infections (89), past infections (20) and seronegatives (8) in immunocompetent individuals. In panel B, patients with a high number of reactivations were included: immunosuppressed patients (37), lymphoma (19), nasopharyngeal carcinoma (10), chronic fatigue syndrome (14). Blood donors (43) and cross-reactive sera (29) were added as controls. Line blot and IFA were concordant in 94% of primary infections, 100% of seronegatives and 100% of past infections, similar to ELISA. Results differed significantly with regard to reactivations. When compared with IFA, the incidence of reactivations was overestimated by the blot, 24 and 58% in blood donors and cross-reactive sera, respectively. ELISA showed a similar problems with 21 and 34% indeterminate results, respectively. The line blot is easy to carry out, has a good concordance with the reference IFA for primary infections, and is, therefore, a sufficient

				choice for distinguishing primary infection from seronegative and past infection. EBV reactivation assessment will require other methods such as EBV viral load.
Gilhooly PE, Ottenweller JE, Lange G, Tiersky L, Natelson BH.	Veterans Administration, New Jersey Health Care System, 385 Tremont Avenue, East Orange, NJ 07018, USA. PEGMD6@aol.com	Chronic fatigue and sexual dysfunction in female Gulf War veterans.	J Sex Marital Ther. 2001 Oct-Dec;27(5):483-7.	Chronic fatigue (CF) is one of the most common conditions reported by Gulf War veterans. This study evaluated female sexual dysfunction (FSD) in veterans with or without complaints of CF. Subjects were screened for medical and psychiatric causes of CF. They included 22 healthy subjects and 26 with fatiguing symptoms. FSD was reported by 10% of controls and by 60% of the fatigued ($p < .002$) while 19% versus 81% ($p < .001$) noted decreased libido. FSD was more prevalent in fatigued veterans than in the controls. This relationship was not mediated by an Axis I diagnosis. This appears to be the first report of sexual dysfunction in CF.
Gorman D, Monigatti J, Glass B, Gronwall D, Beasley M.	University of Auckland, New Zealand. d.gorman@auckland.ac.nz	Assessment of pentachlorophenol-exposed timber workers using a test-of-poisoning model.	Int J Occup Environ Health. 2001 Jul-Sep;7(3):189-94.	Sixty-two former New Zealand timber workers who were exposed to pentachlorophenol (PCP) at work were interviewed, examined, and assessed both by laboratory investigations and psychometrically for clinical syndromes that could be related to PCP exposure. Three such syndromes were identified: an acute complex of fever, headaches, upper and lower respiratory tract and eye irritation, skin disease, and foul smelling and discolored sweat; a chronic fatigue syndrome, beginning while still at work and frequently persisting; and a delayed encephalopathy. Neither of the sustained syndromes was considered characteristic of PCP poisoning, and many confounders were identified. An exposure index and a test-of-poisoning score had a statistically insignificant correlation.
Goudsmit E.		Response to Renckens.	J Psychosom Obstet Gynaecol. 2001 Mar;22(1):61-3. Comment on: J Psychosom Obstet Gynaecol. 2000 Dec;21(4):235-9.	
Goudsmit EM.		Measuring the quality of trials of treatments for chronic fatigue syndrome.	JAMA. 2001 Dec 26;286(24):3078-9. Comment on: JAMA. 2001 Sep 19;286(11):1360-8 Erratum in: JAMA 2002 Mar 20;287(11):1401.	
Gow JW, Simpson K, Behan PO, Chaudhuri A, McKay IC, Behan WM.	Department of Neurology, University of Glasgow, Scotland, United Kingdom.	Antiviral pathway activation in patients with chronic fatigue syndrome and acute infection.	Clin Infect Dis. 2001 Dec 15;33(12):2080-1. Epub 2001 Nov 06. Comment in: Clin Infect Dis. 2002 May 15;34(10):1420-1;	Gene expression of key enzymes in 2 antiviral pathways (ribonuclease latent [RNase L] and RNA-regulated protein kinase [PKR]) was compared in 22 patients with chronic fatigue syndrome (CFS), 10 patients with acute gastroenteritis, and 21 healthy volunteers. Pathway activation in the group of patients with infections differed significantly from that of the other 2 groups, in whom there was no evidence of upregulation. Therefore, assay of activation is unlikely to provide the basis for a diagnostic test for CFS.

			discussion 1421-2.	
Gray D, Parker-Cohen NY, White T, Clark ST, Seiner SH, Achilles J, McMahon WM.	Department of Psychiatry, University of Utah, Salt Lake City 84108, USA. Douglas.gray@hsc.utah.edu	A comparison of individual and family psychology of adolescents with chronic fatigue syndrome, rheumatoid arthritis, and mood disorders.	J Dev Behav Pediatr. 2001 Aug;22(4):234-42.	Chronic fatigue syndrome (CFS) is a controversial diagnosis with unknown cause. Adult studies indicate high rates of psychosocial dysfunction and psychiatric comorbidity. The authors compared three groups of pediatric patients selected by diagnosis-(1l) CFS (n = 15), (2) juvenile rheumatoid arthritis (n = 15), and (3) mood disorders (n = 15)-across many psychological measures. CFS subjects had dramatic elevation of the Somatic Complaints subscale (mean T score = 75), whereas the mood disorders group had higher externalizing scores (mean T score = 68) on the Child Behavior Checklist. The CFS subjects missed significantly more school compared with the two control groups. After the onset of CFS, 13 of 15 of the CFS patients required significant educational accommodation. Only 4 of the 15 CFS patients had an Axis I psychiatric diagnosis, as determined by the Computerized Diagnostic Interview for Children. Despite a low rate of psychiatric diagnosis in the CFS sample, these data attest to their psychosocial and school dysfunction.
Grossman ER.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1889-90. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
Grubb BP, Kanjwal MY, Kosinski DJ.	Electrophysiology Section, Division of Cardiology, Department of Medicine, The Medical College of Ohio, Toledo OH 43614-2598, USA. bgrubb@mco.edu	Review: The postural orthostatic tachycardia syndrome: current concepts in pathophysiology diagnosis and management.	J Interv Card Electrophysiol. 2001 Mar;5(1):9-16.	
Hamilos DL, Nutter D, Gershtenson J, Ikle D, Hamilos SS, Redmond DP, Di Clementi JD, Schmaling KB, Jones JF.	Washington University School of Medicine, Division of Allergy and Immunology, Euclid Avenue, St Louis, Missouri, USA. dhamilos@im.wustl.edu	Circadian rhythm of core body temperature in subjects with chronic fatigue syndrome.	Clin Physiol. 2001 Mar;21(2):184-95.	The pathophysiological basis for chronic fatigue syndrome (CFS) remains poorly understood. Certain symptoms of CFS, namely fatigue, neurocognitive symptoms and sleep disturbance, are similar to those of acute jet lag and shift work syndromes thus raising the possibility that CFS might be a condition associated with disturbances in endogenous circadian rhythms. In this study, we tested this hypothesis by examining the circadian rhythm of core body temperature (CBT) in CFS and control subjects. Continuous recordings of CBT were obtained every 5 min over 48 h in a group of 10 subjects who met the Center for Disease Control (CDC) definition of CFS and 10 normal control subjects. Subjects in the two groups were age, sex and weight-matched and were known to have normal basal metabolic rates and thyroid function. CBT recordings were performed under ambulatory conditions in a clinical research centre with the use of an ingestible radio frequency transmitter pill and a belt-worn receiver-logger. CBT time series were analysed by a cosinor analysis and by a harmonic-regression-plus-correlated-noise model to estimate the mean,

				amplitude and phase angle of the rhythm. The goodness of fit of each model was also compared using the Akaike Information Criterion (AIC) and sigma2. Average parameters for each group were compared by Student's t-test. By cosinor analysis, the only significant difference between CFS and control groups was in the phase angle of the third harmonic (P=0.02). The optimal harmonic-regression-plus-correlated-noise models selected were ARMA(1,1): control 7, CFS 6; ARMA(2,0): control 1, CFS 4; and ARMA(2,1): control 2 subjects. The optimal fit ARMA model contained two harmonics in eight of 10 control subjects but was more variable in the CFS subjects (1 harmonic: 5 subjects; 2 harmonics: 1 subject; 3 harmonics: 4 subjects). The goodness of fit measures for the optimal ARMA model were also better in the control than the CFS group, but the differences were not statistically significant. We conclude that, measured under ambulatory conditions, the circadian rhythm of CBT in CFS is nearly indistinguishable from that of normal control subjects although there was a tendency for greater variability in the rhythm. Hence, it is unlikely that the symptoms of CFS are because of disturbance in the circadian rhythm of CBT.
Hamilton W..	Chronic fatigue syndrome		Br J Gen Pract. 2001 Dec;51(473):1015. Comment on: Br J Gen Pract. 2001 Jul;51(468):553-8. Br J Gen Pract. 2001 Sep;51(470):758.	
Hamilton WT, Hall GH, Round AP.	North and East Devon Health Authority, Exeter. w.hamilton@cwcom.net	Frequency of attendance in general practice and symptoms before development of chronic fatigue syndrome: a case-control study.	Br J Gen Pract. 2001 Jul;51(468):553-8. Comment in: Br J Gen Pract. 2001 Dec;51(473):1015. Br J Gen Pract. 2001 Sep;51(470):758.	BACKGROUND: Chronic fatigue syndrome (CFS) research has concentrated on infective, immunological, and psychological causes. Illness behaviour has received less attention, with most research studying CFS patients after diagnosis. Our previous study on the records of an insurance company showed a highly significant increase in illness reporting before development of CFS. AIM: To investigate the number and type of general practitioner (GP) consultations by patients with CFS for 15 years before they develop their condition. DESIGN OF STUDY: Case-control study in 11 general practices in Devon. SETTING: Forty-nine patients with CFS (satisfying the Centers for Disease Control criteria), 49 age, sex, and general practice matched controls, and 37 patients with multiple sclerosis (MS) were identified from the general practices' computerised databases. METHOD: The number of general practice consultations and symptoms recorded in three five-year periods (quinquennia) were counted before development of the patients' condition. RESULTS: The median number of consultations was significantly higher for CFS patients than that of matched controls in each of the quinquennia: ratios for first quinquennium = 1.88, P = 0.01; second quinquennium = 1.70, P = 0.005; last quinquennium = 2.25, P < 0.001. More CFS patients than controls attended for 13 of the 18 symptoms studied. Significant increases were found for upper respiratory tract infection (P < 0.001), lethargy (P < 0.001), and vertigo (P = 0.02). Similar results were found for CFS patients when

				compared with MS. CONCLUSIONS: CFS patients consulted their GP more frequently in the 15 years before development of their condition, for a wide variety of complaints. Several possibilities may explain these findings. The results support the hypothesis that behavioural factors have a role in the aetiology of CFS.
Hammond DC.	Department of Physical Medicine & Rehabilitation, University of Utah School of Medicine, Salt Lake City, UT, USA. D.C.Hammond@m.cc.utah.edu	Treatment of chronic fatigue with neurofeedback and self-hypnosis.	NeuroRehabilitation. 2001;16(4):295-300.	A 21 year old patient reported a relatively rapid onset of serious chronic fatigue syndrome (CFS), with her worst symptoms being cognitive impairments. Congruent with research on rapid onset CFS, she had no psychiatric history and specialized testing did not suggest that somatization was likely. Neuroimaging and EEG research has documented brain dysfunction in cases of CFS. Therefore, a quantitative EEG was done, comparing her to a normative data base. This revealed excessive left frontal theta brainwave activity in an area previously implicated in SPECT research. Therefore, a novel treatment approach was utilized consisting of a combination of EEG neurofeedback and self-hypnosis training, both of which seemed very beneficial. She experienced considerable improvement in fatigue, vigor, and confusion as measured pre-post with the Profile of Mood States and through collaborative interviews with both parents. Most of the changes were maintained at 5, 7, and 9 month follow-up testing.
Hanson SJ, Gause W, Natelson B.	Department of Psychology, Rutgers University, Newark, New Jersey 07102, USA. jose@kreizler.rutgers.edu	Detection of immunologically significant factors for chronic fatigue syndrome using neural-network classifiers.	Clin Diagn Lab Immunol. 2001 May;8(3):658-62.	Neural-network classifiers were used to detect immunological differences in groups of chronic fatigue syndrome (CFS) patients that heretofore had not shown significant differences from controls. In the past linear methods were unable to detect differences between CFS groups and non-CFS control groups in the nonveteran population. An examination of the cluster structure for 29 immunological factors revealed a complex, nonlinear decision surface. Multilayer neural networks showed an over 16% improvement in an n-fold resampling generalization test on unseen data. A sensitivity analysis of the network found differences between groups that are consistent with the hypothesis that CFS symptoms are a consequence of immune system dysregulation. Corresponding decreases in the CD19(+) B-cell compartment and the CD34(+) hematopoietic progenitor subpopulation were also detected by the neural network, consistent with the T-cell expansion. Of significant interest was the fact that, of all the cytokines evaluated, the only one to be in the final model was interleukin-4 (IL-4). Seeing an increase in IL-4 suggests a shift to a type 2 cytokine pattern. Such a shift has been hypothesized, but until now convincing evidence to support that hypothesis has been lacking.
Hardt J, Buchwald D, Wilks D, Sharpe M, Nix WA, Egle UT.	Department of Psychosomatic Medicine and Psychotherapy, University of Mainz, Untere Zahlbacher 8, D-55101, Mainz, Germany. hardt@mail.uni-	Health-related quality of life in patients with chronic fatigue syndrome: an international study.	J Psychosom Res. 2001 Aug;51(2):431-4.	OBJECTIVE: Chronic fatigue syndrome (CFS) has been reported worldwide. Our objectives were to determine if patients from different countries have similar profiles of impairments. METHODS: Health-related quality of life (HRQoL) was assessed in 740 CFS patients in the US, 82 in the UK, and 65 in Germany using the eight subscales of the Short-Form General Health Survey (SF-36). To examine the internal structure, factor analyses were performed. RESULTS: Overall, there was a remarkable similarity in HRQoL among all CFS patients, regardless of location. Patients scored two to three standard deviations below normal on six subscales and one standard deviation below normal on the other two subscales. Factor analysis suggested a two-factor model where the same six subscales constitute the first

	mainz.de			factor and the two others the second factor. CONCLUSION: HRQoL is poor in CFS patients from three countries. This study is a first step towards conducting further comparative cross-cultural and international studies.
Hausotter W.		[Modern illnesses from the critical viewpoint] [Article in German]	Versicherungsmedizin. 2001 Dec 1;53(4):177-81. Comment in: Versicherungsmedizin. 2002 Sep 1;54(3):149-50; discussion 150.	Psychosomatic illness as "modern diseases" are of increasing interest to the public. Environmental illnesses, for example assumed intoxication with organic solvents, multiple chemical sensitivity, sick building syndrome, chronic fatigue syndrome, fibromyalgia, the influence of amalgam or of electromagnetic waves and ozone are often causes of anxiety. There are many hypotheses about the origin of these diseases. Some scientists emphasize an organic basis; however, this is not generally accepted. Very often with good reason a psychological cause is supposed. Objective diagnostic criteria are not available, therefore these diagnoses may only be applied after sufficient exclusion of other known organic diseases. Mostly a psychological treatment is refused by the person affected, and a scientifically based somatic concept for the therapy does not exist. The medicolegal problems are important and often the reason for prolonged forensic confrontations.
Hickie IB, Bansal AS, Kirk KM, Lloyd AR, Martin NG.	School of Psychiatry, University of New South Wales, Sydney, Australia. i.hickie@unsw.edu.au	A twin study of the etiology of prolonged fatigue and immune activation.	Twin Res. 2001 Apr;4(2):94-102.	Risk factors to prolonged fatigue syndromes (PFS) are controversial. Pre-morbid and/or current psychiatric disturbance, and/or disturbed cell-mediated immunity (CMI), have been proposed as etiologic factors. Self-report measures of fatigue and psychologic distress and three in vitro measures of CMI were collected from 124 twin pairs. Crosstwin-crosstrait correlations were estimated for the complete monozygotic (MZ; 79 pairs) and dizygotic (DZ; 45 pairs) twin groups. Multivariate genetic and environmental models were fitted to explore the patterns of covariation between etiologic factors. For fatigue, the MZ correlation was more than double the DZ correlation (0.49 versus 0.16) indicating strong genetic control of familial aggregation. By contrast, for in vitro immune activation measures MZ and DZ correlations were similar (0.49-0.69 versus 0.42-0.53) indicating the etiologic role of shared environments. As small univariate associations were noted between prolonged fatigue and the in vitro immune measures (r = -0.07 to -0.12), multivariate models were fitted. Relevant etiologic factors included: a common genetic factor accounting for 48% of the variance in fatigue which also accounted for 4%, 6% and 8% reductions in immune activation; specific genetic factors for each of the in vitro immune measures; a shared environment factor influencing the three immune activation measures; and, most interestingly, unique environmental influences which increased fatigue but also increased markers of immune activation. PFS that are associated with in vitro measures of immune activation are most likely to be the consequence of current environmental rather than genetic factors. Such environmental factors could include physical agents such as infection and/or psychologic stress.
Hickie IB, Davenport TA, Hadzi-Pavlovic D, Koschera A, Naismith SL, Scott EM, Wilhelm KA.	School of Psychiatry, University of New South Wales, Sydney. ian.hickie@beyondblue.org.au	Development of a simple screening tool for common mental disorders in general practice.	Med J Aust. 2001 Jul 16;175 Suppl:S10-7. Comment in: Med J Aust. 2001 Jul 16;175 Suppl:S6-7	OBJECTIVE: To develop and validate a self-report screening tool for common mental disorders. DESIGN AND SETTING: Sequential development and validation studies in three cohorts of patients in general practice and one cohort of patients in a specialist psychiatry clinic. PARTICIPANTS: 1585 patients in general practice examined cross-sectionally and longitudinally; 46515 patients attending 386 general practitioners nationwide; 364 patients

				participating in a longitudinal study of psychiatric disorders in general practice; and 522 patients attending a specialist psychiatry clinic. MAIN OUTCOME MEASURES: Performance of the 12 items from the 34-item SPHERE questionnaire against DSM-III-R and DSM-IV diagnoses of psychiatric disorder, self-reported Brief Disability Questionnaire findings, GPs' ratings of patients' needs for psychological care and degree of risk resulting from mental disorder, and patients' and GPs' reports of reasons for presentation. RESULTS: Six somatic and six psychological questions identify two levels (and three types) of mental disorder: patients reporting both characteristic psychological and somatic symptoms (Level 1, Type 1), and patients reporting either psychological symptoms (Level 2, Type 2) or somatic symptoms (Level 2, Type 3). This classification system predicts disability ratings (Level 1, 8.2 "days out of role in the last month" and Level 2, 4.1 and 5.4 "days out of role in the last month" for Types 2 and 3, respectively), rates of lifetime psychiatric diagnoses (Level 1, 63% and Level 2, 59% and 48%, respectively), both patients' and GPs' report of reasons for presentation, and doctors' ratings of risk as a result of mental disorder. There are important and differing sociodemographic correlates for the three types of mental disorders. CONCLUSION: A classification system based on the 12 items from the 34-item SPHERE questionnaire can be used to identify common mental disorders. This system has acceptable validity and reliability, and is suited specifically for general practice settings.
Inbar O, Dlin R, Rotstein A, Whipp BJ.	Department of Life Sciences, Zinman College, Wingate Institute, Netania, Israel. inbar@macam98.ac.il	Physiological responses to incremental exercise in patients with chronic fatigue syndrome.	Med Sci Sports Exerc. 2001 Sep;33(9):1463-70.	PURPOSE: The purpose of this investigation was to characterize the physiological response profiles of patients with chronic fatigue syndrome (CFS), to an incremental exercise test, performed to the limit of tolerance. METHODS: Fifteen patients (12 women and three men) who fulfilled the case definition for chronic fatigue syndrome, and 15 healthy, sedentary, age- and sex-matched controls, performed an incremental progressive all-out treadmill test (cardiopulmonary exercise test). RESULTS: As a group, the CFS patients demonstrated significantly lower cardiovascular as well as ventilatory values at peak exercise, compared with the control group. At similar relative submaximal exercise levels (% peak VO(2)), the CFS patients portrayed response patterns (trending phenomenon) characterized, in most parameters, by similar intercepts, but either lower (VCO(2), HR, O(2pulse), V(E), V(T), PETCO(2)) or higher (B(f), V(E)/VCO(2)) trending kinetics in the CFS compared with the control group. It was found that the primary exercise-related physiological difference between the CFS and the control group was their significantly lower heart rate at any equal relative and at maximal work level. Assuming maximal effort by all (indicated by RER, PETCO(2), and subjective exhaustion), these results could indicate either cardiac or peripheral insufficiency embedded in the pathology of CFS patients. CONCLUSION: We conclude that indexes from cardiopulmonary exercise testing may be used as objective discriminatory indicators for evaluation of patients complaining of chronic fatigue syndrome.
Jason LA, Eisele H, Taylor RR.	DePaul University, USA.	Assessing attitudes toward new names for chronic fatigue	Eval Health Prof. 2001 Dec;24(4):424-35.	A questionnaire was distributed at the American Association of Chronic Fatigue Syndrome's biannual convention in Washington in January 2001 as well as through various Internet Web sites and listserves during early February and March of 2001. The sample

		syndrome.		consisted of 432 respondents. Most respondents (86%) indicated they wanted a name change, although more patients than scientists were in favor of this change. It was also apparent that the patients and physicians were clearly split between adopting a name such as myalgic encephalopathy versus one such as neuro-endocrine immune disorder. Also, among those respondents who selected either of these two choices for a new name, less than 30% of them supported the other name. Although the majority of respondents feel the name should be changed at this time, this survey suggests there are different stakeholders involved in the name-change process, each with strong and sometimes disparate feelings about changing the name.
Jason LA, Taylor RR, Carrico AW.	DePaul University, Department of Psychology, Chicago, IL 60614, USA. ljason@wppost.depaul.edu	A community-based study of seasonal variation in the onset of chronic fatigue syndrome and idiopathic chronic fatigue.	Chronobiol Int. 2001 Mar;18(2):315-9.	One proposed hypothesis regarding the etiology of chronic fatigue syndrome (CFS) is that there is a subgroup of patients in which symptom onset is precipitated by a viral infection. If this is indeed true, then one would anticipate a greater incidence of the emergence of CFS symptoms during months when viral infections occur with the greatest frequency. The current community-based epidemiology study examined the month of symptom onset for 31 patients with CFS and 44 others with idiopathic chronic fatigue (ICF). It was determined that the distribution of the month of illness onset for the CFS and ICF groups was nonrandom, with greater numbers of participants than expected reporting an onset of CFS and ICF during January.
Jason LA, Taylor RR, Kennedy CL, Harding ST, Song S, Johnson D, Chimata R.		Subtypes of Chronic Fatigue Syndrome: A Review of Findings	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 1	Most studies of Chronic Fatigue Syndrome (CFS) have been based on patients recruited from primary or tertiary care settings. Patients from such settings might not be typical of patients in the general population and may not accurately reflect the heterogeneity among individuals diagnosed with this condition. The current paper reviews four community-based studies that examined subtypes of individuals with CFS. Distinctions between subtype groups based on sociodemographics, illness onset and duration, stressful precipitating events, symptom frequency, and comorbidity characteristics are made with respect to outcome measures of fatigue and symptom severity, functional ability, and psychiatric comorbidity.
Jason LA, Taylor RR.		Measuring Attributions About Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 31	Three studies explored the effects of different diagnostic labels and different types of recommended treatments for Chronic Fatigue Syndrome upon attributions regarding its cause, nature, severity, contagion, prognosis, and treatment. Attributions for Chronic Fatigue Syndrome appear to change based upon the diagnostic label given for the syndrome and the type of t reatment recommended. Results suggest that, in comparison to the Chronic Fatigue Syndrome label, the Myalgic Encephalopathy label prompts attributions that this syndrome is a serious condition associated with a physiologically-based etiology, a poor prognosis, and decreased potential for organ donation. Results also suggest that, compared with cognitive coping skills treatment, treatment with ampligen appears to be associated with perceptions of chronic fatigue syndrome as an accurate diagnosis and as a severely disabling condition.
Jay SJ.		Orthostatic hypotension and	JAMA. 2001 Mar 21;285(11):1442-3.	

		chronic fatigue syndrome.	Comment on: JAMA. 2001 Jan 3;285(1):52-9.	
Johnson SK, Lange G, Tiersky L, DeLuca J, Natelson BH.		Health-Related Personality Variables in Chronic Fatigue Syndrome and Multiple Sclerosis	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 41	This study investigated personality variables in patients with Chronic Fatigue Syndrome (CFS) and Multiple Sclerosis (MS), with healthy, sedentary subjects as controls. CFS and MS groups were higher on alexithymia, characterized as difficulty in describing and differentiating emotions and marked externalization. CFS and MS groups reported a more depressive attributional style than healthy participants, reflecting beliefs that causes for good events are not diffused into other areas of life while causes for bad events will always be present. The CFS group was significantly lower on Doctors/Others locus of control indicating lack of trust in medical professionals. Results indicate that CFS and MS are similar to each other while different from the healthy group on certain personality variables that likely reflect the demoralizing effects of coping with a chronic, disabling illness marked by uncertainty.
Kaminaga T, Kunimatsu N, Chikamatsu T, Furui S.	Department of Radiology, Teikyo University School of Medicine, Tokyo, Japan. kami@med.teikyo-u.ac.jp	Validation of CBF measurement with non-invasive microsphere method (NIMS) compared with autoradiography method (ARG).	Ann Nucl Med. 2001 Feb;15(1):61-4.	The purpose of this study is to examine the correlation of measured regional cerebral blood flow (rCBF) by means of a new microsphere method (non-invasive microsphere method), to the autoradiography (ARG) method, which is an established quantification method for 123I-IMP brain SPECT. The non-invasive microsphere (NIMS) method and ARG method were simultaneously applied to 30 patients, and quantified rCBF maps were calculated with each method. A significant correlation ($r = 0.70$: $p < 0.001$) was detected between mCBF values calculated with the NIMS and ARG methods. This new method seems to reliably quantify rCBF with brain SPECT.
Karpukhin IV.		[Use of local negative pressure in combination with electric sleep or Charcot's douche for treatment of erectile dysfunctions] [Article in Russian]	Vopr Kurortol Fizioter Lech Fiz Kult. 2001 Jul-Aug;(4):32-4.	43 patients with psychogenic erectile dysfunction aged 20-43 years received therapeutic complex including local negative pressure and electric sleep or Charcot's douche. The results obtained show that this complex in effective in erectile dysfunctions secondary to stress, neurosis and chronic fatigue syndrome.
Kenny RA, Graham LA.		Chronic fatigue syndrome symptoms common in patient with vasovagal syncope.	Am J Med. 2001 Feb 15;110(3):242-3.	
Kerr JR, Barah F, Mattey DL, Laing I, Hopkins SJ, Hutchinson IV, Tyrrell DA.	Department of Microbiology, Royal Brompton Hospital, National Heart and Lung Institute,	Circulating tumour necrosis factor-alpha and interferon-gamma are detectable during	J Gen Virol. 2001 Dec;82(Pt 12):3011-9.	To investigate whether cytokine responses may have a bearing on the symptoms and outcome of parvovirus B19 infection, circulating cytokines were measured during acute infection (n=51), follow-up of acute infection (n=39) and in normal healthy controls (n=50). At acute B19 virus infection (serum anti-B19 IgM-positive), patients ranged in age from 4 to 54 years, with a mean age of 28.2 years. The male:female ratio was 1:4.1 and symptoms

	Imperial College School of Medicine, Sydney Street, London SW3 6NP, UK. j.kerr@ic.ac.uk	acute and convalescent parvovirus B19 infection and are associated with prolonged and chronic fatigue.		were rash (n=15), arthralgia (n=31), fatigue (n=8), lymphadenopathy (n=4), foetal hydrops (n=3), transient aplastic crisis (n=2), neutropenia (n=2), myelodysplasia (n=1), thrombocytopenia (n=1) and pancytopenia (n=1). Of these patients, 39 were contacted after a follow-up period of 2-37 months (mean of 22.5 months). In comparison with normal controls, detectable IL-6 was associated with acute B19 virus infection (26%; P=0.0003), but not with follow-up (6%; P=0.16). Detection of interferon (IFN)-gamma was associated with acute B19 virus infection (67%; P<0.0001) and follow-up (67%; P<0.0001). Detection of tumour necrosis factor (TNF)-alpha was associated with acute B19 virus infection (49%; P<0.0001) and follow-up (56%; P<0.0001). IL-1beta was detected in acute infection (20%), but not at follow-up. At acute B19 virus infection, detection of serum/plasma IL-6 was associated with rheumatoid factor (P=0.038) and IFN-gamma (> or =7 pg/ml) was associated with fatigue in those patients of > or =15 years of age (P=0.022). At follow-up, fatigue was associated with IFN-gamma (> or =7 pg/ml) and/or TNF-alpha (> or =40 pg/ml) (P=0.0275). Prolonged upregulation of serum IFN-gamma and TNF-alpha appears to represent a consistent host response to symptomatic B19 virus infection.
Klimas NG, Patarca-Montero R, Maher K, Smith M, Bathe O, Fletcher MA.		Clinical and Immunologic Effects of Autologous Lymph Node Cell Transplant in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(1): 39	An open labeled, phase 1, safety and feasibility study using lymph node extraction, ex vivo lymph node cell expansion, followed by autologous cell reinfusion was evaluated as a potential immunomodulatory treatment strategy in patients with chronic fatigue syndrome (CFS). The experimental therapy utilized the cells of the lymph node, activated and grown in culture with defined media, interleukin-2 (IL-2) and anti-CD3 to activate and enhance cellular immunological functions. This procedure was designed to change the cytokine pattern of the lymph node lymphocytes to favor expression of T-helper (Th)1-type over Th2-type cytokines. The mixed population of ex vivo immune-enhanced cells were reinfused into the donor, who was carefully monitored for adverse events and possible clinical benefit. There were no adverse events. There were significant improvements in clinical status in association with a significant decrease in Th2-type cytokine production.
Kovaleva AI, Pyshnov GIu.		[Problems of chronic fatigue] [Article in Russian]	Med Tr Prom Ekol. 2001;(11):1-5.	The review covers some human pathologic conditions defined as chronic fatigue syndrome, caroshi, burnout. Concerning nonspecific manifestations, one could characterize these conditions as general overfatigue of human. The authors attempt to consider these conditions from the viewpoint of occupationally induced disorders.
Krueger GR, Koch B, Hoffmann A, Rojo J, Brandt ME, Wang G, Buja LM.	Department of Pathology & Laboratory Medicine, University of Texas-Houston Medical School, 6431 Fannin St, MSB 2.246, Houston, Texas 77030, USA. Gerhard.Krueger@ut	Dynamics of chronic active herpesvirus-6 infection in patients with chronic fatigue syndrome: data acquisition for computer modeling.	In Vivo. 2001 Nov-Dec;15(6):461-5.	Ten adult patients with persistent active HHV-6 variant A infection and clinical chronic fatigue syndrome (CFS) were studied over a period of 24 months after initial clinical diagnosis. CFS was diagnosed according to IIIP-revised CDC-criteria as defined by the CFS Expert Advisory Group to the German Federal Ministry of Health in 1994. Changes in HHV-6 antibody titer, viral DNA load, peripheral blood T lymphocytes and subpopulations, as well as CD4/CD8 cell ratio and cell death (apoptosis) were monitored. Data were collected for comparison with respective changes in acute HHV-6 infection and as a basis for future computer simulation studies. The results showed variable but slightly elevated numbers of HHV-6 DNA copies in the blood of patients with CFS, while PBL (peripheral blood lymphocyte) apoptosis rates were clearly increased. CD4/CD8 cell ratios varied from below

	htmcedu			1 up to values as seen in autoimmune disorders. Contrary to acute HHV-6 infection, T lymphocytes do not exhibit the usual response to HHV-6, that is elevation of mature and immature populations suggesting a certain degree of unresponsiveness. The data suggest that persistent low-dose stimulation by HHV-6 may favor imbalanced immune response rather than overt immune deficiency. This hypothesis requires confirmation through additional functional studies.
Kuratsune H, Kondo K, Ikuta K, Yamanishi K, Watanabe Y, Kitani T.		[Chronic fatigue syndrome (CFS)] [Article in Japanese]	Nippon Naika Gakkai Zasshi. 2001 Dec 10;90(12):2431-7.	
LaManca JJ, Peckerman A, Sisto SA, DeLuca J, Cook S, Natelson BH.	Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, New Jersey, USA.	Cardiovascular responses of women with chronic fatigue syndrome to stressful cognitive testing before and after strenuous exercise.	Psychosom Med. 2001 Sep-Oct;63(5):756-64.	OBJECTIVE: The purpose of this study was to compare the cardiovascular responses of patients with chronic fatigue syndrome (CFS) to healthy control subjects when performing stressful cognitive tasks before and after strenuous exercise. METHOD: Beat-by-beat blood pressure and electrocardiogram were recorded on 19 women with CFS and 20 healthy nonexercising (ie, sedentary) women while they performed cognitive tests before, immediately after, and 24 hours after incremental exercise to exhaustion. RESULTS: Diminished heart rate ($p < .01$) and systolic ($p < .01$) and diastolic ($p < .01$) blood pressure responses to stressful cognitive testing were seen in patients with CFS when compared with healthy, sedentary controls. This diminished stress response was seen consistently in patients with CFS across three separate cognitive testing sessions. Also, significant negative correlations between self-ratings of CFS symptom severity and cardiovascular responses were seen ($r = -0.62$, $p < .01$). CONCLUSIONS: Women with CFS have a diminished cardiovascular response to cognitive stress; however, exercise did not magnify this effect. Also, the data showed that the patients with the lowest cardiovascular reactivity had the highest ratings of CFS symptom severity, which suggests that the individual response of the patient with CFS to stress plays a role in the common complaint of symptoms worsening after stress.
Lange G, Holodny AI, DeLuca J, Lee HJ, Yan XH, Steffener J, Natelson BH.	Departments of Psychiatry and Radiology, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, 30 Bergen Street, Newark, NJ 07107, USA. langegu@umdnj.edu	Quantitative assessment of cerebral ventricular volumes in chronic fatigue syndrome.	Appl Neuropsychol. 2001;8(1):23-30.	Previous qualitative volumetric assessment of lateral ventricular enlargement in chronic fatigue syndrome (CFS) has provided evidence for subtle structural changes in the brains of some individuals with CFS. The aim of this pilot study was to determine whether a more sensitive quantitative assessment of the lateral ventricular system would support the previous qualitative findings. In this study, we compared the total lateral ventricular volume, as well as the right and left hemisphere subcomponents in 28 participants with CFS and 15 controls. Ventricular volumes in the CFS group were larger than in control groups, a difference that approached statistical significance. Group differences in ventricular asymmetry were not observed. The results of this study provide further evidence of subtle pathophysiological changes in the brains of participants with CFS.
Lange G, Tiersky LA, Scharer JB, Policastro	Center for Environmental	Cognitive functioning in Gulf War Illness.	J Clin Exp Neuropsychol. 2001	A comprehensive neuropsychological battery was administered to 48 veterans with Gulf War Illness (GWI) characterized by severe fatigue (GV-F) and 39 healthy veterans (GV-H).

T, Fiedler N, Morgan TE, Natelson BH.	Hazards Research, DVA NJ Health Care System, East Orange, NJ, USA. langegu@umdnj.edu		Apr;23(2):240-9.	Subjects were matched on intelligence and did not differ on age, gender, race, and alcohol consumption. Compared to GVs-H, GVs-F were significantly impaired on four tasks: three attention, concentration, information processing tasks and one measure of abstraction and conceptualization. After considering the presence of post-war Axis I psychopathology, GWI remained a significant predictor of cognitive performance on one of the attention, concentration, and information processing tasks and one abstraction and conceptualization measure. Performance on the remaining two attention, concentration, and information processing tasks was only significantly predicted by Axis I psychopathology with post-war onset. The results suggest that Gulf War Illness is associated with some aspects of cognitive dysfunction in Gulf Veterans, over and above the contribution of psychopathology.
Lassesen KM.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):239; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Lerner AM, Zervos M, Chang CH, Beqaj S, Goldstein J, O'Neill W, Dworkin H, Fitgerald T, Deeter RG.		A small, randomized, placebo-controlled trial of the use of antiviral therapy for patients with chronic fatigue syndrome.	Clin Infect Dis. 2001 Jun 1;32(11):1657-8. Comment on: Clin Infect Dis. 1999 Sep;29(3):526-7.	
Levin AM.		Chronic Fatigue Syndrome: The Yeast Concept	Journal of Chronic Fatigue Syndrome 2001; 8(2): 71	Many theories abound as to the cause of CFS, but none have been proven conclusively. Because of the prevalence of the condition in many different countries throughout the world, it is becoming increasingly necessary to find a common link in the causative mechanism. The cause must be present at an international level. The overgrowth of bowel yeast and its infiltration through the bowel wall into the blood stream would appear to be the starting point in the development of CFS. This invasion of yeast can occur for different reasons. Therapeutic interventions based on the years of hypothesis are suggested.
Levin J, Steele L.		On the epidemiology of 'mysterious' phenomena.	Altern Ther Health Med. 2001 Jan;7(1):64-6.	In the field of epidemiology, research topics are favored or dismissed depending on whether respective variables under investigation are believed to exist according to current scientific theories. Unconventional independent variables or exposures, such as religiousness and spirituality, and controversial dependent variables or outcomes, such as chronic fatigue syndrome, may be considered unacceptable topics for researchers because they do not fit comfortably into the consensus clinical perspectives of mainstream medical scientists or physicians. Disapproval of research in these and other taboo areas is generally masked by claims that such studies are "pseudoscientific," despite hundreds or thousands of peer-reviewed publications on these topics. In reality, seemingly "mysterious" variables are equally as amenable to epidemiologic research as any other exposure or disease.

				Similarly, alternative therapies are able to be investigated using existing methods, despite claims to the contrary. Such research is vital for scientific understanding to be expanded into new areas of inquiry.
Levine PH, Klimas N, Armitage R, Fredericks R, Stewart J, Torch W, Schwartz S, Suhadolnik R, Reichenbach NL, Rhodes L.		Nevada Chronic Fatigue Syndrome Consensus Conference	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 53	
Levine S, Eastman H, Ablashi DV.		Prevalence of IgM and IgG Antibody to HHV-6 and HHV-8 and Results of Plasma PCR to HHV-6 and HHV-7 in a Group of CFS Patients and Healthy Donors	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 31	Human herpes virus-6 is a beta herpes virus that was first described in 1986 and which occurs in the form of at least two variants, A and B. Healthy donors in the general population are carriers for mainly the B variant, in whom 90% harbor the DNA of this type in their peripheral blood mononuclear cells (PBMNC). A higher prevalence of this virus has been detected by testing of plasma and PBMNCs by IFA, ELISA and by the nested PCR technique, in addition to direct culture for HHV-6 in certain groups of immunesuppressed patients such as those with multiple sclerosis and HIV. It has also been isolated to a greater degree using these techniques from patients who meet the case definition for the chronic fatigue syndrome (CFS). We determined IgG and IgM antibody titers to HHV-6; IgG to HHV-8 and performed PCR testing for HHV-6 on the plasma of 46 patients with CFS and on 7 healthy donors (HD). We also performed PCR testing for HHV-7 on 15 CFS patients and on 4 HD(s). We found a higher prevalence of IgM antibody in CFS patients 23/36 (50%) versus 2/7 (28.5%) of HD. The prevalence of IgG antibody to HHV-8 was zero among both CFS patients and HD. Three out of forty six (6.5%) of CFS patients demonstrated a positive plasma by PCR to HHV-6 compared to zero out of 7 HD(s). Finally, four out of fifteen (26.7%) CFS patients and zero out of four HD (s) demonstrated a positive plasma PCR to HHV-7. Our results were influenced by the presence of various subpopulations of CFS patients among our study group, in addition to our reliance on the results of single specimens as opposed to a series of multiple samples over time in individual subjects, and by methodological variability (decreasing our yield because of diminished viral shedding in cell-free samples or increasing it compared to other research groups who failed to co-culture the PBMNCs with indicator cells, e.g., PHA-stimulated human cord blood cells or human fibroblasts for short-term culture [15 day]). Nevertheless, it is clear that the study of plasma and perhaps other tissue samples, such as cerebral spinal fluid and gastric mucosa from patients with CFS in better defined subgroups, as well as defined population of HDs using a variety of methodological techniques will increase our knowledge about the role of HHV-6 in this complex disorder.
Levine S.		Prevalence in the Cerebrospinal Fluid of the Following	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 41	Over the last decade a wide variety of infectious agents has been associated with the chronic fatigue syndrome (CFS) as potential etiologies for this disorder by researchers from all over the world. Many of these agents are neurotrophic and have been linked previously

		Infectious Agents in a Cohort of 12 CFS Subjects: Human Herpes Virus-6 and 8; Chlamydia Species; Mycoplasma Species; EBV; CMV; and Coxsackievirus		to other diseases involving the central nervous system (CNS). Human herpes virus-6 (HHV-6), especially the B variant, has been found in autopsy specimens of patients who suffered from multiple sclerosis. Because patients with CFS manifest a wide range of symptoms involving the CNS as shown by abnormalities on brain MRIs, SPECT scans of the brain and results of tilt table testing we sought to determine the prevalence of HHV-6, HHV-8, Epstein-Barr virus (EBV), cytomegalovirus (CMV), Mycoplasma species, Chlamydia species, and Coxsackie virus in the spinal fluid of a group of 12 patients with CFS. Although we intended to search mainly for evidence of actively replicating HHV-6, a virus that has been associated by several researchers with this disorder, we found evidence of HHV-8, Chlamydia species, CMV and Coxsackie virus in 6/12 samples. Attempts were made to correlate the clinical presentations of each of these patients, especially the neurological exams and results of objective testing of the CNS, with the particular infectious agent isolated. It was also surprising to obtain such a relatively high yield of infectious agents on cell free specimens of spinal fluid that had not been centrifuged. Future research in spinal fluid analysis, in addition to testing tissue samples by polymerase chain reaction (PCR) and other direct viral isolation techniques will be important in characterizing subpopulations of CFS patients, especially those with involvement of the CNS.
Lewis DH, Mayberg HS, Fischer ME, Goldberg J, Ashton S, Graham MM, Buchwald D.	Departments of Radiology, University of Washington, Seattle, USA.	Monozygotic twins discordant for chronic fatigue syndrome: regional cerebral blood flow SPECT.	Radiology. 2001 Jun;219(3):766-73.	PURPOSE: To evaluate the relationship between regional cerebral blood flow (rCBF) and chronic fatigue syndrome (CFS) in monozygotic twins discordant for CFS. MATERIALS AND METHODS: The authors conducted a co-twin control study of 22 monozygotic twins in which one twin met criteria for CFS and the other was healthy. Twins underwent a structured psychiatric interview and resting technetium 99m-hexamethyl-propyleneamine oxime single photon emission computed tomography of the brain. They also rated their mental status before the procedure. Scans were interpreted independently by two physicians blinded to illness status and then at a blinded consensus reading. Imaging fusion software with automated three-dimensional matching of rCBF images was used to coregister and quantify results. Outcomes were the number and distribution of abnormalities at both reader consensus and automated quantification. Mean rCBF levels were compared by using random effects regression models to account for the effects of twin matching and potential confounding factors. RESULTS: The twins with and those without CFS were similar in mean number of visually detected abnormalities and in mean differences quantified by using image registration software. These results were unaltered with adjustments for fitness level, depression, and mood before imaging. CONCLUSION: The study results did not provide evidence of a distinctive pattern of resting rCBF abnormalities associated with CFS. The described method highlights the importance of selecting well-matched control subjects.
Lipschitz EL		Chronic fatigue syndrome and posttraumatic stress disorder.	JAMA. 2001 Aug 22-29;286(8):916-7. Comment on: JAMA. 2001 May 23-	

			30;285(20):2557-9.	
Logan AC, Wong C.	CFS/FM Integrative Care Centre, Toronto, ON, Canada. alancloganND@excite.com	Chronic fatigue syndrome: oxidative stress and dietary modifications.	Altern Med Rev. 2001 Oct;6(5):450-9.	Chronic fatigue syndrome (CFS) is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various body systems. The etiology of CFS remains unclear; however, a number of recent studies have shown oxidative stress may be involved in its pathogenesis. The role of oxidative stress in CFS is an important area for current and future research as it suggests the use of antioxidants in the management of CFS. Specifically, the dietary supplements glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins, Ginkgo biloba, and Vaccinium myrtillus (bilberry) may be beneficial. In addition, research on food intolerance is discussed, since food intolerance may be involved in CFS symptom presentation and in oxidation via cytokine induction. Finally, recent evidence suggests celiac disease can present with neurological symptoms in the absence of gastrointestinal symptoms; therefore, celiac disease should be included in the differential diagnosis of CFS.
Logan AC.		Nutritional strategies for treating chronic fatigue syndrome.	Altern Med Rev. 2001 Feb;6(1):4-6. Comment on: Altern Med Rev. 2000 Apr;5(2):93-108.	
Manuel y Keenoy B, Moorkens G, Vertommen J, De Leeuw I.	University Hospital, University of Antwerp, Belgium. begona@uia.ua.ac.be	Antioxidant status and lipoprotein peroxidation in chronic fatigue syndrome.	Life Sci. 2001 Mar 16;68(17):2037-49.	The aetiology and pathogenesis of the Chronic Fatigue Syndrome (CFS) are still largely unresolved. Accompanying metabolic disorders such as selective n-6 fatty acid depletion suggest that oxidative stress and more specifically lipid peroxidation might play a role in its pathogenesis. In order to investigate this hypothesis, oxidant-antioxidant status and its impact on lipoprotein peroxidation in vitro was examined in 61 patients with unexplained fatigue lasting more than 1 month. They were subdivided into 2 groups: group CFS+ (33 subjects) fulfilled the 1988 Center of Disease Control criteria for CFS and group CFS- did not but was similar as regards age, sex distribution and clinical characteristics. Antioxidant status was similar in the 2 groups except for lower serum transferrin in the CFS + (mean (95 % CI) 2.41 (2.28-2.54) versus 2.73 (2.54-2.92) g/L in the CFS-, p = 0.009) and higher lipoprotein peroxidation in vitro: 6630 (5949-7312) versus 5581 (4852-6310) nmol MDA/mg LDL and VLDL cholesterol x minutes, p = 0.035). CFS intensified the influence of LDL cholesterol (p = 0.012) and of transferrin (p = 0.045) on peroxidation in vitro, suggesting additional pro-oxidant effects. These results indicate that patients with CFS have increased susceptibility of LDL and VLDL to copper-induced peroxidation and that this is related both to their lower levels of serum transferrin and to other unidentified pro-oxidising effects of CFS.
Maquet D, Croisier JL, Crielaard JM.	Medecine de l'appareil locomoteur, CHU Sart Tilman, 4000 Liege, Belgique, France.	[What happens to the fibromyalgia syndrome?] [Article in French]	Ann Readapt Med Phys. 2001 Jul;44(6):316-25.	OBJECTIVE: To realize a clarification about fibromyalgia, attempting to consider diagnostic criteria, prevalence, pathophysiology and therapeutic approach. METHOD: A systematic literature search was conducted to select articles about fibromyalgia and connected diseases. The database are Premedline, Medline and Medlineplus. RESULTS: Fifty-eight articles about fibromyalgia and twelve articles about connected diseases were selected to

	d.maquet@belgacom.net			realize this review of literature. DISCUSSION: Fibromyalgia constitutes a syndrome characterized by widespread musculo-skeletal pain, present above the waist and below the waist and in the axial skeleton. Widespread pain must have been present for at least three months. "Spasmophilie", chronic fatigue syndrome and myofascial syndrome represent diseases connected with fibromyalgia: differential diagnosis must be established. Researches related to fibromyalgia suggest a reduction of muscular performances associated with histological and biochemical anomalies. Patients are characterized by shorter and nonrestorative sleep. Psychological, neuroendocrine and central alterations appear often associated with fibromyalgia. The reduction of pressure tolerance and pain thresholds may be linked to the alterations of neuroendocrine substances. Literature recommend a multidisciplinary therapeutic approach in management of fibromyalgia. CONCLUSION: The pathophysiologic mechanisms in fibromyalgia appear multiple and interdependent. With the aim to optimizing treatment, investigations are necessary to determine biochemical repercussions of various therapeutic approaches.
Martinez-Lavin M.	Rheumatology Department, Instituto Nacional de Cardiologia Ignacio Chavez, Juan Badiano 1., 14080 Mexico, D.F. Mexico. mmlavin@infosel.net.mx	Overlap of fibromyalgia with other medical conditions.	Curr Pain Headache Rep. 2001 Aug;5(4):347-50.	Fibromyalgia is a multisystem illness. One of its defining features, generalized pain, may also be present in other rheumatic entities. The diagnosis of fibromyalgia is not easy by any means, it requires a profound knowledge of internal medicine. This article discusses the different rheumatic and nonrheumatic diseases that overlap or are prone to be confused with fibromyalgia. It emphasizes the key points in the differential diagnosis.
Masuda A, Nakayama T, Yamanaka T, Hatsutanmaru K, Tei C.	First Department of Internal Medicine, Kagoshima University.	Cognitive behavioral therapy and fasting therapy for a patient with chronic fatigue syndrome.	Intern Med. 2001 Nov;40(11):1158-61.	Cognitive behavioral therapy temporarily alleviated symptoms of a chronic fatigue syndrome patient but the anxiety about rehabilitation into work became stronger and his symptoms worsened. This patient was successfully rehabilitated by fasting therapy. Natural killer cell activity and serum acylcarnitine levels recovered after fasting therapy. Though fasting therapy transiently increased physical and mental subjective symptoms, the patient gained self-confidence by overcoming difficulties after fasting therapy. A combination of cognitive behavioral therapy and fasting therapy is promising as a treatment for chronic fatigue syndrome.
Michiels V, Cluydts R. Department of Psychology, Free University of Brussels, Belgium.		Neuropsychological functioning in chronic fatigue syndrome: a review.	Acta Psychiatr Scand. 2001 Feb;103(2):84-93.	OBJECTIVE: In this paper we review critically the current status of neurocognitive studies in patients with chronic fatigue syndrome (CFS). METHOD: CFS literature was monitored as part of a large research project which involved several neuropsychological and psychopathological studies. The literature survey was the result of several consecutive searches on Medline and PsycInfo databases. RESULTS: The neurocognitive studies are reviewed in terms of scientificaly accepted aspects of attention and memory. In addition, we review possible explanations for cognitive dysfunction in CFS. This is preceded with a discussion of the methodological limitations that are considered to explain inconcistencies across neuropsychological studies in CFS. CONCLUSION: The current research shows that

				slowed processing speed, impaired working memory and poor learning of information are the most prominent features of cognitive dysfunctioning in patients with CFS. Furthermore, to this date no specific pattern of cerebral abnormalities has been found that uniquely characterizes CFS patients. There is no overwhelming evidence that fatigue is related to cognitive performance in CFS, and researchers agree that their performance on neuropsychological tasks is unlikely to be accounted solely by the severity of the depression and anxiety.
Miike T.	Department of Child Development, Kumamoto University School of Medicine.	[Chronic fatigue syndrome] [Article in Japanese]	Nippon Rinsho. 2001 Dec;59 Suppl 8:414-21.	
Miller CS.	Department of Family and Community Medicine, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78229-3900, USA. millercs@uthscsa.edu	Toxicant-induced loss of tolerance.	Addiction. 2001 Jan;96(1):115-37.	Drug addiction and multiple chemical intolerance (abdiction) appear to be polar opposites--the former characterized by craving and dependency, the latter by aversion. However, when the two are viewed in juxtaposition similarities emerge, revealing a common underlying dynamic, one which appears to be a new paradigm of disease. TILT, or toxicant-induced loss of tolerance, bridges the gap between addiction and abduction and has the potential to explain a variety of illnesses, including certain cases of asthma, migraine headaches and depression, as well as chronic fatigue syndrome, fibromyalgia and "Gulf War syndrome". This paper argues that both addiction and chemical intolerance involve a fundamental breakdown in innate tolerance, resulting in an amplification of various biological effects, particularly withdrawal symptoms. While addicts seek further exposures so as to avoid unpleasant withdrawal symptoms, chemically intolerant individuals shun their problem exposures, but for the same reason--to avoid unpleasant withdrawal symptoms. These observations raise critical questions: do addictive drugs and environmental pollutants initiate an identical disease process? Once this process begins, can both addictants and pollutants trigger symptoms and cravings? TILT opens a new window between the fields of addiction and environmental medicine, one that has the potential to transform neighboring realms of medicine, psychology, psychiatry and toxicology.
Morrison RE, Keating HJ 3rd.	Department of Medicine, Division of General Internal Medicine, University of Tennessee at Memphis, Memphis, Tennessee, USA.	Fatigue in primary care.	Obstet Gynecol Clin North Am. 2001 Jun;28(2):225-40, v-vi.	Fatigue is a common problem in primary care that may represent a reaction to life problems or be a component of a disease state. A careful history, physical examination, and a few directed laboratory tests can usually allow the physician to differentiate between fatigue caused by depression, situational stress, or physical causes such as postviral or drug-induced fatigue, endocrine disorders, sleep disorders, infectious diseases, autoimmune disorders, or neurologic disease. Uncommonly, patients may have otherwise unexplained fatigue lasting 6 months or more that fulfills the criteria of chronic fatigue syndrome. A range of diagnostic skills coupled with a therapeutic physician-patient relationship will usually be successful in treating women with symptoms of fatigue.
Moss-Morris R, Petrie KJ.	Health Psychology Research Group,	Discriminating between chronic	Psychol Med. 2001 Apr;31(3):469-79.	BACKGROUND: Chronic fatigue syndrome (CFS) and depression share a number of common symptoms and the majority of CFS patients meet lifetime criteria for depression.

	Faculty of Medical and Health Science, The University of Auckland, New Zealand.	fatigue syndrome and depression: a cognitive analysis.		While cognitive factors seem key to the maintenance of CFS and depression, little is known about how the cognitive characteristics differ in the two conditions. METHODS: Fifty-three CFS patients were compared with 20 depressed patients and 38 healthy controls on perceptions of their health, illness attributions, self-esteem, cognitive distortions of general and somatic events, symptoms of distress and coping. A 6 month follow-up was also conducted to determine the stability of these factors and to investigate whether CFS-related cognitions predict ongoing disability and fatigue in this disorder. RESULTS: Between-group analyses confirmed that the depressed group was distinguished by low self-esteem, the propensity to make cognitive distortions across all situations, and to attribute their illness to psychological factors. In contrast, the CFS patients were characterized by low ratings of their current health status, a strong illness identity, external attributions for their illness, and distortions in thinking that were specific to somatic experiences. They were also more likely than depressed patients to cope with their illness by limiting stress and activity levels. These CFS-related cognitions and behaviours were associated with disability and fatigue 6 months later. CONCLUSIONS: CFS and depression can be distinguished by unique cognitive styles characteristic of each condition. The documented cognitive profile of the CFS patients provides support for the current cognitive behavioural models of the illness.
Mouterde O.		Myalgic encephalomyelitis in children.	Lancet. 2001 Feb 17;357(9255):562. Comment in: Lancet. 2001 Jun 9;357(9271):1889.	
Mueller D.	Division of Neurosurgery, University of Missouri Hospital and Clinics, USA. muellerdm@health.missouri.edu	Brainstem conundrum: the Chiari I malformation.	J Am Acad Nurse Pract. 2001 Apr;13(4):154-9.	PURPOSE: To describe the Chairi I Malformation in relation to the anatomy of the brain and spinal cord, the common manifestations of the condition, diagnostic considerations, and management for the primary care provider. DATA SOURCES: Extensive review of the world-wide scientific literature on the condition, supplemented with actual case studies. CONCLUSIONS: The adult Chairi I Malformation is an insidious congenital brainstem anomaly that consists of caudal displacement of the cerebellar tonsils, brainstem and fourth ventricle into the upper cervical space, resulting in overcrowding of the posterior fossa. IMPLICATIONS FOR PRACTICE: Due to the vague, and often ambiguous presenting symptoms of Chiari I Malformation, many patients are misdiagnosed with conditions such as multiple sclerosis, fibromyalgia, chronic fatigue syndrome, or psychiatric disorders. Patients frequently experience symptoms months to years prior to accurate diagnosis and often incur irreversible neurologic deficits.
Mullington JM, Hinze-Selch D, Pollmacher T.	Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School,	Mediators of inflammation and their interaction with sleep: relevance for chronic fatigue	Ann N Y Acad Sci. 2001 Mar;933:201-10.	In humans, activation of the primary host defense system leads to increased or decreased NREM sleep quality, depending on the degree of early immune activation. Modest elevations of certain inflammatory cytokines are found during experimental sleep loss in humans and, in addition, relatively small elevations of cytokines are seen following commencement of pharmacological treatments with clozapine, a CNS active antipsychotic

	Boston, Massachusetts 02215, USA. jmulling@caregroup.harvard.edu	syndrome and related conditions.		agent, known to have immunomodulatory properties. Cytokines such as TNF-alpha, its soluble receptors, and IL-6, present in the periphery and the CNS, comprise a link between peripheral immune stimulation and CNS-mediated behaviors and experiences such as sleep, sleepiness, and fatigue. The debilitating fatigue experienced in chronic fatigue syndrome and related diseases may also be related to altered cytokine profiles.
Murdoch JC.	Chronic fatigue syndrome.		Br J Gen Pract. 2001 Sep;51(470):758. Comment on: Br J Gen Pract. 2001 Jul;51(468):553-8.	
Naschitz JE, Rozenbaum M, Rosner I, Sabo E, Priselac RM, Shaviv N, Ahdoot A, Ahdoot M, Gaitini L, Eldar S, Yeshurun D.	Departments of Internal Medicine A, Rheumatology, Anesthesiology, and Surgery, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.	Cardiovascular response to upright tilt in fibromyalgia differs from that in chronic fatigue syndrome.	J Rheumatol. 2001 Jun;28(6):1356-60.	OBJECTIVE: To compare the cardiovascular response during postural challenge of patients with fibromyalgia (FM) to those with chronic fatigue syndrome (CFS). METHODS: Age and sex matched patients were studied, 38 with FM, 30 with CFS, and 37 healthy subjects. Blood pressure (BP) and heart rate (HR) were recorded during 10 min of recumbence and 30 min of head-up tilt. Differences between successive BP values and the last recumbent BP, their average, and standard deviation (SD) were calculated. Time curves of BP differences were analyzed by computer and their outline ratios (OR) and fractal dimensions (FD) were measured. HR differences were determined similarly. Based on the latter measurements, each subject's discriminant score (DS) was computed. RESULTS: For patients and controls average DS values were: FM: -3.68 (SD 2.7), CFS: 3.72 (SD 5.02), and healthy controls: -4.62 (SD 2.24). DS values differed significantly between FM and CFS ($p < 0.0001$). Subgroups of FM patients with and without fatigue had comparable DS values. CONCLUSION: The DS confers numerical expression to the cardiovascular response during postural challenge. DS values in FM were significantly different from DS in CFS, suggesting that homeostatic responses in FM and CFS are dissimilar. This observation challenges the hypothesis that FM and CFS share a common derangement of the stress-response system.
Naschitz JE, Sabo E, Naschitz S, Shaviv N, Rosner I, Rozenbaum M, Gaitini L, Ahdoot A, Ahdoot M, Priselac RM, Eldar S, Zukerman E, Yeshurun D.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.	Hemodynamic instability in chronic fatigue syndrome: indices and diagnostic significance.	Semin Arthritis Rheum. 2001 Dec;31(3):199-208.	OBJECTIVES: To evaluate the cardiovascular response to postural challenge in patients with chronic fatigue syndrome (CFS) and to determine whether the degree of instability of the cardiovascular response may aid in diagnosing CFS. METHODS: Patients with CFS (n = 25) and their age- and gender-matched healthy controls (n = 37), patients with fibromyalgia (n = 30), generalized anxiety disorder (n = 15), and essential hypertension (n = 20) were evaluated with the aid of a standardized tilt test. The blood pressure (BP) and heart rate (HR) were recorded during 10 minutes of recumbence and 30 minutes of head-up tilt. We designated BP changes as the differences between successive BP values and the last recumbent BP. The average and standard deviation (SD) were calculated. Time curves of BP differences were loaded into a computerized image analyzer, and their outline ratios and fractal dimensions were measured. HR changes were determined similarly. The average and SD of the parameters were calculated, and intergroup comparisons were performed. RESULTS: On multivariate analysis, the independent predictors of CFS patients versus healthy controls were the fractal dimension of absolute values of the systolic BP changes

				(SYST-FD.abs), the standard deviation of the current values of the systolic BP changes (SYST-SD.cur), and the standard deviation of the current values of the heart rate changes (HR-SD.cur). The following equation was deduced to calculate the hemodynamic instability score (HIS) in the individual patient: HIS = 64.3303 + (SYST-FD.abs x -68.0135) + (SYST-SD.cur x 111.3726) + (HR-SD.cur x 60.4164). The best cutoff differentiating CFS from the healthy controls was -0.98. HIS values >-0.98 were associated with CFS (sensitivity 97%, specificity 97%). The HIS differed significantly between CFS and other groups (P <.0001) except for generalized anxiety disorder. Group averages (SD) of HIS were CFS = +3.72 (5.02), healthy = -4.62 (2.26), fibromyalgia = -3.27 (2.63), hypertension = -5.53 (2.24), and generalized anxiety disorder = +1.08 (5.2). CONCLUSION: The HIS adds objective criteria confirming the diagnosis of CFS. Copyright 2001 by W.B. Saunders Company
Natelson BH.	Fatigue Research Center, New Jersey Medical School, 88 Ross St, East Orange, NJ 07018. bhn@njneuromed.org	Chronic fatigue syndrome.	JAMA. 2001 May 23-30;285(20):2557-9. Comment in: JAMA. 2001 Aug 22-29;286(8):916-7.	
Nelson JJ, Natelson BH, Peckerman A, Pollet C, Lange G, Tiersky L, Servatius RJ, Policastro T, Fiedler N, Ottenweller JE.	Center for Environmental Hazards Research, Department of Veterans Affairs Medical Center, East Orange, NJ 07018, USA.	Medical follow-up of Persian Gulf War Veterans with severe medically unexplained fatigue: a preliminary study.	Mil Med. 2001 Dec;166(12):1107-9.	An important question for researchers interested in long-term consequences of military service is the health outcome of symptomatic Persian Gulf War Veterans. From an original group of 76 Gulf War Veterans who received the diagnosis of severe fatiguing illness, we attempted to get 58 veterans to return to our center for a second evaluation. Thirteen returned. Two had recovered by the time of revisit, but the rest remained ill; however, only one was so ill as to be unable to work. The data suggest that the medical consequences of serving in the Persian Gulf are not transient. The difficulty in getting veterans to return to our center suggests potential problems in the proposed nation-wide longitudinal health outcome study of Persian Gulf War Veterans.
Nesher G, Margalit R, Ashkenazi YJ.	Department of Rheumatology Service, Hebrew University Medical School, Jerusalem, Israel. nesher@inter.net.il	Anti-nuclear envelope antibodies: Clinical associations.	Semin Arthritis Rheum. 2001 Apr;30(5):313-20.	OBJECTIVES: Characterization of the clinical associations and clinical implications of antibodies reacting with antigens of the nuclear envelope. METHODS: Description of an illustrative case and a MEDLINE search-assisted literature review of relevant cases. RESULTS: With indirect immunofluorescence, autoantibodies directed against various antigens of the nuclear envelope stain the nucleus in a ring-like (rim) pattern. Autoantibodies against 5 antigenic components of the nuclear envelope have been described: anti-gp210, p62, lamina, lamina-associated polypeptides, and lamin B receptor. Antibodies to antigens of the nuclear pore complex, such as gp210 and p62, are highly specific (> 95%) for primary biliary cirrhosis and may aid in the serologic diagnosis of this condition, especially in cases in which antimitochondrial antibodies are not detectable. In contrast, antilamin antibodies are not disease-specific but seem to be associated with lupus anticoagulant or anticardiolipin antibodies, antiphospholipid syndrome, thrombocytopenia, autoimmune liver diseases, and arthralgia. High-titered antilamin

				antibodies help to define a subset of lupus patients with antiphospholipid antibodies who are at a lower risk of developing thrombotic events. In addition, preliminary data suggest that the presence of antilamin antibodies may be helpful in the diagnosis of chronic fatigue syndrome. CONCLUSIONS: Each of the antibodies reacting with nuclear membrane antigens has its own spectrum of disease associations. RELEVANCE: Determination of anti-nuclear envelope antibody pattern by indirect immunofluorescence, with subsequent determination of the specific antibody, carries important diagnostic and prognostic implications in various autoimmune conditions.
Nishikai M, Tomomatsu S, Hankins RW, Takagi S, Miyachi K, Kosaka S, Akiya K.	National Tokyo Medical Center, Tokyo, Japan.	Autoantibodies to a 68/48 kDa protein in chronic fatigue syndrome and primary fibromyalgia: a possible marker for hypersomnia and cognitive disorders.	Rheumatology (Oxford). 2001 Jul;40(7):806-10.	OBJECTIVE: To identify antinuclear antibodies (ANA) specific for chronic fatigue syndrome (CFS), and in related conditions such as fibromyalgia (FM) or psychiatric disorders. METHODS: One hundred and fourteen CFS patients and 125 primary and secondary FM patients were selected based on criteria advocated by the Centers for Disease Control and Prevention and by the American College of Rheumatology, respectively. As controls, healthy subjects and patients with either various psychiatric disorders or diffuse connective tissue diseases were included. Autoantibodies were examined by immunoblot utilizing HeLa cell extracts as the antigen. RESULTS: Autoantibodies to a 68/48 kDa protein were present in 13.2 and 15.6% of patients with CFS and primary FM, respectively. In addition, autoantibodies to a 45 kDa protein were found in 37.1 and 21.6% of the patients with secondary FM and psychiatric disorders, respectively. Meanwhile, these two autoantibodies were not found at all in connective tissue disease patients without FM, nor in healthy subjects ($P<0.05$). As a group, the anti-68/48 kDa-positive CFS patients presented more frequently with hypersomnia ($P<0.005$), short-term amnesia ($P<0.07$) or difficulty in concentration ($P<0.05$) than those CFS patients without the antibodies. CONCLUSIONS: The presence of the anti-68/48 kDa protein antibodies in a portion of both CFS and primary FM patients suggests the existence of a common immunological background. These antibodies may find utility as possible markers for a clinicoserological subset of CFS/FM patients with hypersomnia and cognitive complaints.
Nonaka I.	National Center of Neurology and Psychiatry.	[Complex III (ubiquinone-cytochrome c reductase) deficiency] [Article in Japanese]	Ryoikibetsu Shokogun Shirizu. 2001;(36):135-6.	
Nye F..		Infectious mononucleosis: not always what it seems	Hosp Med. 2001 Jul;62(7):388-9. Comment in: Hosp Med. 2002 Jan;63(1):54.	
Okuyama T, Tanaka K, Akechi T, Kugaya A, Okamura H,	Psycho-Oncology Division, National Cancer Center	Fatigue in ambulatory patients with advanced lung	J Pain Symptom Manage. 2001 Jul;22(1):554-64.	Although it has been indicated that patients with lung cancer experience higher level of fatigue than patients with other cancers, few published studies have focused on the characteristics of this fatigue and how it interferes with daily activities. The purpose of this

Nishiwaki Y, Hosaka T, Uchitomi Y.	Research Institute East, Kashiwa, Japan.	cancer: prevalence, correlated factors, and screening.		study was to clarify fatigue prevalence and the factors correlated with fatigue, and to develop a screening method for fatigue in patients with advanced lung cancer. One hundred fifty-seven patients completed two fatigue scales (Cancer Fatigue Scale [CFS], and Fatigue Numerical Scale [FNS]) plus other measures, along with a self-administered questionnaire asking whether fatigue had interfered with any of 7 areas of daily activities. Fifty-nine percent of patients had experienced clinical fatigue, which was defined as fatigue that interfered with any daily activities. Logistic regression analysis demonstrated that symptoms of dyspnea on walking, appetite loss, and depression were significant correlated factors. Both CFS and FNS were found to have sufficient sensitivity and specificity for use as a screening tool. The results indicated that fatigue is a frequent and important symptom, which is associated with both physical and psychological distress in this population. The CFS and FNS were confirmed to have sufficient screening ability.
Ottenweller JE, Sisto SA, McCarty RC, Natelson BH.	Department of Neurosciences, New Jersey Medical School, University of Medicine and Dentistry of New Jersey, Newark, USA. jeo@nbunj.jvnc.net	Hormonal responses to exercise in chronic fatigue syndrome.	Neuropsychobiology. 2001 Jan;43(1):34-41.	Chronic fatigue syndrome (CFS) is a debilitating disease characterized by severe, unexplained fatigue and postexertional exacerbation of symptoms. We examined basal endocrine function in a group of CFS patients and a carefully matched group of sedentary controls. The subjects then completed a graded, maximal exercise test on a treadmill, and additional blood samples were drawn 4 min and a day after the end of exercise. There were no differences in basal hormone levels before exercise. Plasma adrenocorticotropin, epinephrine, prolactin and thyrotropin responses 4 min after exercise were lower in the CFS group, but the growth hormone response may have been exaggerated, and the plasma norepinephrine response was similar to that in controls. The next day, there were no differences in hormone levels between the groups, which suggests that long-term changes in endocrine function are unlikely to be a cause of the prolonged fatigue that occurs in CFS patients after a bout of exertion. Copyright 2001 S. Karger AG, Basel
Overstreet DH, Djuric V.	Department of Psychiatry and Center for Alcohol Studies, University of North Carolina at Chapel Hill, 27599-7178, USA. dhover@med.unc.edu	A genetic rat model of cholinergic hypersensitivity: implications for chemical intolerance, chronic fatigue, and asthma.	Ann N Y Acad Sci. 2001 Mar;933:92-102.	The fact that only some individuals exposed to environmental chemicals develop chemical intolerance raises the possibility that genetic factors could be contributing factors. The present communication summarizes evidence from a genetic animal model of cholinergic supersensitivity that suggests that an abnormal cholinergic system could be one predisposing genetic factor. The Flinders Sensitive Line (FSL) rats were established by selective breeding for increased responses to an organophosphate. It was subsequently found that these FSL rats were also more sensitive to direct-acting muscarinic agonists and had elevated muscarinic receptors compared to the selectively bred parallel group, the Flinders Resistant Line (FRL) rats, or randomly bred control rats. Increased sensitivity to cholinergic agents has also been observed in several human populations, including individuals suffering from chemical intolerance. Indeed, the FSL rats exhibit certain behavioral characteristics such as abnormal sleep, activity, and appetite that are similar to those reported in these human populations. In addition, the FSL rats have been reported to exhibit increased sensitivity to a variety of other chemical agents. Peripheral tissues, such as intestinal and airway smooth muscle, appear to be more sensitive to both cholinergic agonists and an antigen, ovalbumin. Hypothermia, a centrally mediated response, is more

				pronounced in the FSL rats after nicotine and alcohol, as well as agents that are selective for the dopaminergic and serotonergic systems. In some cases, the increased sensitivity has been detected in the absence of any changes in the receptors with which the drugs interact (dopamine receptors), while receptor changes have been seen in other cases (nicotine receptors). Therefore, there may be multiple mechanisms underlying the multiple chemical sensitivity-chemical intolerance of the FSL rats. An elucidation of these mechanisms may provide useful clues to those involved in chemical intolerance in humans.
Pall ML, Satterle JD.	School of Molecular Biosciences, Washington State University, Pullman 99164-4660, USA. martin_pall@wsu.edu	Elevated nitric oxide/peroxynitrite mechanism for the common etiology of multiple chemical sensitivity, chronic fatigue syndrome, and posttraumatic stress disorder.	Ann N Y Acad Sci. 2001 Mar;933:323-9.	Various types of evidence implicate nitric oxide and an oxidant, possibly peroxynitrite, in MCS and chemical intolerance (CI). The positive feedback loops proposed earlier for CFS may explain the chronic nature of MCS (CI) as well as several of its other reported properties. These observations raise the possibility that this proposed elevated nitric oxide/peroxynitrite mechanism may be the mechanism of a new disease paradigm, answering the question raised by Miller earlier: "Are we on the threshold of a new theory of disease?"
Pall ML.		Cobalamin Used in Chronic Fatigue Syndrome Therapy Is a Nitric Oxide Scavenger	Journal of Chronic Fatigue Syndrome 2001; 8(2): 39	Cobalamin (vitamin B12) in the form of hydroxocobalamin or cyanocobalamin injections has been widely used to treat chronic fatigue syndrome (CFS). Hydroxocobalamin is a nitric oxide scavenger and is proposed here to act as such a scavenger in CFS treatment. Its possible efficacy in CFS treatment, if further substantiated, may provide confirmation of a prediction of the elevated nitric oxide/peroxynitrite theory of CFS etiology. This interpretation of the possible role of cobalamin in CFS treatment suggests a useful perspective for confirming and optimizing this treatment.
Pall ML.	School of Molecular Biosciences and Program in Medical Sciences, Washington State University, Pullman, 99164-4660, USA. pall@mail.wsu.edu	Common etiology of posttraumatic stress disorder, fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity via elevated nitric oxide/peroxynitrite.	Med Hypotheses. 2001 Aug;57(2):139-45.	Three types of overlap occur among the disease states chronic fatigue syndrome (CFS), fibromyalgia (FM), multiple chemical sensitivity (MCS) and posttraumatic stress disorder (PTSD). They share common symptoms. Many patients meet the criteria for diagnosis for two or more of these disorders and each disorder appears to be often induced by a relatively short-term stress which is followed by a chronic pathology, suggesting that the stress may act by inducing a self-perpetuating vicious cycle. Such a vicious cycle mechanism has been proposed to explain the etiology of CFS and MCS, based on elevated levels of nitric oxide and its potent oxidant product, peroxynitrite. Six positive feedback loops were proposed to act such that when peroxynitrite levels are elevated, they may remain elevated. The biochemistry involved is not highly tissue-specific, so that variation in symptoms may be explained by a variation in nitric oxide/peroxynitrite tissue distribution. The evidence for the same biochemical mechanism in the etiology of PTSD and FM is discussed here, and while less extensive than in the case of CFS and MCS, it is nevertheless suggestive. Evidence supporting the role of elevated nitric oxide/peroxynitrite in these four disease states is summarized, including induction of nitric oxide by common apparent inducers of these disease states, markers of elevated nitric oxide/peroxynitrite in patients and evidence for an inductive role of elevated nitric oxide in animal models. This theory

				appears to be the first to provide a mechanistic explanation for the multiple overlaps of these disease states and it also explains the origin of many of their common symptoms and similarity to both Gulf War syndrome and chronic sequelae of carbon monoxide toxicity. This theory suggests multiple studies that should be performed to further test this proposed mechanism. If this mechanism proves central to the etiology of these four conditions, it may also be involved in other conditions of currently obscure etiology and criteria are suggested for identifying such conditions. Copyright 2001 Harcourt Publishers Ltd.
Papp KK, Erokwu B, Decker M, Strohl KP.	Louis B. Stokes Cleveland V.A. Medical Center and Case Western Reserve University School of Medicine, Cleveland, Ohio, USA. kkp4@po.cwru.edu	Medical student competence in eliciting a history for "chronic fatigue".	Sleep Breath. 2001 Sep;5(3):123-9.	PURPOSE: We report an observational study of medical students' abilities in taking a complex history for which sleep disorders is one of several possible conditions. METHODS: Students are observed taking a focused history from a simulated patient whose chief complaint is "I am tired. I cannot get anything done." Nine groups of students (n = 360) completing the internal medicine core-clerkship were evaluated by one of three examiners. Students received full, partial, or no credit for each item on a uniform behavioral checklist, which included prompts for common medical and psychiatric disorders associated with chronic fatigue. RESULTS: Observed means were lowest for items pertaining to sleep behaviors and head trauma. Fewer than half of the students inquired about whether or not the person had difficulty falling asleep at night, family history of sleep apnea, and frequency and length of naps. In contrast, the majority of students inquired about heart disease, metabolic disorders, the use of illicit drugs, alcohol consumption, and the taking of medications. Examiners accounted for a significant source of variance in scores; yet the station discriminated among top and bottom students as measured by the Objective Structured Clinical Examination (OSCE) overall. No statistically significant differences were observed on the basis of clerkship site, primary care versus traditional-track students, time of year, or gender. CONCLUSION: A majority of students do not adequately cover issues relevant to sleep in contrast to other associated disorders when taking a focused history for chronic fatigue.
Parker AJ, Wessely S, Cleare AJ.	Department of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine and the Institute of Psychiatry, London.	The neuroendocrinology of chronic fatigue syndrome and fibromyalgia.	Psychol Med. 2001 Nov;31(8):1331-45.	BACKGROUND: Disturbance of the HPA axis may be important in the pathophysiology of chronic fatigue syndrome (CFS) and fibromyalgia. Symptoms may be due to: (1) low circulating cortisol; (2) disturbance of central neurotransmitters; or (3) disturbance of the relationship between cortisol and central neurotransmitter function. Accumulating evidence of the complex relationship between cortisol and 5-HT function, make some form of hypothesis (3) most likely. We review the methodology and results of studies of the HPA and other neuroendocrine axes in CFS. METHOD: Medline, Embase and Psychlit were searched using the Cochrane Collaboration strategy. A search was also performed on the King's College CFS database, which includes over 3000 relevant references, and a citation analysis was run on the key paper (Demitrack et al. 1991). RESULTS: One-third of the studies reporting baseline cortisol found it to be significantly low, usually in one-third of patients. Methodological differences may account for some of the varying results. More consistent is the finding of reduced HPA function, and enhanced 5-HT function on

				neuroendocrine challenge tests. The opioid system, and arginine vasopressin (AVP) may also be abnormal, though the growth hormone (GH) axis appears to be intact, in CFS. CONCLUSIONS: The significance of these changes, remains unclear. We have little understanding of how neuroendocrine changes relate to the experience of symptoms, and it is unclear whether these changes are primary, or secondary to behavioural changes in sleep or exercise. Longitudinal studies of populations at risk for CFS will help to resolve these issues.
Patarca R.	Department of Medicine, University of Miami School of Medicine, Florida 33101, USA. rpatarca@pol.net	Cytokines and chronic fatigue syndrome.	Ann N Y Acad Sci. 2001 Mar;933:185-200.	Chronic fatigue syndrome (CFS) patients show evidence of immune activation, as demonstrated by increased numbers of activated T lymphocytes, including cytotoxic T cells, as well as elevated levels of circulating cytokines. Nevertheless, immune cell function of CFS patients is poor, with low natural killer cell cytotoxicity (NKCC), poor lymphocyte response to mitogens in culture, and frequent immunoglobulin deficiencies, most often IgG1 and IgG3. Immune dysfunction in CFS, with predominance of so-called T-helper type 2 and proinflammatory cytokines, can be episodic and associated with either cause or effect of the physiological and psychological function derangement and/or activation of latent viruses or other pathogens. The interplay of these factors can account for the perpetuation of disease with remission/exacerbation cycles. A T-helper type 2 predominance has been seen among Gulf War syndrome patients and this feature may also be present in other related disorders, such as multiple chemical sensitivity. Therapeutic intervention aimed at induction of a more favorable cytokine expression pattern and immune status appears promising.
Patarca-Montero R, Antoni M, Fletcher MA, Klimas NG.	E. M. Papper Laboratory of Clinical Immunology, Center for Behavioral Medicine Research, Miami Veterans Administration Medical Center, University of Miami School of Medicine, P.O. Box 016960, Miami, FL 33101, USA.	Cytokine and other immunologic markers in chronic fatigue syndrome and their relation to neuropsychological factors.	Appl Neuropsychol. 2001;8(1):51-64.	The literature is reviewed and data are presented that relate to a model we have developed to account for the perpetuation of the perplexing disorder currently termed chronic fatigue syndrome (CFS). In patients with CFS there is chronic lymphocyte overactivation with cytokine abnormalities that include perturbations in plasma levels of proinflammatory cytokines and decrease in the ratio of Type 1 to Type 2 cytokines produced by lymphocytes in vitro following mitogen stimulation. The initiation of the syndrome is frequently sudden and often follows an acute viral illness. Our model for the subsequent chronicity of this disorder holds that the interaction of psychological factors (distress associated with either CFS-related symptoms or other stressful life events) and the immunologic dysfunction contribute to (a) CFS-related physical symptoms (e.g., perception of fatigue and cognitive difficulties, fever, muscle and joint pain) and increases in illness burden and (b) impaired immune surveillance associated with cytotoxic lymphocytes with resulting activation of latent herpes viruses.
Patarca-Montero R, Klimas NG, Fletcher MA.		Immunotherapy of Chronic Fatigue Syndrome: Therapeutic Interventions Aimed at Modulating the	Journal of Chronic Fatigue Syndrome 2001; 8(1): 3	Based on the postulates of viral and autoimmune etiologies of CFS, several interventions have been designed and tested by different research groups around the world, including the United States, Sweden, United Kingdom, Italy, and Japan. This review addresses those interventions aimed at altering the balance of certain cytokines, the mediators of immune responses. Patients with CFS who show evidence of activation of the immune system have poor immune cell function and a predominance of what is called a T-helper (Th)2-type

		Th1/Th2 Cytokine Expression Balance		cytokine response when their lymphocytes are activated. A Th2-type response, which is characterized by production of cytokines such as interleukin (IL)-4, -5, and -10, favors the function of B lymphocytes, the cellular factories of immunoglobulins. A predominance of a Th2-type response is therefore consistent with pathologies, such as autoimmunity and atopy, which are based on inappropriate production of immunoglobulins. Many of the CFS therapies discussed decrease the Th2-type predominance seen at baseline in CFS patients, thereby allowing a greater predominance of a Th1-type response, which favors the function of macrophages and natural killer cells. The function of the latter cells, which have the natural ability of directly destroying invading microbes and cancer cells, is defective in untreated CFS patients. Typical Th1-type cytokines include IL-2 and interferon-gamma, and some of the therapies induce their production. The interventions discussed in this review cover a wide spectrum of therapeutic tools ranging from lymph node cell immunotherapy, herbal products, and small molecules to vaccines. Despite the controversies on the etiology of CFS, immunotherapy research is useful and necessary.
Patarca-Montero R.		Fibromyalgia: Literature in Review (1999-2000)	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 63	Definition of Fibromyalgia, Disability and Functional Status Assessments, Endocrinology, Epidemiology, Immunology, Microbiology, Neurology, Pathophysiology, Pediatrics, Psychiatry, Psychology, Related Disorders and Complications, Treatment.
Patarca-Montero R.		Fibromyalgia	Journal of Chronic Fatigue Syndrome 2001; 9(3/4): 21 - 161	Although much has been learned over the last decade about fibromyalgia, much remains to be learned about its causes, nosology, treatment, and overlap with a variety of rheumatic and nonrheumatic conditions. Advances in rheumatology, cardiovascular medicine, endocrinology, epidemiology, immunology, infectious diseases, neurology, psychiatry, and psychology have served as the basis for the formulation of new lines of research and novel therapeutic interventions. The purpose of this review is to summarize the knowledge gained and published mainly within the last decade.
Pauk J, Buchwald D, Corey L.		Letter to the editor: human herpesvirus 6 serologic responses.	J Clin Virol. 2001 Apr;21(1):103-4.	
Paul LM, Wood L, Maclaren W.	Department of Physiotherapy, Podiatry and Radiography, Glasgow Caledonian University, City Campus, Cowcaddens Road, Scotland G4 OBA, Glasgow, UK. l.paul@gcal.ac.uk	The effect of exercise on gait and balance in patients with chronic fatigue syndrome.	Gait Posture. 2001 Jul;14(1):19-27.	This study investigated anecdotal reports of gait and balance abnormalities in subjects with Chronic Fatigue Syndrome (CFS) by examining the effects of a light exercise test on postural sway and various gait parameters. Tests were performed on 11 CFS patients and 11 age- and sex-matched sedentary controls. Results demonstrated that postural sway was not significantly different in both groups before or after the exercise test. There were, however, significant differences in gait parameters between the two groups confirming anecdotal evidence, but these differences were not exacerbated by the exercise test. Heart rate responses demonstrated that both groups were exercising at similar loads, although this was perceived to be higher by the CFS group.
Peachey E.	Salisbury District Hospital.	Myalgic encephalomyelitis. Myth, mystery or	Pract Midwife. 2001 Apr;4(4):29-31.	

		misunderstood?		
Petri H, Graffelman AW, Knuistingh Neven A, Springer MP, Mearin L, Von Blomberg BM, Visser JT.		Coeliac disease and chronic fatigue syndrome.	Int J Clin Pract. 2001 Jan-Feb;55(1):71.	
Petrie KJ, Sivertsen B, Hysing M, Broadbent E, Moss-Morris R, Eriksen HR, Ursin H.	Health Psychology Research Group, Faculty of Medicine and Health Sciences, The University of Auckland, Auckland, New Zealand. kj.petrie@auckland.ac.nz	Thoroughly modern worries: the relationship of worries about modernity to reported symptoms, health and medical care utilization.	J Psychosom Res. 2001 Jul;51(1):395-401.	OBJECTIVE: There is now greater public concern about how features of modern life pose threats to personal health. In two studies, we investigated the relationship between individuals' worries about modernity affecting health to symptom reports, perceptions of health and health care utilization. METHODS: In the first study, 526 University students completed a questionnaire measuring modern health worries (MHW), symptom reports and health perceptions. A second study utilized an existing national survey database of 7869 New Zealanders. Part of the survey examined people's concerns of modernity affecting their health in the past 12 months, as well as the use of conventional medical and alternative health care. RESULTS: We found concerns about modernity affecting health were made up of four major components: environmental pollution, toxic interventions, tainted food and radiation. MHW were significantly associated with somatic complaints and ratings of the importance of health to the individual. We also found individuals with high levels of MHW had a higher rate of food intolerance and chronic fatigue syndrome (CFS). In the second study, we found MHW to be associated with medical care utilization, particularly of alternative health practitioners. CONCLUSIONS: The results of these studies suggest concerns about modernity do cause changes in the way individuals interpret somatic information and may play a role in undermining perceptions of health. The area of MHW is worthy of study and may hold importance for understanding aspects of functional disorders.
Powell P, Bentall RP, Nye FJ, Edwards RH.	Regional Infectious Diseases Unit, University Hospital Aintree, Liverpool L9 7AL.	Randomised controlled trial of patient education to encourage graded exercise in chronic fatigue syndrome.	BMJ. 2001 Feb 17;322(7283):387-90. Comment in: ACP Journal Club 2001 Sep-Oct;135(2):46. BMJ. 2001 Jun 23;322(7301):1545-6.	OBJECTIVE: To assess the efficacy of an educational intervention explaining symptoms to encourage graded exercise in patients with chronic fatigue syndrome. DESIGN: Randomised controlled trial. SETTING: Chronic fatigue clinic and infectious diseases outpatient clinic. SUBJECTS: 148 consecutively referred patients fulfilling Oxford criteria for chronic fatigue syndrome. INTERVENTIONS: Patients randomised to the control group received standardised medical care. Patients randomised to intervention received two individual treatment sessions and two telephone follow up calls, supported by a comprehensive educational pack, describing the role of disrupted physiological regulation in fatigue symptoms and encouraging home based graded exercise. The minimum intervention group had no further treatment, but the telephone intervention group received an additional seven follow up calls and the maximum intervention group an additional seven face to face sessions over four months. MAIN OUTCOME MEASURE: A score of >/=25 or an increase of >/=10 on the SF-36 physical functioning subscale (range 10 to 30) 12 months after randomisation. RESULTS: 21 patients dropped out, mainly from the

				intervention groups. Intention to treat analysis showed 79 (69%) of patients in the intervention groups achieved a satisfactory outcome in physical functioning compared with two (6%) of controls, who received standardised medical care (P<0.0001). Similar improvements were observed in fatigue, sleep, disability, and mood. No significant differences were found between the three intervention groups. CONCLUSIONS: Treatment incorporating evidence based physiological explanations for symptoms was effective in encouraging self managed graded exercise. This resulted in substantial improvement compared with standardised medical care.
Prins JB, Bleijenberg G, Bazelmans E, Elving LD, de Boo TM, Severens JL, van der Wilt GJ, Spinhoven P, van der Meer JW.	Department of Medical Psychology, University Medical Centre, Nijmegen, The Netherlands. j.prins@cksmps.azn.nl	Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial.	Lancet. 2001 Mar 17;357(9259):841-7.	BACKGROUND: Cognitive behaviour therapy (CBT) seems a promising treatment for chronic fatigue syndrome (CFS), but the applicability of this treatment outside specialised settings has been questioned. We compared CBT with guided support groups and the natural course in a randomised trial at three centres. METHODS: Of 476 patients diagnosed with CFS, 278 were eligible and willing to take part. 93 were randomly assigned CBT (administered by 13 therapists recently trained in this technique for CFS), 94 were assigned the support-group approach, and 91 the control natural course. Multidimensional assessments were done at baseline, 8 months, and 14 months. The primary outcome variables were fatigue severity (on the checklist individual strength) and functional impairment (on the sickness impact profile) at 8 and 14 months. Data were analysed by intention to treat. FINDINGS: 241 patients had complete data (83 CBT, 80 support groups, 78 natural course) at 8 months. At 14 months CBT was significantly more effective than both control conditions for fatigue severity (CBT vs support groups 5.8 [2.2-9.4]; CBT vs natural course 5.6 [2.1-9.0]) and for functional impairment (CBT vs support groups 263 [38-488]; CBT vs natural course 222 [3-441]). Support groups were not more effective for CFS patients than the natural course. Among the CBT group, clinically significant improvement was seen in fatigue severity for 20 of 58 (35%), in Karnofsky performance status for 28 of 57 (49%), and self-rated improvement for 29 of 58 (50%). Prognostic factors for outcome after CBT were a higher sense of control predicting more improvement, and a passive activity pattern and focusing on bodily symptoms predicting less improvement. INTERPRETATION: CBT was more effective than guided support groups and the natural course in a multicentre trial with many therapists. Our study showed a lower proportion of patients with improvement than CBT trials with a few highly skilled therapists.
Proctor SP, Heaton KJ, White RF, Wolfe J.	Boston Environmental Hazards Center (116B-4), 150 South Huntington Avenue, Boston, MA 02130-4893, USA. sproctor@bu.edu	Chemical sensitivity and chronic fatigue in Gulf War veterans: a brief report.	J Occup Environ Med. 2001 Mar;43(3):259-64.	The foci of this brief report are to (1) describe the prevalence of chemical sensitivity (CS) and chronic fatigue (CF) symptomatology and of presumptive multiple CS and CF syndrome diagnoses, and (2) explore the potential overlap between one purported case definition (i.e., chronic multi-symptom illness) and these unexplained symptom syndromes in a well-characterized group of Gulf War veterans. The number of subjects with CS and CF symptomatology and presumptive multiple CS and CF syndrome diagnoses was higher in the Gulf War-deployed group compared with a group deployed to Germany during the Gulf War. However, the percent differences were not significant when comparing the presumptive diagnoses of multiple CS and CF syndrome. The characteristic differences

				between the groups and the overlap with chronic multi-symptom illness are also discussed.
Racciatti D, Guagnano MT, Vecchiet J, De Remigis PL, Pizzigallo E, Della Vecchia R, Di Sciascio T, Merlitti D, Sensi S.	Clinic of Infectious Diseases, University of Chieti, Chieti, Italy.	Chronic fatigue syndrome: circadian rhythm and hypothalamic-pituitary-adrenal (HPA) axis impairment.	Int J Immunopathol Pharmacol. 2001 Jan-Apr;14(1):11-15.	Chronic Fatigue Syndrome (CFS) is a clinical condition characterized by a persistent or relapsing debilitating fatigue at rest, lasting more than 6 months, and made worse by exercise. At the present moment, there are three potential etiopathogenic factors: immunologic, viral and neuroendocrine. The purpose of our study was to evaluate possible alterations of the hypothalamic-pituitary-adrenal (HPA) axis in our CFS patients by studying the circadian rhythms of prolactin (PRL), thyrotropic hormone (TSH), adrenocorticotropic hormone (ACTH), and cortisol (CS). A total of 36 patients were enrolled according to the Centers for Disease Control and Prevention case-definition criteria. Twenty healthy subjects were included as controls. Blood samples were taken every 4 hours during a single 24-hour period. We performed a fluorometric enzyme immunoassay with serum PRL, cortisol and TSH, and an immunoradiometric assay with plasma ACTH. The circadian rhythms of PRL, TSH, ACTH and CS were statistically significant in both CFS and control groups. At 24:00 and 04:00 hrs the CFS patients showed lower ACTH levels than healthy subjects (p < 0.001); the PRL levels were higher at 04.00 h in CFS patients than in healthy subjects.
Racciatti D, Vecchiet J, Ceccomancini A, Ricci F, Pizzigallo E.	Department of Infectious Diseases, G. D'Annunzio University, Chieti Scalo, Italy. racciatt@unich.it	Chronic fatigue syndrome following a toxic exposure.	Sci Total Environ. 2001 Apr 10;270(1-3):27-31.	Chronic fatigue syndrome (CFS) is a clinical entity characterized by severe fatigue lasting more than 6 months and other well-defined symptoms. Even though in most CFS cases the etiology is still unknown, sometimes the mode of presentation of the illness implicates the exposure to chemical and/or food toxins as precipitating factors: ciguatera poisoning, sick building syndrome, Gulf War syndrome, exposure to organochlorine pesticides, etc. In the National Reference Center for CFS Study at the Department of Infectious Diseases of 'G. D'Annunzio' University (Chieti) we examined five patients (three females and two males, mean age: 37.5 years) who developed the clinical features of CFS several months after the exposure to environmental toxic factors: ciguatera poisoning in two cases, and exposure to solvents in the other three cases. These patients were compared and contrasted with two sex- and age-matched subgroups of CFS patients without any history of exposure to toxins: the first subgroup consisted of patients with CFS onset following an EBV infection (post-infectious CFS), and the second of patients with a concurrent diagnosis of major depression. All subjects were investigated by clinical examination, neurophysiological and immunologic studies, and neuroendocrine tests. Patients exposed to toxic factors had disturbances of hypothalamic function similar to those in controls and, above all, showed more severe dysfunction of the immune system with an abnormal CD4/CD8 ratio, and in three of such cases with decreased levels of NK cells (CD56+). These findings may help in understanding the pathogenetic mechanisms involved in CFS.
Redelmeier DA, Tu JV, Schull MJ, Ferris LE, Hux JE.	Department of Medicine, University of Toronto, Toronto, Ont. dar@ices.on.ca	Problems for clinical judgement: 2. Obtaining a reliable past medical history.	CMAJ. 2001 Mar 20;164(6):809-13.	Ordinary human reasoning may lead patients to provide an unreliable history of past experiences because of errors in comprehension, recall, evaluation and expression. Comprehension of a question may change depending on the definition of periods of time and prior questions. Recall fails through the loss of relevant information, the fabrication of misinformation and distracting cues. Evaluations may be mistaken because of the "halo

				effect" and a reluctance to change personal beliefs. Expression is influenced by social culture and the environment. These errors can also occur when patients report a history of present illness, but they tend to be more prominent with experiences that are more remote. An awareness of these specific human fallibilities might help clinicians avoid some errors when eliciting a patient's past medical history.
Regland, Zachrisson O, Stejskal V, Gottfries C-G.		Nickel Allergy Is Found in a Majority of Women with Chronic Fatigue Syndrome and Muscle Pain-And May Be Triggered by Cigarette Smoke and Dietary Nickel Intake	Journal of Chronic Fatigue Syndrome 2001; 8(1): 57	Two hundred and four women with chronic fatigue and muscle pain, with no signs of autoimmune disorder, received immune stimulation injections with a Staphylococcus vaccine at monthly intervals over 6 months. Good response was defined as a decrease by at least 50% of the total score on an observer's rating scale. Nickel allergy was evaluated as probable if the patient had a positive history of skin hypersensitivity from cutaneous exposure to metal objects. The patient's smoking habits were recorded. Fifty-two percent of the patients had a positive history of nickel contact dermatitis. There were significantly more good responders among the non-allergic non-smokers (39%) than among the allergic smokers (6%). We also present case reports on nickel-allergic patients who apparently improved after cessation of cigarette smoking and reducing their dietary nickel intake. Our observations indicate that exposure to nickel, by dietary intake or inhalation of cigarette smoke, may trigger systemic nickel allergy and contribute to syndromes of chronic fatigue and muscle pain.
Reid S, Hotopf M, Hull L, Ismail K, Unwin C, Wessely S.	Academic Department of Psychiatry, Guy's King's and St. Thomas' School of Medicine and Institute of Psychiatry, London, United Kingdom.	Multiple chemical sensitivity and chronic fatigue syndrome in British Gulf War veterans.	Am J Epidemiol. 2001 Mar 15;153(6):604-9.	The objective of this study was to measure the prevalence of multiple chemical sensitivity (MCS) and chronic fatigue syndrome (CFS) in British Gulf War veterans and to investigate their association with reported exposures and psychologic morbidity. In 1997--1998, the authors undertook a cross-sectional survey of three cohorts of British military personnel comprising Gulf veterans (n = 3,531), those who had served in Bosnia (n = 2,050), and those serving during the Gulf War but not deployed there (Era cohort, n = 2,614). MCS and CFS were defined according to operational criteria. The prevalence of MCS in the Gulf, Bosnia, and Era cohorts was 1.3%, 0.3%, and 0.2%, respectively. For CFS, the prevalence was 2.1% (Gulf cohort), 0.7% (Bosnia cohort), and 1.8% (Era cohort). In Gulf veterans, MCS was strongly associated with exposure to pesticides (adjusted odds ratio = 12.3, 95% confidence interval: 5.1, 30.0). Both syndromes were associated with high levels of psychologic morbidity. These findings suggest that CFS and MCS account for some of the medically unexplained illnesses reported by veterans after deployment to the Gulf. MCS was particularly associated with Gulf deployment and self-reported exposure to pesticides, findings that merit further exploration given the controversial status of this diagnosis and the potential for recall bias in a questionnaire survey.
Reinhart WH, Fleisch F.	Departement Innere Medizin, Kantonsspital Chur. walter.reinhart@ksc.gr.ch	[Fatigue] [Article in German	Schweiz Rundsch Med Prax. 2001 Nov 15;90(46):2015-8.	Fatigue is one of the most frequent symptoms in medicine. A detailed history must include sleeping habits, other diseases, drugs, and concomitant symptoms. A physical examination is necessary, followed by laboratory tests and imaging techniques, which must be used in a cost-effective manner. When underlying diseases are excluded, a chronic fatigue syndrome may be present. Its pathogenesis is largely unknown. Established treatment options in chronic fatigue syndrome are graded exercise, antidepressants in case of depression and

				anxiety, and cognitive behaviour treatment. The large number of other treatments including diets have no proven value. Fatigue remains a diagnostic and therapeutic challenge to the physician.
Repka-Ramirez MS, Naranch K, Park YJ, Velarde A, Clauw D, Baraniuk JN.	Department of Medicine, Georgetown University, Washington, DC 20007-2197, USA.	IgE levels are the same in chronic fatigue syndrome (CFS) and control subjects when stratified by allergy skin test results and rhinitis types.	Ann Allergy Asthma Immunol. 2001 Sep;87(3):218-21.	BACKGROUND: Chronic fatigue syndrome (CFS) has an uncertain pathogenesis. Allergies have been suggested as one cause. OBJECTIVE: The aim of this study was to compare serum immunoglobulin (Ig)E in CFS and control subjects to determine whether IgE levels were elevated in CFS. This would be suggestive of increased atopy in CFS. METHODS: IgE was measured by quantitative ELISA (sandwich) immunoassay in 95 CFS and 109 non-CFS control subjects. Subjects were classified by positive or negative allergy skin tests (AST) and rhinitis questionnaires (rhinitis score, RhSc) into four rhinitis types: nonallergic rhinitis (NAR with positive RhSc and negative AST); allergic rhinitis (AR with positive AST and RhSc); atopic/no rhinitis (AST positive/RhSc negative); and nonatopic/no rhinitis (both AST and RhSc negative) subjects. RESULTS: IgE was not significantly different between control (128 +/- 18 IU/mL, mean +/- SEM) and CFS (133 +/- 43 IU/mL) groups, or between control and CFS groups classified into the four rhinitis types. IgE was significantly higher in subjects with positive AST whether or not they had positive RhSc or CFS symptoms. CONCLUSIONS: Elevated IgE and positive AST indicate allergen sensitization, but are not necessarily indicators of symptomatic allergic diseases. There was no association between IgE levels and CFS, indicating that atopy was probably not more prevalent in CFS. Therefore, TH2-lymphocyte and IgE-mast cell mechanisms are unlikely causes of CFS.
Richardson J.		Viral Isolation from Brain in Myalgic Encephalomyelitis	Journal of Chronic Fatigue Syndrome 2001; 9(3/4): 15 - 19	
Ridsdale L, Godfrey E, Chalder T, Seed P, King M, Wallace P, Wessely S; Fatigue Trialists' Group.	Department of General Practice, Guy's, King's and St Thomas's School of Medicine, King's College, 5 Lambeth Walk, London SE11 6SP. L.Ridsdale@iop.kcl.ac.uk	Chronic fatigue in general practice: is counselling as good as cognitive behaviour therapy? A UK randomised trial.	Br J Gen Pract. 2001 Jan;51(462):19-24. Comment in: Br J Gen Pract. 2001 Apr;51(465):316-7. Br J Gen Pract. 2001 Apr;51(465):317-8.	BACKGROUND: Fatigue is a common symptom for which patients consult their doctors in primary care. With usual medical management the majority of patients report that their symptoms persist and become chronic. There is little evidence for the effectiveness of any fatigue management in primary care. AIM: To compare the effectiveness of cognitive behaviour therapy (CBT) with counselling for patients with chronic fatigue and to describe satisfaction with care. DESIGN OF STUDY: Randomised trial with parallel group design. SETTING: Ten general practices located in London and the South Thames region of the United Kingdom recruited patients to the trial between 1996 and 1998. Patients came from a wide range of socioeconomic backgrounds and lived in urban, suburban, and rural areas. METHOD: Data were collected before randomisation, after treatment, and six months later. Patients were offered six sessions of up to one hour each of either CBT or counselling. Outcomes include: self-report of fatigue symptoms six months later, anxiety and depression, symptom attributions, social adjustment and patients' satisfaction with care. RESULTS: One hundred and sixty patients with chronic fatigue entered the trial, 45 (28%) met research criteria for chronic fatigue syndrome; 129 completed follow-up. All patients met Chalder et al's standard criteria for fatigue. Mean fatigue scores were 23 on entry (at baseline) and 15 at six months' follow-up. Sixty-one (47%) patients no longer met

				standard criteria for fatigue after six months. There was no significant difference in effect between the two therapies on fatigue (1.04 [95% CI = -1.7 to 3.7]), anxiety and depression or social adjustment outcomes for all patients and for the subgroup with chronic fatigue syndrome. Use of antidepressants and consultations with the doctor decreased after therapy but there were no differences between groups. CONCLUSION: Counselling and CBT were equivalent in effect for patients with chronic fatigue in primary care. The choice between therapies can therefore depend on other considerations, such as cost and accessibility.
Robertson-Ritchie H.		Toward a new definition of chronic fatigue syndrome.	West J Med. 2001 Apr;174(4):241.	
Robinson GL, McGregor NR, Roberts TK, Dunstan RH, Butt H.	Special Education Centre, University of Newcastle, Callaghan, New South Wales, Australia.	A biochemical analysis of people with chronic fatigue who have Irlen Syndrome: speculation concerning immune system dysfunction.	Percept Mot Skills. 2001 Oct;93(2):486-504.	This study investigated the biological basis of visual processing disabilities in adults with Chronic Fatigue Syndrome. The study involved 61 adults with symptoms of Chronic Fatigue Syndrome who were screened for visual processing problems (Irlen Syndrome) and divided into two groups according to the severity of symptoms of Irlen Syndrome. Significant variations were identified in blood lipids and urine amino and organic acids of the two groups, which may be indicative of activation of the immune system due to some infective agent. It was suggested that metabolic profiling may help the development of more valid diagnostic categories and allow more investigation of immune system dysfunction as a possible causal factor in a range of learning and behaviour disorders.
Roelens S, Herst CV, D'Haese A, De Smet K, Frémont M, De Meirleir K, Englebienne P.		G-Actin Cleavage Parallels 2-5A-Dependent RNase L Cleavage in Peripheral Blood Mononuclear Cells-Relevance to a Possible Serum-Based Screening Test for Dysregulations in the 2-5A Pathway	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 63	A dysregulation in the 2N,5N-oligoadenylate (2-5A)-dependent RNase L antiviral pathway has been detected in peripheral blood mononuclear cells (PBMC) of chronic fatigue syndrome (CFS) patients, which is characterized by an unregulated RNase L activity and the presence of a low molecular weight (LMW) 2-5A-binding protein (37-kDa 2-5A-BP). This study was undertaken to test the possibility that the 37-kDa 2-5A-BP of CFS is produced by proteolytic cleavage of the 80-kDa monomeric enzyme. Incubation of the 80-kDa human recombinant RNase L (r-hRNase L) with PBMC extracts either positive or negative for the presence of 37-kDa 2-5A-BP, respectively, demonstrates that the LMW protein is produced by the former, not the latter, and that the size of the fragment generated from the recombinant protein matches the 37-kDa size of the fragment observed in the original PBMC. Digestion of r-hRNase L with calpain generated the same 37-kDa 2-5A-BP observed in PBMC extracts, and calpain immunoprecipitation from PBMC extracts reduced their proteolytic activity, an observation that suggests that calpain may be involved in the cleavage. We further examined G-actin, a known calpain substrate, for possible cleavage in PBMC. Actin fragments were observed of which the presence correlated with the presence of 37-kDa 2-5-BP. Since G-actin is cleared by serum transport, we further screened serum samples for the presence of LMW forms. A single LMW actin fragment could be detected in serum, the presence of which correlated significantly with the presence of both G-actin and RNase L fragments in PBMC. This latter observation offers the opportunity to screen large populations of patients for dysregulations in the RNase L pathway by a serum-based

				assay.
Rosenqvist P.	Psykiatriska kliniken, Kalmar, per.rosenqvist@ltblekinge.se	[Stress-related fatigue--some therapeutic experiences] [Article in Swedish]	Lakartidningen. 2001 Nov 28;98(48):5549-50, 5553.	
Ross S, Fantie B, Straus SF, Grafman J.	Department of Psychology, American University, Washington, DC, USA.	Divided attention deficits in patients with chronic fatigue syndrome.	Appl Neuropsychol. 2001;8(1):4-11.	Chronic fatigue syndrome (CFS) patients and controls were compared on a variety of mood state, personality, and neuropsychological measures, including memory, word finding, and attentional tasks that required participants to focus, sustain, or divide their attention, or to perform a combination of these functions. CFS patients demonstrated a selective deficit on 3 measures of divided attention. Their performance on the other neuropsychological tests of intelligence, fluency, and memory was no different than that of normal controls despite their reports of generally diminished cognitive capacity. There was an inverse relation between CFS patient fatigue severity and performance on 1 of the divided attention measures. Given these findings, it is probable that CFS patients will report more cognitive difficulties in real-life situations that cause them to divide their effort or rapidly reallocate cognitive resources between 2 response channels (vision and audition).
Rowe PC, Calkins H, DeBusk K, McKenzie R, Anand R, Sharma G, Cuccherini BA, Soto N, Hohman P, Snader S, Lucas KE, Wolff M, Straus SE.	Departments of Pediatrics and Medicine, Johns Hopkins Hospital, 600 N Wolfe St, Baltimore, MD 21287, USA.	Fludrocortisone acetate to treat neurally mediated hypotension in chronic fatigue syndrome: a randomized controlled trial.	JAMA. 2001 Jan 3;285(1):52-9. Comment in: JAMA. 2001 Mar 21;285(11):1441-2; discussion 1443. JAMA. 2001 Mar 21;285(11):1442-3. JAMA. 2001 Mar 21;285(11):1442; discussion 1443.	CONTEXT: Patients with chronic fatigue syndrome (CFS) are more likely than healthy persons to develop neurally mediated hypotension (NMH) in response to prolonged orthostatic stress. OBJECTIVE: To examine the efficacy of fludrocortisone acetate as monotherapy for adults with both CFS and NMH. DESIGN: Randomized, double-blind, placebo-controlled trial conducted between March 1996 and February 1999. SETTING: Two tertiary referral centers in the United States. PATIENTS: One hundred individuals aged 18 to 50 years who satisfied Centers for Disease Control and Prevention criteria for CFS and had NMH provoked during a 2-stage tilt-table test. Eighty-three subjects had adequate outcome data to assess efficacy. INTERVENTION: Subjects were randomly assigned to receive fludrocortisone acetate, titrated to 0.1 mg/d (n = 50) or matching placebo (n = 50) for 9 weeks, followed by 2 weeks of observation after discontinuation of therapy. MAIN OUTCOME MEASURE: Proportion of subjects in each group with at least a 15-point improvement on a 100-point global wellness scale. RESULTS: Baseline demographic and illness characteristics between the groups were similar; CFS had been present for at least 3 years in 71%. Using an intention-to-treat analysis, 7 subjects (14%) treated with fludrocortisone experienced at least a 15-point improvement in their wellness scores compared with 5 (10%) among placebo recipients (P =.76). No differences were observed in several other symptom scores or in the proportion with normal follow-up tilt test results at the end of the treatment period. CONCLUSIONS: In our study of adults with CFS, fludrocortisone as monotherapy for NMH was no more efficacious than placebo for amelioration of symptoms. Failure to identify symptomatic improvement with fludrocortisone does not disprove the hypothesis that NMH could be contributing to some of the symptoms of CFS. Further studies are needed to determine whether other

				medications or combination therapy are more effective in treating orthostatic intolerance in patients with CFS.
Ruchko VM, Makhlai LI, Borisevich SV, Makhlai AA.		[Chronic fatigue and immune dysfunction syndrome] [Article in Russian]	Vopr Virusol. 2001 May-Jun;46(3):46-8.	
Sachs L.	Department of Communication Studies, Linkoping University, Sweden. lisbeth.sachs@swipnet.se	From a lived body to a medicalized body: diagnostic transformation and chronic fatigue syndrome.	Med Anthropol. 2001;19(4):299-317. Comment in: Med Anthropol. 2001;19(4):411-3.	This paper addresses the diagnostic dilemma posed by chronic illness that offers no demonstrable evidence of serious physical disorders or pathology. Is a diagnosis such as chronic fatigue syndrome (CFS) disabling because it encourages people to identify with it? Does it become a self-fulfilling prophecy? In providing people with a name, and thus allowing them to confirm the legitimacy of their suffering, a diagnosis of CFS may help them to relate to their world and, hence, facilitate their recovery. One of the most relevant questions pertaining to a diagnosis of CFS concerns how people deal with suffering when it does not come with a biomedically established pathology. I draw upon material provided by 21 men and women diagnosed with CFS. My analysis concerns the ambivalence involved in the diagnostic process and its implications for the relationship between self-identity and chronicity.
Sakaino H.	Department of Oral Surgery, Kurume University School of Medicine, Kurume 830-0011, Japan.	The biochemical study of intermaxillary fixation (IMF) stress in oral surgery inpatients.	Kurume Med J. 2001;48(1):71-7.	Although intermaxillary fixation (IMF) is performed to treat the patients with maxillary fracture, this procedure is very stressful to the patients. IMF has been reported to increase noradrenaline (NA) release in the brain and elevate plasma corticosterone contents in the rat. These changes were significantly attenuated by diazepam, an anxiolytic of the benzodiazepine family. These results suggest that IMF could greatly affect the pituitary-adrenal system as a stress. In the present study, in order to examine the influence of IMF on the human body function, we measured levels of 17-hydrocorticosteroids (17-OHCS) and 17-ketosteroid (17-KS), which are metabolites of the adreno-cortical hormone cortisol, in the urine of inpatients undergoing IMF. The subjects were requested to fill out a questionnaire on irritableness caused by IMF. In these patients, urinary 17-OHCS levels were significantly increased after IMF and well correlated to the results of the questionnaire. The finding suggested that urinary 17-OHCS levels reflect stress related to IMF, and that such stress mainly causes an irritated feeling. Natural killer cell activity (NK activity), which is considered to be related to stress, was measured in these patients. The relationship between 17-OHCS levels and NK activity was examined in reference to the results of the questionnaire. Questionnaire showed that most patients noted insomnia and an irritated feeling during IMF. To examine the influence of anxiolytic agents on stress related to IMF, an anxiolytic agent, ethyl loflazepate, was administered during IMF, and urinary 17-OHCS levels were measured. There was no correlation between 17-OHCS levels and NK activity in the patients. Furthermore, no correlation was observed between visual analogue scale (VSA) and NK activity. Increases in 17-OHCS levels in the group treated with ethyl loflazepate, an anxiolytic of the benzodiazepine family, were significantly lower than in the untreated group. This suggests that ethyl loflazepate reduced stress responses to

				IMF. It has been reported that NK activity is reduced inpatients with depression or chronic fatigue syndrome. However, NK activity may not be affected by mechanical stress such as IMF. The finding that an anxiolytic agent, ethyl loflazepate, inhibited stress responses to IMF further suggests that anxiolytic drugs are very useful for treatment of irritated feeling of the patients undergoing IMF.
Schacterle RS, Conti Fabrizio, Magrini L, Komaroff AL, Valesini G.		Increased Eosinophil Protein X Levels in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 9(1/2): 21	Chronic fatigue syndrome is a condition of unknown etiology characterized by severe fatigue and accompanied by symptoms including cognitive difficulties, myalgias, and headaches. Studies of this illness have found chronic activation of the immune system, including one reporting elevated levels of eosinophil cationic protein, considered an eosinophil activation marker. The aim of this study was to measure serum levels of eosinophil protein X, a cationic protein not measured previously in this illness. Measurements are reported on serum samples from 29 patients meeting the Centers for Disease Control and Prevention criteria for chronic fatigue syndrome, and 30 healthy controls of similar age and gender. The median serum eosinophil protein X level in patients was higher than controls: 37.9 vs. 25.3 µg/L (p = 0.037). Forty-eight percent of patients versus 23% of controls had levels above the normal range. The marked increase in serum levels of eosinophil protein X in chronic fatigue syndrome patients could reflect eosinophil activation in this illness.
Selvaratnam P.	Monash University, Melbourne.	Post-operative exercise improves pain, disability and spinal function following microdiscectomy.	Aust J Physiother. 2001;47(3):218.	
Servaes P, van der Werf S, Prins J, Verhagen S, Bleijenberg G.	Dutch Fatigue Research Group, Department of Medical Psychology (118), University Hospital Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. P.Servaes@cksmps.azn.nl	Fatigue in disease-free cancer patients compared with fatigue in patients with chronic fatigue syndrome.	Support Care Cancer. 2001 Jan;9(1):11-7.	The goal of our work was to assess fatigue in disease-free cancer patients with help of a validated fatigue questionnaire. Furthermore, we wished to analyse the relationship between severe fatigue and former treatment modalities, problems of concentration and motivation, physical activity, functional impairment, depression and anxiety and finally, to compare severely fatigued disease-free cancer patients and patients with Chronic Fatigue Syndrome (CFS). The participants were 85 adult cancer patients and 16 patients with CFS. The cancer patients were all disease-free and had been off treatment for a minimum of 6 months. They were asked to participate in this study by their physician when they came to the hospital for control visits. Patients who were willing to participate completed four questionnaires. The Checklist Individual Strength was used to measure fatigue. In addition, the Beck Depression Inventory, the Spielberger Trait Anxiety Inventory and the Nottingham Health Profile were used. Results indicate that 19% of the disease-free cancer patients were severely fatigued. Their fatigue experience is comparable to that of patients with CFS. Severe fatigue is associated with problems of concentration and motivation, reduced physical activity, emotional health problems and pain. Furthermore, a relation was found between fatigue and depression and anxiety. No relation was found between fatigue and

				type of cancer, former treatment modalities, duration of treatment and time since treatment ended. In conclusion, for one fifth of a group of disease-free cancer patients fatigue is a severe problem long after treatment. In addition to fatigue, these patients experience several psychological and physical problems.
Sharma A, Oyebode F, Kendall MJ, Jones DA.	Department of Medicine, Queen Elizabeth Hospital, Birmingham, Edgbaston, Birmingham B15 2TH, UK. a.sharma.1@bham.ac.uk	Recovery from chronic fatigue syndrome associated with changes in neuroendocrine function.	J R Soc Med. 2001 Jan;94(1):26-7.	
Shephard RJ.	Defence & Civil Institute of Environmental Medicine, and Faculty of Physical Education & Health, University of Toronto, Ontario, Canada. royjshep@mountain-inter.net	Chronic fatigue syndrome: an update.	Sports Med. 2001;31(3):167-94.	The chronic fatigue syndrome is characterised by a fatigue that is disproportionate to the intensity of effort that is undertaken, has persisted for 6 months or longer, and has no obvious cause. Unless there has been a long period of patient- or physician-imposed inactivity, objective data may show little reduction in muscle strength or peak aerobic power, but the affected individual avoids heavy activity. The study of aetiology and treatment has been hampered by the low disease prevalence (probably <0.1% of the general population), and (until recently) by a lack of clear and standardised diagnostic criteria. It is unclear how far the aetiology is similar for athletes and nonathletes. It appears that in top competitors, overtraining and/or a negative energy balance can be precipitating factors. A wide variety of other possible causes and/or precipitating factors have been cited in the general population, including psychological stress, disorders of personality and affect, dysfunction of the hypothalamic-pituitary-adrenal axis, hormonal imbalance, nutritional deficits, immune suppression or activation and chronic infection. However, none of these factors have been observed consistently. The prognosis is poor; often disability and impairment of athletic performance are prolonged. Prevention of overtraining by careful monitoring seems the most effective approach in athletes. In those where the condition is established, treatment should aim at breaking the vicious cycle of effort avoidance, deterioration in physical condition and an increase in fatigue through a combination of encouragement and a progressive exercise programme.
Shepherd C.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):239; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Shetzline SE, Suhadolnik RJ.	Department of Biochemistry and the	Characterization of a 2',5'-oligoadenylate	J Biol Chem. 2001 Jun 29;276(26):23707-11.	Upregulation of key components of the 2',5'-oligoadenylate (2-5A) synthetase/RNase L pathway has been identified in extracts of peripheral blood mononuclear cells from

	Fels Institute for Cancer Research and Molecular Biology, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA.	(2-5A)-dependent 37-kDa RNase L: azido photoaffinity labeling and 2-5A-dependent activation.	Epub 2001 Apr 25. Erratum in: J Biol Chem 2001 Aug 24;276(34):32392.	individuals with chronic fatigue [corrected] syndrome, including the presence of a low molecular weight form of RNase L. In this study, analysis of 2',5'-Oligoadenylate (2-5A) binding and activation of the 80- and 37-kDa forms of RNase L has been completed utilizing photolabeling/immunoprecipitation and affinity assays, respectively. Saturation of photolabeling of the 80- and the 37-kDa RNase L with the 2-5A azido photoprobe, [(32)P]pApAp(8-azidoA), was achieved. Half-maximal photoinsertion of [(32)P]pApAp(8-azidoA) occurred at 3.7 x 10(-8) m for the 80-kDa RNase L and at 6.3 x 10(-8) m for the 37-kDa RNase L. Competition experiments using 100-fold excess unlabeled 2-5A photoaffinity probe, pApAp(8-azidoA), and authentic 2-5A (p(3)A(3)) resulted in complete protection against photolabeling, demonstrating that [(32)P]pApAp(8-azidoA) binds specifically to the 2-5A-binding site of the 80- and 37-kDa RNase L. The rate of RNA hydrolysis by the 37-kDa RNase L was three times faster than the 80-kDa RNase L. The data obtained from these 2-5A binding and 2-5A-dependent activation studies demonstrate the utility of [(32)P]pApAp(8-azidoA) for the detection of the 37-kDa RNase L in peripheral blood mononuclear cell extracts.
Sirois DA, Natelson B.	Department of Oral Medicine, New York University College of Dentistry, New York, USA.	Clinicopathological findings consistent with primary Sjogren's syndrome in a subset of patients diagnosed with chronic fatigue syndrome: preliminary observations.	J Rheumatol. 2001 Jan;28(1):126-31.	OBJECTIVE: Some patients diagnosed with chronic fatigue syndrome (CFS) have symptoms commonly observed in Sjogren's syndrome (SS), particularly xerophthalmia and xerostomia, leading to speculation that some patients with CFS might have primary SS or that the 2 disorders share common pathophysiological features. We investigated the prevalence of symptoms of mucosal dryness, salivary gland pathology, lacrimal hyposecretion, and autoantibodies (antinuclear antibody, SSA/SSB) among patients diagnosed with CFS. METHODS: Twenty-five subjects with CFS and 18 healthy control subjects were interviewed and examined, had a Schirmer test and fluorescein tear dilution, and underwent minor salivary gland (MSG) biopsy. Antibody to nuclear antigen as well as anti-La (SSA) and anti-Ro (SSB) antibody were available for subjects with CFS. Pathologists unaware of the subject group assignment examined labial salivary gland biopsy specimens and calculated a standard MSG score for each specimen. RESULTS: Mucosal dryness was reported by 13/25 (52%) subjects with CFS, of which 8 (32%) also had MSG score, low Schirmer test value, and symptoms consistent with primary SS (p = 0.05). No control subject met diagnostic criteria for primary SS. MSG focus scores < or =1 were common among both groups (CFS 14/25; controls 15/18). MSG results without pathological alteration were rare, seen in only one control and no CFS patients. Low Schirmer values were found in 10/25 (40%) CFS patients and 1/18 (6%) control (p = 0.01). CONCLUSION: A subset of patients with CFS may have primary SS.
Skowera A, Peakman M, Cleare A, Davies E, Deale A, Wessely S.		High prevalence of serum markers of coeliac disease in patients with chronic fatigue syndrome.	J Clin Pathol. 2001 Apr;54(4):335-6.	
Snell CR, Stevens SR,		Chronic Fatigue	Journal of Chronic	The purpose of this investigation was to identify significant quality-of-life issues for two

VanNess JM.		Syndrome, Ampligen, and Quality of Life: A Phenomenological Perspective	Fatigue Syndrome 2001; 8(3/4): 117	women previously diagnosed with chronic fatigue syndrome (CFS), and their families. Both women were participants in a cost-recovery, clinical trial of the antiviral and immunomodulatory drug, Ampligen. A qualitative, case study approach was adopted to access information not normally available from clinical trials. Specifically, semi-structured, in-depth interviews were conducted with the CFS patients, and their spouses, to discover if these families perceived any changes in their patterns of daily living contingent with participation in the Ampligen trial. Patient diaries were also analyzed for the purpose of triangulation. Content analysis of the interview transcripts and diary entries revealed a number of significant quality of life improvements for the women and their families, for which they perceived the drug therapy responsible. After an initial acclimation period, and with the exception of the day when the drug was administered, both women reported a reduction in pain, increased energy levels, and improved cognitive functioning. They each cited numerous cases to illustrate their improvement.
Soderberg S, Evengard B.	Huddinge University Hospital, M42, SE-141 86 Huddinge, Sweden. stina.soderberg@hs.sll.se	Short-term group therapy for patients with chronic fatigue syndrome.	Psychother Psychosom. 2001 Mar-Apr;70(2):108-11.	BACKGROUND: This study presents experiences of focused short-term group therapy for patients with chronic fatigue syndrome (CFS). METHODS: Fourteen women diagnosed as CFS patients were randomly placed into two groups. The control group received group therapy 5 months after the first group. The project consisted of 10 group sessions of 1.5 h per week. Sense of coherence (SOC) was used for measuring coping resources, and self-rating scales of quality of life and of fatigue were compared before and after group therapy. RESULTS: The most valuable aspect was the sharing of experiences. More than half of the patients also felt that the sessions had improved psychological well-being through adjustment of ambitions and improved coping with symptoms. CONCLUSION: The study encourages further research. If group therapy is chosen as treatment for these patients, a longer period is recommended. A possible alternative is individualized short-term therapy adapted to each patient's needs, problems and circumstances. Copyright 2001 S. Karger AG, Basel
Speight N, Franklin A.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1890. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
Spence VA, Abbot NC.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):239-40; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
St Clair Gibson A, Lambert ML, Noakes TD.	The Medical Research Council, Department of Human Biology,	Neural control of force output during maximal and	Sports Med. 2001;31(9):637-50.	A common belief in exercise physiology is that fatigue during exercise is caused by changes in skeletal muscle metabolism. This 'peripheral' fatigue results either from substrate depletion during submaximal exercise or metabolite accumulation during maximal exercise

	University of Cape Town, South Africa. agibson@sports.uct.ac.za	submaximal exercise.		in the exercising muscles. However, if substrate depletion alone caused fatigue, intracellular ATP levels would decrease and lead to rigor and cellular death. Alternatively, metabolite accumulation would prevent any increase in exercise intensity near the end of exercise. At present, neither of these effects has been shown to occur, which suggests that fatigue may be controlled by changes in efferent neural command, generally described as 'central' fatigue. In this review, we examine neural efferent command mechanisms involved in fatigue, including the concepts of muscle wisdom during short term maximal activity, and muscle unit rotation and teleoanticipation during submaximal endurance activity. We propose that neural strategies exist to maintain muscle reserve, and inhibit exercise activity before any irreparable damage to muscles and organs occurs. The finding that symptoms of fatigue occur in the nonexercising state in individuals with chronic fatigue syndrome indicates that fatigue is probably not a physiological entity, but rather a sensory manifestation of these neural regulatory mechanisms.
Staub F, Bogousslavsky J.		[Is there such a thing as brain fatigue?] [Article in French]	Rev Neurol (Paris). 2001 Mar;157(3):259-62.	
Stein E.		Chronic Fatigue Syndrome: Overcoming the Attitudinal Impasse	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 53	Context: Patients with Chronic Fatigue Syndrome and their physicians are often in conflict about the etiology and treatment of CFS. Objectives: 1. Survey the literature regarding physician's attitudes towards CFS; 2. Examine the contributing factors to physician's attitude towards the disorder; and 3. Suggest solutions. Data Sources: The relevant medical and psychological literature (years 1988- 2000) was searched using the search term "Chronic Fatigue Syndrome." This was supplemented with papers from the bibliographies of the retrieved papers, additional related literature, and clinical experience. Data Synthesis: Forty-six to ninty percent of GPs accept CFS as a discrete clinical entity and 30-82% are willing to make the diagnosis in qualifying patients. Conclusions: CFS is a heterogeneous, multifactorial host response disorder that is inadequately described by the biomedical model. Despite substantial evidence of multisystemic physical abnormality in CFS, the lack of pathognomic tests and the female gender predominance cause some physicians to continue to treat CFS as a psychosocial disorder. This leads to conflict between patients and physicians. CFS challenges physicians to think beyond current disease models, to tolerate diagnostic and therapeutic uncertainty, and to work collaboratively with patients rather than taking the role of expert.
Stein MT, First LR, Friedman SB.	University of California, San Diego, USA.	Twelve-year-old girl with chronic fatigue, school absence, and fluctuating somatic symptoms.	J Dev Behav Pediatr. 2001 Apr;22(2 Suppl):S151-6.	
Stevens DL.	Department of Medicine, New York University School of	Chronic fatigue.	West J Med. 2001 Nov;175(5):315-9.	

	Medicine, Gouverneur Hospital, 227 Madison St, New York, NY 10024, USA. dls3@nyu.edu			
Stewart JM.		Orthostatic Intolerance: A Review with Application to the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(2): 45	The symptoms of the chronic fatigue syndrome closely match those of chronic orthostatic intolerance and research suggests that orthostatic intolerance plays a role in the symptomatology of CFS. Recent investigations support the hypothesis that findings in CFS patients result at least in part from impaired blood pressure and heart rate regulation. Orthostatic intolerance has been implicated. Effective and specific treatment for chronic orthostatic intolerance can only be developed when a specific etiology or etiologies are discovered.
Streeten DH.	Department of Medicine, SUNY Upstate Medical University, Syracuse, New York 13210, USA.	Role of impaired lower-limb venous innervation in the pathogenesis of the chronic fatigue syndrome.	Am J Med Sci. 2001 Mar;321(3):163-7.	BACKGROUND: In patients with acute orthostatic hypotension, there is excessive pooling of blood in the legs, which may result from the strikingly subnormal compliance that is demonstrable in the pedal veins during norepinephrine infusion. The common occurrence of delayed orthostatic hypotension and/or tachycardia in the chronic fatigue syndrome (CFS) led to the present studies of foot vein compliance in CFS patients with a linear variable differential transformer. METHODS: Seven patients with CFS were compared with 7 age- and gender matched healthy control subjects in their blood pressure, heart-rate, and plasma norepinephrine responses to prolonged standing and in measurements of their foot vein contractile responses to intravenous norepinephrine infusions with the linear variable differential transformer. RESULTS: Excessive, delayed (usually after 10 min) orthostatic reductions in systolic and diastolic blood pressure ($P < 0.01$) and inconsistently excessive increases in heart rate were found in the CFS patients, in whom venous compliance in response to infused norepinephrine was significantly reduced ($P < 0.05$). CONCLUSIONS: In these patients with CFS, delayed orthostatic hypotension was clearly demonstrable, and, as in previously reported patients with orthostatic hypotension of acute onset, this was associated with reduced pedal vein compliance during norepinephrine infusion, implying impaired sympathetic innervation of foot veins. The rapid symptomatic improvement demonstrated in previous studies of CFS patients during correction of orthostatic venous pooling by inflation of military antishock trousers (MAST) to 35 mm Hg may suggest that excessive lower body venous pooling, perhaps by reducing cerebral perfusion, is involved in the orthostatic component of fatigue in these patients.
Strickland PS, Levine PH,. Peterson DL, O'Brien K, Fears T.		Neuromyasthenia and Chronic Fatigue Syndrome (CFS) in Northern Nevada/California: A Ten-Year Follow-Up of an Outbreak	Journal of Chronic Fatigue Syndrome 2001; 9(3/4): 3 - 14	In 1984-87, an outbreak of debilitating fatigue was reported by two physicians in the private practice of internal medicine in Incline Village, Nevada. Follow-up questionnaires were sent in 1995 to the 259 patients in this outbreak. The results were analyzed to determine how many patients met the latest Centers for Disease Control and Prevention (CDC) case definition for Chronic Fatigue Syndrome (CFS), Idiopathic Chronic Fatigue (ICF), or Prolonged Fatigue (PF). Data were analyzed separately for those living in the Lake Tahoe area and those referred from other locales. Of those returning questionnaires (123/259),

				41% met the CDC case definition for CFS, 56% met the criteria for inclusion in the subgroup ICF, and 3% experienced PF. In the populationbased Lake Tahoe group, symptomatic women were more likely to have CFS than ICF whereas symptomatic men were likely to fit ICF criteria. Also in this group, full recovery was reported more often among Lake Tahoe participants classified as having ICF (43%) than participants classified as having CFS (15%).
Tarello W.	Veterinary Surgeon, Castiglione del Lago, Perugia, Italy.	Chronic fatigue syndrome in horses: diagnosis and treatment of 4 cases.	Comp Immunol Microbiol Infect Dis. 2001 Jan;24(1):57-70.	A report from England has suggested that Chronic Fatigue Syndrome exists in equines and constitutes an emerging veterinary problem. Preliminary epidemiological studies seem to confirm the zoonotic implications of CFS. An arsenical drug, sodium thiacetarsamide, was administered to four horses with a diagnosis of Chronic Fatigue Syndrome (CFS), already treated unsuccessfully with different medications. The CFS-like lethargy, with accompanying symptoms and signs, of the four animals obtained a complete remission after intravenous treatment with this drug at low dosage (0.1 mg/kg/day). No adverse side effects were ever noticed. This clinical response was associated with recovery from anaemia and decrease of muscular enzyme values in two of the four horses. In all patients, micrococci-like bacteria found before treatment adhering to the outer surface of many red blood cells, disappeared at post-treatment controls. Considerations are made on the possible action of an arsenical drug, used in isolation, in the treatment of CFS.
Tarello W.	tarello@iol.it	Chronic Fatigue Syndrome (CFS) in 15 dogs and cats with specific biochemical and microbiological anomalies.	Comp Immunol Microbiol Infect Dis. 2001 Jul;24(3):165-85.	A great deal of controversy and speculation surrounds the etiology of Chronic Fatigue Syndrome (CFS) in human patients and the existence of a similar illness in animals. To evaluate the association with a presumptive staphylococcal infection and bacteremia, seven dogs and eight cats diagnosed with CFS (two meeting the CDC working case definition) were submitted to rapid blood cultures and fresh blood smears investigations. Nine out of 15 blood cultures proved Staph-positive and four isolates were specified as S. xilosus (3) and S. intermedius (1). The presence of micrococci-like organisms in the blood was of common observation among these subjects, in association with fatigue/pain-related symptoms and biochemical abnormalities suggestive of a myopathy. Following treatment with a low dosage arsenical drug (thiacetarsamide sodium, Caparsolate, i.v., 0.1 ml/kg/day) all patients experienced complete remission. Micrococci disappeared from the blood at post-treatment controls made 10-30 days later. The outcomes were compared with those of five healthy controls and five 'sick with other illness' patients showing significant difference.
Tarello W.	wtarello@supereva.it	Chronic fatigue syndrome (CFS) associated with Staphylococcus spp. bacteremia, responsive to potassium arsenite 0.5% in a veterinary surgeon and his	Comp Immunol Microbiol Infect Dis. 2001 Oct;24(4):233-46.	Chronic fatigue syndrome (CFS) in human patients remain a controversial and perplexing condition with emerging zoonotic aspects. Recent advances in human medicine seem to indicate a bacterial etiology and the condition has already been described in horses, dogs, cats and birds of prey in association with micrococci-like organisms in the blood. To evaluate the possibility of a chronic bacteremia, a veterinary surgeon (the author) and his coworking wife, both diagnosed with CFS and meeting the CDC working case definition, were submitted to rapid blood cultures and fresh blood smears investigations. Blood cultures proved Staph-positive and micrococci-like organisms in the blood were repeatedly observed in the 3-year period preceding the arsenical therapy, during which several

		coworking wife, handling with CFS animal cases.		medicaments, including antibiotics, proved unsuccessful. Following treatment with a low dosage arsenical drug (potassium arsenite 0.5%, im., 1 ml/12 h, for 10 days) both patients experienced complete remission. At the post-treatment control made 1 month later, micrococci had disappeared from the blood, and the CD4/CD8 ratio was raising.
Taylor RR, Jason LA.	Department of Occupational Therapy, University of Illinois at Chicago, 60612, USA.	Sexual abuse, physical abuse, chronic fatigue, and chronic fatigue syndrome: a community-based study.	J Nerv Ment Dis. 2001 Oct;189(10):709-15.	Using a randomly selected community-based sample, this investigation examined whether histories of childhood sexual, physical, and death threat abuse predicted adulthood outcomes of specific medical and psychiatric conditions involving chronic fatigue. This study also tested prior suggestions that most individuals with chronic fatigue syndrome report a past history of interpersonal abuse. Multinomial logistic regression was used to examine the relationship between abuse history and chronic fatigue group outcomes while controlling for the effects of sociodemographics. Compared with healthy controls, childhood sexual abuse was significantly more likely to be associated with outcomes of idiopathic chronic fatigue, chronic fatigue explained by a psychiatric condition, and chronic fatigue explained by a medical condition. None of the abuse history types were significant predictors of chronic fatigue syndrome. A closer examination of individuals in the chronic fatigue syndrome group revealed that significantly fewer individuals with CFS reported abuse as compared with those who did not. The implications of these findings are discussed.
Teitelbaum JE, Bird B, Greenfield RM, Weiss A, Muenz L, Gould L.		Effective Treatment of Chronic Fatigue Syndrome and Fibromyalgia–A Randomized, Double-Blind, Placebo-Controlled, Intent-To-Treat Study	Journal of Chronic Fatigue Syndrome 2001; 8(2): 3	Background: Hypothalamic dysfunction has been suggested in fibromyalgia (FMS) and chronic fatigue syndrome (CFS). This dysfunction may result in disordered sleep, subclinical hormonal deficiencies, and immunologic changes. Our previously published open trial showed that patients usually improve by using a protocol which treats all the above processes simultaneously. The current study examines this protocol using a randomized, double-blind design with an intent-to-treat analysis. Methods: Seventy-two FMS patients (38 active:34 placebo; 69 also met CFS criteria) received all active or all placebo therapies as a unified intervention. Patients were treated, as indicated by symptoms and/or lab testing, for: (1) subclinical thyroid, gonadal, and/or adrenal insufficiency, (2) disordered sleep, (3) suspected neurally mediated hypotension (NMH), (4) opportunistic infections, and (5) suspected nutritional deficiencies. Results: At the final visit, 16 active patients were "much better," 14 "better," 2 "same," 0 "worse," and 1 "much worse" vs. 3, 9, 11, 6, and 4 in the placebo group ($p < .0001$, Cochran-Mantel-Haenszel trend test). Significant improvement in the FMS Impact Questionnaire (FIQ) scores (decreasing from 54.8 to 33.2 vs. 51.4 to 47.7) and Analog scores (improving from 176.1 to 310.3 vs. 177.1 to 211.9) (both with $p < .0001$ by random effects regression), and Tender Point Index (TPI) (31.7 to 15.5 vs. 35.0 to 32.3, $p < .0001$ by baseline adjusted linear model) were seen. Long term follow-up (mean 1.9 years) of the active group showed continuing and increasing improvement over time, despite patients being able to discontinue most treatments. Conclusions: Significantly greater benefits were seen in the active group than in the placebo group for all primary outcomes. An integrated treatment approach appears effective in the treatment of FMS/CFS.

Tiersky LA, DeLuca J, Hill N, Dhar SK, Johnson SK, Lange G, Rappolt G, Natelson BH.	School of Psychology, Fairleigh Dickinson University, 1000 River Road, Mail Stop T-WH1-01, Teaneck, NJ 07666, USA.	Longitudinal assessment of neuropsychological functioning, psychiatric status, functional disability and employment status in chronic fatigue syndrome.	Appl Neuropsychol. 2001;8(1):41-50.	The longitudinal course of subjective and objective neuropsychological functioning, psychological functioning, disability level, and employment status in chronic fatigue syndrome (CFS) was examined. The relations among several key outcomes at follow-up, as well as the baseline characteristics that predict change (e.g., improvement), were also evaluated. The study sample consisted of 35 individuals who met the 1988 and 1994 CFS case definition criteria of the Centers for Disease Control (CDC) at intake. Participants were evaluated a mean of 41.9 (SEM = 1.7) months following their initial visit (range = 24-63 months). Results indicated that objective and subjective attention abilities, mood, level of fatigue, and disability improve over time in individuals with CFS. Moreover, improvements in these areas were found to be interrelated at follow-up. Finally, psychiatric status, age, and between-test duration were significant predictors of outcome. Overall, the prognosis for CFS appears to be poor, as the majority of participants remained functionally impaired over time and were unemployed at follow-up, despite the noted improvements.
Ting JY, Brown AF.	Department of Emergency Medicine, Princess Alexandra Hospital, Brisbane, Queensland, Australia.	Ciguatera poisoning: a global issue with common management problems.	Eur J Emerg Med. 2001 Dec;8(4):295-300.	Ciguatera poisoning, a toxinological syndrome comprising an enigmatic mixture of gastrointestinal, neurocutaneous and constitutional symptoms, is a common food-borne illness related to contaminated fish consumption. As many as 50000 cases worldwide are reported annually, and the condition is endemic in tropical and subtropical regions of the Pacific Basin, Indian Ocean and Caribbean. Isolated outbreaks occur sporadically but with increasing frequency in temperate areas such as Europe and North America. Increase in travel between temperate countries and endemic areas and importation of susceptible fish has led to its encroachment into regions of the world where ciguatera has previously been rarely encountered. In the developed world, ciguatera poses a public health threat due to delayed or missed diagnosis. Ciguatera is frequently encountered in Australia. Sporadic cases are often misdiagnosed or not medically attended to, leading to persistent or recurrent debilitating symptoms lasting months to years. Without treatment, distinctive neurologic symptoms persist, occasionally being mistaken for multiple sclerosis. Constitutional symptoms may be misdiagnosed as chronic fatigue syndrome. A common source outbreak is easier to recognize and therefore notify to public health organizations. We present a case series of four adult tourists who developed ciguatera poisoning after consuming contaminated fish in Vanuatu. All responded well to intravenous mannitol. This is in contrast to a fifth patient who developed symptoms suggestive of ciguatoxicity in the same week as the index cases but actually had staphylococcal endocarditis with bacteraemia. In addition to a lack of response to mannitol, clinical and laboratory indices of sepsis were present in this patient. Apart from ciguatera, acute gastroenteritis followed by neurological symptoms may be due to paralytic or neurotoxic shellfish poisoning, scombroid and pufferfish toxicity, botulism, enterovirus 71, toxidromes and bacteraemia. Clinical aspects of ciguatera toxicity, its pathophysiology, diagnostic difficulties and epidemiology are discussed.
Tomita K, Sakurada S, Minami S.	Department of Chemistry, College of	Enzymatic determination of	J Pharm Biomed Anal. 2001 Mar;24(5-	An enzymatic method was proposed for determination of acetylcarnitine (AcCar), even when carnitine (Car), non-acetylated form, co-exists. The method is consisted of four

	Engineering, Kanto Gakuin University, 4834 Mutsuura, Kanazawa-ku, Yokahama 236-8501, Japan. tomitak@kanto-gakuin.ac.jp	acetylcarnitine for diagnostic applications.	6):1147-50.	enzymatic reactions: First, AcCar is hydrolysed by acylcarnitine hydrolase to yield acetate; followed by the other three reactions coupled with three enzymes, respectively, acetate kinase, pyruvate kinase and lactate dehydrogenase; finally, the acetate formation causes a decrease in NADH. The amount of AcCar is then evaluated as the change in absorbance at 340 nm. The reagent composition of the reaction mixture was determined, and the characteristics of the method were investigated. The dilution test showed a good linearity over a wide range. The precision and accuracy tests produced satisfactory results. The co-existence of Car gave no effect on the measurement. The present method was found to be used easily, simply and rapidly for the selective determination of AcCar.
Tomoda, Jhodoi T, Miike T.		Chronic Fatigue Syndrome and Abnormal Biological Rhythms in School Children	Journal of Chronic Fatigue Syndrome 2001; 8(2): 29	Chronic fatigue syndrome occurring in previously healthy children and adolescents is one of the most vexing problems encountered by pediatric practitioners. To investigate the biological rhythms in the pediatric patients with CFS, we examined sleep pattern, and the circadian rhythm of core body temperature (CBT), and plasma cortisol in 41 patients, aged between 10 and 19 years, who did not have any physical or psychiatric disorders, but had non-specific complaints, and were suspected to have a circadian rhythm disturbance. They were diagnosed as having CFS on the basis of published criteria. Circadian variation of CBT in the CFS patients did not present a clear rhythm, and appearance time of their lowest CBT was significantly delayed compared to healthy subjects. Amplitude of circadian CBT changes, fitted to a cosinor curve by the least square method, was significantly smaller in the patients than in healthy subjects. Moreover, circadian rhythm of plasma cortisol in the patients appeared to be quite different, compared to healthy subjects. These findings suggest that their clinical psychosomatic symptoms (e.g., fatigue and sleep disturbance) might be closely related to the desynchronization of their biorhythms, particularly the circadian rhythm of body temperature and cortisol rhythm.
Tomonaga K, Kobayashi T, Ikuta K.	Department of Virology, Research Institute for Microbial Diseases, Osaka University.	[The neuropathogenesis of Borna disease virus infection] [Article in Japanese]	Nippon Rinsho. 2001 Aug;59(8):1605-13.	Borna disease virus(BDV) is a noncytolytic, neurotropic RNA virus that causes a disease of the central nervous system(CNS) in several vertebrate species, including horses, sheep, cats and ostriches. Epidemiological studies using peripheral blood or brain samples revealed that BDV can infect humans and that it may be related with certain neuropsychiatric disorders. The unique genetic and biological properties of BDV indicate that BDV develops a persistent infection in the CNS. Furthermore, a line of recent evidences suggests that BDV infection causes direct effects on brain functions in the absence of immunopathology-related brain damage. In this review, we discuss about recent data regarding neuropathogenesis of BDV infections in animals and humans.
Torpy DJ, Bachmann AW, Grice JE, Fitzgerald SP, Phillips PJ, Whitworth JA, Jackson RV.	Department of Medicine, University of Queensland, Greenslopes Private Hospital, Brisbane, Queensland 4120, Australia.	Familial corticosteroid-binding globulin deficiency due to a novel null mutation: association with fatigue and relative hypotension.	J Clin Endocrinol Metab. 2001 Aug;86(8):3692-700.	Corticosteroid-binding globulin is a 383-amino acid glycoprotein that serves a hormone transport role and may have functions related to the stress response and inflammation. We describe a 39-member Italian-Australian family with a novel complete loss of function (null) mutation of the corticosteroid-binding globulin gene. A second, previously described, mutation (Lyon) segregated independently in the same kindred. The novel exon 2 mutation led to a premature termination codon corresponding to residue -12 of the procorticosteroid-binding globulin molecule (c.121G-->A). Among 32 family members there

				were 3 null homozygotes, 19 null heterozygotes, 2 compound heterozygotes, 3 Lyon heterozygotes, and 5 individuals without corticosteroid-binding globulin mutations. Plasma immunoreactive corticosteroid-binding globulin was undetectable in null homozygotes, and mean corticosteroid-binding globulin levels were reduced by approximately 50% at 18.7 +/- 1.3 microg/ml (reference range, 30-52 microg/ml) in null heterozygotes. Morning total plasma cortisol levels were less than 1.8 microg/dl in homozygotes and were positively correlated to the plasma corticosteroid-binding globulin level in heterozygotes. Homozygotes and heterozygote null mutation subjects had a high prevalence of hypotension and fatigue. Among 19 adults with the null mutation, the systolic blood pressure z-score was 12.1 +/- 3.5; 11 of 19 subjects (54%) had a systolic blood pressure below the third percentile. The mean diastolic blood pressure z-score was 18.1 +/- 3.4; 8 of 19 subjects (42%) had a diastolic blood pressure z-score below 10. Idiopathic chronic fatigue was present in 12 of 14 adult null heterozygote subjects (86%) and in 2 of 3 null homozygotes. Five cases met the Centers for Disease Control criteria for chronic fatigue syndrome. Fatigue questionnaires revealed scores of 25.1 +/- 2.5 in 18 adults with the mutation vs. 4.2 +/- 1.5 in 23 healthy controls ($P < 0.0001$). Compound heterozygosity for both mutations resulted in plasma cortisol levels comparable to those in null homozygotes. Abnormal corticosteroid-binding globulin concentrations or binding affinity may lead to the misdiagnosis of isolated ACTH deficiency. The mechanism of the association between fatigue and relative hypotension is not established by these studies. As idiopathic fatigue disorders are associated with relatively low plasma cortisol, abnormalities of corticosteroid-binding globulin may be pathogenic.
Underhill JA, Mahalingam M, Peakman M, Wessely S.	Institute of Liver Studies, Department of Immunology, and Department of Psychological Medicine, Guy's, King's & St Thomas' School of Medicine, London, UK.	Lack of association between HLA genotype and chronic fatigue syndrome.	Eur J Immunogenet. 2001 Jun;28(3):425-8.	Although the aetiology of chronic fatigue syndrome is controversial, evidence that infective agents including viruses may have a role in the development of the condition has led to studies seeking an association with the immunomodulatory HLA genes. In the present study, we sought to extend previous work using a well-characterized patient group and modern HLA genotyping techniques. Fifty-eight patients were phenotyped for HLA A and B by microcytotoxicity and genotyped for HLA DRB, DQB and DPB by PCR oligoprobing, and the frequencies of antigens so assigned were compared with those from a control group of 134. No significant differences in HLA frequencies were found between patient and control groups. Thus, this study does not confirm previous findings of an HLA association with chronic fatigue syndrome, suggesting that neither presentation of viral antigen by HLA class I nor antigen processing genes in the HLA region is a major contributory factor in the development of the disease.
Underwood M, Eldridge S.		Chronic fatigue in general practice.	Br J Gen Pract. 2001 Apr;51(465):317-8. Comment on: Br J Gen Pract. 2001 Jan;51(462):19-24.	
Ursin H, Eriksen HR.	Department of	Sensitization,	Ann N Y Acad Sci.	The purpose of this presentation is to discuss the possibility that sensitization is a

	Biological and Medical Psychology, University of Bergen, Norway.	subjective health complaints, and sustained arousal.	2001 Mar;933:119-29.	psychobiological mechanism underlying not only multiple chemical sensitivity (MCS), but a much more general cluster of illness, referred to as "subjective health complaints". Sustained arousal, or sustained "stress" responses, may be an important factor for the development of these conditions. Patients with subjective complaints without objective changes are sometimes referred to as having "fashionable diagnoses" or "unexplained symptoms". They may be given diagnoses like MCS, epidemic fatigue, chronic fatigue syndrome, burnout, stress, a variety of intoxications, environmental illness, radiation, multiple chemical hypersensitivity, food intolerance, functional dyspepsia, irritable bowel, myalgic encephalitis, postviral syndrome, yuppie flu, fibromyalgia, or vital exhaustion. One issue is whether this is one general condition or separate entities. Another issue is whether sensitization may be the psychobiological mechanism for most or all of these conditions. Finally, is it likely that sustained arousal may facilitate the development of sensitization in some or many neural circuits? In this review, the main emphasis will be on musculoskeletal pain. This is the most frequent and most expensive condition for sickness compensation and disability. The comorbidity of other complaints, however, will also be taken into account.
Valentine AD, Meyers CA.	Department of Neuro-Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77030, USA.	Cognitive and mood disturbance as causes and symptoms of fatigue in cancer patients.	Cancer. 2001 Sep 15;92(6 Suppl):1694-8.	Fatigue, cognitive dysfunction, and depression are very common in cancer patients. A relationship among the three entities is recognized but poorly understood. Factors that contribute to this poor understanding are the subjective nature of the symptoms, multiple potential causes, and a lack of reliable assessment tools. An understanding of fatigue in cancer patients may benefit from studies of chronic fatigue syndrome (CFS) and other nonmalignant diseases indicating that cognitive impairment varies with physical and mental fatigue, and that symptoms of depression experienced by patients with physical illnesses and primary mood disorders are qualitatively different. The multidimensional nature of fatigue suggests that interventions should be patient-specific. They could be related to lifestyle or involve the use of specific behavioral or pharmacologic therapies. As is the case with depression and cognitive disorders, targeted interventions against cancer-related fatigue will benefit from a better understanding of its potential biologic causes. Consideration of cognitive dysfunction and depression complicates the understanding of cancer-related fatigue; however, it provides opportunities to assist patients who must deal with this serious problem. Copyright 2001 American Cancer Society.
Van Houdenhove B, Neerinckx E, Lysens R, Vertommen H, Van Houdenhove L, Onghena P, Westhovens R, D'Hooghe MB.	Department of Psychosomatic Rehabilitation, Katholieke Universiteit Leuven, Belgium. dewijn.VanHoudenhove@uz.kuleuven.ac.be	Victimization in chronic fatigue syndrome and fibromyalgia in tertiary care: a controlled study on prevalence and characteristics.	Psychosomatics. 2001 Jan-Feb;42(1):21-8.	The authors studied the prevalence and characteristics of different forms of victimization in 95 patients suffering from chronic fatigue syndrome (CFS) or fibromyalgia (FM) compared with a chronic disease group, including rheumatoid arthritis (RA) and multiple sclerosis (MS) patients, and a matched healthy control group. The authors assessed prevalence rates, nature of victimization (emotional, physical, sexual), life period of occurrence, emotional impact, and relationship with the perpetrator by a self-report questionnaire on burdening experiences. CFS and FM patients showed significantly higher prevalences of emotional neglect and abuse and of physical abuse, with a considerable subgroup experiencing lifelong victimization. The family of origin and the partner were the

				most frequent perpetrators. With the exception of sexual abuse, victimization was more severely experienced by the CFS/FM group. No differences were found between healthy control subjects or RA/MS patients, and between CFS and FM patients. These findings support etiological hypotheses suggesting a pivotal role for chronic stress in CFS and FM and may have important therapeutic implications.
Van Houdenhove B, Neerinckx E, Onghena P, Lysens R, Vertommen H.	Faculty of Medicine, K.U. Leuven, Leuven, Belgium. boudewijn.vanhoudenhove@uz.kuleuven.ac.be	Premorbid "overactive" lifestyle in chronic fatigue syndrome and fibromyalgia. An etiological factor or proof of good citizenship?	J Psychosom Res. 2001 Oct;51(4):571-6.	OBJECTIVE: In a former study, we have shown that patients suffering from chronic fatigue syndrome (CFS) or chronic pain, when questioned about their premorbid lifestyle, reported a high level of "action-proneness" as compared to control groups. The aim of the present study was to control for the patients' possible idealisation of their previous attitude towards action. METHODS: A validated Dutch self-report questionnaire measuring "action-proneness" (the HAB) was completed by 62 randomly selected tertiary care CFS and fibromyalgia (FM) patients, as well as by their significant others (SOs). RESULTS: HAB scores of the patients and those of the SOs were very similar and significantly higher than the norm values. Whether or not the SO showed sympathy for the patient's illness did not influence the results to a great extent. SOs with a negative attitude towards the illness even characterized the patients as more "action-prone." CONCLUSIONS: These results provide further support for the hypothesis that a high level of "action-proneness" may play a predisposing, initiating and/or perpetuating role in CFS and FM.
van Houdenhove B.		Does myalgic encephalomyelitis exist?	Lancet. 2001 Jun 9;357(9271):1889. Comment on: Lancet. 2001 Feb 17;357(9255):562.	
van Middendorp H, Geenen R, Kuis W, Heijnen CJ, Sinnema G.	Department of Pediatric Psychology, University Medical Center Utrecht, Wilhelmina Children's Hospital, The Netherlands.	Psychological adjustment of adolescent girls with chronic fatigue syndrome.	Pediatrics. 2001 Mar;107(3):E35.	OBJECTIVE: To examine psychosocial problems and adaptation of adolescent girls with chronic fatigue syndrome (CFS). METHODOLOGY: Thirty-six adolescent girls with CFS (mean age: 15.2 years; mean syndrome duration: 19.7 months) who fulfilled the criteria of the Centers for Disease Control and Prevention were examined by interviews regarding premorbid problems and by questionnaires regarding psychosocial functioning and distress, psychological attitudes, and coping resources. Data were compared with normative data. RESULTS: Of the adolescents, 86.1% reported 1 or more premorbid problems (58.3% physical, 38.9% psychological, and 52.8% familial). Normal adjustment was reported for psychosocial self-esteem, social abilities, and attentional abilities. High adjustment to adult social standards of behavior was found, but low perceived competence in specific adolescent domains, such as athletic ability, romance, and participation in recreational activities. The girls reported predominantly internalizing problems. Normal achievement motivation, no debilitating fear of failure, and high internal locus of control were observed. Palliative reaction patterns and optimism were predominantly used as coping strategies. CONCLUSIONS: The large number of premorbid problems suggests a possible contributing factor to the onset of the syndrome, although there were no reference data of healthy adolescents. In distinct domains of psychosocial

				adjustment, the adolescent girls with CFS showed strengths such as adequate self-esteem and scholastic and social abilities, and weaknesses such as low competence in adolescent-specific tasks and internalizing distress, which may partly be explained by syndrome-specific somatic complaints. The use of optimistic and palliative reaction patterns as coping strategies in this patient group indicates that the patients with CFS seem to retain an active and positive outlook on life, which may result in a rather adequate psychological adaptation to the syndrome, but also in maintenance of the syndrome by exceeding the physical limits brought about by the CFS. Our results on adjustment and coping strategies may be helpful to implement (individual) rehabilitation programs.
van Rensburg SJ, Potocnik FC, Kiss T, Hugo F, van Zijl P, Mansvelt E, Carstens ME, Theodorou P, Hurly PR, Emsley RA, Taljaard JJ.	Department of Chemical Pathology, University of Stellenbosch Medical School, Tygerberg Hospital, Tygerberg, South Africa. sjvr@gerga.sun.ac.za	Serum concentrations of some metals and steroids in patients with chronic fatigue syndrome with reference to neurological and cognitive abnormalities.	Brain Res Bull. 2001 May 15;55(2):319-25.	Chronic fatigue syndrome is defined by the Atlanta Centers for Disease Control (Atlanta, GA, USA) as debilitating fatigue lasting for longer than 6 months. Symptoms include disturbances of cognition. Certain factors have in the past been shown to influence cognition, including metals such as aluminum, iron, and zinc; and steroids such as dehydroepiandrosterone. In the present study, concentrations of these factors were determined in the serum and plasma of patients and their age- and gender-matched healthy controls (10 women and 5 men in each group). In addition, copper, dehydroepiandrosterone sulphate, cortisol, cholesterol, hemoglobin, ferritin and transferrin concentrations, as well as transferrin genetic subtypes were determined in both groups. The results indicate that patients had significantly increased serum aluminum and decreased iron compared to controls. In the females, serum iron and dehydroepiandrosterone sulphate were significantly decreased and correlated. Total cholesterol was significantly increased, and significantly negatively correlated with dehydroepiandrosterone sulphate. There were no differences in zinc, copper, cortisol, hemoglobin, transferrin and ferritin concentrations, or in transferrin genetic subtypes.
VanNess JM, Snell CR, Fredrickson DM, Strayer DR, Stevens SR.		Assessment of Functional Impairment by Cardiopulmonary Exercise Testing in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2001; 8(3/4): 103	Functional impairment in a population of patients with chronic fatigue syndrome (CFS) was determined by exercise testing. The criteria established by Weber and Janicki were employed because impairment levels are based on maximal oxygen consumption. Oxygen consumption was obtained by cardiopulmonary exercise testing and was used to classify subjects according to the severity of impairment. All the subjects in this study met the CDC case definition for CFS. All patients underwent at least two maximal graded exercise tests in which expired air was collected for assessment of VO2max. Data are included for eighty-seven CFS patients, the highest VO2 was used for determining impairment. Although all patients met the CDC case definition for CFS, only 35 (40%) would be classified as having greater than "Mild" functional impairment. The highest VO2 of any of the patients in this study was 29.5 ml/kg/min, very close to what normative data predicts to be the average maximal value for the entire group. Without a sedentary control group it is unclear if the low VO2 in this population is due to the pathology of CFS or results from the inactivity that accompanies the disease. However, use of maximal VO2 during exercise can clearly discriminate between levels of functional impairment and may be efficacious for diagnosis of CFS. Additionally, in cases where cardiopulmonary analysis is unavailable, exercise

				duration on a standardized test may also be employed.
Vassallo CM, Feldman E, Peto T, Castell L, Sharpley AL, Cowen PJ.	University Department of Psychiatry, Warneford Hospital, Oxford.	Decreased tryptophan availability but normal post-synaptic 5-HT2c receptor sensitivity in chronic fatigue syndrome.	Psychol Med. 2001 May;31(4):585-91.	BACKGROUND: Chronic fatigue syndrome (CFS) has been associated with increased prolactin (PRL) responses to the serotonin (5-HT) releasing agent fenfluramine. It is not known whether this abnormality is due to increased 5-HT release or heightened sensitivity of post-synaptic 5-HT receptors. METHODS: We measured the increase in plasma PRL produced by the directly acting 5-HT receptor agonist, m-chlorophenylpiperazine (mCPP), in patients with CFS and healthy controls. We also compared the ability of mCPP to lower slow wave sleep (SWS) in the sleep polysomnogram of both subject groups. Finally, we measured plasma amino-acid levels to determine whether tryptophan availability differed between CFS subjects and controls. RESULTS: mCPP elevated plasma PRL equivalently in patients with CFS and controls. Similarly, the decrease in SWS produced by mCPP did not differ between the two subject groups. Plasma-free tryptophan was significantly decreased in CFS. CONCLUSIONS: The sensitivity of post-synaptic 5-HT2c receptors is not increased in patients with CFS. This suggests that the increased PRL response to fenfluramine in CFS is due to elevated activity of pre-synaptic 5-HT neurones. This change is unlikely to be due to increased peripheral availability of tryptophan.
Vermeulen RC, Scholte HR, Bezemer PD.		Cognitive behaviour therapy for chronic fatigue syndrome.	Lancet. 2001 Jul 21;358(9277):238; author reply 240-1. Comment on: Lancet. 2001 Mar 17;357(9259):841-7	
Visser J, Graffelman W, Blauw B, Haspels I, Lentjes E, de Kloet ER, Nagelkerken L.	Division of Immunological and Infectious Diseases, TNO Prevention and Health, P.O. Box 2215, 2301 CE, Leiden, The Netherlands.	LPS-induced IL-10 production in whole blood cultures from chronic fatigue syndrome patients is increased but supersensitive to inhibition by dexamethasone.	J Neuroimmunol. 2001 Oct 1;119(2):343-9.	Several causes have been held responsible for the chronic fatigue syndrome (CFS), including an altered hypothalamus-pituitary-adrenal gland (HPA)-axis activity, viral infections and a reduced Th1 activity. Therefore, it was investigated whether the regulation of IL-10 is different in CFS. LPS-induced cytokine secretion in whole blood cultures showed a significant increase in IL-10 and a trend towards a decrease in IL-12 as compared with healthy controls. In patients and controls, IL-12 secretion was equally sensitive to suppression by dexamethasone, whereas IL-10 secretion appeared more sensitive in CFS-patients. In controls, IL-10 and IL-12 secretion were inversely correlated with free serum cortisol ($r=-0.492$, $p<0.02$ and $r=-0.434$, $p<0.05$, respectively). In CFS, such an inverse correlation was found for IL-12 ($r=-0.611$, $p<0.02$) but not for IL-10 ($r=-0.341$, ns). These data are suggestive for a disturbed glucocorticoid regulation of IL-10 in CFS.
Visser J, Lentjes E, Haspels I, Graffelman W, Blauw B, de Kloet R, Nagelkerken L.	Division of Immunological and Infectious Diseases, TNO Prevention and Health, Leiden, The Netherlands.	Increased sensitivity to glucocorticoids in peripheral blood mononuclear cells of chronic fatigue syndrome patients, without evidence for	J Investig Med. 2001 Mar;49(2):195-204.	BACKGROUND: In this study we tested the hypothesis that the increased sensitivity to glucocorticoids in chronic fatigue syndrome (CFS)-patients can be attributed to an altered functioning of their glucocorticoid receptors (GR). METHODS: For this purpose, affinity and distribution of the GR were studied in purified, peripheral blood mononuclear cells (PBMC) of 10 CFS patients and 14 controls along with the responsiveness of these cells to glucocorticoids in vitro. RESULTS: Affinity (Kd) and number of GR was not different in PBMC of CFS patients when compared with the controls (Kd, 12.9 +/- 8.9 nmol vs 18.8 +/- 16.2

		altered density or affinity of glucocorticoid receptors.		nmol and GR number, 4,839 +/- 2,824/ cell vs 4,906 +/- 1,646/cell). Moreover, RT-PCR revealed no differences in GR messenger RNA expression. Nevertheless, PBMC from CFS patients showed an increased sensitivity to glucocorticoids in vitro. In CFS patients 0.01 micromol dexamethasone suppressed PBMC proliferation by 37%, whereas the controls were only suppressed by 17% (P < 0.01). Addition of phorbol 12-myristate 13-acetate to the cultures rendered the cells resistant to dexamethasone with regard to proliferation and IL-10 and IFN-gamma production, but not to IL-2 and TNF-alpha production in both patients and controls. No difference between patients and controls was observed in this respect CONCLUSIONS: In conclusion, PBMC of CFS patients display an increased sensitivity to glucocorticoids, which cannot be explained by number or affinity of the GR but should rather be attributed to molecular processes beyond the actual binding of the ligand to the GR.
Vives-Bauza C, Gamez J, Roig M, Briones P, Cervera C, Solano A, Montoya J, Andreu AL.	Research Centre for Biochemistry and Molecular Biology, Universitary Hospital Vall d'Hebron, Barcelona, Spain.	Exercise intolerance resulting from a muscle-restricted mutation in the mitochondrial tRNA(Leu (CUN)) gene.	Ann Med. 2001 Oct;33(7):493-6.	BACKGROUND: Some patients presenting with isolated lifelong exercise intolerance and ragged-red fibres, harbour skeletal-muscle restricted mutations in their mitochondrial DNA. AIM: To identify the molecular defect in a patient presenting with lifelong exercise intolerance, ragged-red fibres and deficiencies of complexes III and IV in skeletal muscle. METHODS: The muscle biopsy was studied for activities of the respiratory chain, histochemical stains, and sequencing the tRNA genes of mitochondrial DNA. RESULTS: The patient had a heteroplasmic mutation in the tRNA(Leu (CUN)) gene of mitochondrial DNA (G12334A). Clinical and morphological data as well as restriction fragment length polymorphism (RFLP) and single-fibre polymerase chain reaction (PCR) analyses strongly indicate that this molecular defect is the primary cause of the myopathy. CONCLUSION: Mutations in any mitochondrial gene should be considered in the differential diagnosis of patients with lifelong exercise intolerance, even when the neurological examination is normal.
Walsh CM, Zainal NZ, Middleton SJ, Paykel ES.	University Department of Psychiatry, Addenbrooke's Hospital, Cambridge, UK.	A family history study of chronic fatigue syndrome.	Psychiatr Genet. 2001 Sep;11(3):123-8.	Chronic fatigue syndrome (CFS) is characterized by unexplained, disabling fatigue and is associated with high rates of comorbid depression. While the aetiology is unknown, findings from recent twin surveys suggest that genetic factors may be relevant to prolonged fatigue states (> 1 month). To date, however, there has been no exploration of the role of familial/genetic factors in operationally defined CFS. The aims of the present study were: (i) to examine whether CFS is familial by comparing the rates of CFS in the first-degree relatives of CFS cases and medical control subjects; and (ii) to determine whether the high rate of comorbid depression in CFS is reflected in a greater familial loading for affective disorder. Twenty-five CFS cases and 36 medical control subjects were assessed for fatigue symptoms based on the Centre for Disease Control (CDC) criteria for CFS, and for lifetime psychiatric symptoms using the Schedule for Schizophrenia and Affective Disorders-Lifetime Version. Informant family history was obtained regarding first-degree relatives using the CDC criteria and the Family History Research Diagnostic Criteria. In addition, informant history was supplemented by sending a questionnaire to first-degree relatives. There were significantly higher rates of CFS in the relatives of CFS cases

				compared with the relatives of control subjects. The rate of depression in the CFS cases was similar to previous studies but did not appear to reflect a greater familial loading for depression when compared with control subjects. However, these analyses were complicated by higher than expected rates of depression in the control group. These findings suggest that familial factors are important in the aetiology of chronic fatigue syndrome.
Wessely S.	Guy's, King's, and St Thomas's School of Medicine and Institute of Psychiatry, London, United Kingdom. s.wessely@iop.kcl.ac.uk	Chronic fatigue: symptom and syndrome.	Ann Intern Med. 2001 May 1;134(9 Pt 2):838-43.	Chronic fatigue is common, is difficult to measure, can be associated with considerable morbidity, and is rarely a subject of controversy. The chronic fatigue syndrome also presents problems in definition and measurement, is associated with even more morbidity than chronic fatigue itself, and is often controversial. Particularly unclear is the way in which chronic fatigue and the chronic fatigue syndrome relate to each other: Is one the severe form of the other, or are they qualitatively and quantitatively different? We know that many things can cause chronic fatigue, and this is probably true for the chronic fatigue syndrome, too. We can anticipate that discrete causes of the chronic fatigue syndrome will be found in the future, even if these causes are unlikely to fall neatly along the physical-psychological divide that some expect. The causes of chronic fatigue are undoubtedly many, both in a population and in any individual person, even when a discrete cause, such as depression or cancer, is identified. Social, behavioral, and psychological variables are important in both chronic fatigue and the chronic fatigue syndrome. Interventions that address these general variables can be successful, and currently they are often more successful than interventions directed at specific causes.
Wessely S.	Department of Psychological Medicine, Guy's King and St Thomas' School of Medicine, 103 Denmark Hill, London, England SE5 8AF. sphascw@iop.bpmf.ac.uk	Chronic fatigue syndrome--trials and tribulations.	JAMA. 2001 Sep 19;286(11):1378-9. Comment on: JAMA. 2001 Sep 19;286(11):1360-8.	
White PD, Thomas JM, Kangro HO, Bruce-Jones WD, Amess J, Crawford DH, Grover SA, Clare AW.	Department of Psychological Medicine, St Bartholomew's and the Royal London School of Medicine and Dentistry, London, UK. P.D. White@qmul.ac.uk	Predictions and associations of fatigue syndromes and mood disorders that occur after infectious mononucleosis.	Lancet. 2001 Dec 8;358(9297):1946-54.	BACKGROUND: Certain infections can trigger chronic fatigue syndromes (CFS) in a minority of people infected, but the reason is unknown. We describe some factors that predict or are associated with prolonged fatigue after infectious mononucleosis and contrast these factors with those that predicted mood disorders after the same infection. METHODS: We prospectively studied a cohort of 250 primary-care patients with infectious mononucleosis or ordinary upper-respiratory-tract infections until 6 months after clinical onset. We sought predictors of both acute and chronic fatigue syndromes and mood disorders from clinical, laboratory, and psychosocial measures. FINDINGS: An empirically defined fatigue syndrome 6 months after onset, which excluded comorbid psychiatric disorders, was most

				reliably predicted by a positive Monospot test at onset (odds ratio 2.1 [95% CI 1.4-3.3]) and lower physical fitness (0.35 [0.15-0.8]). Cervical lymphadenopathy and initial bed rest were associated with, or predicted, a fatigue syndrome up to 2 months after onset. By contrast, mood disorders were predicted by a premorbid psychiatric history (2.3 [1.4-3.9]), an emotional personality score (1.21 [1.11-1.35]), and social adversity (1.7 [1.0-2.9]). Definitions of CFS that included comorbid mood disorders were predicted by a mixture of those factors that predicted either the empirically defined fatigue syndrome or mood disorders. INTERPRETATION: The predictors of a prolonged fatigue syndrome after an infection differ with both definition and time, depending particularly on the presence or absence of comorbid mood disorders. The particular infection and its consequent immune reaction may have an early role, but physical deconditioning may also be important. By contrast, mood disorders are predicted by factors that predict mood disorders in general.
Whiting P, Bagnall AM, Sowden AJ, Cornell JE, Mulrow CD, Ramirez G.	National Health Service Centre for Reviews and Dissemination, University of York, York, England, YO10 5DD. pfw2@york.ac.uk	Interventions for the treatment and management of chronic fatigue syndrome: a systematic review.	JAMA. 2001 Sep 19;286(11):1360-8. Erratum in: JAMA 2002 Mar 20;287(11):1401.	CONTEXT: A variety of interventions have been used in the treatment and management of chronic fatigue syndrome (CFS). Currently, debate exists among health care professionals and patients about appropriate strategies for management. OBJECTIVE: To assess the effectiveness of all interventions that have been evaluated for use in the treatment or management of CFS in adults or children. DATA SOURCES: Nineteen specialist databases were searched from inception to either January or July 2000 for published or unpublished studies in any language. The search was updated through October 2000 using PubMed. Other sources included scanning citations, Internet searching, contacting experts, and online requests for articles. STUDY SELECTION: Controlled trials (randomized or nonrandomized) that evaluated interventions in patients diagnosed as having CFS according to any criteria were included. Study inclusion was assessed independently by 2 reviewers. Of 350 studies initially identified, 44 met inclusion criteria, including 36 randomized controlled trials and 8 controlled trials. DATA EXTRACTION: Data extraction was conducted by 1 reviewer and checked by a second. Validity assessment was carried out by 2 reviewers with disagreements resolved by consensus. A qualitative synthesis was carried out and studies were grouped according to type of intervention and outcomes assessed. DATA SYNTHESIS: The number of participants included in each trial ranged from 12 to 326, with a total of 2801 participants included in the 44 trials combined. Across the studies, 38 different outcomes were evaluated using about 130 different scales or types of measurement. Studies were grouped into 6 different categories. In the behavioral category, graded exercise therapy and cognitive behavioral therapy showed positive results and also scored highly on the validity assessment. In the immunological category, both immunoglobulin and hydrocortisone showed some limited effects but, overall, the evidence was inconclusive. There was insufficient evidence about effectiveness in the other 4 categories (pharmacological, supplements, complementary/alternative, and other interventions). CONCLUSIONS: Overall, the interventions demonstrated mixed results in terms of effectiveness. All conclusions about effectiveness should be considered together with the methodological inadequacies of the studies. Interventions which have shown

				promising results include cognitive behavioral therapy and graded exercise therapy. Further research into these and other treatments is required using standardized outcome measures.
Wiesmuller GA, Ebel H, Hornberg C.	Institut fur Hygiene und Umweltmedizin, Universitatsklinikums, RWTH Aachen. GA.Wiesmueller@post.rwth-aachen.de	[Syndromes in environmental medicine: variants of somatoform disorders] [Article in German]	Fortschr Neurol Psychiatr. 2001 Apr;69(4):175-88.	Concerning the syndromes in environmental medicine, like Multiple Chemical Sensitivities (MCS), Idiopathic Environmental Intolerances (IEI), Sick Building Syndrome (SBS), Chronic Fatigue Syndrome (CFS), Candida Syndrome (CS), and Burnout Syndrome (BS), scientific knowledge in etiology, pathology, pathophysiology, diagnosis, therapy, prevention and prognosis is still lacking until now. A critical comparison shows that it is still impossible to find a scientifically satisfying delimitation. Syndromes in environmental medicine show clinical similarities to somatoform disorders. Furthermore, there are the following possible explanations for the existence of these syndromes: Firstly, they may be a complex interaction of environmental impacts, individual predispositions, psychological influences, as well as processes of mental perception and interpretation. Secondly, they may be an effect of distress influenced by culture and social structures and/or thirdly, they may be an latrogenic determination. A more comprehensive characterisation which better considers the complex clinical manifestations is overdue. Although there are neither scientifically validated procedures for diagnosis or therapy nor prophylactic measures, a hardly comprehensible number of partly unvalidated methods is in practical use. Until the syndromes are not finally defined the terms for the syndromes should not be applied to a certain disease. Despite all uncertainities in the evaluation of syndromes in environmental medicine, physicians have the duty to take the affected persons' problems seriously.
Wikland B, Lowhagen T, Sandberg PO.		Fine-needle aspiration cytology of the thyroid in chronic fatigue.	Lancet. 2001 Mar 24;357(9260):956-7. Comment in: Lancet. 2001 Jul 14;358(9276):151.	
Wilke WS.	Department of Rheumatology, Cleveland Clinic, U.S.A.	Can fibromyalgia and chronic fatigue syndrome be cured by surgery?	Cleve Clin J Med. 2001 Apr;68(4):277-9. Comment in: Cleve Clin J Med. 2002 Jan;69(1):89-91.	
Wilson A, Hickie I, Hadzi-Pavlovic D, Wakefield D, Parker G, Straus SE, Dale J, McCluskey D, Hinds G, Brickman A, Goldenberg D, Demitrack M, Blakely T, Wessely S, Sharpe	University of New South Wales, Sydney, Australia.	What is chronic fatigue syndrome? Heterogeneity within an international multicentre study.	Aust N Z J Psychiatry. 2001 Aug;35(4):520-7.	OBJECTIVE: We sought to compare the characteristics of patients presenting with chronic fatigue (CF) and related syndromes in eight international centres and to subclassify these subjects based on symptom profiles. The validity of the subclasses was then tested against clinical data. METHOD: Subjects with a clinical diagnosis of CF completed a 119-item self-report questionnaire to provide clinical symptom data and other information such as illness course and functional impairment. Subclasses were generated using a principal components-like analysis followed by latent profile analysis (LPA). RESULTS: 744 subjects returned complete data sets (mean age 40.8 years, mean length of illness 7.9 years, female to male ratio 3:1). Overall, the subjects had a high rate of reporting typical CF symptoms

M, Lloyd A.				(fatigue, neuropsychological dysfunction, sleep disturbance). Using LPA, two subclasses were generated. Class one (68% sample) was characterized by: younger age, lower female to male ratio; shorter episode duration; less premorbid, current and familial psychiatric morbidity; and, less functional disability. Class two subjects (32%) had features more consistent with a somatoform illness. There was substantial variation in subclass prevalences between the study centres (Class two range 6-48%). CONCLUSIONS: Criteria-based approaches to the diagnosis of CF and related syndromes do not select a homogeneous patient group. While substratification of patients is essential for further aetiological and treatment research, the basis for allocating such subcategories remains controversial.
Yunus MB.	College of Medicine at Peoria, University of Illinois, One Illini Drive, PO Box 1649, Peoria, IL 61656, USA. Yunus@uic.edu	The role of gender in fibromyalgia syndrome.	Curr Rheumatol Rep. 2001 Apr;3(2):128-34.	Fibromyalgia syndrome (FMS), characterized by widespread pain and tenderness on palpation (tender points), is much more common in women than in men in a proportion of 9:1. Two recent studies have shown important gender differences in various clinical characteristics of FMS. In a community and a clinic sample, women experienced significantly more common fatigue, morning fatigue, hurt all over, total number of symptoms, and irritable bowel syndrome. Women had significantly more tender points. Pain severity, global severity and physical functioning were not significantly different between the sexes, nor were psychologic factors, eg, anxiety, stress, and depression. Gender differences have also been observed in other related syndromes, eg, chronic fatigue syndrome, irritable bowel syndrome, and headaches. The mechanisms of gender differences in these illnesses are not fully understood, but are likely to involve an interaction between biology, psychology, and sociocultural factors.
Zaman R, Puri BK, Main J, Nowicky AV, Davey NJ.	Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, London W6 8RF, UK.	Corticospinal inhibition appears normal in patients with chronic fatigue syndrome.	Exp Physiol. 2001 Sep;86(5):547-50.	The pathogenesis of chronic fatigue syndrome (CFS) remains unknown. Thresholds and latencies of motor evoked potentials (MEPs) in response to transcranial magnetic stimulation (TMS) are normal but intracortical inhibition has not been investigated. Eleven patients with CFS were compared with 11 control subjects. Each patient completed a questionnaire using visual analogue indices of pain, fatigue, anxiety and depression. Subjects released a button to initiate simple (SRTs) and choice reaction time (CRTs) tasks; for each task, movement times were measured between release of the initiation button and depression of a second button 15 cm away. Subjects held a 10 % maximum voluntary contraction in the thenar muscles of their dominant hand while TMS was applied to the motor cortex; the duration and extent of inhibition of surface electromyographic (EMG) activity were assessed at stimulus strengths above and below the threshold for MEPs. Patients had significantly ($P < 0.05$) higher mean indices of fatigue than of pain, anxiety or depression. Mean (+/- S.E.M.) SRTs (but not CRTs) were longer in patients (309 +/- 45 ms) than in controls (218 +/- 9 ms). Movement times were longer in patients for both SRTs and CRTs. TMS thresholds, expressed as a percentage of the maximum stimulator output, were not significantly ($P > 0.05$) different in both groups for both MEPs (patients, 34 +/- 3%; controls, 36 +/- 3%) and inhibition of voluntary contraction (patients, 29 +/- 2%; controls, 34 +/- 4%). The duration and extent of inhibition did not differ significantly between

				groups at any stimulus strength. The pattern of change in duration and extent of inhibition with increasing stimulus intensity was no different in the two groups. The duration and extent of corticospinal inhibition in patients with CFS did not differ from controls, adding further evidence to the notion that the feeling of fatigue and the slowness of movement seen in CFS is not manifest in corticospinal output pathways.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Aaron LA, Buchwald D.	Seattle, Wash.	Tobacco use and chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder	Arch Intern Med 2000 Aug 14;160(15):2398-401	
Aaron LA, Burke MM, Buchwald D.	Department of Medicine, University of Washington, Seattle, USA. laaron@u.washington.edu	Overlapping conditions among patients with chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder.	Arch Intern Med 2000 Jan 24;160(2):221-7Comment in: Arch Intern Med. 2000 Aug 14-28;160(15):2398, 2401	BACKGROUND: Patients with chronic fatigue syndrome (CFS), fibromyalgia (FM), and temporomandibular disorder (TMD) share many clinical illness features such as myalgia, fatigue, sleep disturbances, and impairment in ability to perform activities of daily living as a consequence of these symptoms. A growing literature suggests that a variety of comorbid illnesses also may commonly coexist in these patients, including irritable bowel syndrome, chronic tension-type headache, and interstitial cystitis. OBJECTIVE: To describe the frequency of 10 clinical conditions among patients with CFS, FM, and TMD compared with healthy controls with respect to past diagnoses, degree to which they manifested symptoms for each condition as determined by expert-based criteria, and published diagnostic criteria. METHODS: Patients diagnosed as having CFS, FM, and TMD by their physicians were recruited from hospital-based clinics. Healthy control subjects from a dermatology clinic were enrolled as a comparison group. All subjects completed a 138-item symptom checklist and underwent a brief physical examination performed by the project physicians. RESULTS: With little exception, patients reported few past diagnoses of the 10 clinical conditions beyond their referring diagnosis of CFS, FM, or TMD. In contrast, patients were more likely than controls to meet lifetime symptom and diagnostic criteria for many of the conditions, including CFS, FM, irritable bowel syndrome, multiple chemical sensitivities, and headache. Lifetime rates of irritable bowel syndrome were particularly striking in the patient groups (CFS, 92%; FM, 77%; TMD, 64%) compared with controls (18%) (P<.001). Individual symptom analysis revealed that patients with CFS, FM, and TMD share common symptoms, including generalized pain sensitivity, sleep and concentration difficulties, bowel complaints, and headache. However, several symptoms also distinguished the patient groups. CONCLUSIONS: This study provides preliminary evidence that patients with CFS, FM, and TMD share key symptoms. It also is apparent that other localized and systemic conditions may frequently co-occur with CFS, FM, and TMD. Future research that seeks to identify the temporal relationships and other pathophysiologic mechanism(s) linking CFS, FM, and TMD will likely advance our understanding and treatment of these chronic, recurrent conditions.
Ablashi DV, Eastman HB, Owen CB, Roman	Department of Microbiology,	Frequent HHV-6 reactivation in multiple	J Clin Virol 2000 May;16(3):179-91	BACKGROUND: HHV-6 is a ubiquitous virus and its infection usually occurs in childhood and then becomes a latent infection. HHV-6 reactivation has been shown

MM, Friedman J, Zabriskie JB, Peterson DL, Pearson GR, Whitman JE.	Georgetown University, School of Medicine, Washington, DC, USA. dablashi@abionline.com	sclerosis (MS) and chronic fatigue syndrome (CFS) patients.		to play a role in the pathogenesis of AIDS and several other diseases. OBJECTIVES: To determine what role HHV-6 infection or reactivation plays in the pathogenesis of multiple sclerosis (MS) and chronic fatigue syndrome (CFS). RESULTS: Twenty-one MS and 35 CFS patients were studied and followed clinically. In these patients, we measured HHV-6 IgG and IgM antibody levels and also analyzed their peripheral blood mononuclear cells (PBMCs) for the presence of HHV-6, using a short term culture assay. In both MS and CFS patients, we found higher levels of HHV-6 IgM antibody and elevated levels of IgG antibody when compared to healthy controls. Seventy percent of the MS patients studied contained IgM antibodies for HHV-6 late antigens (capsid), while only 15% of the healthy donors (HD) and 20% of the patients with other neurological disorders (OND) had HHV-6 IgM antibodies. Higher frequency of IgM antibody was also detected in CFS patients (57.1%) compared to HD (16%). Moreover, 54% of CFS patients exhibited antibody to HHV-6 early protein (p41/38) compared to only 8.0% of the HD. Elevated IgG antibody titers were detected in both the MS and the CFS patients. PBMCs from MS, CFS and HD were analyzed in a short term culture assay in order to detect HHV-6 antigen expressing cells and to characterize the viral isolates obtained as either Variant A or B. Fifty-four percent of MS patients contained HHV-6 early and late antigen producing cells and 87% of HHV-6 isolates were Variant B. Isolates from CFS, patients were predominately Variant A (70%) and isolates from HD were predominately Variant B (67%). Moreover, one isolate from OND was also Variant B. Persistent HHV-6 infection was found in two CFS patients over a period of 2.5 years and HHV-6 specific cellular immune responses were detected in PBMCs from ten CFS patients. CONCLUSION: In both MS and CFS patients, we found increased levels of HHV-6 antibody and HHV-6 DNA. A decrease in cellular immune responses was also detected in CFS patients. These data suggest that HHV-6 reactivation plays a role in the pathogenesis of these disorders.
Addington JW.		Chronic Fatigue Syndrome: A Dysfunction of the Hypothalamic-Pituitary-Adrenal Axis	Journal of Chronic Fatigue Syndrome 2000; 7(2): 63	Chronic fatigue syndrome is a severe, often disabling disorder with prevalence as high as 422 cases per 100,000 in the United States. Aside from the adverse effects to patients' quality of life, sequela of the disorder include a negative impact on the economy as well as a burden on public health care costs. Some avenues of current research into the possible genesis of the syndrome are neurally mediated hypotension, viral pathogen, immunological disorders, lymphocyte enzyme system abnormalities, or a purely psychological root. This paper is a review of the literatures as to a neuroendocrinologic cause, namely dysfunction of the hypothalamic-pituitary-adrenal axis.
Afari N, Eisenberg DM, Herrell R, Goldberg J, Kleyman E, Ashton S, Buchwald D.	Department of Medicine, University of Washington, Seattle, WA, USA	Use of alternative treatments by chronic fatigue syndrome discordant twins.	1096-2190 2000 Mar 21;2(2):97-103	Background: Patients with chronic fatigue syndrome (CFS) have been faced with difficulties in diagnosis and lack of effective treatments. Anecdotal evidence suggests that use of alternative treatments may be common in these patients. Our primary objective was to compare the prevalence and patterns of alternative medicine use among twins who met the Centers for Disease Control and Prevention (CDC) CFS

				criteria to that of their non-CFS co-twins. Secondary goals were to assess how often alternative medicine use was discussed with physicians and the perceived benefit of these therapies. Methods: Sixty-three twin pairs discordant for CFS completed a survey about their use of 22 alternative therapies. Matched pair odds ratios and 95% confidence intervals were used to examine differences in the use between CFS twins and their non-CFS co-twins. Results: 91% of twins with CFS and 71% of non-CFS twins had used at least 1 alternative treatment in their lifetime. Twins with CFS were more likely to use homeopathy, mega-vitamins, herbal therapies, biofeedback, relaxation/meditation, guided imagery, massage therapy, energy healing, religious healing by others, and self-help groups than their non-CFS counterparts. A large proportion of all twins found alternative therapies helpful; however, only 42% of those with CFS and 23% of those without CFS discussed their use of alternative medicine with a physician. Conclusions: Individuals with CFS frequently used alternative medical treatments yet rarely communicated this use to their medical doctor. Future research should ascertain the usefulness of alternative practices in the management of CFS.
Afari N, Schmaling KB, Herrell R, Hartman S, Goldberg J, Buchwald DS.	Department of Medicine, University of Washington, Seattle, WA 98104, USA. afari@u.washington.edu	Coping strategies in twins with chronic fatigue and chronic fatigue syndrome.	J Psychosom Res 2000 Jun;48(6):547-54	OBJECTIVES: Individuals with chronic fatigue and chronic fatigue syndrome (CFS) face debilitating symptoms as well as stressful life situations that may result from their condition. The goal of this study was to examine the coping strategies used by fatigue-discordant twin pairs. METHODS: We utilized a co-twin design to assess how twin pairs discordant for chronic fatigue and CFS cope with stress. All twin pairs were administered the Revised Ways of Coping Checklist. RESULTS: Overall, the pattern of coping strategies was similar for fatigued and non-fatigued twins. However, twins with chronic fatigue or CFS utilized more avoidance strategies than their non-fatigued counterparts; those with chronic fatigue also used more avoidance relative to problem-focused coping than their co-twins. CONCLUSIONS: These results suggest that while fatigue-discordant twins generally exhibit similar behavior patterns in order to cope with stress, there may be an association between fatigue and avoidance coping. Future research should focus on the role of avoidance and its relationship to fatiguing illnesses.
Albrecht F.		Chronic fatigue syndrome.	J Am Acad Child Adolesc Psychiatry 2000 Jul;39(7):808-9 Comment on: J Am Acad Child Adolesc Psychiatry. 1999 Dec;38(12):1515-21	
Apel-Paz M, Lior B, Shemesh-Kigli R.		[Chronic fatigue syndrome--the disease and approaches to	Harefuah 2000 Aug;139(3-4):141-9	

		treatment].[article in Hebrew]		
Asa PB, Cao Y, Garry RF.	Department of Microbiology, Tulane Medical School, 1430 Tulane Avenue, New Orleans, Louisiana, 70112, USA. PMBA@aol.com	Antibodies to squalene in Gulf War syndrome.	Exp Mol Pathol 2000 Feb;68(1):55-64	Gulf War Syndrome (GWS) is a multisystemic illness afflicting many Gulf War-era veterans. The molecular pathological basis for GWS has not been established. We sought to determine whether the presence of antibodies to squalene correlates with the presence of signs and symptoms of GWS. Participants in this blinded cohort study were individuals immunized for service in Desert Shield/Desert Storm during 1990-1991. They included 144 Gulf War-era veterans or military employees (58 in the blinded study), 48 blood donors, 40 systemic lupus erythematosus patients, 34 silicone breast implant recipients, and 30 chronic fatigue syndrome patients. Serum antibodies to squalene were measured. In our small cohort, the substantial majority (95%) of overtly ill deployed GWS patients had antibodies to squalene. All (100%) GWS patients immunized for service in Desert Shield/Desert Storm who did not deploy, but had the same signs and symptoms as those who did deploy, had antibodies to squalene. In contrast, none (0%) of the deployed Persian Gulf veterans not showing signs and symptoms of GWS have antibodies to squalene. Neither patients with idiopathic autoimmune disease nor healthy controls had detectable serum antibodies to squalene. The majority of symptomatic GWS patients had serum antibodies to squalene. Copyright 2000 Academic Press.
Ax S.		Coping Differences Between Chronic Fatigue Syndrome Sufferers and Their Carers	Journal of Chronic Fatigue Syndrome 2000; 5(2): 27	The main objective of the present study is to describe the extent to which CFS sufferers and their carers reported to have used a number of coping strategies over the course of the illness, and to find out if reports of coping differ between groups of these. In addition, associations between married sufferers and carers were investigated. From a methodological point of view, the factorial structure and the usefulness of the Ways of Coping Questionnaire (Folkman & Lazarus, 1988) in CFS was studied. The results indicate no gender differences. There are also no differences between sufferers supported and not supported by a carer. However, the results indicate reduced coping responses of carer husbands. From a methodological point of view, the emergence of comparable factors for sufferers and carers, which were also closely related to the original emotion and problem-focused factors, suggested that the use of the questionnaire was appropriate. The importance of these findings for coping research and therapy are discussed.
Axe E, Satz P.	Departments of Epidemiology and Neuropsychology, University of California-Los Angeles, Los Angeles, CA, USA	Psychiatric correlates in chronic fatigue syndrome.	Ann Epidemiol 2000 Oct 1;10(7):458	PURPOSE: This study presents psychiatric correlates in Chronic Fatigue Syndrome (CFS) that emerged from the CDC's Surveillance Study. It seeks to determine the time of onset and rates of syndromal psychiatric disorders and identify the predominant disorder. Other goals are to ascertain whether depression is associated with CFS symptomatology, compare syndromal to self- reported depression, and test for the specificity of the 1988 CDC case definition for CFS.METHODS: All 565 enrolled subjects had fatiguing illnesses and were evaluated for CFS. They completed the Diagnostic Interview Schedule for the DSM-III-R and the Beck Depression Inventory.

				Prevalence estimates for current syndromal psychiatric disorders were calculated. CFS symptoms were compared by depression status. Syndromal and self-reported depression were contrasted. Groups that did and did not meet the case definition were compared by three outcome variables.RESULTS: Rates of current psychiatric disorders were high in CDC subjects compared to the community. The predominant disorder was depression. Although prior disorders tended to persist (75%), many disorders were incident to the fatiguing illness (57%). Depression was not associated with increased CFS symptomatology. There was only weak agreement between measures of syndromal and self-reported depression (kappa = 0.3219). Subjects designated as CFS had similar rates of syndromal psychiatric disorders, syndromal depression, and self-reported depression as did non-CFS subjects.CONCLUSIONS: Current syndrome; psychiatric disorders appear associated with fatiguing illnesses. While prior psychiatric disorders are risk factors for current, the onset was largely concurrent with the fatiguing illnesses. The BDI should probably not be used as a measure for psychiatric morbidity in CFS subjects. Regardless of outcome, there was no evidence of specificity of psychiatric features to the CDC case definition.
Azpiroz F, Dapoigny M, Pace F, Muller-Lissner S, Coremans G, Whorwell P, Stockbrugger RW, Smout A.	Digestive System Research Unit, Hospital General Vall d'Hebron, Barcelona, Spain.	Nongastrointestinal disorders in the irritable bowel syndrome.	Digestion 2000;62(1):66-72	A large proportion of irritable bowel syndrome (IBS) patients also complain of other functional disorders, such as headache, noncardiac chest pain, low back pain, and dysuria. Some of these features, particularly headache, may have a negative influence on the outcome of IBS. In a large proportion of female IBS patients, sexual intercourse triggers the symptoms, and frequently IBS symptoms exacerbate during menses. These gynecological-type symptoms often mislead the patients to the gynecological clinic, which may imply unnecessary investigations and inappropriate treatments. The diagnostic criteria of the fibromyalgia syndrome include IBS, and hence, the apparent relationship of both syndromes is difficult to analyze. On the other hand, no convincing evidence has been produced to date to sustain an association between IBS and the chronic fatigue syndrome. Copyright 2000 S. Karger AG, Basel
Baraniuk JN, Naranch K, Maibach H, Clauw DJ.		Irritant Rhinitis in Allergic, Nonallergic, Control and Chronic Fatigue Syndrome Populations	Journal of Chronic Fatigue Syndrome 2000; 7(2): 3	Background: Irritation symptoms after exposure to ``nonspecific'' stimuli are often attributed to nonallergic rhinitis (vasomotor rhinitis). This is a heterogeneous syndrome of exclusion based on nasal symptoms with negative allergy skin tests. Method: Control (n = 114) and Chronic Fatigue Syndrome (CFS, n = 120) subjects scored the severity of nasal congestion and rhinorrhea sensations that they attributed to 9 irritants. The sum was the ``Irritant Rhinitis Score'' (IRS, maximum 72). A positive IRS of w 19 defined ``Irritant Rhinitis.'' Demographic, allergy skin test and other assessments were done to characterize the Irritant Rhinitis population. Results: Irritant Rhinitis was present in 11% of Control and 47% of CFS subjects. In multivariate analysis, positive IRS was correlated with a history of rhinitis complaints, systemic complaints such as fatigue, sensations of congestion and rhinorrhea induced by meteorological conditions, tobacco smoke, odors, perfumes, and other volatile

				materials, and diagnoses of CFS and Multiple Chemical Sensitivity (MCS). Although atopy was not correlated to Irritant Rhinitis, 51% of allergic rhinitis subjects had a positive IRS. Conclusions: The Irritant Rhinitis Score defined a population with irritant-induced nasal congestion and rhinorrhea who also had significant systemic complaints. Similar neural mechanisms may underlie the spectrum of Irritant Rhinitis, CFS and MCS.
Baraniuk JN, Naranch K, Maibach H, Clauw DJ.		Tobacco Sensitivity in Chronic Fatigue Syndrome (CFS)	Journal of Chronic Fatigue Syndrome 2000; 7(2): 33	Background: Mechanisms responsible for sensitivity to irritants such as tobacco smoke are poorly understood. A Tobacco Score questionnaire was developed to identify and characterize subjects with this sensitivity. For this pilot study, scores were assessed in populations of self-selected controls and a group with irritant sensitivity (Chronic Fatigue Syndrome, CFS). Method: Subjects graded the severity of 21 symptoms associated with tobacco exposure. Results were compared with other instruments and a measure of pain sensitivity (dolorimetry) in 116 control and 103 CFS subjects. Results: The Tobacco Score was positive in 16% of control and 51% of CFS subjects. Significant correlations were found between Tobacco Score, Irritant Rhinitis Score, and history of sinusitis. Intermediate relationships were found with history of allergic rhinitis, Systemic Complaints Score, and Multiple Chemical Sensitivity. Factors having no influence included gender, the severity of CFS symptoms, pain thresholds, and allergy skin tests. Conclusions: Tobacco sensitivity was correlated with measures of upper airway irritation and nonallergic sensitivity to triggers such as weather changes. The spectrum of symptoms, high prevalence in CFS, and absence of a relationship to atopy suggest that these nonallergic irritant syndromes may share a common neuropathophysiology.
Baschetti R.		The 1microg Synacthen test in chronic fatigue syndrome	Clin Endocrinol (Oxf) 2000 Jun;52(6):797-9 Comment on: Clin Endocrinol (Oxf). 1998 Jun;48(6):733-7 Clin Endocrinol (Oxf). 1999 Nov;51(5):625-30.	
Baschetti R.		Chronic fatigue syndrome: a form of Addison's disease.	J Intern Med 2000 Jun;247(6):737-9	
Behan WMH, Holt IJ, Kay DH, Moonie P.		In vitro Study of Muscle Aerobic Metabolism in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 5(1): 3	The purpose of this study was to establish if muscle aerobic metabolism is abnormal in chronic fatigue syndrome (CFS). Myoblast cultures from muscle biopsies of 16 patients with CFS and 10 healthy controls were established. Micromethods were used to determine the lactate/pyruvate (L/P) ratio, respiratory chain function and cytochrome oxidase and lactic dehydrogenase activities. Mitochondrial DNA (mtDNA) volume was measured and mtDNA rearrangements sought. The results showed that myoblasts from ten of 16 cases of CFS had defects in aerobic metabolism: two had

				increased L/P ratios, suggestive of a defect in oxidative phosphorylation while eight had decreased ratios, consistent with a deficiency in pyruvate dehydrogenase. There was a statistically significant broader range of L/P ratios in the patients' cultures, compared to controls (p = 0.011). No mtDNA rearrangements were present. This in vitro study confirms that there is convincing evidence of mild aerobic defects in skeletal muscle in some cases of CFS.
Bell IR, Bootzin RR, Schwartz GER, Baldwin CM, Ballesteros F.		Differing Patterns of Cognitive Dysfunction and Heart Rate Reactivity in Chemically-Intolerant Individuals With and Without Lifestyle Changes	Journal of Chronic Fatigue Syndrome 2000; 5(2): 3	The purpose of the present study was to compare specific neuropsychological, psychological, and family history patterns, as well as cardiovascular reactivity of three community-recruited groups of nonsmoking, nonalcoholic middle-aged individuals with and without the symptom of intolerance to low levels of environmental chemicals (CI). CI is a common symptom in chronic fatigue syndrome and fibromyalgia. The groups included: (i) CI who had made associated lifestyle changes because of the CI (CI/LSC); (ii) CI who had not made such changes (CI); and (iii) normals without CI (N). All subjects underwent an evaluation session followed by two laboratory cognitive and psychophysiological test sessions one week apart. The CI/LSC diverged from the other groups in exhibiting poorer performance on the Continuous Visual Memory Test (CVMT) in terms of more false alarms and fewer correct hits, but normal performance on a visuospatial test of divided attention (DAT). In contrast, the CI group showed progressively poorer performance on the DAT with practice, but were like the N on the CVMT. The CI group showed a complex sensitization (amplification) of heart rate response to the DAT over time. In addition, the CI/LSC had the highest rate of family histories of alcohol problems and of attention deficit disorder, as well as of antihypertensive medication treatment and self-reported past emotional/physical abuse. Taken together, the data suggest that individuals with CI comprise a heterogeneous population requiring careful definition of subtypes for future studies.
Bottero P.		Role of Rickettsiae and Chlamydiae in the Psychopathology of Chronic Fatigue Syndrome (CFS) Patients: A Diagnostic and Therapeutic Report	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 147	Objective: To demonstrate the probable role of intracellular bacteria like Rickettsiae and Chlamydiae in the development of certain chronic psychopathological conditions and according to the efficiency of antibiotic regimes (cyclines and/or macrolides). The latter aim is based on the fact that all the patients that I have seen since 1981 had a sera reaction positive for Rickettsiae and/or Chlamydiae using the micro-agglutination on blade technique of P. Giroud and M.L. Giroud (MAG) by Prof. J.B. Jadin of Antwerpen, Belgium with special antigens cultured on guinea pig lungs and chicken embryos. Methods: This is an open study which began in 1981 in a private medical practice, not versus placebo; but with random choice. Treatment was for a minimum of six months (cyclines and/or macrolides together with vasodilatory medication; chloroquine; warm baths). Group one: 98 CFS cases; women: 78, men: 20; for 67 cases, the ancientness of symptoms is more than 2 years. Group two: 59 psycho-somatic cases; 5 schizophrenia; 3 borderline; 10 children with agressivity, excitement; 1 autistic child; 1 delirium with relapses. Results: Group one: 79.5% good

				and very good results; 4.1% fairly good; 16.4% failed. Group two: 82.3% good and very good results; 2.5% fairly good; 15. 2% failed. Conclusion: This diagnostic and therapeutic study began in 1981. All of the Dr. Bottero's therapeutic results are confirmed since 1991 by Dr. Cecile Jadin of Randburg (South Africa) for more than 3000 CFS and other psychopathological states (300): Sydney 98 CFS Conference, Australia. We have shown that Rickettsiae and Chlamydiae are probably causative factors in many ``psychopathologies.''
Bottero P.		Chronic Psychopathologies Associated with Persistant Rickettsiae and/or Similar Germs (Chlamydiae)	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 163	For 60 cases of diseases that are called ``Psychic'' associated with persistent rickettsiae; we have: 55 good and excellent result, 5 failure, but we still have to wait a confirmation in course of time for many patients.
Brace MJ, Scott Smith M, McCauley E, Sherry DD.	Department of Psychiatry, University of Washington, Seattle, USA.	Family reinforcement of illness behavior: a comparison of adolescents with chronic fatigue syndrome, juvenile arthritis, and healthy controls.	J Dev Behav Pediatr 2000 Oct;21(5):332-9	Parental encouragement of illness behavior is hypothesized to correlate with psychosocial dysfunction in adolescents with chronic illness. To explore this hypothesis, adolescents aged 11 to 17 years with chronic fatigue syndrome (CFS) (n = 10), juvenile rheumatoid arthritis (JRA) (n = 16), and healthy adolescents (n = 14) were recruited for the study. Measures included the Achenbach parent and youth self report forms, the Family Adaptability and Cohesion Evaluation Scale-II (FACES II), the Children's Depression Rating Scale, and number of days absent from school. The Illness Behavior Encouragement Scale (IBES) generated measures of parental reinforcement of illness behavior. As predicted, the teens with CFS scored statistically higher on measures of depression, total competence, and number of days of school missed in the previous 6 months (mean = 40). Children with JRA scored significantly lower than the CFS group on the measure of parental reinforcement of illness behavior. The healthy group produced intermediate scores. Results and implications for future clinical and research activity are discussed.
Bradley LA, McKendree-Smith NL, Alarcon GS.	Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, School of Medicine, 475 Boshell Diabetes Building, 1808 7th Avenue South, Birmingham, AL 35294, USA. larry.bradley@ccc.uab.edu	Pain complaints in patients with fibromyalgia versus chronic fatigue syndrome.	Curr Rev Pain 2000;4(2):148-57	Individuals with fibromyalgia (FM) and/or chronic fatigue syndrome (CFS) report arthralgias and myalgias. However, only persons with FM alone exhibit abnormal pain responses to mild levels of stimulation, or allodynia. We identify the abnormalities in the neuroendocrine axes that are common to FM and CFS as well as the abnormalities in central neuropeptide levels and functional brain activity that differentiate these disorders. These two sets of factors, respectively, may account for the similarities and differences in the pain experiences of persons with FM and CFS.

Brooks JC, Roberts N, Whitehouse G, Majeed T.	Magnetic Resonance and Image Analysis Research Centre, University of Liverpool, Pembroke Place, Liverpool L69 3BX, UK.	Proton magnetic resonance spectroscopy and morphometry of the hippocampus in chronic fatigue syndrome.	Br J Radiol 2000 Nov;73(875):1206-8	Seven patients with chronic fatigue syndrome (CFS) were matched with ten healthy control subjects of similar age. Hippocampal volume, obtained from magnetic resonance images using an unbiased method, showed no difference between the two groups, whereas proton magnetic resonance spectroscopy showed a significantly reduced concentration of N-acetylaspartate in the right hippocampus of CFS patients (p = 0.005).
Buskila D.	Ben Gurion University of the Negev, Faculty of Health Sciences, Soroka Medical Center, Beer Sheva, Israel.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol 2000 Mar;12(2):113-23	Fibromyalgia and widespread pain were common in Gulf War veterans with unexplained illness referred to a rheumatology clinic. Increased tenderness was demonstrated in the postmenstrual phase of the cycle compared with the intermenstrual phase in normally cycling women but not in users of oral contraceptives. Patients with fibromyalgia had high levels of symptoms that have been used to define silicone implant-associated syndrome. Tender points were found to be a common transient finding associated with acute infectious mononucleosis, but fibromyalgia was an unusual long-term outcome. The common association of fibromyalgia with other rheumatic and systemic illnesses was further explored. A preliminary study revealed a possible linkage of fibromyalgia to the HLA region. Patients with fibromyalgia were found to have an impaired ability to activate the hypothalamic pituitary portion of the hypothalamic pituitary adrenal axis as well as the sympathoadrenal system, leading to reduced corticotropin and epinephrine response to hypoglycemia. Much interest has been expressed in the literature on the possible role of autonomic dysfunction in the development or exacerbation of fatigue and other symptoms in chronic fatigue syndrome. Mycoplasma genus and mycoplasma fermentans were detected by polymerase chain reaction in patients with chronic fatigue syndrome. It was reported that myofascial temporomandibular disorder does not run in families. No major therapeutic trials in fibromyalgia, chronic fatigue syndrome, or myofascial pain syndrome were reported over the past year. The effectiveness of cognitive behavioral therapy and behavior therapy for chronic pain in adults was emphasized. A favorable outcome of fibromyalgia and chronic fatigue syndrome in children and adolescents was reported.
Byrne E.	Department of Clinical Neurosciences, St Vincent's Hospital, Fitzroy Victoria, Australia. byrnee@svhm.org.au	Aetiological considerations on some conditions in the borderlands of neurology: chronic fatigue syndrome, pan allergy syndrome and repetitive strain injury--a personal view.	J Clin Neurosci 2000 Jan;7(1):9-12	
Cabane J, Renaud MC,		The Biorhythm of	Journal of Chronic	Evidence is provided for a rhythmic interpretation of fatigue in CFS.

Tiev KP.		Fatigue in Chronic Fatigue Syndrome	Fatigue Syndrome 2000; 6(3/4): 109	
Caccappolo E, Kipen H, Kelly-McNeil K, Knasko S, Hamer RM, Natelson B, Fiedler N.	University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Piscataway 08854, USA.	Odor perception: multiple chemical sensitivities, chronic fatigue, and asthma.	J Occup Environ Med 2000 Jun;42(6):629-38	Patients with multiple chemical sensitivities (MCS) often report heightened sensitivity to odors. Odor detection thresholds to phenyl ethyl alcohol (PEA) and pyridine (PYR) were evaluated as a measure of odor sensitivity for 33 MCS subjects, 13 chronic fatigue syndrome subjects, 16 asthmatic subjects, and 27 healthy controls. Odor identification ability (based on University of Pennsylvania Smell Identification Test results) and ratings in response to four suprathreshold levels of PEA and PYR were also assessed. Odor detection thresholds for PEA and PYR and odor identification ability were equivalent for all groups; however, when exposed to suprathreshold concentrations of PEA, MCS subjects reported significantly more trigeminal symptoms and lower esthetic ratings of PEA. No group differences were found in response to suprathreshold concentrations of PYR. In summary, MCS subjects did not demonstrate lower olfactory threshold sensitivity or enhanced ability to identify odors accurately. Furthermore, they were differentiated from the other groups in their symptomatic and esthetic ratings of PEA, but not PYR.
Chaudhuri A, Behan PO.		Neurological Dysfunction in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 51	Chronic fatigue syndrome (CFS), popularly known in Europe as myalgic encephalomyelitis (ME), is a common but not a new illness. CFS/ME was classified as a neurological disease by the World Health Organisation in 1993. Neurological dysfunction is considered the principal mechanism of both physical and mental fatigue in this condition. This article reviews the neurological symptoms of the epidemic and sporadic forms of the illness. Paroxysmal changes in the severity of symptoms (fatigue and neuropsychiatric) are the hallmark features in the natural history of this disease. Ion channel abnormality leading to neuronal instability in selective anatomical pathways (basal ganglia circuitry) is proposed as the possible mechanism of fluctuating fatigue and related symptoms in CFS.
Chaudhuri A, Watson WS, Pearn J, Behan PO.	University Department of Neurology, Institute of Neurological Sciences, Southern General Hospital, Glasgow, UK.	The symptoms of chronic fatigue syndrome are related to abnormal ion channel function	Med Hypotheses 2000 Jan;54(1):59-63Comment in: Med Hypotheses. 2000 Dec;55(6):524 Med Hypotheses. 2000 Nov;55(5):457.	The pathogenesis of chronic fatigue syndrome (CFS) is unknown but one of the most characteristic features of the illness is fluctuation in symptoms which can be induced by physical and/or mental stress. Other conditions in which fluctuating fatigue occurs are caused by abnormal ion channels in the cell membrane. These include genetically determined channelopathies, e.g. hypokalemic periodic paralysis, episodic ataxia type 2 and acquired conditions such as neuromyotonia, myasthenic syndromes, multiple sclerosis and inflammatory demyelinating polyneuropathies. Our hypothesis is that abnormal ion channel function underlies the symptoms of CFS and this is supported also by the finding of abnormal cardiac-thallium201 SPECT scans in CFS, similar to that found in syndrome X, another disorder of ion channels. CFS and syndrome X can have identical clinical symptoms. CFS may begin after exposure to specific toxins which are known to produce abnormal sodium ion channels. Finally, in CFS, increased resting energy expenditure (REE) occurs, a state influenced by transmembrane ion transport. The hypothesis that ion channels are abnormal in CFS

				may help to explain the fluctuating fatigue and other symptoms.
Cichon MJ, Farrell DL, Ganio SH, Sadler GM.		A Case Series Survey of Silicone Breast Implant Patients	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 119	Objective: To survey the symptoms of a large group of breast implant patients displaying illness and to determine if any clinical or serological features predominate. Design: A case series survey. Setting: A private internal medicine practice. Patients: A referred sample of 415 patients with fatigue of long duration, followed by muscle/joint pain, cognition problems, polyneuropathy, and localized breast pain. Conclusion: Silicone adjuvant breast disease may be a novel disorder, possibly autoimmune, producing atypical syndromes that do not fit within the classic diagnostic criteria of known conditions. Furthermore, the diversity and distinction of silicone adjuvant breast disease may require the medical community to accept it as a new entity, encompassing a neurological and connective tissue disorder.
Clarke JN.	Sociology Department, Wilfrid Laurier University, Waterloo, Ontario, Canada.	The search for legitimacy and the "expertization" of the lay person: the case of chronic fatigue syndrome.	Soc Work Health Care 2000;30(3):73-93	Some "diseases" appear to be recognized first by sufferers. At times these diseases may be disclaimed by medical doctors and elusive to scientific categorization and description. In these cases sufferers may organize themselves together in support groups and lobby for money to finance the discovery of diagnostic markers that would legitimate and medicalize the constellation of symptoms that they experience. Chronic fatigue syndrome is such a disease; and it is characterized by varied and changing symptomatology. Its diagnostic markers are in the process of being refined. Presently, its diagnosis primarily originates in reports of subjective experience of extreme fatigue. Often-times people diagnose themselves after attending a support group and find a doctor through a support group network who believes in the disease. Sometimes, people then return to their own family doctors with information and try to teach their doctors about what they believe to be the nature of their disease, its prognosis and treatment. Through such paths as described in the paper, patients become "experts": they may often know more about the illness than doctors and non-suffering others. This paper moves beyond the experience of chronic illness to describe the processes through which people seek confirmation and legitimation for the way that they feel and in a sense become the "experts."
Cleare AJ, Sookdeo SS, Jones J, O'Keane V, Miell JP.	Department of Psychological Medicine, Guy's King's and St. Thomas' School of Medicine, and the Institute of Psychiatry, London, United Kingdom. a.cleare@iop.kcl.ac.uk	Integrity of the growth hormone/insulin-like growth factor system is maintained in patients with chronic fatigue syndrome.	J Clin Endocrinol Metab 2000 Apr;85(4):1433-9	GH deficiency states and chronic fatigue syndrome (CFS) share several characteristics, and preliminary studies have revealed aspects of GH dysfunction in CFS. This study assessed indexes of GH function in 37 medication-free CFS patients without comorbid psychiatric illness and 37 matched healthy controls. We also assessed GH function before and after treatment with low dose hydrocortisone, which has been shown recently to reduce fatigue in CFS. We measured basal levels of serum insulin-like growth factor I (IGF-I), IGF-II, IGF-binding protein-1 (IGFBP-1), IGFBP-2 and IGFBP-3 together with 24-h urinary GH excretion. We also performed 2 dynamic tests of GH function: a 100-microg GHRH test and an insulin stress test using 0.15 U/kg BW insulin. There were no differences between patients and controls in basal levels of IGF/IGFBP or in urinary GH excretion. GH responses to both the GHRH test and the insulin stress test were no different in patients and controls. CFS patients did have a

				marginally reduced suppression of IGFBP-1 during the insulin stress test. Hydrocortisone treatment had no significant effect on any of these parameters. There is no evidence of GH deficiency in CFS. At the doses used, hydrocortisone treatment appears to have little impact on GH function.
Cocchetto AM, McNamara ME, Jordan EF.		Human Herpes Virus 6 (HHV-6) Infection in Patients with Chronic Fatigue Syndrome and Its Relationship to Activation-Induced Cell Death	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 41	Using evidence-based medical research techniques, current knowledge about the presence of active HHV-6 infections, in a sub-population of patients with chronic fatigue syndrome (CFS), has been reviewed and implications to activation-induced cell death are presented. Therapeutic intervention methods are also disclosed with a call for clinical studies to test the hypothesis presented.
Colquhoun D, Senn S.		Is NADH effective in the treatment of chronic fatigue syndrome?	Ann Allergy Asthma Immunol 2000 Jun;84(6):639-40 Comment on: Ann Allergy Asthma Immunol. 1999 Feb;82(2):185-91	
Couper J.	Department of Psychiatry, St Vincent's Hospital, The University of Melbourne, Fitzroy, Victoria, Australia. couperjw@svhm.org.au	Chronic fatigue syndrome and Australian psychiatry: lessons from the UK experience.	Aust N Z J Psychiatry 2000 Oct;34(5):762-9	OBJECTIVE: The aim of this paper is to outline the opportunities and dangers the chronic fatigue syndrome (CFS) issue presents to Australian psychiatry. METHOD: The scientific literature of the last 50 years on CFS in adults was reviewed and samples of recent media portrayals of CFS in the UK and Australia were collected. The author has worked in both the UK and Australia managing adult CFS patients in specialist outpatient consultation-liaison (C-L) psychiatry settings. RESULTS: Chronic fatigue syndrome has been at the heart of an acrimonious debate in the UK, both within the medical profession and in the wider community. UK psychiatry has been drawn into the debate, at times being the target of strong and potentially damaging criticism, yet UK psychiatry, especially the C-L subspecialty, has played a crucial role in clarifying appropriate research questions and in devising management strategies. The issue has served to enhance and broaden psychiatry's perceived research and clinical role at the important medicine-psychiatry interface in that country. CONCLUSIONS: Handled properly, the CFS issue offers Australian psychiatry, especially C-L psychiatry, an opportunity to make a useful contribution to patient care in a clinically difficult and contentious area, while at the same time serving to help broaden psychiatry's scope in the Australian medical landscape.
Cox DL, Findley LJ.		Severe and Very Severe Patients with Chronic Fatigue Syndrome: Perceived Outcome Following an Inpatient	Journal of Chronic Fatigue Syndrome 2000; 7(3): 33	The Chronic Fatigue Syndrome (CFS) Service within the Essex Neuroscience's Centre has been developing since 1990. The service was established as a comprehensive diagnostic and management service in July 1994. From May 1990 to March 1998, 318 patients with CFS were admitted into the programme and since November 1994, 1189 patients seen as outpatients. A previous survey indicated a positive perceived

		Programme		change in level of ability following the inpatient programme for all levels of CFS from mild to very severe. Of those admitted since 1990, 14% (43/318) were severely affected (extremely restricted mobility) and 9% (29/318) very severely affected (totally bedbound). Most studies on CFS do not include the more severe expressions of the disease; therefore, this descriptive paper aims to show the perceived outcome of these more severely affected patients following the inpatient programme. In particular, the eventual diagnosis, the specific approach to treatment and management and grading of patients will be described and the potential influence of the programme presented. The patients not diagnosed with CFS on discharge appeared to do least well at follow up.
Cruess SE, Klimas N, Antoni MH, Helder L, Maher K, Keller R, Fletcher MA.		Immunologic Status Correlates with Severity of Physical Symptoms and Perceived Illness Burden in Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 2000; 7(1): 39	The purpose of the present study was to investigate the relationship between immunologic status and physical symptoms in Chronic Fatigue Syndrome (CFS) patients. Twenty-seven patients diagnosed with CFS were included. Participants completed a questionnaire including selected subscales of the Sickness Impact Profile, the Cognitive Difficulties Scale, and frequency and severity of CFS-related physical symptoms. Cellular immune markers measured included number and percent of T-helper/inducer cells (CD3+CD4+), T-cytotoxic/suppressor cells (CD3+CD8+), activated T-lymphocytes (CD26+CD2+ CD3+), activated T cytotoxic/suppressor cells (CD38+HLA-DR+CD8+), and CD4/CD8 ratio. Spearman's correlation coefficients revealed significant associations between a number of immunologic measures and severity of illness suggesting that the degree of cellular immune activation was associated with the severity of CFS-related physical symptoms, cognitive complaints, and perceived impairment secondary to CFS. Specifically, elevations in T-helper/inducer cells, activated T-cells, activated cytotoxic/suppressor T-cells, and CD4/CD8 ratio were associated with greater severity of several symptoms. Furthermore, reductions in T-suppressor/cytotoxic cells also appeared related to greater severity of some CFS-related physical symptoms and illness burden. Multiple regression analyses demonstrated that decreased percentage of CD3+CD8+ cells and increased number of CD38+HLA-DR+CD8+ cells were the strongest predictors of total illness burden and fatigue severity, accounting for almost 30% of the variance in these measures.
Cukor D, Tiersky L, Natelson BH.		Psychiatric Comorbidity and Somatic Distress in Sudden and Gradual Onset Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 7(4): 33	The purpose of this study was to examine if type of Chronic Fatigue Syndrome (CFS) onset suggested two distinct illness patterns within CFS. One hundred and seventeen patients diagnosed with CFS by a multidisciplinary team were divided into two groups: sudden versus gradual onset of symptoms. These two subgroups were compared on the presence of lifetime comorbid Axis I diagnoses, the pattern of medically unexplained symptoms, and the number of patients who met criteria for Somatization Disorder (SD). The two subgroups did not differ in any of the experimental variables indicating that onset type is not distinguished by either comorbid psychopathology or medically unexplained symptoms. Implications of

				these findings are discussed.
Dalby JT.		Chronic fatigue syndrome and memory complaints.	Scand J Rheumatol 2000;29(4):271-2	
Davis SD, Kator SF, Wonnett JA, Pappas BL, Sall JL.	Preventive Medicine, Evans US Army Community Hospital, Fort Carson, Colorado, USA. shirley.davis@med.va.gov	Neurally mediated hypotension in fatigued Gulf War veterans: a preliminary report.	Am J Med Sci 2000 Feb;319(2):89-95	BACKGROUND: Many patients with chronic fatigue syndrome (CFS) have neurally mediated hypotension when subjected to head-up tilt, suggesting autonomic nervous system dysfunction. Some Gulf War veterans have symptoms similar to CFS. Whether they also tend to have neurally mediated hypotension is unknown. METHODS: We performed 3-stage tilt-table testing on 14 Gulf War veterans with chronic fatigue, 13 unfatigued control Gulf War veterans, and 14 unfatigued control subjects who did not serve in the Gulf War. Isoproterenol was used in stages 2 and 3 of the tilt protocol. RESULTS: More fatigued Gulf War veterans than unfatigued control subjects had hypotensive responses to tilt ($P < 0.036$). A positive response to the drug-free stage 1 of the tilt was observed in 4 of 14 fatigued Gulf War veterans versus 1 of 27 unfatigued control subjects ($P < 0.012$). Heart rate and heart rate variation during stage 1 was significantly greater in the fatigued group ($P < 0.05$). CONCLUSION: We conclude that more fatigued Gulf War veterans have neurally mediated hypotension than unfatigued control subjects, similar to observations in CFS. Autonomic nervous system dysfunction may be present in some fatigued Gulf War veterans.
De Becker P, Roeykens J, Reynders M, McGregor N, De Meirleir K.	Human Performance Laboratory and Department of Internal Medicine, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, LK-Third Floor, Pleinlaan 2, 1050 Brussels, Belgium. pdbeck@minf.vub.ac.be	Erratum in: Arch Intern Med 2001 Sep 10;161(16):2051-2 Exercise capacity in chronic fatigue syndrome.	Arch Intern Med 2000 Nov 27;160(21):3270-7	BACKGROUND: Patients with chronic fatigue syndrome (CFS) suffer from various symptoms, including debilitating fatigue, muscle pain, and muscle weakness. Patients with CFS can experience marked functional impairment. In this study, we evaluated the exercise capacity in a large cohort of female patients with CFS. METHODS: Patients with CFS and matched sedentary control subjects performed a maximal test with graded increase on a bicycle ergometer. Gas exchange ratio was continuously measured. In a second stage, we examined only those persons who achieved a maximal effort as defined by 2 end points: a respiratory quotient of at least 1.0 and an age-predicted target heart rate of at least 85%. Data were assessed using univariate and multivariate statistical methods. RESULTS: The resting heart rate of the patient group was higher, but the maximal heart rate at exhaustion was lower, relative to the control subjects. The maximal workload and maximal oxygen uptake attained by the patients with CFS were almost half those achieved by the control subjects. Analyzing only those persons who performed a maximal exercise test, similar findings were observed. CONCLUSIONS: When compared with healthy sedentary women, female patients with CFS show a significantly decreased exercise capacity. This could affect their physical abilities to a moderate or severe extent. Reaching the age-predicted target heart rate seemed to be a limiting factor of the patients with CFS in achieving maximal effort, which could be due to autonomic disturbances. Arch Intern Med. 2000;160:3270-3277.
De Meirleir K, Bisbal C,	Department of Human	A 37 kDa 2-5A binding	Am J Med 2000	PURPOSE: Recent studies have revealed abnormalities in the ribonuclease L pathway

Campine I, De Becker P, Salehzada T, Demettre E, Lebleu B.	Physiology and Medicine, Vrije Universiteit Brussels, Belgium.	protein as a potential biochemical marker for chronic fatigue syndrome	Feb;108(2):99-105Comment in: Am J Med. 2000 Aug 15;109(3):257-9 Am J Med. 2000 Dec 15;109(9):744 Am J Med. 2000 Feb;108(2):169-71 Am J Med. 2000 Feb;108(2):172-3.	in peripheral blood mononuclear cells of patients with the chronic fatigue syndrome. We conducted a blinded study to detect possible differences in the distribution of 2-5A binding proteins in the cells of patients with chronic fatigue syndrome and controls. PATIENTS AND METHODS: We studied 57 patients with chronic fatigue syndrome and 53 control subjects (28 healthy subjects and 25 patients with depression or fibromyalgia). A radioactive probe was used to label 2-5A binding proteins in unfractionated peripheral blood mononuclear cell extracts and to compare their distribution in the three groups. RESULTS: A 37 kDa 2-5A binding polypeptide was found in 50 (88%) of the 57 patients with chronic fatigue syndrome compared with 15 (28%) of the 53 controls ($P < 0.01$). When present, the amount of 37 kDa protein was very low in the control groups. When expressed as the ratio of the 37 kDa protein to the 80 kDa protein, 41 (72%) of the 57 patients with chronic fatigue syndrome had a ratio > 0.05, compared with 3 (11%) of the 28 healthy subjects and none of the patients with fibromyalgia or depression. CONCLUSION: The presence of a 37 kDa 2-5A binding protein in extracts of peripheral blood mononuclear cells may distinguish patients with chronic fatigue syndrome from healthy subjects and those suffering from other diseases.
Deale A, Wessely S.	Department of Psychological Medicine, King's College, London, UK. alicia.deale@kcl.ac.uk	Diagnosis of psychiatric disorder in clinical evaluation of chronic fatigue syndrome.	J R Soc Med 2000 Jun;93(6):310-2	The overlap of symptoms in chronic fatigue syndrome (CFS) and psychiatric disorders such as depression can complicate diagnosis. Patients often complain that they are wrongly given a psychiatric label. We compared psychiatric diagnoses made by general practitioners and hospital doctors with diagnoses established according to research diagnostic criteria. 68 CFS patients referred to a hospital fatigue clinic were assessed, and psychiatric diagnoses were established by use of a standardized interview schedule designed to provide current and lifetime diagnoses. These were compared with psychiatric diagnoses previously given to patients. Of the 31 patients who had previously received a psychiatric diagnosis 21 (68%) had been misdiagnosed: in most cases there was no evidence of any past or current psychiatric disorder. Of the 37 patients who had not previously received a psychiatric diagnosis 13 (35%) had a treatable psychiatric disorder in addition to CFS. These findings highlight the difficulties of routine clinical evaluation of psychiatric disorder in CFS patients. We advise doctors to focus on subtle features that discriminate between disorders and to use a brief screening instrument such as the Hospital Anxiety and Depression Scale.
Donnay A, Ziem G.		Prevalence and Overlap of Chronic Fatigue Syndrome and Fibromyalgia Syndrome Among 100 New Patients with Multiple Chemical Sensitivity Syndrome	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 71	Background: Several studies have reported on extensive two-way overlaps found among chronic fatigue syndrome (CFS), fibromyalgia syndrome (FMS) and multiple chemical sensitivity syndrome (MCS) but none have yet reported on the overlap of all three. This study assesses the prevalence of pure MCS, MCS-CFS, MCS-FMS and the overlap of all three among 100 consecutive new patients evaluated for MCS in a private practice specializing in occupational and environmental medicine. Methods: Sixty-eight females and 32 males diagnosed with MCS-based on a medical history of multiple chronic symptoms in multiple organs triggered by multiple chemical

				exposures at or below previously tolerated levels-were also evaluated for CFS and FMS using the diagnostic criteria of the US Centers for Disease Control and the American College of Rheumatology, respectively. Results: Eighty-eight percent of the 100 MCS patients met criteria for CFS, 49% met criteria for FMS, and 47% met both. Slightly more male than female MCS patients had CFS: 91% vs. 87%; while FMS was more than twice as common among female MCS patients: 59% vs. 28%. The majority of women, 56%, met criteria for all three disorders, and an additional 31% had both MCS and CFS. This pattern was reversed in men, only 28% of whom had all three, compared to 63% with MCS and CFS but no FMS. MCS alone was diagnosed in only 10% of the women and 9% of the men. Even rarer was the overlap of MCS and FMS without any CFS, found in just 2 women. Conclusions: At least in this clinic population, MCS seldom occurs alone. The enormous range of diagnostic overlaps reported here and in previous studies of various overlaps among CFS, FMS and MCS highlights the need to screen for all three disorders in studies of any one and to report results in these terms. We recommend this be made standard practice in both clinical settings and research protocols.
Duley JA, Garrick DP, Pratt DA.		Raised Plasma Adenosine Associated with Chronic Fatigue Syndrome: A Preliminary Study	Journal of Chronic Fatigue Syndrome 2000; 7(3): 77	Plasma adenosine levels were measured in a small trial study of eighteen volunteers, aged 36-85 years. Volunteers comprised nine with chronic fatigue syndrome (CFSs), four with `other fatigue' illnesses, and five with no history of fatigue illnesses but some of whom were related to chronic fatigue sufferers. Plasma adenosine was slightly raised above the minimum detectable level (approx. 1 micromole/L) in one healthy non-fatigued volunteer and grossly raised (greater than 5 micromoles/L) in two non-fatigued volunteers, both of whom were related to CFSs. Among the nine CFSs, all had plasma adenosine raised above baseline, and seven were grossly raised. High adenosine levels were also seen in two of the volunteers with `other fatigue.' Raised adenosine occurred among certain families, suggesting a genetic metabolic element. Instability of adenosine in frozen stored plasma was noted. High levels of adenosine probably do not exist freely within peripheral plasma but may be released from blood cells locally within tissues or in response to venipuncture stress or other factors. The results may be highly relevant to other pathologies such as heart disease.
Duncan RB.		Latency Immunity and Therapy: A Clinical Study of Latent Epstein Barr Virus Incidence in 297 Idiopathic Chronic Fatigue Patients with Plausible Hypotheses	Journal of Chronic Fatigue Syndrome 2000; 5(2): 77	Organ cells of the body retain an Immune Activity System comparable to protozoa. The cells' immunity memory templates are latent proteins, microbes, their toxins and chemicals (latentees). Excess latentees are detected and excreted by latency therapy. Their excretion induces immediate and/or delayed symptoms and signs recognized by the patient. Foreign latent materials (latentors) enter the body and bypass the Natural Immune System to be taken up selectively by organ cell groups. Active infection/disease and allergens (antigens) involve the Natural Immune System antibodies. Latent infection/disease and allergens (latentors) involve the Organ Cell Immunity as intracellular latentees. Clinical laboratory testing is inappropriate. This Clinical Anecdotal Study compiles 297 patients who obtained little or no relief from

				conventional and alternative medicine (duration: 63% > three years.) Patients provoked symptoms to two or more of 16 viruses, in particular Epstein Barr Virus. Latency therapy (heat, saunas, massage, tolerated exercise and sweating during sleep, the auto-sauna) dilutions stimulated excretion until symptoms/signs cleared. The principals were Epstein Barr Virus 67.3%, 200 patients; 13 individual viruses 30.0%, 89 patients; non-viral 2.6%, 8 patients. Latency therapy < 50% improvement = 16.5%; 50% to 80% = 26.6%; 80% to 100% = 46. 7%; failures = 11%. Fourteen patients gave positive Epstein Barr Virus serology. A latency immunity concept explains affected subjective symptoms and illnesses and offers a treatment which complements related medical therapies.
Dunstan RH, McGregor NR, Roberts T K, Butt H, Niblett SH, Rothkirch T.		The Development of Laboratory-Based Tests in Chronic Pain and Fatigue: 1. Muscle Catabolism and Coagulase Negative Staphylococci Which Produce Membrane Damaging Toxins	Journal of Chronic Fatigue Syndrome 2000; 7(1): 23	Background: The diagnosis of chronic fatigue syndrome (CFS) requires the exclusion of other known fatigue-related diseases because the core symptoms of CFS represent a general host response to many well-defined diseases. The patient set derived by this process is heterogeneous in their polysymptomatic presentation and has proved very difficult to study clinically and scientifically. Objectives: To investigate the alterations in urine excretion and microbiology in patients with CFS. Results: CFS patients had multiple anomalies in their amino and organic acid homeostasis. Sub-groups of CFS patients could be delineated on the basis of their urine excretion and their symptom presentation. The most common feature was an active muscle catabolism resulting in a depletion of amino acids and associated organic and keto-acids. The extent of muscle catabolism was directly correlated to pain severity. The carriage of toxin-producing coagulase negative staphylococci (MDT-CoNS) was strongly correlated with the catabolic response and pain severity. Conclusions: An hypothesis has been constructed where an occult pathogen, such as MDT-CoNS, may be an aetiological agent contributing to the sustenance of a chronic fatigue/pain disorder, a comorbid pathogen. Urine analysis offers an opportunity for assessment of muscle catabolism and sub-classification of chronic fatigue patients leading to a number of management options. The detection of MDT-CoNS identifies potentially treatable agents that contribute to the fatigue and pain condition.
Dunstan RH, McGregor NR, Roberts T K, Butt H, Niblett SH, Rothkirch T.		The Development of Laboratory-Based Tests in Chronic Pain and Fatigue: 1. Muscle Catabolism and Coagulase Negative Staphylococci Which Produce Membrane Damaging Toxins	Journal of Chronic Fatigue Syndrome 2000; 7(2): 53	Background: The diagnosis of chronic fatigue syndrome (CFS) requires the exclusion of other known fatigue-related diseases because the core symptoms of CFS represent a general host response to many well-defined diseases. The patient set derived by this process is heterogeneous in their polysymptomatic presentation and has proved very difficult to study clinically and scientifically. Objectives: To investigate the alterations in urine excretion and microbiology in patients with CFS. Results: CFS patients had multiple anomalies in their amino acid and organic acid homeostasis. Sub-groups of CFS patients could be delineated on the basis of their urine excretion and their symptom presentation. The most common feature was an active muscle catabolism resulting in a depletion of amino acids and associated organic and keto-acids. The extent of muscle catabolism was directly correlated to pain severity. The

				carriage of toxin-producing coagulase negative staphylococci (MDT-CoNS) was strongly correlated with the catabolic response and pain severity. Conclusions: An hypothesis has been constructed where an occult pathogen, such as MDT-CoNS, may be an aetiological agent contributing to the sustenance of a chronic fatigue/pain disorder, a comorbid pathogen. Urine analysis offers an opportunity for assessment of muscle catabolism and sub-classification of chronic fatigue patients leading to a number of management options. The detection of MDT-CoNS identifies potentially treatable agents that contribute to the fatigue and pain condition.
Dunstan RH, McGregor NR, Roberts T K, Butt H, Taylor WG, Carter A.		The Development of Laboratory-Based Tests in Chronic Pain and Fatigue: 2. Essential Fatty Acids and Cholesterol	Journal of Chronic Fatigue Syndrome 2000; 7(2): 59	Objectives: To investigate fatty acid and sterol homeostasis in patients with CFS. Methods: Plasma samples were collected from CFS and control subjects and analyzed for lipid composition by GC-MS metabolic profiling techniques. Results: CFS patients had significantly different profiles of fatty acids and sterols compared with control subjects. The 1st and 2nd most important factors discriminating the CFS patients from the controls, were a decrease in elaidic acid (trans-9-octadecenoic acid) and an increase in stearic acid (octadecanoic acid), respectively. The CFS patients also had lower levels of cholesterol, which has potential impact on membrane integrity and function, steroid hormone synthesis, energy metabolism and bile production. The CFS patients could also be subdivided into subgroups based on their fatty acid and sterol composition. The results of cluster analyses and multivariate analyses revealed that several types of homeostasis exist in different types of CFS patients, whereas the control group was largely homogeneous. Viral infections can contribute to the nature of the lipid-based anomalies in CFS patients and lipid profiles from patients with prior viral infections could be differentiated from those without viral histories. Conclusions: The assessment of fatty acids and sterols in fasting plasma samples can indicate essential fatty acid deficits, suggest appropriate types of essential fatty acid oils for formulations, indicate potential cholesterol deficit-associated anomalies, provide evidence for mitochondrial dysfunction and categorize CFS patients into biochemical subgroups. These evaluations provide a basis for devising individually tailored patient management protocols.
Durstine JL, Painter P, Franklin BA, Morgan D, Pitetti KH, Roberts SO.	Department of Exercise Science, University of South Carolina, Columbia 29208, USA. ldurstine@sophe.sph.sc.edu	Physical activity for the chronically ill and disabled.	Sports Med 2000 Sep;30(3):207-19	Exercise prescription principles for persons without chronic disease and/or disability are based on well developed scientific information. While there are varied objectives for being physically active, including enhancing physical fitness, promoting health by reducing the risk for chronic disease and ensuring safety during exercise participation, the essence of the exercise prescription is based on individual interests, health needs and clinical status, and therefore the aforementioned goals do not always carry equal weight. In the same manner, the principles of exercise prescription for persons with chronic disease and/or disability should place more emphasis on the patient's clinical status and, as a result, the exercise mode, intensity, frequency and duration are usually modified according to their clinical condition. Presently, these exercise prescription principles have been scientifically defined for

				clients with coronary heart disease. However, other diseases and/or disabilities have been studied less (e.g. renal failure, cancer, chronic fatigue syndrome, cerebral palsy). This article reviews these issues with specific reference to persons with chronic diseases and disabilities.
Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES.	Inflammatory Joint Diseases Section, Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland, USA.	The sympathetic nerve--an integrative interface between two supersystems: the brain and the immune system.	Pharmacol Rev 2000 Dec;52(4):595-638	The brain and the immune system are the two major adaptive systems of the body. During an immune response the brain and the immune system "talk to each other" and this process is essential for maintaining homeostasis. Two major pathway systems are involved in this cross-talk: the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS). This overview focuses on the role of SNS in neuroimmune interactions, an area that has received much less attention than the role of HPA axis. Evidence accumulated over the last 20 years suggests that norepinephrine (NE) fulfills the criteria for neurotransmitter/neuromodulator in lymphoid organs. Thus, primary and secondary lymphoid organs receive extensive sympathetic/noradrenergic innervation. Under stimulation, NE is released from the sympathetic nerve terminals in these organs, and the target immune cells express adrenoreceptors. Through stimulation of these receptors, locally released NE, or circulating catecholamines such as epinephrine, affect lymphocyte traffic, circulation, and proliferation, and modulate cytokine production and the functional activity of different lymphoid cells. Although there exists substantial sympathetic innervation in the bone marrow, and particularly in the thymus and mucosal tissues, our knowledge about the effect of the sympathetic neural input on hematopoiesis, thymocyte development, and mucosal immunity is extremely modest. In addition, recent evidence is discussed that NE and epinephrine, through stimulation of the beta(2)-adrenoreceptor-cAMP-protein kinase A pathway, inhibit the production of type 1/proinflammatory cytokines, such as interleukin (IL-12), tumor necrosis factor-alpha, and interferon-gamma by antigen-presenting cells and T helper (Th) 1 cells, whereas they stimulate the production of type 2/anti-inflammatory cytokines such as IL-10 and transforming growth factor-beta. Through this mechanism, systemically, endogenous catecholamines may cause a selective suppression of Th1 responses and cellular immunity, and a Th2 shift toward dominance of humoral immunity. On the other hand, in certain local responses, and under certain conditions, catecholamines may actually boost regional immune responses, through induction of IL-1, tumor necrosis factor-alpha, and primarily IL-8 production. Thus, the activation of SNS during an immune response might be aimed to localize the inflammatory response, through induction of neutrophil accumulation and stimulation of more specific humoral immune responses, although systemically it may suppress Th1 responses, and, thus protect the organism from the detrimental effects of proinflammatory cytokines and other products of activated macrophages. The above-mentioned immunomodulatory effects of catecholamines and the role of SNS are also discussed in the context of their clinical implication in certain infections, major injury and

				sepsis, autoimmunity, chronic pain and fatigue syndromes, and tumor growth. Finally, the pharmacological manipulation of the sympathetic-immune interface is reviewed with focus on new therapeutic strategies using selective alpha(2)- and beta(2)-adrenoreceptor agonists and antagonists and inhibitors of phosphodiesterase type IV in the treatment of experimental models of autoimmune diseases, fibromyalgia, and chronic fatigue syndrome.
Enbom M, Linde A, Evengard B.		No evidence of active infection with human herpesvirus 6 (HHV-6) or HHV-8 in chronic fatigue syndrome.	J Clin Microbiol 2000 Jun;38(6):2457	
Endicott NA.		Chronic Fatigue Syndrome in Psychiatric Patients: Evidence of Premorbid Anomalous Patterns of Brain Organization	Journal of Chronic Fatigue Syndrome 2000; 5(1): 29	Forty-six patients with chronic fatigue syndrome (CFS) were matched with two control groups: one chosen on the basis of relatively good physical health (N = 92) and the other without regard to physical health (N = 46). All patients were from the same psychiatric practice. The groups were compared on 20 anomalous brain conditions or phenomena (ABCP) used as markers of patterns of brain organization. The results suggest that psychiatric patients who subsequently develop CFS have a higher number of pre-CFS ABCP, of both childhood and adult onset, than psychiatric patients who have not developed this condition.
Enserink M. News		Chronic fatigue syndrome. CDC struggles to recover from debacle over earmark	Science 2000 Jan 7;287(5450):22-3 Comment on: Science. 2000 Jan 21;287(5452):427.	
Evans P.		Chronic fatigue syndrome	Aust Fam Physician 2000 Jul;29(7):625-6 Comment on: Aust Fam Physician. 2000 Jan;29(1):76-7.	
Feinberg M.		Chronic fatigue syndrome and the aviator.	Aviat Space Environ Med 2000 Sep;71(9 Pt 1):965	
Ferrari R.		The biopsychosocial model--a tool for rheumatologists.	Baillieres Best Pract Res Clin Rheumatol 2000 Dec;14(4):787-95	Rheumatologists grapple in daily practice with many controversial syndromes including fibromyalgia, late whiplash syndrome, chronic fatigue syndrome, Gulf War syndrome, the adverse outcomes of silicon breast implants and so on. For decades, much of the debate surrounding, and the approach to these controversial syndromes has centred on a model creating two camps-organic versus non-organic. While each camp has its support, this model seems to have failed in achieving the desired understanding of these syndromes, most particularly in offering the rheumatologist a practical and coherent approach to effective treatment. This chapter will thus

				introduce the biopsychosocial model, its elements, its advantages over the traditional model and the practical application of this model. Examples will be given of how rheumatologists can approach the treatment of these syndromes through patient education and the implementation of a change in illness behaviour. Copyright 2000 Harcourt Publishers Ltd.
Fiedler N, Lange G, Tiersky L, DeLuca J, Policastro T, Kelly-McNeil K, McWilliams R, Korn L, Natelson B.	Department of Environmental and Community Medicine, UMDNJ-Robert Wood Johnson Medical School, 170 Frelinghuysen Road, Piscataway, NJ 08854, USA. nfiedler@eohsi.rutgers.edu	Stressors, personality traits, and coping of Gulf War veterans with chronic fatigue.	J Psychosom Res 2000 Jun;48(6):525-35	OBJECTIVES: preliminary surveys of Persian Gulf veterans revealed a significant prevalence of self-reported symptoms consistent with chronic fatigue syndrome (CFS). The purpose of this study was to compare self-reported life stressors, combat, and chemical exposures, personality and coping between Gulf War veterans with CFS and healthy veterans. METHODS: following a complete physical, psychiatric, and neuropsychological evaluation, 45 healthy veterans, 35 veterans with CFS and co-morbid psychiatric disorder, and 23 veterans with CFS and no co-morbid psychiatric disorder completed questionnaires assessing war and non-war-related life stressors, self-reports of environmental exposure (e.g. oil well fires, pesticides), personality, and coping. RESULTS: measures of personality, self-reported combat and chemical exposures, and negative coping strategies significantly differentiated healthy veterans from those with CFS. CONCLUSION: a biopsychosocial model of veterans' illness was supported by the fact that personality, negative coping strategies, life stress after the war, and environmental exposures during the war were significant predictors of veterans' current physical function.
Fletcher MA, Maher K, Patarca-Montero R, Klimas N.		Comparative Analysis of Lymphocytes in Lymph Nodes and Peripheral Blood of Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 7(3): 65	Blood and lymph node samples were obtained from patients with chronic fatigue syndrome (CFS) who had volunteered to undergo a lymph node biopsy while participating in a phase 1 clinical trial of a novel immunomodulatory therapy. The surface marker phenotypes of the peripheral blood and lymph node samples were examined using four-color flow cytometry and compared to published proportions of cells in peripheral blood and lymph nodes from control individuals. While a greater proportion of T lymphocytes from both lymph nodes and peripheral blood of control subjects are immunologically ``naive'' (CD45RA+), the proportions of lymphocytes with a ``memory'' phenotype predominate in lymph nodes and peripheral blood of CFS patients. CFS has been proposed to be a disease of autoimmune etiology and in this respect it is interesting to note that decreased proportions of CD45RA+ T (``naive'') cells are also seen in the peripheral blood of patients with autoimmune diseases.
Friedberg F, Dechene L, McKenzie MJ 2nd, Fontanetta R.	Department of Mathematics, Fitchburg State College, MA, USA.	Symptom patterns in long-duration chronic fatigue syndrome.	J Psychosom Res 2000 Jan;48(1):59-68	OBJECTIVE: Our objective was to evaluate symptom patterns in patients with chronic fatigue syndrome (CFS) who were ill for 10 or more years. METHODS: This cross-sectional self-report study compared patient groups with long-duration (median = 18 years; n = 258) and short-duration (median = 3 years; n = 28) CFS to a group of healthy significant others (n = 79) on symptomatic, neurocognitive, and psychological variables. Data were gathered from a 574-item postal questionnaire. RESULTS: A principal-components analysis of CFS symptom data yielded a three-factor solution:

				cognitive problems; flu-like symptoms; and neurologic symptoms. Compared with the short-duration CFS group, the long-duration group had significantly higher CFS symptom severity scores ($p < 0.04$), largely attributable to increased cognitive difficulties. A subgroup comparison of subjects ill for < 3 years versus those ill 4-7 years suggested that denial coping strategies were more likely in those participants with the shorter illness duration. Significant differences between both CFS groups and healthy controls were found in a number of comorbid disorders. Participants with CFS most often endorsed immune/viral abnormalities and persistent stress as important perceived causes of their illness. CONCLUSION: Participants with long-duration CFS reported a large number of specific cognitive difficulties that were greater in severity than those reported by participants with short-duration CFS. The pattern of comorbid disorders in the CFS groups was consistent with hypersensitivity and viral reactivation hypotheses.
Friedberg F.		A Subgroup Analysis of Cognitive-Behavioral Treatment Studies	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 149	Several studies of graded activity-oriented cognitive behavioral treatment for chronic fatigue syndrome (CFS), all conducted in England, have reported dramatic improvements in functioning and substantial reductions in symptomatology. On the other hand, cognitive behavioral intervention studies conducted in Australia and the United States have not found significant improvements in functioning or CFS symptoms. Based on a review and synthesis of data from these clinical trials, naturalistic outcome investigations, and illness comparison studies, this articles argues that two CFS subgroups, distinguished by functional status and symptom severity, may account, in part, for the differences in outcome in cognitive behavioral treatment studies. It is also argued that differences in treatment duration may have influenced clinical outcomes. This article concludes with recommendations for specific cognitive behavioral interventions in CFS.
Friedberg F.		An Overview of Psychometric Assessment	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 161	The assessment of a number of behavioral and psychosocial domains may be important in baseline and outcome evaluations of CFS patients. These domains include mood disturbance, functional status, sleep disturbance, global well-being (i.e., psychiatric status), pain, behavioral coping, social support, locus of control, illness behavior and illness attribution. This article describes a variety of pen-and-paper measures designed to assess these behavioral dimensions and summarizes their psychometric properties and applicability to CFS populations.
Fulcher KY, White PD.	National Sports Medicine Institute, St Bartholomew's and the Royal London School of Medicine and Dentistry, Charterhouse Square, London EC1M 6BQ, UK.		J Neurol Neurosurg Psychiatry 2000 Sep;69(3):302-7Comment in: J Neurol Neurosurg Psychiatry. 2000 Sep;69(3):289 Strength and physiological response	OBJECTIVE: To measure strength, aerobic exercise capacity and efficiency, and functional incapacity in patients with chronic fatigue syndrome (CFS) who do not have a current psychiatric disorder. METHODS: Sixty six patients with CFS without a current psychiatric disorder, 30 healthy but sedentary controls, and 15 patients with a current major depressive disorder were recruited into the study. Exercise capacity and efficiency were assessed by monitoring peak and submaximal oxygen uptake, heart rate, blood lactate, duration of exercise, and perceived exertion during a treadmill walking test. Strength was measured using twitch interpolated voluntary

			to exercise in patients with chronic fatigue syndrome.	isometric quadriceps contractions. Symptomatic measures included physical and mental fatigue, mood, sleep, somatic amplification, and functional incapacity. RESULTS: Compared with sedentary controls, patients with CFS were physically weaker, had a significantly reduced exercise capacity, and perceived greater effort during exercise, but were equally unfit. Compared with depressed controls, patients with CFS had significantly higher submaximal oxygen uptakes during exercise, were weaker, and perceived greater physical fatigue and incapacity. Multiple regression models suggested that exercise incapacity in CFS was related to quadriceps muscle weakness, increased cardiovascular response to exercise, and body mass index. The best model of the increased exercise capacity found after graded exercise therapy consisted of a reduction in submaximal heart rate response to exercise. CONCLUSIONS: Patients with CFS were weaker than sedentary and depressed controls and as unfit as sedentary controls. Low exercise capacity in patients with CFS was related to quadriceps muscle weakness, low physical fitness, and a high body mass ratio. Improved physical fitness after treatment was associated with increased exercise capacity. These data imply that physical deconditioning helps to maintain physical disability in CFS and that a treatment designed to reverse deconditioning helps to improve physical function.
Fulle S, Mecocci P, Fano G, Vecchiet I, Vecchini A, Racciotti D, Cherubini A, Pizzigallo E, Vecchiet L, Senin U, Beal MF.	Lab. Interuniversitario di Miologia, Dip. Biologia Cellulare e Molecolare, Universita di Perugia, Perugia, Italy.	Specific oxidative alterations in vastus lateralis muscle of patients with the diagnosis of chronic fatigue syndrome.	Free Radic Biol Med 2000 Dec 15;29(12):1252-9	Chronic fatigue syndrome (CFS) is a poorly understood disease characterized by mental and physical fatigue, most often observed in young white females. Muscle pain at rest, exacerbated by exercise, is a common symptom. Although a specific defect in muscle metabolism has not been clearly defined, yet several studies report altered oxidative metabolism. In this study, we detected oxidative damage to DNA and lipids in muscle specimens of CFS patients as compared to age-matched controls, as well as increased activity of the antioxidant enzymes catalase, glutathione peroxidase, and transferase, and increases in total glutathione plasma levels. From these results we hypothesize that in CFS there is oxidative stress in muscle, which results in an increase in antioxidant defenses. Furthermore, in muscle membranes, fluidity and fatty acid composition are significantly different in specimens from CFS patients as compared to controls and to patients suffering from fibromyalgia. These data support an organic origin of CFS, in which muscle suffers oxidative damage.
Furst G.		Measuring Fatigue in Chronic Fatigue Syndrome: Why and How	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 55	Fatigue is a common symptom occurring in a wide range of acute and chronic illnesses. It is multidimensional and subjective and because of this it has been difficult to define and quantify. Fatigue is one of several significant symptoms in diseases such as rheumatoid arthritis and multiple sclerosis, but for persons with chronic fatigue syndrome (CFS), it is often the most debilitating symptom. The need for valid and reliable assessments of fatigue is necessary for health care providers as we are increasingly required to document outcomes of care for professional and insurance purposes.
Gelman IH, Unger ER,	Department of	Chronic fatigue	Mol Diagn 2000	

Mawle AC, Nisenbaum R, Reeves WC.	Microbiology, Mount Sinai School of Medicine, New York, NY, USA.	syndrome is not associated with expression of endogenous retroviral p15E.	Jun;5(2):155-6	
Gilbert RB, Kaan R, Lipkin DM, Lepp M.		Chronic fatigue: syndrome or disease?	JAMA 2000 Feb 9;283(6):744-5	
Gimenez HB, Cash P, Laing RBS, Douglas JG.		Cytokine Expression and Morphology of in vitro Grown Monocytes from Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 5(1): 47	Although underlying metabolic cause of chronic fatigue syndrome (CFS) is unknown, specific defects have been proposed to exist in the skeletal muscle, the immune system and the neuroendocrine system. Peripheral blood mononuclear cells from CFS patients and healthy controls were fractionated as adherent cells (monocyte-enriched fraction) and non-adherent cells. We have investigated some activities of the former during in vitro culture. It was observed that the morphology (shape and size) of adherent cells from CFS patients, co-cultivated with homologous non-adherent cells, differed between CFS patients and healthy controls for 21 out of 25 (84%) paired samples (i.e., CFS patient and healthy control). Cytokine expression was examined for the adherent cell population collected from 14 CFS patients and 12 healthy controls. Unstimulated and LPS stimulated tumour necrosis factor-a (TNFa) expression was higher for monocytes from 7 out of 14 CFS patients. Unstimulated interleukin-1b (IL-1b) expression was higher for monocytes from 10 out of 14 CFS patients, whereas LPS-stimulated IL-1b expression was higher for 8 out of 14 CFS patients. The proportional increase of IL-1b and TNFa following LPS stimulation was lower for the majority of the CFS patients studied, suggesting that the monocytes from CFS patients were less responsive to LPS than the respective healthy controls. The basis for the abnormal in vitro monocyte maturation, the elevated unstimulated levels of IL-1b expression and the abnormal response of the monocytes to LPS is unknown. The relevance of these findings to CFS pathogenesis is discussed.
Glass RT.		The Human/Animal Interaction in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: A Look at 127 Patients	Journal of Chronic Fatigue Syndrome 2000; 6(2): 65	Objective: To evaluate the interaction between Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) patients and domestic animals (pets). Design: Retrospective study of criteria-met ME/CFS patients using a standardized questionnaire which included patient comments. Setting: University medical center and ME/CFS support groups throughout the United States. Patients: A total of 127 patients met the surveillance criteria of the Centers for Disease Control and Prevention (CDC) for the establishment of the diagnosis of ME/CFS and were included in the study. Measurements: Information from the standardized questionnaire was compiled and appropriate statistical tests, including mean, median, Z test, multivariant analysis, and Chi-square test, were used. This information was compared to national statistical information on animal interaction compiled by the American Veterinary Medicine Association. Results: The most striking result of the study was the association between ME/CFS patients and animals (usually indoor pets) and the

				number of animals per ME/CFS patient. 97% of the ME/CFS patients had animal contact (expected national contact: 57.9%), with only 2 males and 2 females not reporting animal contact. Reported dog ownership/household for ME/CFS males was 9.5 and for ME/CFS females was 7.9 (expected national average: 1.52). Reported cat ownership/household for ME/CFS males was 6.1 and for ME/CFS females was 8.7 (expected national average: 1.95). 106 of the respondents (83.5%) reported that their animals (pets) had atypical diseases with symptoms which mimicked ME/CFS in humans. Of the 106 ME/CFS patients, 100 (94.3%) either were the primary caregiver for the sick animals or had intimate contact (sleeping with, being bitten or scratched by, or kissing the animal). Conclusions: ME/CFS patients have a significant animal interaction and a large number of these animals have atypical or unusual diseases which at least mimic ME/CFS.
Glass RT.		Abnormal Signs Found in Animals of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome Patients: A Look at 463 Animals	Journal of Chronic Fatigue Syndrome 2000; 6(2): 73	Objective: To evaluate the abnormal signs found in the domestic animals (pets) of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) patients. Design: Retrospective study of the domestic animals (pets) of criteria-met ME/CFS patients using a standardized questionnaire which included patient comments. Setting: University medical center and ME/CFS support groups throughout the United States. Patients: A total of 127 patients met the surveillance criteria of the Centers for Disease Control and Prevention (CDC) for the establishment of the diagnosis of ME/CFS and were included in the study. This group of patients had a total of 463 domestic animals (pets), of which 348 animals demonstrated abnormal signs and 115 were considered healthy. Measurements: Information from the standardized questionnaire was compiled and appropriate statistical tests, including mean, median, Z test, multivariant analysis, and Chi-square test, were used. Results: One hundred six (83%) of the 127 ME/CFS surveyed reported that at least one of their animals (predominantly domestic pets) showed a wide range of unusual or atypical signs, many of which mimicked the signs and symptoms of ME/CFS. The sick animals' signs were divided into General (40%), Neurological (35%), Gastrointestinal (10%), Reticuloendothelial/Blood (9%), Neoplasia (4%), and Endocrine (2%). One of the most striking result of the study was that 113 of the 127 ME/CFS patients surveyed felt their ME/CFS symptoms were somehow associated with their animals contact. Ninety (71%) of the 127 ME/CFS patients reported that they were the primary caretakers for multiple animals. Other less common findings were: the onset of ME/CFS being associated with obtaining the animal; the onset of ME/CFS being associated with a flea bite episode; prior residents having sick animals and ME/CFS; other family member contracting ME/CFS from their close association with the sick animal (as opposed to their association with the family members who had ME/CFS); ME/CFS symptoms decreasing after the pet leaving or dying. Conclusions: A large number of animals of ME/CFS patients have atypical or unusual diseases which at least mimic ME/CFS. Most of the 127 ME/CFS patients surveyed have significant animal

				interactions.
Goodwin SS.	Pacific Lutheran University, Tacoma, WA 98447, USA. goodwisd@plu.edu	Couples' perceptions of wives' CFS symptoms, symptom change, and impact on the marital relationship.	Issues Ment Health Nurs 2000 Jun;21(4):347-63	The purpose of this descriptive correlational study was to describe the differences in couples' perceptions of wives' Chronic Fatigue Syndrome (CFS) symptoms and to describe the relationship between changing symptoms and the marital relationship. The convenience sample of 131 wives with CFS and their spouses reported symptom changes similarly. However, wives reported significantly higher problem levels for constitutional, fatigue, cognition, central nervous system (CNS), musculoskeletal, and allergy symptom domains and significantly less problem levels of mood disturbance domain than their husbands. Husbands who reported more symptom changes also reported lower marital adjustment, less empathy and support from their wives, and more conflict within the relationship. Wives who reported more symptom changes reported lower marital adjustment, less empathy for their husbands, and more conflict within the relationship and had husbands who reported lower marital adjustment and less empathy and support by the wives.
Gordon R, Michalewski HJ, Nguyen T, Starr A.		Premovement and Cognitive Brain Potentials in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 137	Brain potentials from normals and patients with Chronic Fatigue Syndrome (CFS) were recorded in four different experimental tasks: (1) Auditory target detection, (2) Short-term memory scanning, (3) Fore-warned reaction time (contingent negative variation) and, (4) Self-paced movement. In the auditory target detection task, a slow negative potential shift (maximum at Cz), appears prior to stimulus onset in normals, but is markedly reduced in amplitude in patients with CFS. However, all other sensory and cognitive brain potentials do not differ between normals and CFS. Reaction times are slower in CFS compared to normals. In the memory task, a slow negative shift associated with memory scanning is reduced in patients with CFS. For the fore-warned reaction time and self-paced movement tasks, no differences were found between the patients and normals. The finding of premovement related potential abnormalities in CFS supports the concept that central motor preparation and execution are impaired in CFS. In certain tasks, measures of neural processes related to sensory processing and attention are normal for these patients. Results from the memory task suggest that neural processes related to short-term memory are also altered in CFS.
Goudsmit E.		Chronic fatigue syndrome and depression	Br J Psychiatry 2000 Nov;177:470 Comment on: Br J Psychiatry. 2000 Jun;176:550-6.	
Green J, Romei J, Natelson BH.		Stigma and Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 5(2): 63	We predicted that the largely female population seeking relief from the incapacitating symptoms of chronic fatigue syndrome (CFS), an enigmatic illness, would feel stigmatized, and that attribution of CFS symptoms to psychological causes by physicians would contribute significantly to the CFS-related stigma. Most subjects scored high on measures of stigma: 95% had feelings of estrangement, 70% believed that others attributed their CFS symptoms to psychological causes, 77% coped by

				using an educational strategy (disclosure) and 39% saw a need to be secretive about their symptoms in some circumstances. Most subjects (77%) were labeled as `psychological cases' by one or more of the physicians (mean = 8) consulted, but of the 4 stigma measures, only disclosure was related to physician labeling. Such factors as duration of illness and unemployment, dissatisfaction with spouse, and symptom severity correlated significantly with measures of stigma. That many physicians were reportedly ignorant or skeptical of CFS (male more so than female M.D.'s) may influence attempts of CFS patients to legitimize their symptoms by disclosure and lead to high rates of health care system use.
Greenlee JE, Rose JW.	Neurology Service, Veterans Affairs Medical Center and Department of Neurology, University of Utah Health Science Center, Salt Lake City 84148-001, USA.	Controversies in neurological infectious diseases.	Semin Neurol 2000;20(3):375-86	The past several years have seen major advances in our understanding of neurological infectious diseases, their diagnosis, and their treatment. Along with these advances, however, new information about infectious agents and new therapeutic options have also introduced both uncertainty and controversy in the approach and management of patients with diseases of the central nervous system. Here, we discuss six such areas: the long-term efficacy of HAART therapy in treatment of HIV infection; the role of viral infection in chronic fatigue syndrome; Rasmussen's encephalitis as an infectious or autoimmune disease; the spectrum of neurological diseases caused by rickettsial infection; the role of Mycoplasma pneumoniae in human central nervous system disease; and the possible association of Chlamydia pneumoniae and human herpesvirus 6 with multiple sclerosis. Review, Academic
Grimaud J.	Service de Neurologie A, Hopital Neurologique et Neurochirurgical Pierre Wertheimer, Lyon.	[Relationship between fatigue in multiple sclerosis and the chronic fatigue syndrome].[article in French]	Rev Neurol (Paris) 2000 Nov;156(11):1044-5	
Hack AD.		Divalent Cations, Hormones, Psyche and Soma: Four Case Reports	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 117	Objectives: The steroid hormone, vitamin D and the peptide hormone, parathormone are reported to influence not only bone metabolism, but also other metabolic and nervous, cardiovascular and immune functions, and mood. Regular actions of these hormones depend highly on intracellular magnesium content. Although symptoms are recognized, they usually are not correlated to these hormones. Foregoing case studies have revealed that vitamin D and/or parathormone disorders are common causes of CFS-fibromyalgia like symptoms. Methods: Four patients with chronic fatigue-like symptoms and vitamin D (25OHD3) and parathormone (PTH intact) disorders are illustrated to demonstrate conflicting laboratory results. Patients were treated with 5,000 to 10,000 IU cholecalciferol, plus multiminerals and trace elements. Clinical outcome was assessed and treatment difficulties are reported. Results: Diagnostic pitfalls are shown. Vitamin D and parathormone disorders are not completely detectable by calcium and phosphate screening. In 2 of this 4

				demonstrated cases treatable diagnosis would have been missed without endocrinological screening. In the case of undetected long-standing disorder of these hormones, intracellular mineral derangement follows, thus inducing vitamin D resistance and parathormone ineffectiveness which makes therapy difficult. Combining vitamin D therapy with multiminerals possibly may overcome these obstacles. Conclusions: Vitamin D and parathormone disturbance should not be overlooked in chronic fatigue. Appropriate therapy is easy, inexpensive and harmless. Early diagnosis and treatment might be essential to avoid chronic fatigue syndrome. The complexity of diagnosis, therapy and scientific background may lead to a new understanding of ``psycho-somatic'' disease. The relation between intracellular minerals, trace elements, cellular energy supply and responsible hormones should become clearer.
Hadzi-Pavlovic D, Hickie IB, Wilson AJ, Davenport TA, Lloyd AR, Wakefield D.	Mood Disorders Unit, Prince of Wales Hospital, Randwick, NSW, Australia. D.Hadzi-Pavlovic@unsw.edu.au	Screening for prolonged fatigue syndromes: validation of the SOFA scale.	Soc Psychiatry Psychiatr Epidemiol 2000 Oct;35(10):471-9	BACKGROUND: The identification of syndromes characterised by persistent and disabling mental and/or physical fatigue is of renewed interest in psychiatric epidemiology. This report details the development of two specific instruments: the SOFA/CFS for identification of patients with chronic fatigue syndrome (CFS) in specialist clinics and the SOFA/GP for identification of prolonged fatigue syndromes (PFS) in community and primary care settings. METHODS: Patients with clinical diagnoses of CFS (n = 770) and consecutive attenders at primary care (n = 1593) completed various self-report questionnaires to assess severity of current fatigue-related symptoms and other common somatic and psychological symptoms. Quality receiver operating characteristic curves were used to derive appropriate cut-off scores for each of the instruments. Comparisons with other self-report measures of anxiety, depression and somatic distress are noted. Various multivariate statistical modelling techniques [latent class analysis (LCA), longitudinal LCA] were utilised to define the key features of PFS and describe its longitudinal characteristics. RESULTS: The SOFA/CFS instrument performs well in specialist samples likely to contain a high proportion of patients with CFS disorders. Cut-off scores of either 1/2 or 2/3 can be used, depending on whether the investigators wish to preferentially emphasise false-negatives or false-positives. Patients from these settings can be thought of as consisting not only of those with a large number of unexplained medical symptoms, but also those with rather specific musculoskeletal and pain syndromes. The SOFA/GP instrument has potential cut-off scores of 1/2 or 2/3, with the latter preferred as it actively excludes all non-PFS cases (sensitivity = 81%, specificity = 100%). Patients with these syndromes in the community represent broader sets of underlying classes, with the emergence of not only musculoskeletal and multisymptomatic disorders, but also persons characterised by significant cognitive subjective impairment. Twelve-month longitudinal analyses of the primary care sample indicated that the underlying class structure was preserved over time. Comparisons with other measures of psychopathology indicated the relative

				independence of these constructs from conventional notions of anxiety and depression. CONCLUSIONS: The SOFA/GP instrument (which is considerably modified from the SOFA/CFS in terms of anchor points for severity and chronicity) is preferred for screening in primary care and community settings. Patients with PFS and CFS present a range of psychopathology that differs in its underlying structure, cross-sectionally and longitudinally, from coventional notions of anxiety and depression.
Hannan KL, Berg DE, Baumzweiger W, Harrison HH, Berg LH, Ramirez R, Nichols D.	Osceola Hospital, Kissimmee, Orlando, Florida, USA.	Activation of the coagulation system in Gulf War Illness: a potential pathophysiologic link with chronic fatigue syndrome. A laboratory approach to diagnosis.	Blood Coagul Fibrinolysis 2000 Oct;11(7):673-8	Most symptoms of Gulf War Illness (GWI) are similar to Chronic Fatigue Syndrome (CFS) and/or Fibromyalgia (FM). We investigated whether these symptoms are associated with an activated coagulation system as has been reported in some cases of CFS/FM. The coagulation assays include activation markers of the cascade, platelet activation and hereditary risk factors. Our findings show activation of the coagulation system in GWI. This evidence of a hypercoagulable state suggests that symptoms may be due to poor blood flow and, therefore, a basis for the potential utility of anticoagulant therapy.
Hart B, Grace VM.	Department of Feminist Studies, University of Canterbury, Christchurch, New Zealand. blossom@expansive.co.nz	Fatigue in chronic fatigue syndrome: a discourse analysis of women's experiential narratives.	Health Care Women Int 2000 Apr-May;21(3):187-201	Chronic fatigue syndrome (CFS) is a debilitating condition. Approximately 75% of sufferers are women. The etiology of CFS is debated, but remains inconclusive. "Fatigue" is ill defined and conceptually problematic. The international multidisciplinary literature on CFS reveals a paucity of studies on women. Qualitative research to analyze women's discourses on CFS is virtually absent. Eleven New Zealand women of European descent with experience of CFS were interviewed in depth. Within the complex facets of CFS, this article reports specifically on an analysis of discourses on "fatigue." The predominant theme that emerged was that fatigue is articulated as "lack" or absence, which is not representable as an identifiable entity in biomedical terms. Parallels with chronic pain are briefly drawn. We conclude that approaches to CFS must respond to the diverse and complex constructions of the experience of fatigue evident in women's narratives.
Hazendonk KM, Crowe SF.	School of Psychological Science, La Trobe University, Bundoora, Victoria, Australia.	A neuropsychological study of the postpolio syndrome: support for depression without neuropsychological impairment.	Neuropsychiatry Neuropsychol Behav Neurol 2000 Apr;13(2):112-8	OBJECTIVE: This study aimed to examine cognitive functioning in postpolio syndrome (PPS) after controlling for the effects of depression and illness behavior. BACKGROUND: Few studies have investigated the possible cognitive sequelae of PPS, despite widespread documented subjective complaints of "mental fatigue." METHOD: A total of 23 PPS sufferers, 20 polio survivors without PPS, and 22 matched controls were compared using the Beck Depression Inventory-II; the Illness Behaviour Questionnaire; a chronic fatigue syndrome symptom checklist; and several measures of memory, attention, and concentration, including the Brown-Petersen Task, Stroop Test, Austin Maze, California Verbal Learning Test, Trail Making Test, Controlled Oral Word Association Test, and Symbol-Digit Modalities Test. RESULTS: In those participants with a medically confirmed diagnosis of PPS, there was a significantly higher level of depressive and hypochondriacal symptomatology as compared with the other two groups. Nevertheless, no significant differences existed between the three groups on neuropsychological measures. CONCLUSIONS: These results indicate

				that the attention and memory difficulties reported by PPS sufferers may be linked to the physical or psychological manifestations of the illness rather than to objective decrements in cognitive performance.
Heim C, Ehlert U, Hellhammer DH.	Center for Psychobiological and Psychosomatic Research, University of Trier, Germany.	The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders.	Psychoneuroendocrinology 2000 Jan;25(1):1-35	Representing a challenge for current concepts of stress research, a number of studies have now provided convincing evidence that the adrenal gland is hypoactive in some stress-related states. The phenomenon of hypocortisolism has mainly been described for patients, who experienced a traumatic event and subsequently developed post-traumatic stress disorder (PTSD). However, as presented in this review, hypocortisolism does not merely represent a specific correlate of PTSD, since similar findings have been reported for healthy individuals living under conditions of chronic stress as well as for patients with several bodily disorders. These include chronic fatigue syndrome, fibromyalgia, other somatoform disorders, rheumatoid arthritis, and asthma, and many of these disorders have been related to stress. Although hypocortisolism appears to be a frequent and widespread phenomenon, the nature of the underlying mechanisms and the homology of these mechanisms within and across clinical groups remain speculative. Potential mechanisms include dysregulations on several levels of the hypothalamic-pituitary adrenal axis. In addition, factors such as genetic vulnerability, previous stress experience, coping and personality styles may determine the manifestation of this neuroendocrine abnormality. Several authors proposed theoretical concepts on the development or physiological meaning of hypocortisolism. Based on the reviewed findings, we propose that a persistent lack of cortisol availability in traumatized or chronically stressed individuals may promote an increased vulnerability for the development of stress-related bodily disorders. This pathophysiological model may have important implications for the prevention, diagnosis and treatment of the classical psychosomatic disorders.
Hickie IB, Wilson AJ, Wright JM, Bennett BK, Wakefield D, Lloyd AR.	School of Psychiatry, University of New South Wales, Sydney, Australia. i.hickie@unsw.edu.au	A randomized, double-blind placebo-controlled trial of moclobemide in patients with chronic fatigue syndrome.	J Clin Psychiatry 2000 Sep;61(9):643-8	BACKGROUND: Chronic fatigue syndrome is characterized by prolonged and disabling fatigue and a range of neuropsychiatric symptoms including depressed and/or irritable mood. To date, no medical or psychotropic therapies have provided clear symptomatic benefit. METHOD: Ninety patients with chronic fatigue syndrome, diagnosed with our system that approximates CDC criteria, participated in a randomized, placebo-controlled, double-blind trial of 450 to 600 mg/day of moclobemide, a novel reversible inhibitor of monoamine oxidase-A. RESULTS: Fifty-one percent (24/47) of patients receiving moclobemide improved compared with 33% (14/43) of patients receiving placebo (odds ratio = 2.16, 95% confidence interval [CI] = 0.9 to 5.1). Drug response was best characterized symptomatically by an increase in the subjective sense of vigor and energy rather than a reduction in depressed mood. The effect of moclobemide on subjective energy was detectable within the first 2 weeks of treatment and increased across the course of the study. The greatest reduction in clinician-rated disability was in patients with concurrent

				immunologic dysfunction (mean difference in standardized units of improvement = 0.8, 95% CI = 0.03 to 1.6). CONCLUSION: Moclobemide produces some improvement in key symptoms experienced by patients with chronic fatigue syndrome. This effect is not dependent on the presence of concurrent psychological distress and is likely to be shared with other monoamine oxidase inhibitors.
Hoskin L, Clifton-Bligh P, Hansen R, Fulcher G, Gates F.	Department of Diabetes, Endocrinology, and Metabolic Medicine, Royal North Shore Hospital, St. Leonards, New South Wales, Australia. lhoskin@doh.health.nsw.gov.au	Bone density and body composition in young women with chronic fatigue syndrome.	Ann N Y Acad Sci 2000 May;904:625-7	
Huber M.	Institut und der Poliklinik fur Psychosomatik und Psychotherapie der Universitat zu Koln.	[Aspects of occupational disability in psychosomatic disorders].[article in German]	Versicherungsmedizin 2000 Jun 1;52(2):66-75	In 1997, 30% of the persons going into early retirement because of occupational disability and received pensions were psychosomatically ill. An additional large number of retirees suffered from untreatable pain such as chronic low back pain, some of them might as well have a chronic somatoform pain disorder. The article describes frequent psychosomatic diseases like somatization disorder, fibromyalgia and chronic fatigue syndrome with respect to their pathophysiology and psychological aspects as well as therapeutic advancements. It is postulated that an interdisciplinary access to these patients early in the course of their illness involving both somatic medical and psychiatric competence is the most promising means to tackle this enormous medical and health protection problem.
Hurwitz BE, Brownley KA, Fletcher MA, Klimas NG.		Chronic Fatigue Syndrome: Evidence Supporting the Hypothesis of a Behaviorally-Activated Neuromodulator of Fatigue	Journal of Chronic Fatigue Syndrome 2000; 6(2): 45	Chronic Fatigue Syndrome (CFS) is a disorder characterized by a prolonged, debilitating fatigue of unknown etiology. In addition, patients with CFS frequently report enhanced fatigue symptoms following even mild physical exertion, and their tolerance for physical exercise is limited relative to healthy individuals. The physiological mechanisms underlying the excessive fatigue and weakness common to this disorder remain an issue of scientific debate. Collectively, the available data suggest that fatigue in CFS is not due to any neuromuscular dysfunction, per se, but possibly is caused or influenced by some centrally acting mediator that is released during behavioral activities that require physical or mental exertion. In addition to persistent fatigue, there is growing evidence that many CFS patients exhibit alterations in hypothalamic-pituitary-adrenal (HPA) axis and autonomic function, including the inability to maintain the blood pressure response to orthostatic challenge. When an individual engages in mental or physical behavioral activation, there is a release of numerous centrally acting neuromodulators, some of which have been postulated to influence fatigue. This paper examines the evidence supporting a

				common pathway through which these centrally-mediated psychological and autonomic abnormalities may be linked. It is hypothesized that as a consequence of behavioral activation there is an abnormality in neuromodulator release or action in individuals with CFS, and that this abnormal neuromodulator activity results in increased fatigue. Furthermore, it is postulated that the CNS initiates a counter-regulatory mechanism to reduce the activity of those systems responsible for the production of the neuromodulator; and that the consequence of this counter-regulatory maneuver is the prevailing dysregulation of the autonomic and HPA axes and other dysfunctional cardiovascular and immunological sequelae.
Jadin CL.		Common Clinical and Biological Windows of CFS and Rickettsial Diseases	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 133	From 1991, links between CFS and Rickettsial Diseases were uncovered because of their similar clinical presentation. Further research linked them even more. Five Rickettsia strains, suspected to be the cause, or an important factor in CFS, were identified by means of the Giroud Micro-Agglutination test and were widely found to be positive in patients' serum, diagnosed as suffering from CFS, Fibromyalgia, Rheumatoid Arthritis, Multiple Sclerosis, Depression, Psychosis, Heart Diseases, and Auto-Immune Diseases. This finding leads us to submit those originally differently diagnosed patients to the same Tetracycline treatment. This proved to be a great success. The increasing number of patients gave us the opportunity to establish a biological checklist (regardless of the diversity of the pathology) of infections, organs' functions and auto-immune profile. We found the differences in positivity to depend on four factors: length of illness, virulence of germs, cohabitation of germs, and the state of the host immune system. These studies suggest that auto-immune diseases could have an infectious origin. Better knowledge and mastery of the co-factors would be determinant in speeding recovery. With this approach, CFS patients are being treated for the cause of their illness rather than symptomatically.
Jason LA, Fennell PA, Klein S, Fricano G, Halpert J.		An Investigation of the Different Phases of the CFS Illness	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 35	The present study examined the factor structure of the Fennell Phase Inventory, an instrument designed to measure the phases of the illness known as chronic fatigue syndrome. Four hundred participants were recruited and randomly assigned to two equally sized groups. A similar three-factor solution emerged for both samples, suggesting that three phases characterize this illness: a Crisis phase, a Stabilization phase, and an Integration phase. Factor scores on the Crisis Factor were significantly related to levels of fatigue and disability. The Fennell Phase Inventory appears to be a promising way of differentiating the different phases that are experienced by patients with CFS. The implications of these findings are discussed.
Jason LA, Fennell PA,Taylor RR, Fricano G, Halpert JA.		An Empirical Verification of the Fennell Phases of the CFS Illness	Journal of Chronic Fatigue Syndrome 2000; 6(1): 47	The Fennell Phase Inventory is an instrument designed to measure the phases typically experienced by individuals with chronic fatigue syndrome. In a previous study, a three-factor solution emerged. A cluster analysis was then conducted using the three mean scores for each individual, and four clusters emerged. These clusters matched the four phases predicted by Fennell. The Fennell Phase Inventory appears to be a promising way of differentiating the phases that are experienced by

				individuals with CFS.
Jason LA, Fricano G, Taylor RR, Halpert J, Fennell PA, Klein S, Levine S.	Department of Psychology, DePaul University, Chicago, IL 60614, USA. ljason@wppost.depaul.edu	Chronic fatigue syndrome: an examination of the phases.	J Clin Psychol 2000 Dec;56(12):1497-508	The present study examined the Fennell Phase Inventory, an instrument designed to measure the phases typically experienced by individuals with chronic fatigue syndrome (CFS). This inventory yields three factor scores of Crisis, Stabilization, and Integration. These factor scores have been employed in a cluster analysis, yielding four clusters that matched the four phases predicted by Fennell: Crisis, Stabilization, Resolution, and Integration. The present study represents a partial replication study of a prior investigation of the Fennell Phase Inventory by Jason et al. (in press), but that earlier study did not have an independent physician examination to diagnose patients with CFS. In the present study, 65 patients diagnosed with chronic fatigue syndrome by a physician were recruited and administered the Fennell Phase Inventory and other measures assessing CFS-related symptoms, disability, and coping. Each of the 65 patients was classified into one of four predefined clusters measuring a Crisis phase, a Stabilization phase, a Resolution phase, and an Integration phase. Relationships were explored between three of these cluster groupings and measures of symptoms, disability, and coping. Results confirmed Fennell's model, revealing significant differences between the three clusters in terms of levels of disability and modes of coping. Results suggest that the Fennell Phase Inventory accurately differentiates phases of adaptation to illness experienced by individuals with CFS.
Jason LA, King CP, Taylor RR, Kennedy C.		Defining Chronic Fatigue Syndrome: Methodological Challenges	Journal of Chronic Fatigue Syndrome 2000; 7(3): 17	Accurate diagnosis of Chronic Fatigue Syndrome (CFS) is greatly complicated by the vague wording of many of the major diagnostic criteria (i.e., substantial reductions in previous levels of occupational, educational, social, or personal activities) and the absence of guidelines for health care professionals to follow. The lack of operationally explicit criteria has forced health care professionals to rely heavily on their own clinical judgement, which may be biased by personal and highly idiosyncratic factors. Thus, in the case of CFS, the lack of consensus among clinicians regarding the interpretation and application of the diagnostic criteria has likely produced problems in diagnostic reliability. Data from a recent community based epidemiologic study are presented to illustrate these problems and provide recommendations for improving criterion reliability.
Jason LA, King CP, Richman JA, Taylor RR, Torres SR, Song S.		U.S. Case Definition of Chronic Fatigue Syndrome: Diagnostic and Theoretical Issues	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 3	In 1994, researchers from the U.S. Centers for Disease Control and Prevention developed a revised case definition of chronic fatigue syndrome (CFS) (1), a complex illness characterized by debilitating fatigue and a number of accompanying flu-like symptoms. Although Fukuda and associates intended to resolve complexities surrounding the classification of individuals with CFS stemming from previous definitional criteria (1), significant problems with the revised criteria endure. This article highlights reliability issues and other conceptual and operational difficulties inherent in the current U.S. definition of CFS (1). We employ case studies derived from a community-based epidemiological study of chronic fatigue syndrome (2) to

				illustrate examples of the potential for misclassification of individuals with CFS using the current U. S. criteria (1). Moreover, we suggest alternative approaches to classification and ways to operationalize specific concepts embedded in the current U.S. criteria (1).
Jason LA, Taylor RR, Kennedy CL, Jordan K, Song S, Johnson DE, Torres SR.	Department of Psychology, DePaul University, Chicago, Illinois 60614, USA.	Chronic fatigue syndrome: sociodemographic subtypes in a community-based sample.	Eval Health Prof 2000 Sep;23(3):243-63	Most chronic fatigue syndrome (CFS) studies are based on information about patients from primary or tertiary care settings. These patients might not be typical of patients in the general population. This investigation involved examinations of individuals with CFS from a community-based study. A random sample of 18,675 in Chicago was interviewed by telephone. Individuals with chronic fatigue and at least four minor symptoms associated with CFS were given medical and psychiatric examinations. A group of physicians then diagnosed individuals with CFS, who were then subclassified based on three sociodemographic categories--gender, ethnicity, and work status. Sociodemographic subgroups were analyzed in terms of symptom severity, functional disability, coping, optimism, perceived stress, and psychiatric comorbidity. Women, minorities, and nonworking individuals with CFS reported greater levels of functional disability, symptom severity, and poorer psychosocial functioning than men, Caucasians, and working individuals, suggesting sociodemographic characteristics may be associated with poorer outcomes in urban, community-based samples of CFS individuals.
Jason LA, Taylor RR, Kennedy CL, Song S, Johnson D, Torres S.	Department of Psychology, DePaul University, Chicago, Illinois 60614, USA.	Chronic fatigue syndrome: occupation, medical utilization, and subtypes in a community-based sample.	J Nerv Ment Dis 2000 Sep;188(9):568-76	Most studies of chronic fatigue syndrome (CFS) have been based on patients recruited from primary or tertiary care settings. Patients from such settings might not be typical of patients in the general population. The present investigation involved examining individuals with CFS from a community-based study. A random sample of 18,675 respondents in Chicago was first interviewed by telephone. A group of individuals with chronic fatigue accompanied by at least four minor symptoms associated with CFS were given medical and psychiatric examinations. From this sample, a physician review group diagnosed individuals with CFS. Those diagnosed with CFS were subclassified based on a variety of categories, including duration of illness, mode of illness onset, and presence or absence of a stressful life event directly preceding onset. In addition, we examined medical utilization among those diagnosed with CFS, as well as whether individuals with CFS were disproportionately represented in health care professions. Important differences emerged on measures of sociodemographics, symptoms, and functional disability. The implications of these findings and others are discussed.
Jason LA, Taylor RR, Kennedy CL.	Department of Psychology, DePaul University, Chicago 60614, IL, USA. ljason@wppost.depaul.edu	Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based	Psychosom Med 2000 Sep-Oct;62(5):655-63	OBJECTIVE: The aim of this study was to determine illness comorbidity rates for individuals with chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivities (MCS). An additional objective was to identify characteristics related to the severity of fatigue, disability, and psychiatric comorbidity in each of these illness groups. METHODS: A random sample of 18,675 residents in Chicago, Illinois, was first interviewed by telephone. A control group and a group of individuals

		sample of persons with chronic fatigue syndrome-like symptoms.		with chronic fatigue accompanied by at least four minor symptoms associated with CFS received medical and psychiatric examinations. RESULTS: Of the 32 individuals with CFS, 40.6% met criteria for MCS and 15.6% met criteria for FM. Individuals with MCS or more than one diagnosis reported more physical fatigue than those with no diagnosis. Individuals with more than one diagnosis also reported greater mental fatigue and were less likely to be working than those with no diagnosis. Individuals with CFS, MCS, FM, or more than one diagnosis reported greater disability than those with no diagnosis. CONCLUSIONS: Rates of coexisting disorders were lower than those reported in prior studies. Discrepancies may be in part attributable to differences in sampling procedures. People with CFS, MCS, or FM endure significant disability in terms of physical, occupational, and social functioning, and those with more than one of these diagnoses also report greater severity of physical and mental fatigue. The findings illustrate differences among the illness groups in the range of functional impairment experienced.
Jay SJ.		Tobacco use and chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder.	Arch Intern Med 2000 Aug 14-28;160(15):2398, 2401 Comment on: Arch Intern Med. 2000 Jan 24;160(2):221-7	
Jiaxu C, Weiyi Y.		Treatment of Chronic Fatigue Syndrome with Chinese Medicine	Journal of Chronic Fatigue Syndrome 2000; 5(1): 61	Chronic fatigue syndrome (CFS) is a severe, debilitating disorder, which prominently features self-reported impairments in concentration and short-term memory, and disturbances in sleep and emotions, all of which can affect any one and seriously affect quality of life. In 1987, the Centers for Disease Control and Prevention (CDC) defined CFS as persistent or relapsing fatigue, with at least 50% reduction of baseline activity level lasting for at least 6 months, as one of the main symptoms. Since its cause is still unknown, treatment of CFS has been palliative and has included usually orally administered products, such as vitamin B12, vitamin C, folic acid, iron, magnesium, essential fatty acids, coenzyme Q10 and nicotinamide adenine dinucleotide (NADH), among others. The latter therapeutic modalities can only relieve some symptoms to some extent, but cannot fundamentally eliminate fatigue. It is, therefore, urgent to seek safe and effective drugs for the treatment of fatigue. We propose here that regulating homeostasis and enhancing immunity are important for the treatment of fatigue. In China, many Chinese herbs with such functions have been proven effective, an observation which opens the possibility of a new therapeutic method of eliminating fatigue with traditional Chinese medicine (TCM).
Jordan KM, Ayers PM. Jahn SC, Taylor KK, Huang C-F, Richman J, Jason LA.		Prevalence of Fatigue and Chronic Fatigue Syndrome-Like Illness in Children and	Journal of Chronic Fatigue Syndrome 2000; 6(1): 3	A community-based screening of over 12,000 households was conducted in order to determine the prevalence of fatigue and CFS-like illness in a sample of 5 to 17 year olds. Results indicate that over 4% of the sample was fatigued and that 2. 05% were diagnosed with CFS-like illness. Adolescents had a slightly higher rate of CFS-like

		Adolescents		illness (2.91%) than did pre-pubescent children (1.96%). Those with CFS-like illness were almost evenly divided between male (47.5%) and female (52. 5%). Youngsters of Latino origin had the highest representation in the CFS-like group. Symptom data, family patterns, and other data are presented for both the CFS-like group and the entire sample.
Kahn MF.		Chronic fatigue syndrome. New developments.	Joint Bone Spine 2000;67(5):359-61	
Kaur G, Kulkarni SK.		Comparative Study of Antidepressants and Herbal Psychotropic Drugs in a Mouse Model of Chronic Fatigue	Journal of Chronic Fatigue Syndrome 2000; 6(2): 23	This study examined the effects and comparative efficacy of various antidepressants and herbal psychotropic drugs in a mouse model of chronic fatigue. Animals were subjected daily to forced swimming (Porsolt's forced swimming test) and the duration of the immobility period was recorded in 6-minute sessions on each day for 7 days. Chronic forced swimming resulted in significant increases in immobility time on day 7 as compared to day 1 in control mice. Pretreatment with imipramine (10 mg/kg, i.p.), desipramine (10 mg/kg, i.p.), tranylcypromine (10 mg/kg, i.p.), alprazolam (0.5 mg/kg, i.p.), fluoxetine (10 mg/kg, i.p.) and melatonin (10 mg/kg, i.p.) produced significant decreases in immobility time as compared to controls on each day. Similar decreases in immobility periods were observed with herbal psychotropic preparations-Withania somnifera root extract (100 mg/kg, p.o.), BR-16AR (200 mg/kg, p.o.), siotoneR granules (200 mg/kg, p.o.) and evening primrose oil (0.2 ml/20g, p.o.). However, trazodone and idazoxan failed to modify the immobility times on all the days. The present observations underscore the established use of antidepressants in providing symptomatic relief of fatigue in Chronic Fatigue Syndrome (CFS) patients and further reinforce the potential therapeutic usefulness of herbal psychotropic preparations in CFS patients.
Kavelaars A, Kuis W, Knook L, Sinnema G, Heijnen CJ.	Department of Pediatric Immunology, Wilhelmina Children's Hospital of the University Medical Center Utrecht, The Netherlands. a.kavelaars@wkz.azu.nl	Disturbed neuroendocrine-immune interactions in chronic fatigue syndrome.	J Clin Endocrinol Metab 2000 Feb;85(2):692-6	The present study was designed to investigate the interaction between neuroendocrine mediators and the immune system in chronic fatigue syndrome (CFS). We examined the sensitivity of the immune system to the glucocorticoid agonist dexamethasone and the beta2-adrenergic agonist terbutaline in 15 adolescent girls with CFS and 14 age- and sex-matched controls. Dexamethasone inhibits T-cell proliferation in healthy controls and in CFS patients. However, the maximal effect of dexamethasone on T-cell proliferation is significantly reduced in CFS patients as compared with controls. The beta2-adrenergic receptor agonist terbutaline inhibits tumor necrosis factor-alpha production and enhances interleukin-10 production by monocytes. Our data demonstrate that the capacity of a beta2-adrenergic agonist to regulate the production of these two cytokines is also reduced in CFS patients. We did not observe differences in baseline or CRH-induced cortisol and ACTH between CFS patients and controls. Baseline noradrenaline was similar in CFS and controls, whereas baseline adrenaline levels were significantly higher in CFS patients. We conclude that CFS is accompanied by a relative resistance of the

				immune system to regulation by the neuroendocrine system. Based on these data, we suggest CFS should be viewed as a disease of deficient neuroendocrine-immune communication.
Kerr JR, Cunniffe VS.	Departments of Medical Microbiology and Virology, Manchester Royal Infirmary, Oxford Road, Manchester M13 9WL, UK.	Antibodies to parvovirus B19 non-structural protein are associated with chronic but not acute arthritis following B19 infection.	Rheumatology (Oxford) 2000 Aug;39(8):903-8	OBJECTIVE: To determine the incidence and significance of antibodies to the parvovirus B19 non-structural (NS1) protein in B19-infected persons during acute infection and convalescence. METHODS: The B19 NS1 protein was expressed in SF9 cells using the baculovirus expression system and was used to prepare immunofluorescence slides. These were used in a fluorescent antibody test to determine anti-B19 NS1 IgG in a well-characterized cohort of 53 persons at the time of acute B19 infection and again after a follow-up period of 26-85 months. Results were examined for statistical significance by the use of Fisher's exact test. RESULTS: NS1 antibodies were detected in five of 32 persons with acute B19 infection (four with arthritis) and 10 of 53 persons with past B19 infection (six with chronic arthritis and two with chronic arthritis and chronic fatigue syndrome). Regarding the correlation of NS1 antibodies and arthritis, at the time of acute infection four of 24 persons with arthritis had NS1 antibodies detected compared with one of eight persons with any other symptoms (P: = 1). During convalescence, eight of 20 persons with chronic arthritis had NS1 antibodies compared with two of 33 with symptoms of any other category (all except one were asymptomatic) (P: = 0.007). All 10 patients with NS1 antibodies during convalescence had arthritis during acute infection, which persisted in eight persons until the time of follow-up. CONCLUSION: Antibodies to parvovirus B19 NS1 protein are associated with chronic but not with acute arthritis after B19 infection.
Klimas N, Wallace M.		Toward optimal health: the experts discuss chronic fatigue syndrome: interview by Jodi Godfrey Meisler.	J Womens Health Gend Based Med 2000 Jun;9(5):477-82	
Knook L, Kavelaars A, Sinnema G, Kuis W, Heijnen CJ.	Department of Pediatric Immunology, Wilhelmina Children Hospital of the University Medical Center Utrecht, The Netherlands.	High nocturnal melatonin in adolescents with chronic fatigue syndrome.	J Clin Endocrinol Metab 2000 Oct;85(10):3690-2	Decreased quality of sleep is frequently reported by chronic fatigue syndrome (CFS) patients. The pineal hormone melatonin is involved in regulation of sleep. We analyzed the nocturnal rise in melatonin in 13 adolescent CFS patients and 15 healthy age-matched controls. Saliva samples were collected at hourly intervals between 1700 and 0200 h. Nocturnal saliva melatonin levels were significantly higher in CFS patients, compared with controls, at midnight, 0100 h, and 0200 h ($P < 0.001$). No differences were observed in timing of melatonin increase in saliva between patients and controls. Time of sleep onset and duration of sleep did not differ significantly between patients and controls. However, all CFS patients and only one of the controls in our study group reported unrefreshing sleep. Our data demonstrate that sleep problems in adolescents with CFS are associated with increased melatonin levels during the first part of the night. Based on these data, we suggest that there is

				no indication for melatonin supplementation in adolescents with CFS.
Komaroff AL. Editorial		The biology of chronic fatigue syndrome.	Am J Med 2000 Feb;108(2):169-71Comment in: Am J Med. 2000 Aug 15;109(3):257-9 Comment on: Am J Med. 2000 Feb;108(2):99-105	
Korszun A, Young EA, Engleberg NC, Masterson L, Dawson EC, Spindler K, McClure LA, Brown MB, Crofford LJ.	Department of Psychological Medicine, University of Wales College of Medicine, Cardiff, UK. akorszun@umich.edu	Follicular phase hypothalamic-pituitary-gonadal axis function in women with fibromyalgia and chronic fatigue syndrome.	J Rheumatol 2000 Jun;27(6):1526-30	OBJECTIVE: Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are clinically overlapping stress associated disorders. Neuroendocrine perturbations have been noted in both syndromes, and they are more common in women, suggesting abnormalities of gonadal steroid hormones. We tested the hypothesis that women with FM and CFS manifest abnormalities of the hypothalamic-pituitary-gonadal (HPG) hormonal axis. METHODS: We examined the secretory characteristics of estradiol, progesterone, follicle stimulating hormone (FSH), and luteinizing hormone (LH), including a detailed analysis of LH in premenopausal women with FM (n = 9) or CFS (n = 8) during the follicular phase of the menstrual cycle compared to matched healthy controls. Blood was collected from an indwelling intravenous catheter every 10 min. over a 12 h period. LH was assayed from every sample; pulses of LH were identified by a pulse-detection program. FSH and progesterone were assayed from a pool of hourly samples for the 12 h period and estradiol from samples pooled over four 3 h time periods. RESULTS: There were no significant differences in FSH, progesterone, or estradiol levels in patients versus controls. There were no significant differences in pulsatile secretion of LH. CONCLUSION: There is no indication of abnormal gonadotropin secretion or gonadal steroid levels in this small, but systematic, study of HPG axis function in patients with FM and CFS.
Korszun A.	Department of Psychological Medicine, University of Wales College of Medicine, Heath Park Cardiff CF4 4XN, UK. akorszun@umich.edu	Sleep and circadian rhythm disorders in fibromyalgia.	Curr Rheumatol Rep 2000 Apr;2(2):124-30	Fibromyalgia (FM) is a syndrome of generalized muscle pain that is also associated with equally distressing symptoms of sleep disturbance and fatigue. FM shows clinical overlap with other stress-associated disorders, including chronic fatigue syndrome (CFS) and depression. All of these conditions have the features of disrupted sleep patterns and dysregulated biologic circadian rhythms, such as stress hormone secretion. This review focuses on the role of sleep and circadian rhythm disorders in FM and, in the absence of any specific treatment for FM, presents a pragmatic therapeutic approach aimed at identifying and treating comorbid sleep and depressive disorders, optimizing sleep habits, and judicious use of pharmacologic agents.
Kuratsune H.	Department of Hematology and Oncology, Osaka	[Chronic fatigue syndrome].[article in Japanese]	Ryoikibetsu Shokogun Shirizu 2000;(32):531-4	

	University Graduate School of Medicine.			
Lane R.	Division of Clinical Neurosciences and Psychological Medicine Imperial College School of Medicine London UK r.lane@ic.ac.uk.	Chronic fatigue syndrome: is it physical?	West J Med 2000 Dec;173(6):416-7	
Lane R. Editorial		Chronic fatigue syndrome: is it physical	J Neurol Neurosurg Psychiatry 2000 Sep;69(3):289 Comment on: J Neurol Neurosurg Psychiatry. 2000 Sep;69(3):302-7?	
Lawrie SM, MacHale SM, Cavanagh JT, O'Carroll RE, Goodwin GM.	Department of Psychiatry, University of Edinburgh.	The difference in patterns of motor and cognitive function in chronic fatigue syndrome and severe depressive illness.	Psychol Med 2000 Mar;30(2):433-42	BACKGROUND: Chronic fatigue syndrome (CFS) and major depressive disorder (MDD) share many symptoms and aetiological factors but may have different neurobiological underpinnings. We wished to determine the profile of the biological variables disturbed in CFS and MDD, and identify any critical factors that differentiate the disorders. METHODS: Thirty patients with CFS, 20 with MDD and 15 healthy controls matched group-wise for age and sex were recruited. Subjects were given a detailed battery of motor and cognitive tests, including measures of psychomotor speed, memory and maximal voluntary muscle contraction in both the morning and evening that were balanced to avoid order effects. RESULTS: CFS patients generally performed worse on cognitive tests than healthy controls, but better than patients with MDD. Both patient groups had markedly impaired motor function compared with healthy controls. MDD subjects showed a significantly greater diurnal improvement in maximal voluntary contraction than healthy controls. CONCLUSIONS: Patients with CFS and MDD show similarly substantial motor impairment, but cognitive deficits are generally more marked in MDD. Diurnal changes in some functions in MDD may differentiate the disorder from CFS.
Laylander JA.		A Nutrient/Toxin Interaction Theory of the Etiology and Pathogenesis of Chronic Pain-Fatigue Syndromes: Part I	Journal of Chronic Fatigue Syndrome 2000; 5(1): 67	Recent research suggests that Chronic Fatigue Syndrome (CFS), Fibromyalgia Syndrome (FMS), and Persian Gulf Syndrome (PGS) may represent the effects of dysfunctions involving the central and/or peripheral nervous system, neuroendocrine system, neuromuscular system, immune system, metabolism, or sleep patterns. Each systemic dysfunction is accepted here as being central to these syndromes but not causal. This two-part review introduces the theory that the syndromes listed above represent finitely variable combinations of multiple systemic dysfunctions which all share a common underlying etiology at the subcellular level: magnesium deficiency plus concomitant fluoride excess (MDFE). The theory is introduced in Part I; detailed evidence which supports the theory is presented in Part II. Treatment suggestions are

				listed at the end of Part II through a call for clinical trials to test this theory.
Laylander JA.		A Nutrient/Toxin Interaction Theory of the Etiology and Pathogenesis of Chronic Pain-Fatigue Syndromes: Part II	Journal of Chronic Fatigue Syndrome 2000; 5(1): 93	This second part of the review paper covers the evidence in favor of the theory which proposes that Chronic Fatigue Syndrome, Fibromyalgia Syndrome, and Persian Gulf Syndrome represent finitely variable combinations of multiple systemic dysfunctions which share a common underlying etiology at the subcellular level: magnesium deficiency plus concomitant fluoride excess (MDFE). Treatment suggestions are listed at the end of the manuscript through a call for clinical trials to test the theory presented.
Le Bon O, Hoffmann G, Murphy J, De Meirleir K, Cluydts R, Pelc I.	Brugmann University Hospital, Brussels 1020, Belgium. lebono@resulb.ulb.ac.be	How significant are primary sleep disorders and sleepiness in the chronic fatigue syndrome?	Sleep Res Online 2000;3(2):43-8	In order to study both the prevalence of Primary Sleep Disorders (PSD) and sleepiness, and their association to the Chronic Fatigue Syndrome (CFS), 46 unselected outpatients (34 women, mean age 36.5) were examined clinically and underwent two nights of all-night polysomnography and multiple sleep latency tests (MSLT). Forty-six percent presented with a Sleep Apnea/Hypopnea Syndrome Index (AHI>=5), 5% with a Periodic Limb Movements syndrome. No subject received a diagnosis of Narcolepsy or Idiopathic Hypersomnia. Thirty percent showed the presence of objective sleepiness as measured by MSLT<10 minutes. Objective and subjective measures of sleepiness were not associated with CFS, nor with the double diagnosis of CFS and a PSD. The presence of PSD or sleepiness was not associated with any of the clinical scales that were used to measure anxiety, depression, somatisation, physical or mental fatigue, or functional status impairment. Fifty-four percent of CFS patients had no PSD, and 69% no sleepiness. These patients could not be distinguished clinically from patients having a PSD or from those with sleepiness. Therefore, it is unlikely that CFS is simply a somatic expression of any PSD observed in our sample or of sleepiness per se.
Lee S, Yu H, Wing Y, Chan C, Lee AM, Lee DT, Chen C, Lin K, Weiss MG.	Department of Psychiatry, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin. singlee@cuhk.edu.hk	Psychiatric morbidity and illness experience of primary care patients with chronic fatigue in Hong Kong.	Am J Psychiatry 2000 Mar;157(3):380-4	OBJECTIVE: The authors' goal was to examine the prevalence and experience of psychiatric morbidity among primary care patients with chronic fatigue in Hong Kong. METHOD: One hundred adult patients with medically unexplained fatigue for 6 or more months were assessed with the Explanatory Model Interview Catalogue, psychopathological rating scales, and an enhanced version of the Structured Clinical Interview for DSM-III-R. RESULTS: The lifetime prevalence of DSM-III-R depressive and anxiety disorders was 54%. Current depressive and anxiety disorders were identified in 28 patients, who exhibited more psychopathology and functional impairment than other patients. Thirty-three patients had somatoform pain disorder, and 30 had undifferentiated somatoform disorder, but most of them could also be diagnosed as having shenjing shuairuo (weakness of nerves) and, to a lesser extent, ICD-10 neurasthenia. Chronic fatigue syndrome diagnosed according to the 1988 Centers for Disease Control criteria was rare (3%) and atypical. Generally, patients mentioned fatigue if asked, but pains (36%), insomnia (20%), and worries (13%) were the most troublesome symptoms. Most patients attributed illness onset to psychosocial sources. CONCLUSIONS: Psychiatric morbidity was common among primary care

				patients with chronic fatigue. Subthreshold psychiatric morbidity was very common and was more validly represented by the disease construct of shenjing shuairuo or neurasthenia than somatoform disorder.
Leonhardt T.	Medicinkliniken i Vanersborg-Trollhattan.	[Chronic fatigue syndrome--old wine in new bottles].[article in Swedish]	Lakartidningen 2000 Jan 19;97(3):182-4	
Levine PH, Clauw DJ, Claman HC, Robertson AD, Ketch L.		Silicone Breast Implants, Chronic Fatigue Syndrome and Fibromyalgia	Journal of Chronic Fatigue Syndrome 2000; 7(1): 53	Clinical studies have continued to suggest a relationship between silicone breast implants and chronic fatigue syndrome. Extensive epidemiologic studies, however, indicate that such a relationship is likely to be by chance and the successful lawsuits against producers of silicone breast implants are based on factors other than scientific proof. We present several perspectives on this issue which are probably relevant to other reports of putative etiologic agents for chronic fatigue syndrome.
Levine PH, Pilkington D, Strickland P, Peterson D.		Chronic Fatigue Syndrome and Cancer	Journal of Chronic Fatigue Syndrome 2000; 7(1): 29	Several studies have indicated a link between chronic fatigue syndrome (CFS) and cancer, most of them based on anecdotal observations. We have attempted to use more population-based data to determine if the reported relationship is meaningful. Two outbreaks of a fatiguing illness which included well documented cases of CFS were evaluated ten years after the reported outbreak for long-term effects, particularly cancer. We found an unusual pattern of cancer which, in view of an increased incidence of brain tumors and non-Hodgkin's lymphoma (NHL) reported in other studies involving CFS, indicates the need for further study. At the present time this link, which is often presumed to be due to immune dysfunction, has not yet been documented. Not all CFS patients have apparent dysregulation of the immune system and a single causative agent is highly unlikely, making the study of two heterogeneous illnesses, CFS and cancer, highly problematic. With the continuing focus on subgroups, however, this area of research may prove to be more productive.
Levine S.		Borna Disease Virus Proteins in Patients with CFS	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 199	Bornavirus is a member of a newly recognized virus family, Bornaviridae, and is neurotropic for a wide range of animal species, including birds, rodents, horses, and humans. Although little is known about its mode of transmission and it has not been clearly linked to any human disease, an association between bornaviruses and neuropsychiatric disorders has been suggested. Several researchers have also isolated this organism from patients who meet the clinical criteria for the Chronic Fatigue Syndrome (CFS). However, due to non-standardization of assay protocols, lack of a large study population and the possibility of contamination in certain laboratory settings, the true prevalence of Bornaviral proteins and their possible role in the pathogenesis of at least a subgroup of CFS patients remains undefined. We analyzed the serum immune reactivity to Borna Disease Virus (BDV) in 77 CFS patients and in 33 healthy normal controls using an ELISA based assay of 3 different recombinant BDV proteins. Of the 6 samples that displayed immunoreactivity to 2 or

				more BDV proteins, S were from patients (83.3%). Two samples, both from CFS patients, displayed immunoreactivity to 3 BDV proteins.
Lindberg NE, Lindberg E.		[Use available knowledge--also when it is not complete. Current example: chronic fatigue syndrome, fibromyalgia].[Article in Swedish]	Lakartidningen 2000 May 24;97(21):2651-2	
Lloyd AR, Hickie IB, Loblay RH.		Illness or disease? The case of chronic fatigue syndrome.	Med J Aust 2000 May 15;172(10):471-2	
Lofqvist AH.		Functional Somatic Syndromes-A Matter of Stress Response Patterns?	Journal of Chronic Fatigue Syndrome 2000; 7(2): 75	This hypothesis deals with reactions described in functional somatic syndromes and postulates that these reactions be described in terms of active/passive and external/internal. The reflex character of these reactions explain the variation in symptom intensity which in turn is projected to doctors as feelings of lacking understanding, especially when disease parameters are normal.
Loganovsky KN.		Vegetative-Vascular Dystonia and Osteoalgetic Syndrome or Chronic Fatigue Syndrome as a Characteristic After-Effect of Radioecological Disaster: The Chernobyl Accident Experience	Journal of Chronic Fatigue Syndrome 2000; 7(3): 3	The aim of this study was to determine whether the Chronic Fatigue Syndrome (CFS) definition could be applicable to the assessment of the medical aftermath of radioecological disasters and to investigate a possible psychophysiological basis of fatigue in Chernobyl accident survivors. One hundred randomly selected clean-up workers of the Chernobyl accident who presented with complains of fatigue were examined neuropsychiatrically using MMPI profiles, Quantitative Electroencephalography (QEEG) and Somatosensory evoked potentials (SSEP). Twenty-six percent of them met the CFS diagnostic criteria. Their absorbed radiation doses were less than 0.3 Sv, an exposure level that is not expected to produce a clear deterministic radiation effect. Clinical symptomatology included persistent fatigue, odd skin sensations, bizarre feelings in bones, muscles and joints, irritability, headache, vertigo, pain in the chest area, emotional lability, irritability, lack of concentration and memory, cognitive deterioration, depression signs and sleep disorders. Liquidators with CFS had the characteristic MMPI profile with increased hypochondria, depression, clear hypochondria, schizophrenia, hysteria, psychasthenia, and bizarre sensory perception scales. Spectral analysis of QEEG showed lateralised (left-sided) increase of q-power ($P < 0.001$) and lateralised (left-sided) decrease of a-power ($P < 0.001$) and lateralised (left-sided) increase of b-power ($P < 0.01$). SSEP were characterized by increased latencies and decreased amplitudes. SSEP significantly differed by topographic abnormalities in the left temporoparietal area in liquidators with CFS. Associations between schizophrenia-like, hypochondriac and psychasthenic psychopathology and an increase of latency of

				SSEP P300 and N400 in liquidators with CFS were revealed. Thus, ``Vegetative-Vascular Dystonia'' and ``Osteoalgetic Syndrome'' cases following exposure to ionizing radiation as a result of the Chernobyl accident can be classified as CFS cases. The psychophysiological basis of fatigue in liquidators consists of dysfunction of the cortico-limbical structures of the left, dominating, hemisphere. CFS is one of the most important consequences of radioecological disaster, which results from an interaction of different hazardous environmental factors.
MacHale SM, Lawrie SM, Cavanagh JT, Glabus MF, Murray CL, Goodwin GM, Ebmeier KP.	University Department of Psychiatry, Royal Edinburgh Hospital.		192: Br J Psychiatry 2000 Jun;176:550-6Comment in: Br J Psychiatry. 2000 Nov;177:470 Cerebral perfusion in chronic fatigue syndrome and depression.	BACKGROUND: Patients with chronic fatigue syndrome (CFS) and depressive illness share many, but not all, features. AIMS: To test the hypothesis that patients with CFS have abnormal cerebral perfusion, that differs from that in patients with depressive illness. METHOD: We recruited 30 patients with CFS who were not depressed, 12 depressed patients and 15 healthy volunteers. Regional cerebral perfusion at rest was assessed using region of interest (ROI) and voxel-based statistical parametric mapping (SPM) techniques. RESULTS: On SPM analysis there was increased perfusion in the right thalamus, pallidum and putamen in patients with CFS and in those with depressive illness. CFS patients also had increased perfusion in the left thalamus. Depressed patients differed from those with CFS in having relatively less perfusion of the left prefrontal cortex. The results were similar on ROI analysis. CONCLUSIONS: Abnormal cerebral perfusion patterns in CFS subjects who are not depressed are similar but not identical to those in patients with depressive illness. Thalamic overactivity may be a correlate of increased attention to activity in CFS and depression; reduced prefrontal perfusion in depression may be associated with the greater neuropsychological deficits in that disorder.
Mahowald ML, Mahowald MW.	Department of Medicine, Minneapolis Veteran's Administration Medical Center, University of Minnesota Medical School, MN, Minneapolis, USA	Nighttime sleep and daytime functioning (sleepiness and fatigue) in less well-defined chronic rheumatic diseases with particular reference to the 'alpha-delta NREM sleep anomaly'	1389-9457 2000 Jul 1;1(3):195-207	For the past 25 years, the 'alpha-delta NREM sleep abnormality' has been used by some as a defining or legitimizing marker for poorly defined rheumatic diseases such as fibromyalgia and chronic fatigue syndrome. Comprehensive review of the literature reveals no support for such a conclusion. Most studies involve small numbers of patients. The lack of control subjects, non-standardized recording techniques, and confusion between tonic and phasic alpha frequency activity patterns make comparison difficult. There is much evidence that this sleep EEG pattern is not only non-specific, but may actually reflect a sleep maintaining process. The 'sleep fragmentation' theory of the complaint of non-restorative sleep in this patient population is invalidated by the fact that conditions characterized by severe sleep fragmentation, such as obstructive sleep apnea, are not associated with musculoskeletal symtoms. It is difficult to attribute musculoskeletal symptoms to disorders of sleep in view of the fact that the only organ of the body known to benefit from sleep, or to be adversely affected by lack of sleep, is the brain. It is concluded that fibromyalgia and chronic fatigue syndrome are associated with subjective sleep complaints, but do not represent sleep disorders.
Manu P. Editorial		Chronic fatigue	Am J Med 2000	

Review Review, Tutorial		syndrome: the fundamentals still apply	Feb;108(2):172-3Comment in: Am J Med. 2000 Aug 15;109(3):257-9 and Am J Med. 2000 Feb;108(2):99-105.	
Manuel y Keenoy B, Moorkens G, Vertommen J, Noe M, Neve J, De Leeuw I.	Laboratory of Endocrinology, University of Antwerp, Belgium.	Magnesium status and parameters of the oxidant-antioxidant balance in patients with chronic fatigue: effects of supplementation with magnesium.	J Am Coll Nutr 2000 Jun;19(3):374-82	OBJECTIVE: Magnesium deficiency and oxidative stress have both been identified as pathogenic factors in aging and in several age-related diseases. The link between these two factors is unclear in humans although, in experimental animals, severe Mg deficiency has been shown to lead to increased oxidative stress. METHODS: The relationship between Mg body stores, dietary intakes and supplements on the one hand and parameters of the oxidant-antioxidant balance on the other was investigated in human subjects. RESULTS: The study population consisted of 93 patients with unexplained chronic fatigue (median age 38 years, 25% male, 16% smokers and 54% with Chronic Fatigue Syndrome (CFS). Mg deficient patients (47%) had lower total antioxidant capacity in plasma (p=0.007) which was related to serum albumin. Mg deficient patients whose Mg body stores did not improve after oral supplementation with Mg (10 mg/kg/day) had persistently lower blood glutathione levels (p=0.003). In vitro production of thiobarbituric acid reactive substances (TBARS) by non-HDL lipoproteins incubated with copper was related to serum cholesterol (p<0.001) but not to Mg or antioxidants and did not improve after Mg supplementation. In contrast, velocity of formation of fluorescent products of peroxidation (slope) correlated with serum vitamin E (p<0.001), which was, in turn, related to Mg dietary intakes. Both slope and serum vitamin E improved after Mg supplementation (p<0.001). CONCLUSIONS: These results show that the lower antioxidant capacity found in moderate Mg deficiency was not due to a deficit in Mg dietary intakes and was not accompanied by increased lipid susceptibility to in vitro peroxidation. Nevertheless, Mg supplementation was followed by an improvement in Mg body stores, in serum vitamin E and its interrelated stage of lipid peroxidation.
Maquet D, Croisier JL, Crielaard JM.	Universite de Liege, Medecine de l'Appareil Locomoteur.	[Fibromyalgia in the year 2000].[article in French]	Rev Med Liege 2000 Nov;55(11):991-7	Musculoskeletal pain is common in the population. Several pathologies like fibromyalgia (FM), chronic fatigue syndrome (CFS) or spasmophilia are associated with functional myalgia. The etiology of FM remains elusive, but the diagnosis is well established. The criteria for the classification are widespread pain combined with tenderness at 11 or more of the 18 specific tender points sites. The prevalence is 2% in the general population. This article reviews recent data on the pathophysiology and treatment of FM.
Martinsen EW.	Psykiatrisk klinikk, Sentralsjukehuset i Sogn og Fjordane, Forde.	[Physical activity for mental health].[article in Norwegian]	Tidsskr Nor Laegeforen 2000 Oct 20;120(25):3054-6	BACKGROUND: About 50% of the population will be affected by a mental disorder during their lifetime; the most common forms are mood and anxiety disorders and abuse of or dependence on drugs or alcohol. The standard forms of therapy are medication and various forms of psychotherapy. The cost of treating disease is

	egilwm@online.no			escalating, and the health care system will never be able to meet the need for treatment in this large group of patients. Hence, development of effective self help strategies is important. MATERIAL AND METHODS: In this paper, the scientific basis for promoting exercise as treatment for mental disorders is evaluated on the basis of a review of the literature. RESULTS: Beneficial psychological effects of exercise are best documented for mild to moderate forms of unipolar depression and chronic fatigue syndrome; in these disorders, exercise is an alternative to traditional forms of treatment. A therapeutic effect may also be achieved in panic and generalised anxiety disorder, schizophrenia, conversion and somatoform pain disorder, and alcohol abuse and dependence. INTERPRETATION: Beneficial effects of exercise are well documented. A simple and inexpensive approach like exercise is helpful and might be important for public health.
McGregor NR, Niblett S, Clifton Bligh P, Dunstan RH, Fulcher G, Hoskin L, Butt HL, Roberts TK,King K, Klineberg I.		The Biochemistry of Chronic Pain and Fatigue	Journal of Chronic Fatigue Syndrome 2000; 7(1): 3	Background: Chronic pain and fatigue represent major reasons for seeking medical treatments, however, the mechanisms are poorly understood. Onset of these disorders has been associated with events (infections, trauma, stress) which initiate a host response requiring increased energy demands. Objectives: To investigate the biochemical mechanisms of chronic pain and fatigue. Methods: Data will be presented from 4 separate investigations of CFS and myofascial pain syndrome (MFPS) patients, and from age/sex-matched controls, using metabolite profiling techniques. Results: Several types of chronic pain and fatigue disorders were discerned on the basis of their biochemistry. The metabolic events associated with chronic pain were distinct from those associated with chronic fatigue. The investigations have shown that chronic pain was associated with reductions in serum sodium, changes in urinary volume and output of amino and organic acids, increases in levels of markers of tissue damage (ALT, AST), and increases in the tyrosine: leucine ratio, which represents alterations in protein turnover. Fatigue was associated with alterations in urine excretion of amino and organic acids associated with tricarboxylic acid cycle (TCA) function. Levels of RNase-L were correlated with the expression of chronic fatigue related symptoms and were a good marker for CFS. Increased carriage of toxin-producing coagulase negative staphylococci was evident in MFPS and CFS patients, and this carriage was correlated with increased tyrosine: leucine ratios and pain severity. The toxin producing staphylococci appear to be a co-morbid pathogen that contributes to CFS patient morbidity. Conclusion: These studies indicated that changes in nitrogen homeostasis were associated with pain and fatigue symptoms and carriage of certain pathogens may sustain or exaggerate the chronic disorder.
McKenzie R, Reynolds JC, O'Fallon A, Dale J, Deloria M, Blackwelder W, Straus	Division of Microbiology and Infectious Diseases, National Institute of	Decreased bone mineral density during low dose glucocorticoid	J Rheumatol 2000 Sep;27(9):2222-6	OBJECTIVE: While osteoporosis and bone fractures are clearly recognized side effects of high dose glucocorticoids, the effect of low dose glucocorticoids remains controversial. We investigated the effect of 3 months of low dose hydrocortisone on bone mineral density (BMD). METHODS: Subjects, 18 to 55 years old with chronic

SE.	Allergy and Infectious Diseases, National Institute of Health, Bethesda, Maryland , USA.	administration in a randomized, placebo controlled trial.		fatigue syndrome and no medical or psychiatric illness requiring medication, were randomized in a double blind, placebo controlled trial to receive oral hydrocortisone, 13 mg/m2 body surface area every morning and 3 mg/m2 every afternoon (25 to 35 mg/day, equivalent to about 7.5 mg prednisone/day) or placebo for 12 weeks. Before and after treatment BMD of the lumbar spine was measured by dual energy x-ray absorptiometry. RESULTS: We studied 23 subjects (19 women, 4 men). For the 11 hydrocortisone recipients there was a mean decrease in BMD: mean change from baseline of the lateral spine was -2.0% (95% CI -3.5 to -0.6. p = 0.03) and mean change of the anteroposterior spine was -0.8% (95% CI -1.5 to -0.1, p = 0.06). Corresponding changes for the 12 placebo recipients were +1.0% (95% CI -1.0 to 3.0, p = 0.34) and +0.2% (95% CI -1.4 to 1.5, p = 0.76). CONCLUSION: A 12 week course of low dose glucocorticoids given to ambulatory subjects with chronic fatigue syndrome was associated with a decrease in BMD of the lumbar spine. This decrease was statistically significant in lateral spine measurements and nearly so in anteroposterior spine measurements.
Merz S.	write.me@mail.bip.net	[Chronic fatigue syndrome. Different definitions are confusing].[article in Swedish]	Lakartidningen 2000 Aug 23;97(34):3642-4	
Moorkens G, Berwaerts J, Wynants H, Abs R.	Departments of Internal Medicine; Endocrinology, University Hospital Antwerp, Belgium.	Characterization of pituitary function with emphasis on GH secretion in the chronic fatigue syndrome.	Clin Endocrinol (Oxf) 2000 Jul;53(1):99-106	OBJECTIVE: Previous studies have revealed that hormonal disturbances may accompany the chronic fatigue syndrome (CFS). Changes in the secretion of the pituitary-adrenal axis have been demonstrated, as well as abnormalities in the GH-IGF-I axis. However, data have not always been well characterized and were sometimes conflicting. The small number of CFS patients investigated in earlier studies may have played a role in the interpretation of the results. SUBJECTS AND DESIGN: Hormonal testing was performed in 73 nonobese CFS patients and nonobese 21 age-and gender-matched healthy controls. We investigated GH, ACTH and cortisol responses to insulin-induced hypoglycaemia. In a subgroup of patients arginine and clonidine stimulation for GH was also performed. Nocturnal secretion of GH, ACTH and cortisol were determined. Serum levels of IGF-I, prolactin, TSH, and free thyroxine were also measured. Visceral fat mass was assessed by CT scanning. RESULTS: GH response to insulin induced hypoglycaemia assessed by peak value (17.0 +/- 13.1 microg/l vs. 22. 1 +/- 9.8 microg/l; P = 0.01) and by AUC (450.0 +/- 361.3 microg/l vs. 672.3 +/- 393.0 microg/l; P = 0.002) was significantly decreased in CFS patients vs. controls. Nocturnal GH secretion assessed by GH peak value (5.4 +/- 3.7 vs. 9.0 +/- 5.1 microg/l; P = 0.44) and by AUC (34.4 +/- 20.2 vs. 67.4 +/- 43.1; P = 0.045) was also significantly impaired in CFS patients. Arginine and clonidine administration showed no differences in GH secretion between CFS patients and controls. In the CFS group, GH peak values were significantly higher after ITT than

				after arginine (P = 0.017) or clonidine (P = 0.001). No differences in serum IGF-I levels were found between CFS patients and controls. Except for a significantly lower nocturnal cortisol peak value, no differences were found in ACTH and cortisol secretion between CFS patients and controls. Significantly higher serum prolactin levels (7.4 +/- 4.7 microg/l vs. 4.4 +/- 1.3 microg/l; P = 0.004) and significantly higher serum TSH levels (1.6 +/- 1.0 mU/l vs. 1.0 +/- 0.4 mU/l; P = 0.011) were found in CFS patients. Serum free thyroxine was comparable in both groups. Visceral fat mass was significantly higher in CFS patients (86.6 +/- 34.9 cm2 vs. 51.5 +/- 15.7 cm2; P < 0.001). CONCLUSIONS: We observed a significant impairment of GH response during insulin-induced hypoglycaemia and a low nocturnal GH secretion in CFS patients. These changes did, however, not lead to different concentrations in serum IGF-I. The clinical expression of this inadequate GH secretion can thus be questioned, although the alteration in body composition may be related to this relative GH deficiency. Significantly increased prolactin and TSH levels were found when compared to controls. These findings give support to the hypothesis of a decreased dopaminergic tone in CFS. Further investigations are required in order to identify specific adaptations within the neurotransmitter system in CFS and to determine the clinical importance of the impaired GH homeostasis.
Naschitz JE, Rosner I, Rozenbaum M, Gaitini L, Bistritzki I, Zuckerman E, Sabo E, Yeshurun D.	Department of Internal Medicine A, Bnai Zion Medical Center and Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.	The capnography head-up tilt test for evaluation of chronic fatigue syndrome.	Semin Arthritis Rheum 2000 Oct;30(2):79-86	OBJECTIVES: To compare the hemodynamic and ventilatory responses to autonomic challenge evoked by upright tilt table testing in patients with chronic fatigue syndrome (CFS) to healthy individuals. METHODS: Thirty-two consecutive patients with CFS and 32 healthy volunteers were evaluated with the aid of the recently introduced capnography head-up tilt test (CHUTT). The main outcome measures were values of blood pressure (BP), heart rate (HR), respiratory rate (RR), and end-tidal pressure of co2 (ETPco2) recorded during recumbence and tilt. In addition, the end points of vasodepressor and cardioinhibitory reactions, hyperventilation (defined by ETPco2 <25 mm Hg) and the postural tachycardia syndrome, were recorded. RESULTS: The BP, HR, RR, and ETPco2 recorded during recumbence were similar in both groups. During tilt, patients with CFS developed significantly lower systolic BP, diastolic BP, and ETPco2, and a significant rise in HR and RR (P<.01). In CFS patients, the postural tachycardia syndrome occurred in 44%, vasodepressor reaction in 41%, cardioinhibitory reaction in 13%, and hyperventilation in 31% of cases. One or more end points of the CHUTT were reached in 78% of patients with CFS but in none of the controls (P<.0001). CONCLUSIONS: In most patients with CFS, a spectrum of abnormal homeostatic reactions is diagnosed with the aid of the CHUTT. Data provided by the CHUTT may reinforce the clinical diagnosis by adding objective and unbiased criteria to the subjective assessment of CFS.
Nawab SS, Miller CS, Dale JK, Greenberg BD, Friedman TC, Chrousos	Section on Biological Rhythms, National Institute of Mental	Self-reported sensitivity to chemical exposures in five	Psychiatry Res 2000 Jul 24;95(1):67-74	Two hundred and twenty-five subjects, including normal volunteers and patients with previously documented seasonal affective disorder (SAD), chronic fatigue syndrome (CFS), Cushing's syndrome, Addison's disease and obsessive-compulsive disorder

GP, Straus SE, Rosenthal NE.	Health, Bethesda, MD 20892-1390, USA. ssnawab@hotmail.com	clinical populations and healthy controls.		(OCD), completed a self-rated inventory of reported sensitivity to various chemical exposures. Patients with CFS, Addison's disease and SAD self-reported more sensitivity to chemical exposures than normal controls. In addition, women reported more sensitivity than men. This report suggests that chemical sensitivity may be a relevant area to explore in certain medical and psychiatric populations. A possible relationship between reported chemical sensitivity and hypothalamic-pituitary-adrenal (HPA)-axis functioning is discussed.
Neeck G, Crofford LJ.	Department of Rheumatology, University of Giessen, Bad Nauheim, Germany. gunther.neeck@kerckhoff.med.uni-giessen.de	Neuroendocrine perturbations in fibromyalgia and chronic fatigue syndrome.	Rheum Dis Clin North Am 2000 Nov;26(4):989-1002	A large body of data from a number of different laboratories worldwide has demonstrated a general tendency for reduced adrenocortical responsiveness in CFS. It is still not clear if this is secondary to CNS abnormalities leading to decreased activity of CRH- or AVP-producing hypothalamic neurons. Primary hypofunction of the CRH neurons has been described on the basis of genetic and environmental influences. Other pathways could secondarily influence HPA axis activity, however. For example, serotonergic and noradrenergic input acts to stimulate HPA axis activity. Deficient serotonergic activity in CFS has been suggested by some of the studies as reviewed here. In addition, hypofunction of sympathetic nervous system function has been described and could contribute to abnormalities of central components of the HPA axis. One could interpret the clinical trial of glucocorticoid replacement in patients with CFS as confirmation of adrenal insufficiency if one were convinced of a positive therapeutic effect. If patient symptoms were related to impaired activation of central components of the axis, replacing glucocorticoids would merely exacerbate symptoms caused by enhanced negative feedback. Further study of specific components of the HPA axis should ultimately clarify the reproducible abnormalities associated with a clinical picture of CFS. In contrast to CFS, the results of the different hormonal axes in FMS support the assumption that the distortion of the hormonal pattern observed can be attributed to hyperactivity of CRH neurons. This hyperactivity may be driven and sustained by stress exerted by chronic pain originating in the musculoskeletal system or by an alteration of the CNS mechanism of nociception. The elevated activity of CRH neurons also seems to cause alteration of the set point of other hormonal axes. In addition to its control of the adrenal hormones, CRH stimulates somatostatin secretion at the hypothalamic level, which, in turn, causes inhibition of growth hormone and thyroid-stimulating hormone at the pituitary level. The suppression of gonadal function may also be attributed to elevated CRH because of its ability to inhibit hypothalamic luteinizing hormone-releasing hormone release; however, a remote effect on the ovary by the inhibition of follicle-stimulating hormone-stimulated estrogen production must also be considered. Serotonin (5-HT) precursors such as tryptophan (5-HTP), drugs that release 5-HT, or drugs that act directly on 5-HT receptors stimulate the HPA axis, indicating a stimulatory effect of serotonergic input on HPA axis function. Hyperfunction of the HPA axis could also reflect an elevated serotonergic tonus in the

				CNS of FMS patients. The authors conclude that the observed pattern of hormonal deviations in patients with FMS is a CNS adjustment to chronic pain and stress, constitutes a specific entity of FMS, and is primarily evoked by activated CRH neurons.
Neerinckx E, Van Houdenhove B, Lysens R, Vertommen H, Onghena P.	Department of Psychosomatic Rehabilitation, University Hospital Katholieke Universiteit Leuven, Belgium. eneerinckx@mail.phlimburg.be	Attributions in chronic fatigue syndrome and fibromyalgia syndrome in tertiary care.	J Rheumatol 2000 Apr;27(4):1051-5	OBJECTIVE: To evaluate the attributions of patients with chronic fatigue syndrome (CFS) and fibromyalgia (FM) consulting at a university fatigue and pain clinic. METHODS: Consecutive attenders (n = 192) who met the CFS criteria (n = 95) or FM criteria (n = 56) or who had medically unexplained chronic pain and/or fatigue without meeting both criteria (CPF) (n = 41) were evaluated. All subjects completed an extended form of the Cause of Illness Inventory. Descriptive statistics, frequency analyses, chi-square tests, one-way analysis of variance, and sequential Fisher least significant difference tests were performed. RESULTS: In total, 48 patients reported physical causes only and 10 patients psychosocial causes only; the majority (70%) mentioned both types of causes. With regard to the contents, "a chemical imbalance in my body" (61%), "a virus" (51%), "stress" (61%), and "emotional confusion" (40%) were reported most frequently. The diagnostic label did not have a significant influence on number and type of attributions. Small to moderate effect sizes were registered concerning the association of specific attributions and diagnosis, sex, duration of the symptoms, contact with a self-help group, and premorbid depression. CONCLUSION: The majority of patients with CFS, FM, and CPF reported a great diversity of attributions open to a preferably personalized cognitive behavioral approach. Special attention should be paid to patients with symptoms existing for more than one year and those who had previous contacts with a self-help group. They particularly show external, stable, and global attributions that may compromise feelings of self-efficacy in dealing with the illness.
Nicolson GL. Nasralla MY, Franco AR, De Meirleir K, Nicolson NL, Ngwenya R, Haier J.		Role of Mycoplasmal Infections in Fatigue Illnesses: Chronic Fatigue and Fibromyalgia Syndromes, Gulf War Illness and Rheumatoid Arthritis	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 23	Bacterial and viral infections are purported to be associated with several fatigue illnesses, including Chronic Fatigue Syndrome (CFS), Fibromyalgia Syndrome (FMS), Gulf War Illnesses (GWI) and Rheumatoid Arthritis (RA), as causative agents, cofactors or opportunistic infections. We and others have looked for the presence of invasive pathogenic mycoplasmal infections in patients with CFS, FMS, GWI and RA and have found significantly more mycoplasmal infections in CFS, FMS, GWI and RA patients than in healthy controls. Most patients had multiple mycoplasmal infections (more than one species). Patients with chronic fatigue as a major sign often have different clinical diagnoses but display overlapping signs/symptoms similar to many of those found in CFS/FMS. When a chronic fatigue illness, such as GWI, spreads to immediate family members, they present with similar signs/symptoms and mycoplasmal infections. CFS/FMS/GWI patients with mycoplasmal infections generally respond to particular antibiotics (doxycycline, minocycline, ciprofloxacin, azithromycin and clarithromycin), and their long-term administration plus nutritional support, immune enhancement and other supplements appear to be necessary for

				recovery. Examination of the efficacy of antibiotics in recovery of chronic illness patients reveals that the majority of mycoplasma-positive patients respond and many eventually recover. Other chronic infections, such as viral infections, may also be involved in various chronic fatigue illnesses with or without mycoplasmal and other bacterial infections, and these multiple infections could be important in causing patient morbidity and difficulties in treating these illnesses.
Nisenbaum R, Jones A, Jones J, Reeves W.	Centers for Disease Control and Prevention, Atlanta, GA, USA	Longitudinal analysis of symptoms reported by patients with chronic fatigue syndrome.	Ann Epidemiol 2000 Oct 1;10(7):458	PURPOSE: To determine the effect of chronic fatigue syndrome (CFS) illness duration and onset type on the likelihood of reporting a symptom during successive follow-up periods.METHODS: In 1997, a two-phase RDD survey in Wichita, Kansas, was conducted to estimate the prevalence of CFS. Phase I identified 56,154 respondents 18-69 years of age and screened for severe fatigue, extreme tiredness or exhaustion lasting for 1 month or longer. In phase II an equal number of fatigued (n = 7,176) and randomly selected non-fatigued subjects were asked about 8 CFS and 13 non-CFS symptoms, as well as the presence of specific medical and psychiatric conditions. Eligible respondents were clinically evaluated to establish CFS diagnosis. Phase II respondents were re-contacted at 12- (n = 4,331) and 24-months (n = 4,266) for additional follow-up and diagnosis. In this study we considered symptoms reported as being present most of the time during each successive observation period. Generalized estimating equations were used to model symptoms over time and to address study questions. Such a model accounts for correlations among repeated symptoms for each subject. We used an auto-regressive structure for the correlation matrix, assuming the correlations between each pair of repeated symptoms should decrease as the time between symptoms increased.RESULTS: There were 74 CFS patients who had been ill for 1 to 20 years (median = 6.3 years). Among these, 46 reported gradual and 28 reported sudden onset. Symptoms fluctuated over the course of illness. However, only stomach pain (non-CFS symptom) was more likely to be reported as duration of illness increased ($p < 0.05$). There was no association between onset type and the likelihood of reporting a symptom during an interview, except that chills and severe headaches were more likely to be reported by sudden cases.CONCLUSIONS: The likelihood of expressing CFS and non-CFS symptom "most of the time" is the same across years of illness. More analyses are warranted to consider expression of symptoms for >/=6 months and severe symptoms.
Nores J-M.		The Philosophy of Pain: New Concepts	Journal of Chronic Fatigue Syndrome 2000; 5(2): 99	This article examines the concept of physical pain and its relationship to philosophy within the context of ethics. The first question posing a problem is: should pain be added to or included in the list of the five senses? Whether sensation is present or not, pain does exist. Pain is part of the ``immediate data of consciousness'' dear to philosophers. Pain is at the heart of ontology, philosophy of the being and existential ontology, which places existence above essence. Pain is mine and teaches me that I exist. Pain conveys my existence more than thought. Why shouldn't we enrich Descartes's cogito? ``I suffer, therefore I exist'' rather than ``I think, therefore I exist''

				or even ``I am something which suffers'' rather than ``I am a thing which thinks'' by Descartes. As pain is the witness of their existence, other beings resemble me. The use of physical pain to cause harm is the best transition towards the following question, that is, what is the relationship between pain and evil or harm? This is a question which is primordial and concerns philosophers, moralists and theologians. There is just pain which is harmful and is our enemy to be conquered. This would seem to be what philosophy has to teach those of us who are doctors fighting pain.
Nowotny N, Kolodziejek J.		9 Demonstration of borna disease virus nucleic acid in a patient with chronic fatigue syndrome	J Infect Dis 2000 May;181(5):1860-2 Comment on: J Infect Dis. 1999 Nov;180(5):1695-.	
Oldmeadow M.		Chronic fatigue syndrome.	Aust Fam Physician 2000 Jan;29(1):76-7Comment in: Aust Fam Physician. 2000 Jul;29(7):625-6	
Pall ML.		Elevated Peroxynitrite as the Cause of Chronic Fatigue Syndrome: Other Inducers and Mechanisms of Symptom Generation	Journal of Chronic Fatigue Syndrome 2000; 7(4): 45	In an earlier paper, I proposed that chronic fatigue syndrome (CFS) is caused by a response to infection, involving the induction of inflammatory cytokines which induce, in turn, the inducible nitric oxide synthase, producing elevated nitric oxide. Nitric oxide reacts with superoxide to form the potent oxidant, peroxynitrite. Six positive feedback loops were proposed by which peroxynitrite may stay elevated, acting to increase levels of both nitric oxide and superoxide, which react to form more peroxynitrite. This vicious cycle based on known biochemistry is proposed to be the central cause of CFS. The current paper discusses additional inducers which may act by increasing nitric oxide (physical or psychological trauma) or increasing superoxide (hypoxia) and the role of orthostatic intolerance, Ehlers-Danlos syndrome, excessive exercise, exercise intolerance and carbon monoxide in inducing hypoxia and consequently superoxide and peroxynitrite. The major symptoms of CFS can all be interpreted as relatively direct consequences of the pathophysiology predicted by the elevated peroxynitrite theory of CFS. Attractive mechanisms are proposed by which elevated peroxynitrite, nitric oxide and/or related physiological changes may induce CFS symptoms including fatigue, immune dysfunction, learning and memory dysfunction, multi-organ pain, exercise intolerance/postexertional malaise and orthostatic intolerance. Roles are discussed for six factors likely to influence the frequency of CFS induction in response to infection or other inducing events.
Pall ML.	Department of Biochemistry/Biophysics and Program in Basic	Elevated, sustained peroxynitrite levels as the cause of chronic	Med Hypotheses 2000 Jan;54(1):115-25	The etiology of chronic fatigue syndrome (CFS) has been both obscure and highly contentious, leading to substantial barriers to both clear diagnosis and effective treatment. I propose here a novel hypothesis of CFS in which either viral or bacterial

	Medical Sciences, Washington State University, Pullman 99164-4660, USA. pall@mail.wsu.edu	fatigue syndrome.		infection induces one or more cytokines, IL-1beta IL-6, TNF-alpha and IFN-gamma. These induce nitric oxide synthase (iNOS), leading to increased nitric oxide levels. Nitric oxide, in turn, reacts with superoxide radical to generate the potent oxidant peroxynitrite. Multiple amplification and positive feedback mechanisms are proposed by which once peroxynitrite levels are elevated, they tend to be sustained at a high level. This proposed mechanism may lower the HPA axis activity and be maintained by consequent lowered glucocorticoid levels. Similarities are discussed among CFS and autoimmune and other diseases previously shown to be associated with elevated peroxynitrite. Multiple pharmacological approaches to the treatment of CFS are suggested by this hypothesis.
Patarca-Montero R, Mark T, Fletcher MA, Klimas NG.		Immunology of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 69	A review of the literature on the immunology of CFS reveals that people who have Chronic Fatigue Syndrome (CFS) have two basic problems with immune function that have been documented by most research groups: 1. immune activation, as demonstrated by elevation of activated T lymphocytes, including cytotoxic T cells, as well as elevations of circulating cytokines; and 2. poor cellular function, with low natural killer cell cytotoxicity (NKCC), poor lymphocyte response to mitogens in culture, and frequent immunoglobulin deficiencies, most often IgG1 and IgG3. These findings have a waxing and waning temporal pattern which is consistent with episodic immune dysfunction (with predominance of so called T-helper type 2 and proinflammatory cytokines and low NKCC and lymphoproliferation) that can be associated as cause or effect of the physiological and psychological function derangement and/or activation of latent viruses or other pathogens. The interplay of these factors can account for the perpetuation of disease with remission/exacerbation cycles. Therapeutic intervention aimed at induction of a more favorable cytokine expression pattern and immune status is discussed.
Pearn J.		Differential Diagnosis: The Challenge of Chronic Fatigue	Journal of Chronic Fatigue Syndrome 2000; 7(4): 17	The chronic fatigue syndrome comprises one of the most challenging issues in contemporary medicine. The condition remains distressing for patients and perplexing to medical science. Clinicians face a management path which has no ``gold standard'' of investigational mileposts; and are locked into a progression where the extremes of either undertreatment or over-investigation may lead to iatrogenic disaster. The themes of investigation, diagnosis and management of patients with the chronic fatigue syndrome remain controversial. This condition joins in historical perspective a series of other diseases such as pink disease, post traumatic stress disorder (by a variety of names), the Royal Free disease, Q Fever, Ross River disease and chronic ciguatera-all of which have occupied windows of historical time in the twentieth century during which their genesis remained an enigma. In some cases, they still do. New and puzzling diseases will undoubtedly arise in the future. Both patients and medical science are best served if the formal discipline of differential diagnosis is followed unswervingly under these circumstances or ``new'' diseases. The rigour of this discipline-the rank listing of formal possibilities after the clinical

				history and objective signs have been elicited-forms the pivot of best-practice contemporary medicine. An example of its power is no more dramatically illustrated by the example of a ``new'' enigmatic disease, chronic ciguatera, which ``reappeared'' in the 1950s. Ciguatoxins are some of the most potent biological substances known. Their neurotropic effects produce a protean array of symptoms which are distressing in the acute-phase syndrome and which are enervating throughout the often-prolonged progression of convalescence. It is now appreciated that such effects are due to sodium channel activation and subsequent dysfunction at the receptor sites on the cell surface of all excitable tissues. Dr. A. Melvin Ramsay, the Honorary Consultant Physician in Infectious Diseases at the Royal Free Hospital in London, was at the clinical epicentre of the presentation of another new disease in July 1955. His approach to its diagnosis, in the best traditions of differential diagnosis, is an exemplar of the objective response to the appearance of a new or enigmatic disease; and especially to that type in which experience has not generated sufficient case familiarity to define syndrome barriers or to establish pathogenesis. Under such conditions, the correct diagnostic paradigm is to follow the discipline of differential diagnosis, an evolved phenomenon of the last one hundred years of medicine. This paper traces the evolution of the process of differential diagnosis, in the perspective of the enigma of chronic fatigue, which remains an unmet challenge today.
Pearn J.	Australian Defence Force, Royal Children's Hospital, Brisbane, Queensland, Australia.	Traumatic stress disorders: a classification with implications for prevention and management.	Mil Med 2000 Jun;165(6):434-40	The management and prevention of acute and post-traumatic stress disorders are current themes of great importance to the defense health services of many nations. Currently, between 2% and 8% of service members deployed on combat operations, United Nations peacekeeping tasks, and humanitarian and disaster relief operations present with one or more stress disorders within 3 years of deployment. The management of acute stress disorders and the prevention and management of post-traumatic stress disorders necessitate an understanding of the nosology of this group of illnesses. Research into some preventive options--such as critical incident stress debriefing--also necessitates the selection of syndrome-specific subjects during case finding if controversies about the efficacy of such interventions are to be resolved. Diagnostic features, a summary of the nosological evolution, and key points of differential treatment options are presented for 5 acute operational stress disorders (acute combat stress disorder, conversion reactions, the counter-disaster syndrome, peacekeeper's acute stress syndrome, and the Stockholm syndrome) and for 11 post-traumatic disorders, including classic post-traumatic stress disorder, chronic fatigue syndrome, Gulf War syndrome, peacekeeper's stress syndrome, survivor's guilt syndrome, and the syndrome of lifestyle and cultural change.
Peckerman A, LaManca JJ, Smith SL, Taylor A, Tiersky L, Pollet C, Korn LR,	Center for Environmental Hazards Research, Environmental and	Cardiovascular stress responses and their relation to symptoms in Gulf War veterans	Psychosom Med. 2000 Jul-Aug;62(4):509-16.	OBJECTIVE: The objective of this study was to examine whether inappropriate cardiovascular responses to stressors may underlie symptoms in Gulf War veterans with chronic fatigue. METHODS: Psychophysiological stress testing was performed on 51 Gulf War veterans with chronic fatigue (using the 1994 case definition of the

Hurwitz BE, Ottenweller JE, Natelson BH.	Occupational Health Sciences Institute, Robert Wood Johnson Medical School, Piscataway, NJ, USA. apeckerm@nbunj.jvnc.net	with fatiguing illness.		Centers for Disease Control and Prevention) and 42 healthy veterans. Hemodynamic responses to cold pressor, speech, and arithmetic stressors were evaluated using impedance cardiography. RESULTS: Veterans with chronic fatigue had diminished blood pressure responses during cognitive (speech and arithmetic) stress tests due to unusually small increases in total peripheral resistance. The cold pressor test, however, evoked similar blood pressure responses in the chronic fatigue and control groups. Low reactivity to cognitive stressors was associated with greater fatigue ratings among ill veterans, whereas an opposite relation was observed among healthy veterans. Self-reported neurocognitive decline was associated with low reactivity to the arithmetic task. CONCLUSIONS: These results suggest a physiological basis for some Gulf War veterans' reports of severe chronic fatigue. A greater deficit with responses processed through cerebral centers, as compared with a sensory stimulus (cold pressor), suggests a defect in cortical control of cardiovascular function. More research is needed to determine the specific mechanisms through which the dissociation between behavioral and cardiovascular activities identified in this study may be contributing to symptoms in Gulf War veterans.
Petzke F, Clauw DJ.	Division of Rheumatology, Immunology, and Allergy, Georgetown University Medical Center, LL Gorman Building, 3800 Reservoir Road NW, Washington, DC 20007. petzkef@gusun.georgetown.edu	Sympathetic nervous system function in fibromyalgia.	Curr Rheumatol Rep 2000 Apr;2(2):116-23	This review focuses on studies of the sympathetic nervous system in fibromyalgia (FM). First, a brief review of the sympathetic system, and its relationship to the human stress response, is outlined. Then various studies of functional assessment of sympathetic function in FM are highlighted. Certain methods of assessment (eg, heart rate variability, biochemical, and psychophysical responses to various stressors) that we believe to be of specific importance for future research are discussed in greater detail. Finally, findings on autonomic function in related disorders--specifically, chronic fatigue syndrome, irritable bowel syndrome, and migraine--will be briefly presented.
Podell RN.		Chronic fatigue syndrome: the fundamentals still apply.	Am J Med 2000 Jun 1;108(8):677	
Poole J, Herrell R, Ashton S, Goldberg J, Buchwald D.	Harborview Medical Center, 325 Ninth Ave, Box 359780, Seattle, WA 98104, USA.	Results of isoproterenol tilt table testing in monozygotic twins discordant for chronic fatigue syndrome.	Arch Intern Med 2000 Dec 11-25;160(22):3461-8	BACKGROUND: The pathogenesis of chronic fatigue syndrome (CFS) is unknown. Neurally mediated hypotension (NMH) has been suggested as a common comorbid condition or a potential underlying cause. METHODS: We conducted a cotwin control study of 21 monozygotic twins who were discordant for CFS. One twin met the 1994 Centers for Disease Control and Prevention criteria for CFS, and the other twin was healthy and denied chronic fatigue. The twins were selected from a volunteer twin registry in which at least 1 member reported persistent fatigue. As part of a 7-day clinical evaluation, all 21 twin pairs were evaluated with a 3-stage tilt table test with isoproterenol hydrochloride for the assessment of NMH. The presence of NMH was

				defined as syncope or presyncope associated with a decrease of 25 mm Hg in blood pressure and no associated increase in heart rate. RESULTS: A positive tilt table test result was observed in 4 twins with CFS (19%) and in 4 healthy twins (19%). This difference was not statistically significant (matched pair odds ratio, 1.0; 95% confidence interval, 0.2-5.4; P>.90). Compared with the healthy twins, the twins with CFS reported more severe symptoms of CFS and NMH both in the week before and during the tilt table test. CONCLUSIONS: These results do not support a major role for NMH in CFS. They highlight the importance of selecting well-matched control subjects, as well as the unique value of the monozygotic cotwin control design in the study of this illness. Arch Intern Med. 2000;160:3461-3468.
Price JR, Couper J.	Department of Psychiatry, University of Oxford, The Warneford Hospital, Oxford, UK, OX3 7JX. jonathan.price@psych.ox.ac.uk	Cognitive behaviour therapy for adults with chronic fatigue syndrome.	Cochrane Database Syst Rev 2000;(2):CD001027	OBJECTIVES: 1. To systematically review all randomised controlled trials of cognitive-behaviour therapy (CBT) for adults with chronic fatigue syndrome (CFS); 2. To test the hypothesis that CBT is more effective than orthodox medical management or other interventions in adults with CFS. SEARCH STRATEGY: 1. Electronic searching of bibliographic databases, including Medline, PsycLIT, Biological Abstracts, Embase, SIGLE, Index to Theses, Index to Scientific and Technical Proceedings, and Science Citation Index, using multiple search terms in order to perform a highly sensitive search. 2. Electronic searching of the Trials Register of the Depression, Anxiety and Neurosis group. 3. Citation lists of relevant studies and reviews were perused for other relevant trials. 4. Contact with the principal authors of relevant studies, and with researchers in the field. SELECTION CRITERIA: All randomised controlled trials were included in which - adult patients with CFS; - received CBT or a control intervention, being either orthodox medical management or another intervention; - and whose outcomes were assessed in an appropriate way. CBT could be either type 'A' (encouraging return to 'normal' levels of rest and activity) or type 'B' (encouraging rest and activity which were within levels imposed by the disorder). DATA COLLECTION AND ANALYSIS: The two reviewers worked independently throughout the selection of trials and data extraction, comparing findings only when there was disagreement. Relevant trials were allocated to one of three quality categories. Full data extraction, using a standardised data extraction sheet, was performed on studies which were of high or moderate quality. Trials of low quality were excluded from the review. The comparisons made to test the review hypothesis were of type 'A' CBT versus other intervention(s), and of type 'B' CBT versus other intervention(s). Functional outcome was used as the main outcome for comparison, but other appropriate outcomes were compared where possible. Results were synthesised using the Review Manager software. For dichotomous data, the odds ratio was calculated for each study. For continuous data, effect sizes were obtained and the standardised mean difference, with 95% confidence intervals, was calculated. MAIN RESULTS: Only three relevant trials of adequate quality were found. These trials demonstrated that CBT significantly benefits physical functioning in adult out-

				patients with CFS when compared to orthodox medical management or relaxation. It is necessary to treat about two patients to prevent one additional unsatisfactory physical outcome about six months after treatment end. CBT appeared highly acceptable to the patients in these trials. There is no satisfactory evidence for the effectiveness of CBT in patients with the milder forms of CFS found in primary care or in patients who are so disabled that they are unable to attend out-patients. Additionally, there is no satisfactory evidence for the effectiveness of group CBT. REVIEWER'S CONCLUSIONS: Cognitive behaviour therapy appears to be an effective and acceptable treatment for adult out-patients with chronic fatigue syndrome. CFS is a common and disabling disorder. Its sufferers deserve the medical profession to be more aware of the potential of this therapy to bring lasting functional benefit, and health service managers to increase its availability. Further research is needed in this important area. Trials should conform to accepted standards of reporting and methodology. The effectiveness of CBT in more and less severely disabled patients than those usually seen in out-patient clinics needs to be assessed. Trials of group CBT and in-patient CBT compared to orthodox medical management, and of CBT compared to graded activity alone, also need to be conducted. Review, Academic
Prins JB, Bleijenberg G, Rouweler EK, van Weel C, van der Meer JWM.		Doctor-Patient Relationship in Primary Care of Chronic Fatigue Syndrome: Perspectives of the Doctor and the Patient	Journal of Chronic Fatigue Syndrome 2000; 7(4): 3	Background: Chronic Fatigue Syndrome (CFS) is characterized by severe debilitating fatigue for at least six months. The lack of a known origin could have consequences for the way general practitioners deal with the diagnosis CFS and their perception of CFS patients. The aims of the study were to investigate the use of the diagnosis CFS by GPs and their reactions to self-diagnosis and to explore opinions of GPs about causes of CFS and the communication with CFS patients as well as opinions of CFS patients about their GPs. Method: One hundred twenty-one GPs completed questionnaires and 12 were interviewed. Data of 211 CFS patients were analyzed as well. Results: Only half of the GPs used the diagnosis CFS. The main reason for not diagnosing CFS was ignorance of the criteria. GPs reported self-diagnosis in 68% of the CFS patients. More than half of the GPs could sympathize less with the complaints of CFS patients compared with other patients. These GPs experienced more problems in communicating with CFS patients and judged co-operation and contact as poor. As to the causes for CFS a discrepancy was found. GPs mainly attributed the complaints to psychosocial factors, whereas patients mainly had physical attributions. Conclusion: In CFS, GPs should be explicit about the diagnosis. As to the discrepancy in presumed causes of CFS between GPs and CFS patients, it may be helpful for GPs to discuss the distinction between initiating and perpetuating factors of CFS. We argue that this attitude of GPs would be beneficial to the course of the complaints of CFS patients.
Racciatti D, Barberio A,Vecchiet J, Pizzigallo E.		Clinical and Pathogenetical Characterization of 238	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 61	Prolonged fatigue is a common complaint in the community and is usually transitory. If fatigue continues for more than six months, is disabling, and is accompanied by other constitutional and neuropsychiatric symptoms, then a diagnosis of chronic

		Patients of a Chronic Fatigue Syndrome Italian Center		fatigue syndrome (CFS) should be considered. CFS probably is an heterogeneous disease, maybe multifactorial, or it includes different pathologies which manifest with the same symptoms. In some cases, the mode of presentation of the illness implicate the exposure to chemical and/or food toxins as precipitating factors (e.g., ciguatera poisoning, Gulf War Syndrome, etc.). In other CFS cases, the etiology is still unknown: there are various hypotheses on pathogenetic events which, alone or in association with each other, may precipitate the illness. In fact, it is probable an involvement of multiple events in CFS onset where different precipitating factors can interact each other, even if not always all present in the single patient: latent and/or chronic viral infections, immunologic and neuroendocrine dysfunctions, psychological, environmental and mood factors. In accordance to this theory, we consider various subgroups of CFS patients on the basis of the pathway and the mode of presentation of the disease. The Clinic of Infectious Diseases of ``G. D'Annunzio'' University of Chieti is one of the main National Reference Centers for the CFS Study in Italy. From January 1992 to January 1998, 238 patients came to our observation: 89 of them met CDC criteria for CFS (1994), 127 did not; the other 22 patients are still under evaluation. Our patients underwent physical examination (including tests for searching for the possible coexistence of a fibromyalgia syndrome), psychiatric interview with several neuropsychological tests, laboratory tests (including magnesium determination on serum), neuroendocrine evaluation (circadian rhythm of several hormones, buspirone challenge test), SPECT scans to evaluate cerebral perfusion, and other examinations where necessary in according to the symptomatology of each patient (e.g., orthopedic, ORL, EMG, muscle biopsy, etc.). According to our preliminary results, we subdivided our patients in different subgroups and we studied them comparatively. We report the more significant data collected from this evaluation that might lead to a better understanding of the syndrome and in particular of its pathways course, a knowledge that will help is choosing appropriate therapies for each subgroups.
Rangel L, Garralda E, Levin M, Roberts H.	Academic Unit of Pediatrics, Imperial College School of Medicine, London, UK.	Personality in adolescents with chronic fatigue syndrome.	Eur Child Adolesc Psychiatry 2000 Mar;9(1):39-45	Our aim was to study the presence of personality traits and disorder in adolescents with Chronic Fatigue Syndrome (CFS). Personality was then compared to other measures of functioning such as presence of psychiatric disorder and rating on the Child Behavior Checklist 4-18 (CBCL) and in relation to CFS outcome. Twenty-five adolescents with CFS followed-up after contacts with tertiary paediatric/psychiatric clinics were compared with 15 matched healthy controls. Interviews and questionnaires from parents and youngsters included Personality Assessment Schedule (PAS), Kiddie-SADS Psychiatric Interview, Child Behavior Checklist. CFS subjects were significantly more likely than controls to have personality difficulty or disorder. Personality features significantly more common amongst them were conscientiousness, vulnerability, worthlessness and emotional lability. There was a nonsignificant association between personality disorder and worse CFS outcome.

				Personality difficulty or disorder was significantly associated with psychological symptoms and decreased social competence on the CBCL but it was distinguishable from episodic psychiatric disorder. Personality difficulty and disorder are increased in adolescents with a history of CFS. Personality disorder may be linked to poor CFS outcome.
Rangel L, Garralda ME, Levin M, Roberts H.	Academic Unit of Child and Adolescent Psychiatry, Imperial College School of Medicine, St Mary's Hospital, London, UK.		J R Soc Med 2000 Mar;93(3):129-34Comment in: J R Soc Med. 2000 Jun;93(6):337-8 The course of severe chronic fatigue syndrome in childhood.	Little has been reported on prognostic indicators in children with chronic fatigue syndrome (CFS). We used interviews with children and parents, a mean of 45.5 months after illness onset, to follow up 25 cases of CFS referred to tertiary paediatric psychiatric clinics. At its worst, the illness had been markedly handicapping (prolonged bed-rest and school absence in two-thirds); mean time out of school was one academic year. Two-thirds, however, had recovered and resumed normal activities--mean duration of illness to recovery/assessment 38 months--and none had developed other medical conditions. Recovery was associated with specific physical triggers to the illness, with start of illness in the autumn school term and with higher socioeconomic status. Severe fatigue states in children can cause serious and longlasting handicap but most children recover.
Ray DE.	Medical Research Council Toxicology Unit, Leicester, United Kingdom. der@le.ac.uk	Pesticide neurotoxicity in Europe: real risks and perceived risks.	Neurotoxicology 2000 Feb-Apr;21(1-2):219-21	The same classes of pesticides are used all over the world, but conditions of use vary widely, and public perceptions of risk vary more widely still. Within Western Europe pesticide residues in commercially traded foodstuffs are subject to international standards and are closely monitored. Hence risks to consumers from such foods are negligible. The major hazards are poisoning associated with high acute/chronic operator exposures due to occasional pesticide misuse. In addition pesticides provide a convenient means of attempting suicide in agricultural areas. In contrast, public perception of risks from pesticides centres on low level exposures, and is heightened by several factors. These are: poisonings associated with pesticide misuse; the indirect nature of the benefit to the consumer (cf. medicines or public health uses); and commercially motivated marketing of pesticide-free produce. In press reports pyrethroid insecticides have been linked to "Multiple Chemical Sensitivity" in Germany, and organophosphates to "Chronic Fatigue Syndrome" in the UK. A number of pressure groups are actively campaigning to ban all uses of organophosphorus pesticides. Unfortunately evaluation of the real risks of pesticide exposure is rendered less certain by the lack of any very useful retrospective exposure measures with which biological effects of uncertain aetiology might be correlated. This means that although we can be sure that pesticides pose no gross threat to health in the general population, subtle effects on more highly exposed sub-populations are, as yet, more difficult to rule out.
Redman DA.	American University, Washington, DC, USA.	Ruscus aculeatus (butcher's broom) as a potential treatment for orthostatic	J Altern Complement Med 2000 Dec;6(6):539-49	CONTEXT: Chronic orthostatic hypotension (OH) is frequently a severely debilitating disease that affects large groups of the population with autonomic insufficiency--the elderly; patients with diabetes, Parkinson's disease, and chronic fatigue syndrome; and anyone on drugs that affect the autonomic nervous system. Unfortunately, even

		hypotension, with a case report.		though more than 60 medications are currently being used to treat OH, none of them is particularly or consistently effective. Ruscus aculeatus, a phytotherapeutic agent that is well known in Europe, may, however, change this. Its vasoconstrictive and venotonic properties make it ideally suited to treat the pooling of blood in the limbs, lack of venous tone, and lack of neurally mediated vasoconstriction that frequently characterize OH. Although it has never been suggested as a treatment for OH, it already has a long, proven record of use in Europe for treating a variety of circulatory disorders. OBJECTIVE: To provide evidence for what appears to be an effective, safe, inexpensive botanical therapy for OH and encourage further studies on the efficacy of Ruscus for OH patients. DESIGN: Review of OH and therapies currently available for OH and evaluation of the properties of Ruscus aculeatus, its mechanism of action, and its suitability as a therapeutic agent for treatment of OH. RESULTS: A review of the many pharmacologic and nonpharmacologic agents for treating OH reveals that all of the drug therapies are disappointing and marginally useful. Although nonpharmacologic management is preferred, in the many cases in which OH becomes debilitating, pharmacologic intervention becomes a last resort. But drug therapy may not always be necessary, because Ruscus aculeatus, a phytotherapeutic agent containing ruscogenins and flavonoids, may prove useful for the treatment of OH if denervation is not so advanced that it has compromised receptor activity at the venous wall. Ruscus aculeatus is an alpha-adrenergic agonist that causes venous constriction by directly activating postjunctional alpha1- and alpha2-receptors, in turn stimulating the release of noradrenaline at the level of the vascular wall. It also possesses venotonic properties: it reduces venous capacity and pooling of blood in the legs and exerts protective effects on capillaries, the vascular endothelium, and smooth muscle. Its flavonoid content strengthens blood vessels, reduces capillary fragility, and helps maintain healthy circulation. Unlike most of the drug therapies used to treat OH, Ruscus aculeatus does not cause supine hypertension. It also appears to do something no other therapy can offer--alleviate the worsening effects of OH in environmentally hot conditions. Finally, it is an extremely safe, inexpensive, over-the-counter botanical medicine. CONCLUSION: With proven phlebotherapeutic properties, including vasoconstrictive action and venotonic properties, Ruscus aculeatus shows great promise for ameliorating the symptoms of OH and improving the quality of life for large groups in the population. It clearly deserves to be the object of wider research and study as a treatment for OH.
Reeves WC, Stamey FR, Black JB, Mawle AC, Stewart JA, Pellett PE.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and	Human herpesviruses 6 and 7 in chronic fatigue syndrome: a case-control study.	Clin Infect Dis 2000 Jul;31(1):48-52	We conducted this study to determine whether infection with human herpesvirus (HHV) 6A, HHV-6B, or HHV-7 differed between patients with chronic fatigue syndrome and control subjects. We recruited 26 patients and 52 nonfatigued matched control subjects from Atlanta. Serum samples were tested by enzyme immunoassay for seroreactivity to HHV-6, and all were seropositive. Lymphocyte specimens were cocultivated with cord blood lymphocytes and assayed for HHV-6

	Prevention, Atlanta, GA, 30333, USA. wcr1@cdc.gov			and HHV-7; neither virus was isolated. Finally, lymphocytes were tested by use of 3 polymerase chain reaction methods for HHV-6A, HHV-6B, and HHV-7 DNA. HHV-6A or HHV-6B DNA was detected in 17 (22.4%) of 76 samples, and there were no significant differences (by matched analyses) between patients (3 [11.5%] of 26) and control subjects (14 [28%] of 50). HHV-7 DNA was detected in 14 subjects, and although control subjects (12 [24%]) were more likely than patients (2 [7.7%]) to be positive, the difference was not statistically significant. We found no evidence that active or latent infection with HHV-6A, HHV-6B, HHV-7, or any combination these 3 HHVs is associated with chronic fatigue syndrome.
Regland B.		[Two contributions on chronic fatigue syndrome: biological causes are involved in most cases]. [Article in Swedish]	Lakartidningen 2000 Mar 8;97(10):1168	
Reid S, Chalder T, Cleare A, Hotopf M, Wessely S.	Guy's, Kings, and St Thomas's School of Medicine and Institute of Psychiatry, London SE5 8AZ. steve.reid@kcl.ac.uk	Chronic fatigue syndrome.	BMJ 2000 Jan 29;320(7230):292-6	
Reyes M, Dobbins JG, Nisenbaum R, Subedar NS, Randall B, Reeves C.		Chronic Fatigue Syndrome Progression and Self-Defined Recovery: Evidence from the CDC Surveillance System	Journal of Chronic Fatigue Syndrome 2000; 5(1): 17	Objective: To examine the presence of symptoms associated with chronic fatigue syndrome (CFS) over the course of the illness and determine the probability of self-defined recovery by duration of illness. Design: Follow-up study. Subjects: One hundred fifty-five CFS patients enrolled in the Centers for Disease Control and Prevention's (CDC) CFS surveillance system between August 1989 and July 1993 and followed to November 1997. Measurements: Presence of symptoms, a self-defined period of recovery from CFS, and demographic differences between patients reporting and not reporting recovery. Period life-table methods were used to compute the probability of recovery from CFS for specific years of illness duration. Results: At illness onset, the most commonly reported CFS symptoms (w 45%) were sore throat, fever, tender lymph nodes, general weakness, and muscle pain. As the illness progressed, the percentages of patients reporting symptoms fluctuated. At illness onset, patients with a sudden onset of CFS reported significantly higher frequencies of sore throat, fever, tender lymph nodes, chills, hypersomnia, difficulty thinking or concentrating, and depression when compared to patients with a gradual onset. As the illness progressed, these differences disappeared, but gradual onset cases reported more hypersomnia than sudden onset cases (p = 0.001). The cumulative probability of recovery from CFS was 31.4% during the first 5 years of illness and 48.1% during the first 10 years of illness. For each year of illness through

				year 15, both sudden and gradual onset cases had similar recovery probabilities. Thereafter, gradual onset cases had higher recovery probabilities, but these differences were not statistically significant. Patients reporting recovery and those remaining ill were similar demographically. Conclusions: A period of recovery could be reported at any time during the course of CFS, but was more likely in the early years. Additional longitudinal studies are required to adequately describe the course of CFS in the early stages of illness, determine if the illness recurs over time, and predict the occurrence of symptoms over the course of illness. We recommend that researchers develop a standard definition of recovery from CFS and that future studies take into account the variable duration of illness and follow-up
Richards RS, Roberts TK, Dunstan RH, McGregor NR, Butt HL.	Department of Biological Sciences, University of Newcastle, New South Wales, Australia.	Free radicals in chronic fatigue syndrome: cause or effect?	Redox Rep 2000;5(2-3):146-7	We have demonstrated that certain morphological and biochemical changes occur in chronic fatigue syndrome (CFS) and in rheumatoid arthritis (RA). These changes in RA can be explained by the well-established inappropriate increase in free radical generation. The similar changes in CFS suggest a similar explanation and a possible role for free radicals in the aetiology of this condition.
Richards RS, Roberts TK, Mathers D, Dunstan RH, McGregor NR, Butt HL.		Erythrocyte Morphology in Rheumatoid Arthritis and Chronic Fatigue Sydrome: A Preliminary Study	Journal of Chronic Fatigue Syndrome 2000; 6(1): 23	Erythrocyte deformability and erythrocyte membrane stability are dependent on the erythrocyte cytoskeleton and its relationship with the contents of the cell. Certain internal occurrences such as oxidation of sulphydryl groups on the membrane cytoskeleton or the haemoglobin molecule could alter this relationship and as a consequence, alter the membrane properties and the shape of the cell. It is thus conceivable that in conditions where there is a potential increase in the generation of free radicals, erythrocyte shape could be altered. We investigated the possibility that predictable shape changes occur in erythrocytes from patients with rheumatoid arthritis (RA), a condition associated with free radical damage. We also investigated this possibility in patients with chronic fatigue syndrome (CFS) and whether any such change could be correlated with those seen in RA. Patients with CFS could be divided into two groups based on their erythrocyte morphology. Patients in one of these groups had increased numbers of stomatocytes. Patients with RA had increased numbers of leptocytes.
Richards RS, Roberts TK, Mathers D, Dunstan RH, McGregor NR, Butt HL.		Investigation of Erythrocyte Oxidative Damage in Rheumatoid Arthritis and Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 6(1): 37	A role of free radical scavenging for erythrocytes has previously been demonstrated, which is additional to their established role of gas exchange. In carrying out this role, erythrocytes become damaged by oxidation, which consumes endogenous reducing substances. It was therefore proposed that there exists a link between erythrocyte metabolism (particularly redox metabolism) and erythrocyte shape and that both of these should be related to erythrocyte deformability. To look for evidence of oxidative damage in vivo, the erythrocytes were assessed for reduced glutathione (GSH), malondialdehyde (MDA), methaemoglobin (metHb) and 2,3-diphosphoglyceric acid (2,3-DPG) in patients suffering from rheumatoid arthritis (RA), chronic fatigue syndrome (CFS) and healthy control subjects. Full blood counts, serum vitamin B12, erythrocyte folate, serum ferritin, serum iron, serum iron binding capacity and

				erythrocyte magnesium were also performed on all samples. Patients with RA had increased 2, 3-DPG, GSH and metHb when compared with the control group as well as the expected decreased haemoglobin, haematocrit, and serum iron. There was evidence of oxidative damage in CFS with 2,3-DPG metHb and MDA increased in this group. An increase in GSH could also be demonstrated in a sub-group of the CFS patients. This damage may explain the shape changes (presumably accompanied by increased rigidity) that have been reported in erythrocytes in patients suffering from CFS and suggests a role for free radicals in the pathogenesis of CFS.
Richards RS, Roberts TK, McGregor NR, Dunstan RH, Butt HL.	Department of Biological Sciences, University of Newcastle, Australia.	Blood parameters indicative of oxidative stress are associated with symptom expression in chronic fatigue syndrome.	Redox Rep 2000;5(1):35-41	Full blood counts, ESR, CRP, haematinics and markers for oxidative stress were measured for 33 patients diagnosed with chronic fatigue syndrome (CFS) and 27 age and sex matched controls. All participants also completed symptom questionnaires. CFS patients had increases in malondialdehyde (P <0.006), methaemoglobin (P <0.02), mean erythrocyte volume (P <0.02) and 2,3-diphosphoglycerate (P <0.04) compared with controls. Multiple regression analysis found methaemoglobin to be the principal component that differentiated between CFS patients and control subjects. Methaemoglobin was found to be the major component associated with variation in symptom expression in CFS patients (R(2) = 0.99, P <0.00001), which included fatigue, musculoskeletal symptoms, pain and sleep disturbance. Variation in levels of malondialdehyde and 2,3-diphosphoglycerate were associated with variations in cognitive symptoms and sleep disturbance (R(2) = 0.99, P <0.00001). These data suggest that oxidative stress due to excess free radical formation is a contributor to the pathology of CFS and was associated with symptom presentation.
Richardson J.		Four Cases of Pesticide Poisoning, Presenting as ``ME,'' Treated with a Choline and Ascorbic Acid Mixture	Journal of Chronic Fatigue Syndrome 2000; 6(2): 11	Objectives: 1. To demonstrate in four patients, in whom the correct diagnosis of pesticide poisoning had been missed, the injustices inflicted on them when they are told ME does not exist. 2. To show how closely the features of such poisoning, especially by organochlorines, resemble those of the much more classic ME which is usually due, at least in the author's practice in the northern region of the UK, to persistent enteroviral infection. 3. To draw attention to a new and apparently successful form of treatment with an oral mixture of choline and ascorbic acid. 4. To suggest reasons why this treatment merits further scientific investigation. Setting: A charity based private practice involved in the investigation of viral mediated disease. Subjects: Four patients, two male and two female, each referred with a diagnosis of ME. Intervention: a. Samples of blood were sent to Biolab Medical Unit where a variety of pesticide residues, including the very persistent organochlorines, were identified, and progress in detoxification was monitored. b. All four cases were treated orally with a choline and ascorbic acid mixture. Results: After a variable number of months, during the early phase of which the blood levels of some of the toxins rose, possibly due to mobilization from fatty stores, all symptoms cleared as blood levels fell. KEY Messages: The term ME comprises a number of clinical features, characterizing a patient who is ill. To refuse to recognize their existence does the

				patient much injustice. Some cases of ME may be found to have pesticide poisoning. The possibility of it should always be borne in mind. The source may be either in the UK or abroad. A positive enquiry and a single blood test will provide a diagnosis. Organochlorines may persist in the body for many years, as may the symptoms derived from them. A detoxification program based on oral administration of a choline and ascorbic acid mixture has shown much promise and deserves verification of its value. Conclusions: Amongst the group of clinical features known as ME, the possibility of pesticide poisoning should always be borne in mind. Treatment with choline and ascorbic acid mixture is worth trying, pending its more formal investigation.
Richman JA, Jason LA, Taylor RR, Jahn SC.	Department of Psychiatry, University of Illinois, Chicago 60612, USA. JRichman@uic.edu	Feminist perspectives on the social construction of chronic fatigue syndrome.	Health Care Women Int 2000 Apr-May;21(3):173-85	We contrast Western medical views of chronic fatigue syndrome (CFS) etiology, diagnosis, and treatment with views maintained by a predominantly female CFS population. We argue that the failure of Western medicine to demonstrate a viral etiology for CFS led to a paradigmatic shift in research perspectives, which then embraced psychiatric and sociocultural explanations for CFS. As a result, CFS was delegitimized as a biomedical phenomenon within medical, academic, governmental, and public arenas. We compare alternative social constructions of CFS with issues pertaining to multiple sclerosis (MS), an illness that similarly predominates among women. Patient perspectives suggest that the history of medical attitudes toward CFS may eventually parallel the transformations that occurred in relation to MS. In particular, the discovery of biological markers for CFS may lay to rest the categorization of CFS as largely within the psychiatric realm. Review Literature
Rosner I, Rozenbaum M, Naschitz JE, Sabo E, Yeshurun D.	Department of Hematology, Bnai Zion Medical Center, Haifa, Israel.	Dysautonomia in chronic fatigue syndrome vs. fibromyalgia.	Isr Med Assoc J 2000 Dec;2 Suppl:23-4	
Rowe KS.		Five-Year Follow-Up of Young People with Chronic Fatigue Syndrome Following the Double Blind Randomised Controlled Intravenous Gammaglobulin Trial	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 97	Three and 5 year follow-up studies of eighty-nine young people with Chronic Fatigue Syndrome who completed a double blind randomized controlled trial of intravenous gammaglobulin has been conducted to determine whether the improvement following the intravenous gammaglobulin was sustained. Initial telephone contact and a questionnaire that assessed functional outcomes including, physical activity, social activities, work/school attendance and work/school workload was used. Strategies and treatment that were found helpful and ways to improve management were also asked. Follow-up data were obtained on 86 of 89 after the study concluded. The 3-year follow-up yielded a 75% response to the questionnaire. A 78% follow up response rate at 5 years was achieved for those enrolled in the study with 84% (n = 74) of those who completed the study being traced. The mean follow-up time from commencement of illness was 56 months (s.d. 25 months), range 15-112 months. There was no persistent deterioration in function related to CFS in any young person. Four had reported recurrence of symptoms lasting 3-8 months and

				again improved. Others remained `improved' or continued to improve. Seventeen per cent of those who responded were still moderately unwell with another 23% `not back to normal yet.' Sixty per cent of participants considered they were `well' at the last follow-up with 45% scoring 10/10. Seventeen (20%) had another condition during or after their illness. Anergy or hypoergy did not predict functional outcome at five years after the trial, although an earlier improvement was noted in those who were anergic and who received gammaglobulin. There was no deterioration in overall function over the 5 years following participation in the gammaglobulin trial, and young people continued to improve although a significant number were still disabled. The significance of the abnormal delayed type hypersensitivity reaction for the response to gammaglobulin is uncertain and warrants further investigation.
Sachs L, Evengard B.	Tema Kommunikation, Linkopings universitet.	[The special physician-patient relation in connection to chronic fatigue syndrome. Anthropologists and physicians search for a new contact-model].[article in Swedish]	Lakartidningen 2000 Jan 19;97(3):176-8, 181	
Sadlier M, Evans JR, Phillips C, Broad A.		A Preliminary Study into the Effectiveness of Multi-Convergent Therapy in the Treatment of Heterogeneous Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 7(1): 93	In this preliminary study twenty-eight heterogeneous Chronic Fatigue Syndrome (CFS) patients were treated with Multi-Convergent Therapy (MCT). This form of therapy has been used successfully for over ten years in the treatment of Irritable Bowel Syndrome, Tinnitus, Hyperventilation Syndrome, Chronic Pain and Anxiety Disorders. This small study was undertaken to assess whether MCT is effective in the treatment of CFS and to examine whether a more extensive investigation is warranted. Due to heterogeneity of symptoms, outcome measures were established on the basis of a shared decision-making process between patient and therapist. One patient dropped out of the study. All twenty-seven remaining patients achieved significant recoveries. Twelve patients recorded a mean improvement on baseline symptoms of 61%, eight patients who completed a Quality of Life questionnaire demonstrated a mean change from 2.4 to 6.3 (out of 10). Five patients reported a return to full normal function and two patients returned to school or work and regular exercise. At follow up nine-months to one-year later all eighteen patients who responded reported either continued improvements or maintenance of a well state. The findings of this study support the use of MCT in the management of patients with Chronic Fatigue Syndrome and justify the implementation of a major clinical trial.
Schmaling KB, Smith WR, Buchwald DS.	University of Washington, Seattle	Significant other responses are	Psychosom Med 2000 May-Jun;62(3):444-50	OBJECTIVE: The predictive power of partners' responses to illness behavior for illness outcomes was investigated among couples in which one person had chronic fatigue

	98195-6560, USA. karens@u.washington.edu	associated with fatigue and functional status among patients with chronic fatigue syndrome.		syndrome (CFS). METHODS: One hundred nineteen participants who met case-definition criteria for CFS and were living with a significant other (SO) completed self-report measures of relationship satisfaction, responses of their SO to fatigue symptoms, and outcome measures of fatigue and functional status. RESULTS: The results indicated that more frequent solicitous SO responses to illness behavior were predictive of greater fatigue-related severity and bodily pain. Solicitous SO responses to fatigue behavior were particularly influential in the context of a satisfactory relationship. In highly satisfactory relationships, solicitous SO responses were associated with significantly greater fatigue severity and fatigue-related disability than in relationships characterized by low or average satisfaction. CONCLUSIONS: Solicitous SO responses to CFS-related symptoms are associated with poorer patient outcomes, especially in the context of a satisfactory intimate relationship. Because of the cross-sectional nature of the study, the direction of effects cannot be interpreted unambiguously. SOs may be inadvertently positively reinforcing illness-related behavior: Solicitous partners may help the patient more with tasks of daily living, thereby decreasing the patient's activity level, which may lead to deconditioning and disability. Alternatively, patients with more severe symptoms and disability may present more opportunities for concerned SO responses, which again may be heightened in the context of a caring, satisfactory relationship. In either case, the results suggest that additional research on the role of solicitous SO responses is warranted.
Schwartz SN, Jones R.		Measuring Outcomes of Treatment in Chronic Fatigue Syndrome: A Comparison of Simple Questioning vs. Use of a Validated Outcome Instrument (Short Form 36)	Journal of Chronic Fatigue Syndrome 2000; 6(2): 3	Purpose: To compare the outcome of treatment of chronic fatigue syndrome measured by a validated outcome instrument to patients' perception of outcome based on simple questioning. Subjects and Methods: Results of a single self-report question (``Are you much better, better, about the same, worse or much worse?'') at the end of approximately one year of treatment of 45 patients were compared to results of the Short Form 36 obtained at the beginning and end of that year. Results: There was no correlation between the results of the single self-report question and the interval change in the Short Form 36 summary scales and 7 of 8 component scales. Conclusions: Appropriate outcomes measurements can increase reliability of clinical practice results as well as treatment trials. Studies based only on answers to simple self-report questions may yield unreliable results.
Scott LV, Svec F, Dinan T.	Department of Psychiatry, Trinity College Medical School, St. James' Hospital, 8, Dublin, Ireland.	A preliminary study of dehydroepiandrosterone response to low-dose ACTH in chronic fatigue syndrome and in healthy subjects.	Psychiatry Res 2000 Dec 4;97(1):21-8	Abnormalities of the production of dehydroepiandrosterone (DHEA), the adrenal androgen, have been linked with disorders such as obesity and psychological disorders such as major depression. Adrenocorticotropin (ACTH) is the primary stimulant of DHEA, and cortisol, from the adrenal. We chose to examine the DHEA and DHEA/cortisol response to the novel low-dose ACTH test in healthy subjects and a cohort with chronic fatigue syndrome (CFS): this test is useful in assessing subtle irregularities of pituitary-adrenal activity. Nineteen CFS subjects (diagnosed by CDC criteria) and 10 healthy subjects were examined. We demonstrated that 1 &mgr;g

				ACTH significantly elevates DHEA levels, with no difference in output between CFS and healthy subjects. The DHEA/cortisol ratio decreased in response to ACTH stimulation in healthy subjects but not in the CFS cohort. We suggest this divergence of response between the two groups represents an imbalance in the relative synthetic pathways of the CFS group which, if present chronically and if comparable to daily stressors, may manifest itself as an inappropriate response to stress. This difference may be important in either the genesis or propagation of the syndrome.
Shannon M, Clovis LL.		Health Care Workers, Predominant Gender Females at High Risk: Turning the Spotlight on the Endocrine System	Journal of Chronic Fatigue Syndrome 2000; 7(1): 75	``Cluster Outbreaks'' of Chronic Fatigue (Immune Dysfunction) Syndrome CFIDS)/ Myalgic Encephalomyelitis (ME) have been well documented in the Healthcare professions. Large bodies of scientific evidence suggest that the endocrine system is very involved. In fact, it may be the most critical piece of the puzzle that needs to be examined in all future research. Although some subtle immunologic changes have been documented in persons with ME/CFIDS, recent studies on the endocrine system suggest that several hormonal abnormalities may account for the myriad of symptoms. Calkins and colleagues at Johns Hopkins have found that most patients have delayed orthostatic hypotension. Streeten and Bell extended these studies finding that most patients studied have severe hypovolemia. Hormones that prevent these conditions in healthy people are controlled by the pituitary and hypo-thalamus. It is interesting that the symptoms experienced by patients with Pan-Hypothyroidism are virtually identical to CFIDS/ME Endocrine research shows that most patients have low Cortisol levels. Overwhelming research shows a similar pattern to the many autoimmune diseases that occur predominantly in females. What looks like a multi-systemic disease, therefore, could be an endocrine disorder and could possibly explain the predisposition of the female gender. As health care professionals living with the disease, we would like to bridge the gap and help you help us return to our normal, pre-CFIDS/ME lives as best we can.
Soderlund A, Skoge AM, Malterud K.	Department of Public Health and Primary Health Care, University of Bergen, Norway.	"I could not lift my arm holding the fork...". Living with chronic fatigue syndrome.	Scand J Prim Health Care 2000 Sep;18(3):165-9	OBJECTIVES: To explore and describe symptoms and their consequences for patients suffering from chronic fatigue syndrome (CFS). DESIGN: Qualitative data from a group interview, written answers to a questionnaire and a follow-up meeting analysed in accordance with Giorgi's phenomenological approach. SUBJECTS: Purposeful sample of 10 women and 2 men of various ages recruited from the local self-help patient organisation. MAIN OUTCOME MEASURES: Descriptions reflecting the nature, extent and consequences of symptoms regarded as the most substantial by the informants across the group. RESULTS: Extreme exhaustion exceeding the nature of everyday weariness was reported as the worst symptom. The informants perceived reduced muscular strength, continuous weakness and recurrent pain, problems related to memory and concentration, sleep disturbances and excessive sensitivity towards smell, light and sound. Learning abilities had deteriorated, and housework, conversation, reading and watching TV were characterised as exhausting, leading to an unpredictability of everyday life-disturbing social relations. CONCLUSION: The

				extent and nature of symptoms suggest that CSF is an essentially different and far more serious condition than the strains of everyday life. Our findings suggest immunological processes affecting the neuromuscular and central neural system comparable to the effects of cytostatic medication.
Soetekouw PM, Wevers RA, Vreken P, Elving LD, Janssen AJ, van der Veen Y, Bleijenberg G, van der Meer JW.	Department of Medicine, Division of General Internal Medicine 541, University Medical Center St. Radboud, P.O. Box 9101, 6500 HB, Nijmegen, The Netherlands. p.soetekouw@aig.azn.nl	Normal carnitine levels in patients with chronic fatigue syndrome.	Neth J Med 2000 Jul;57(1):20-4	BACKGROUND: Patients with chronic fatigue syndrome (CFS) complain of muscle pain and impaired exercise tolerance. Previous studies show that this is due to systemic carnitine deficiency. We investigated the hypothesis that carnitine deficiency plays an important role in CFS in female CFS patients and compared their results with neighbourhood controls. METHODS: The level of total carnitine, free carnitine, acylcarnitine and carnitine esters were measured in 25 female CFS patients and 25 healthy matched neighbourhood controls in a blinded fashion. RESULTS: The previously reported decreased level of acylcarnitine in CFS patients was not confirmed. There were also no significant differences in levels of total carnitine, free carnitine and 20 carnitine esters between CFS patients and controls. CONCLUSIONS: The present study demonstrates that serum carnitine deficiency does not contribute to or causes the symptoms in many CFS patients.
Spath M, Welzel D, Farber L.	Friedrich-Baur-Institut, University of Munich, MunchenGermany. Michael.Spaeth@LRZ.uni-muenchen.de	Treatment of chronic fatigue syndrome with 5-HT3 receptor antagonists--preliminary results.	Scand J Rheumatol Suppl 2000;113:72-7	OBJECTIVE: The serotonin system presumably is involved in the pathogenesis of chronic fatigue syndrome (CFS). Results from a few studies led to the hypothesis of a "postsynaptic hyperresponsiveness" in CFS. Therefore we intended to evaluate the efficacy of 5-HT3 receptor antagonists in the treatment of CFS. PATIENTS AND METHODS: 2 patient groups (10 patients each; CFS according to the CDC classification criteria) received either oral tropisetron (5 mg once daily) or oral ondansetron (2 x 8 mg daily), open-labelled. Treatment duration was 15 days. Treatment response was evaluated by visual analog scales (VAS) for fatigue and capability. RESULTS: 19 patients finished their respective study. In the tropisetron group 6/9 (VAS fatigue) and 7/9 (VAS capability) patients documented benefit, 8/10 rsp. 8/10 patients in the ondansetron group. The score changes (VAS before and after treatment) in case of response were more pronounced in the tropisetron group. The frequency of concomitant symptoms did not differ significantly in the treatment groups. The overall analysis of both studies showed a remarkable improvement (> or = 35%) of approximately one third of the patients in both VAS. Treatment was well tolerated. CONCLUSION: Our preliminary results encourage to perform placebo-controlled, double-blind studies to further evaluate the efficacy of 5-HT3 receptor antagonists in the treatment of CFS.
Spence VA, Khan F, Belch JJ.	University Department of Medicine, Ninewells Hospital and Medical School, Dundee, Scotland.	Enhanced sensitivity of the peripheral cholinergic vascular response in patients with chronic fatigue syndrome.	Am J Med 2000 Jun 15;108(9):736-9Comment in: Am J Med. 2000 Dec 15;109(9):744	

Starr A, Scalise A, Gordon R, Michalewski HJ, Caramia MD.	Department of Neurology, University of California, Irvine, CA 92697-4290, USA. astarr@uci.edu	Motor cortex excitability in chronic fatigue syndrome.	Clin Neurophysiol 2000 Nov;111(11):2025-31	OBJECTIVE: To use transcranial magnetic stimulation (TMS) to define motor cortical excitability in chronic fatigue syndrome (CFS) subjects during a repetitive, bilateral finger movement task. METHODS: A total of 14 CFS patients were tested and compared with 14 age-matched healthy control subjects. TMS of the motor cortex (5% above threshold) was used to elicit motor evoked potentials (MEPs). Subjects performed regular (3-4/s) repetitive bilateral opening-closing movements of the index finger onto the thumb. MEPs of the first dorsal interosseus (FDI) were measured before, immediately following exercise periods of 30, 60 and 90 s, and after 15 min of rest. RESULTS: Performance, defined by rate of movement, was significantly slower in CFS subjects (3.5/s) than in controls (4. 0/s) independent of the hand measured. The rate, however, was not significantly affected by the exercise duration for either group. The threshold of TMS to evoke MEPs from the FDI muscle was significantly higher in CFS than in control subjects, independent of the hemisphere tested. A transient post-exercise facilitation of MEP amplitudes immediately after the exercise periods was present in controls independent of the hemisphere tested, but was absent in CFS subjects. A delayed facilitation of MEPs after 15-30 min of rest was restricted to the non-dominant hemisphere in controls; delayed facilitation was absent in CFS subjects. CONCLUSIONS: Individuals with CFS do not show the normal fluctuations of motor cortical excitability that accompany and follow non-fatiguing repetitive bimanual finger movements.
Steven ID, McGrath B, Qureshi F, Wong C, Chern I, Pearn-Rowe B.	Royal Australian College of General Practitioners, South Australia.	General practitioners' beliefs, attitudes and reported actions towards chronic fatigue syndrome.	Aust Fam Physician 2000 Jan;29(1):80-5	OBJECTIVE: To undertake a survey of Australian general practitioners (GPs) to explore their beliefs, attitudes and reported actions with respect to chronic fatigue syndrome (CFS). METHOD: A random sample of 2090 Australian GPs, stratified by state, was surveyed in May-August 1995. RESULTS: A 77% response rate was obtained. For the majority of practitioners who pursue a diagnosis of CFS, six symptoms were considered to be of significance: chronic unremitting fatigue for over 6 months; failure to recover energy after rest; reduced exercise tolerance; prostration for several days after exercise; generalised myalgia and poor concentration. Individual counselling was the most frequently used treatment. Thirty-one percent of practitioners reported that they did not believe that CFS is a distinct syndrome. Of these, 70% reported that the most likely cause of chronic fatigue was depression. CONCLUSION: There is considerable diversity of opinion between practitioners about CFS. The diversity extends from questioning whether the syndrome even exists to different strategies for diagnosis and management.
Stewart JM.	Department of Pediatrics, The Center for Pediatric Hypotension, New York Medical College, Valhalla 10595, USA.	Autonomic nervous system dysfunction in adolescents with postural orthostatic tachycardia syndrome and chronic fatigue	Pediatr Res 2000 Aug;48(2):218-26	The objective was to determine the nature of autonomic and vasomotor changes in adolescent patients with orthostatic tachycardia associated with the chronic fatigue syndrome (CFS) and the postural orthostatic tachycardia syndrome (POTS). Continuous electrocardiography and arterial tonometry was used to investigate the heart rate and blood pressure responses before and 3-5 min after head-up tilt in 22 adolescents with POTS and 14 adolescents with CFS, compared with control subjects

		syndrome is characterized by attenuated vagal baroreflex and potentiated sympathetic vasomotion.		comprising 10 healthy adolescents and 20 patients with simple faint. Heart rate and blood pressure variability, determined baroreceptor function using transfer function analysis, and measured cardiac vagal and adrenergic autonomic responses were calculated using timed breathing and the quantitative Valsalva maneuver. Two of 10 healthy controls and 14 of 20 simple faint patients experienced vasovagal syncope during head-up tilt. By design, all CFS and POTS patients experienced orthostatic tachycardia, often associated with hypotension. R-R interval and heart rate variability were decreased in CFS and POTS patients compared with control subjects and remained decreased with head-up tilt. Low-frequency (0.05-0.15 Hz) blood pressure variability reflecting vasomotion was increased in CFS and POTS patients compared with control subjects and increased further with head-up tilt. This was associated with depressed baroreflex transfer indicating baroreceptor attenuation through defective vagal efferent response. Only the sympathetic response remained. Heart rate variability declined progressively from normal healthy control subjects through syncope to POTS to CFS patients. Timed breathing and Valsalva maneuver were most often normal in CFS and POTS patients, although abnormalities in select individuals were found. Heart rate and blood pressure regulation in POTS and CFS patients are similar and indicate attenuated efferent vagal baroreflex associated with increased vasomotor tone. Loss of beat-to-beat heart rate control may contribute to a destabilized blood pressure resulting in orthostatic intolerance. The dysautonomia of orthostatic intolerance in POTS and in chronic fatigue are similar.
Stough C, Withers G.		Sleep Disturbance in Patients with Chronic Fatigue Syndrome and Chronic Fatigue	Journal of Chronic Fatigue Syndrome 2000; 6(2): 37	To examine whether the identification of patients with Chronic Fatigue Syndrome can be made using more objective criteria than presently available (1), we compared 14 patients with Chronic Fatigue Syndrome and 12 patients with chronic fatigue (but who did not meet the criteria for Chronic Fatigue Syndrome) on sleep architecture, continuity, and sleep abnormalities from polysomnography recordings. No differences in sleep continuity or architecture were found between the two groups, except that patients with Chronic Fatigue Syndrome recorded significantly increased sleep latencies. There were no differences in the frequency of sleep disorders. Results indicated that apart from sleep latency, other sleep variables do not adequately differentiate patients with CFS from those with chronic fatigue and that other variables should be examined, which may validly diagnose patients with CFS.
Streeten DH, Thomas D, Bell DS.	Department of Medicine, State University of New York Health Science Center, Syracuse 13210, USA.	The roles of orthostatic hypotension, orthostatic tachycardia, and subnormal erythrocyte volume in the pathogenesis of the chronic fatigue	Am J Med Sci 2000 Jul;320(1):1-8	BACKGROUND: Orthostatic hypotension during upright tilt is an important physical disorder in patients with chronic fatigue syndrome. We have tested its occurrence during prolonged standing, whether it is correctable, and whether reduced circulating erythrocyte volume is present. METHODS: Fifteen patients were randomly selected from a large population of patients with chronic fatigue syndrome, studied, and observed for several years (by DSB). Blood pressure (BP) and heart rate (HR) measured with Dinamap every minute for 30 minutes supine and 60 minutes standing were compared with these findings in 15 healthy age- and gender-matched

		syndrome.		control subjects and later during lower body compression with military antishock trousers (MAST). Plasma catecholamines and circulating erythrocyte and plasma volumes were also measured by isotopic dilution methods. RESULTS: Abnormal findings in the patients included excessive orthostatic reductions in systolic (P < 0.001) and diastolic BP (P < 0.001) and excessive orthostatic tachycardia (P < 0.01), together with presyncopal symptoms in 11 of the 15 patients and in none of the control subjects after standing for 60 min. Lower body compression with the MAST restored all orthostatic measurements to normal and overcame presyncopal symptoms within 10 min. Circulating erythrocyte but not plasma volumes were subnormal in the 12 women (P < 0.01) and plasma norepinephrine concentration rose excessively after standing for 10 min. CONCLUSION: Delayed orthostatic hypotension and/or tachycardia caused by excessive gravitational venous pooling, which is correctable with external lower-body compression, together with subnormal circulating erythrocyte volume, are very frequent, although not invariably demonstrable, findings in moderate to severe chronic fatigue syndrome. When present, they may be involved in its pathogenesis.
Suhadolnik RJ, Peterson DL, Cheney PR, Horvath SE, Reichenbach NL, O'Brien K, Lombardi V, Welsch S, Furr EG, Charubala R, Pfleiderer W.		Biochemical Dysregulation of the 2-5A Synthetase/RNase L Antiviral Defense Pathway in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 223	The aim of the current study was to examine the biochemical defects in KEY components of the 2i,5i-oligoadenylate (2-5A) synthetase/RNase L antiviral pathway in an extended cohort of patients with chronic fatigue syndrome (CFS) from two sites. CFS patients, who met the CDC criteria for CFS, and matched controls were assessed with respect to their general health, depression, and pain. Biochemical assays were completed for three blood draws over a period of one year. Analysis of the mean values for bioactive 2-5A, RNase L activity, low molecular weight (LMW) RNase L in CFS PBMC extracts confirmed the statistically significant upregulation of the 2-5A synthetase/RNase L pathway compared to control PBMC extracts (p = .001, .002, and .007, respectively). Clinical correlates to the biochemical findings included a negative correlation between Karnofsky Performance Score and bioactive 2-5A (p = .025) or RNase L activity (p = .002) and positive correlation between Metabolic Screening Questionnaire and RNase L activity (p = .01) and between interferon- and LMW RNase L (p = .05). The evidence presented in this study more firmly establishes the dysregulation of the 2-5A synthetase/RNase L pathway in CFS.
Sweetman BJ.		Chronic fatigue syndrome in mother and child.	J R Soc Med 2000 Jun;93(6):337-8 Comment on: J R Soc Med. 2000 Mar;93(3):129-34	
Takahashi Y, Ohta S, Sano A, Kuroda Y, Kaji Y, Matsuki M, Matsuo M.	Department of Pediatrics, Tenri Hospital, Nara, Japan.	Does severe nutcracker phenomenon cause pediatric chronic fatigue?	Clin Nephrol 2000 Mar;53(3):174-81	BACKGROUND: In the past five years we experienced 9 fatigued disabled children who were intermittently or persistently absent from school. PATIENTS: They had been suspected to be burdened with psychosomatic disorders, having orthostatic hypotension, postural tachycardia, or other autonomic dysfunction symptoms.

				RESULTS: Investigating the cause of moderate orthostatic proteinuria in some of them, we found by chance severe typical nutcracker phenomenon (NC), which was present in all 9 children complaining of chronic fatigue. CONCLUSION: Their symptoms filled the criteria of chronic fatigue syndrome or idiopathic chronic fatigue (CFS/CF). An association between severe NC and autonomic dysfunction symptoms in children with CFS/CF has been presented.
Takahashi Y, Sano A, Matsuo M.		An effective "transluminal balloon angioplasty" therapy for pediatric chronic fatigue syndrome with nutcracker phenomenon.	Clin Nephrol 2000 Jan;53(1):77-8	
Taylor RR, Jason LA, Torres A.	Department of Psychology, DePaul University, Chicago, IL 60614, USA.	Fatigue rating scales: an empirical comparison.	Psychol Med 2000 Jul;30(4):849-56	BACKGROUND: There has been limited research comparing the efficacy of different fatigue rating scales for use with individuals with chronic fatigue syndrome (CFS). This investigation explored relationships between two commonly-used fatigue rating scales in CFS research, the Fatigue Scale and the Fatigue Severity Scale. Theoretically, these scales have been described as measuring different aspects of the fatigue construct. The Fatigue Scale was developed as a measure of the severity of specific fatigue-related symptoms, while the Fatigue Severity Scale was designed to assess functional outcomes related to fatigue. METHODS: Associations of these scales with the eight definitional symptoms of CFS and with eight domains of functional disability were examined separately in: (1) an overall sample of individuals with a wide range of fatigue severity and symptomatology; (2) a subsample of individuals with CFS-like symptomatology, and, (3) a subsample of healthy controls. RESULTS: Findings revealed that both scales are appropriate and useful measures of fatigue-related symptomatology and disability within a general population of individuals with varying levels of fatigue. However, the Fatigue Severity Scale appears to represent a more accurate and comprehensive measure of fatigue-related severity, symptomatology, and functional disability for individuals with CFS-like symptomatology.
Tomoda A, Miike T, Yamada E, Honda H, Moroi T, Ogawa M, Ohtani Y, Morishita S.	Department of Child Development, Kumamoto University School of Medicine, Japan. tomo@kaiju.medic.kumamoto-u.ac.jp	Chronic fatigue syndrome in childhood.	Brain Dev 2000 Jan;22(1):60-4	Chronic fatigue occurring in previously healthy children and adolescents is one of the most vexing problems encountered by pediatric practitioners. We report three cases, 11, 12 and 13-year-old children, with chronic fatigue syndrome (CFS). They initially developed a low grade fever and generalized fatigue, followed by sleep disturbance and psychosomatic symptoms, and their performance ability deteriorated. They were diagnosed as having CFS on the basis of criteria. To investigate the brain function in CFS patients, we examined the regional cerebral blood flow by single-photon emission-computed tomography (SPECT) with 111 MBq [123I]-iodoamphetamine (123I-IMP) or xenon-computed tomography (Xe-CT), and brain metabolic levels by MR spectroscopy (MRS). Blood flow, expressed as the corticocerebellar ratio (CCR), in

				the left temporal and occipital lobes was markedly lower in cases 2 and 3 than that in healthy subjects reported by another investigator. In case 1, however, blood flow in the left basal ganglia and thalamus was markedly higher than in healthy subjects. The MR spectroscopy (MRS) study revealed remarkable elevation of the choline/creatine ratio in the patients with CFS. None of our patients exhibited evidence of focal structural abnormalities on MRI. These findings suggest that the various clinical symptoms in CFS patients may be closely related to an abnormal brain function.
Treib J, Grauer MT, Haass A, Langenbach J, Holzer G, Woessner R.	Department of Neurology, University Hospital of the Saarland, Homburg, Germany.	Chronic fatigue syndrome in patients with Lyme borreliosis.	Eur Neurol 2000;43(2):107-9	Several authors have reported a chronic fatigue-like syndrome in patients that have suffered from Lyme borreliosis in the past. To further investigate this suspicion of an association without sample bias, we carried out a prospective, double-blind study and tested 1, 156 healthy young males for Borrelia antibodies. Seropositive subjects who had never suffered from clinically manifest Lyme borreliosis or neuroborreliosis showed significantly more often chronic fatigue (p = 0.02) and malaise (p = 0.01) than seronegative recruits. Therefore we believe it is worth examining whether an antibiotic therapy should be considered in patients with chronic fatigue syndrome and positive Borrelia serology. Copyright 2000 S. Karger AG, Basel.
Tuck I, Wallace D, Casalnuova G, May B.		Psychosocial Response of Sufferers of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 2000; 7(3): 49	Chronic Fatigue Syndrome (CFS) is a chronic debilitating disease that affects two to five million persons in the United States. Previous studies examined theories of etiology and have resulted in contradictory findings. This study explored the psychosocial factors associated with CFS. Questionnaires were administered to 49 CFS sufferers and a matched sample of non-CFS sufferers. Significant differences were found in the perception of stress and its causes, coping styles, and emotional responses to affective states as measured by the Ways of Coping, Derogatis Stress, Trait Anger, Perceived Stress, and Profile of Moods scales. Groups were not different on the measure of trait anger. The findings indicated that associated psychosocial factors do influence the illness trajectory and the quality of life of CFS sufferers. These findings have implications for nursing practice.
Tuck I, Wallace D.	School of Nursing, Virginia Commonwealth University, 1220 East Broad Street, P.O. Box 980567, Richmond, VA 23298-0567, USA. ituck@hsc.vcu.edu	Chronic fatigue syndrome: a woman's dilemma.	Health Care Women Int 2000 Jul-Aug;21(5):457-66	Chronic Fatigue Syndrome (CFS) is an illness characterized by fatigue with varying levels of disability. According to the Centers for Disease Control (CDC) there are 2 to 5 million people in the United States who suffer from CFS and a disproportionate number are women. There are many theories of etiology of the condition and controversy has surrounded recommendations for diagnosis and treatment. CFS can mimic other diseases and women are doubly affected since many have comorbid conditions. While diagnoses and treatment are critical to the health of women, having the disease and coping with the symptoms may have a greater impact on their well-being and quality of life. The authors report qualitative data describing the experience of having CFS (N = 22) and quantitative responses of 42 CFS sufferers reporting psychosocial factors. The psychosocial factors were measured by the Derogatis Stress Profile (DSP), Spielberger Trait-Anger Scale, Ways of Coping Survey, Profile of Moods States (POMS) Survey, and the Perceived Stress Scale. The findings

				indicate that CFS changes the lives of women who suffer with the disease and disrupts their relationships, careers, and perceptions of themselves.
Uter W.		Chronic fatigue syndrome and nickel allergy	Contact Dermatitis 2000 Jan;42(1):56-7 Comment on: Contact Dermatitis. 1999 May;40(5):269-72.	
Valling RS.		Report on the Second World Congress on Chronic Fatigue Syndrome and Related Disorders: Towards Effective Diagnosis and Treatment in the 21st Century	Journal of Chronic Fatigue Syndrome 2000; 6(3/4): 3	
van der Steen WJ.	Faculties of Biology and Philosophy, Vrije Universiteit, Amsterdam, The Netherlands. wvds@bio.vu.nl	Chronic fatigue syndrome: a matter of enzyme deficiencies?	Med Hypotheses 2000 May;54(5):853-4	The etiology of chronic fatigue syndrome (CFS) remains an enigma. But literature concerning chronic fatigue which does not focus on CFS points to all sorts of enzyme deficiencies as possible causes. The deficiencies are probably dismissed as causes of CFS because other characteristic symptoms are lacking in CFS patients. But these symptoms are often also lacking in patients with a deficiency. Symptom patterns in enzyme deficiencies are extremely variable. Therefore, patients with CFS should be screened systematically for enzyme deficiencies. Copyright 2000 Harcourt Publishers Ltd.
van der Werf SP, Prins JB, Jongen PJ, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	Abnormal neuropsychological findings are not necessarily a sign of cerebral impairment: a matched comparison between chronic fatigue syndrome and multiple sclerosis.	Neuropsychiatry Neuropsychol Behav Neurol 2000 Jul;13(3):199-203	OBJECTIVE: The aim of this study was to assess the potential impact of effort in comparative studies assessing neurocognitive dysfunction in patients with and without a neurologic diagnosis. BACKGROUND: It was hypothesized that a subgroup within a group of patients with prominent neurocognitive complaints but without a neurologic diagnosis would have impaired performance on a task originally designed to detect malingering. METHOD: We compared the neuropsychological performance of a group of 40 patients with a definite diagnosis of multiple sclerosis (MS) with that of 67 patients with chronic fatigue syndrome (CFS). The Amsterdam Short-Term Memory Test, a forced-choice memory task, served as measure to detect submaximal effort. In addition, we administered a regular neuropsychological task generally considered to be sensitive for cognitive deterioration. RESULTS: Compared with the MS group (13%), a larger proportion of the matched CFS group (30%) obtained scores indicative of reduced effort. In contrast, the proportions of patients scoring below the cutoff value on a conventional neuropsychological test did not differ significantly (17% of MS patients and 16% of CFS patients). CONCLUSIONS: The results obtained raise the question of to what extent abnormal test findings in the absence of documented neurologic impairment should be interpreted as a sign of cerebral

				impairment. The suggestion has been made to screen more often for biased results in comparative research studies so as to enhance valid interpretation of neuropsychological findings.
van der Werf SP, Prins JB, Vercoulen JH, van der Meer JW, Bleijenberg G.	The Netherlands Fatigue Research Group Nijmegen, Department of Medical Psychology and Internal Medicine, University Hospital Nijmegen, Post Box 9101, 6500 HB, Nijmegen, The Netherlands. s.vanderwerf@cksmps.azn.nl	Identifying physical activity patterns in chronic fatigue syndrome using actigraphic assessment.	J Psychosom Res 2000 Nov;49(5):373-9	OBJECTIVE: Changes in physical activity are thought to play an important role in maintaining symptoms in chronic fatigue syndrome (CFS). The aim of this study was to describe intraindividual physical activity patterns in more detail and to identify pervasively passive patients. METHODS: With help of a movement-sensing device, physical activity levels were registered continuously over a 12-day period in 277 CFS patients. Within this registration period, the 10 largest activity peaks were computed. The intensity and duration of these activity peaks and their subsequent rest periods were described and compared to those of 47 healthy controls. In addition, the patients' 12 daily activity scores were used to identify patients who were characterised by low levels of physical activity throughout the registration period. RESULTS: The CFS sample had less intense and shorter activity peaks, while the average rest periods that followed these peaks lasted longer. Approximately one-fourth of the CFS sample differed distinctly from the control group and was labelled as pervasively passive. CONCLUSION: The measurements and classification of actual physical activity levels were found to reduce heterogeneity in the CFS population and therefore could provide the opportunity to optimise behavioural intervention protocols for CFS.
Van Houdenhove B, Vanthuyne S, Neerinckx E		Chronic fatigue syndrome.	Am J Med 2000 Aug 15;109(3):257-9 Comment on: Am J Med. 2000 Feb;108(2):99-105 Am J Med. 2000 Feb;108(2):169-71 Am J Med. 2000 Feb;108(2):172-3	
Visser JT, De Kloet ER, Nagelkerken L.	TNO Prevention and Health, Division of Immunological and Infectious Diseases, P.O. Box 2215, 2301 CE Leiden, The Netherlands.	Altered glucocorticoid regulation of the immune response in the chronic fatigue syndrome.	Ann N Y Acad Sci 2000;917:868-75	It is increasingly recognized that glucocortiocoids (GCs) can have subtle modulatory effects in immunoregulation rather than having generalized immunosuppressive effects. GCs suppress Th1 cells and cellular immunity, but may favor Th2 responses and humoral immunity. The chronic fatigue syndrome (CFS) appears to be associated with a disturbed HPA-axis. Moreover, CFS patients show several immunological changes suggestive of decreased cellular immunity. It is postulated herein that in CFS patients a decreased Th1/Th2 balance may be the result of selective effects of GC on the IL-10/IL-12 regulatory circuit.
Vojdani A, Franco R.		Muliplex PCR for the Detection of Mycoplasma	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 187	A multiplex polymerase chain reaction (PCR) was used to detect mycoplasma infection in human DNA samples of patients with CFS and related illnesses. One set of oligonucleotide primers which are specific for a highly conserved region among all

		fermentans, M. hominis, and M. penetrans in Patients with Chronic Fatigue Syndrome, Fibromyalgia, Rheumatoid Arthritis, and Gulf War Syndrome		members of the genus Mycoplasma along with three other primer sets which are specific for Mycoplasma fermentans, M. hominis, and M. penetrans species were used in this assay. The sensitivity of detection was determined by adding known mycoplasma DNA copy numbers to 1 mg of genomic DNA from healthy subjects. Each sample was subjected to 40 cycles of amplification. The detection level was determined to be 7, 7, 9, and 15 mycoplasma DNA copies per mg of human genomic DNA for M. genus, M. fermentans, M. hominis, and M. penetrans, respectively. The assay was applied to DNA extracted from the PBMCs of individuals suffering from chronic fatigue syndrome (CFS) (n = 100), fibromyalgia (FMS) (n = 40), rheumatoid arthritis (RA) (n = 60), and gulf war syndrome (GWS) (n = 60) and compared to age- and sex-matched healthy individuals (n = 160). The percentage of M. genus infection detected in CFS, FMS, RA, and GWS was 52, 54, 49, and 55%, respectively. M. fermentans was detected in 32, 35, 23, and 36%, M. hominis was detected in 9, 8, 11, and 5%, and M. penetrans was detected in 6, 4, 7, and 3% of CFS, FMS, RA, and GWS patients, respectively. M. genus, M. fermentans, M. hominis, and M. penetrans were detected in 15, 8, 3, and 2% of healthy matched controls. This assay provides a rapid and cost efficient procedure to screen clinical samples for the presence of three potentially pathogenic species of Mycoplasma with a high level of sensitivity and specificity.
Vojdani A, Lapp CW.		The Relationship Between Chronic Fatigue Syndrome and Chemical Exposure	Journal of Chronic Fatigue Syndrome 2000; 5(3/4): 207	Overlapping symptomatologies between chronic fatigue syndrome (CFS) and chemical sensitivity have been observed by different investigators. Interferon-induced proteins 2-5A synthetase and protein kinase RNA (PKR) have been implicated in the viral induction of CFS. The objective of this study was to measure 2-5A and PKR activity in patients with CFS and toxic chemical exposure. Based on the CDC definition and criteria, twenty CFS patients who were positive for viral genome(s) (mainly HHV6; HTLV II, EBV, and CMV) and did not have any history of exposure to toxic chemicals were included in this study. As a comparison, the second group of patients consisted of twenty individuals from the same geographical area who were negative for viral genomes but had been exposed to methyl tertiary-butyl ether concentration of up to 70 ppb and benzene concentration up to 14 ppb. All patients complained of fatigue and other symptoms overlapping between the two groups. From all 40 patients, blood was drawn, leukocyte extract was prepared and assayed for 2-5A synthetase and PKR activity. Clinical specimens which were positive for viral genomes showed from 2. 2-38.7 fold increase in 2-5A activity and 1.3-13.5 fold increase in PKR activities over the background of the healthy controls. Similarly, the second group (negative for viral genomes, but exposed to chemicals) showed a 1.1-29.2 fold increase for 2-5A synthetase and a 1.3-11.6 fold increase for PKR when they were compared to healthy subjects. To elucidate mechanisms involved in viral versus chemical induction of 2-5A synthetase and PKR, MDBK cell lines were cultured either in the presence or absence of HHV6, MTBE, or benzene. 2-5A and PKR activities were

				measured in all the above conditions. A clear induction of 2-5A and PKR was observed when MDBK cells were exposed to HHV6, MTBE, and benzene indicating that induction of interferon-induced proteins are not unique to viruses. We conclude that 2-5A and PKR are not only biomarkers for viral induction of CFS, but biomarkers to other stressors that include MTBE and benzene.
Waxman SG, Ptacek LJ.		Chronic fatigue syndrome and channelopathies	Med Hypotheses 2000 Nov;55(5):457Comment in: Med Hypotheses. 2000 Dec;55(6):524 and Med Hypotheses. 2000 Jan;54(1):59-63.	
Werbach MR.	UCLA School of Medicine, California, USA.	Nutritional strategies for treating chronic fatigue syndrome.	Altern Med Rev 2000 Apr;5(2):93-108	Despite considerable worldwide efforts, no single etiology has been identified to explain the development of chronic fatigue syndrome (CFS). It is likely that multiple factors promote its development, sometimes with the same factors both causing and being caused by the syndrome. A detailed review of the literature suggests a number of marginal nutritional deficiencies may have etiologic relevance. These include deficiencies of various B vitamins, vitamin C, magnesium, sodium, zinc, L-tryptophan, L-carnitine, coenzyme Q10, and essential fatty acids. Any of these nutrients could be marginally deficient in CFS patients, a finding that appears to be primarily due to the illness process rather than to inadequate diets. It is likely that marginal deficiencies not only contribute to the clinical manifestations of the syndrome, but also are detrimental to the healing processes. Therefore, when feasible, objective testing should identify them and their resolution should be assured by repeat testing following initiation of treatment. Moreover, because of the rarity of serious adverse reactions, the difficulty in ruling out marginal deficiencies, and because some of the therapeutic benefits of nutritional supplements appear to be due to pharmacologic effects, it seems rational to consider supplementing CFS patients with the nutrients discussed above, along with a general high-potency vitamin/mineral supplement, at least for a trial period.
White C, Schweitzer R.	Department of Psychology and Counselling, Queensland University of Technology, Brisbane, Australia.	The role of personality in the development and perpetuation of chronic fatigue syndrome.	J Psychosom Res 2000 Jun;48(6):515-24	OBJECTIVES: Qualitative evidence suggests that personality may have special relevance to the predisposition, precipitation and perpetuation of chronic fatigue syndrome (CFS). This study compares three dimensions of personality - perfectionism, self-esteem, and emotional control in the personality profiles of CFS patients (N=44) and a control group (N=44) without a history of CFS, matched for age and gender. METHODS: Participants were assessed on the MPS [Frost RO, Marten P, Lahart C, Rosenblate R. The dimensions of perfectionism. Cognit Ther Res 1990;14:449-468.]; the Rosenberg Self-Esteem Scale [Rosenberg M. Society and the Adolescent Self-image. Princeton, NJ: Princeton Univ Press, 1965.]; the Courtauld Emotional Scale [Watson M, Greer S. Development of a questionnaire measure of emotional control. J Psychosom Res 1983;27:299-305.] and the Marlowe-Crowne

				Social Desirability Scale [Crowne DP, Marlowe D. A new scale of social desirability independent of psychopathology. J Consult Psychol 1960;24:349-354.]. RESULTS: Analyses revealed that the CFS group reported higher levels than the control group on the Total Perfectionism score and Doubts about Actions and the Concern over Mistakes subscales. Furthermore, the CFS group also reported lower self-esteem than the control group. No difference between the two groups was found on the dimensions of emotional control and social desirability response bias. CONCLUSION: A developmental model of CFS, which considers the predisposing, precipitating, and perpetuating factors that may account for the course of the disorder irrespective of etiology, is proposed. In the context of the results, recommendations for practice and future research are discussed.
White KP, Speechley M, Harth M, Ostbye T.	Department of Medicine, University of Western Ontario, London, Canada. kevin.white@lhsc.on.ca	Co-existence of chronic fatigue syndrome with fibromyalgia syndrome in the general population. A controlled study.	Scand J Rheumatol 2000;29(1):44-51	OBJECTIVE: To determine the proportion of adults with fibromyalgia syndrome (FMS) in the general population who also meet the 1988 Centre for Disease Control (CDC) criteria for chronic fatigue syndrome (CFS). METHODS: Seventy-four FMS cases were compared with 32 non-FMS controls with widespread pain and 23 with localized pain, all recruited in a general population survey. RESULTS: Among females, 58.0% of fibromyalgia cases met the full criteria for CFS, compared to 26.1% and 12.5% of controls with widespread and localized pain, respectively (p=0.0006). Male percentages were 80.0, 22.2, and zero, respectively (p=0.003). Compared to those with FMS alone, those meeting the case definitions for both FMS and CFS reported a worse course, worse overall health, more dissatisfaction with health, more non-CFS symptoms, and greater disease impact. The number of total symptoms and non-CFS symptoms were the best predictors of co-morbid CFS. CONCLUSIONS: There is significant clinical overlap between CFS and FMS.
White PD.		The role of physical inactivity in the chronic fatigue syndrome.	J Psychosom Res 2000 Nov;49(5):283-4	
Wittrup IH, Christensen LS, Jensen B, Danneskiold-Samsee B, Bliddal H, Wiik A.	Parker Research Institute, Dept. of Rheumatology, Frederiksberg University Hospital, Copenhagen, Denmark. Irenewittrup@fh.hosp.dk	Search for Borna disease virus in Danish fibromyalgia patients.	Scand J Rheumatol 2000;29(6):387-90	OBJECTIVE: The purpose of this study was to look for Borna disease virus (BDV) in 18 patients with acute onset of fibromyalgia (FMS) following a "flu-like" episode. BDV is a neurotropic RNA virus affecting horses and sheep. Infections in animals have been reported to cause immune mediated disease characterized by abnormalities in behavior. A possible link between BDV and neuropsychiatric diseases in man has been described, and lately a connection to chronic fatigue syndrome (CFS) has been suggested. METHODS: A BDV-specific nested PCR (RT-PCR) was performed on serum and spinal fluid. RESULTS: The BDV genome was not detected in any of the FMS cases. CONCLUSION: Although BDV was not demonstrated in spinal fluid or serum from the tested patients with FMS, we believe that it is important to report our results, since FMS can exhibit many manifestations in common with CFS. Possible reasons for the discrepant findings are discussed.
Woo SB, Schacterle RS,	Dept of Oral Medicine	Salivary gland changes	Oral Surg Oral Med	OBJECTIVE: The purpose of this preliminary study is to compare labial salivary gland

Komaroff AL, Gallagher GT.	and Diagnostic Sciences, Harvard School of Dental Medicine, Brigham and Women's Hospital, USA.	in chronic fatigue syndrome: a case-controlled preliminary histologic study.	Oral Pathol Oral Radiol Endod 2000 Jul;90(1):82-7	changes of 11 patients with chronic fatigue syndrome with control subjects. STUDY DESIGN: Changes in labial salivary glands were graded from 0 to 3+ for acinar dilatation, ductal dilatation, periductal fibrosis, plasmacytic infiltrate, lymphocytic infiltrate, mast cell infiltrate, and lymphocytic aggregates or foci. RESULTS: Four of the 11 subjects had 2+ to 3+ changes in at least 4 of the 7 parameters examined. Only the presence of mast cells was statistically significant between the 2 groups. Two of these 4 patients had 1 lymphocytic focus per 4 mm(2) of tissue. CONCLUSIONS: The salivary gland changes in patients with chronic fatigue syndrome show varying degrees of ductal and acinar dilatation, periductal fibrosis, lymphoplasmacytic infiltrates, and occasional lymphocytic foci, all suggestive of primary gland damage. The one parameter that showed statistical significance was the presence of mast cells (Fisher exact test, 0.0125).
Zhang QW, Natelson BH, Ottenweller JE, Servatius RJ, Nelson JJ, De Luca J, Tiersky L, Lange G.	Department of Neurosciences, University of Medicine and Dentistry-New Jersey Medical School, Newark, USA.	Chronic fatigue syndrome beginning suddenly occurs seasonally over the year.	Chronobiol Int 2000 Jan;17(1):95-9	The fact that many patients with chronic fatigue syndrome (CFS) have an infectious like sudden onset to their illness has led to the hypothesis that CFS is a medical illness. If CFS were, on the other hand, a psychiatric disorder related to symptom amplification, one would expect illness onset to occur randomly over the calendar year. This study tested that hypothesis with 69 CFS patients whose illness was on the more severe side of the illness spectrum; all patients reported sudden illness onset with the full syndrome of sore throat, fatigue/malaise, and diffuse achiness developing over no longer than a 2-day period. Date of illness onset was distinctly nonrandom. It peaked from November through January and was at its lowest from April through May. These data support the hypothesis that an infectious illness can trigger the onset of CFS.

1999				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Arpino C, Carrieri MP, Valesini G, Pizzigallo E, Rovere P, Tirelli U, Conti F, Dialmi P, Barberio A, Rusconi N, Bosco O, Lazzarin A, Saracco A, Moro ML, Vlahov D.	Laboratorio di Epidemiologia e Biostatistica, Istituto Superiore di Sanita, Rome, Italy.	Idiopathic chronic fatigue and chronic fatigue syndrome: a comparison of two case-definitions.	Ann Ist Super Sanita 1999;35(3):435-41	The aim of the study was to compare the signs and symptoms of individuals meeting two different definitions of chronic fatigue syndrome (CFS). Ninety-four patients fitting the eligibility criteria for idiopathic fatigue were enrolled into the study. Of the 94 patients, 48 met the 1988 definition of CFS, 20 the 1994 (but not the 1988) definition of CFS, and 26 met neither definition. The 1994 defined cases were more likely than 1988 defined cases, and non-syndromal individuals to be male, married, and high school educated. The 1994 cases were less likely than 1988 cases to present acute onset, self reported sore throat, mild fever lymphadenopathy, pharyngitis. In conclusion, the 1994 criteria increased the number of patients classified as CFS; however, those who fit only the 1994 criteria were less likely to have an acute symptomatic onset and signs and symptoms suggestive of an infectious process.
Ax S		Coping Differences Between Chronic Fatigue Syndrome Sufferers and Their Carers	Journal of Chronic Fatigue Syndrome 1999: 5(2): 27 - 62	The main objective of the present study was to describe the extent to which CFS sufferers and their carers reported to have used a number of coping strategies over the course of the illness, and to find out if reports of coping differed between groups of these. In addition, associations between married sufferers and carers were investigated. From a methodological point of view, the factorial structure and the usefulness of the Ways of Coping Questionnaire (Folkman & Lazarus, 1988) in CFS was studied. The results indicated no gender differences. There were also no differences between sufferers supported and not supported by a carer. However, the results indicated reduced coping responses of carer husbands. From a methodological point of view, the emergence of comparable factors for sufferers and carers, which were also closely related to the original emotion and problem-focused factors, suggested that the use of the questionnaire was appropriate. The importance of these findings for coping research and therapy are discussed.
Barsky AJ, Borus JF.	Division of Psychiatry, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.	Functional somatic syndromes.	Ann Intern Med 1999 Jun 1;130(11):910-21Comment in: Ann Intern Med. 2000 Feb 15;132(4):327-8; discussion 329-30 Ann Intern Med. 2000 Feb 15;132(4):327; discussion 329-30 Ann Intern Med. 2000 Feb 15;132(4):328-9; discussion 329-30 Ann Intern Med. 2000 Feb 15;132(4):328;	The term functional somatic syndrome has been applied to several related syndromes characterized more by symptoms, suffering, and disability than by consistently demonstrable tissue abnormality. These syndromes include multiple chemical sensitivity, the sick building syndrome, repetition stress injury, the side effects of silicone breast implants, the Gulf War syndrome, chronic whiplash, the chronic fatigue syndrome, the irritable bowel syndrome, and fibromyalgia. Patients with functional somatic syndromes have explicit and highly elaborated self-diagnoses, and their symptoms are often refractory to reassurance, explanation, and standard treatment of symptoms. They share similar phenomenologies, high rates of co-occurrence, similar epidemiologic characteristics, and higher-than-expected prevalences of psychiatric comorbidity. Although discrete pathophysiologic causes may ultimately be found in some patients with functional somatic syndromes, the suffering of these patients is exacerbated by a self-perpetuating, self-validating cycle in which common, endemic, somatic symptoms are incorrectly attributed to serious

			discussion 329-30 Ann Intern Med. 2000 Feb 15;132(4):329; discussion 329-30	abnormality, reinforcing the patient's belief that he or she has a serious disease. Four psychosocial factors propel this cycle of symptom amplification: the belief that one has a serious disease; the expectation that one's condition is likely to worsen; the "sick role," including the effects of litigation and compensation; and the alarming portrayal of the condition as catastrophic and disabling. The climate surrounding functional somatic syndromes includes sensationalized media coverage, profound suspicion of medical expertise and physicians, the mobilization of parties with a vested self-interest in the status of functional somatic syndromes, litigation, and a clinical approach that overemphasizes the biomedical and ignores psychosocial factors. All of these influences exacerbate and perpetuate the somatic distress of patients with functional somatic syndromes, heighten their fears and pessimistic expectations, prolong their disability, and reinforce their sick role. A six-step strategy for helping patients with functional somatic syndromes is presented here. Review, Academic
Baschetti R.		Chronic fatigue syndrome.	N Z Med J 1999 Jun 25;112(1090):242 Comment on: N Z Med J. 1999 Mar 26;112(1084):104-5	
Baschetti R.		Psychological factors and chronic fatigue syndrome.	N Z Med J 1999 Feb 26;112(1082):58-9 Comment on: N Z Med J. 1998 Oct 23;111(1076):410-2	
Baschetti R.		Hydrocortisone and chronic fatigue syndrome.	Lancet 1999 May 8;353(9164):1618; discussion 1619-20 Comment on: Lancet. 1999 Feb 6;353(9151):455-8	
Baschetti R.		Low-dose hydrocortisone for chronic fatigue syndrome.	JAMA 1999 May 26;281(20):1887; discussion 1888-9 Comment on: JAMA. 1998 Sep 23-30;280(12):1061-6	
Baschetti R.		Cortisol deficiency may account for elevated apoptotic cell population in patients	J Intern Med 1999 Apr;245(4):409-10Comment in: J Intern Med. 1999	

		with chronic fatigue syndrome.	Apr;245(4):410-2 Comment on: J Intern Med. 1997 Dec;242(6):465-78	
Baschetti R.		Investigations of hydrocortisone and fludrocortisone in the treatment of chronic fatigue syndrome.	J Clin Endocrinol Metab 1999 Jun;84(6):2263-4	
Baschetti R.		Overlap of chronic fatigue syndrome with primary adrenocortical insufficiency.	Horm Metab Res 1999 Jul;31(7):439 Comment on: Horm Metab Res. 1999 Jan;31(1):18-21	
Baschetti R.		Fibromyalgia, chronic fatigue syndrome, and Addison disease	Arch Intern Med 1999 Nov 8;159(20):2481; discussion 2482-3 Comment on: Arch Intern Med. 1999 Apr 26;159(8):777-85.	
Bazelmans E, Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van Weel C, van der Meer JW, Bleijenberg G.	University Hospital Nijmegen, Department of Medical Psychology, The Netherlands.	Chronic Fatigue Syndrome and Primary Fibromyalgia Syndrome as recognized by GPs.	Fam Pract 1999 Dec;16(6):602-4	BACKGROUND: Prevalence studies on Chronic Fatigue Syndrome (CFS) are rare. Because of the similarity in symptoms, the prevalence of Primary Fibromyalgia Syndrome (PFS) was investigated at the same time. OBJECTIVES: To determine the prevalence of CFS and PFS as recognized by GPs in The Netherlands and to inform them of the existence of CFS. METHODS: A postal questionnaire was sent to all GPs. RESULTS: The questionnaire was returned by 60% of the GPs. Seventy-three per cent reported one or more CFS patients and 83% one or more PFS patients in their practice. CONCLUSION: The estimated prevalence of CFS as recognized by GPs of 112 (PFS 157) patients per 100,000 is a minimum estimate.
Bell IR, Richard R. Bootzin, Gary E. R. Schwartz, Carol M. Baldwin RN, Faith Ballesteros		Differing Patterns of Cognitive Dysfunction and Heart Rate Reactivity in Chemically-Intolerant Individuals With and Without Lifestyle Changes	Journal of Chronic Fatigue Syndrome 1999: 5(2): 3 - 25	The purpose of the present study was to compare specific neuropsychological, psychological, and family history patterns, as well as cardiovascular reactivity of three community-recruited groups of nonsmoking, nonalcoholic middle-aged individuals with and without the symptom of intolerance to low levels of environmental chemicals (CI). CI is a common symptom in chronic fatigue syndrome and fibromyalgia. The groups included: (i) CI who had made associated lifestyle changes because of the CI (CI/LSC); (ii) CI who had not made such changes (CI); and (iii) normals without CI (N). All subjects underwent an evaluation session followed by two laboratory cognitive and psychophysiological test sessions one week apart. The CI/LSC diverged from the other groups in exhibiting poorer performance on the Continuous Visual Memory Test (CVMT) in terms of more false alarms and fewer correct hits, but normal performance on a visuospatial test of divided attention

				(DAT). In contrast, the CI group showed progressively poorer performance on the DAT with practice, but were like the N on the CVMT. The CI group showed a complex sensitization (amplification) of heart rate response to the DAT over time. In addition, the CI/LSC had the highest rate of family histories of alcohol problems and of attention deficit disorder, as well as of antihypertensive medication treatment and self-reported past emotional/physical abuse. Taken together, the data suggest that individuals with CI comprise a heterogeneous population requiring careful definition of subtypes for future studies.
Bell IR, Szarek MJ, Dicenso DR, Baldwin CM, Schwartz GE, Bootzin RR.	Department of Psychology, The University of Arizona, Tucson 85721, USA. IBELL@U.ARIZONA.EDU	Patterns of waking EEG spectral power in chemically intolerant individuals during repeated chemical exposures.	Int J Neurosci 1999 Mar;97(1-2):41-59	Previous studies indicate that low level chemical intolerance (CI) is a symptom of several different controversial conditions with neuropsychiatric features, e.g., chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and "Persian Gulf Syndrome". Prior studies suggest that limbic and/or mesolimbic sensitization may contribute to development of CI. The purpose of this report was to document the waking electroencephalographic (EEG) patterns of individuals with CI during chemical exposures presented over repeated sessions. Three groups of adult subjects who were recruited from the community participated in the study: self-reported CI who had made associated lifestyle changes due to their intolerance (CI/ LSC), self-reported CI who had not made such changes (CI), and normal controls without self-reported CI. Subjects underwent two sessions involving one-minute EEG recordings during exposures to low level chemical odors (a probe for limbic activation). The CI, but not the CI/ LSC, subjects had increased absolute delta power after the chemical exposures during the second, but not the first, session. The findings support the neural sensitization hypothesis for intolerance to low levels of environmental chemicals in vulnerable individuals. As in human studies of stimulant drug sensitization, those with the strongest past history with sensitizing agents may not show-term sensitization to low level exposures in the laboratory.
Berg D, Berg LH, Couvaras J, Harrison H.	HEMEX Laboratories, Inc., Phoenix, Arizona 85021, USA.	Chronic fatigue syndrome and/or fibromyalgia as a variation of antiphospholipid antibody syndrome: an explanatory model and approach to laboratory diagnosis.	Blood Coagul Fibrinolysis 1999 Oct;10(7):435-8	Chronic Fatigue and/or Fibromyalgia have long been diseases without definition. An explanatory model of coagulation activation has been demonstrated through use of the ISAC panel of five tests, including, Fibrinogen, Prothrombin Fragment 1+2, Thrombin/ AntiThrombin Complexes, Soluble Fibrin Monomer, and Platelet Activation by flow cytometry. These tests show low level coagulation activation from immunoglobulins (Igs) as demonstrated by Anti-B2GPI antibodies, which allows classification of these diseases as a type of antiphospholipid antibody syndrome. The ISAC panel allows testing for diagnosis as well as monitoring for anticoagulation protocols in these patients.
Bickerton S.		How she learned to live with chronic fatigue syndrome.	Nurs Times 1999 Jun 2-8;95(22):39	
Blenkiron P, Edwards R, Lynch S.	Division of Psychiatry and Behavioural	Associations between perfectionism, mood,	J Nerv Ment Dis 1999 Sep;187(9):566-70	This study investigated possible associations between perfectionistic personality traits, mood, and fatigue in chronic fatigue syndrome (CFS). Forty CFS sufferers

	Sciences in Relation to Medicine, St. James's University Hospital, Leeds, United Kingdom.	and fatigue in chronic fatigue syndrome: a pilot study.		referred to tertiary care and 31 control healthy subjects completed the Multidimensional Perfectionism Scale (MPS), Chalder Fatigue Questionnaire, and Hospital Anxiety and Depression (HAD) scale. Total perfectionism scores did not correlate with fatigue, anxiety, or depression in either group. Other-oriented MPS scores were significantly lower among CFS sufferers (p = .0019), especially women, and correlated negatively with physical fatigue levels overall (R = -0.27, p = .02). Total and socially prescribed MPS scores correlated with age for the CFS group alone (p = .05). Possible reasons why this study did not confirm a positive association between perfectionism and CFS are discussed. The finding that CFS sufferers set lower standards and have lower expectations for significant others may have implications for rehabilitation and recovery from this disorder.
Bounous G, Molson J.	Department of Surgery, McGill University, and Medical Research Council of Canada.	Competition for glutathione precursors between the immune system and the skeletal muscle: pathogenesis of chronic fatigue syndrome.	Med Hypotheses 1999 Oct;53(4):347-9	The chronic fatigue syndrome (CFS) is typically associated or follows a recognized or presumed infection. Abnormalities of both humoral and cellular immunity have been demonstrated in a substantial proportion of patients with CFS. The most consistent findings are of impaired lymphocyte responses to mitogen. As an antioxidant, glutathione (GSH) is essential for allowing the lymphocyte to express its full potential without being hampered by oxiradical accumulation. Hence, protracted challenge of the immunocytes may lead to cellular GSH depletion. Because GSH is also essential to aerobic muscular contraction, an undesirable competition for GSH precursors between the immune and muscular systems may develop. It is conceivable that the priority of the immune system for the survival of the host has drawn to this vital area the ever-diminishing GSH precursors, thus depriving the skeletal muscle of adequate GSH precursors to sustain a normal aerobic metabolism resulting in fatigue and eventually myalgia.
Breau LM, McGrath PJ, Ju LH.	Department of Psychology, Dalhousie University, Halifax, Canada.	Review of juvenile primary fibromyalgia and chronic fatigue syndrome.	J Dev Behav Pediatr 1999 Aug;20(4):278-88	This article reviews the current literature on childhood fibromyalgia and chronic fatigue syndrome. In doing so, it questions assumptions about the presumed nature of the disorders-that they are distinct from each other and are duplicates of their adult counterparts. It also attempts to synthesize the available data to reach some preliminary judgments about these disorders: that fibromyalgia and chronic fatigue syndrome may be related in children and may not be duplicates of the adult disorders; that psychological and psychosocial factors are unlikely contributors to the etiology of these disorders; and that the evidence is increasingly pointing to a role for genetic factors in their etiology. A discussion of the research into treatments for childhood fibromyalgia and chronic fatigue syndrome highlights the lack of well-designed, controlled studies. Finally, directions for future research are offered where results of the current literature are unclear.
Brunello N, Akiskal H, Boyer P, Gessa GL, Howland RH, Langer SZ, Mendlewicz J, Paes	Center of Neuropharmacology, Institute of Pharmacological	Dysthymia: clinical picture, extent of overlap with chronic fatigue syndrome,	J Affect Disord 1999 Jan-Mar;52(1-3):275-90	Dysthymia, as defined in the American Psychiatric Association and International Classification of Mental Disorders, refers to a prevalent form of subthreshold depressive pathology with gloominess, anhedonia, low drive and energy, low self-esteem and pessimistic outlook. Although comorbidity with panic, social phobic, and

de Souza M, Placidi GF, Racagni G, Wessely S.	Sciences, University of Milan, Italy. brunello@isfunix.farma.unimi.it	neuropharmacological considerations, and new therapeutic vistas.		alcohol use disorders has been described, the most significant association is with major depressive episodes. Family history is loaded with affective, including bipolar, disorders. The latter finding explains why dysthymia, especially when onset is in childhood, can lead to hypomanic switches, both spontaneously and upon pharmacologic challenge in as many as 30%. Indeed, antidepressants from different classes -tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), reversible inhibitors of monoamine oxidase A (RIMAs), selective serotonin-reuptake inhibitors (SSRIs) and, more recently, amisulpride, and spanning noradrenergic, serotonergic as well as dopaminergic mechanisms of action - have been shown to be effective against dysthymia in an average of 65% of cases. This is a promising development because social and characterologic disturbances so pervasive in dysthymia often, though not always, recede with continued pharmacotherapy beyond acute treatment. Despite symptomatic overlap of dysthymia with chronic fatigue syndrome - especially with respect to the cluster of symptoms consisting of low drive, lethargy, lassitude and poor concentration - neither the psychopathologic status, nor the pharmacologic response profile of the latter syndrome is presently understood. Chronic fatigue today is where dysthymia was two decades ago. We? submit that the basic science - clinical paradigm that has proven so successful in dysthymia could, before too long, crack down the conundrum of chronic fatigue as well. At a more practical level, we raise the possibility that a subgroup within the chronic fatigue group represents a variant of dysthymia.
Buchwald D, Herrell R, Ashton S, Belcourt M, Schmaling K, Goldberg J.	Department of Medicine, University of Washington, Seattle, USA. dedra@u.washington.edu	The Chronic Fatigue Twin Registry: method of construction, composition, and zygosity assignment.	Twin Res 1999 Sep;2(3):203-11	Chronic fatigue syndrome (CFS) and the symptom of chronic fatigue are conditions of unknown etiology. The Centers for Disease Control and Prevention (CDC) define CFS as an illness characterized by > or = 6 months of disabling fatigue associated with muscle pain, pharyngitis, and alterations in mood, sleep and neurocognition. We constructed a registry of twins with chronic fatigue to facilitate research on the impact of illness, the associated medical and psychosocial factors, and the heterogeneous proposed mechanisms for these conditions. We have recruited 204 twin pairs in which one or both members reported persistent fatigue through patient support group newsletters (60%), clinicians/researchers familiar with CFS (12%), notices placed on electronic bulletin boards for CFS (11%), twin organizations and researchers (6%), relatives and friends (3%) and other sources (8%). Complete data are available for 177 pairs (87%). Twins completed an extensive questionnaire booklet that included measures of physical and mental health, functional status, and psychosocial factors; a structured psychiatric interview was also conducted by telephone. Twins were classified using three increasingly more stringent diagnostic criteria for chronic fatigue: 1) > or = 6 months of fatigue (115 discordant and 61 concordant pairs); 2) chronic fatigue with additional symptoms and application of the medial exclusions of the CDC CFS case definition as obtained by self-report (92 discordant and 41 concordant pairs) and; 3) chronic fatigue with additional symptoms

				unexplained by self-reported medical conditions and psychiatric diagnoses as determined by the structured interview (69 discordant pairs and 25 concordant pairs). Despite the limitations of a volunteer registry, the Chronic Fatigue Twin Registry promises to be an important resource for research on CFS and chronic fatigue.
Buckley L, MacHale SM, Cavanagh JT, Sharpe M, Deary IJ, Lawrie SM.	Department of Psychiatry, University of Edinburgh and Royal Edinburgh Hospital, UK.	Personality dimensions in chronic fatigue syndrome and depression.	J Psychosom Res 1999 Apr;46(4):395-400	Chronic fatigue syndrome (CFS) is a poorly understood condition. Possible etiological factors include infectious agents, psychiatric disorders, and personality characteristics. We examined personality dimensions in 30 nondepressed patients with CFS, 20 patients with major depressive disorder (MDD), and 15 healthy controls. On the NEO-FFI, patients with CFS scored significantly lower than healthy controls on the extroversion subscale. On the neuroticism dimension of the Eysenck Personality Questionnaire (EPQ), patients with MDD scored higher than those with CFS, who in turn scored significantly higher than the healthy controls. CFS patients rated themselves as higher on neuroticism and less extroverted when ill than when they were well. Our results suggest that high scores on neuroticism and low scores on extroversion in CFS could be a reaction to chronic illness. Controlled Clinical Trial
Buskila D.	Department of Medicine B, Soroka Medical Center, Beer Sheva, Israel.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol 1999 Mar;11(2):119-26	Fibromyalgia was almost completely absent from an urban affluent population compared with poor urban and rural communities. Seventeen percent of Gulf War veterans with soft tissue syndromes had fibromyalgia, a much higher rate than was seen in previous studies of rheumatic disease in the military population. A state of central hyperexcitability in the nociceptive system was reported in fibromyalgia. Altered functioning of the stress-response system has been further documented in fibromyalgia and chronic fatigue syndrome. Administration of growth hormone to patients with fibromyalgia who have low levels of insulin-like growth factor 1 resulted in improvement in their symptoms and tenderness. An association between chronic fatigue syndrome and initial infections was demonstrated. A correlation between particular immunologic abnormalities and measures of disease severity was documented in chronic fatigue syndrome. Concomitant fibromyalgia in other rheumatic diseases was a major contributor to poor quality of life. A favorable outcome of fibromyalgia in children was reported; the majority of patients improved over 2 to 3 years of follow-up. Treatment of patients with fibromyalgia continues to be of limited success.
Cannon JG, Angel JB, Ball RW, Abad LW, Fagioli L, Komaroff AL.	Department of Medicine, New England Medical Center, Boston, Massachusetts 02111, USA. jgc2@psu.edu	Acute phase responses and cytokine secretion in chronic fatigue syndrome.	J Clin Immunol 1999 Nov;19(6):414-21	This study addresses the hypothesis that clinical manifestations of chronic fatigue syndrome (CFS) are due in part to abnormal production of or sensitivity to cytokines such as interleukin-1beta (IL-1beta) and IL-6 under basal conditions or in response to a particular physical stress: 15 min of exercise consisting of stepping up and down on a platform adjusted to the height of the patella. The study involved 10 CFS patients and 11 age-, sex-, and activity-matched controls: of these, 6 patients and 4 controls were tested in both the follicular and the luteal phases of the menstrual cycle, and the remainder were tested in only one phase, for a total of 31 experimental sessions.

				Prior to exercise, plasma concentrations of the acute phase reactant alpha2-macroglobulin were 29% higher in CFS patients (P < 0.008) compared to controls. Secretion of IL-6 was generally higher for CFS patients (approximately 38%), however, this difference was statistically significant only if all values over a 3-day period were analyzed by repeated-measures ANOVA (P = 0.035). IL-6 secretion correlated with plasma alpha2-macroglobulin in control subjects at rest (R = 0.767, P = 0.001). Immediately after exercise, the CFS patients reported greater ratings of perceived exertion (P=0.027) compared to the healthy control subjects. Ratings of perceived exertion correlated with IL-1beta secretion by cells from healthy control subjects (R = 0.603, P = 0.022), but not from CFS patients, and IL-1beta secretion was not different between groups. Exercise induced a slight (< 12%) but significant (P = 0.006) increase in IL-6 secretion, but the responses of the CFS patients were not different than controls. Furthermore, no significant exercise-induced changes in body temperature or plasma alpha2-macroglobulin were observed. These data indicate that under basal conditions, CFS is associated with increased IL-6 secretion which is manifested by chronically elevated plasma alpha2-macroglobulin concentrations. These modest differences suggest that cytokine dysregulation is not a singular or dominant factor in the pathogenesis of CFS.
Castell LM, Yamamoto T, Phoenix J, Newsholme EA.	University Department of Biochemistry, Oxford, UK. cat@bioch.ox.ac.uk	The role of tryptophan in fatigue in different conditions of stress.	Adv Exp Med Biol 1999;467:697-704	Tryptophan is the precursor for the neurotransmitter 5-hydroxytryptamine (5-HT), which is involved in fatigue and sleep. It is present in bound and free from in the blood, where the concentration is controlled by albumin binding to tryptophan. An increase in plasma free tryptophan leads to an increased rate of entry of tryptophan into the brain. This should lead to a higher level of 5-HT which may cause central fatigue. Central fatigue is implicated in clinical conditions such as chronic fatigue syndrome and post-operative fatigue. Increased plasma free tryptophan leads to an increase in the plasma concentration ratio of free tryptophan to the branched chain amino acids (BCAA) which compete with tryptophan for entry into the brain across the blood-brain barrier. The plasma concentrations of these amino acids were measured in chronic fatigue syndrome patients (CFS) before and after exercise (Castell et al., 1998), and in patients undergoing major surgery (Yamamoto et al., 1997). In the CFS patients, the pre-exercise concentration of plasma free tryptophan was higher than in controls (p < 0.05) but did not change during or after exercise. This might indicate an abnormally high level of brain 5-HT in CFS patients leading to persistent fatigue. In the control group, plasma free tryptophan was increased after maximal exercise (p < 0.001), returning towards baseline levels 60 min later. The apparent failure of the CFS patients to change the plasma free tryptophan concentration or the free tryptophan/BCAA ratio during exercise may indicate increased sensitivity of brain 5-HT receptors, as has been demonstrated in other studies (Cleare et al., 1995). In post-operative recovery after major surgery plasma free tryptophan concentrations were markedly increased compared with baseline

				levels; the plasma free tryptophan/BCAA concentration ratio was also increased after surgery. Plasma albumin concentrations were decreased after surgery: this may account for the increase in plasma free tryptophan levels. Provision of BCAA has improved mental performance in athletes after endurance exercise (Blomstrand et al., 1995, 1997). It is suggested that BCAA supplementation may help to counteract the effects of an increase in plasma free tryptophan, and may thus improve the status of patients during or after some clinically stressful conditions.
Charnock D, Shepperd S, Needham G, Gann R.	University of Oxford, Division of Public Health and Primary Health Care, Institute of Health Sciences.	DISCERN: an instrument for judging the quality of written consumer health information on treatment choices.	J Epidemiol Community Health 1999 Feb;53(2):105-11	OBJECTIVE: To develop a short instrument, called DISCERN, which will enable patients and information providers to judge the quality of written information about treatment choices. DISCERN will also facilitate the production of new, high quality, evidence-based consumer health information. DESIGN: An expert panel, representing a range of expertise in consumer health information, generated criteria from a random sample of information for three medical conditions with varying degrees of evidence: myocardial infarction, endometriosis, and chronic fatigue syndrome. A graft instrument, based on this analysis, was tested by the panel on a random sample of new material for the same three conditions. The panel re-drafted the instrument to take account of the results of the test. The DISCERN instrument was finally tested by a national sample of 15 information providers and 13 self help group members on a random sample of leaflets from 19 major national self help organisations. Participants also completed an 8 item questionnaire concerning the face and content validity of the instrument. RESULTS: Chance corrected agreement (weighted kappa) for the overall quality rating was kappa = 0.53 (95% CI kappa = 0.48 to kappa = 0.59) among the expert panel, kappa = 0.40 (95% CI kappa = 0.36 to kappa = 0.43) among information providers, and kappa = 0.23 (95% CI kappa = 0.19 to kappa = 0.27) among self help group members. Higher agreement levels were associated with experience of using the instrument and with professional knowledge of consumer health information. Levels of agreement varied across individual items on the instrument, reflecting the need for subjectivity in rating certain criteria. The trends in levels of agreement were similar among all groups. The final instrument consisted of 15 questions plus an overall quality rating. Responses to the questionnaire after the final testing revealed the instrument to have good face and content validity and to be generally applicable. CONCLUSIONS: DISCERN is a reliable and valid instrument for judging the quality of written consumer health information. While some subjectivity is required for rating certain criteria, the findings demonstrate that the instrument can be applied by experienced users and providers of health information to discriminate between publications of high and low quality. The instrument will also be of benefit to patients, though its use will be improved by training.
Chia JK, Chia LY.	Torrance Memorial Medical Center, California, USA.	Chronic Chlamydia pneumoniae infection: a treatable cause of	Clin Infect Dis 1999 Aug;29(2):452-3	

	chiasann@pol.net	chronic fatigue syndrome.		
Christodoulou C, Deluca J, Johnson SK, Lange G, Gaudino EA, Natelson BH.	University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, USA. cchristo@kmrrec.org	Examination of Cloninger's basic dimensions of personality in fatiguing illness: chronic fatigue syndrome and multiple sclerosis.	J Psychosom Res 1999 Dec;47(6):597-607	Relatively few studies have examined the personality characteristics of patients with chronic fatigue syndrome (CFS). The personality profiles of 38 CFS subjects were compared with 40 healthy controls and 40 subjects with multiple sclerosis (MS), a chronic illness that shares many symptoms with CFS (e.g., fatigue), but has a known neurological substrate. Subjects were examined within Cloninger's biosocial theory of personality, which delineates basic dimensions of temperament. Both illness groups displayed similarly elevated levels of Harm Avoidance, and lower levels of Reward Dependence as compared with healthy controls. The MS group showed a lower level of Persistence than controls and CFS subjects. Implications for the relationship between chronic illness and personality are discussed.
Clapp LL, Richardson MT, Smith JF, Wang M, Clapp AJ, Pieroni RE.	Health, Physical Education, and Recreation Department, Southwest Texas State University, San Marcos 78666, USA. ll12@swt.edu	Acute effects of thirty minutes of light-intensity, intermittent exercise on patients with chronic fatigue syndrome.	Phys Ther 1999 Aug;79(8):749-56Comment in: Phys Ther. 2000 Jan;80(1):115	BACKGROUND AND PURPOSE: Currently, there is no consensus on exercise prescription for patients with chronic fatigue syndrome (CFS). This investigation examined whether light-intensity, intermittent physical activity exacerbated symptoms in patients with CFS immediately following exercise to 7 days following exercise. Subjects. Subjects were 9 women (mean age=44.2 years, SD=8.4, range=29-56; mean weight=74.2 kg, SD=18.8, range=56.36-110.91; and mean height=1.63 m, SD=0.8, range=1.55-1.78) and 1 man (age=48 years, weight=97.1 kg, and height= 1.98 m) who met the Centels for Disease Control and Prevention's criteria fi)r (FS. METHODS: Subjects performed 10 discontinuous 3-minute exercise bouts (separated by 3 minutes of recovery) at a self-selected, comfortable walking pace on a treadmill. Oxygen consumption, minute ventilation, respiratory exchange ratio, and heart rate were measured every minute during the exercise session. To assess degree of disability, general health status, activity level, symptoms, and mood, subjects completed various questionnaires before and after exercise. RESULTS: Results indicated that degree of disability, general health status, symptoms, and mood did not change immediately and up to 7 days following exercise. CONCLUSION AND DISCUSSION: Thirty minutes of intermittent walking did not exacerbate symptoms in subjects with CFS. The physiological data did not show any abnormal response to exercise. Although this study did not determine whether 30 minutes of continuous versus intermittent exercise would exacerbate symptoms, all 10 subjects felt that they could not exercise continuously for 30 minutes without experiencing symptom exacerbation. Despite this limitation, the results indicate that some individuals with CFS may be able to use low-level, intermittent exercise without exacerbating their symptoms.
Clarke JN.	Department of Sociology and Anthropology, Wilfrid Laurier University,	Chronic fatigue syndrome: gender differences in the search for legitimacy.	Aust N Z J Ment Health Nurs 1999 Dec;8(4):123-33	This study employs qualitative research methods to describe and compare the experiences of men and women with chronic fatigue syndrome (CFS), focusing on respondents' self-perceived illness experience and relationship with medical practitioners. Data were collected from 59 respondents (18 male, 41 female) in

	Waterloo, Ontario, Canada.			telephone interviews using an open-ended focus interview schedule. While respondents explained the causes of the disease in ways that were largely gender appropriate, they did not experience the disease itself in gender different ways. The evidence of the study points to a clear dichotomy between ways in which men and women experience the disease and differences in the ways in which they are treated by the medical profession.
Cleare AJ, Heap E, Malhi GS, Wessely S, O'Keane V, Miell J.	Department of Psychological Medicine, Guy's King's and St Thomas' School of Medicine and the Institute of Psychiatry, London, UK. a.cleare@iop.bpmf.ac.uk	Low-dose hydrocortisone in chronic fatigue syndrome: a randomised crossover trial.	Lancet 1999 Feb 6;353(9151):455-8Comment in: Lancet. 1999 Feb 6;353(9151):424-5 Lancet. 1999 May 8;353(9164):1618-9; discussion 1619-20 Lancet. 1999 May 8;353(9164):1618; discussion 1619-20 Lancet. 1999 May 8;353(9164):1619-20	BACKGROUND: Reports of mild hypocortisolism in chronic fatigue syndrome led us to postulate that low-dose hydrocortisone therapy may be an effective treatment. METHODS: In a randomised crossover trial, we screened 218 patients with chronic fatigue. 32 patients met our strict criteria for chronic fatigue syndrome without co-morbid psychiatric disorder. The eligible patients received consecutive treatment with low-dose hydrocortisone (5 mg or 10 mg daily) for 1 month and placebo for 1 month; the order of treatment was randomly assigned. Analysis was by intention to treat. FINDINGS: None of the patients dropped out. Compared with the baseline self-reported fatigue scores (mean 25.1 points), the score fell by 7.2 points for patients on hydrocortisone and by 3.3 points for those on placebo (paired difference in mean scores 4.5 points [95% CI 1.2-7.7], p=0.009). In nine (28%) of the 32 patients on hydrocortisone, fatigue scores reached a predefined cut-off value similar to the normal population score, compared with three (9%) of the 32 on placebo (Fisher's exact test p=0.05). The degree of disability was reduced with hydrocortisone treatment, but not with placebo. Insulin stress tests showed that endogenous adrenal function was not suppressed by hydrocortisone. Minor side-effects were reported by three patients after hydrocortisone treatment and by one patient after placebo. INTERPRETATION: In some patients with chronic fatigue syndrome, low-dose hydrocortisone reduces fatigue levels in the short term. Treatment for a longer time and follow-up studies are needed to find out whether this effect could be clinically useful.
Csef H.	Medizinischen Poliklinik, Universitat Wurzburg.	[Similarities of chronic fatigue syndrome, fibromyalgia and multiple chemical sensitivity].[article in German]	Dtsch Med Wochenschr 1999 Feb 12;124(6):163-9	
De Becker P, De Meirleir K, Joos E, Campine I, Van Steenberge E, Smitz J, Velkeniers B.	Faculty of Medicine and Pharmacy, Vrije Universiteit Brussel, Belgium. pdbeck@minf.vub.ac.be	Dehydroepiandrosterone (DHEA) response to i.v. ACTH in patients with chronic fatigue syndrome.	Horm Metab Res 1999 Jan;31(1):18-21Comment in: Horm Metab Res. 1999 Jul;31(7):439	Previous studies have demonstrated concentrating neuroendocrinological disturbances in chronic fatigue syndrome (CFS) patients, concentrating in particular on low cortisol levels and a hypothalamic deficiency. In order to investigate the dynamic response of the adrenal glands, we measured dehydroepiandrosterone (DHEA) in serum after adreno-corticotropic hormone (ACTH) stimulation during 60 minutes in 22 CFS-patients and 14 healthy controls. We found normal basal DHEA levels, but a blunted serum DHEA response curve to i.v. ACTH injection. This

				observation adds to the large amount of evidence of endocrinological abnormalities in CFS. Relative glucocorticoid deficiency might contribute to the overall clinical picture in CFS, and could explain some of the immunological disturbances observed in this syndrome.
Dessein PH, Shipton EA.		Hydrocortisone and chronic fatigue syndrome.	Lancet 1999 May 8;353(9164):1618; discussion 1619-20 Comment on: Lancet. 1999 Feb 6;353(9151):455-8	
Doyle JP, Frank E, Saltzman LE, McMahon PM, Fielding BD.	Division of General Medicine, Rollins School of Public Health, Emory University School of Medicine, Atlanta, Georgia 30303, USA.	Domestic violence and sexual abuse in women physicians: associated medical, psychiatric, and professional difficulties.	J Womens Health Gend Based Med 1999 Sep;8(7):955-65	Physicians have been called on to identify victims of domestic violence (DV) and sexual abuse (SA). Few data exist, however, on the prevalence of DV and SA in physicians themselves or on the personal or professional sequelae of such experiences. We determined the reported lifetime prevalence of DV and SA among women physicians and the personal characteristics, health-related factors, and work-related factors associated with these forms of abuse. We used data from the Women Physicians' Health Study, a large (n = 4501 respondents), nationally distributed questionnaire study that included questions on DV and SA histories, personal characteristics, and psychiatric, medical, and work-related histories. We compared the characteristics of women physicians with and without histories of DV or SA. The logistic models indicate that women physicians reporting DV histories (3.7% of the population) were significantly ($p < 0.05$) less likely to be single and significantly more likely to report depression histories, suicide attempts, substance abuse, current or past cigarette smoking, severe daily stress at home, chronic fatigue syndrome, and DV experienced by their mothers. Women physicians reporting SA histories (4.7% of the population) were significantly more likely to be younger than 60 years, identify themselves as homosexual or bisexual, to have specialized in psychiatry, obstetrics and gynecology, or emergency medicine, and to report histories of depression, suicide attempts, eating disorders, and fair or poor perceived health status. Although the reported lifetime prevalence of DV and SA among women physicians is below other reported figures, such experiences are associated with medical and psychiatric difficulties that could negatively affect them personally and professionally.
Duncan RB		Latency Immunity and Therapy: A Clinical Study of Latent Epstein Barr Virus Incidence in 297 Idiopathic Chronic Fatigue Patients with Plausible Hypotheses	Journal of Chronic Fatigue Syndrome 1999: 5(2): 77 - 95	Organ cells of the body retain an Immune Activity System comparable to protozoa. The cells' immunity memory templates are latent proteins, microbes, their toxins and chemicals (latentees). Excess latentees are detected and excreted by latency therapy. Their excretion induces immediate and/or delayed symptoms and signs recognized by the patient. Foreign latent materials (latentors) enter the body and bypass the natural immune system to be taken up selectively by organ cell groups. Active infection/disease and allergens (antigens) involve the natural immune system antibodies. Latent infection/disease and allergens (latentors) involve the Organ Cell

				Immunity as intracellular latentees. Clinical laboratory testing is inappropriate. This Clinical Anecdotal Study compiles 297 patients who obtained little or no relief from conventional and alternative medicine (duration: 63% > three years). Patients provoked symptoms to two or more of 16 viruses, in particular Epstein Barr Virus. Latency therapy (heat, saunas, massage, tolerated exercise and sweating during sleep, the auto-sauna) dilutions stimulated excretion until symptoms/signs cleared. The principals were Epstein Barr Virus 67.3%, 200 patients; 13 individual viruses 30.0%, 89 patients; non-viral 2.6%, 8 patients. Latency therapy < 50% improvement = 16.5%; 50% to 80% = 26.6%; 80% to 100% = 46.7%; failures = 11%. Fourteen patients gave positive Epstein Barr Virus serology. A latency immunity concept explains affected subjective symptoms and illnesses and offers a treatment which complements related medical therapies
Elkins LE, Pollina DA, Scheffer SR, Krupp LB.	Department of Neurology, State University of New York at Stony Brook 11794-8121, USA.	Psychological states and neuropsychological performances in chronic Lyme disease.	Appl Neuropsychol 1999;6(1):19-26	The neuropsychiatric sequelae of chronic Lyme disease remains unclear. This study sought to characterize the psychological status of a group of participants who met criteria for post-Lyme syndrome (PLS). These measures were then used to examine the influence of psychological status on neuropsychological performances. Thirty PLS participants completed a structured psychiatric interview, the Positive and Negative Affect Schedule, the Lyme Symptom Checklist, and a battery of neuropsychological tests. As a group, the PLS participants did not appear to have an elevated incidence of psychiatric disorders, and psychiatric history was not useful for understanding neuropsychological performances or symptom reports. The mood of the PLS participants was characterized by lowered levels of positive affect (PA) and typical levels of negative affect. This combination can be distinguished from depression and is consistent with previous findings of affect patterns in individuals with chronic fatigue syndrome. PA was also linked to both total symptom severity and severity of cognitive complaints, but not to duration of illness, neurological manifestations at initial diagnosis, or treatment history. Relative to published normative data, neuropsychological performances were not in the impaired range on any measure. Neither psychological status nor symptom report were useful for understanding any aspect of cognitive functioning. It is concluded that decreased PA is the most useful marker of psychological functioning in PLS.
Endicott NA.	Department of Research, Assessment & Training, New York State Psychiatric Institute, New York, USA.	Chronic fatigue syndrome in private practice psychiatry: family history of physical and mental health.	J Psychosom Res 1999 Oct;47(4):343-54	Forty-five psychiatric patients with chronic fatigue syndrome (CFS) were compared, using the case-control method, to two control groups selected from the same practice and matched on age, gender, and psychiatric diagnosis. The first control group (C-I, N=90) was selected on the basis of relatively good physical health. The second control group (C-II, N=45) was selected without regard to physical health. The reported family history of physical health revealed: the CFS mothers died at a younger age than the C-II mothers; both parents died before age 65 among the CFS parents more frequently than did the C-I parents; and the CFS parents had an increased prevalence of cancer, autoimmune disorders, and CFS-like conditions as

				compared to the families of one or both control groups. The reported family history of mental disorders revealed no significant differences in any of these conditions between the CFS patients and either control group.
Evengard B, Briese T, Lindh G, Lee S, Lipkin WI.	Department of Immunology, Microbiology, Pathology and Infectious Diseases, Clinic for Infectious Diseases, Karolinska Institutet at Huddinge University Hospital.	Absence of evidence of Borna disease virus infection in Swedish patients with Chronic Fatigue Syndrome.	J Neurovirol 1999 Oct;5(5):495-9	Chronic Fatigue Syndrome (CFS) is characterized by debilitating fatigue, somatic symptoms and cognitive impairment. An infectious basis has been proposed; candidate agents include enteroviruses, herpesviruses, retroviruses and Borna disease virus (BDV), a novel neurotropic virus associated with neuropsychiatric disorders. Sera and peripheral blood mononuclear cells (PBMC) from Swedish CFS patients were assayed for evidence of infection using ELISA and Western immunoblot for detection of antibodies to BDV proteins N, P and gp18; and using nested reverse transcriptase polymerase chain reaction (RT-PCR) for detection of BDV N- and P-gene transcripts. No specific immunoreactivity to BDV proteins was found in sera from 169 patients or 62 controls. No BDV N- or P-gene transcripts were found through RT-PCR analysis of PBMC from 18 patients with severe CFS. These results do not support a role for BDV in pathogenesis of CFS.
Evengard B, Komaroff AL.	Infektionskliniken, Huddinge sjukhus.	[Chronic fatigue syndrome does exist. Changes of biological parameters are measurable].[article in Swedish]	Lakartidningen 1999 Jun 30;96(26-27):3166-9	Chronic fatigue syndrome is a debilitating condition characterised by neurocognitive and somatic symptoms. Although many patients report an infectious onset, there is no unequivocal evidence to support this. The immune system is activated, and the hypothalamic-pituitary-adrenal axis is involved. The aetiology is complex, and its understanding may require modification of our views on ill-health and disease.
Evengard B, Schacterle RS, Komaroff AL.	Division of Infectious Diseases, Department of Immunology, Karolinska Institute at Huddinge University Hospital, Huddinge, Sweden. birgitta.evengardinfect.hs.sll.se	Chronic fatigue syndrome: new insights and old ignorance.	J Intern Med 1999 Nov;246(5):455-69	Chronic fatigue syndrome (CFS) is a condition characterized by impairment of neurocognitive functions and quality of sleep and of somatic symptoms such as recurrent sore throat, muscle aches, arthralgias, headache, and postexertional malaise. A majority of patients describe an infectious onset but the link between infections and CFS remains uncertain. Findings show an activation of the immune system, abberations in several hypothalamic-pituitary axes and involvement of other parts of the central nervous system. The origin is bound to be complex and it may well be that the solution will come together with a more generally altered view about mind-body dualism, and the concept of illness and disease.
Forsyth LM, Preuss HG, MacDowell AL, Chiazze L Jr, Birkmayer GD, Bellanti JA.	Department of Pediatrics, Georgetown University School of Medicine, Washington, D.C., USA.	Therapeutic effects of oral NADH on the symptoms of patients with chronic fatigue syndrome.	Ann Allergy Asthma Immunol 1999 Feb;82(2):185-91Comment in: Ann Allergy Asthma Immunol. 2000 Jun;84(6):639-40	BACKGROUND: Chronic fatigue syndrome (CFS) is a disorder of unknown etiology, consisting of prolonged, debilitating fatigue, and a multitude of symptoms including neurocognitive dysfunction, flu-like symptoms, myalgia, weakness, arthralgia, low-grade fever, sore throat, headache, sleep disturbances, and swelling and tenderness of lymph nodes. No effective treatment for CFS is known. OBJECTIVE: The purpose of the study was to evaluate the efficacy of the reduced form of nicotinamide adenine dinucleotide (NADH) i.e., ENADA the stabilized oral absorbable form, in a randomized, double-blind, placebo-controlled crossover study in patients with CFS. Nicotinamide adenine dinucleotide is known to trigger energy production through ATP generation which may form the basis of its potential effects. METHODS: Twenty-

				six eligible patients who fulfilled the Center for Disease Control and Prevention criteria for CFS completed the study. Medical history, physical examination, laboratory studies, and questionnaire were obtained at baseline, 4, 8, and 12 weeks. Subjects were randomly assigned to receive either 10 mg of NADH or placebo for a 4-week period. Following a 4-week washout period, subjects were crossed to the alternate regimen for a final 4-week period. RESULTS: No severe adverse effects were observed related to the study drug. Within this cohort of 26 patients, 8 of 26 (31%) responded favorably to NADH in contrast to 2 of 26 (8%) to placebo. Based upon these encouraging results we have decided to conduct an open-label study in a larger cohort of patients. CONCLUSION: Collectively, the results of this pilot study indicate that NADH may be a valuable adjunctive therapy in the management of the chronic fatigue syndrome and suggest that further clinical trials be performed to establish its efficacy in this clinically perplexing disorder.
Frank E, Dingle AD.	Department of Family and Preventive Medicine, Emory University School of Medicine, Atlanta, GA 30303, USA. efrank@fpm.eushc.org	Self-reported depression and suicide attempts among U.S. women physicians.	Am J Psychiatry 1999 Dec;156(12):1887-94	OBJECTIVE: Studies examining suicide rates for U.S. women physicians and other U.S. women have found odds ratios as high as 4 to 1. Although such reports are controversial and are based on small groups (N = 17 to 49 suicides), they are often cited as evidence of a high prevalence of psychopathology among women physicians. METHOD: The authors used the results of the Women Physicians' Health Study (N = 4,501), a large, nationally distributed questionnaire, to assess the lifetime prevalence of self-identified depression and suicide attempts among U.S. women physicians. RESULTS: An estimated 1.5% (N = 61) of U.S. women physicians have attempted suicide, and 19.5% (N = 808) have a history of depression. Those who were born in the United States, were not Asian, had histories of cigarette smoking, alcohol abuse or dependence, sexual abuse, domestic violence, poor current mental health, more severe harassment, or a family history of psychiatric disorders were significantly more likely to report suicide attempts or depression. Depression was more common among those who were not partnered, were childless, had a household gun, had more stress at home, drank alcohol, had worse health, or had a history of obesity, chronic fatigue syndrome, substance abuse, an eating disorder, or another psychiatric disorder and among those who reported working too much, career dissatisfaction, less control at work, and high job stress. Strata reporting higher rates of depression tended to show higher (although usually nonsignificant) rates of suicide attempts. CONCLUSIONS: Depression is approximately as common among U.S. women physicians as among other U.S. women, but suicide attempts may be fewer. A number of conditions may help identify women physicians at high risk for suicide attempts and depression.
Friedman TC, Adesanya A, Poland RE.		Low-dose hydrocortisone for chronic fatigue syndrome.	JAMA 1999 May 26;281(20):1888-9 Comment on: JAMA. 1998 Sep 23-	

			30;280(12):1061-6	
Garralda E, Rangel L, Levin M, Roberts H, Ukoumunne O.	Academic Unit of Child and Adolescent Psychiatry, Imperial College School of Medicine, St. Mary's Hospital, London, England. e.garralda@ic.ac.uk	Psychiatric adjustment in adolescents with a history of chronic fatigue syndrome.	J Am Acad Child Adolesc Psychiatry 1999 Dec;38(12):1515-21Comment in: J Am Acad Child Adolesc Psychiatry. 2000 Jul;39(7):808-9	OBJECTIVE: To ascertain psychiatric adjustment in youngsters with a history of childhood chronic fatigue syndrome (CFS). METHOD: Subjects were 25 children and adolescents with CFS who were seen in tertiary pediatric/psychiatric clinics (mean age 15.6 years, seen a mean of 45.5 months after illness onset; 17 subjects had recovered and 8 were still ill) and 15 healthy matched controls. Youngsters and their parents (usually mothers) were interviewed and completed questionnaires. Instruments used included the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS), the Child Behavior Checklist (CBCL), and the Harter Self-Esteem Questionnaire. RESULTS: At assessment, psychiatric disorders (mainly anxiety and depressive disorders) were present in half the subjects with a history of CFS, a rate significantly higher than in healthy controls. On the CBCL youngsters with a history of CFS had an excess of psychological symptoms and decreased social competence. On the Harter Self-Esteem Questionnaire they reported reduced self-esteem, especially in social competence. Anxiety disorders were significantly more common in recovered subjects than in those with active CFS illness status. CONCLUSIONS: Psychiatric disorders were found to be increased in adolescents with a history of severe CFS; CFS may enhance the risk for or share common predisposing factors with anxiety disorders.
Gil'miiarova FN, Radomskaia VM, Kretova IG, Vinogradova LN, Samykina LN, Sheshunov IV, Babichev AV, Sharafutdinova IM, Ponomareva LA.		[Chronic fatigue syndrome:objective criteria of metabolic defects].[article in Russian]	Klin Lab Diagn 1999 Feb;(2):9-11	Multi-level system of defense mechanisms is studied in 206 normal subjects living in an ecologically unfavorable region and working at chemical plants. Control group consisted of 24 subjects living in en ecologically safe region. The content of total protein and albumin and its effective and binding capacity were decreased, while the content of medium molecular weight peptides increased in the blood of subjects exposed to technogenic environmental pollution. The detected shifts are regarded as a mechanism of development of chronic fatigue syndrome.
Godwin M, Delva D, Miller K, Molson J, Hobbs N, MacDonald S, MacLeod C.	Department of Family Medicine, Queen's University, Kingston, ON.	Investigating fatigue of less than 6 months' duration. Guidelines for family physicians.	Can Fam Physician 1999 Feb;45:373-9Comment in: Can Fam Physician. 1999 Apr;45:872-3 Can Fam Physician. 1999 May;45:1152	OBJECTIVE: To develop an evidence-based systematic approach to assessment of adult patients who present to family physicians complaining of fatigue of less than 6 months' duration. The guidelines present investigative options, making explicit what should be considered in all cases and what should be considered only in specific situations. They aim to provide physicians with an approach that, to the extent possible, is based on evidence so that time and cost are minimized and detection and management of the cause of the fatigue are optimized. QUALITY OF EVIDENCE: MEDLINE was searched from 1966 to 1997 using the key words "family practice" and "fatigue." Articles about chronic fatigue syndrome were excluded. Articles with level 3 evidence were found, but no randomized trials, cohort studies, or case-control studies were found. Articles looking specifically at the epidemiology, demographics, investigations, and diagnoses of patients with fatigue were chosen. Articles based on

				studies at referral and specialty centres were given less weight than those based on studies in family physicians' offices. MAIN MESSAGE: Adherence to these guidelines will decrease the cost of investigating the symptom of fatigue and optimize diagnosis and management. This needs to be proved in practice, however, and with research that produces level 1 and 2 evidence. CONCLUSIONS: Adults presenting with fatigue of less than 6 months' duration should be assessed for psychosocial causes and should have a focused history and physical examination to determine whether further investigations should be done. The guidelines outline investigations to be considered. The elderly require special consideration. These guidelines have group validation, but they need to be tested by more physicians in various locations and types of practices.
Goodnick PJ, Jorge CM.		Treatment of chronic fatigue syndrome with nefazodone.	Am J Psychiatry 1999 May;156(5):797-8	
Gordon R, Michalewski HJ, Nguyen T, Gupta S, Starr A.	Department of Neurology, University of California, Irvine, Med. Surge I, Room 154, Irvine, CA 92697-4290, USA.	Cortical motor potential alterations in chronic fatigue syndrome.	Int J Mol Med 1999 Nov;4(5):493-9	Premovement, sensory, and cognitive brain potentials were recorded from patients with Chronic Fatigue Syndrome (CFS) in four tasks: i) target detection, ii) short-term memory, iii) self-paced movement, and iv) expectancy and reaction time (CNV). Accuracy and reaction times (RTs) were recorded for tasks i, ii, and iv. Results from CFS patients were compared to a group of healthy normals. Reaction times were slower for CFS patients in target detection and significantly slower in the short-term memory task compared to normals. In target detection, the amplitude of a premovement readiness potential beginning several hundred milliseconds prior to stimulus onset was reduced in CFS, whereas the poststimulus sensory (N100) and cognitive brain potentials (P300) did not differ in amplitude or latency. In the memory task, a negative potential related to memory load was smaller in CFS than normals. The potentials to self-paced movements and to expectancy and RT (CNV) were not different between groups. The findings in CFS of slowed RTs and reduced premovement-related potentials suggest that central motor mechanisms accompanying motor response preparation were impaired in CFS for some tasks. In contrast, measures of neural processes related to both sensory encoding (N100) and to stimulus classification (P300) were normal in CFS.
Granzow B.		[Mutual features of chronic fatigue syndrome, fibromyalgia and multiple chemical sensitivity].[article in German]	Dtsch Med Wochenschr 1999 Oct 15;124(41):1224	
Gray GC, Kaiser KS, Hawksworth AW, Hall	Emerging Illness Division, Naval Health	Increased postwar symptoms and	Am J Trop Med Hyg 1999 May;60(5):758-66	To investigate reports on war-related morbidity, 527 active-duty Gulf War veterans and 970 nondeployed veterans from 14 Seabee commands were studied in 1994 with

FW, Barrett-Connor E.	Research Center, San Diego, California 92186-5122, USA.	psychological morbidity among U.S. Navy Gulf War veterans.		a questionnaire, sera collection, handgrip strength, and pulmonary function testing. The questionnaire assessed postwar symptoms, war exposures, and screened for chronic fatigue syndrome, post-traumatic stress disorder, and psychological symptoms suggesting neurosis (Hopkins Symptom Checklist). Sera were tested with four nonspecific reactant assays: C-reactive protein, transferrin, ferritin, and haptoglobin. Gulf War veterans reported a higher prevalence for 35 of 41 symptoms, scored higher on psychological symptom scales, were more likely to screen for post-traumatic stress disorder, had lower handgrip strength, and had higher serum ferritin assay results. Numerous comparisons of these morbidity outcomes with 30 self-reported exposures demonstrated many associations, but no unique exposure or group of exposures were implicated. Morbidity data are consistent with other postwar observations, but the etiology for morbidity findings remains uncertain.
Green JL, Jennifer Romei, Benjamin Natelson		Stigma and Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1999: 5(2): 63 - 75	We predicted that the largely female population seeking relief from the incapacitating symptoms of chronic fatigue syndrome (CFS), an enigmatic illness, would feel stigmatized, and that attribution of CFS symptoms to psychological causes by physicians would contribute significantly to the CFS-related stigma. Most subjects scored high on measures of stigma: 95% had feelings of estrangement, 70% believed that others attributed their CFS symptoms to psychological causes, 77% coped by using an educational strategy (disclosure) and 39% saw a need to be secretive about their symptoms in some circumstances. Most subjects (77%) were labeled as 'psychological cases' by one or more of the physicians (mean = 8) consulted, but of the 4 stigma measures, only disclosure was related to physician labeling. Such factors as duration of illness and unemployment, dissatisfaction with spouse, and symptom severity correlated significantly with measures of stigma. That many physicians were reportedly ignorant or skeptical of CFS (male more so than female MD's) may influence attempts of CFS patients to legitimize their symptoms by disclosure and lead to high rates of health care system use
Gupta S, Aggarwal S, Starr A.	Department of Medicine, University of California, Irvine, CA 92697, USA.	Increased production of interleukin-6 by adherent and non-adherent mononuclear cells during 'natural fatigue' but not following 'experimental fatigue' in patients with chronic fatigue syndrome.	Int J Mol Med 1999 Feb;3(2):209-13	In an investigator-blinded study, adherent (monocytes) and non-adherent cells (lymphocytes) from patients with chronic fatigue syndrome (CFS) were examined on two separate occasions (when feeling 'fatigued' and when feeling 'rested') for in vitro spontaneous, phytohemagglutinin- (PHA, for lymphocytes), and lipopolysaccharide- (LPS, for monocytes) induced production of IL-6 by ELISA assay. A group of CFS patients and controls were also subjected to exercise-induced fatigue ('experimental fatigue') and IL-6 production was compared, in a double-blinded manner, prior to and following induction of fatigue. A significant increase in spontaneous, PHA- and LPS-induced IL-6 secretion by both lymphocytes and monocytes was observed in CFS patients during 'natural fatigue' as compared to during state. However, no such changes in IL-6 production were observed during 'experimental fatigue'. These data suggest a role of IL-6 in natural symptomatology and perhaps in the pathogenesis of CFS. In addition, the data demonstrate that laboratory-induced fatigue (experimental

				fatigue) may not be a good model to study immunological changes in CFS; immunological parameters should be studied in a longitudinal manner during the natural course of the disease.
Hartz AJ, Kuhn EM, Bentler SE, Levine PH, London R.	Department of Family Medicine, University of Iowa College of Medicine, Iowa City, USA.	Prognostic factors for persons with idiopathic chronic fatigue.	Arch Fam Med 1999 Nov-Dec;8(6):495-501	BACKGROUND: The simultaneous examination of a large number of patient characteristics in a prospective study of patients with chronic fatigue. OBJECTIVE: To compare the relative importance of these characteristics as prognostic factors. METHODS: The data analyzed were from 199 subjects in a registry of persons who were aged 18 years or older and had idiopathic fatigue for at least 6 months. All subjects completed an extensive baseline questionnaire that provided information about fatigue, demographic characteristics, medical conditions, lifestyle, sleeping habits, psychological characteristics, and the presence of criteria for chronic fatigue syndrome. Changes in fatigue severity from baseline to 2-year follow-up were tested for an association with risk factors at baseline and with changes in symptoms other than fatigue during the follow-up period. RESULTS: The following characteristics at baseline significantly and independently predicted greater fatigue improvement: less unclear thinking, fewer somatoform symptoms not used to define chronic fatigue syndrome, infrequent awakening, fewer hours sleeping, and being married. Of 29 subjects who at baseline reported no somatoform symptoms unrelated to chronic fatigue syndrome and who thought clearly most of the time, 8 substantially improved, compared with 1 of 29 subjects who had more than 2 somatoform symptoms and never thought clearly (P = .01). Improvements in the following symptoms were significantly and independently associated with improvements in fatigue: unclear thinking, depression, muscle aches, and trouble falling asleep. CONCLUSIONS: This study identified characteristics of subjects that seem to be of prognostic importance for idiopathic chronic fatigue. Symptoms that change concomitantly with changes in fatigue may be intrinsically linked to fatigue.
Heap LC, Peters TJ, Wessely S.	Department of Clinical Biochemistry, King's College School of Medicine, London, UK.	Vitamin B status in patients with chronic fatigue syndrome.	J R Soc Med 1999 Apr;92(4):183-5	Some patients with chronic fatigue syndrome say they benefit from taking vitamin supplements. We assessed functional status for the B vitamins pyridoxine, riboflavin and thiamine in 12 vitamin-untreated CFS patients and in 18 healthy controls matched for age and sex. Vitamin-dependent activities--aspartate aminotransferase (AST) for pyridoxine, glutathione reductase (GTR) for riboflavin, transketolase (TK) for thiamine--were measured in erythrocyte haemolysates before and after in-vitro addition of the relevant vitamin. For all three enzymes basal activity (U/g Hb) was lower in CFS patients than in controls: AST 2.84 (SD 0.62) vs 4.61 (1.43), $P < 0.001$; GTR 6.13 (1.89) vs 7.42 (1.25), $P < 0.04$; TK 0.50 (0.13) vs 0.60 (0.07), $P < 0.04$. This was also true of activated values: AST 4.91 (0.54) vs 7.89 (2.11), $P < 0.001$; GTR 8.29 (1.60) vs 10.0 (1.80), $P < 0.001$; TK 0.56 (0.19) vs 0.66 (0.08), $P < 0.07$. The activation ratios, however, did not differ between the groups. These data provide preliminary evidence of reduced functional B vitamin status, particularly of pyridoxine, in CFS patients.

Hickie I.	St George Hospital and Community Service, Kogarah, New South Wales, Australia. i.hickie@unsw.edu.au	Nefazodone for patients with chronic fatigue syndrome.	Aust N Z J Psychiatry 1999 Apr;33(2):278-80	OBJECTIVE: Patients with chronic fatigue syndrome (CFS) present with a variety of musculoskeletal, neurocognitive, sleep disturbance and mood symptoms. An open evaluation of the clinical utility of the novel antidepressant compound, nefazodone, was completed. METHOD: Ten patients with CFS presenting for assessment by a specialist psychiatrist were treated with nefazodone. Patients treated within this specialist service are also advised to engage in appropriate behavioural and sleep-wake cycle strategies to improve their level of functioning. RESULTS: Of the 10 patients, eight (80%) reported at least some improvement in the key symptom of fatigue, with four (40%) reporting moderate or marked symptom relief. Additionally, sleep disturbance and mood were both moderately or markedly improved in seven (70%) and eight (80%) of the patients, respectively. Five of the patients (50%) achieved at least a moderate improvement in overall functional outcome and were able to return to work or their previous level of role function. The mean dose of nefazodone was 370 mg/day (range = 200-800 mg), with a strong preference for nocturnal dosing. Seven of the patients had previously failed to respond to moclobemide, while seven had previously failed to respond to conventional antidepressant therapy. CONCLUSION: Nefazodone appears to be worthy of further systematic investigation in patients with CFS. Given its effects on sleep, mood and anxiety symptoms, it may have particular advantages in patients with this disorder.
Hill NF, Tiersky LA, Scavalla VR, Lavietes M, Natelson BH.	Chronic Fatigue Syndrome Center, Department of Neurosciences, University of Medicine and Dentistry-New Jersey Medical School, Newark, USA.	Natural history of severe chronic fatigue syndrome.	Arch Phys Med Rehabil 1999 Sep;80(9):1090-4	OBJECTIVE: To evaluate the natural history of chronic fatigue syndrome (CFS) in a severely ill group of patients at three points in time. DESIGN: Patients were enrolled from April 1992 to February 1994 and were evaluated three times. Time 1 (at enrollment): history, physical evaluation, and psychiatric evaluation; Time 2 (median = 1.6yrs after initial evaluation): postal questionnaire to assess current condition; Time 3 (median = 1.8 yrs after Time 2): medical and psychiatric evaluations. SETTING: The New Jersey CFS Cooperative Research Center, an ambulatory setting. PATIENTS: Twenty-three patients fulfilled the 1988 case definition for CFS and had symptom complaints that were substantial or worse in severity. All patients were ill less than 4.5 years; and none had a DSM-III-R psychiatric disorder in the 5 years before illness onset; none had substance abuse in the 10 years before enrollment. MAIN OUTCOME MEASURES: Severity of CFS symptoms was assessed by self-report questionnaires, laboratory tests, and medical examination. Psychological status was assessed using the Q-D15 and the Centers for Epidemiological Study-Depression Scale. At each time of evaluation, patients were categorized as severe, slightly improved, improved, and recovered. RESULTS: Over the 4 years of the study, 13 patients remained severely ill, 9 improved but still fulfilled the 1994 case definition for CFS, and 1 recovered. Illness duration, mode of onset, psychiatric status or depressed mood at intake, or chemical sensitivity did not predict illness outcome. One patient was diagnosed with an alternate illness, but it probably did not explain her CFS symptoms. Mood improved for those patients whose illness lessened. CONCLUSIONS: The prognosis for recovery

				was extremely poor for the severely ill subset of CFS patients. The majority showed no symptom improvement and only 4% of the patients recovered. Illness severity between Times 2 and 3 remained stable.
Hodgson MJ, Kipen HM.	Department of Medicine, University of Connecticut Health Center, Farmington, USA.	Gulf War illnesses: causation and treatment.	J Occup Environ Med 1999 Jun;41(6):443-52	Soldiers returning from the Gulf War in 1991 described a range of symptoms, including some consistent with the chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity. Well-defined adverse health events attributable to service in the Gulf occurred. However, controlled epidemiological studies in Gulf War veterans and controls describe significant excesses of symptoms that were not clearly associated with pathologic disease. At least 12% of veterans currently receive some form of disability from the Department of Veterans Affairs. A number of reports outline theories proposed to explain the excess, but few are scientifically supported. Management guidelines for this spectrum of disorders resembles that of many of "emerging overlap syndromes," including multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. They include the establishment of a trusting doctor-patient relationship, negotiations around a common ground of scientific and etiologic beliefs, non-labeling of the disorder, and work toward recovery in the absence of clear etiologic answers.
Hotopf M, Wessely S.		Chronic fatigue syndrome--mapping the interior.	Psychol Med 1999 Mar;29(2):255-8	
Hudson M, Cleare AJ.	Department of Psychological Medicine, Guy's King's and St Thomas' School of Medicine and the Institute of Psychiatry, London, UK.	The 1microg short Synacthen test in chronic fatigue syndrome.	Clin Endocrinol (Oxf) 1999 Nov;51(5):625-30 Comment in: Clin Endocrinol (Oxf). 2000 Jun;52(6):797-9	OBJECTIVE: Many studies suggest mild hypocortisolism in chronic fatigue syndrome (CFS), usually assumed to be due to reduced suprahypothalamic drive to the hypothalamo-pituitary-adrenal (HPA) axis. We wished to explore further the state of the HPA axis in CFS using the 1 microg low dose short Synacthen test. DESIGN: Subjects received an intravenous bolus of 1 microg Synacthen; samples for cortisol estimation were taken at baseline and 2, 10, 20, 30, 40 and 60 minutes after injection. PATIENTS: We tested 20 subjects suffering from CFS according to the criteria of the Center for Diseases Control without psychiatric comorbidity and 20 matched healthy controls. All subjects were drug free for at least 1 month. MEASUREMENTS: We calculated the cortisol responses to the test as the maximum cortisol attained, the incremental rise in cortisol over baseline (Deltavalue) and as the integrated area under the curve. RESULTS: There were no significant differences in baseline cortisol or cortisol responses between patients and controls. However, responses generally were low, and many subjects' peak responses were prior to the standard 30 minute sampling time., CONCLUSIONS These results do not lend support to the theory that patients with chronic fatigue syndrome have a low adrenal reserve. However, results from studies assessing the HPA axis are proving to be inconsistent. We suggest that many other factors may be contributing to HPA axis alterations in chronic fatigue syndrome, including sleep disturbance, inactivity, altered circadian rhythmicity, illness chronicity, concomitant medication and comorbid psychiatric

				disturbance. These sources of heterogeneity need to be considered in future studies, and may explain the inconsistent findings to date.
Itoh Y, Igarashi T, Tatsuma N, Imai T, Yoshida J, Tsuchiya M, Murakami M, Fukunaga Y.	Department of Pediatrics, Nippon Medical School, Tokyo, Japan.	[Autoimmune fatigue syndrome and fibromyalgia syndrome].[article in Japanese]	Nippon Ika Daigaku Zasshi 1999 Aug;66(4):239-44	We have encounted two patients with fibromyalgia (FM) initially diagnosed as having autoimmune fatigue syndrome (AIFS). To investigate the relationship between AIFS and FM, the distribution of the tender points in patients with AIFS was assessed according to the ACR criteria for FM. It was revealed that AIFS patients had 5.6 tender points on averages. Patients with headaches, digestive problems, or difficulty going to school had more tender points than patients without. Patients with ANA titers < 1: 160 had more tender points than patients with ANA > or = 1: 160. Anti-Sa negative patients had more tender points than positive patients. These results suggest a relationship between AIFS and FM in terms of the pathophysiologic mechanisms of the numerous tender points. In other words, ANA-positive FM patients could be one form of AIFS, as well as ANA-positive chronic fatigue syndrome patients. Thus, autoimmunity could explain the controversial disease entities of FM and/or CFS.
Jackson EL.		The effects on siblings in families with a child with chronic fatigue syndrome.	J Child Health Care 1999 Summer;3(2):27-32	Paediatric CFS/ME is a stressor, which affects not only the sufferer but also the whole family. The sibling bond exerts a great influence on all the children in the family. Healthy siblings are often overlooked as attention is focused on the child with CFS/ME or other chronic illness. Individual children react in different ways to serious illness in another sibling by adopting a variety of coping mechanisms. There is a need for health and education professionals to consider the whole family when caring for and working with a child with CFS/ME.
Jahn K, Klenke T.	kj@multimedica.de	[Web sites on tinnitus, fibromyalgia, chronic fatigue syndrome, etc. Here your patients seek information].[article in German]	MMW Fortschr Med 1999 Dec 16;141(51-52):14	
Jason LA, King CP, Frankenberry EL, Jordan KM, Tryon WW, Rademaker F, Huang CF.	Department of Psychology, DePaul University, Chicago, IL 60613, USA.	Chronic fatigue syndrome: assessing symptoms and activity level.	J Clin Psychol 1999 Apr;55(4):411-24	Current approaches to the diagnosis and assessment of Chronic Fatigue Syndrome (CFS) rely primarily on scales that measure only the occurrence of various symptoms related to CFS. Such approaches do not provide information on either the severity of symptoms or on fluctuations in symptom severity and activity level that occur over time. As a result, these measures do not reflect the complexities and the interrelations among symptoms. By obscuring the fluctuating nature of CFS and its high variability, current assessment procedures may prevent health care professionals from understanding the complexities of this disease. The present study provides two CFS case studies to illustrate the advantages of using self-reporting rating scales in combination with a device used to measure the frequency and intensity of activity. The implications of this assessment system, which captures the symptom dynamics and variability involved in CFS, are discussed.

Jason LA, Melrose H, Lerman A, Burroughs V, Lewis K, King CP, Frankenberry EL.	DePaul University, Chicago, IL, USA.	Managing chronic fatigue syndrome: overview and case study.	AAOHN J 1999 Jan;47(1):17-21	1. The basic principles of envelope theory are explained. By not overexerting themselves, people with CFS can avoid the setbacks and relapses that commonly occur in response to overexertion while increasing their tolerance to activity. 2. By collecting time series data on fluctuations in energy levels, important clinical observations can be made in respect to a client's unique condition and experience with CFS.
Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, Taylor RR, McCready W, Huang CF, Plioplys S.	Department of Psychology, DePaul University, Chicago, IL 60614, USA. ljason@wppost.depaul.edu	A community-based study of chronic fatigue syndrome.	Arch Intern Med 1999 Oct 11;159(18):2129-37	BACKGROUND: Most previous estimates of the prevalence of chronic fatigue syndrome (CFS) have derived largely from treated populations, and have been biased by differential access to health care treatment linked with sex, ethnic identification, and socioeconomic status. OBJECTIVE: To assess the point prevalence of CFS in an ethnically diverse random community sample. DESIGN AND PARTICIPANTS: A sample of 28,673 adults in Chicago, Ill, was screened by telephone, and those with CFS-like symptoms were medically evaluated. MAIN OUTCOME MEASURES AND ANALYSES: Self-report questionnaires, psychiatric evaluations, and complete medical examinations with laboratory testing were used to diagnose patients with CFS. Univariate and multivariate statistical techniques were used to delineate the overall rate of CFS in this population, and its relative prevalence was subcategorized by sex, ethnic identification, age, and socioeconomic status. RESULTS: There was a 65.1% completion rate for the telephone interviews during the first phase of the study. Findings indicated that CFS occurs in about 0.42% (95% confidence interval, 0.29%-0.56%) of this random community-based sample. The highest levels of CFS were consistently found among women, minority groups, and persons with lower levels of education and occupational status. CONCLUSIONS: Chronic fatigue syndrome is a common chronic health condition, especially for women, occurring across ethnic groups. Earlier findings suggesting that CFS is a syndrome primarily affecting white, middle-class patients were not supported by our findings.
Jason LA, Tryon WW, Taylor RR, King C, Frankenberry EL, Jordan KM.	Department of Psychology, DePaul University, Chicago, IL 60614, USA.	Monitoring and assessing symptoms of chronic fatigue syndrome: use of time series regression.	Psychol Rep 1999 Aug;85(1):121-30	Chronic Fatigue Syndrome's principal symptoms are severe and include prolonged fatigue and a number of other minor symptoms. Behavioral data collection methods were used in a case study to show some of the benefits that can be derived from monitoring symptoms hourly and daily. Using time series regression, several statistically significant correlates of fatigue were found both within days and between days. Perceived energy, physical exertion, and mental exertion were significantly related to fatigue in both analyses. Collection of such data may help resolve a number of theoretical and methodological problems in research on the Chronic Fatigue Syndrome.
Jeffcoate WJ.	Department of Diabetes and Endocrinology, City Hospital, Nottingham, UK.	Chronic fatigue syndrome and functional hypoadrenia--fighting vainly the old ennui.	Lancet 1999 Feb 6;353(9151):424-5Comment in: Lancet. 1999 Feb 6;353(9151):445-8	

			Lancet. 1999 May 8;353(9164):1619-20	
Johnson SK, DeLuca J, Natelson BH.	Department of Psychology, University of North Carolina, Charlotte 28223, USA.	Chronic fatigue syndrome: reviewing the research findings.	Ann Behav Med 1999 Summer;21(3):258-71	This article reviews the current state of research in chronic fatigue syndrome (CFS). The evolving definition, prevalence, and prognosis of this controversial illness are presented. We review studies examining psychiatric, personality, and psychosocial etiology for CFS. The evidence for pathophysiology in CFS is also presented, and studies investigating viral, immune, neuroimaging, neuroendocrine, and central and autonomic nervous system abnormalities in CFS are assessed. Current evidence indicates that CFS is multi-determined and heterogeneous and that subgrouping patients according to factors such as psychiatric state and symptom onset may be fruitful. The current state of treatment for CFS is reviewed, and the challenges for research aimed at resolving this prototypical mind/body problem are discussed.
Jones E, Wessely S.	Department of Psychological Medicine, Guy's, King's, and St Thomas's School of Medicine, London SE5 8AZ. E.Jones@hogarth7.demon.co.uk	Case of chronic fatigue syndrome after Crimean war and Indian mutiny.	BMJ 1999 Dec 18-25;319(7225):1645-7	
Kakumanu S, Yeager M, Craig TJ.	Pennsylvania State University, College of Medicine, Hershey, USA.	Chronic fatigue syndrome.	J Am Osteopath Assoc 1999 Oct;99(10 Su Pt 1):S1-5	The chronic fatigue syndrome is an illness of unknown etiology characterized by severe fatigue, myalgias, lymphadenopathy, arthralgias, chills, fevers, and postexertional malaise. Recognizing chronic fatigue syndrome is primarily a method of exclusion with no definitive diagnostic test or physical findings. As research continues to delve into the many possible etiologic agents for chronic fatigue syndrome--infectious, immunologic, neurologic, or psychiatric alone or in combination--the answer remains elusive. What is known is that chronic fatigue syndrome is a heterogeneous disorder very possibly involving an interaction of biological systems. Therefore, chronic fatigue syndrome may describe a large subset of patients, each exhibiting unique symptoms and serologic profiles dependent on the nature of the onset of illness and the genetic profile of individual patients.
Keenan PA. Editorial		Brain MRI abnormalities exist in chronic fatigue syndrome.	J Neurol Sci 1999 Dec 1;171(1):1-2 Comment on: J Neurol Sci. 1999 Dec 1;171(1):3-7	
Kenter EG, Okkes IM.	Academisch Medisch Centrum/Universiteit van Amsterdam, afd. Huisartsgeneeskunde.	[Patients with fatigue in family practice: prevalence and treatment].[article in Dutch]	Ned Tijdschr Geneeskd 1999 Apr 10;143(15):796-801	OBJECTIVE: To gain insight into the prevalence and treatment of severe fatigue in general practice. DESIGN: Secondary data analysis. METHOD: By means of an episode-oriented morbidity registration by 54 GPs throughout the Netherlands over the period 1985-1994 it was established how often in the course of one year 'fatigue' was listed as the reason for consultation, what diagnoses were then made, how long

				episodes of care because of 'fatigue' lasted and what interventions took place (n = 93,297). Of the patients with a care episode because of 'fatigue' lasting at least 6 months, age, sex, comorbidity and consumption of care were established; for this purpose use was also made of a file containing data on 4 years in succession (n = 9630). RESULTS: Per annum, 92 per 1000 listed patients consulted the GP because of fatigue. Somatic or psychic diagnoses were made in 27.7 per 1000 patients listed. The episode of care lasted 4 weeks at most in 86% and at least 6 months in approximately 4%. The GPs' management of patients with 'fatigue' included physical examination in 63% and blood testing in 34%, conversation in 35%, prescription of medication in 24% and referral to a specialist in 3%. Of the 97 patients with fatigue lasting longer than 6 months, 61% had a chronic disease or psychic problems. CONCLUSION: Fatigue is frequently encountered in general practice, but the estimate that one per 1000 listed patients meets the criteria of the chronic fatigue syndrome looks a little high. It appears that GPs, in accordance with recommendations, mostly adopt a policy of wait and see.
Kipen HM, Hallman W, Kang H, Fiedler N, Natelson BH.	New Jersey Center for Environmental Hazards Research, East Orange, USA.	Prevalence of chronic fatigue and chemical sensitivities in Gulf Registry Veterans.	Arch Environ Health 1999 Sep-Oct;54(5):313-8Comment in: Arch Environ Health. 1999 Sep-Oct;54(5):309-11	More than 68000 of the 700000 veterans of the Gulf War have become members of the Veteran Affairs' Gulf War Registry. In 1995, we undertook a questionnaire study of the symptoms and medical histories reported by a randomly selected subsample of 1935 of these veterans to characterize their complaints. All results reported were based on questionnaire responses without face-to-face evaluation or physical examinations. Inasmuch as initial registry symptoms overlapped those of Chronic Fatigue Syndrome and Multiple Chemical Sensitivities, we also included standard questions for these syndromes in the questionnaire. A total of 1161 (60%) individuals responded, and there were no major demographic biases; therefore, 15.7% of registry veterans qualified for Chronic Fatigue Syndrome in accordance with the 1994 Centers for Disease Control definition. In addition, 13.1% qualified for multiple chemical sensitivities in accordance with a widely used definition, and 3.3% of the respondents had both conditions. There were no effects of gender, race, branch, duty status (active or reserve), or rank, although Multiple Chemical Sensitivities was somewhat more prevalent in women and African Americans. The data gleaned in this study suggested that the unexplained symptom syndromes of Chronic Fatigue and Multiple Chemical Sensitivities may characterize an appreciable portion of the complaints of those who volunteered for the Veterans Affairs' Gulf War Registry, and further investigation is warranted.
Knobeloch L, Jackson R.	Bureau of Environmental Health, Wisconsin Division of Public Health, Madison 53703-3043, USA.	Recognition of chronic carbon monoxide poisoning.	WMJ 1999 Sep-Oct;98(6):26-9	Chronic exposure to low levels of carbon monoxide can cause vague symptoms that are easily mistaken for other common illnesses. During the past 5 years, three families have contacted the Wisconsin Division of Public Health to report illnesses that may have been caused by chronic exposure to carbon monoxide. Members of these families were diagnosed with a variety of conditions including chronic fatigue syndrome, depression and influenza. Carbon monoxide exposure was not suspected

				as a cause of these illnesses until heating contractors discovered that gas appliances in these families' homes were not properly vented. These cases serve as reminders that carbon monoxide exposure should be considered in the differential diagnosis of patients who present with chronic symptoms of headache, fatigue, dizziness, nausea and mental confusion--especially when these symptoms onset during the winter heating season.
Korszun A, Sackett-Lundeen L, Papadopoulos E, Brucksch C, Masterson L, Engelberg NC, Haus E, Demitrack MA, Crofford L.	Department of Psychiatry, University of Michigan Medical Center, Ann Arbor, USA. akorszun@umich.edu	Melatonin levels in women with fibromyalgia and chronic fatigue syndrome.	J Rheumatol 1999 Dec;26(12):2675-80	OBJECTIVE: Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are stress associated disorders mainly affecting women. FM is characterized primarily by widespread musculoskeletal pain, and CFS by profound debilitating fatigue, but there is considerable overlap of clinical symptoms between these 2 syndromes. Neuroendocrine abnormalities have been noted in both FM and CFS and desynchronization of circadian systems has been postulated in their etiology. The pineal hormone melatonin is involved in synchronizing circadian systems and the use of exogenous melatonin has become widespread in patients with FM and CFS. METHODS: We examined the characteristics and relationship of melatonin and cortisol levels in premenopausal women with FM (n = 9) or CFS (n = 8), compared to age and menstrual cycle phase matched controls. Blood was collected from an indwelling intravenous catheter every 10 min over 24 h, and plasma melatonin and cortisol were determined by radioimmunoassay at 60 and 10 min intervals, respectively. RESULTS: Night time (23:00-06:50) plasma melatonin levels were significantly higher in FM patients compared to controls ($p<0.05$), but there was no significant difference in melatonin levels between CFS patients and controls. No differences in the timing of cortisol and melatonin secretory patterns and no internal desynchronization of the 2 rhythms were found in either patient group, compared to controls. CONCLUSION: Raised plasma melatonin concentrations have been documented in several other conditions that are associated with dysregulation of neuroendocrine axes. Increased melatonin levels may represent a marker of increased susceptibility to stress induced hypothalamic disruptions. These data indicate that there is no rationale for melatonin replacement therapy in patients with FM and CFS.
Kreyberg S.		[A close meeting with chronic fatigue syndrome].[article in Norwegian]	Tidsskr Nor Laegeforen 1999 Jun 10;119(15):2229-31	
Kreyberg S.		[Management of chronic fatigue syndrome reflects the physician's "illness belief" letter)]. [Article in Swedish]	Lakartidningen 1999 Dec 1;96(48):5342	

LaManca JJ, Peckerman A, Walker J, Kesil W, Cook S, Taylor A, Natelson BH.	CFS Cooperative Research Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA.	Cardiovascular response during head-up tilt in chronic fatigue syndrome.	Clin Physiol 1999 Mar;19(2):111-20	This study examined the cardiovascular response to orthostatic challenge, and incidence and mechanisms of neurally mediated hypotension in chronic fatigue syndrome (CFS) during a head-up tilt test. Stoke volume was obtained by a thoracic impedance cardiograph, and continuous heart rate and blood pressure were recorded during a 45-min 70 degrees head-up tilt test. Thirty-nine CFS patients and 31 healthy physically inactive control subjects were studied. A positive tilt, i.e. a drop in systolic blood pressure of > 25 mmHg, no concurrent increase in heart rate and/or development of presyncopal symptoms, was seen in 11 CFS patients and 12 control subjects (P > 0.05). During baseline and the first 5 min of head-up tilt, CFS patients had higher heart rate and smaller pulsatile-systolic area than control subjects (P < 0.05). Among subjects who completed the test, those with CFS had higher heart rate and smaller stroke volume (P < 0.05) than corresponding control subjects. When comparing those who had a positive test outcome in each group, CFS patients had higher heart rates and lower pulse pressure and pulsatile-systolic areas during the last 4 min before being returned to supine (P < 0.05). These data show that there are baseline differences in the cardiovascular profiles of CFS patients when compared with control subjects and that this profile is maintained during head-up tilt. However, the frequency of positive tilts and the haemodynamic adjustments made to this orthostatic challenge are not different between groups.
LaManca JJ, Sisto SA, Zhou XD, Ottenweller JE, Cook S, Peckerman A, Zhang Q, Denny TN, Gause WC, Natelson BH.	NJ CFS Cooperative Research Center, UMDNJ-New Jersey Medical School, Newark 07103, USA.	Immunological response in chronic fatigue syndrome following a graded exercise test to exhaustion.	J Clin Immunol 1999 Mar;19(2):135-42	This study was conducted to evaluate the immunological response to an exhaustive treadmill exercise test in 20 female chronic fatigue syndrome patients compared to 14 matched sedentary controls. Venipuncture was performed at baseline and 4 min, 1 hr, and 24 hr postexercise. White blood cells were labeled for monoclonal antibody combinations and were quantified by FACsan. Cytokines were assayed utilizing quantitative RT/PCR. No group difference was seen in VO2peak (28.6 +/- 1.6 vs 30.9 +/- 1.2 ml.kg-1.min-1; P > 0.05). However, 24 hr after exercise the patients' fatigue levels were significantly increased (P < 0.05). The counts of WBC, CD3+ CD8+ cells, CD3+ CD4+ cells, T cells, B cells, natural killer cells, and IFN-gamma changed across time (P's < 0.01). No group differences were seen for any of the immune variables at baseline or after exercise (P's > 0.05). The immune response of chronic fatigue syndrome patients to exhaustive exercise is not significantly different from that of healthy nonphysically active controls.
Lange G, DeLuca J, Maldjian JA, Lee H, Tiersky LA, Natelson BH.	Department of Psychiatry, UMDNJ-New Jersey Medical School, MSB E-561, 185 S. Orange Avenue, Newark, NJ 07103-2714, USA.	Brain MRI abnormalities exist in a subset of patients with chronic fatigue syndrome.	J Neurol Sci 1999 Dec 1;171(1):3-7Comment in: J Neurol Sci. 1999 Dec 1;171(1):1-2	Presence of MRI brain abnormalities in patients with Chronic Fatigue Syndrome (CFS) was determined and the profile of MRI abnormalities was compared between 39 CFS patients, 18 with (CFS-Psych) and 21 without (CFS-No Psych) a DSM-III-R Axis I psychiatric diagnosis since illness onset, and 19 healthy, sedentary controls (HC). Two neuroradiologists, blind to group membership, separately read the MR films using a detailed protocol for rating and categorizing abnormal signal changes. When findings were incongruent, the two neuroradiologists met to try to reach consensus, otherwise a third neuroradiologist evaluated the MR images and served as a tie-

				breaker. The CFS-No Psych group showed a significantly larger number of brain abnormalities on T2 weighted images than the CFS-Psych and HC groups. Cerebral changes in the CFS-No Psych group consisted mostly of small, punctate, subcortical white matter hyperintensities, found predominantly in the frontal lobes. No significant difference was found when both CFS groups were combined and compared to the HC group. The use of stratification techniques is an important strategy in understanding the pathophysiology of CFS. This frontal lobe pathology could explain the more severe cognitive impairment previously reported in this subset of CFS patients.
Lange G, Tiersky L, DeLuca J, Peckerman A, Pollet C, Policastro T, Scharer J, Ottenweller JE, Fiedler N, Natelson BH.	Center for Environmental Hazards Research, VA Medical Center, East Orange, NJ, USA. langegu@umdnj.edu	Psychiatric diagnoses in Gulf War veterans with fatiguing illness.	Psychiatry Res 1999 Dec 13;89(1):39-48	The purpose of this study was to determine whether Gulf War Illness (GWI) can be explained by the presence of psychiatric disorders as assessed by DSM-III-R. To reduce the heterogeneity amongst Persian Gulf War veterans with GWI (PGV-F), only those were studied who presented with severe fatigue as a major complaint and also fulfilled clinical case definitions for Chronic Fatigue Syndrome, Idiopathic Chronic Fatigue, and/or Multiple Chemical Sensitivity. A total of 95 Registry PGVs were examined; 53 presented with GWI and 42 did not report any post-war health problems (PGV-H). All subjects were assessed for the presence of DSM-III-R Axis I psychiatric disorders. Compared to PGV-Hs, 49% of PGV-Fs had similar post-war psychiatric profiles: either no, or only one, psychiatric disorder was diagnosed. Psychiatric profiles of the remaining 51% of PGV-Fs were significantly different from PGV-Hs in that most of these veterans suffered from multiple post-war psychiatric diagnoses. The presence of psychiatric disorders as assessed by DSM-III-R criteria cannot explain symptoms of Gulf War Illness among all Persian Gulf veterans with severe fatiguing illness.
Lloyd AR, Hickie I, Peterson PK.	School of Pathology, University of New South Wales, Australia.	Chronic fatigue syndrome: current concepts of pathogenesis and treatment.	Curr Clin Top Infect Dis 1999;19:135-59	
Lovell DM.	Oxford University Psychiatry Department, Warneford Hospital, Oxford, England.	Chronic fatigue syndrome among overseas development workers: A qualitative study.	J Travel Med 1999 Mar;6(1):16-23	BACKGROUND: A relatively high proportion of overseas development workers may develop chronic fatigue syndrome (CFS). A qualitative study was conducted in order to investigate how such people perceived their condition. METHODS: Twelve people who had developed CFS while working overseas with development organizations, or shortly after visiting development projects, were interviewed about their experiences. Their responses were analyzed using a grounded theory approach. RESULTS: Most of the participants considered themselves to have been extremely healthy before they developed CFS. The syndrome did not appear to have been caused by depression. The symptoms which were reported covered the range of symptoms typically found in studies of CFS. Respondents described difficulty in receiving, and accepting, a diagnosis. All of the participants attributed the CFS to

				multiple causes, the principal causes being overwork, stress and infections. Among the consequences of CFS reported to be the most difficult were having to leave the development project prematurely; pain; powerlessness; loss of independence, and the unpredictability of CFS. Factors which had helped respondents cope with these difficulties included religious beliefs; comparisons with people who were worse off than they were; thinking about positive consequences of the condition, and talking with supportive people. CONCLUSIONS: Some theories have suggested that CFS symptoms arise as a result of depression or other emotional difficulties, which the individual is not able to acknowledge. The results indicated that such theories may not apply to this subgroup of people with CFS. Further research on the etiology of CFS is warranted. Respondents described high levels of work-related stress as common to the experience of development work. It might be beneficial to train development workers in stress management techniques. Development organizations should be encouraged to ensure that their workers take sufficient time to rest, and attempts should be made to reduce work pressures.
Lundin A.		[Chronic fatigue syndrome is not medically explained. Biomedical explanation is confusing for the patient].[article in Swedish]	Lakartidningen 1999 Oct 6;96(40):4350-52	
Magdic B, Ilic T, Jovankic O, Cedic V.		[The chronic fatigue syndrome--a clinical entity or a complex of symptoms of various pathologic conditions].[article in Serbo-Croatian (Cyrillic)]	Vojnosanit Pregl 1999 Mar-Apr;56(2):167-71	
Marcusson JA, Lindh G, Evengard B.	Department of Dermatology, Huddinge University Hospital, Sweden.	Chronic fatigue syndrome and nickel allergy.	Contact Dermatitis 1999 May;40(5):269-72Comment in: Contact Dermatitis. 2000 Jan;42(1):56-7	50 patients with chronic fatigue syndrome (CFS) and 73 controls were patch tested with 8 metal allergens. We found an overrepresentation of allergies among the CFS patients, which was not significant. However, allergy to nickel occurred in 36% of patients in the CFS group and in 19% of subjects in the control group ($p<0.05$). The high frequency of nickel allergy was more noteworthy in females in the CFS group than among female controls (52% and 24%, respectively, $p<0.05$). Similarly, in the males the figures were 14% and 9%. We suggest that in vivo immunoactivation by ions of nickel, or metal cross-reacting with nickel, could be an etiological factor in CFS.
Marcusson JA.		The frequency of	Contact Dermatitis	

		mercury intolerance in patients with chronic fatigue syndrome and healthy controls.	1999 Jul;41(1):60-1	
Marshall GS.	Department of Pediatrics, University of Louisville School of Medicine, Louisville, Kentucky, USA. Review Review, Multicase	Report of a workshop on the epidemiology, natural history, and pathogenesis of chronic fatigue syndrome in adolescents.	J Pediatr 1999 Apr;134(4):395-405	
Martin WJ.	Center for Complex Infectious Diseases, Rosemead, California 91770, USA.	Stealth adaptation of an African green monkey simian cytomegalovirus.	Exp Mol Pathol 1999 Apr;66(1):3-7	DNA extracted from cultures of a cytopathic virus isolated from a patient with chronic fatigue syndrome was cloned into pBluescript plasmid. The nucleotide sequences of the plasmid inserts were analyzed using the BlastN and BlastX programs of the National Center for Biotechnology Information. In confirmation of earlier studies, many of the sequences show partial homology to various regions within the genome of human cytomegalovirus (HCMV). The matching regions were unevenly distributed throughout the HCMV genome. No matches were seen with either the UL55 or the UL83 genes, which provide the major antigenic targets for anti-HCMV cytotoxic T-cell-mediated immunity. This finding is consistent with the notion that certain viruses can avoid immune elimination by deleting genes required for effective antigenic recognition by the cellular immune system. The term "stealth" has been applied to such viruses. Comparisons were also made between the sequences of the stealth virus and the limited sequence data available on cytomegaloviruses from rhesus monkeys and from African green monkeys. These comparisons unequivocally establish that the virus was derived from an African green monkey simian cytomegalovirus. Copyright 1999 Academic Press.
Matsuda J, Gohchi K.	Department of Clinical Biochemistry, Faculty of Pharmaceutical Sciences, Teikyo University.	[Chronic fatigue syndrome].[article in Japanese]	Ryoikibetsu Shokogun Shirizu 1999;(24 Pt 2):161-5	
Matsumoto Y.	Center of Rheumatic Diseases, Toyokawa City Hospital.	[Fibromyalgia syndrome].[article in Japanese]	Nippon Rinsho 1999 Feb;57(2):364-9	Fibromyalgia syndrome (FMS) is recognizable syndrome characterized by chronic, diffuse pain, an absence of inflammatory or structural muscloskeletal abnormalities, and a range of symptoms that include fatigue, and sleep and mood disturbances. Physical examination and laboratory testing are unrevealing, except for the presence of pain on palpation of characteristic soft-tissue sites, the tender points. Despite the recognition of FMS by the World Health Organization, it remains a controversial condition and its existence as a distinct entity remains uncertain. However, the concept of FMS is a useful one, allowing many investigations to be avoided and

				appropriate advice on treatment to be given. FMS may overlap with symptoms of, and the patient further impaired by, anxiety and depression. The term FMS dose not imply causation and merely describes the most common symptoms. Many patients with chronic fatigue syndrome(CFS) fulfill the criteria of FMS and represent one end of a spectrum of presentation. Evidence for triggering viral infection and the lower level of serum acylcarnitine, observed in CFS patients, is lacking in the majority of patients with FMS. These findings are suggestive to be distinctively another disorders between FMS and CFS.
Matsumoto Y.		[Immunological aspects of pathophysiology of chronic fatigue syndrome].[article in Japanese]	Nihon Rinsho Meneki Gakkai Kaishi 1999 Jun;22(3):111-22	
McCully KK, Natelson BH.	Department of Medicine, Medical College of Pennsylvania and Hahnemann University, Philadelphia, PA 19129, USA. kmccully@coe.uga.edu	Impaired oxygen delivery to muscle in chronic fatigue syndrome.	Clin Sci (Colch) 1999 Nov;97(5):603-8; discussion 611-3Comment in: Clin Sci (Colch). 1999 Nov;97(5):611-3	The purpose of this study was to determine if chronic fatigue syndrome (CFS) is associated with reduced oxygen delivery to muscles. Patients with CFS according to CDC (Center for Disease Control) criteria (n=20) were compared with normal sedentary subjects (n=12). Muscle oxygen delivery was measured as the rate of post-exercise and post-ischaemia oxygen-haem resaturation. Oxygen-haem resaturation was measured in the medial gastrocnemius muscle using continuous-wavelength near-IR spectroscopy. Phosphocreatine resynthesis was measured simultaneously using (31)P magnetic resonance spectroscopy. The time constant of oxygen delivery was significantly reduced in CFS patients after exercise (46.5+/-16 s; mean+/-S.D.) compared with that in controls (29.4+/-6.9 s). The time constant of oxygen delivery was also reduced (20.0+/-12 s) compared with controls (12.0+/-2.8 s) after cuff ischaemia. Oxidative metabolism was also reduced by 20% in CFS patients, and a significant correlation was found between oxidative metabolism and recovery of oxygen delivery. In conclusion, oxygen delivery was reduced in CFS patients compared with that in sedentary controls. This result is consistent with previous studies showing abnormal autonomic control of blood flow. Reduced oxidative delivery in CFS patients could be specifically related to CFS, or could be a non-specific effect of reduced activity levels in these patients. While these results suggest that reduced oxygen delivery could result in reduced oxidative metabolism and muscle fatigue, further studies will be needed to address this issue.
Meggs WJ. Editorial		Gulf War Syndrome, Chronic Fatigue Syndrome, and the Multiple Chemical Sensitivity Syndrome: stirring the cauldron of confusion.	Arch Environ Health 1999 Sep-Oct;54(5):309-11 Comment on: Arch Environ Health. 1999 Sep-Oct;54(5):313-8	

Merz S.		Lakartidningen. 1999 Nov 10;96(45):4904 [Treatment of chronic fatigue syndrome].[article in Swedish]	Lakartidningen 1999 Oct 13;96(41):4409 Comment in: Lakartidningen. 1999 Dec 15;96(50):5610	
Michiels V, de Gucht V, Cluydts R, Fischler B.	Free University of Brussels (VUB), Belgium.	Attention and information processing efficiency in patients with Chronic Fatigue Syndrome.	J Clin Exp Neuropsychol 1999 Oct;21(5):709-29	In this study a battery of attentional tests and a verbal memory task were administered to outpatients with Chronic Fatigue Syndrome (CFS) in order to evaluate aspects of attention that have not been explored in this group to date. In addition, this study was designed to further examine memory function and to extend the few reports investigating the rate of cognitive processing independent of motor speed and the possibility of a modality-specific impairment of information processing. Twenty-nine patients with CFS and 22 healthy controls matched for age, gender, intelligence, and education were included in this study. The results show that patients with CFS do not seem to be impaired for modification of phasic arousal level, nor for visual selective attention requiring shifting of attention in the visuospatial field. The results further support the presence of reduced information processing speed and efficiency, and strengthen the evidence of a global non-modality-specific attentional dysfunction in patients with CFS. In this study the poor performance of patients with CFS on recall of verbal information was due to poor initial storage rather than to a retrieval failure.
Mojarro Praxedes MD, Benjumea Pino P.	Servicio de Psiquiatria,Hospital Clinico Universitario, Sevilla, Sevilla, 41009,Espana.	[The chronic fatigue and neurasthenia in the student population].[article in Spanish]	Actas Esp Psiquiatr 1999 Jan-Feb;27(1):14-21	INTRODUCTION: Fatigue is one of the most common symptoms in community studies, primary care and other medical setting. In spite of a high frequency of fatigue, the incidence of chronic fatigue syndrome is very low. In this paper, we want to know the frequency of chronic fatigue syndrome and neurasthenia; we want to know the association between fatigue and depressive symptoms in students. METHODS: We studied 277 medical student, administering: 1. a center for disease control questionnaire to assess major criteria and minor criteria of chronic fatigue syndrome, 2. ICD 10 criteria for the diagnoses of neurasthenia and 3. Beck depression inventory. RESULTS AND CONCLUSIONS: We found that the 37,55% of the subjects suffer fatigue. 9 subjects (3,25% of the total) meet the criteria of neurasthenia. 2 subjects (0,72% of the total) meet the chronic fatigue syndrome criteria. The depressive symptoms are most frequent in the subjects with fatigue, but we don't know if they are the cause or the consequence of the fatigue. With the factorial analyses, we find that symtoms of physical fatigue, mental fatigue and cognitive difficulties are factor independent of each other.
Morriss RK, Ahmed M, Wearden AJ, Mullis R, Strickland P, Appleby L, Campbell IT,	Department of Community Psychiatry, Royal Preston Hospital, University of	The role of depression in pain, psychophysiological syndromes and	J Affect Disord 1999 Oct;55(2-3):143-8	BACKGROUND: The association between depression and pain, function, medically unexplained symptoms and psychophysiological syndromes such as irritable bowel syndrome has not been explored before in chronic fatigue syndrome. METHODS: Cross-sectional controlled study of the current prevalence of psychophysiological

Pearson D.	Manchester, UK.	medically unexplained symptoms associated with chronic fatigue syndrome.		syndromes, pain, function and lifetime prevalence of medically unexplained symptoms in 77 out-patients with chronic fatigue syndrome (CFS) without DSM-III-R depression, 42 CFS out-patients with DSM-III-R depression and 26 out-patient with primary DSM-III-R depression. RESULTS: Both CFS groups differed significantly from the primary depression group but not each other in the prevalence of tension headaches (P < 0.001), reporting of widespread bodily pain (P < 0.001) and the number of lifetime medically unexplained symptoms (P < 0.001). The three groups did not significantly differ in the prevalence of irritable bowel syndrome or fibromyalgia. CFS patients with depression were more impaired in social function than other CFS patients. CONCLUSION: Depression is not associated with the reporting of pain, psychophysiological syndromes and medically unexplained symptoms in CFS patients. Depression is associated with decreased social function in CFS patients. LIMITATIONS: Study depended on recall of symptoms, not confirmed by medical records and current investigations. Patients with depression were taking antidepressants. CLINICAL RELEVANCE: Treating depression in chronic fatigue syndrome is unlikely to diminish reporting of pain and medically unexplained symptoms but may improve social function.
Moss RB, Mercandetti A, Vojdani A.	The Immune Response Corporation, Carlsbad, California 92008, USA. shotdoc@imnr.com	TNF-alpha and chronic fatigue syndrome.	J Clin Immunol 1999 Sep;19(5):314-6	Based upon the clinical presentation of chronic fatigue syndrome (CFS), we hypothesized that proinflammatory cytokines may play a role in the pathogenesis of the disease. We therefore undertook a retrospective cross-sectional study to examine the role of TNF-alpha in patients with CFS. Our results suggest a significant increase serum TNF-alpha in patients with CFS (P<0.0001) compared to non-CFS controls. This study supports the further examination of the role of proinflammatory mediators in CFS. Furthermore, the clinical testing of TNF-alpha blockers and other antiinflammatory agents for the treatment of this disease is warranted.
Mullis R, Campbell IT, Wearden AJ, Morriss RK, Pearson DJ.	Department of Physiotherapy Studies, University of Keele, Staffordshire, United Kingdom.	Prediction of peak oxygen uptake in chronic fatigue syndrome.	Br J Sports Med 1999 Oct;33(5):352-6	OBJECTIVES: To establish a simple, valid, and acceptable method of predicting peak oxygen uptake (VO2peak) in patients with chronic fatigue syndrome (CFS), which could provide a basis for subsequent exercise prescription at an appropriate intensity as part of a clinical rehabilitation programme. METHODS: A total of 130 patients who met UK research criteria for CFS were taken from consecutive referrals for chronic fatigue to the University Department of Medicine at Withington Hospital, Manchester. VO2peak was determined using an incremental graded exercise test to exhaustion. Respiratory gas exchange, work rate, and heart rate were monitored throughout. RESULTS: In all patients, VO2peak was found to correlate strongly and significantly with peak work rate (WRpeak) during testing (r2 = 0.88, p<0.001). In patients who exercised for longer than two minutes (n = 119), regression analysis established the relation as Vo2peak = 13.1 x WRPpeak + 284, where VO2 is given in ml/min and WR in W. The mean error between the measured VO2peak and the predicted value was 10.7%. The relation between increase in work rate and oxygen uptake across the group was highly significant (r2 = 0.87, p<0.001), and given as

				VO2increase = 12.0 x WRincrease, this value being similar to that expected for healthy individuals. Almost all (97%) subjects reported no exacerbation of symptoms after maximal exercise testing. CONCLUSIONS: Using a simple to administer maximal exercise test on a cycle ergometer, it is possible to predict accurately the VO2peak of a patient with CFS from peak work rate alone. This value can then be used as an aid to setting appropriate exercise intensity for a rehabilitation programme. The increase in VO2 per unit increase in workload was consistent with that expected in healthy individuals, suggesting that the physiological response of the patients measured here was not abnormal. Contrary to the belief of many patients, maximal exercise testing to the point of subjective exhaustion proved to be harmless, with no subjects suffering any lasting deterioration in their condition after assessment.
Myers C, Wilks D.	Regional Infectious Diseases Unit, Western General Hospital, Edinburgh, UK.	Comparison of Euroqol EQ-5D and SF-36 in patients with chronic fatigue syndrome.	Qual Life Res 1999;8(1-2):9-16	The objective of the study was to compare the Euroqol EQ-5D (Euroqol) and short-form 36 (SF-36) health questionnaires in patients with chronic fatigue syndrome (CFS). One hundred and twenty-seven outpatients referred to a hospital-based infectious disease clinic with a diagnosis of CFS were contacted by post and asked to complete both questionnaires. Additional data were determined from hospital casenotes. Eighty-five patients returned correctly completed questionnaires. Euroqol health values and visual analogue scale (VAS) scores were strongly and significantly correlated with all dimensions of the SF-36, with the exception of physical limitation of role. SF-36 dimensions were in turn strongly and significantly correlated with each other, with the same exception. Patients reported a high degree of physical disability and a moderate degree of emotional or psychological ill-health. The Euroqol elements dealing with mobility and self-care referred to inappropriately severe degrees of disability for these patients with CFS. Similarly some dimensions in the SF-36 were oversensitive and did not discriminate between patients with moderate or severe disability. It was concluded that Euroqol scores correlated strongly with SF-36 scores and provided useful information about patients with CFS and that Euroqol would be a useful tool for the rapid assessment of health status in CFS. The current Euroqol instrument refers to inappropriately severe degrees of disability for patients with CFS and would need to be modified to be maximally useful in this situation.
Nakaya T, Takahashi H, Nakamur Y, Kuratsune H, Kitani T, Machii T, Yamanishi K, Ikuta K.	Section of Serology, Institute of Immunological Science, Hokkaido University, Sapporo, Japan.	Borna disease virus infection in two family clusters of patients with chronic fatigue syndrome.	Microbiol Immunol 1999;43(7):679-89	A high rate of Borna disease virus (BDV) infection has been demonstrated in patients with chronic fatigue syndrome (CFS). Herein, we focused on BDV infection in two family clusters of patients with CFS: a father, mother, two sons and one daughter (family #1); and a father, mother, two daughters and one son (family #2). All members, except for the elder son in family #1 and the father and son in family #2, were diagnosed with CFS. The results supported that all the family members with CFS were infected with BDV, as evidenced by the presence of antibodies to viral p40, p24 and/or gp18 and BDV p24 RNA in peripheral blood mononuclear cells. The healthy members, except for the father of family #2 who was positive for antibody to p24, were all negative by both assays. Follow-up studies in family #1 continued to reveal

				BDV antibodies and BDV RNA, except in the mother, who lost the RNA upon slight recovery from the disease.
Nasralla M, Haier J, Nicolson GL.	The Institute for Molecular Medicine, Huntington Beach, CA 92649-1041, USA.	Multiple mycoplasmal infections detected in blood of patients with chronic fatigue syndrome and/or fibromyalgia syndrome.	Eur J Clin Microbiol Infect Dis 1999 Dec;18(12):859-65	The aim of this study was to investigate the presence of different mycoplasmal species in blood samples from patients with chronic fatigue syndrome and/or fibromyalgia syndrome. Previously, more than 60% of patients with chronic fatigue syndrome/fibromyalgia syndrome were found to have mycoplasmal blood infections, such as Mycoplasma fermentans infection. In this study, patients with chronic fatigue syndrome/fibromyalgia syndrome were examined for multiple mycoplasmal infections in their blood. A total of 91 patients diagnosed with chronic fatigue syndrome/fibromyalgia syndrome and with a positive test for any mycoplasmal infection were investigated for the presence of Mycoplasma fermentans, Mycoplasma pneumoniae, Mycoplasma hominis and Mycoplasma penetrans in blood using forensic polymerase chain reaction. Among these mycoplasma-positive patients, infections were detected with Mycoplasma pneumoniae (54/91), Mycoplasma fermentans (44/91), Mycoplasma hominis (28/91) and Mycoplasma penetrans (18/91). Multiple mycoplasmal infections were found in 48 of 91 patients, with double infections being detected in 30.8% and triple infections in 22%, but only when one of the species was Mycoplasma pneumoniae or Mycoplasma fermentans. Patients infected with more than one mycoplasmal species generally had a longer history of illness, suggesting that they may have contracted additional mycoplasmal infections with time.
Natelson BH, Denny T, Zhou XD, LaManca JJ, Ottenweller JE, Tiersky L, DeLuca J, Gause WC.	Department of Neuroscience, UMDNJ-New Jersey Medical School, East Orange, Newark 07103, USA.	Is depression associated with immune activation?	J Affect Disord 1999 May;53(2):179-84	BACKGROUND: Some research immunologists have suggested that major depression amd chronic fatigue syndrome (CFS) are characterized by immune activation. To test this hypothesis, we compared immunological function in patients with major depression and in patients with CFS who developed major depression after the onset of CFS to that of sedentary healthy controls. METHODS: Subjects completed the Centers for Epidemiological Study-Depression (CES-D) questionnaire and allowed venisection. We performed flow cytometric analysis on 13 groups of white blood cells and used a reverse transcriptase PCR method to assay m-RNA of eight cytokines. RESULTS: CES-D scores were high in both patient groups and did not differ significantly. We found no evidence for immune activation in either patient group. Instead the data suggested immunological downregulation in depression. LIMITATIONS: Not all the subjects in the two patient groups were off antidepressants. CONCLUSIONS: The data indicate that immune activation is not necessary in depression--either alone or with CFS.
Nores JM		The Philosophy of Pain: New Concepts	Journal of Chronic Fatigue Syndrome 1999: 5(2): 99 - 105	This article examines the concept of physical pain and its relationship to philosophy within the context of ethics. The first question posing a problem is: should pain be added to or included in the list of the five senses? Whether sensation is present or not, pain does exist. Pain is part of the ''immediate data of consciousness'' dear to philosophers. Pain is at the heart of ontology, philosophy of the being and existential

				ontology, which places existence above essence. Pain is mine and teaches me that I exist. Pain conveys my existence more than thought. Why shouldn't we enrich Descartes's cogito? ''I suffer, therefore I exist'' rather than ''I think, therefore I exist'' or even ''I am something which suffers'' rather than ''I am a thing which thinks'' by Descartes. As pain is the witness of their existence, other beings resemble me. The use of physical pain to cause harm is the best transition towards the following question, that is, what is the relationship between pain and evil or harm? This is a question which is primordial and concerns philosophers, moralists and theologians. There is just pain which is harmful and is our enemy to be conquered. This would seem to be what philosophy has to teach those of us who are doctors fighting pain.
Onouchi H, Muro Y, Tomita Y.	Department of Dermatology, Nagoya University School of Medicine, Nagoya, Japan.	Clinical features and IgG subclass distribution of anti-p80 coilin antibodies.	J Autoimmun 1999 Sep;13(2):225-32	We examined the clinical features of patients presenting antinuclear autoantibodies against p80-coilin and the IgG subclass distribution of anti- p80-coilin antibodies. Sera from 365 Japanese patients were analysed. Immunoblotting and indirect immunofluorescence microscopy techniques were used with a polyclonal rabbit antiserum against p80-coilin. Eleven patients with anti-p80-coilin antibodies were found. All the patients were female and nine were in their twenties. None could be diagnosed with differentiated rheumatic disease except for one case of systemic scleroderma and another of Sjogren's syndrome. Most patients had general fatigue, arthralgia, headaches, dysmenorrhea, lymph node swelling and/or low grade fever such as chronic fatigue syndrome (CFS), and showed low complement. One patient fulfilled the criteria for CFS. All were younger females than those often diagnosed with rheumatic disease in previous reports. Patients' sera had a predominant distribution of subclass IgG(1)anti-p80-coilin antibodies and five sera had concomitant subclass IgG(2). Two rheumatic disease patients had a relatively high titer of IgG(2)anti-p80-coilin antibodies. The IgG(2)subclass of anti-p80-coilin antibodies may be a specific marker for systemic autoimmune disease. Copyright 1999 Academic Press.
Pagani M, Lucini D.	Centro Ricerca Terapia Neurovegetativa, Ospedale L. Sacco, University of Milan, Via G.B. Grassi, 74, 20157 Milan, Italy.	Chronic fatigue syndrome: a hypothesis focusing on the autonomic nervous system.	Clin Sci (Colch) 1999 Jan;96(1):117-25Comment in: Clin Sci (Colch). 1999 Sep;97(3):319-22	Chronic fatigue syndrome is a debilitating illness of unknown aetiology, with estimated levels of prevalence of up to about 8. 7/100 000 in the U.S.A. Like pain fatigue it is a personal, emotionally rich experience, which may originate from peripheral or central sites (or both). The nature of the symptoms is complex and reflects the interaction of the patient with the environment and cultural milieu. Accordingly the common use of the same terminology for different types of fatigue may be misleading. Autonomic activation is a key component of both real and simulated physical exercise. Alterations in autonomic nervous system activity are a key component of several physiopathological conditions. In chronic fatigue syndrome disturbances in autonomic activity, and in other homoeostatic mechanisms, such as the hormonal and immune systems, have been reported recently. In this review we followed the hypothesis that in chronic fatigue syndrome the paradoxical condition of disturbing somatic symptoms in the absence of organic evidence of disease might

				be addressed by focusing on attending functional correlates. In particular we addressed possible alterations in cardiovascular autonomic control, as can be assessed by spectral analysis of R-R interval and systolic arterial pressure variability. With this approach, in subjects complaining of unexplained fatigue, we obtained data suggesting a condition of prevailing sympathetic modulation of the sino-atrial node at rest, and reduced responsiveness to excitatory stimuli. Far from considering the issue resolved, we propose that in the context of the multiple physiological and psychological interactions involved in the perception and self-reporting of symptoms, attendant changes in physiological equivalents might furnish a convenient assessment independent from subjective components. Indices of sympathetic modulation could, accordingly, provide quantifiable signs of the interaction between subject's efforts and environmental demands, independently of self descriptions, which could provide convenient measurable outcomes, both for diagnosis and treatment titration in chronic fatigue syndrome.
Paul L, Wood L, Behan WM, Maclaren WM.	Department of Physiotherapy, Glasgow Caledonian University, Glasgow, Scotland.	Demonstration of delayed recovery from fatiguing exercise in chronic fatigue syndrome.	Eur J Neurol 1999 Jan;6(1):63-9	Patients with the chronic fatigue syndrome (CFS) complain consistently of delay in recovery of peripheral muscle function after exercise. The purpose of this study was to try to confirm this observation. A fatiguing exercise test was carried out on the quadriceps muscle group of ten patients and ten control subjects. The test consisted of 18 maximum voluntary contractions (MVCs) with a 50% duty cycle (10 s contraction, 10 s rest), and the force generated by each contraction was recorded using a KinCom dynamometer. This was followed by a recovery phase lasting 200 min in which quadriceps strength was evaluated at increasing intervals, and a follow-up session at 24 h post-exercise involving three 10 s MVCs. Throughout the exercise period, the MVCs obtained from the control group were significantly higher than those of the patient group ($P = 0.006$), but both groups showed a parallel decline in force over the 18 contractions, in keeping with a similar endurance capacity. Recovery was prolonged in the patient group, however, with a significant difference compared to initial MVCs being evident during the recovery phase after exercise ($P = 0.001$) and also at 24 h ($P < 0.001$). In contrast, the control group achieved MVCs which were not significantly different from initial values during the recovery phase, and maintained these at 24 h. These findings support the clinical complaint of delayed recovery after exercise in patients with CFS. Copyright 1999 Lippincott Williams & Wilkins
Perry LD.		Chronic fatigue syndrome?	Pediatrics 1999 Jul;104(1 Pt 1):130, discussion 131-2	
Pheley AM, Melby D, Schenck C, Mandel J, Peterson PK.	Ohio University College of Osteopathic Medicine, Athens, USA.	Can we predict recovery in chronic fatigue syndrome?	Minn Med 1999 Nov;82(11):52-6	PURPOSE: To determine if selected demographic or clinical features of chronic fatigue syndrome (CFS) are associated with recovery. PATIENTS AND METHODS: A follow-up questionnaire was mailed to 341 patients who had been ill on average for nine years to ascertain "recovery" rate (defined as self-reported recovery on a visual

				analog scale). Baseline demographic and clinical features (functional status and psychological status) recorded at the time of the initial (baseline) clinical visit were analyzed for their association with recovery at the time of follow-up. RESULTS: Of the 177 patients who responded to the follow-up questionnaire, only 21 (12%) reported "recovery." Patients with higher levels of physical and social functioning and lower levels of anxiety and obsessive-compulsiveness at baseline were more likely to report recovery at follow-up ($p < 0.05$). No specific demographic characteristics were associated with recovery. CONCLUSION: These findings support previous research that complete recovery from CFS is rare and that patients with less severe illness at the initial clinic visit are more likely to have a positive prognosis for recovery. However, considerable overlap in illness severity was observed between the recovered and nonrecovered groups, suggesting that accurate prediction of recovery in individual CFS patients is not currently feasible.
Plioplys AV.		Chronic fatigue syndrome?	Pediatrics 1999 Jul;104(1 Pt 1):130-2	
Prins JB, Bleijenberg G.	Department of Medical Psychology, Hospital Nijmegen, The Netherlands. j.prins@cksmps.az.nl	Cognitive behavior therapy for chronic fatigue syndrome: a case study.	J Behav Ther Exp Psychiatry 1999 Dec;30(4):325-39	The case of a 26-year old woman with Chronic Fatigue Syndrome (CFS) is presented. Multidimensional assessment showing severe debilitating fatigue and considerable psychological, social and occupational impairment confirmed the diagnosis. Cognitive behavior therapy (CBT) was based on a tested causal model of CFS and individual behavioral analyses. Key elements in CBT were process variables from the CFS model, like sense of control, causal attributions, physical activity and focusing on bodily functions. Goals were recovery from fatigue, returning to work and relapse prevention. The course of therapy is described in detail to illustrate difficulties in treating CFS. Assessments were made five times, at baseline and at 8, 14, 21 and 33 months. Comparison of the pretest, post-test and follow-up scores of the outcome variables, fatigue and functional impairment and of the process variables showed clinically significant improvement from the range of CFS patients to the range of healthy controls.
Propsner NM.	The classic profile of the chronic fatigue syndrome (CFS) patient is a white, middle-age female. Characterized by profound fatigue, CFS often starts with an acute viral infection. While today's medicine provides symptomatic relief, research is offering in	Fatigue that doesn't go away.	N J Med 1999 Jun;96(6):29-31	

Rea T, Buchwald D.		Hydrocortisone and chronic fatigue syndrome.	Lancet 1999 May 8;353(9164):1618-9; discussion 1619-20 Comment on: Lancet. 1999 Feb 6;353(9151):455-8	
Riem L.		[Etiology and therapy of chronic fatigue syndrome. Too tired for life. Press Conference: Fatigue--Paralyzing Symptom in Cancer Patients, Cologne, 17 September 1999].[article in German]	MMW Fortschr Med 1999 Nov 11;141(45):16-8	
Robertson TJ.		Misunderstood illnesses: fibromyalgia and chronic fatigue syndrome.	Alta RN 1999 May-Jun;55(3):6-7	
Rowe PC, Barron DF, Calkins H, Maumenee IH, Tong PY, Geraghty MT.	Department of Pediatrics, Center for Hereditary Eye Diseases, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.	Orthostatic intolerance and chronic fatigue syndrome associated with Ehlers-Danlos syndrome.	J Pediatr 1999 Oct;135(4):494-9	OBJECTIVE: To report chronic fatigue syndrome (CFS) associated with both Ehlers-Danlos syndrome (EDS) and orthostatic intolerance. STUDY DESIGN: Case series of adolescents referred to a tertiary clinic for the evaluation of CFS. All subjects had 2-dimensional echocardiography, tests of orthostatic tolerance, and examinations by both a geneticist and an ophthalmologist. RESULTS: Twelve patients (11 female), median age 15.5 years, met diagnostic criteria for CFS and EDS, and all had either postural tachycardia or neurally mediated hypotension in response to orthostatic stress. Six had classical-type EDS and 6 had hypermobile-type EDS. CONCLUSIONS: Among patients with CFS and orthostatic intolerance, a subset also has EDS. We propose that the occurrence of these syndromes together can be attributed to the abnormal connective tissue in dependent blood vessels of those with EDS, which permits veins to distend excessively in response to ordinary hydrostatic pressures. This in turn leads to increased venous pooling and its hemodynamic and symptomatic consequences. These observations suggest that a careful search for hypermobility and connective tissue abnormalities should be part of the evaluation of patients with CFS and orthostatic intolerance syndromes.
Russell IJ, Vipraio GA, Michalek JE, Craig FE, Kang YK, Richards AB.	Department of Medicine, University Clinical Research Center, The University	Lymphocyte markers and natural killer cell activity in fibromyalgia syndrome: effects of	J Interferon Cytokine Res 1999 Aug;19(8):969-78	A clinical study was designed to utilize flow cytometric immunophenotyping and chromium release from cultured tumor target cells to characterize peripheral blood mononuclear leukocyte (PBML) subpopulations and natural killer activity in healthy normal controls (n = 18) and in patients with fibromyalgia syndrome (FMS) at

	of Texas Health Science Center, San Antonio 78284-7868, USA. russell@uthscsa.edu	low-dose, sublingual use of human interferon-alpha.		baseline (n = 124) and again after 6 weeks of treatment with low-doses of orally administered human interferon-alpha (IFN-alpha). Volunteer subjects discontinued all analgesic and sedative hypnotic medications for 2 weeks prior to the baseline phlebotomy. Laboratory measures included a complete blood count; a phenotypic analysis of PBML by flow cytometry; and in vitro natural killer (NK) cell activity. After baseline blood sample collection, the FMS patients were randomized to one of four parallel treatment groups (n = 28/group) to receive sublingual IFN-alpha (15 IU, 50 IU, 150 IU), or placebo every morning for 6 weeks. The tests were repeated at week 6 to evaluate treatment effects. At baseline, FMS patients exhibited fewer lymphocytes and more CD25+ T lymphocytes than did normal controls. By week 6, the main significant and consistent change was a decrease in the HLA-DR+ CD4+ subpopulation in the 15 IU and 150 IU treatment groups. These data do not support an immunologically dysfunctional PBML phenotype among patients with FMS as has been observed in the chronic fatigue syndrome.
Sacco P, Hope PA, Thickbroom GW, Byrnes ML, Mastaglia FL.	Australian Neuromuscular Research Institute, QE II Medical Centre, Nedlands, WA, Australia. psacco@cyllene.uwa.edu.au	Corticomotor excitability and perception of effort during sustained exercise in the chronic fatigue syndrome.	Clin Neurophysiol 1999 Nov;110(11):1883-91	OBJECTIVE: We have investigated the possibility of a central basis for the complaints of fatigue and poor exercise tolerance in subjects with chronic fatigue syndrome (CFS). METHODS: Transcranial magnetic stimulation of the motor cortex was used to measure sequential changes in motor evoked potential (MEP) amplitude, post-excitatory silent period (SP) duration and twitch force of the biceps brachii muscle during a 20% maximum isometric elbow flexor contraction maintained to the point of exhaustion. Ten patients with post-infectious CFS and 10 age- and sex-matched control subjects were studied. Results were analysed using non-parametric repeated measures analysis of variance (Friedman's test) and Mann-Whitney U-tests for intra- and inter-group comparisons respectively. RESULTS: Mean endurance time for the CFS group was lower (13.1+/-3.2 min, mean +/- SEM) than controls (18.6+/-2.6 min, P < 0.05) and CFS subjects reported higher ratings of perceived exertion. During the exercise period MEP amplitude and SP duration increased in both groups but to a lesser extent in CFS subjects. Interpolated twitch force amplitude also increased during exercise, being more pronounced in CFS subjects. CONCLUSION: The findings are in keeping with an exercise-related diminution in central motor drive in association with an increased perception of effort in CFS.
Saheki T.	Department of Biochemistry, Faculty of Medicine, Kagoshima University.	[Carnitine as a vitamin-like biofactor].[article in Japanese]	Nippon Rinsho 1999 Oct;57(10):2270-5	Carnitine is a well-known cofactor for the beta-oxidation of long-chain fatty acid. It also plays a role in transport of acetyl moity for fatty acid and cholesterol synthesis, excretion of organic acid and xenobiotic acid as carnitine ester, and control of ratio of acetylCoA to CoA. Therapeutic effect of acetylcarnitine on Alzheimer disease and HIV-infection, and aberrant incorporation acetylcarnitine into brain under chronic fatigue syndrome have been reported. Carnitine deficiency causes hyperammonemia through suppression of gene expression of urea cycle enzymes. On the other hand, a large amount of carnitine has a therapeutic effect on hyperammonemia by still unclear mechanism. These suggest carnitine as a multifunctional biofactor. Review

				Literature
Saul JP.	MUSC, Charleston 29425, USA.	Syncope: etiology, management, and when to refer.	J S C Med Assoc 1999 Oct;95(10):385-7	An abnormality of blood pressure control is by far the most likely cause of syncope in children; however, syncope in children may be due to primary cardiac dysrhythmias, particularly in the presence of structural heart disease. An appropriate work-up should include an ECG with a 60-second rhythm strip at first presentation. Tilt testing can usually wait until after a second occurrence on non-pharmacologic therapy. Patients who require more than a history and ECG by the algorithm in the Figure should probably be referred to a cardiologist familiar with the evaluation of syncope. The common form of neurally mediated syncope is also probably related to both breath-holding spells in toddlers, and to many of the cases of chronic fatigue syndrome.
Schondorf R, Benoit J, Wein T, Phaneuf D.	Department of Neurology, McGill University, Sir Mortimer B. Davis Jewish General Hospital, Montreal, Quebec, Canada. cxrs@musica.mcgill.ca	Orthostatic intolerance in the chronic fatigue syndrome.	J Auton Nerv Syst 1999 Feb 15;75(2-3):192-201	This study aims to investigate the prevalence and pathophysiology of orthostatic intolerance (OI) and its potential contribution to symptoms of a group of unselected patients with chronic fatigue syndrome (CFS). Seventy five patients (65 women, 10 men) with CFS were evaluated. During an initial visit, a clinical suspicion as to the likelihood of observing laboratory evidence of OI was assigned. Laboratory investigation consisted of beat-to-beat recordings of heart rate, blood pressure (Finapres), and stroke volume (impedance cardiograph) while supine and during 80 degrees head-up tilt (HUT), during rhythmic deep breathing (6 breaths/min) and during the Valsalva maneuver. The responses of 48 age-matched healthy controls who had no history of OI were used to define the range of normal responses to these three maneuvers. Forty percent of patients with CFS had OI during head-up tilt. Sixteen exhibited neurally-mediated syncope alone, seven tachycardia (> 35 bpm averaged over the whole of the head-up tilt) and six a mixture of tachycardia and syncope. Eight of 48 controls exhibited neurally-mediated syncope. The responses to the Valsalva maneuver and to deep breathing were similar in controls and patients. On average, the duration of disease and patient age were significantly less and the onset of symptoms was more often subacute in patients with OI than in those without OI. We conclude that there exists a clinically identifiable subgroup of patients with CFS and OI that differs from control subjects and from those with CFS without OI for whom treatment specifically aimed at improving orthostatic tolerance may be indicated.
Schondorf R, Freeman R.	Dept. of Neurology, McGill University, Sir Mortimer B. Davis Jewish General Hospital, Montreal, Quebec, Canada. cxrs@musica.mcgill.ca	The importance of orthostatic intolerance in the chronic fatigue syndrome.	Am J Med Sci 1999 Feb;317(2):117-23	Chronic fatigue syndrome (CFS) or myalgic encephalomyelitis is a clinically defined syndrome characterized by persistent or relapsing debilitating fatigue for longer than 6 months in the absence of any definable medical diagnosis. The cause of this syndrome is unknown. Symptoms of orthostatic intolerance, such as disabling fatigue, dizziness, diminished concentration, tremulousness, and nausea, are often found in patients with CFS. In this review, we critically evaluate the relationship between orthostatic intolerance and CFS. Particular emphasis is placed on clinical diagnosis, laboratory testing, pathophysiology, and therapeutic management. It is

				hoped that this review will provide a stimulus for further study of this complex and disabling condition.
Schutzer SE, Natelson BH.	Department of Medicine, University of Medicine and Dentistry, New Jersey Medical School, Newark 07103, USA. schutzer@umdnj.edu	Absence of Borrelia burgdorferi-specific immune complexes in chronic fatigue syndrome.	Neurology 1999 Oct 12;53(6):1340-1	Chronic fatigue syndrome (CFS) and Lyme disease often share clinical features, especially fatigue, contributing to concern that Borrelia burgdorferi (Bb), the cause of Lyme disease, may underlie CFS symptoms. We examined 39 CFS patients and 40 healthy controls with a Bb immune complex test. Patients and controls were nonreactive. Centers for Disease Control and Prevention-defined CFS patients lacking antecedent signs of Lyme disease--erythema migrans, Bell's palsy, or large joint arthritis--are not likely to have laboratory evidence of Bb infection.
Scott LV, Dinan TG.	Department of Psychiatry, Trinity College Medical School, St James' Hospital, Dublin, Ireland. Review, Academic	The neuroendocrinology of chronic fatigue syndrome: focus on the hypothalamic-pituitary-adrenal axis.	Funct Neurol 1999 Jan-Mar;14(1):3-11	
Scott LV, Medbak S, Dinan TG.	Department of Psychiatry, Trinity College Medical School, St. James' Hospital, Dublin, Ireland.	Desmopressin augments pituitary-adrenal responsivity to corticotropin-releasing hormone in subjects with chronic fatigue syndrome and in healthy volunteers.	Biol Psychiatry 1999 Jun 1;45(11):1447-54	BACKGROUND: Corticotropin-releasing hormone (CRH) and vasopressin (VP) are the two principal neuropeptide regulators of the hypothalamic-pituitary-adrenal axis in man, with VP serving to augment CRH-induced adrenocorticotropic hormone (ACTH) release. Unlike VP, desmopressin (DDAVP), which is a synthetic analogue of VP, when administered alone, has not been shown in healthy subjects to have consistent ACTH-releasing properties. It has been suggested that chronic fatigue syndrome (CFS), characterized by profound fatigue and a constellation of other symptoms, may be caused by a central deficiency of CRH. METHODS: We administered 100 micrograms ovine CRH (oCRH) and 10 micrograms DDAVP, both alone and in combination, to a group of subjects with CFS, and to a group of healthy volunteers. Our aim was to establish the effect of DDAVP on CRH-induced ACTH release in these two groups. RESULTS: The delta-ACTH responses to oCRH were attenuated in the CFS (21.0 +/- 4.5 ng/L) compared to the control subjects (57.8 +/- 11.0 ng/L; $t = 3.2$, $df = 21$, $p < .005$). The delta-cortisol responses were also reduced in the CFS (157.6 +/- 40.7 nmol/L) compared to the healthy subjects (303.5 +/- 20.9 nmol/L; $t = 3.1$, $df = 21$, $p < .01$). The delta-ACTH and delta-cortisol responses to DDAVP alone did not differ between the two groups. On administration of both CRH and DDAVP no response differences between the two groups for either ACTH ($p = .3$) or cortisol output ($p = .87$) were established. Comparing the ACTH and cortisol responses to CRH and CRH/DDAVP in only those individuals from each group who had both tests, the cortisol output to the combination was significantly greater in the CFS compared to the healthy group. The ACTH output was also increased in the former group, though this was not significant. CONCLUSIONS: DDAVP augments CRH-mediated pituitary-adrenal responsivity in healthy subjects and in patients with CFS. That DDAVP was capable of normalizing

				the pituitary-adrenal response to oCRH in the CFS group suggests there may be increased vasopressinergic responsivity of the anterior pituitary in CFS and/or that DDAVP may be exerting an effect at an adrenal level.
Scott LV, Salahuddin F, Cooney J, Svec F, Dinan TG.	Department of Psychiatry, Trinity College Medical School, Dublin, Ireland.	Differences in adrenal steroid profile in chronic fatigue syndrome, in depression and in health.	J Affect Disord 1999 Jul;54(1-2):129-37	BACKGROUND: Hyperactivity and hypoactivity of the HPA have been forwarded as of pathophysiological relevance in major depressive disorder and chronic fatigue syndrome (CFS), respectively. METHODS: This study examines cortisol levels in the two disorders, and also assesses levels of the adrenal androgens, dehydroepiandrosterone (DHEA) and its sulphate derivative (DHEA-S), and 17-alpha-hydroxyprogesterone; 15 subjects with CFS diagnosed according to CDC criteria, 15 subjects with DSM III-R major depression and 11 healthy subjects were compared. RESULTS: DHEA and DHEA-S levels were significantly lower in the CFS compared to the healthy group; DHEA-S levels, but not DHEA, were lower in the depressives; cortisol and 17-alpha-hydroxyprogesterone did not differ between the three groups. CONCLUSIONS: A potential role for DHEA, both therapeutically and as a diagnostic tool, in CFS, is suggested.
Scott LV, Teh J, Reznek R, Martin A, Sohaib A, Dinan TG.	Department of Psychiatry, Trinity College Dublin Medical School, St. James's, Hospital, Ireland.	Small adrenal glands in chronic fatigue syndrome: a preliminary computer tomography study.	Psychoneuroendocrinology 1999 Oct;24(7):759-68	No inclusive or satisfactory biomedical explanation for chronic fatigue syndrome (CFS) has as yet been forwarded. Recent research suggests that a dysregulated hypothalamic-pituitary-adrenal axis (HPA) may be contributory, and in particular that there may be diminished forward drive and adrenal under-stimulation. In this preliminary study we wished to examine a cohort of CFS patients in whom evidence for such hypofunctioning was found. Our aim was to establish whether these patients had altered adrenal gland size. Patients were recruited from a fatigue clinic. Those who fulfilled the Centre for Disease Control and Prevention (CDC) criteria underwent a 1 microgram adrenocorticotropin (ACTH) stimulation test, a test of adrenal gland functioning. Eight subjects (five females, three males) with a subnormal response to this test underwent a computer tomography (CT) adrenal gland assessment. Measurements were compared with those from a group of 55 healthy subjects. The right and left adrenal gland bodies were reduced by over 50% in the CFS subjects indicative of significant adrenal atrophy in a group of CFS patients with abnormal endocrine parameters. This is the first study to use imaging methods to measure adrenal gland size in CFS. It is a limitation of this study that a selected CFS sample was employed. A future larger study would optimally employ an unselected cohort of CFS patients. This study has implications not only for the elucidation of CFS pathophysiology, but also for possible therapeutic strategies.
Shepherd C.		Hydrocortisone and chronic fatigue syndrome.	Lancet 1999 May 8;353(9164):1619-20 Comment on: Lancet. 1999 Feb 6;353(9151):424-5 Lancet. 1999 Feb	

			6;353(9151):455-8	
Shlaes JL, Jason LA, Ferrari JR.	DePaul University, Department of Psychology, Chicago, IL 60614, USA.	The development of the Chronic Fatigue Syndrome Attitudes Test. A psychometric analysis.	Eval Health Prof 1999 Dec;22(4):442-65	Chronic Fatigue Syndrome (CFS) is characterized by debilitating symptoms including persistent or relapsing fatigue. As a result of CFS, some individuals experience significant stigma that is attached to this illness. Many medical professionals are skeptical of the validity of the illness, and employers often fail to appreciate the seriousness of the symptoms. Although negative attitudes greatly affect the lives of individuals with CFS, there is presently no measurement of attitudes toward this illness and people who have CFS. The purpose of the present studies was to create a scale that measures attitudes toward individuals with CFS--the Chronic Fatigue Attitudes Test (CAT)--and to assess the scale's reliability and validity. The 13-item scale was created using several constructs outlined in the literature regarding negative attitudes toward people with CFS, disabilities, and AIDS. Theoretical implications of the findings and the utility of the CAT are discussed.
Smith AP, Borysiewicz L, Pollock J, Thomas M, Perry K, Llewelyn M.	Department of Experimental Psychology, University of Bristol.	Acute fatigue in chronic fatigue syndrome patients.	Psychol Med 1999 Mar;29(2):283-90	BACKGROUND: Chronic fatigue syndrome (CFS) patients often complain that they are more susceptible to acute mental fatigue. It is important to determine whether this is observed using objective tests of sustained attention and responding. METHODS: Sixty-seven patients who fulfilled the criteria for CFS proposed by Sharpe et al. (1991) were compared with 126 matched healthy controls. Acute fatigue was assessed by comparing performance at the start and end of a lengthy test session and by examining changes over the course of individual tasks. RESULTS: CFS patients showed impaired performance compared to the controls and these differences increased as the volunteers developed acute fatigue. In addition, differences between the two groups were larger at the end of the test session. CONCLUSIONS: The present results show that CFS patients are more susceptible to acute fatigue than healthy controls. This could reflect motor fatigue or an inability to compensate for fatigue with increased effort. This profile is consistent with previous research on fatigue and suggests that interpretation of certain aspects of CFS may be helped by considering it as the end point of a continuum of fatigue rather than a distinct disease.
Social Security Administration.	Notice of Social Security ruling.	Social Security Ruling, SSR 99-2p.; titles II and XVI; evaluating cases involving chronic fatigue syndrome (CFS).	Fed Regist 1999 Apr 30;64(83):23380-4	In accordance with 20 CFR 402.35(b)(1), the Commissioner of Social Security gives notice of Social Security Ruling, SSR 99-2p. This Ruling clarifies disability policy for the evaluation and adjudication of disability claims involving Chronic Fatigue Syndrome (CFS). This Ruling explains that, when it is accompanied by appropriate medical signs or laboratory findings, CFS is a medically determinable impairment that can be the basis for a finding of "disability." This Ruling ensures that all adjudicators will use the same policies and procedures in evaluating disability claims involving CFS, and provides a consolidated statement of these policies and procedures.
Soetekouw PM, Lenders JW, Bleijenberg G, Thien T, van der Meer JW.	Department of Medicine, St. Radboud University Hospital, Nijmegen, The	Autonomic function in patients with chronic fatigue syndrome.	Clin Auton Res 1999 Dec;9(6):334-40	Subtle signs of autonomic dysfunction and orthostatic intolerance have been reported in patients with chronic fatigue syndrome (CFS). To assess cardiovascular autonomic function noninvasively in an unselected group of patients with CFS, we examined responsiveness to several cardiovascular reflex tests in 37 CFS patients and

	Netherlands.			38 healthy control subjects. Blood pressure and heart rate (HR) were recorded continuously by a Finapres device before and during forced breathing, standing up, Valsalva maneuver, and sustained handgrip exercise (HG). In addition, a mental arithmetic test was carried out and questionnaires to assess the severity of CFS symptoms were completed. At rest, there were no significant differences in blood pressure or in HR between the two groups. The in- and expiratory difference in HR tended to be lower in CFS patients (28.4 +/- 10.5 beats) than in healthy controls (32.2 +/- 9.5) ($p = 0.11$). The maximal increase in HR during standing up was not significantly different between the CFS group (37.6 +/-8.9 beats) and the control group (40.2 +/- 8.9 beats). There were no significant differences between both groups with regard to the Valsalva ratio, but the systolic and diastolic blood pressure responses were significantly larger in CFS patients, despite the fact that many CFS patients were not able to sustain the Valsalva maneuver. The HR response to MA was significantly less in the CFS group (22.6 +/- 9.9) than in the control group (29.5 +/- 16.7) ($p < 0.05$), suggesting impaired cardiac sympathetic responsiveness to mental stress. The lower HR responses could not be explained by the level of concentration in the CFS group. During HG exercise, the hemodynamic responses were lower in the CFS group than in the control group, but this might be attributed to the lower level of muscle exertion in CFS patients. There were no significant differences between CFS patients with and without symptoms of autonomic dysfunction regarding the hemodynamic responses to the cardiovascular reflex tests. The findings of the study suggest that there are no gross alterations in cardiovascular autonomic function in patients with CFS.
Sorenson WG.	Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, WV 26505, USA. wgs1@cdc.gov	Fungal spores: hazardous to health?	Environ Health Perspect 1999 Jun;107 Suppl 3:469-72	Fungi have long been known to affect human well being in various ways, including disease of essential crop plants, decay of stored foods with possible concomitant production of mycotoxins, superficial and systemic infection of human tissues, and disease associated with immune stimulation such as hypersensitivity pneumonitis and toxic pneumonitis. The spores of a large number of important fungi are less than 5 microm aerodynamic diameter, and therefore are able to enter the lungs. They also may contain significant amounts of mycotoxins. Diseases associated with inhalation of fungal spores include toxic pneumonitis, hypersensitivity pneumonitis, tremors, chronic fatigue syndrome, kidney failure, and cancer.
Starcevic V.	University of Belgrade School of Medicine, Yugoslavia.	Neurasthenia: cross-cultural and conceptual issues in relation to chronic fatigue syndrome.	Gen Hosp Psychiatry 1999 Jul-Aug;21(4):249-55	The purpose of this study was to examine several conceptual and cross-cultural issues in neurasthenia, particularly in terms of their relationship to chronic fatigue syndrome. A review of this relationship led to the conclusion that these conditions are much more alike in Western countries than in countries such as China, where neurasthenia could almost be regarded as a "culture-bound syndrome." This may be a consequence of factors such as the heterogeneous nature of neurasthenia and different diagnostic practices in different countries, despite the ICD-10 definition of neurasthenia, intended for worldwide use. Likewise, there is no consensus on what

				the "core" characteristics of neurasthenia are, because its clinical presentation and key features in different countries are very different. Despite the finding of relatively low comorbidity rates between neurasthenia and other mental disorders, clinical experience suggests that features of neurasthenia frequently overlap with those of depression, chronic anxiety, and somatoform disorders. There is no convincing evidence that in cases of overlap or comorbidity, other diagnoses should automatically have "primacy" over neurasthenia nor should the diagnosis of neurasthenia thereby be excluded. Although some aspects of its validity have improved recently, especially its descriptive validity, the overall validity of the diagnosis of neurasthenia is still not satisfactory. Suggestions for further research, aimed at improving the diagnostic validity of neurasthenia, are offered in this paper.
Stark FM, Sobetzko HM.	Klinik fur Psychiatrie und Psychotherapie, Universitatskrankenhaus Eppendorf, Hamburg, Germany.	Approaches to coping with chronic fatigue syndrome (CFS).	Zentralbl Hyg Umweltmed 1999 Aug;202(2-4):179-90	The 1994 approach to the definition of Chronic Fatigue Syndrome (CFS) describes a severe disorder with unknown etiology and pathophysiology. It results in substantial reduction in previous levels of occupational, educational, social, or personal activities. Most patients cannot continue their usual lifestyle. No causal treatments or other therapies suitable for all patients exist so far. Therefore it was intended to identify approaches to an effective disease management by the long time escort and observation of a CFS support group. CFS should be diagnosed according to the actual CDC guidelines. Conditions with similar symptoms explaining chronic fatigue have to be ruled out first. Then an individually shaped disease management comprising of different components plays a central role in the coping process. Medical long time care performed by a general practitioner and the membership in a suitable support group are integrated within this approach.
Stejskal VD, Danersund A, Lindvall A, Hudecek R, Nordman V, Yaqob A, Mayer W, Bieger W, Lindh U.	Dept Clinical Chemistry, Danderyd Hospital and Karolinska Institute, Stockholm, Sweden. vera.melisa@swipnet.se	Metal-specific lymphocytes: biomarkers of sensitivity in man.	Neuroendocrinol Lett 1999;20(5):289-298	Many patients attribute their health problems to amalgam and other dental metals. In genetically susceptible indviduals, mercury and gold may function as haptens and elicit allergic and autoimmune reactions. The frequency of metal-induced lymphocyte responses was examined in 3,162 patients in three European laboratories using MELISA(R), an optimized lymphocyte proliferation test. The patients suffered from local and systemic symptoms attributed to dental restorations. The effect of dental metal removal was studied in 111 patients with metal hypersensitivity and symptoms resembling Chronic Fatigue Syndrome (CFS). After consultation with a dentist the patients decided to replace their metal restorations with non-metallic materials. The changes in health and in vitro lymphocyte reactivity were studied by inquiries and follow-up MELISA(R). Lymphocyte reactivity was also analyzed in 116 healthy subjects with no complaints of metal allergy. A significant number of patients had metal-specific lymphocytes in the blood. Nickel was the most common sensitizer, followed by inorganic mercury, gold, phenylmercury, cadmium and palladium. As compared to lymphocyte responses in healthy subjects, the CFS group had significantly increased responses to several metals, especially to inorganic mercury, phenylmercury and gold. Following dental metal removal, 83 patients (76%) reported long-term health

				improvement. Twenty-four patients (22%) reported unchanged health and two (2%) reported worsening of symptoms. Following dental metal replacement, the lymphocyte reactivity to metals decreased as well. We propose that an inflammatory process induced by metals may modulate the hypothalamic-pituitary-adrenal axis (HPA axis) and trigger multiple non-specific symptoms characterizing CFS and other chronic conditions like myalgic encephalitis (ME) and multiple chemical sensitivity (MCS).
Sterzl I, Prochazkova J, Hrda P, Bartova J, Matucha P, Stejskal VD.	Institute of Endocrinology, Prague, Czech Republic.	Mercury and nickel allergy: risk factors in fatigue and autoimmunity.	Neuroendocrinol Lett 1999;20(3-4):221-228	This study examined the presence of hypersensitivity to dental and environmental metals in patients with clinical disorders complicated with chronic fatigue syndrome. Three groups of patients were examined through medical history, dental examination, and by using a modified test of blast transformation for metals-MELISA(R). The three groups consisted of the following: 22 patients with autoimmune thyroiditis with or without polyglandular autoimmune activation; 28 fatigued patients free from endocrinopathy; and 22 fatigued professionals without evidence of autoimmunity. As controls, a population sample or 13 healthy subjects without any evidence of metal sensitivity was included. Healthy controls did not complain of marked fatigue and their laboratory tests did not show signs of autoimmunity and endocrinopathy. We have found that fatigue, regardless of the underlying disease, is primarily associated with hypersensitivity to inorganic mercury and nickel. The lymphocyte stimulation by other metals was similar in fatigued and control groups. To evaluate clinical relevance of positive in vitro findings, the replacement of amalgam with metal-free restorations was performed in some of the patients. At a six-month follow-up, patients reported considerably alleviated fatigue and disappearance of many symptoms previously encountered; in parallel, lymphocyte responses to metals decreased as well. We suggest that metal-driven inflammation may affect the hypothalamic-pituitary-adrenal axis (HPA axis) and indirectly trigger psychosomatic multisymptoms characterizing chronic fatigue syndrome, fibromyalgia, and other diseases of unknown etiology.
Stewart JM, Gewitz MH, Weldon A, Arlievsky N, Li K, Munoz J.	Department of Pediatrics, New York Medical College, Valhalla, New York, USA.	Orthostatic intolerance in adolescent chronic fatigue syndrome.	Pediatrics 1999 Jan;103(1):116-21	OBJECTIVES: To demonstrate the association between orthostatic intolerance and the chronic fatigue syndrome (CFS) in adolescents and to delineate the form that orthostatic intolerance takes in these children. STUDY DESIGN: We investigated the heart rate and blood pressure (BP) responses to head-up tilt (HUT) in 26 adolescents aged 11 to 19 years with CFS compared with responses in adolescents referred for the evaluation of simple faint and to responses in 13 normal healthy control children of similar age. RESULTS: A total of 4/13 of the controls and 18/26 simple faint patients experienced typical faints with an abrupt decrease in BP and heart rate associated with loss of consciousness. One CFS patient had a normal HUT. A total of 25/26 CFS patients experienced severe orthostatic symptoms associated with syncope in 7/25, orthostatic tachycardia with hypotension in 15/25, and orthostatic tachycardia without significant hypotension in 3/25. Acrocyanosis, cool extremities,

				and edema indicated venous pooling in 18/25. None of the control or simple faint patients experienced comparable acral or tachycardic findings. CONCLUSIONS: We conclude that chronic fatigue syndrome is highly related to orthostatic intolerance in adolescents. The orthostatic intolerance of CFS often has heart rate and BP responses similar to responses in the syndrome of orthostatic tachycardia suggesting that a partial autonomic defect may contribute to symptomatology in these patients.
Stewart JM, Gewitz MH, Weldon A, Munoz J.	Department of Pediatrics, Division of Cardiology, New York Medical College, Valhalla 10595, USA.	Patterns of orthostatic intolerance: the orthostatic tachycardia syndrome and adolescent chronic fatigue.	J Pediatr 1999 Aug;135(2 Pt 1):218-25	OBJECTIVES: To describe the orthostatic tachycardia syndrome (OTS) in adolescents, similarities to and differences from chronic fatigue syndrome (CFS), and patterns of orthostatic intolerance during head-up tilt (HUT). STUDY DESIGN: Using electrocardiography and arterial tonometry, we investigated the heart rate and blood pressure responses during HUT in 20 adolescents with OTS compared with 25 adolescents with CFS, 13 healthy control subjects, and 20 patients with simple faint. RESULTS: Of the control subjects, 4 of 13 experienced typical vasovagal faints with an abrupt fall in blood pressure and heart rate, and 14 of 20 patients with simple faint experienced similar HUT responses. All patients with CFS (25/25) experienced severe orthostatic symptoms with syncope in 2 of 25, early orthostatic tachycardia during HUT in 16 of 23 (13/16 hypotensive), and delayed orthostatic tachycardia in 7 of 23 (6/7 hypotensive). Acrocyanosis and edema occurred in 18 of 25. Early orthostatic tachycardia occurred in 10 of 20 patients with OTS. Of these, 9 of 10 were hypotensive, but hypotension was delayed in 4 of 9. Delayed tachycardia occurred in 10 of 20 (all hypotensive). Acrocyanosis and edema occurred in most patients with CFS, fewer patients with OTS, and in one patient with simple faint. Orthostatic symptoms were similar but more severe in patients with CFS compared with patients with OTS. CONCLUSIONS: Symptoms and patterns of orthostatic heart rate and blood pressure change in OTS overlap strongly with those of CFS. Orthostatic intolerance in OTS may represent an attenuated form of chronic fatigue pathophysiology.
Streeten DH, Bell DS.		Long- and short-term blood pressure and RR-interval variability and psychosomatic distress in chronic fatigue syndrome.	Clin Sci (Colch) 1999 Sep;97(3):319-22 Comment on: Clin Sci (Colch). 1998 Jan;94(1):57-63 Clin Sci (Colch). 1999 Jan;96(1):117-25	
Teitelbaum JE, Bird B, Weiss A, Gould L.		Low-dose hydrocortisone for chronic fatigue syndrome.	JAMA 1999 May 26;281(20):1887-8; discussion 1888-9 Comment on: JAMA. 1998 Sep 23-30;280(12):1061-6	
Terra JL.	Departement	[Symptomatic and	Rev Prat 1999 Apr	The symptomatic and concurrent depressions description need to resort to

	d'information et d'evaluation medicales, Centre hospitalier specialise Le Vinatier, Bron.	concurrent depressions].[article in French]	1;49(7):727-31	comorbidity and symptomatic co-occurrence concepts. Patients with depressive symptoms or in a major depressive episode may also be suffering from another nonmood psychiatric disorders as alcoholism, anxiety or eating disorders. Many general medical conditions which are link with depression are illustrated with the examples of cancer, coronary artery disease, endocrinologic diseases, dementia, stroke and chronic fatigue syndrome. When depression and another psychiatric or medical conditions occur together, it is important to provide to the practitioner guidelines for the decision to treat one of the two disorders. This paper contains an example of decisional algorithm.
Theorell T, Blomkvist V, Lindh G, Evengard B.	National Institute for Psychosocial Factors and Health, Stockholm, Sweden.	Critical life events, infections, and symptoms during the year preceding chronic fatigue syndrome (CFS): an examination of CFS patients and subjects with a nonspecific life crisis.	Psychosom Med 1999 May-Jun;61(3):304-10	OBJECTIVE: The purpose of this study was to describe the sequence of psychosocial events and infections preceding the onset of chronic fatigue syndrome (CFS). This information was related to the temporal development of crucial symptoms in relation to the onset of, namely, fatigue, sadness, irritability, pain, and feeling of fever. METHODS: A personal interview was conducted in 46 patients (mean age, 39.5 years; SD, 9 years) who fulfilled international CFS criteria. These patients were matched with regard to age and gender to 46 carefully matched control subjects. Twenty-three percent of the study subjects were men, and 77% were women. The patient at first identified the month that coincided with the onset of CFS. Similarly, each control subject was asked to identify a "very difficult period" within approximately the same period as the patient with whom the control subject was matched. A list of 14 different life events was perused. Participants were asked to identify for each month whether each of the listed events had occurred. Furthermore, they were asked to rate the importance of the events they had experienced. In addition, for each of the cardinal symptoms (fatigue, sadness, irritability, pain, and feeling of fever) and for each month, the subjects were asked to rate, on a visual analogue scale, the symptom intensity. Also, the number of infections was noted. RESULTS: A statistically significant group difference in fatigue intensity existed during the period 4 to 10 months before the onset of CFS. During the 3 months preceding the diagnosis for the CFS patients or the peak of the crisis for the control group, there was a dramatic rise in fatigue in both groups. The CFS group reached a much higher fatigue level, which leveled off somewhat during the first year of follow-up but still remained very high in comparison with the control group, which reached precrisis levels 4 months after the peak. Similar patterns were observed for fever and pain. With regard to sadness and irritability, no group difference was observed during the period preceding the crisis. In the patient group, the level stayed high throughout the whole first year of follow-up, whereas a slow return started in the control group; precrisis levels were reached after 1 year in this group. The prevalence ratio (CFS patients/control subjects) for negative events was around 1.0 for the periods 4 to 12 months preceding CFS but 1.9 during the quarter year preceding the onset. For infections, the prevalence ratio increased successively during the four quarters preceding CFS (from 1.4 to 2.3).

				CONCLUSIONS: According to the retrospective self-reports, there were differences between the groups in fatigue, pain, and feeling of fever during the months preceding the crisis. With regard to depressive and irritable feelings, no preillness differences were reported between the groups. There was a reported excess prevalence of both infections and negative life events during the quarter year preceding the onset of CFS or crisis. Potential sources of error are discussed. These findings must be replicated in longitudinal studies.
Vermel' AE.		[Chronic fatigue syndrome].[article in Russian]	Klin Med (Mosk) 1999;77(7):11-5	
Vojdani A, Lapp CW.	Immunosciences Laboratory Inc., Beverly Hills, California, USA. immunsci@ix.netcom.com	Interferon-induced proteins are elevated in blood samples of patients with chemically or virally induced chronic fatigue syndrome.	Immunopharmacol Immunotoxicol 1999 May;21(2):175-202	Overlapping symptomatologies between Chronic Fatigue Syndrome (CFS) and Chemical Sensitivity have been observed by different investigators. Therefore, it is of great importance to develop biomarker(s) for possible differentiation between viral induced CFS (without sensitivity to chemicals) versus chemically induced CFS. Since interferon induced proteins 2-5A Synthetase and Protein Kinase RNA (PKR) have been implicated in the viral induction of CFS, the objective of this study was to utilize 2-5A and PKR activity for differentiation between CFS induced by either viruses or chemicals. Based on the CDC definition and criteria, twenty CFS patients who were positive for viral genome(s) (mainly HHV6; HTLVII, EBV, and CMV) and did not have any history of exposure to toxic chemicals were included in this study. As a comparison, the second group of patients consisted of twenty individuals from the same geographical area who were negative for viral genomes but had been exposed to methyl tertiary-butyl ether concentration of up to 70 ppb and benzene concentration up to 14 ppb. All patients complained of fatigue and other symptoms overlapping between the two groups. From all 40 patients, blood was drawn, leukocyte extract was prepared and assayed for 2-5A Synthetase and PKR activity. Clinical specimens which were positive for viral genomes showed from 2.2-38.7 fold increase in 2-5A activity and 1.3-13.5 fold increase in PKR activities over the background of the healthy controls. Similarly, the second group (negative for viral genomes, but exposed to chemicals) showed a 1.1-29.2 fold increase for 2-5A Synthetase and a 1.3-11.6 fold increase for PKR when they were compared to healthy subjects. To elucidate mechanisms involved in viral versus chemical induction of 2-5A Synthetase and PKR, MDBK cell lines were cultured either in the presence or absence of HHV6, MTBE, or Benzene, heat shock proteins and interferon-beta. 2-5A and PKR activities were measured in all the above conditions. A clear induction of 2-5A and PKR was observed when MDBK cells were exposed to HHV6, MTBE, and Benzene. This induction was more significant with HSP90, HSP70, and IFN-beta indicating their involvement in the mechanism of action. However, when MDBK cells were incubated either with MTBE + Benzene or HHV6 in the presence or absence of anti IFN-beta or anti-HSP-70, the activities of both 2-5A and PKR in HHV6 infected cells were inhibited

				by more than 90% due to addition of anti IFN-beta, and only 20% by addition of anti-HSP70. While in MTBE + Benzene exposed cells anti IFN-beta reduced the activity of these enzymes by 40% and anti-HSP70 by more than 90%. This variation in the induction of 2-5A and PKR by anti-HSP70 or IFN-beta indicates involvement of IFN-beta in viral induction 2-5A and PKR, and HSP involvement in chemical induction of these enzymes. We conclude that 2-5A and PKR are not only biomarkers for viral induction of CFS, but biomarkers to other stressors that include MTBE and Benzene.
Wagenmakers AJ.	Department of Human Biology, Maastricht University, PO Box 616, 6200 MD Maastricht, The Netherlands.	Chronic fatigue syndrome: the physiology of people on the low end of the spectrum of physical activity?	Clin Sci (Colch) 1999 Nov;97(5):611-3 Erratum in: Clin Sci (Colch) 1999 Dec;97(6):719 Comment on: Clin Sci (Colch). 1999 Nov;97(5):603-8; discussion 611-3	
Wagner-Raphael LI, Jason LA, Ferrari JR.	Department of Psychology, DePaul University, USA. lwagner@mcw.edu	Chronic fatigue syndrome, chronic fatigue, and psychiatric disorders: predictors of functional status in a national nursing sample.	J Occup Health Psychol 1999 Jan;4(1):63-71	Members of 2 nurses' associations (N = 71) were assessed using 2 mail questionnaires, a telephone questionnaire, the Diagnostic Interview Schedule, and medical records. Physicians reviewed participants to determine whether they met current criteria for chronic fatigue syndrome (CFS). Stepwise multivariate regression analyses were conducted to identify predictors of functional status scores. Impairments in physical, role, and social functioning increased as fatigue severity increased. Bodily pain increased as fatigue severity increased, and ratings of overall health increased as severity of fatigue decreased. Nurses with a current psychiatric diagnosis reported more impairments in emotional functioning than nurses with a lifetime diagnosis or no psychiatric diagnosis. Quality of life decreased as fatigue severity increased. Nurses with fatigue not meeting CFS criteria reported better quality of life than those with CFS or medical exclusions.
Walker TL.	Parke-Davis, Ann Arbor, MI, USA.	Chronic fatigue syndrome. Do you know what it means?	Am J Nurs 1999 Mar;99(3):70-4, 76	
Wallace HL 2nd, Natelson B, Gause W, Hay J.	Department of Microbiology, State University of New York at Buffalo, Buffalo, New York 14214, USA.	Human herpesviruses in chronic fatigue syndrome.	Clin Diagn Lab Immunol 1999 Mar;6(2):216-23	We have conducted a double-blind study to assess the possible involvement of the human herpesviruses (HHVs) HHV6, HHV7, Epstein-Barr virus (EBV), and cytomegalovirus in chronic fatigue syndrome (CFS) patients compared to age-, race-, and gender-matched controls. The CFS patient population was composed of rigorously screened civilian and Persian Gulf War veterans meeting the Centers for Disease Control and Prevention's CFS case definition criteria. Healthy control civilian and veteran populations had no evidence of CFS or any other exclusionary medical or psychiatric condition. Patient peripheral blood mononuclear cells were analyzed by PCR for the presence of these HHVs. Using two-tailed Fisher's exact test analyses, we

				were unable to ascertain any statistically significant differences between the CFS patient and control populations in terms of the detection of one or more of these viruses. This observation was upheld when the CFS populations were further stratified with regard to the presence or absence of major axis I psychopathology and patient self-reported gradual versus acute onset of disease. In tandem, we performed serological analyses of serum anti-EBV and anti-HHV6 antibody titers and found no significant differences between the CFS and control patients.
Ware NC.	Department of Social Medicine, Harvard Medical School, Boston, MA 02115, USA.	Toward a model of social course in chronic illness: the example of chronic fatigue syndrome.	Cult Med Psychiatry 1999 Sep;23(3):303-31	Retrospective, narrative accounts of illness experience in chronic fatigue syndrome provide the empirical basis for a preliminary conceptual model of social course in chronic illness. Qualities of distress interact with culturally specific expectations for social life and personal conduct to trigger microsocial processes of marginalization: role constriction, delegitimation, impoverishment, and social isolation. Marginalizing processes are opposed by acts of resistance initiated by ill individuals and directed toward integration in social worlds. Social distance from the perceived centers of CFS sufferers' interpersonal worlds expands and contracts with the changing predominance of marginalizing and resisting influences over time. Social course thus consists of successive, bi-directional movements along a 'continuum of marginality' by persons living lives with chronic illness.
Warren G, McKendrick M, Peet M.	The University of Sheffield, Section of Psychiatry, Northern General Hospital, UK.	The role of essential fatty acids in chronic fatigue syndrome. A case-controlled study of red-cell membrane essential fatty acids (EFA) and a placebo-controlled treatment study with high dose of EFA.	Acta Neurol Scand 1999 Feb;99(2):112-6	OBJECTIVE: To replicate the treatment study by Behan et al. (1990) using current research criteria for Chronic Fatigue Syndrome (CFS). METHOD: Fifty patients who fulfilled the Oxford Criteria for CFS were randomly allocated to treatment with either Efamol Marine or placebo for 3 months. They were seen monthly and completed a physical symptoms checklist and the Beck Inventory for Depression and reported if they were the same, better or worse at the end of the study. RESULTS: Symptoms generally improved with time but not significantly and there were no significant differences between the treatment and placebo groups. Pretreatment red-cell membrane (RBC) lipids of patients compared with age-and sex-matched normal controls showed no significant differences. DISCUSSION: The results of this study contrast sharply with the previous study where 85% of patients had a clinically significant improvement of symptoms with Efamol Marine over a 3-month treatment period.
Wessely S, Hotopf M.	Academic Department of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine, London, UK.	Is fibromyalgia a distinct clinical entity? Historical and epidemiological evidence.	Baillieres Best Pract Res Clin Rheumatol 1999 Sep;13(3):427-36	Most medical specialities have defined medically unexplained syndromes such as fibromyalgia, to categorize patients with prominent but unexplained symptoms. Other such syndromes include irritable bowel syndrome, chronic fatigue syndrome and atypical chest pain. In this chapter we present evidence to suggest that fibromyalgia is not a unique clinical entity, but shares much with these other syndromes. We use historical, clinical and epidemiological evidence to illustrate this idea. The historical data emphasize the essentially arbitrary way in which fibromyalgia developed. The clinical evidence shows the considerable overlap between patients with fibromyalgia and those with other unexplained syndromes.

				From an epidemiological perspective we emphasize the strong associations between symptoms such as myalgia and fatigue. We conclude by suggesting that fibromyalgia is one of many medically unexplained syndromes which have more similarities than differences between them.
Wessely S, Nimnuan C, Sharpe M.	Department of Psychological Medicine, Guy's, King's and St Thomas' School of Medicine, London, UK.	Functional somatic syndromes: one or many?	Lancet 1999 Sep 11;354(9182):936-9Comment in: Lancet. 1999 Dec 11;354(9195):2078; discussion 2078-9 Lancet. 1999 Dec 11;354(9195):2079 Lancet. 1999 Dec 11;354(9195):2079-80 Lancet. 1999 Dec 11;354(9195):2080	We review the concept and importance of functional somatic symptoms and syndromes such as irritable bowel syndrome and chronic fatigue syndrome. On the basis of a literature review, we conclude that a substantial overlap exists between the individual syndromes and that the similarities between them outweigh the differences. Similarities are apparent in case definition, reported symptoms, and in non-symptom association such as patients' sex, outlook, and response to treatment. We conclude that the existing definitions of these syndromes in terms of specific symptoms is of limited value; instead we believe a dimensional classification is likely to be more productive.
Wood B, Wessely S.	Maudsley Hospital and the Institute of Psychiatry, London, UK.	Personality and social attitudes in chronic fatigue syndrome.	J Psychosom Res 1999 Oct;47(4):385-97	One hundred one chronic fatigue syndrome (CFS) patients attending a specialist CFS clinic were compared with 45 rheumatoid arthritis (RA) patients on a range of standardized questionnaire measures, to investigate whether CFS patients are characterized by particular personality traits or social attitudes. No differences were found between CFS and RA patients in measures of perfectionism, attitudes toward mental illness, defensiveness, social desirability, or sensitivity to punishment (a concept related to neuroticism), on either crude or adjusted analyses. Alexithymia scores were greater in the RA patient group ($p<0.05$). Social adjustment, based on subjective assessment of overall restriction in activities and relationship difficulties, was substantially poorer in the CFS group ($p<0.001$). This was highly associated with depressive symptoms, but remained significant even after adjusting for depressive symptomatology. There was no evidence from this study of major differences between the personalities of CFS patients and RA patients. The stereotype of CFS sufferers as perfectionists with negative attitudes toward psychiatry was not supported.
Yamaguchi K, Sawada T, Naraki T, Igata-Yi R, Shiraki H, Horii Y, Ishii T, Ikeda K, Asou N, Okabe H, Mochizuki M, Takahashi K, Yamada S, Kubo K, Yashiki S, Waltrip RW 2nd, Carbone KM.	Blood Transfusion Service and Internal Medicine, Kumamoto University School of Medicine, Kumamoto, Japan. kyama@gpo.kumamoto-u.ac.jp	Detection of borna disease virus-reactive antibodies from patients with psychiatric disorders and from horses by electrochemiluminescence immunoassay.	Clin Diagn Lab Immunol 1999 Sep;6(5):696-700	The prevalence of Borna disease virus (BDV)-specific antibodies among patients with psychiatric disorders and healthy individuals has varied in several reports using several different serological assay methods. A reliable and specific method for anti-BDV antibodies needs to be developed to clarify the pathological significance of BDV infections in humans. We developed a new electrochemiluminescence immunoassay (ECLIA) for the antibody to BDV that uses two recombinant proteins of BDV, p40 and p24 (full length). Using this ECLIA, we examined 3,476 serum samples from humans with various diseases and 917 sera from blood donors in Japan for the presence of anti-BDV antibodies. By ECLIA, 26 (3.08%) of 845 schizophrenia patients and 9

				(3.59%) of 251 patients with mood disorders were seropositive for BDV. Among 323 patients with other psychiatric diseases, 114 with neurological diseases, 75 with chronic fatigue syndrome, 85 human immunodeficiency virus-infected patients, 50 with autoimmune diseases including rheumatoid arthritis and systemic lupus erythematosis and 17 with leprosy, there was no positive case except one case each with alcohol addiction, AIDS, and dementia. Although 19 (1.36%) of 1,393 patients with various ocular diseases, 10 (1.09%) of 917 blood donors, and 3 (4.55%) of 66 multitransfused patients were seropositive for BDV-specific antigen, high levels of seroprevalence in schizophrenia patients and young patients (16 to 59 years old) with mood disorders were statistically significant. The immunoreactivity of seropositive sera could be verified for specificity by blocking with soluble p40 and/or p24 recombinant protein. Anti-p24 antibody was more frequent than p40 antibody in most cases, and in some psychotic patients antibody profiles showed only p40 antibody. Although serum positive for both p40 and p24 antibodies was not found in this study, the p40 ECLIA count in schizophrenia patients was higher than that of blood donors. Furthermore, we examined 90 sera from Japanese feral horses. Antibody profiles of control human samples are similar to that of naturally BDV-infected feral horses. We concluded that BDV infection was associated in some way with psychiatric disorders.
Zhang Q, Zhou XD, Denny T, Ottenweller JE, Lange G, LaManca JJ, Lavietes MH, Pollet C, Gause WC, Natelson BH.	Center for Environmental Hazards Research, DVA Medical Center, E. Orange, New Jersey 07018, USA.	Changes in immune parameters seen in Gulf War veterans but not in civilians with chronic fatigue syndrome.	Clin Diagn Lab Immunol 1999 Jan;6(1):6-13	The purpose of this study was to evaluate immune function through the assessment of lymphocyte subpopulations (total T cells, major histocompatibility complex [MHC] I- and II-restricted T cells, B cells, NK cells, MHC II-restricted T-cell-derived naive and memory cells, and several MHC I-restricted T-cell activation markers) and the measurement of cytokine gene expression (interleukin 2 [IL-2], IL-4, IL-6, IL-10, IL-12, gamma interferon [IFN-gamma], and tumor necrosis factor alpha [TNF-alpha]) from peripheral blood lymphocytes. Subjects included two groups of patients meeting published case definitions for chronic fatigue syndrome (CFS)-a group of veterans who developed their illness following their return home from participating in the Gulf War and a group of nonveterans who developed the illness sporadically. Case control comparison groups were comprised of healthy Gulf War veterans and nonveterans, respectively. We found no significant difference for any of the immune variables in the nonveteran population. In contrast, veterans with CFS had significantly more total T cells and MHC II+ T cells and a significantly higher percentage of these lymphocyte subpopulations, as well as a significantly lower percentage of NK cells, than the respective controls. In addition, veterans with CFS had significantly higher levels of IL-2, IL-10, IFN-gamma, and TNF-alpha than the controls. These data do not support the hypothesis of immune dysfunction in the genesis of CFS for sporadic cases of CFS but do suggest that service in the Persian Gulf is associated with an altered immune status in veterans who returned with severe fatiguing illness.

1998				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Abu-Judeh HH, Levine S, Kumar M, el-Zeftawy H, Naddaf S, Lou JQ, Abdel-Dayem HM.	Department of Radiology, St. Vincent's Hospital, New York, NY 10011, USA.	Comparison of SPET brain perfusion and 18F-FDG brain metabolism in patients with chronic fatigue syndrome.	Nucl Med Commun 1998 Nov;19(11):1065-71	Chronic fatigue syndrome is a clinically defined condition of uncertain aetiology. We compared 99Tcm-HMPAO single photon emission tomography (SPET) brain perfusion with dual-head 18F-FDG brain metabolism in patients with chronic fatigue syndrome. Eighteen patients (14 females, 4 males), who fulfilled the diagnostic criteria of the Centers for Disease Control for chronic fatigue syndrome, were investigated. Thirteen patients had abnormal SPET brain perfusion scans and five had normal scans. Fifteen patients had normal glucose brain metabolism scans and three had abnormal scans. We conclude that, in chronic fatigue syndrome patients, there is discordance between SPET brain perfusion and 18F-FDG brain uptake. It is possible to have brain perfusion abnormalities without corresponding changes in glucose uptake.
Ambrogetti A, Leslie G. Olson, David C. Sutherland, John A. Malcolm, David Bliss, Stephen G. Gyulay		Daytime Sleepiness and REM Sleep Abnormalities in Chronic Fatigue A Case Series	Journal of Chronic Fatigue Syndrome 1998: 4(1): 23 - 35	Objective: To describe a subgroup of patients with chronic fatigue in whom there is increased physiological sleep tendency. Design: Prospective case series. Setting and Patients: Fifty-six consecutive patients with a working diagnosis of chronic fatigue syndrome underwent a sleep interview, overnight polysomnography and a Multiple Sleep Latency Test in a regional Sleep Disorders Center. Results: Of the 56 patients, 14 satisfied the current International Classification of Sleep Disorders criteria for the diagnosis of narcolepsy. Four of these patients had both excessive somnolence and clear-cut cataplexy and 10 pathological somnolence and polysomnographic criteria for narcolepsy. A further 35 had either increased daytime sleepiness, abnormal REM sleep regulation or both. Despite the objective evidence of daytime increased sleep tendency, the majority of the patients complained of fatigue and not of sleepiness. Twenty-nine patients were treated with either dexamphetamine or methylphenidate with good results in about half. Conclusion: We conclude that among patients investigated for chronic fatigue syndrome it is possible to identify a subgroup with significant daytime sleepiness and REM sleep abnormalities. Symptomatic treatment of these patients is often rewarding.
Andersson M, Bagby JR, Dyrehag L, Gottfries C.	Pain Unit, Kungalv Hospital, Sweden	Effects of staphylococcus toxoid vaccine on pain and fatigue in patients with fibromyalgia/chronic fatigue syndrome.	Eur J Pain 1998;2(2):133-142	Positive results of pilot studies of the effect of staphylococcus toxoid vaccine in patients with fibromyalgia and chronic fatigue syndrome were the incitement to the present, placebo-controlled study. It included 28 patients who fulfilled the criteria for both fibromyalgia and chronic fatigue syndrome. The effect of vaccination with a staphylococcus toxoid was compared with the effect of injections of sterile water. Psychometric assessment was made using 15 items from the comprehensive psychopathological rating scale (CPRS), Zung's self-rating depression scale and clinical global impressions (CGI). The visual analogue scale (VAS) was used to measure pain levels, and a hand-held electronic pressure algometer was used to measure pressure pain thresholds. Significant improvement was seen in seven of the 15 CPRS items in the vaccine group when pretreatment values were compared to post-treatment values. In CPRS <<fatiguability>>, there were significant intergroup differences, and in

				CPRS <<pain>> intergroup differences bordered on significance. There was no significant improvement in CPRS items in the placebo group. Clinical global impressions showed significant improvement in the vaccine-treated group, and VAS did so in both groups. In a follow-up study of 23 patients, the vaccine treatment was continued for 2-6 years. Fifty percent were rehabilitated successfully and resumed half-time or full-time work. The results of this study support the authors>> hypothesis that treatment with staphylococcus toxoid may be a fruitful strategy in patients with fibromyalgia and chronic fatigue syndrome. Copyright 1998 European Federation of Chapters of the International Association for the Study of Pain.
Arzomand ML		Chronic Fatigue Syndrome Among School Children and Their Special Educational Needs	Journal of Chronic Fatigue Syndrome 1998: 4(3): 59 - 69	Objectives: To determine the prevalence of Chronic Fatigue Syndrome (CFS) in school children. To explore their Special Educational Needs (SEN) arrangements. To evaluate the views of their parents, the educational and medical professionals involved in the process of special education needs assessment. Design: A postal questionnaire survey. Setting: The Merton and Sutton Junior and High Schools. Subjects: Pupils diagnosed with CFS. Main Outcome Measures: Responses to CFS about special educational needs and case details. Results: With a 53.8% return rate, 22 cases were identified giving an overall point prevalence of 0.07%. Of these 22 cases, 21 were in Sutton and one in Merton. There were equal numbers of boys and girls. Although the respondent groups generally agreed about Special Educational Needs arrangements, differences existed on home tuition and physical education (PE) at school. Parents were more against PE, 5 (71%) vs. 2 (14%) and 4 (11%) of doctors and educational staff, respectively (P = 0.001). Four out of seven parents (57%) said home tuition was necessary, while only one doctor (7%) and nine educational staffs (25.7%) agreed with this (P = 0.044). Conclusion: The estimated overall prevalence is consistent with previous paediatric studies. Two different findings, however, emerged. The equal prevalence in boys and girls (in contrast to previous studies) and the highly significant difference of case numbers between these two neighbouring boroughs (21 vs. 1). Further research is needed for possible explanation of these differences.
Ayres JG, Flint N, Smith EG, Tunnicliffe WS, Fletcher TJ, Hammond K, Ward D, Marmion BP.	Department of Respiratory Medicine, Heartlands Hospital, Birmingham, UK.	Post-infection fatigue syndrome following Q fever.	QJM 1998 Feb;91(2):105-23	In 1989, 147 individuals in the West Midlands, UK, were infected with Q fever. Five years later, following anecdotal reports of fatigue, we used a questionnaire-based case-control study to determine the prevalence of chronic fatigue syndrome symptoms in this group. Replies from 71 patients were compared with those from 142 age- and sex-matched controls. Increased sweating (52.9% vs. 31.6%, p = 0.006), breathlessness (50.7% vs. 30.6%, p = 0.006), blurred vision (34.3% vs. 17.8%, p = 0.016) and undue tiredness (68.7% vs. 51.5%, p = 0.03) were found in controls compared to cases. These findings were similar to those in Australian abbatoir workers occupationally exposed to Q fever. CDC criteria for chronic fatigue syndrome were fulfilled by 42.3% of cases and 26% of controls. Using visual analogue scores, symptoms were more severe in cases than in controls. Our findings support the existence of a chronic fatigue state following acute Q fever, in a group of patients

				exposed just once to the organism, and in circumstances free of such confounding factors as lawsuits over compensation.
Baraniuk JN, Clauw D, Yuta A, Ali M, Gaumond E, Upadhyayula N, Fujita K, Shimizu T.	Division of Rheumatology and Immunology and Allergy, Georgetown University, Washington, D.C. 20007-2197, USA.	Nasal secretion analysis in allergic rhinitis, cystic fibrosis, and nonallergic fibromyalgia/chronic fatigue syndrome subjects.	Am J Rhinol 1998 Nov-Dec;12(6):435-40	Rhinitis symptoms are present in approximately 70% of subjects with fibromyalgia and chronic fatigue syndrome (FM/CFS). Because only 35% to 50% have positive allergy skin tests, nonallergic mechanisms may also play a role. To better understand the mechanisms of nonallergic rhinitis in FM/CFS, nasal lavages were performed, and markers of vascular permeability, glandular secretion, and neutrophil and eosinophil infiltration measured in 27 nonallergic FM/CFS, 7 allergic rhinitis, 7 cystic fibrosis, and 9 normal subjects. Allergic rhinitis subjects had significantly increased vascular permeability (IgG) and ECP levels. Cystic fibrosis subjects had significantly higher elastase and total protein levels. There were no significant differences between FM/CFS and normal lavage fluids. Analysis of the constituents of nasal mucus provides information about ongoing secretory processes in rhinitis. There were no differences in the basal secretion of these markers of vascular permeability, submucosal gland serous cell secretion, eosinophil and neutrophil degranulation in nonallergic FM/CFS subjects. This suggests that constitutively active secretory processes that regulate continuous production of nasal secretions are not altered in FM/CFS. Future studies should examine alternative mechanisms such as inducible, irritant-activated, or reflex-mediated effects.
Baraniuk JN, Clauw DJ, Gaumond E.	Division of Rheumatology, Immunology and Allergy, Georgetown University, Washington, DC 20007-2197, USA.	Rhinitis symptoms in chronic fatigue syndrome.	Ann Allergy Asthma Immunol 1998 Oct;81(4):359-65	BACKGROUND: Atopy and allergic rhinitis are thought to be increased in prevalence in chronic fatigue syndrome (CFS). METHODS: To investigate this hypothesis, 51 CFS (CFS), 34 normal (N), 27 allergic rhinitis (AR), and 17 patients with other rheumatologic diseases filled out an Airway Symptom Severity self-report questionnaire to determine the frequencies of nasal, sinus, and chest symptoms, and a Systemic Complaints self-report questionnaire to determine the frequencies of complaints referable to neurologic, rheumatologic, gastrointestinal, and other systems. All subjects received a standard set of allergy skin tests, and were subdivided into those with positive and negative results. RESULTS: Allergy skin tests were positive in 35% of CFS and 44% of N subjects (difference not significant by Chi2). Significant rhinitis complaints were present in 83% of skin test positive CFS, 76% of skin test negative CFS, 74% of AR, and 23% of N subjects. Systemic Complaints scores were significantly elevated in skin test positive (94%) and negative (94%) CFS groups compared with AR (35%) and N (6%) groups. This score could significantly discriminate between CFS and N subjects. CONCLUSIONS: These data indicate that in this CFS population, 24% had no significant rhinitis complaints, 30% had positive skin tests suggesting the potential for allergic rhinitis complaints, and 46% had nonallergic rhinitis. The mechanism of the nonallergic component may offer insights into the pathogenesis of CFS.
Baraniuk JN, Daniel Clauw, Anna-Louisa		IgE Concentrations in Chronic Fatigue	Journal of Chronic Fatigue Syndrome	Hypothesis: Allergies have been proposed as a cause or contributing factor of chronic Fatigue syndrome (CFS). If this is so, then the stigmata of atopy, such as symptoms of

MacDowell-Carneiro, Joseph Bellanti, Pavani Pandiri, Sukmun Foong, Mushtaq Ali		Syndrome	1998: 4(1): 13 - 21	allergic rhinitis and high serum IgE, should be present in CFS subjects. Methods: Medical records from an allergy and immunology clinic were retrospectively reviewed. All subjects who had had a serum IgE measurement performed over a 4-year period were identified, and allergy history and skin test data reviewed. Patients were then classified as: (a) allergic rhinitis (n = 51), (b) CFS (n = 113, 1992 criteria), and (c) normal subjects without atopy, CFS or immunodeficiency (n = 76). IgE levels were compared between groups. Results: A clinical history of allergic rhinitis was present in 31% (35/113) of thc CFS subjects. The IgE levels of allergic rhinitis subjects and the subset of CPS subjects with allergic rhinitis were 392 ± 73 and 406 ± 123 IU/ml, respectively. In contrast, normal subjects and CFS subjccts who did not give a history of allergic rhinitis had normal IgE levels of 49 ± 9 and 33 ± 4 IU/ml, respectively. Conclusion: Atopy with clinically defined allergic rhinitis, high IgE, positive allergy skin tests and the presumed TH2 lymphocyte-IgE-mast cell-eosinophil axis overactivity and immediate hypersensitivity (Type I) immune response was present in a minority of CFS subjects. While atopy may coexist in some CFS subjects, it is unlikely that atopy plays a causal role in CFS pathogenesis.
Baschetti R.		Chronic fatigue syndrome.	Postgrad Med J 1998 Nov;74(877):701 Comment on: Postgrad Med J. 1998 Apr;74(870):229-32	
Baschetti R.		Chronic fatigue syndrome.	JAMA 1998 Feb 11;279(6):431-2; discussion 432-3 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Baschetti R.		Treatment for chronic fatigue syndrome.	Arch Intern Med 1998 Nov 9;158(20):2266-7 Comment on: Arch Intern Med. 1998 Apr 27;158(8):908-14	
Behan WMH, Ian J. Holt, David H. Kay, Pamela Moonie		In vitro Study of Muscle Aerobic Metabolism in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 5(1): 3 - 16	The purpose of this study was to establish if muscle aerobic metabolism is abnormal in chronic fatigue syndrome (CFS). Myoblast cultures from muscle biopsies of 16 patients with CFS and 10 healthy controls were established. Micromethods were used to determine the lactate/pyruvate (L/P) ratio, respiratory chain function and cytochrome oxidase and lactic dehydrogenase activities. Mitochondrial DNA (mtDNA) volume was measured and mtDNA rearrangements sought. The results showed that myoblasts from ten of 16 cases of CFS had defects in aerobic metabolism: two had increased L/P ratios, suggestive of a defect in oxidative phosphorylation while eight

				had decreased ratios, consistent with a deficiency in pyruvate dehydrogenase. There was a statistically significant broader range of L/P ratios in the patients' cultures, compared to controls (p = 0.011). No mtDNA rearrangements were present. This in vitro study confirms that there is convincing evidence of mild aerobic defects in skeletal muscle in some cases of CFS
Bell IR, Baldwin CM, Russek LG, Schwartz GE, Hardin EE.	Department of Psychiatry, University of Arizona, Tucson, USA.	Early life stress, negative paternal relationships, and chemical intolerance in middle-aged women: support for a neural sensitization model.	J Womens Health 1998 Nov;7(9):1135-47	This study (ntotal = 35) compared early life stress ratings, parental relationships, and health status, notably orthostatic blood pressures, of middle-aged women with low-level chemical intolerance (CI group) and depression, depressives without CI (DEP group), and normals. Environmental chemical intolerance is a symptom of several controversial conditions in which women are overrepresented, that is, sick building syndrome, multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia. Previous investigators have postulated that people with CI have variants of somatization disorder, depression, posttraumatic stress disorder (PTSD) initiated by childhood abuse or a toxic exposure event. One neurobehavioral model for CI, somatization disorder, recurrent depression, and PTSD is neural sensitization, that is, the progressive amplification of host responses (e.g., behavioral, neurochemical) to repeated intermittent stimuli (e.g., drugs, chemicals, endogenous mediators, stressors). Females are more vulnerable to sensitization than are males. Limbic and mesolimbic pathways mediate central nervous system sensitization. Although both CI and DEP groups had high levels of life stress and past abuse, the CI group had the most distant and weak paternal relationships and highest limbic somatic dysfunction subscale scores. Only the CI group showed sensitization of sitting blood pressures over sessions. Together with prior evidence, these data are consistent with a neural sensitization model for CI in certain women. The findings may have implications for poorer long-term medical as well as neuropsychiatric health outcomes of a subset of women with CI. Subsequent research should test this model in specific clinical diagnostic groups with CI.
Bell IR, Baldwin CM, Schwartz GE.	Department of Psychiatry, University of Arizona, Tucson Veterans Affairs Medical Center, 85723, USA.	Illness from low levels of environmental chemicals: relevance to chronic fatigue syndrome and fibromyalgia.	Am J Med 1998 Sep 28;105(3A):74S-82S	This article summarizes (1) epidemiologic and clinical data on the symptoms of maladies in association with low-level chemicals in the environment, i.e., environmental chemical intolerance (CI), as it may relate to chronic fatigue syndrome (CFS) and fibromyalgia; and (2) the olfactory-limbic neural sensitization model for CI, a neurobehavioral synthesis of basic and clinical research. Severe CI is a characteristic of 20-47% of individuals with apparent CFS and/or fibromyalgia, all patients with multiple chemical sensitivity (MCS), and approximately 4-6% of the general population. In the general population, 15-30% report at least minor problems with CI. The levels of chemicals reported to trigger CI would normally be considered nontoxic or subtoxic. However, host factors--e.g., individual differences in susceptibility to neurohormonal sensitization (amplification) of endogenous responses--may contribute to generating a disabling intensity to the resultant multisystem dysfunctions in CI. One site for this amplification may be the limbic system of the

				brain, which receives input from the olfactory pathways and sends efferents to the hypothalamus and the mesolimbic dopaminergic [reward] pathway. Chemical, biologic, and psychological stimuli can initiate and elicit sensitization. In turn, subsequent activation of the sensitized limbic and mesolimbic pathways can then facilitate dysregulation of behavioral, autonomic, endocrine, and immune system functions. Research to date has demonstrated the initiation of neurobehavioral sensitization by volatile organic compounds and pesticides in animals, as well as sensitizability of cardiovascular parameters, beta-endorphin levels, resting EEG alpha-wave activity, and divided-attention task performance in persons with CI. The ability of multiple types of widely divergent stimuli to initiate and elicit sensitization offers a new perspective on the search for mechanisms of illness in CFS and fibromyalgia with CI.
Bell IR, Patarca R, Baldwin CM, Klimas NG, Schwartz GE, Hardin EE.	Department of Psychiatry, Psychology, Family and Community Medicine, University of Arizona Health Sciences Center, and the Department of Psychiatry, Tucson Veterans Affairs Medical Center, Tucson, Ariz., USA.	Serum neopterin and somatization in women with chemical intolerance, depressives, and normals.	Neuropsychobiology 1998;38(1):13-8	The symptom of intolerance to low levels of environmental chemicals (CI, chemical intolerance) is a feature of several controversial polysymptomatic conditions that overlap symptomatically with depression and somatization, i.e., chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, and Persian Gulf syndrome. These syndromes can involve many somatic symptoms consistent with possible inflammation. Immunological or neurogenic triggering might account for such inflammation. Serum neopterin, which has an inverse relationship with l-tryptophan availability, may offer a marker of inflammation and macrophage/monocyte activation. This study compared middle-aged women with CI (who had high levels of affective distress; n = 14), depressives without CI (n = 10), and normals (n = 11). Groups did not differ in 4 p.m. resting levels of serum neopterin. However, the CI alone had strong positive correlations between neopterin and all of the scales measuring somatization. These preliminary findings suggest the need for additional research on biological correlates of 'unexplained' multiple somatic symptoms in subtypes of apparent somatizing disorders.
Bennett R.	Department of Medicine, Oregon Health Sciences Center, Portland 97201, USA.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain.	Curr Opin Rheumatol 1998 Mar;10(2):95-103	Epidemiologic studies continue to provide evidence that fibromyalgia is part of a spectrum of chronic widespread pain. The prevalence of chronic widespread pain is several times higher than fibromyalgia as defined by the 1990 American College of Rheumatology guidelines. There is now compelling evidence of a familial clustering of fibromyalgia cases in female sufferers; whether this clustering results from nature or nature remains to be elucidated. A wide spectrum of fibromyalgia-associated symptomatology and syndromes continues to be described. During the past year the association with interstitial cystitis has been explored, and neurally mediated hypotension has been documented in both fibromyalgia and chronic fatigue syndrome. Abnormalities of the growth hormone-insulin-like growth factor-1 axis have been also documented in both fibromyalgia and chronic fatigue syndrome. The commonly reported but anecdotal association of fibromyalgia with whiplash-type neck trauma was validated in a report from Israel. However, unlike North America,

				100% of Israeli patients with posttraumatic fibromyalgia returned to work. Basic research in fibromyalgia continues to pinpoint abnormal sensory processing as being integral to understanding fibromyalgia pain. Drugs such as ketamine, which block N-methyl-D-aspartate receptors (which are often upregulated in central pain states) were shown to benefit fibromyalgia pain in an experimental setting. The combination of fluoxetine and amitriptyline was reported to be more beneficial than either drug alone in patients with fibromyalgia. A high prevalence of autoantibodies to cytoskeletal and nuclear envelope proteins was found in chronic fatigue syndrome, and an increased prevalence of antipolymer antibodies was found in symptomatic silicone breast implant recipients who often have fibromyalgia.
Berwaerts J, Greta Moorkens, Roger Abs		Review of Neuroendocrine Disturbances in the Chronic Fatigue Syndrome Indications for a Role of the Growth Hormone-IGF-1 Axis in the Pathogenesis	Journal of Chronic Fatigue Syndrome 1998: 4(4): 81 - 91	The investigation of the growth hormone (GH)-IGF-1 axis in patients with chronic fatigue syndrome (CFS) may be important for different reasons. Some of the disturbances of the hypothalamic-pituitaryadrenal axis and central serotoninergic (5-HT) function in CFS will be reviewed, before elaborating on three hypotheses that may explain thc role of a disturbed GH axis activity in CFS. Firstly, the disturbed central 5-HT receptor activity may be the cause of GH axis dysfunction. Secondly, CFS may be considered as a "stress-related illness," in which the disturbed central 5-HT function is a result rather than the cause of impaired neuroendocrine stress responses. Finally, by analogy with fibromyalgia, sleep abnormalities in CFS may impair nocturnal GH secretion. Whether the disturbed GH axis activity is a primary or secondary phenomenon in the pathogenesis of CFS, should be elucidated by future clinical investigations.
Berwaerts J, Moorkens G, Abs R.	Department of Endocrinology, Middelheim Hospital, Antwerp, Belgium.	Secretion of growth hormone in patients with chronic fatigue syndrome.	Growth Horm IGF Res 1998 Apr;8 Suppl B:127-9	Decreased serum levels of insulin-like growth factor I (IGF-I) are common in patients with fibromyalgia, which is frequently associated with chronic fatigue syndrome (CFS). Twenty patients with CFS (7 men, 13 women; age range, 30-60 years) and age- and sex-matched controls were tested for peak GH responses to insulin-induced hypoglycaemia and arginine administration. Nocturnal secretion of GH and serum levels of IGF-I were also measured. Serum IGF-I SDS (SD) was significantly lower in patients with CFS than in controls (SDS, -0.39 1.07 vs 0.33 0.84; P = 0.02). Patients with CFS also tended to have reduced nocturnal secretion of GH (area under the curve, 32.4 18.3 vs 62.7 43.7 microg/l/15 minutes; P= 0.06), but peak GH responses to insulin-induced hypoglycaemia and arginine administration did not differ significantly between the two groups. It is not clear whether the tendency for impaired spontaneous nocturnal GH secretion in patients with CFS is a cause or an effect of the condition.
Blackwood SK, MacHale SM, Power MJ, Goodwin GM, Lawrie SM.	Edinburgh University Department of Psychiatry, Royal Edinburgh Hospital, UK.	Effects of exercise on cognitive and motor function in chronic fatigue syndrome and depression.	J Neurol Neurosurg Psychiatry 1998 Oct;65(4):541-6	OBJECTIVES: Patients with chronic fatigue syndrome complain of physical and mental fatigue that is worsened by exertion. It was predicted that the cognitive and motor responses to vigorous exercise in patients with chronic fatigue syndrome would differ from those in depressed and healthy controls. METHODS: Ten patients with chronic fatigue syndrome, 10 with depressive illness, and 10 healthy controls completed

				cognitive and muscle strength testing before and after a treadmill exercise test. Measures of cardiovascular functioning and perceived effort, fatigue, and mood were taken during each stage of testing. RESULTS: Depressed patients performed worst on cognitive tests at baseline. During the treadmill test, patients with chronic fatigue syndrome had higher ratings of perceived effort and fatigue than both control groups, whereas patients with depression reported lower mood. After exertion, patients with chronic fatigue syndrome showed a greater decrease than healthy controls on everyday tests of focused (p=0.02) and sustained (p=0.001) attention, as well as greater deterioration than depressed patients on the focused attention task (p=0.03). No between group differences were found in cardiovascular or symptom measures taken during the cognitive testing. CONCLUSIONS: Patients with chronic fatigue syndrome show a specific sensitivity to the effects of exertion on effortful cognitive functioning. This occurs despite subjective and objective evidence of effort allocation in chronic fatigue syndrome, suggesting that patients have reduced working memory capacity, or a greater demand to monitor cognitive processes, or both. Further insight into the pathophysiology of the core complaints in chronic fatigue syndrome is likely to be realised by studying the effects of exercise on other aspects of everyday functioning.
Block W, Traber F, Kuhl CK, Keller E, Lamerichs R, Karitzky J, Rink H, Schild HH.	Radiologische Klinik der Universitat Bonn. block@uni-bonn.de	[31P-mr spectroscopy of peripheral skeletal musculature under load: demonstration of normal energy metabolites compared with metabolic muscle diseases].[article in German]	Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 1998 Mar;168(3):250-7	PURPOSE: 31P-MR spectroscopy of skeletal muscle under exercise was used to obtain the range of normal variation and comparison was made for different neuromuscular diseases. METHODS: 41 examinations of 24 volunteers and 41 investigations in 35 patients were performed on 1.5 T MR systems (Gyroscan 515 und S15/ACSII, Philips). Localised 31P-MR spectra of the calf muscle were obtained in time series with a resolution of 12 s. RESULTS: Two types of muscle energy metabolism were identified from the pattern of spectroscopic time course in volunteers: While the first group was characterised by a remarkable decline to lower pH values during exercise, the second group showed only small pH shifts (minimum pH: 6.48 0.13 vs 6.87 0.07, p < 10(-6)) although comparable workload conditions were maintained. The pH-values correlated well with blood lactate analysis. Patients with metabolic disorders and chronic fatigue syndrome (CFS) showed decreased resting values of PCr/(PCr Pi) and increased pH levels during exercise. PCr recovery was significantly delayed (0.31 vs 0.65 min-1, p < 0.00005) in metabolic muscle disorders but was normal in CFS patients. CONCLUSION: Findings in volunteers indicate utilisation of different metabolic pathways which seems to be related to the fibre type composition of muscle. Reduced resting levels for PCr/(PCr Pi), altered pH time courses, and decreased PCr recovery seem to be helpful indicators for diagnosis of metabolic muscle disorders.
Borish L, Schmaling K, DiClementi JD, Streib J, Negri J, Jones JF.	Department of Medicine, National Jewish Medical and	Chronic fatigue syndrome: identification of	J Allergy Clin Immunol 1998 Aug;102(2):222-30	BACKGROUND: We investigated a role for allergic inflammation and psychologic parameters in the development of chronic fatigue syndrome (CFS). METHODS: The design was a comparison between subjects with CFS and age- and sex-matched

	Research Center, University of Colorado Health Sciences Center, Denver 80206, USA.	distinct subgroups on the basis of allergy and psychologic variables.		control cohorts. Studies were performed on CFS subjects (n = 18) and control cohorts consisting of normal subjects (n = 11), allergic subjects (n = 14), and individuals with primary depression (n = 12). We quantified cytokines at baseline as cell-associated immunoreactive peptides and as transcripts evaluated by means of semiquantitative RNA-based polymerase chain reactions. Psychologic evaluations included administration of the Diagnostic Interview Schedule, the Structured Clinical Interview, and the Symptom Checklist 90-Revised. RESULTS: Increases in tumor necrosis factor (TNF)-alpha were identified in individual subjects with CFS (50.1 14.4 pg TNF-alpha per 10(7) peripheral blood mononuclear cells [PBMCs]; mean SEM) and allergic subjects (41.6 7.6) in comparison with normal subjects (13.1 8.8) (P < .01 and P < .05, respectively). Similar trends were observed for interferon (IFN)-alpha in allergic subjects (3.0 1.7 pg/10(7) PBMCs) and subjects with CFS (6.4 3.4) compared with normal subjects (1.9 1.4). A significant increase (P < .05) in TNF-alpha transcripts was demonstrated between subjects with CFS and depressed subjects. In contrast to these proinflammatory cytokines, both subjects with CFS (2.6 1.8 pg/10(7) PBMCs) and allergic subjects (3.4 2.8) were associated with a statistically significant (P < .01) decrease in IL-10 concentrations compared with normal subjects (60.2 18.2). As shown in other studies, most of our subjects with CFS were allergic (15 of 18) and therefore presumably demonstrated cytokine gene activation on that basis. The seasonal exacerbation of allergy was associated with a further increase in cellular IFN-alpha (from 2.1 1.2 to 14.2 4.5 pg/107 PBMCs; P < .05) but no further modulation of TNF-alpha or IL-10. Similarly, self-reported exacerbations of CFS were associated with a further increase in IFN-alpha (from 2.5 1.0 to 21.9 7.8; P < .05) and occurred at times of seasonal exposures to allergens. This linkage does not permit making any definitive conclusions regarding a causative influence of either seasonal allergies or the increase in cellular IFN-alpha with the increase in CFS symptoms. The close association between atopy and CFS led us to speculate that CFS may arise from an abnormal psychologic response to the disordered expression of these proinflammatory and antiinflammatory cytokines. Psychologic variables were predictive of immune status within the CFS sample (65.9% of the variance in immune status; F (3,10) = 6.44, P < .05). Specifically, the absence of a personality disorder but greater endorsement of global psychiatric symptoms was predictive of immune activation. CONCLUSIONS: Most of our subjects with CFS were allergic, and the CFS and allergy cohorts were similar in terms of their immune status. However, the CFS subjects could be discriminated by the distinct psychologic profiles among subjects with and without immune activation. We propose that in at least a large subgroup of subjects with CFS who had allergies, the concomitant influences of immune activation brought on by allergic inflammation in an individual with the appropriate psychologic profile may interact to produce the symptoms of CFS. In a psychologically predisposed individual, symptoms associated with allergic inflammation are

				recognized as illness.
Borok G		Chronic Fatigue Syndrome An Atopic State	Journal of Chronic Fatigue Syndrome 1998: 4(3): 39 - 57	The cause of the tiredness and depression, may be due to a virus in the acute or recuperative phase, but in the long-term fatigue must be due to other mechanisms. As varied as are our size, shape, skin and eye colour so are the more subtle nuances of antibodies and enzymes which each cell produces. It is postulated that it is mostly atopic patients who will also react abnormally to certain foods, inhalants and skin applications. Sugars (refined foods) play a major role in leading to fatigue by their chemical, physiological, pharmacological and glycosylogical properties. Bread plays a major role in provoking the symptoms of depression in the chronic fatigue syndrome. What is suggested is that in a genetically predisposed group of people food intolerance causes symptoms akin to both the major and minor criteria of CFS.
Brown SL, Langone JJ, Brinton LA.		Silicone breast implants and autoimmune disease.	J Am Med Womens Assoc 1998 Winter;53(1):21-4, 40	In 1992, the Food and Drug Administration requested a voluntary moratorium on the scale and implantation of silicone-gel-filled breast implants because of growing concern over the lack of scientific and clinical data supporting their safety and effectiveness. Breast implants had been reported to cause serious local complications, and new questions about breast implants and increased risk for autoimmune disease, including the rare but sometimes fatal connective tissue disease scleroderma, were also raised. Since that time, clinical studies have focused on the adjuvant effect of silicone and of potential autoantibody production. Epidemiologic studies have ruled out a large increased risk for connective tissue disease overall in women with breast implants, but samples were too small to rule out an increase in rare connective tissue diseases. Nor were studies properly designed to address whether an atypical syndrome might develop in women with breast implants. Meta-analyses of these studies cannot remedy their underlying methodologic weaknesses. While the question of whether rare connective tissue disease is associated with breast implants may never be answered definitively, recent progress in identifying new syndromes such as fibromyalgia and chronic fatigue syndrome may provide an insight into methodology for evaluating the existence of a silicone-related syndrome in women with breast implants.
Bruno RL, Creange SJ, Frick NM.	Kids' Fatigue Management Program and The Post-Polio Institute, Englewood Hospital and Medical Center, New Jersey 07631, USA.	Parallels between post-polio fatigue and chronic fatigue syndrome: a common pathophysiology?	Am J Med 1998 Sep 28;105(3A):66S-73S	Fatigue is the most commonly reported and most debilitating of post-polio sequelae affecting the >1.8 million North American polio survivors. Post-polio fatigue is characterized by subjective reports of difficulty with attention, cognition, and maintaining wakefulness. These symptoms resemble those reported in nearly 2 dozen outbreaks of post-viral fatigue syndromes (PVFS) that have recurred during this century and that are related clinically, historically, anatomically, or physiologically to poliovirus infections. This article reviews recent studies that relate the symptoms of post-polio fatigue and chronic fatigue syndrome (CFS) to clinically significant deficits on neuropsychologic tests of attention, histopathologic and neuroradiologic evidence of brain lesions, impaired activation of the hypothalamic-pituitary-adrenal axis, increased prolactin secretion, and electroencephalogram (EEG)

				slow-wave activity. A possible common pathophysiology for post-polio fatigue and CFS, based on the Brain Fatigue Generator Model of PVFS, and a possible pharmacotherapy for PVFS based on replacement of depleted brain dopamine, will be described.
Bruno RL, Susan Creange, Jerald R. Zirnmerman Nancy M. Frick		Elevated Plasma Prolactin and EEG Slow Wave Power in Post-Polio Fatigue Implications for a Dopamine Deficiency Underlying Post-Viral Fatigue Syndromes	Journal of Chronic Fatigue Syndrome 1998: 4(2): 61 - 75	To test the hypothesis that plasma prolactin and electroencephalographic (EEG) slow wave activity are correlated with fatigue, 33 polio survivors without medical or psychologic comorbidities were studied. Subjects were administered the Post-Polio Fatigue Questionnaire (PFQ) and had resting measurement of both plasma prolactin and bilateral temporal-occipital power across the EEG frequency spectrum. Typical daily fatigue severity on the PFQ was significantly correlated with daily difficulty with attention, staying awake and motivation, but not with measures of acute polio severity or the number of limbs affected by late-onset Post-Polio Sequelae symptoms. Prolactin was significantly correlated with daily fatigue severity on the PFQ ($r = .39$; $p < .05$). EEG power was equal between the two hemispheres across all frequency bands. However, EEG slow wave power in the right hemisphere was significantly correlated with daily fatigue severity and prolactin level ($r = .37$; $p < .05$). Using multiple linear regression, age at acute polio, frequency of difficulty with attention on the PFQ, prolactin and right hemisphere slow wave power predicted 72% of the variance of the daily fatigue severity rating ($r = 85$; $p < .0001$). These data suggest that increased prolactin secretion and EEG slowing are related to the severity of post-polio fatigue, findings similar to those in patients with acute paralytic and non-paralytic poliomyelitis and with chronic fatigue syndrome. A primary role is suggested for a dopamine deficiency (versus serotonergic receptor supersensitivity) underlying impaired cortical activation and the symptoms associated with putative post-viral fatigue syndromes.
Calkins H, Rowe PC.	The Johns Hopkins University School of Medicine, Baltimore, Maryland.	Relationship Between Chronic Fatigue Syndrome and Neurally Mediated Hypotension.	Cardiol Rev 1998 May;6(3):125-134	Chronic fatigue syndrome is a chronic debilitating disease that afflicts 4/1000 of the general population. The pathophysiologic basis for this condition is unknown, and no known consistently effective therapy has been identified. Recent studies have reported a link between the chronic fatigue syndrome and neurally mediated hypotension, a common abnormality of blood pressure regulation. In nonrandomized studies, treatment directed at neurally mediated hypotension has been effective in treating the symptoms of the chronic fatigue syndrome in two-thirds of patients. Prospective randomized trials are now in progress.
Cannon JG, Angel JB, Abad LW, O'Grady J, Lundgren N, Fagioli L, Komaroff AL.	Department of Medicine, New England Medical Center, Boston, Massachusetts, USA. jgc2@psu.edu	Hormonal influences on stress-induced neutrophil mobilization in health and chronic fatigue syndrome.	J Clin Immunol 1998 Jul;18(4):291-8	This investigation tested the hypotheses that women diagnosed with chronic fatigue syndrome (CFS) would exhibit significantly greater systemic indices of exercise-induced leukocyte mobilization and inflammation (neutrophilia, lactoferrin release, complement activation) than controls matched for age, weight, and habitual activity and that responses in the luteal phase of the menstrual cycle would be greater than in the follicular phase. Subjects stepped up and down on a platform adjusted to the height of the patella for 15 min, paced by metronome. Blood samples were collected

				under basal conditions (the day before exercise) and following exercise for determination of circulating neutrophils and plasma concentrations of lactoferrin, C3a des arg, and creatine kinase. Complete, 24-hr urine collections were made for determination of cortisol excretion. For all subjects, circulating neutrophil counts increased 33% (P < 0.0001) and lactoferrin increased 27% (P = 0.0006) after exercise, whereas plasma C3a des arg and creatine kinase did not increase. No indication of an exaggerated or excessive response was observed in the CFS patients compared to the controls. In healthy women, circulating neutrophil numbers exhibited previously described relationships with physiological variables: basal neutrophil counts correlated with plasma progesterone concentrations (R = 0.726, P = 0.003) and the exercise-induced neutrophilia correlated with both urinary cortisol (R = 0.660, P = 0.007) and plasma creatine kinase (R = 0.523, P = 0.038) concentrations. These relationships were not observed in the CFS patients (R = 0.240, P = 0.370; R = 0.042, P = 0.892; and R = 0.293, P = 0.270; respectively). These results suggest that normal endocrine influences on the circulating neutrophil pool may be disrupted in patients with CFS.
Capen K.		Chronic fatigue syndrome get court's nod of approval as legitimate disorder.	CMAJ 1998 Sep 8;159(5):533-4Comment in: CMAJ. 1999 Mar 9;160(5):636, 638 CMAJ. 1999 Mar 9;160(5):638	Lawyer Karen Capen looks at the implications of a recent Alberta court case involving chronic fatigue syndrome. She thinks Canada's physicians should pay close attention to this precedent-setting case.
Caplan C.		Chronic fatigue syndrome or just plain tired?	CMAJ 1998 Sep 8;159(5):519-20Comment in: CMAJ. 1999 Mar 9;160(5):636, 638 CMAJ. 1999 Mar 9;160(5):638	
Cathebras P, Lauwers A, Rousset H.	Service de Medecine Interne, Hopital Nord, Saint-Etienne.	[Fibromyalgia. A critical review].[article in French]	Ann Med Interne (Paris) 1998 Nov;149(7):406-14	Fibromyalgia is a chronic pain syndrome, more common in women. Its prevalence is estimated around 2% in the general population, and up to 20% among rheumatology outpatients. Besides musculoskeletal pain, symptoms as fatigue and sleep disturbance are considered characteristic. Research criteria have been set up, but their seemingly preciseness is unable to distinguish clearly between fibromyalgia and other functional somatic syndromes (chronic fatigue syndrome, irritable bowel syndrome) and psychiatric disorders (depression, anxiety), with which a striking comorbidity is documented. The diagnosis of fibromyalgia does not theoretically require the exclusion of muscle, joint, or metabolic diseases, but in clinical practice this problem proves to be of crucial importance. There are numbers of

				pathophysiological hypothesis for fibromyalgia, but none of them is fully satisfying: muscle is probably innocent; sleep disturbance, although sometimes considered a landmark of the syndrome, is unspecific; stress response studies show subtle anomaly; psychiatric disorders may represent factors of vulnerability and perpetuation rather than causes. We propose to include some of these etiological contributors in vicious circles leading to a "final common pathway" characterized by generalized hyperalgesia. Treatments of fibromyalgia, whether pharmacological (antidepressants) or psychological (cognitive-behavioral therapies) are of little efficacy, and the global prognosis of fibromyalgia is poor. However, the outcome might prove better outside the specialized clinics in which studies of chronic sufferers with severe abnormal illness behaviors are done. The social consequences of the popularization of the diagnosis of fibromyalgia should not be neglected.
Chester AC.		Chronic fatigue syndrome.	JAMA 1998 Feb 11;279(6):432; discussion 432-3 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Choppa PC, Vojdani A, Tagle C, Andrin R, Magtoto L.	Immunosciences Lab Incorporated Beverly Hills, CA, USA.	Multiplex PCR for the detection of Mycoplasma fermentans, M. hominis and M. penetrans in cell cultures and blood samples of patients with chronic fatigue syndrome.	Mol Cell Probes 1998 Oct;12(5):301-8	A multiplex polymerase chain reaction (PCR) was initially developed to detect the presence of mycoplasma genus DNA sequences in cell cultures and to differentiate between three human pathogenic mycoplasma species simultaneously. The assay in turn, proved to be a useful tool for the detection of mycoplasma infection in human DNA samples. One set of oligonucleotide primers which are specific for a highly conserved region among all members of the genus mycoplasma along with three other primer sets which are specific for Mycoplasma fermentans, Mycoplasma hominis andMycoplasma penetrans species were used in this assay. The sensitivity of detection was determined by infecting peripheral blood mononuclear cells (PBMC) of healthy individuals with known bacterial copy numbers from each species, extracting the DNA, and subjecting 1 microgram of DNA from each sample to 40 cycles of amplification. By using agarose gel electrophoresis the detection level was determined to be 7, 7, 9 and 15 mycoplasma cells per microgram of human genomic DNA for M. genus,M. fermentans, M. hominis and M. penetrans, respectively. The assay was applied to DNA extracted from the PBMCs of individuals suffering from chronic fatigue syndrome (CFS) (n=100) as determined by the Center for Disease Control (CDC) criteria, and compared to healthy individuals (n=100). The percentage of M. genus infection was found to be 52% in CFS patients and only 15% in healthy individuals.Mycoplasma fermentans, M. hominis andM. penetrans were detected in 32, 9 and 6% of the CFS patients while they were detected in 8, 3 and 2% of the healthy control subjects, respectively. This assay provides a rapid and cost efficient procedure to screen either cell cultures or clinical samples for the presence of three

				potentially pathogenic species of mycoplasma with a high level of sensitivity and specificity. Copyright 1998 Academic Press.
Christodoulou C, DeLuca J, Lange G, Johnson SK, Sisto SA, Korn L, Natelson BH.	University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, USA.	Relation between neuropsychological impairment and functional disability in patients with chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1998 Apr;64(4):431-4Comment in: J Neurol Neurosurg Psychiatry. 1998 Apr;64(4):430	OBJECTIVES: To examine the relation between neuropsychological impairment and functional disability in patients with chronic fatigue syndrome, and determine whether the relation is independent of psychiatric factors. METHODS: The subjects were 53 patients with chronic fatigue syndrome and 32 healthy controls who did not exercise regularly. Subjects were administered a structured psychiatric interview and completed questionnaires focusing on depression and functional disability. They also completed a battery of standardised neuropsychological tasks focusing on the cognitive domains that patients with chronic fatigue syndrome experience as particularly difficult: memory (verbal and visual), and attention/concentration. A test score was defined as failing when it was > or =2 SD below the mean of the healthy controls after controlling for demographic factors. RESULTS: Those patients with chronic fatigue syndrome with higher numbers of failing neuropsychological test scores reported significantly more days of general inactivity in the past month than those with fewer failing scores. This result remained significant even after partialling out the contribution of the presence of a comorbid axis I psychiatric episode and the overall level of depressive symptomology. Patients with failing verbal memory scores were particularly functionally disabled compared with those with passing scores. CONCLUSION: A relation was found between cognitive impairment and functional disability which could not be explained entirely on the basis of psychiatric factors.
Cohen SI.		Increased illness experience preceding chronic fatigue syndrome.	J R Coll Physicians Lond 1998 May-Jun;32(3):274Comment in: J R Coll Physicians Lond. 1998 Jul-Aug;32(4):389 and 1998 Jan-Feb;32(1):44-8	
Conti F, Pittoni V, Sacerdote P, Priori R, Meroni PL, Valesini G.	Istituto di Clinica Medica I, Universita degli Studi di Roma La Sapienza, Rome, Italy.	Decreased immunoreactive beta-endorphin in mononuclear leucocytes from patients with chronic fatigue syndrome.	Clin Exp Rheumatol 1998 Nov-Dec;16(6):729-32	OBJECTIVE: To investigate beta-endorphin concentrations in the peripheral blood mononuclear cells (PBMC) of patients with chronic fatigue syndrome (CFS). METHODS: Sixteen patients with CFS were enrolled in this study. Ten healthy subjects were studied as controls. Beta-endorphin concentrations were measured in PBMC by radioimmunoassay performed with antibodies specific for the C-terminal portion of human beta-endorphin. RESULTS: Beta-endorphin concentrations in the PBMC of chronic fatigue patients were significantly lower ($p < 0.001$) than in healthy subjects (mean SD: 8.5 7.0 vs. 42.6 22.6). CONCLUSION: Patients with CFS were found to have low levels of PBMC beta-endorphin. This finding may reflect the condition of chronic immune activation in CFS that has been reported in previous investigations. Beta-endorphin concentrations in PBMC seem to mirror the central nervous system

				homeostasis of the opioid. Therefore, we would postulate that the fatigue and weakness typical of CFS could be related to low beta-endorphin concentrations at the central nervous system level.
Corrado G, Riezzo G, Rea P, Pacchiarotti C, Cavaliere M, Cardi E.		Normal gastric emptying time and myoelectrical activity in an adolescent with chronic fatigue syndrome.	Ital J Gastroenterol Hepatol 1998 Aug;30(4):444-5	
Crofford LJ.	Division of Rheumatology, University of Michigan, Ann Arbor 48109-0680, USA. crofford@umich.edu	The hypothalamic-pituitary-adrenal stress axis in fibromyalgia and chronic fatigue syndrome.	Z Rheumatol 1998;57 Suppl 2:67-71	HPA axis abnormalities in FM, CFS, and other stress-related disorders must be placed in a broad clinical context. We know that interventions providing symptomatic improvement in patients with FM and CFS can directly or indirectly affect the HPA axis. These interventions include exercise, tricyclic anti-depressants, and serotonin reuptake inhibitors. There is little direct information as to how the specific HPA axis perturbations seen in FM can be related to the major symptomatic manifestations of pain, fatigue, sleep disturbance, and psychological distress. Since many of these somatic and psychological symptoms are present in other syndromes that exhibit HPA axis disturbances, it seems reasonable to suggest that there may be some relationship between basal and dynamic function of the HPA axis and clinical manifestations of FM and CFS.
Csef H.	Med. Poliklinik der Univ. Wurzburg.	[The non-specific environmental syndromes MCS (Multiple Chemical Sensitivity), IEI (Idiopathic Environmental Intolerance) and SBS (Sick Building Syndrome)].[article in German]	Fortschr Med 1998 Nov 30;116(33):18-20, 22, 24	This review starts with a clinical description of the most common unspecific environmental diseases, such as Multiple Chemical Sensitivities (MCS), Idiopathic Environmental Intolerances (IEI) and Sick Building Syndrome (SBS). These syndromes are very controversial discussed between scientific medicine and "clinical ecology". In addition, they have fundamental similarities to Chronic Fatigue Syndrome (CFS) and Fibromyalgia. Finally the spectrum of therapeutic approaches is discussed.
Cuykx V, Van Houdenhove B, Neerinckx E.		Childhood abuse, personality disorder and chronic fatigue syndrome.	Gen Hosp Psychiatry 1998 Nov;20(6):382-4 Comment on: Gen Hosp Psychiatry. 1994 Sep;16(5):319-25	
De Becker P, Dendale P, De Meirleir K, Campine I, Vandenborne K,	Department of Human Physiology, University Hospital, Free University, Brussels,	Autonomic testing in patients with chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):22S-26S	The purpose of this study was to determine whether chronic fatigue syndrome (CFS) patients show autonomic dysfunction at the cardiac level and if so, to discover whether these abnormalities explain the fatiguability and/or other symptoms in CFS. The study population consisted of 21 CFS patients (Centers for Disease Control and

Hagers Y.	Belgium.			Prevention [CDC] criteria, 1988) and 13 age- and sex-matched healthy controls. The autonomic testing consisted of: (1) postural challenge: registration of heart rate and blood pressure (BP) and heart rate variability in supine and in upright position (tilted to 70 degrees); (2) Valsalva maneuver; (3) handgrip test; (4) cold pressor test; and (5) heart rate response to deep breathing. Statistical analysis was performed using the Mann Whitney rank sum test; results of the test were considered significant at the 0.05 level. After tilting heart rate was significantly higher in CFS patients compared with healthy controls (mean CFS = 88.9 beats/min vs control = 77.9 beats/min; P <0.01). Low frequency power after tilting was significantly higher in CFS patients compared with controls (mean CFS = 0.603 vs control = 0.428; P = 0.02). There was a trend toward an increased heart rate during the cold pressor test. Other parameters did not differ between the CFS and control populations. The observed changes point toward a sympathetic overactivity in CFS patients when they are exposed to stress. Parasympathetic abnormalities could not be observed. Therefore, our findings provide no real explanation for the fatigue and intolerance to physical exertion in these patients.
De Lorenzo F, Hargreaves J, Kakkar VV.	Beatrice Research Centre, London, UK.	Phosphate diabetes in patients with chronic fatigue syndrome.	Postgrad Med J 1998 Apr;74(870):229-32Comment in: Postgrad Med J. 1998 Nov;74(877):701	Phosphate depletion is associated with neuromuscular dysfunction due to changes in mitochondrial respiration that result in a defect of intracellular oxidative metabolism. Phosphate diabetes causes phosphate depletion due to abnormal renal re-absorption of phosphate be the proximal renal tubule. Most of the symptoms presented by patients with phosphate diabetes such as myalgia, fatigue and mild depression, are also common in patients with chronic fatigue syndrome, but this differential diagnosis has not been considered. We investigated the possible association between chronic fatigue syndrome and phosphate diabetes in 87 patients who fulfilled the criteria for chronic fatigue syndrome. Control subjects were 37 volunteers, who explicitly denied fatigue and chronic illness on a screening questionnaire. Re-absorption of phosphate by the proximal renal tubule, phosphate clearance and renal threshold phosphate concentration were the main outcome measures in both groups. Of the 87 patients with chronic fatigue syndrome, nine also fulfilled the diagnostic criteria for phosphate diabetes. In conclusion, we report a previously undefined relationship between chronic fatigue syndrome and phosphate diabetes. Phosphate diabetes should be considered in differential diagnosis with chronic fatigue syndrome; further studies are needed to investigate the incidence of phosphate diabetes in patients with chronic fatigue syndrome and the possible beneficial effect of vitamin D and oral phosphate supplements.
De Lorenzo F, Xiao H, Mukherjee M, Harcup J, Suleiman S, Kadziola Z, Kakkar VV.	Thrombosis Research Institute, London, UK.	Chronic fatigue syndrome: physical and cardiovascular deconditioning.	QJM 1998 Jul;91(7):475-81	We investigated whether chronic fatigue syndrome (CFS) patients have physical and/or cardiovascular de-conditioning, in 273 CFS patients and 72 healthy controls. We used laboratory tests to assess haematological, biochemical, endocrinological and immunological systems. The cardiovascular system was assessed by echocardiography and carotid echography. Body composition was determined by

				dual energy X-ray absorptiometry (DEXA). CFS patients had smaller left ventricular end systolic ($p < 0.001$) and diastolic ($p = 0.008$) dimensions but thinner posterior walls ($p = 0.02$) than corresponding values in healthy controls. Left ventricular mass was also reduced in CFS patients ($p = 0.006$). Both maximum ($p < 0.001$) and minimum ($p < 0.008$) diameter of the carotid artery were smaller in CFS patients. The laboratory screening tests showed significant differences in serum albumin ($p = 0.05$), phosphate ($p = 0.02$), HDL-cholesterol ($p = 0.03$), HDL:total cholesterol ratio ($p = 0.01$), triglycerides ($p = 0.02$), neutrophils ($p = 0.01$) and thyroid-stimulating hormone ($p = 0.04$) between CFS patients and controls. Male CFS patients had an increased percentage of fat mass compared with healthy male subjects ($p = 0.02$). This large group of CFS patients had evidence of physical and cardiovascular de-conditioning, suggesting that in these patients a graded exercise programme could lead to physical reconditioning and could increase their ability to perform physical activities.
Deale A, Chalder T, Wessely S.	Department of Psychological Medicine, Kings College Hospital, and Institute of Psychiatry, London, UK.	Illness beliefs and treatment outcome in chronic fatigue syndrome.	J Psychosom Res 1998 Jul;45(1 Spec No):77-83	Longitudinal studies have shown that physical illness attributions are associated with poor prognosis in chronic fatigue syndrome (CFS). Speculation exists over whether such attributions influence treatment outcome. This study reports the effect of illness beliefs on outcome in a randomized controlled trial of cognitive-behavior therapy versus relaxation. Causal attributions and beliefs about exercise, activity, and rest were recorded before and after treatment in 60 CFS patients recruited to the trial. Physical illness attributions were widespread, did not change with treatment, and were not associated with poor outcome in either the cognitive-behavior therapy group or the control group. Beliefs about avoidance of exercise and activity changed in the cognitive behavior therapy group, but not in the control group. This change was associated with improved outcome. These findings suggest that physical illness attributions are less important in determining outcome (at least in treatment studies) than has been previously thought. In this study, good outcome is associated with change in avoidance behavior, and related beliefs, rather than causal attributions.
Deale A, Chalder T, Wessely S.	Department of Psychological Medicine, King's College Hospital, London.	Commentary on: Randomised, double-blind, placebo-controlled trial of fluoxetine and graded exercise for chronic fatigue syndrome.	Br J Psychiatry 1998 Jun;172:491-2 Comment on: Br J Psychiatry. 1998 Jun;172 :485-90	
Delbanco TL, Daley J, Hartman EE.		A 56-year-old woman with chronic fatigue syndrome, 1 year later.	JAMA 1998 Jul 22-29;280(4):372 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Demitrack MA,	Lilly Research	Evidence for and	Ann N Y Acad Sci 1998	Chronic fatigue syndrome (CFS) is characterized by profound fatigue and an array of

Crofford LJ.	Laboratories, Lilly Corporate Center, Indianapolis, Indiana 46285, USA.	pathophysiologic implications of hypothalamic-pituitary-adrenal axis dysregulation in fibromyalgia and chronic fatigue syndrome.	May 1;840:684-97	diffuse somatic symptoms. Our group has established that impaired activation of the hypothalamic-pituitary-adrenal (HPA) axis is an essential neuroendocrine feature of this condition. The relevance of this finding to the pathophysiology of CFS is supported by the observation that the onset and course of this illness is excerbated by physical and emotional stressors. It is also notable that this HPA dysregulation differs from that seen in melancholic depression, but shares features with other clinical syndromes (e.g., fibromyalgia). How the HPA axis dysfunction develops is unclear, though recent work suggests disturbances in serotonergic neurotransmission and alterations in the activity of AVP, an important co-secretagogue that, along with CRH, influences HPA axis function. In order to provide a more refined view of the nature of the HPA dusturbance in patients with CFS, we have studied the detailed, pulsatile characteristics of the HPA axis in a group of patients meeting the 1994 CDC case criteria for CFS. Results of that work are consistent with the view that patients with CFS have a reduction of HPA axis activity due, in part, to impaired central nervous system drive. These observations provide an important clue to the development of more effective treatment to this disabling condition.
Demitrack MA.	Lilly Research Laboratories, Indianapolis, Indiana, USA.	Chronic fatigue syndrome and fibromyalgia. Dilemmas in diagnosis and clinical management.	Psychiatr Clin North Am 1998 Sep;21(3):671-92, viii	There has been a resurgence of interest in recent years in both chronic fatigue syndrome and fibromyalgia. These perplexing and common clinical conditions are a source of significant patient morbidity and frame one of the more enduring dilemmas of contemporary Western medical thought, namely the ambiguous interface between mind and body. In this article, the current definitions are reviewed, and a framework for an emerging psychobiological model of these syndromes is presented. These issues are synthesized into a pragmatic approach to clinical management. Review, Academic
Demitrack MA.	Lilly Research Laboratories, Neuroscience Therapeutic Area, Indianapolis, Indiana 46285, USA.	Neuroendocrine aspects of chronic fatigue syndrome: a commentary.	Am J Med 1998 Sep 28;105(3A):11S-14S	
Devitt NF.		Chronic fatigue syndrome.	JAMA 1998 Feb 11;279(6):432; discussion 432-3 Comment on: JAMA. 1997 Oct 8;278(14):1179-85	
Duprez DA, De Buyzere ML, Drieghe B, Vanhaverbeke F, Taes Y, Michielsen W,	Department of Cardiology and Angiology, University Hospital, Gent,	Long- and short-term blood pressure and RR-interval variability and psychosomatic distress	Clin Sci (Colch) 1998 Jan;94(1):57-63Comment in: Clin Sci (Colch). 1999	1. Chronic low blood pressure has been associated with fatigue and low mood. However, in the chronic fatigue syndrome (CFS) the blood pressure (BP) and heart rate profile and their variabilities have not been characterized as yet. 2. We performed office and 24 h ambulatory BP recordings in 38 subjects (age, 34.8 8.0

Clement DL.	Belgium.	in chronic fatigue syndrome.	Sep;97(3):319-22	years) who fulfilled the Holmes criteria for CFS and in 38 healthy control subjects (age 35.6 10.5 years), as well as short-term beat-to-beat BP and RR-interval recordings for 10 min in supine and standing position, and calculated spectral indices. 3. In CFS office (123 19/70 12 mmHg) as well as 24-h, day- and night-time blood pressure values (116 11.1/71 11.1, 121 9.2/77 8.0 and 110 10.5/65 9.2 mmHg respectively) were within reference limits. 4. Heart rate was consistently higher ($P < 0.01$) in CFS patients, based on both office (77 12 compared with 68 12 beats min-1) and 24 h ambulatory recordings (77 12 compared with 67 15 beats min-1). 5. In supine position, spectral indices of BP variability (total, low-frequency and high-frequency variances) were all significantly ($P < 0.01$) lower in CFS. In standing position the differences disappeared. Analysis of RR-interval variability could not detect major alterations in autonomic function in CFS.
Dykman KD, Tone C, Ford C, Dykman RA.	Mannatech Inc., Coppell Texas 75019, USA.	The effects of nutritional supplements on the symptoms of fibromyalgia and chronic fatigue syndrome.	Integr Physiol Behav Sci 1998 Jan-Mar;33(1):61-71	This article reports the results of a within-subject design. Fifty subjects with a physician diagnosis of fibromyalgia (FM) and/or chronic fatigue syndrome (CFS) were interviewed using a structured interview from. Each subject was interviewed initially, and again nine months later (follow-up). Subjects had, on their own, consumed nutritional supplements including freeze-dried aloe vera gel extract; a combination of freeze-dried aloe vera gel extract and additional plant-derived saccharides; freeze-dried fruits and vegetables in combination with the saccharides; and a formulation of dioscorea complex containing the saccharides and a vitamin/mineral complex. With medical treatments, approximately 25 percent of FM patients improve, but the beneficial effects of medical treatment rarely persist more than a few months. All subjects in this study had received some form of medical treatment prior to taking the nutritional supplements, but none with enduring success. Nutritional supplements resulted in a remarkable reduction in initial symptom severity, with continued improvement in the period between initial assessment and the follow-up. Further research is needed to verify these results, specifically crossover designs in well-defined populations.
Empson M.		Celiac disease or chronic fatigue syndrome--can the current CDC working case definition discriminate?	Am J Med 1998 Jul;105(1):79-80	
Endicott NA		Chronic Fatigue Syndrome in Psychiatric Patients: Evidence of Premorbid Anomalous Patterns of Brain Organization	Journal of Chronic Fatigue Syndrome 1998: 5(1): 29 - 45	Forty-six patients with chronic fatigue syndrome (CFS) were matched with two control groups: one chosen on the basis of relatively good physical health (N = 92) and the other without regard to physical health (N = 46). All patients were from the same psychiatric practice. The groups were compared on 20 anomalous brain conditions or phenomena (ABCP) used as markers of patterns of brain organization. The results suggest that psychiatric patients who subsequently develop CFS have a

				higher number of pre-CFS ABCP, of both childhood and adult onset, than psychiatric patients who have not developed this condition
Endicott NA.	Department of Research Assessment and Training, New York State Psychiatric Institute, New York, USA.	Chronic fatigue syndrome in psychiatric patients: lifetime and premorbid personal history of physical health.	Psychosom Med 1998 Nov-Dec;60(6):744-51	OBJECTIVE: This preliminary report compares a group of chronic fatigue syndrome (CFS) patients and controls on several variables of potential significance in the etiology of CFS. METHOD: The lifetime prevalence of reported physical disorders was compared among 46 CFS psychiatric patients, 92 relatively physically healthy psychiatric patients (C-I), and 46 psychiatric patients selected without regard to physical health (C-II). All patients were matched on age, sex, and psychiatric diagnosis and were drawn from the same psychiatric practice. The same groups were compared on a 7-point scale of lifetime physical health by three raters independently evaluating physical health narratives of the CFS patients up to the time of onset of CFS and that of the controls up to the corresponding age. RESULTS: The CFS patients had a significantly higher reported lifetime prevalence of irritable bowel syndrome (IBS), infectious mononucleosis-like syndromes (IM), infectious mononucleosis-like syndromes two or more times (IM x 2), and herpes (other than genital or perioral herpes) than one or both control groups. The CFS group also had a higher incidence of allergic rhinitis or asthma, IBS, IM, and IM x 2 than the combined controls. On the independent ratings, the CFS patients had significantly more impaired physical health up to the time of onset of the CFS than C-I at a comparable age. CONCLUSIONS: The findings suggest that a general health factor may be involved in the pathogenesis of some cases of CFS.
Essame CS, Sue Phelan, Percy Aggett Peter D. White		Pilot Study of a Multidisciplinary Inpatient Rehabilitation of Severely Incapacitated Patients with the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(2): 51 - 60	The outcome of severely incapacitated patients with the chronic fatigue syndrome is poor. We examined the outcome of the first 19 such patients admitted to a psychiatric ward in a general hospital for a multidisciplinary rehabilitation programme. Seventeen (89%) patients had functionally improved by discharge, the median Karnofsky score improvement being 15 points in all 19 patients. All fourteen patients who were followed up had maintained or exceeded their improvement by one year, with a median Karnofsky score improvement of 25 in all 16 followed up patients, compared to admission. Only two patients had not improved by discharge and they were the same or worse at one year. A randomised controlled trial is necessary to confirm the efficacy and acceptability of this form of rehabilitation.
Evengard B, Nilsson CG, Lindh G, Lindquist L, Eneroth P, Fredrikson S, Terenius L, Henriksson KG.	Department of Infectious Diseases, Karolinska Institute at Huddinge Hospital, Stockholm, Sweden.	Chronic fatigue syndrome differs from fibromyalgia. No evidence for elevated substance P levels in cerebrospinal fluid of patients with chronic fatigue syndrome.	Pain 1998 Nov;78(2):153-5	Levels of substance P were determined in the cerebrospinal fluid (CSF) in 15 patients with chronic fatigue syndrome (CFS). All values were within normal range. This is in contrast to fibromyalgia (FM). The majority of patients with FM have increased substance P values in the CSF. The results support the notion that FM and CFS are different disorders in spite of overlapping symptomatology.
Findley JC, Kerns R,	V.A. Connecticut	Self-efficacy as a	J Behav Med 1998	Chronic fatigue syndrome (CFS) is characterized by debilitating fatigue and a variety

Weinberg LD, Rosenberg R.	Healthcare System, West Haven 06516, USA.	psychological moderator of chronic fatigue syndrome.	Aug;21(4):351-62	of somatic symptoms. Few studies have examined psychological aspects of CFS. In the present study, self-efficacy is shown to be a significant predictor of CFS symptoms beyond the variance accounted for by demographic variables and distress. Further psychological CFS research is encouraged by (1) identifying dimensions that are salient in the experience and study of CFS, (2) providing preliminary psychometric data for measures of those dimensions, and (3) identifying psychological variables that serve as moderators of the experience of CFS.
Fischler B, Patrick Flamen Hendrik Everaert Axel Bossuyt Kenny De Meirleir		Physiopathological Significance of 99mTc HMPAO SPECT Scan Anomalies in Chronic Fatigue Syndrome A Replication Study	Journal of Chronic Fatigue Syndrome 1998: 4(4): 15 - 30	Regional cerebral blood flow as measured by 99mTc HMPAO SPECT imaging was compared between chronic fatigue syndrome (CFS) and healthy controls (HC). Larger right(R) > left(L) asymmetry at the parietotemporal level in CFS as compared to HC was observed in accordance with several previous studies. On the contrary, in most regions of interest, hypoperfusion was not confirmed in CFS, and hyperperfusion was demonstrated in several frontal and temporal regions. No significant correlations were found between frontal tracer uptake and R-L parietotemporal asymmetry, on the one hand, and clinically relevant CFS dimensions, on the other.
Franklin A.		How I manage chronic fatigue syndrome.	Arch Dis Child 1998 Oct;79(4):375-8	
Fuller NS, Morrison RE.	Division of General Internal Medicine, University of Tennessee, College of Medicine, Memphis 38103, USA.	Chronic fatigue syndrome. Helping patients cope with this enigmatic illness.	Postgrad Med 1998 Jan;103(1):175-6, 179-84	Chronic fatigue syndrome is a recurring, debilitating illness complicated by the fact that its diagnosis is largely based on subjective complaints and the absence of reproducibly reliable tests. There is no known "cure" for this illness; however, in general, the prognosis for patients is good. Some physicians accept the existence of chronic fatigue syndrome, while others are convinced that it exists only in the minds of its "victims." The majority of physicians, however, are skeptical but open-minded and wish to help their chronically fatigued patients. As more information comes to light, it is likely that modern medicine will have to rethink its views on this elusive illness. In the interim, patients with chronic fatigue syndrome need the support and reassurance of their physicians to help them cope with their symptoms and resume normal, productive lives.
Garcia-Borreguero D, Dale JK, Rosenthal NE, Chiara A, O'Fallon A, Bartko JJ, Straus SE.	Clinical Psychobiology Branch, National Institute of Mental Health, Bethesda, MD 20892, USA.	Lack of seasonal variation of symptoms in patients with chronic fatigue syndrome.	Psychiatry Res 1998 Feb 9;77(2):71-7	Several of the symptoms involved in chronic fatigue syndrome (CFS) such as fatigue, hypersomnia, hyperphagia, weight gain, and mood show seasonal variations in the general population. The aim of this study was to investigate whether patients with CFS experience seasonal fluctuations in these symptoms as well. Seasonal variation of symptoms was assessed in a group of 41 patients with CFS and 41 controls closely matched for age, gender, and city of residence. Participants were recruited across the US and were asked to complete the Seasonal Pattern Assessment Questionnaire (SPAQ) and the Profile of Mood States (POMS). CFS patients showed significantly lower scores on multiple SPAQ-derived measures as compared with controls. These included seasonal variation in energy, mood, appetite, weight, and sleep length. Patients also reported a significantly reduced sensitivity toward sunny, dry, and long days than controls. No association was noted between intensity of seasonal changes

				and severity of depressive symptoms. Patients with CFS exhibit an abnormally reduced seasonal variation in mood and behavior and would not be expected to benefit from light therapy.
Gibbons, Pheby , C. Richards , F. I. Bray		Severe CFS/ME of Juvenile Onset- A Report from the CHROME Database	Journal of Chronic Fatigue Syndrome 1998: 4(4): 67 - 80	CHROME has been collecting data since 1995 on very severely disabled patients in the UK with ME, in order to assess aspects of physical and cognitive levels of disability at the onset of the illness and to monitor progress. Results of the first two years data (225 cases) collection are reported. The modal age of onset for this severe group of patients was 11-15, and the proportion increased with more recent years of onset. Patients tended to deteriorate between onset and recruitment in cognitive and functional ability, and in sensory and sleep disturbance. Statistical significance was assessed using McNemar's Test for comparing correlated proportions.
Gimenez HB, P. Cash, R. B. S. Laing, J. G. Douglas		Cytokine Expression and Morphology of in vitro Grown Monocytes from Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 5(1): 47 - 60	Although the underlying metabolic cause of chronic fatigue syndrome (CFS) is unknown, specific defects have been proposed to exist in the skeletal muscle, the immune system and the neuroendocrine system. Peripheral blood mononuclear cells from CFS patients and healthy controls were fractionated as adherent cells (monocyte-enriched fraction) and non-adherent cells. We have investigated some activities of the former during in vitro culture. It was observed that the morphology (shape and size) of adherent cells from CFS patients, cocultivated with homologous non-adherent cells, differed between CFS patients and healthy controls for 21 out of 25 (84%) paired samples (i.e., CFS patient and healthy control). Cytokine expression was examined for the adherent cell population collected from 14 CFS patients and 12 healthy controls. Unstimulated and LPS stimulated tumour necrosis factor-α (TNFα) expression was higher for monocytes from 7 out of 14 CFS patients. Unstimulated interleukin-1β (IL-1β) expression was higher for monocytes from 10 out of 14 CFS patients, whereas LPS-stimulated IL-1β expression was higher for 8 out of 14 CFS patients. The proportional increase of IL-1β and TNFα following LPS stimulation was lower for the majority of the CFS patients studied, suggesting that the monocytes from CFS patients were less responsive to LPS than the respective healthy controls. The basis for the abnormal in vitro monocyte maturation, the elevated unstimulated levels of IL-1β expression and the abnormal response of the monocytes to LPS is unknown. The relevance of these findings to CFS pathogenesis is discussed
Glaser R, Kiecolt-Glaser JK.	Department of Medical Microbiology and Immunology, Comprehensive Cancer Center, The Ohio State University College of Medicine, Columbus 43210, USA.	Stress-associated immune modulation: relevance to viral infections and chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):35S-42S	The frequent association of an active viral infection with the symptoms of CFS led researchers to hypothesize that chronic fatigue syndrome (CFS) is induced by a virus. Results of these studies indicated that despite clinical support for this hypothesis, there were no clear data linking viruses to CFS. In this overview, we will explore the interrelation of the immune, endocrine, and central nervous systems, and the possibility that stress and/or the reactivation/replication of a latent virus (such as Epstein Barr virus) could modulate the immune system to induce CFS. Relevant research conducted in the developing field of psychoneuroimmunology will be reviewed, with a particular focus on cytokine synthesis, natural killer (NK) cell

				activity, and T-lymphocyte function, as they relate to CFS.
Goshorn RK.	Department of Internal Medicine, Indiana University Hospital, Indianapolis, USA.	Chronic fatigue syndrome: a review for clinicians.	Semin Neurol 1998;18(2):237-42	Syndromes characterized by persistent fatigue, musculoskeletal pain, sleep disturbance, and subjective cognitive impairment have been common problems in clinical practice for decades. The chronic fatigue syndrome case definition was created to standardize the patient population in research studies and to foster a systematic and comprehensive approach to the attempt to define the etiology and pathophysiology of these syndromes. The pathogenesis of chronic fatigue syndrome remains unknown, though it does appear to be associated with subtle neuroendocrine and immunologic abnormalities. Treatment of chronic fatigue syndrome is empirical. Significant palliation is often possible, though treatment success requires skillful practice of the art of medicine.
Hall GH, Hamilton WT, Round AP.		Increased illness experience preceding chronic fatigue syndrome.	J R Coll Physicians Lond 1998 Jul-Aug;32(4):389 Comment on: J R Coll Physicians Lond. 1998 May-Jun;32(3):274	
Hall GH, Hamilton WT, Round AP.		Increased illness experience preceding chronic fatigue syndrome: a case control study.	J R Coll Physicians Lond 1998 Jan-Feb;32(1):44-8Comment in: J R Coll Physicians Lond. 1998 May-Jun;32(3):274	BACKGROUND: Almost all published work on chronic fatigue syndrome (CFS) has involved retrospective surveys of cases, which may introduce recall bias. Only medical records collected before diagnosis of CFS can eliminate this. METHODS: Using data collected several years prior to the development of the illness, we performed a case control study, comparing the reported illness records of all people who subsequently made an insurance claim as a result of CFS, with those of future multiple sclerosis (MS) claimants, and those of non-claimant controls (NC). RESULTS: The study encompassed 133 CFS, 75 MS and 162 NC cases. CFS cases had recorded significantly more illnesses at time of proposal for insurance than the two control groups, and had significantly more claims between proposal and diagnosis of their disorder. Almost all disease categories were reported higher in future CFS sufferers, lethargy having the highest odds ratio after adjustment in a multivariate model. INTERPRETATION: The results of this paper on CFS patients who claim permanent health insurance do not support a specific viral or immunological explanation for CFS. We conclude that abnormal illness behaviour is of greater importance than previously recognised.
Hamilos DL, Nutter D, Gershtenson J, Redmond DP, Clementi JD, Schmaling KB, Make BJ, Jones JF.	National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado, USA.	Core body temperature is normal in chronic fatigue syndrome.	Biol Psychiatry 1998 Feb 15;43(4):293-302	BACKGROUND: Subjects with chronic fatigue syndrome (CFS) frequently report symptoms of subnormal body temperature and low-grade fever. We conducted a study to determine whether CFS subjects manifest any abnormality of core body temperature (CBT) that might help explain their fatigue. METHODS: Continuous 24-hour recordings of CBT measured every 5 min were performed in 7 subjects meeting the Centers for Disease Control definition of CFS. Three additional groups were studied: normal controls, subjects with seasonal allergy, and subjects with major depression. Subjects (n = 7) in each group were age-, sex-, and weight-matched to

				the CFS group and had normal basal metabolic rates, thyroid function, and 24-hour urinary free cortisol excretions. CBT was measured with an ingestible radio frequency transmitter pill and a belt-worn receiver-logger. Each pill was factory-calibrated to 0.1 degree C and field-calibrated with a water bath calibration prior to use. RESULTS: The 24-hour mean calibration-adjusted CBTs of each group were not significantly different (control: 37.00 0.17 degrees C; CFS: 37.04 0.31 degrees C; allergy: 37.15 0.18 degrees C; depression: 37.16 0.18 degrees C). Similarly, the mean peak and trough circadian temperatures were not statistically different. The mean 24-hour profile of CBT for each group showed a similar circadian rhythm. In simultaneously collected blood samples, each group showed a similar circadian profile of serum cortisol with a peak occurring at 08:00. CONCLUSIONS: Subjects with CFS have normal CBT despite frequent self-reports of subnormal body temperature and low-grade fever.
Harlow BL, Signorello LB, Hall JE, Dailey C, Komaroff AL.	Obstetrics and Gynecology Epidemiology Center, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.	Reproductive correlates of chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):94S-99S	A case-control study was conducted to determine whether menstrual and gynecologic abnormalities precede the onset of chronic fatigue syndrome (CFS) in women with this disorder to a greater extent than that observed among healthy controls. We identified 150 women who met the 1988 Centers for Disease Control criteria for CFS from the Brigham and Women's Hospital Cooperative CFS Research Center. A comparison group of 149 women being seen for nongynecologic conditions were selected from the waiting area of the Brigham and Women's Hospital Internal Medicine outpatient department. Women with and without CFS completed self-administered questionnaires on menstrual, reproductive, and medical history. Women with CFS reported increased gynecologic complications and a lower incidence of premenstrual symptomatology. After adjustment for age, a somewhat greater number of cases compared with controls self-reported irregular cycles, periods of amenorrhea, and sporadic bleeding between menstrual periods. Factors suggestive of abnormal ovarian function--such as a history of polycystic ovarian syndrome, hirsutism, and ovarian cysts--were reported more often in CFS cases compared with controls. Frequent anovulatory cycles due to ovarian hyperandrogenism (PCOS) or hyperprolactinemia may increase risk for CFS through loss of the potential immunomodulatory effects of progesterone in the presence of continued estrogen production. We hypothesize that frequent anovulatory cycles due to PCOS and/or hyperprolactinemia may explain the increased reporting of gynecologic complications and the lower reported premenstrual symptomatology observed in women with CFS.
Harrigan P.		Controversy continues over chronic fatigue syndrome.	Lancet 1998 Feb 21;351(9102):574Comment in: Lancet. 1998 Apr 25;351(9111):1292	
Hartz AJ, Evelyn M.		Characteristics of	Journal of Chronic	Background: Characteristics of persons with chronic fatigue syndrome (CFS) have

Kuhn , Paul H. Levine		Fatigued Persons Associated with Features of Chronic Fatigue Syndrome	Fatigue Syndrome 1998: 4(3): 71 - 97	previously been studied by comparing subjects with CFS to subjects with other conditions or no symptoms of fatigue. In the present study of subjects with idiopathic chronic fatigue we examined the association between the number and severity of the features of CFS with other characteristics of the subjects. Methods: Data were obtained from a registry of persons over the age of 17 with fatigue for at least six months. All subjects in the registry completed an extensive questionnaire that provided information about fatigue, demographic characteristics, medical conditions, life style, sleeping habits, and psychological characteristics. The characteristics of the subjects were tested for an association with the number of CFS symptoms and the severity of individual CPS symptoms that are considered to be of fundamental importance and may identify more homogeneous subjects with chronic fatigue. Results: The number of CFS symptoms had a bell shaped distribution. This number was strongly associated with the severity of fatigue, the response of fatigue to mental and physical activity, and the following subject characteristics: a greater frequency of sinus and respiratory infections, a higher frequency of migraine headaches, a greater number of somatoform symptoms that were not included as criteria for CFS, and not drinking alcohol. These same subject characteristics were generally associated with at least one of the individual CFS symptoms but more weakly. Psychological complaints only had a statistically significant positive association with one feature of CFS, neurocognitive complaints. Conclusions: Persons with fatigue can be usefully characterized by the extent to which they meet the CFS criteria.
Hassan IS, Bannister BA, Akbar A, Weir W, Bofill M.	Department of Infectious & Tropical Diseases, Royal Free Hospital, London, England.	A study of the immunology of the chronic fatigue syndrome: correlation of immunologic parameters to health dysfunction.	Clin Immunol Immunopathol 1998 Apr;87(1):60-7	Surface and intracellular immunologic and apoptotic markers and functional lymphocyte assays after stimulation with anti-CD3/anti-CD28 antibodies or phytohemagglutinin (PHA) were studied in 44 patients fulfilling the Oxford criteria for chronic fatigue syndrome (CFS). Results were then correlated to scores for the Short Form-36 health questionnaire (SF-36), which assesses eight aspects of patient's well-being, and for the general health questionnaire (GHQ), which detects current psychiatric disorder. Patients had significantly increased mean fluorescence intensity readings of HLA-DR in CD4 and CD8 cells ($P < 0.05$). Expression of the costimulatory receptor CD28 in CD8 cells was significantly reduced, and the apoptosis repressor ratio of bcl-2/bax in both CD4 and CD8 was increased in patients ($P < 0.05$). Patients with increased HLA-DR expression had significantly lower SF-36 total scores, worse body pains, and poorer general health perception and physical functioning scores. Increased spontaneous lymphocyte proliferation was associated with poor general health perception. PHA proliferative responses were lower in patients with poor emotional and mental health scores, and the anti-CD3/anti-CD28 response was low in those with low general health perception scores. Higher spontaneous proliferation and reduced PHA responses correlated with higher GHQ scores. Similarly, GHQ scores were significantly higher, indicating worse mental health, in those with lower total

				SF-36 scores and worse general and mental health scores in the SF-36 questionnaire. Finally, higher expression of the costimulatory molecule CD28 correlated with higher total SF-36 scores, general health perception and social functioning scores, and with lower role limitation due to physical health. The increased expression of class II antigens and the reduced expression of the costimulatory receptor CD28, which is a marker of terminally differentiated cells, lend further support to the concept of immunoactivation of T-lymphocytes in CFS and may be consistent with the notion of a viral etiopathogenesis in the illness. We report, for the first time, increased expression of the apoptosis repressor protein bcl-2, which may contribute to enhanced survival of activated lymphocytes. Using the SF-36 health assessment questionnaire and the GHQ, we demonstrated changes in different immunological parameters, each of which correlated with particular aspects of disease symptomatology.
Heijmans M, de Ridder D.	Department of Health Psychology, Utrecht University, The Netherlands.	Assessing illness representations of chronic illness: explorations of their disease-specific nature.	J Behav Med 1998 Oct;21(5):485-503	Elaborating on the five-dimensional structure of illness representation, as described in the self-regulation model of Leventhal (1980), the present study is aimed at identifying the relevance of this generic structure for two chronic illnesses: chronic fatigue syndrome (CFS) and Addison's disease (AD). Factor analyses showed the importance of the five dimensions identity, time-line, control/cure, cause, and consequences to differ according to the type of disease. That is, the items representing the five dimensions merged together for CFS patients and AD patients in a different manner and thereby produced different factor solutions for the two patient groups. In CFS patients, a four-factor solution was identified with manageability, seriousness, personal responsibility, and external cause as the factors. In AD patients a four-factor solution was also identified but with seriousness, cause, chronicity, and controllability as the factors. The value of these findings for our understanding of the disease-specific nature of illness representation is discussed.
Heijmans MJ.	Department of Clinical and Health Psychology, Utrecht University, The Netherlands. M.Heijmans@fsw.ruu.nl	Coping and adaptive outcome in chronic fatigue syndrome: importance of illness cognitions.	J Psychosom Res 1998 Jul;45(1 Spec No):39-51	In this study, the relations between illness representations, coping behavior, and adaptive outcomes in chronic fatigue syndrome (CFS) patients (N=98) were examined. Following Leventhal's self-regulation model, it was hypothesized that illness representations would be directly related to coping and, via coping, to adaptive outcome. The results showed patients who considered their illness to be a serious condition, who believed that they had no control over their illness, who saw little possibility for cure, and who believed their illness to have serious consequences to cope with their illness in a passive way, report higher levels of impairment in physical and social functioning and report greater problems in mental health and vitality. A series of regression analyses showed illness representations to be stronger predictors of adaptive outcome than coping scores. The implications of these findings for the treatment of CFS patients are discussed.
Heller U, Becker EW, Zenner HP, Berg PA.	HNO-Klinik, Universitat Tubingen.	[Incidence and clinical relevance of antibodies	HNO 1998 Jun;46(6):583-	Immunoserological assays of patients with sudden deafness and progressive hearing losses have revealed the presence of different antibodies, leading to the assumption

		to phospholipids, serotonin and ganglioside in patients with sudden deafness and progressive inner ear hearing loss].[article in German]	6Comment in: HNO. 1998 Jun;46(6):565-6	that immunological processes may be involved. Recent investigations have demonstrated that these patients have phospholipid antibodies that can cause venous or arterial vasculopathies. In the present study we analyzed the incidence of these antibodies in patients with inner ear disorders. Sera of 55 patients with sudden deafness and 80 patients with progressive hearing loss were tested. Phospholipid antibodies were demonstrable in 49% of the patients with sudden hearing loss and 50% of the patients with progressive hearing loss. Serotonin and ganglioside antibodies were found in 53% of the patients with sudden hearing loss and 63% of the patients with progressive hearing loss. Since these three antibodies are also frequently found in patients with fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS), 28 of the patients studied displayed symptoms typical for these disorders, including fatigue, myalgia, arthralgia, depressions, sicca symptoms and diarrhea. We now recommend questioning patients suffering from inner ear disorders for symptoms typical for FMS or CFS, since these diseases are often closely related to inner ear disorders. If symptoms are present, antibodies should be tested against phospholipids, serotonin and gangliosides. If present, the antibodies are diagnostic for each syndrome. Additionally these immunologic and serologic findings show that these antibodies may play a role in the etiology of hearing loss disorders.
Hicks MH, Kleinman A, Yang L.	Department of Social Medicine, Harvard Medical School, Boston, USA.	The social course of schizophrenia: local and societal factors.	Kaohsiung J Med Sci 1998 Jul;14(7):432-47	In this paper, we propose a model of social course of schizophrenia based on cross-cultural research on the influence of family, wider social network, work, political economy, and legal and mental health care institutions on the experience of illness. We posit the way these ordinary arrangements of daily living organize the course of schizophrenia in part through cultural processes that affect the body-self in suffering and in part through social processes that establish an intersubjective matrix for the experience of illness. We believe this model can be generalized to other chronic illness such as depression, diabetes, asthma, osteoarthritis, chronic pain syndrome, chronic fatigue syndrome, and even heart disease and cancer. We develop the implications of this anthropological approach for research and practice.
Hilgers A, Johannes Frank, Petra Bolte		Prolongation of Central Motor Conduction Time in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(2): 23 - 32	We compared the central motor conduction time (CMCT) obtained by magnetic stimulation of the central nervous system (CNS) of 181 patients who filfilled the criteria (see Fukuda 1994) for CFS with those of 27 healthy control subjects. A cortical and a cervical stimulation was performed on each person under standardised conditions, and the motor evoked potentials (MEP) either from Musculus Abductor Pollicis Brevis (M. APB) or from Musculus Abductor Digiti Minimi (M. ADM) was recorded. For the CFS patients a significant prolongation of the central motor conduction time (M. APB right: $p < 0.0001$; M. ADP left: $p < 0.00005$; M. ADM right: $p < 0.00005$; M. ADM left: $p < 0.005$) was observed compared to controls. The results presented in this study suggest a central nervous system dysfunction in CFS.
Hyman H, Thomas E. Wasser		Gastrointestinal Manifestations of	Journal of Chronic Fatigue Syndrome	Objectives: This study examines the differences in symptoms and Quality of Life (QOL) among patients presenting to a gastrointestinal (GI) service with combinations

		Chronic Fatigue Syndrome (CFS) Symptom Perceptions and Quality of Life	1998: 4(1): 43 - 52	of chronic fatigue syndrome (CFS) and GI complaints. Methods: We conducted a clinical examination of patients from a private GI practice and divided them into three groups: A combination group consisting of patients diagnosed with both CFS and functional bowel disease (FBD) (Group 1, n = 5); those positively diagnosed with CFS, who also reported GI symptoms, but without a prior GI diagnosis (Group 2, n = 6); and those with FBD, but without a diagnosis of CFS (Group 3, n = 11). These groups were prospectively surveyed, using the Medical Outcomes Study Short Form-36 (SF-36) and the Symptom Index Survey (SIS). Results: Data indicate CFS patients report more symptoms than non-CFS patients, as measured by the SIS, in these areas: Allergies, Digestive Tract, Ears, Eyes, Head, Immune, Joints/Muscles and Metabolism/Endocrine. SF-36 data indicated lower QOL for CFS patients compared to FBD alone (Group 3) patients in the General Health and Energy/Fatigue subscales. Conclusions: CFS patients with GI complaints demonstrate a significant relationship between both diagnoses. Since the observed differences occur between Groups 1 and 3, both with GI diagnoses, this indicates that these differences are a result of the presence or absence of CFS. Also, since these differences occur between CFS/ FBD and FBD-only, the classification of irritable bowel syndrome (IBS) should be modified to include a subset of patients who have a combination of CFS and IBS.
Jain SS, DeLisa JA.	Department of Physical Medicine and Rehabilitation, UMDNJ-New Jersey Medical School, Newark, USA.	Chronic fatigue syndrome: a literature review from a physiatric perspective.	Am J Phys Med Rehabil 1998 Mar-Apr;77(2):160-7	To examine the literature on chronic fatigue syndrome (CFS), especially as it relates to cognitive deficits and exercise, more than 200 articles related to CFS were selected from computer-based research as well as pertinent articles noted in the references of individual articles. All were relevant articles on CFS, although articles in a foreign language were excluded. CFS is a controversial diagnosis of exclusion, but certain subgroups do appear to exist. It may represent multiple diseases or multiple stages of the same disease. Although cognitive deficits are commonly reported, the measured impairments are relatively subtle and are in the area of complex information processing speed, or efficiency. Magnetic resonance imaging, single-photon emission computer tomography, and neuroendocrine studies present preliminary evidence suggestive of the cerebral involvement primarily in the white matter. The weakness and fatigue may be the result of alterations in the central nervous system, not in the peripheral muscles. However, it is hard to separate the documented weakness and endurance deficits from deconditioning. Autonomic symptoms such as orthostatic intolerance and a predisposition to neurally mediated syncope may be explained by cardiovascular deconditioning, a postviral idiopathic autonomic neuropathy, or both. The review points out the need for more carefully designed studies of CFS that focus on the relationship between neuropathology, psychopathology and neuropsychologic functioning. The role of exercise as a stimulus for exacerbation or in treatment needs to be further studied using clear diagnostic criteria as well as control groups that carefully match the activity level.
Jason LA, Wagner L,	Department of	Estimating the	Am J Med 1998 Sep	The present study assessed the prevalence of chronic fatigue syndrome (CFS) in a

Rosenthal S, Goodlatte J, Lipkin D, Papernik M, Plioplys S, Plioplys AV.	Psychology, DePaul University, Northwestern Medical School, Rush Presbyterian--St. Luke's Medical Center, Chicago, Illinois 60614, USA.	prevalence of chronic fatigue syndrome among nurses.	28;105(3A):91S-93S	sample of nurses. There is a paucity of studies on the prevalence of CFS in healthcare professionals. Two samples of nurses were recruited through mailed questionnaires. Data were collected on demographic characteristics and symptoms. In addition from the sample, those nurses with CFS-like symptoms were more comprehensively evaluated using a structured clinical interview and reviewing their medical records. A physician review team estimated the prevalence of CFS to be 1,088 per 100,000. These findings suggest that nurses might represent a high-risk group for this illness, possibly due to occupational stressors such as exposure to viruses in the work setting, stressful shift work that is disruptive to biologic rhythms, or to other possible stressors in the work settings (e.g., accidents).
Jiaxu C, Yang Weiyi		Treatment of Chronic Fatigue Syndrome with Chinese Medicine	Journal of Chronic Fatigue Syndrome 1998: 5(1): 61 - 65	Chronic fatigue syndrome (CFS) is a severe, debilitating disorder, which prominently features self-reported impairments in concentration and short-term memory, and disturbances in sleep and emotions, all of which can affect any one and seriously affect quality of life. In 1987, the Centers for Disease Control and Prevention (CDC) defined CFS as persistent or relapsing fatigue, with at least 50% reduction of baseline activity level lasting for at least 6 months, as one of the main symptoms. Since its cause is still unknown, treatment of CFS has been palliative and has included usually orally administered products, such as vitamin B12, vitamin C, folic acid, iron, magnesium, essential fatty acids, coenzyme Q10 and nicotinamide adenine dinucleotide (NADH), among others. The latter therapeutic modalities can only relieve some symptoms to some extent, but cannot fundamentally eliminate fatigue. It is, therefore, urgent to seek safe and effective drugs for the treatment of fatigue. We propose here that regulating homeostasis and enhancing immunity are important for the treatment of fatigue. In China, many Chinese herbs with such functions have been proven effective, an observation which opens the possibility of a new therapeutic method of eliminating fatigue with traditional Chinese medicine (TCM).
Johnson SK.	Department of Psychology, University of North Carolina, 9201 University City Boulevard, Charlotte 28223-0001. skjohnso@email.uncc.edu.	The biopsychosocial model and chronic fatigue syndrome.	Am Psychol 1998 Sep;53(9):1080-2 Comment on: Am Psychol. 1997 Sep;52(9):973-83	
Jordan KM, Landis DA, Downey MC, Osterman SL, Thurm AE, Jason LA.	Department of Psychology, DePaul University, Chicago, Illinois 60614, USA.	Chronic fatigue syndrome in children and adolescents: a review.	J Adolesc Health 1998 Jan;22(1):4-18	
Joyce J, Rabe-Hesketh S, Wessely S.	Institute of Psychiatry, King's College School of	Reviewing the reviews: the example of chronic	JAMA 1998 Jul 15;280(3):264-6	OBJECTIVE: To test the hypothesis that the selection of literature in review articles is unsystematic and is influenced by the authors' discipline and country of residence.

	Medicine, London, England.	fatigue syndrome.		DATA SOURCES: Reviews in English published between 1980 and March 1996 in MEDLINE, EMBASE (BIDS), PSYCHLIT, and Current Contents were searched. STUDY SELECTION: Reviews of chronic fatigue syndrome (CFS) were selected. Articles explicitly concerned with a specialty aspect of CFS and unattributed, unreferenced, or insufficiently referenced articles were discarded. DATA EXTRACTION: Record of data sources in each review was noted as was the departmental specialty of the first author and his or her country of residence. The references cited in each index paper were tabulated by assigning them to 6 specialty categories, by article title, and by assigning them to 8 categories, by country of journal publication. DATA SYNTHESIS: Of 89 reviews, 3 (3.4%) reported on literature search and described search method. Authors from laboratory-based disciplines preferentially cited laboratory references, while psychiatry-based disciplines preferentially cited psychiatric literature (P = .01). A total of 71.6% of references cited by US authors were from US journals, while 54.9% of references cited by United Kingdom authors were published in United Kingdom journals (P = .001). CONCLUSION: Citation of the literature is influenced by review authors' discipline and nationality.
Kawakami N, Iwata N, Fujihara S, Kitamura T.	The Department of Public Health, Gifu University School of Medicine, Japan. norito@cc.gifu-u.ac.jp	Prevalence of chronic fatigue syndrome in a community population in Japan.	Tohoku J Exp Med 1998 Sep;186(1):33-41	In order to know the prevalence of chronic fatigue syndrome (CFS) in a community population in Japan, we analyzed data from a population-based interview survey. Two cases out of 137 respondents experienced chronic fatigue during a period of nine months, suffered from 50% or more reduction of daily activity due to fatigue and had no other physical or psychiatric diagnosis. Both of the two cases fulfilled the 1994 Centers for Disease Control (CDC) criteria and the British criteria. The point and nine-month prevalence rates of CFS were both 1.5% (95% confidence intervals, 0.4-5.2%). None fulfilled the 1989 CDC criteria for CFS. The prevalence rate of CFS was higher than those in previous studies in the Western countries, suggesting a need for future research on cross-cultural differences in the definition, prevalence and symptomatology of CFS.
Kenner C.	Department of Parent-Child Health Nursing, College of Nursing and Health University of Cincinnati, Ohio, USA.	Fibromyalgia and chronic fatigue: the holistic perspective.	Holist Nurs Pract 1998 Apr;12(3):55-63	Fibromyalgia syndrome (FMS) and chronic fatigue syndrome (CFS) are not new conditions, but they are receiving more attention as more research is conducted. These two conditions are primarily women's health problems. In some instances, there may be a genetic predisposition for these conditions. The impact of FMS and CFS can be devastating both physically and emotionally. The treatment plan must be interdisciplinary and holistic and include alternative therapies if the client and family are to be truly supported and helped in coping with these chronic conditions.
Klimas N.	University of Miami School of Medicine/VA Medical Center, Florida, USA.	Pathogenesis of chronic fatigue syndrome and fibromyalgia.	Growth Horm IGF Res 1998 Apr;8 Suppl B:123-6	
Klineberg I, McGregor N, Butt H, Dunstan H,	Faculty of Dentistry, University of Sydney.	Chronic orofacial muscle pain: a new	Alpha Omegan 1998 Jul;91(2):25-8	The initial data from this study indicate that there are clearly identifiable chronic muscle pain conditions in the form of localized pain; myofascial pain or regional pain

Roberts T, Zerbes M.		approach to diagnosis and management.		conditions; and fibromyalgia or generalized pain conditions. A clear difference exists between the prevalence of these conditions in male and female patients, with a higher percentage of female patients suffering generalized pain problems and temporomandibular problems. Generalized or localized pain appears to be an individual variant of a similar problem and pain patients may have a genetically determined vulnerability associated with bacterial toxins, particularly within the genitourinary tract. It appears that in fibromyalgia there is an underlying genetic factor that causes abnormalities in the muscle metabolic cycle, and preliminary data suggest that lipid anomalies predispose to fibromyalgia and possibly chronic fatigue syndrome. Patients report infectious events at/or around onset in more than 60 percent of cases. Seventy percent of fibromyalgic cases report orofacial pain.
Komaroff AL, Buchwald DS.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.	Chronic fatigue syndrome: an update.	Annu Rev Med 1998;49:1-13	Among the many patients who seek medical care for the complaint of fatigue, a small number suffer from chronic fatigue syndrome (CFS). CFS is a poorly understood condition characterized by debilitating fatigue and associated symptoms lasting at least six months. Studies indicate that the illness is not simply a manifestation of an underlying psychiatric disorder, but rather is an illness characterized by activation of the immune system, various abnormalities of several hypothalamic-pituitary axes, and reactivation of certain infectious agents.
Korszun A, Papadopoulos E, Demitrack M, Engleberg C, Crofford L.	Department of Psychiatry and School of Dentistry, University of Michigan, Ann Arbor 48109-0840, USA.	The relationship between temporomandibular disorders and stress-associated syndromes.	Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998 Oct;86(4):416-20	OBJECTIVES: The purpose of this study was to determine the comorbidity of temporomandibular disorders and other stress-associated conditions in patients with chronic fatigue syndrome and fibromyalgia. STUDY DESIGN: Of 92 patients who fulfilled the criteria for chronic fatigue syndrome or fibromyalgia (or both), 39 (42%) reported a prior diagnosis of temporomandibular disorder. Further questionnaires were sent to the members of this group, and 30 patients responded. RESULTS: Of the original 92 patients, of whom 42% reported temporomandibular disorders, 46% had histories of irritable bowel syndrome, 42% of premenstrual syndrome, and 19% of interstitial cystitis. Of the patients with temporomandibular disorders, the great majority reported an onset of generalized symptoms before the onset of facial pain. Despite this, 75% had been treated exclusively for temporomandibular disorders, usually with bite splints. CONCLUSIONS: Patients appearing for treatment with chronic facial pain show a high comorbidity with other stress-associated syndromes. The clinical overlap between these conditions may reflect a shared underlying pathophysiologic basis involving dysregulation of the hypothalamic-pituitary-adrenal stress hormone axis in predisposed individuals. A multidisciplinary clinical approach to temporomandibular disorders would improve diagnosis and treatment outcomes for this group of patients.
Kuratsune H, Yamaguti K, Lindh G, Evengard B, Takahashi M, Machii T, Matsumura K, Takaishi	Hematology and Oncology, Osaka University Medical School, Suita, Osaka	Low levels of serum acylcarnitine in chronic fatigue syndrome and chronic hepatitis type	Int J Mol Med 1998 Jul;2(1):51-6	Recently, we found a serum acylcarnitine (ACR) deficiency in Japanese patients with chronic fatigue syndrome (CFS). To clarify whether this ACR abnormality is a characteristic of CFS or not, we also studied the levels of serum carnitine in Swedish subjects. Both serum ACR and free carnitine (FCR) levels in normal healthy subjects

J, Kawata S, Langstrom B, Kanakura Y, Kitani T, Watanabe Y.	565, Japan.	C, but not seen in other diseases.		were quite different between Japanese (n=131) and Swedish people (n=46) (p<0.001). However, it is confirmed that Swedish patients with CFS (n=57) also had serum ACR deficiency (p<0.001). When we studied the levels of serum ACR and FCR in Japanese patients with various kinds of diseases (CFS, hematological malignancies, chronic pancreatitis, hypertension, diabetes mellitus, chronic hepatitis type C, psychiatric diseases), a significant decrease in the levels of serum ACR was only found in patients with CFS and chronic hepatitis type C (p<0.001). Therefore, we concluded that ACR deficiency in serum might be a characteristic abnormality in only certain types of diseases.
Kuratsune H, Yamaguti K, Sawada M, Kodate S, Machii T, Kanakura Y, Kitani T.	Department of Hematology and Oncology, Osaka University Medical School, Suita city, Osaka 565, Japan.	Dehydroepiandrosterone sulfate deficiency in chronic fatigue syndrome.	Int J Mol Med 1998 Jan;1(1):143-6	The chronic fatigue syndrome (CFS) is a condition of unknown etiology, characterized by a persistent debilitating fatigue, the muscle-related symptoms and the neuropsychiatric symptoms. Recently, it has been reported that the patients with CFS might have impaired activation of the hypothalamic-pituitary-adrenal axis, and suggested that a part of the patho-genesis of CFS might be associated with abnormalities of the endocrine system. Herein, we show that the majority of Japanese patients with CFS had a serum dehydroepiandrosterone sulfate (DHEA-S) deficiency. Serum DHEA-S is one of the most abundantly produced hormones which is secreted from the adrenal glands, and its physiological function is thought to be a precursor of sex steroids. DHEA-S has recently been shown to have physiological properties, such as neurosteroids, which are associated with such psychophysiological phenomena as memory, stress, anxiety, sleep and depression. Therefore, the deficiency of DHEA-S might be related to the neuropsychiatric symptoms in patients with CFS.
LaManca JJ, Sisto SA, DeLuca J, Johnson SK, Lange G, Pareja J, Cook S, Natelson BH.	Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA.	Influence of exhaustive treadmill exercise on cognitive functioning in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):59S-65S	The purpose of this study was to determine the effect of exhaustive exercise on cognitive performance of patients with chronic fatigue syndrome (CFS) and sedentary healthy controls (CON). Subjects were 19 women with CFS and 20 CON. A test battery consisting of 4 cognitive tests (CTB) was given pre-, immediately post-, and 24 hours post-treadmill exercise to exhaustion. No differences were seen on the CTB pre-exercise. CFS patients improved at a slower rate than CON on the Symbol Digit Modalities Test (SDMT), Stroop Word Test (SWT), and Stroop Color Test (SCT). When compared with CON, a lower number of correct responses was seen for the CFS immediately postexercise on the SDMT (61 3 vs 66 2), SWT (137 6 vs 146 6), and SCT (99 4 vs 107 3), and 24 hours postexercise on the SDMT (64 3 vs 69 2), SWT (134 7 vs 148 5), and SCT (101 4 vs 106 3). We conclude that after physically demanding exercise, CFS subjects demonstrated impaired cognitive processing compared with healthy individuals.
Lane RJ, Barrett MC, Taylor DJ, Kemp GJ, Lodi R.	Division of Clinical Neuroscience and Psychological Medicine, Imperial	Heterogeneity in chronic fatigue syndrome: evidence from magnetic	Neuromuscul Disord 1998 May;8(3-4):204-9	It has been shown previously that some patients with chronic fatigue syndrome show an abnormal increase in plasma lactate following a short period of moderate exercise, in the sub-anaerobic threshold exercise test (SATET). This cannot be explained satisfactorily by the effects of 'inactivity' or 'deconditioning', and patients

	College School of Medicine, Charing Cross Hospital, London, UK. r.lane@cxwms.ac.uk	resonance spectroscopy of muscle.		with abnormal lactate responses to exercise (SATET) have been found to have significantly fewer Type 1 muscle fibres in quadriceps biopsies than SATET -ve patients. We performed phosphorus magnetic resonance spectroscopy on forearm muscles of 10 SATET patients, 9 SATET -ve patients and 13 sedentary volunteers. There were no differences in resting spectra between these groups but at the end of exercise, intracellular pH in the SATET patients was significantly lower than in both the SATET -ve cases and controls ($P < 0.03$), and the SATET patients also showed a significantly lower ATP synthesis rate during recovery ($P < 0.01$), indicating impaired mitochondrial oxidative phosphorylation. These observations support other evidence which indicates that chronic fatigue syndrome is a heterogeneous disorder, and confirms the view that some chronic fatigue syndrome patients have a peripheral component to their fatigue.
Lane RJ, Barrett MC, Woodrow D, Moss J, Fletcher R, Archard LC.	Division of Neuroscience and Psychological Medicine, Imperial College School of Medicine, Charing Cross Hospital, London, UK. r.lane@cxwms.ac.uk	Muscle fibre characteristics and lactate responses to exercise in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1998 Mar;64(3):362-7	OBJECTIVES: To examine the proportions of type 1 and type 2 muscle fibres and the degree of muscle fibre atrophy and hypertrophy in patients with chronic fatigue syndrome in relation to lactate responses to exercise, and to determine to what extent any abnormalities found might be due to inactivity. METHODS: Quadriceps needle muscle biopsies were obtained from 105 patients with chronic fatigue syndrome and the proportions of type 1 and 2 fibres and fibre atrophy and hypertrophy factors were determined from histochemical preparations, using a semiautomated image analysis system. Forty one randomly selected biopsies were also examined by electron microscopy. Lactate responses to exercise were measured in the subanaerobic threshold exercise test (SATET). RESULTS: Inactivity would be expected to result in a shift to type 2 fibre predominance and fibre atrophy, but type 1 predominance (23%) was more common than type 2 predominance (3%), and fibre atrophy was found in only 10.4% of cases. Patients with increased lactate responses to exercise did have significantly fewer type 1 muscle fibres ($p<0.043$ males, $p<0.0003$ females), but there was no evidence that this group was less active than the patients with normal lactate responses. No significant ultrastructural abnormalities were found. CONCLUSION: Muscle histometry in patients with chronic fatigue syndrome generally did not show the changes expected as a result of inactivity. However, patients with abnormal lactate responses to exercise had a significantly lower proportion of mitochondria rich type 1 muscle fibres.
Lange G, Wang S, DeLuca J, Natelson BH.	Department of Psychiatry, Chronic Fatigue Syndrome Center, University of Medicine and Dentistry-New Jersey Medical School, Newark, USA.	Neuroimaging in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):50S-53S	The diagnosis of chronic fatigue syndrome (CFS) is made difficult by the absence of specific biomedical markers, and depends primarily on determining whether subjective information provided by the patient meets the clinical case definition of this syndrome. Reported cognitive difficulties and/or complaints of headache may instigate referral for brain imaging. This article will discuss the value of neuroimaging in evaluating CFS, specifically reviewing studies that (1) used static magnetic resonance imaging (MRI) to assess structural abnormalities; and (2) assessed regional cerebral blood flow (rCBF) via detection of Tc-99m hexamethylpropyl-eneamine

				oxime distribution by single-photon emission computed tomography (SPECT). Future research design considerations are explored including (1) the utilization of positron emission tomography (PET) and other emerging neuroimaging technologies; and (2) methodological concerns, i.e., the influence of psychopathology (such as depression) and neurologic disease (such as multiple sclerosis) as possible confounding factors.
Lavietes MH, Michael T. Bergen, Benjamin H. Natelson		Measurement of C02 in Chronic Fatigue Syndrome Patients	Journal of Chronic Fatigue Syndrome 1998: 4(3): 3 - 11	This study has two goals: one, to compare the resting end-tidal pCO2 (PetCO2) and heart rate (HR) of chronic fatigue syndrome patients (CFS) with controls; two, to examine the effects of a mouthpiece and noseclips upon measurements of PetC02 and HR. Patients from the CFS Center came to the University Hospital pulmonary function laboratory for one testing session. Arterial (PaCO2), PetCO2, end-nasal (PenC02) and HR were measured twice; both with and again without the subject breathing through the mouthpiece. We found that PenCO2 was greater and HR lower for both CFS and non-CFS groups when subjects were not confined by the mouthpiece. We conclude that there is no abnormality in the regulation of respiration in CFS patients. Changes in HR accompany changes in PetCO2 in this study. Most likely, both result from anxiety associated with mouthpiece breathing
Laylander JA		A Nutrient/Toxin Interaction Theory of the Etiology and Pathogenesis of Chronic Pain-Fatigue Syndromes: Part II	Journal of Chronic Fatigue Syndrome 1998: 5(1): 93 - 126	This second part of the review paper covers the evidence in favor of the theory which proposes that Chronic Fatigue Syndrome, Fibromyalgia Syndrome, and Persian Gulf Syndrome represent finitely variable combinations of multiple systemic dysfunctions which share a common underlying etiology at the subcellular level: magnesium deficiency plus concomitant fluoride excess (MDFE). Treatment suggestions are listed at the end of the manuscript through a call for clinical trials to test the theory presented
Laylander JA		A Nutrient/Toxin Interaction Theory of the Etiology and Pathogenesis of Chronic Pain-Fatigue Syndromes: Part I	Journal of Chronic Fatigue Syndrome 1998: 5(1): 67 - 91	Recent research suggests that Chronic Fatigue Syndrome (CFS), Fibromyalgia Syndrome (FMS), and Persian Gulf Syndrome (PGS) may represent the effects of dysfunctions involving the central and/or peripheral nervous system, neuroendocrine system, neuromuscular system, immune system, metabolism, or sleep patterns. Each systemic dysfunction is accepted here as being central to these syndromes but not causal. This two-part review introduces the theory that the syndromes listed above represent finitely variable combinations of multiple systemic dysfunctions which all share a common underlying etiology at the subcellular level: magnesium deficiency plus concomitant fluoride excess (MDFE). The theory is introduced in Part I; detailed evidence which supports the theory is presented in Part II. Treatment suggestions are listed at the end of Part II through a call for clinical trials to test this theory.
Layzer RB.		Asthenia and the chronic fatigue syndrome.	Muscle Nerve 1998 Dec;21(12):1609-11	
Lee P.	Institute of Health Policy Studies, University of California,	Recent developments in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):1S	

	San Francisco, 94109, USA.			
Levine PH, Fears TR, Cummings P, Hoover RN.	Division of Cancer Epidemiology and Genetics, NIH, Bethesda, Maryland 20892, USA.	Cancer and a fatiguing illness in Northern Nevada--a causal hypothesis.	Ann Epidemiol 1998 May;8(4):245-9	PURPOSE: We investigated the possibility that chronic fatigue syndrome (CFS) predisposes to cancer by comparing the cancer pattern in an area in northern Nevada, where an outbreak of a fatiguing illness, which included cases of CFS, was reported, to an area in southern Nevada, where no such illness was reported. METHODS: Data from the computerized Nevada Cancer Registry were utilized to compare incidence rates of four malignancies--brain cancer, non-Hodgkin lymphoma (NHL), lung cancer, and breast cancer--in Washoe and Lyon Counties, where an unexplained fatiguing illness was reported during 1984-86, with comparably sized Clark County, where no such illness was reported. RESULTS: Higher incidences of NHL and primary brain tumors were noted in the two northern Nevada counties (Washoe and Lyon) in 1986 and 1987 respectively, compared to the southern Nevada (Clark) county. Similar patterns were not seen for breast or lung cancer. CONCLUSIONS: This study provides a model for investigating the possible predisposition of CFS patients to develop cancer using other cohorts, but it is currently premature to accept such a link at this time.
Levine PH, Whiteside TL, Friberg D, Bryant J, Colclough G, Herberman RB.	National Cancer Institute, Bethesda, Maryland, 20892, USA.	Dysfunction of natural killer activity in a family with chronic fatigue syndrome.	Clin Immunol Immunopathol 1998 Jul;88(1):96-104	A family was identified with 5 of 6 siblings and 3 other immediate family members who had developed chronic fatigue syndrome (CFS) as adults. All 8 met criteria for the CFS case definition as recommended by the Centers for Disease Control and Prevention. Sixty-eight blood samples were obtained over a period of 2 years from 20 family members (8 affected, 12 unaffected) and 8 normal controls. All blood samples were tested for NK activity in 4-h 51Cr-release assays and for the number of circulating CD3-CD56() and CD3-CD16() by flow cytometry. NK activity of the affected immediate family members (cases, n = 8) was significantly lower (P = 0.006, two-sided) than that of the concurrently tested normal controls. The results for unaffected family members were intermediate between these two groups, and the pairwise comparison of unaffected family members to either cases or controls showed no statistically significant difference (P = 0.29, two-sided). No differences were seen between the groups in the absolute number of CD3-CD56() or CD3-CD16() lymphocytes in the peripheral blood. Familial CFS was associated with persistently low NK activity, which was documented in 6/8 cases and in 4/12 unaffected family members. In the family with 5 of 6 siblings who had documented CFS, 2 of their offspring had pediatric malignancies. Low NK activity in this family may be a result of a genetically determined immunologic abnormality predisposing to CFS and cancer.
Levine PH.	Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland, USA.	Chronic fatigue syndrome comes of age.	Am J Med 1998 Sep 28;105(3A):2S-6S	

Levine PH.	George Washington University Medical Center, Washington, DC, USA.	What we know about chronic fatigue syndrome and its relevance to the practicing physician.	Am J Med 1998 Sep 28;105(3A):100S-103S	A number of recent reports have emphasized laboratory abnormalities, clinical tests, and therapeutic approaches that appear to have great promise in the evaluation and management of chronic fatigue syndrome (CFS). Because of the heterogeneity of CFS, the cost of many of these assays and procedures, and the frequent lack of skilled consultants able to apply relevant sophisticated procedures, the solo healthcare provider is often left with uncertain options in patient management. This article summarizes current approaches to patient management, utilizing available information relevant to CFS.
Litzman J, Lokaj J, Fucikova T.	Ustav klinicke imunologie a alergologie, FN u svate Anny, Brno, Praha.	[Chronic fatigue syndrome].[article in Czech]	Cas Lek Cesk 1998 May 18;137(10):295-8	A great concern is recently given to the chronic fatigue syndrome in the Czech Republic. Unfortunately, published data allow us to state neither the etiologic agent nor the pathophysiology of the disease. Although many authors published various laboratory abnormalities, these changes are inconstant and do not allow to state a diagnosis of the chronic fatigue syndrome by a single laboratory test, and effective therapy is not known either. Psychotherapy, and in some cases antidepressants, are recommended by some authors to alleviate patient's symptoms. Neither immunological nor antiviral therapy showed positive results in controlled trials and are not generally used in most centers.
Lloyd AR.	The Inflammation Research Unit, School of Pathology, University of New South Wales, Sydney, Australia.	Chronic fatigue and chronic fatigue syndrome: shifting boundaries and attributions.	Am J Med 1998 Sep 28;105(3A):7S-10S	The subjective symptom of "fatigue" is one of the most widespread in the general population and is a major source of healthcare utilization. Prolonged fatigue is often associated with neuropsychological and musculoskeletal symptoms that form the basis of several syndromal diagnoses including chronic fatigue syndrome, fibromyalgia, and neurasthenia, and is clearly not simply the result of a lack of force generation from the muscle. Current epidemiologic research in this area relies predominantly on self-report data to document the prevalence and associations of chronic fatigue. Of necessity, this subjective data source gives rise to uncertain diagnostic boundaries and consequent divergent epidemiologic, clinical, and pathophysiologic research findings. This review will highlight the impact of the case definition and ascertainment methods on the varying prevalence estimates of chronic fatigue syndrome and patterns of reported psychological comorbidty. It will also evaluate the evidence for a true postinfective fatigue syndrome.
Loblay RH.		Chronic fatigue syndrome.	Lancet 1998 Apr 25;351(9111):1292 Comment on: Lancet. 1998 Feb 21;351(9102):574	
Low PA.	Mayo Medical School, Department of Neurology, Mayo Clinic, Rochester, MN 55905, USA.	Autonomic neuropathies.	Curr Opin Neurol 1998 Oct;11(5):531-7	A limited autonomic neuropathy may underlie some unusual clinical syndromes, including the postural tachycardia syndrome, pseudo-obstruction syndrome, heat intolerance, and perhaps chronic fatigue syndrome. Antibodies to autonomic structures are common in diabetes, but their specificity is unknown. The presence of autonomic failure worsens prognosis in the diabetic state. Some autonomic

				neuropathies are treatable. Familial amyloid polyneuropathy may respond to liver transplantation. There are anecdotal reports of acute panautonomic neuropathy responding to intravenous gamma globulin. Orthostatic hypotension may respond to erythropoietin or midodrine.
Lynch S, Fraser J.		Fluoxetine and graded exercise in chronic fatigue syndrome.	Br J Psychiatry 1998 Oct;173:353 Comment on: Br J Psychiatry. 1998 Jun;172:485-90	
MacHale SM, Cavanagh JT, Bennie J, Carroll S, Goodwin GM, Lawrie SM.	Department of Psychiatry, University of Edinburgh, Edinburgh, UK.	Diurnal variation of adrenocortical activity in chronic fatigue syndrome.	Neuropsychobiology 1998 Nov;38(4):213-7	Baseline morning and evening serum cortisol and ACTH concentrations, and diurnal changes in hormone levels, were measured in 30 patients with chronic fatigue syndrome (CFS) but without concurrent depressive disorder and a control group of 15 weight-, age- and sex-matched healthy volunteers. Morning cortisol levels were non-significantly lower in CFS patients, while evening levels were non-significantly higher. ACTH concentrations were non-significantly higher in both the morning and evening. The diurnal change in cortisol levels was significantly less in CFS than in controls ($p < 0.05$). In CFS subjects, evening levels of cortisol correlated significantly with measures of general health and physical functioning, while diurnal change in cortisol was positively correlated with measures of functional improvement over the past year and current social functioning. These results suggest that there is a relationship between adrenocortical function and disability in CFS, but do not reveal the causal connection.
Mackinnon LT.	Department of Human Movement Studies, The University of Queensland, Australia.	Future directions in exercise and immunology: regulation and integration.	Int J Sports Med 1998 Jul;19 Suppl 3:S205-9; discussion S209-11	Although it is difficult to predict future directions in a rapidly expanding field such as exercise immunology, recently published research along with that presented at this Symposium allow us to ask some key questions which may point to new directions: 1) Are athletes immunocompromised? Athletes are not clinically immunodeficient, yet endurance athletes are at increased risk of illness. Long-term prospective studies are needed to understand the relationship between infection, training variables and immune parameters. 2) Is downregulation of nonspecific immunity beneficial or harmful? In athletes, neutrophils appear to be downregulated, and this may alter resistance to illness. Alternatively, neutrophils are mediators of tissue damage during inflammation. Downregulation of neutrophil function may be protective by limiting chronic inflammation. In athletes, mild immunosuppression may reflect a compromise between the body's attempts to limit inflammation while maintaining immune function. 3) What mediates communication between events in skeletal muscle and the immune system? Leukocyte mobility is affected by metabolic and mechanical factors during exercise. Exercise increases cytokine levels in damaged skeletal muscle and expression of adhesion molecules. Future work is likely to focus on the role of cytokines and adhesion molecules in mediating exercise-induced changes in leukocyte mobility. 4) Can exercise training provide a "countermeasure" against immunosuppressive events? Moderate exercise training may have a role in

				stimulating the immune system during certain diseases (e.g., HIV-infection), immune dysfunction (e.g., chronic fatigue syndrome) or reduced responsiveness (e.g. aging, spaceflight). It is also likely that future study will apply molecular biology techniques to further identify mechanisms by which exercise influences immune function.
Marlin RG, Anchel H, Gibson JC, Goldberg WM, Swinton M.	MRS Health Services, St. Joseph's Hospital, and McMaster University, Hamilton, Ontario, Canada.	An evaluation of multidisciplinary intervention for chronic fatigue syndrome with long-term follow-up, and a comparison with untreated controls.	Am J Med 1998 Sep 28;105(3A):110S-114S	Individuals meeting the Fukuda et al definition for chronic fatigue syndrome completed a multidisciplinary assessment that included medical, psychiatric, behavioral, and psychological evaluations. Patients were then offered a comprehensive multidisciplinary intervention that included (1) bringing the patient under optimal medical management; (2) treating any ongoing affective or anxiety disorder pharmacologically; and (3) implementing a comprehensive cognitive-behavioral treatment program. Fifty-one patients proceeded to treatment. The cognitive-behavioral component was carried out through the use of a therapist working with the patients in their own environments. The program was individually tailored to patients, but included (1) structured physical exercise and activation; (2) sleep management strategies; (3) careful activity management; (4) regulation of stimulant intake and reductions in use of symptomatic medications; (5) cognitive intervention designed to deal with patients' beliefs concerning the nature of their disorder; (6) participation of patients' family; and (7) efforts to establish specific vocational and avocational goals. Third parties were encouraged to collaborate cooperatively. Employers were urged to provide employment opportunities and facilitate a graduated but time-targeted return to work. Disability carriers were encouraged to provide interim financial support in the form of disability benefits, support therapeutic intervention, but also to establish a clear time-frame to access to benefits. Of 51 treated patients, 31 returned to gainful employment, 14 were functioning at a level equivalent to employment, and 6 remained significantly disabled. Twenty of the original 71 patients were contacted an average of 33 months later. Patients who had been treated showed good maintenance of gains. Untreated patients showed improvement in only a minority of cases.
Martin WJ.	Center for Complex Infectious Diseases, Rosemead, Calif 91770, USA.	Cellular sequences in stealth viruses.	Pathobiology 1998;66(2):53-8	Cloned DNA obtained from the culture of an African green monkey simian cytomegalovirus-derived stealth virus contains multiple discrete regions of significant sequence homology (p values ranging from 4 x 10(-3) to 1 x 10(-20)) to portions of known human cellular genes. The stealth virus was cultured from a patient with chronic fatigue syndrome (CFS). Earlier studies had revealed considerable sequence heterogeneity within DNA fragments isolated from virus-infected cells. A set of polymerase chain reaction (PCR) primers generated different PCR products when tested on stealth virus cultures from 4 patients with CFS. Several of the PCR products also contain regions of significant partial homology to distinct cellular sequences, including sequences repetitively expressed throughout the cellular genome. Stealth viruses may play an important role in the origins and in the genetic diversity of both viral and cellular sequences.

McCluskey DR.	Queens University of Belfast, Ireland.	Chronic fatigue syndrome: Its cause and a strategy for management.	Compr Ther 1998 Aug;24(8):357-63	This article describes the features of chronic fatigue syndrome and, by analysis of the many clinical paradoxes which it manifests, attempts to give a unifying explanation of the cause of the disorder and a strategy for management.
McKenzie R, O'Fallon A, Dale J, Demitrack M, Sharma G, Deloria M, Garcia-Borreguero D, Blackwelder W, Straus SE.	Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892-1888, USA.	Low-dose hydrocortisone for treatment of chronic fatigue syndrome: a randomized controlled trial.	JAMA 1998 Sep 23-30;280(12):1061-6Comment in: JAMA. 1999 May 26;281(20):1887-8; discussion 1888-9 JAMA. 1999 May 26;281(20):1887; discussion 1888-9 JAMA. 1999 May 26;281(20):1888-9	CONTEXT: Chronic fatigue syndrome (CFS) is associated with a dysregulated hypothalamic-pituitary adrenal axis and hypocortisolemia. OBJECTIVE: To evaluate the efficacy and safety of low-dose oral hydrocortisone as a treatment for CFS. DESIGN: A randomized, placebo-controlled, double-blind therapeutic trial, conducted between 1992 and 1996. SETTING: A single-center study in a tertiary care research institution. PATIENTS: A total of 56 women and 14 men aged 18 to 55 years who met the 1988 Centers for Disease Control and Prevention case criteria for CFS and who withheld concomitant treatment with other medications. INTERVENTION: Oral hydrocortisone, 13 mg/m2 of body surface area every morning and 3 mg/m2 every afternoon, or placebo, for approximately 12 weeks. MAIN OUTCOME MEASURES: A global Wellness scale and other self-rating instruments were completed repeatedly before and during treatment. Resting and cosyntropin-stimulated cortisol levels were obtained before and at the end of treatment. Patients recorded adverse effects on a checklist. RESULTS: The number of patients showing improvement on the Wellness scale was 19 (54.3%) of 35 placebo recipients vs 20 (66.7%) of 30 hydrocortisone recipients (P =.31). Hydrocortisone recipients had a greater improvement in mean Wellness score (6.3 vs 1.7 points; P=.06), a greater percentage (53% vs 29%; P=.04) recording an improvement of 5 or more points in Wellness score, and a higher average improvement in Wellness score on more days than did placebo recipients (P<.001). Statistical evidence of improvement was not seen with other self-rating scales. Although adverse symptoms reported by patients taking hydrocortisone were mild, suppression of adrenal glucocorticoid responsiveness was documented in 12 patients who received it vs none in the placebo group (P<.001). CONCLUSIONS: Although hydrocortisone treatment was associated with some improvement in symptoms of CFS, the degree of adrenal suppression precludes its practical use for CFS.
Meyer FP.		ber die laquo;Omnipotenz>> der Chelattherapie.	Forsch Komplementarmed 1998;5(6):266-271	About the 'Omnipotence' of the Chelation Therapy In the eighties the 'method of treatment proven in many thousands of cases over 20 years' was transferred from the USA to Germany (enjoys a priori considerable faith) using very dubious promises. It was Clarke et al. who introduced this 'therapy' in 1955. The dubious promise was to maintain that the chelation therapy eliminates or alleviates symptoms in the case of the following illnesses: Alzheimer's disease, senility, schizophrenia, rheumatoid arthritis, osteoarthritis, gout, renal calculus, apoplectic coma, gallstones, multiple sclerosis, osteoporosis, chronic fatigue syndrome, varicose veins, hypertension, failure of memory, scleroderma, Raynaud's disease, digitalis intoxication, intermittent claudication, diabetic ulcer, disturbance of the blood supply, ulcer on the legs, snake

				poison, impotence, emotional difficulties, defective hearing, vision disorder. There is not the slightest proof of effectiveness for any of the listed indications. The burden of proof lies with the supplier. Even in the case of the relatively often examined peripheral atherosclerotic changes (claudicatio intermittens) there is no proof that EDTA has a greater effect than placebo. For coronary heart disease too there is no evidence for any usefulness of the chelation therapy beyond that of a placebo effect. Only controlled studies can help to improve the therapy in the sense of 'Evidence-based medicine'. Retrospective investigations on thousands of patients cannot 'prove' anything, although this is maintained again andagain.
Michiels V, Cluydts R, Fischler B.	Department of Psychology, Free University of Brussels, Belgium. vmichiel@vub.ac.be	Attention and verbal learning in patients with chronic fatigue syndrome.	J Int Neuropsychol Soc 1998 Sep;4(5):456-66	Former neuropsychological studies with Chronic Fatigue Syndrome (CFS) patients evaluated a broad range of cognitive functions. Several, but not all, reported subtle attentional and memory impairments suggesting possible mild cerebral involvement. In this study, a battery of attentional tests and a verbal memory task were administered to 20 CFS patients and 22 healthy controls (HC) in order to clarify the specific nature of attention and memory impairment in these patients. The results provide evidence for attentional dysfunction in patients with CFS as compared to HC. CFS patients performed more poorly on a span test measuring attentional capacity and working memory. Speeded attentional tasks with a more complex element of memory scanning and divided attention seem to be a sensitive measure of reduced attentional capacity in these patients. Focused attention, defined as the ability to attend to a single stimulus while ignoring irrelevant stimuli, appears not to be impaired. CFS patients were poorer on recall of verbal information across learning trials, and poor performance on delayed recall may be due to poor initial learning and not only to a retrieval failure.
Miller BJ, John L. Whiting, Andrew D. Clouston		Coincidental Splenectomy in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(1): 37 - 42	A unique case of coincidental splenectomy for trauma during chronic fatigue syndrome (CFS) is presented. The patient had a two-year history of CFS prior to her involvement in a road crash. Delayed rupture of the spleen ten days later necessitated urgent laparotomy. At operation, the splenic parenchyma was spongy and friable. Splenorrhaphy was considered inadvisable and a splenectomy was performed. Histological examination of the spleen revealed chronic inflammatory changes of uncertain etiology. One year post-operatively, the patient recovered from her CFS symptoms and returned to work. These histopathological changes in the spleen of a patient with CFS have not been described before.
Moorkens G, Wynants H, Abs R.	Department of Internal Medicine, University Hospital Antwerp, Belgium.	Effect of growth hormone treatment in patients with chronic fatigue syndrome: a preliminary study.	Growth Horm IGF Res 1998 Apr;8 Suppl B:131-3	The efficacy of growth hormone (GH) therapy was evaluated in patients with chronic fatigue syndrome (CFS) who had peak serum GH levels below 10 microg/l during stage-controlled sleep. Twenty patients (7 men, 13 women; age range, 30-60 years) with CFS were randomized to receive placebo or GH therapy, 6.7 microg/kg/day (0.02 IU/kg/day), for 12 weeks. Following this double-blind treatment period, the 17 patients remaining in the study were given GH therapy at the above dose for an open period of 9 months. Mean (SD) serum levels of insulin-like growth factor I (IGF-I)

				increased during GH treatment, from 173 46 microg/l to 296 89 microg/l (P < 0.001); IGF-I SDS values increased from -0.45 1.14 to .43 1.09 (P < 0.001). Fat-free mass and total body water were significantly increased after 12 months of treatment. Although quality of life, as assessed using two different questionnaires, did not improve significantly during GH treatment, four patients were able to resume work after a long period of sick leave.
Morehouse RL, Flanigan M, MacDonald DD, Braha D, Shapiro C.	Department of Psychiatry, Dalhousie University, QEII Health Sciences Centre, Halifax, Nova Scotia.	Depression and short REM latency in subjects with chronic fatigue syndrome.	Psychosom Med 1998 May-Jun;60(3):347-51	OBJECTIVE: The hypothesized polysomnographic marker for depression, Rapid Eye Movement Latency (REML), was used to investigate two groups of subjects; Chronic Fatigue Syndrome (CFS)-not depressed and CFS-depressed. METHOD: CFS subjects were classified into depressed and not depressed groups, using the Diagnostic Interview Schedule (DIS), and subsequently were studied in a sleep laboratory to ascertain REML. RESULTS: Short REML showed a statistically significant correlation with the depressed state in CFS subjects. CONCLUSION: Short REM latency is associated with depression in the CFS population.
Morriss RK, Wearden AJ, Mullis R.	Department of Community Psychiatry, University of Manchester, UK.	Exploring the validity of the Chalder Fatigue scale in chronic fatigue syndrome.	J Psychosom Res 1998 Nov;45(5):411-7	The Chalder fatigue scale is widely used to measure physical and mental fatigue in chronic fatigue syndrome patients, but the constructs of the scale have not been examined in this patient sample. We examined the constructs of the 14-item fatigue scale in a sample of 136 chronic fatigue syndrome patients through principal components analysis, followed by correlations with measures of subjective and objective cognitive performance, physiological measures of strength and functional work capacity, depression, anxiety, and subjective sleep difficulties. There were four factors of fatigue explaining 67% of the total variance. Factor 1 was correlated with subjective everyday cognitive difficulties, concentration difficulties, and a deficit in paired associate learning. Factor 2 was correlated with difficulties in maintaining sleep. Factor 3 was inversely correlated with grip strength, peak VO2, peak heart rate, and peak functional work capacity. Factor 4 was correlated with interview and self-rated measures of depression. The results support the validity of mental and physical fatigue subscales and the dropping of the "loss of interest" item in the 11-item version of the fatigue scale.
Morriss RK, Wearden AJ.	Department of Psychiatry, University of Manchester, UK.	Screening instruments for psychiatric morbidity in chronic fatigue syndrome.	J R Soc Med 1998 Jul;91(7):365-8	Physicians require a screening instrument to detect psychiatric disorders in patients with chronic fatigue syndrome (CFS). Different threshold scores on the Hospital Anxiety and Depression scale (HAD) and the mental health scale of the Medical Outcome Survey (MOS) were compared with two gold standards for the presence or absence of psychiatric disorder, standard diagnostic criteria (DSM-III-R) and a threshold score for the number of psychiatric symptoms at a standardized psychiatric interview (Revised Clinical Interview Schedule total cut-off score of 11/12). They were compared by use of validating coefficients and receiver operating characteristics in 136 consecutive CFS medical outpatients. The HAD scale at cut-off of 9/10 was a valid and efficient screening instrument for anxiety and depression by comparison with both gold standards. The MOS mental health scale at its recommended cut-off score

				of 67/68 yielded too many false-positives to be recommended as a psychiatric screening instrument in CFS patients.
Natelson BH, Cheu J, Hill N, Bergen M, Korn L, Denny T, Dahl K.	Department of Neurosciences, University of Medicine and Dentistry of New Jersey, Newark, USA. bhn@nbunj.jvnc.net	Single-blind, placebo phase-in trial of two escalating doses of selegiline in the chronic fatigue syndrome.	Neuropsychobiology 1998;37(3):150-4	AIM: To perform a clinical trial of selegiline in 25 patients with chronic fatigue syndrome (CFS) where patients were told they would receive placebo or active agent at different times during the 6-week trial. We chose selegiline, a specific monoamine oxidase (MAO) B receptor inhibitor, because a prior trial of lowdose phenelzine, a nonspecific MAO inhibitor, showed a small but significant therapeutic effect. METHODS: Questionnaires comprised of 19 tests of mood, fatigue, functional status and symptom severity were collected at the start and end of the trial as well as 2 weeks after its start. The trial was done in three 2-week blocks: in the first, 2 placebo pills were given per day; in the next, one 5-mg tablet of agent and one placebo were given per day, and in the last, a 5-mg tablet of agent was given twice a day. The plan was to compare the changes in the 19 tests during the placebo phase to those found in the active treatment phase in 19 patients completing the trial. FINDINGS: Significant improvement in 3 variables-tension/anxiety, vigor and sexual relations-was found. A significant pattern of improvement compared to worsening was found for the 19 self-report vehicles during active treatment as compared with placebo treatment. Evidence for an antidepressant effect of the drug was not found. CONCLUSIONS: Selegiline has a small but significant therapeutic effect in CFS which appears independent of an antidepressant effect.
Natelson BH, LaManca JJ, Denny TN, Vladutiu A, Oleske J, Hill N, Bergen MT, Korn L, Hay J.	Department of Neurosciences, Chronic Fatigue Syndrome Cooperative Research Center, University of Medicine and Dentistry of New Jersey--New Jersey Medical School, Newark 07018, USA.	Immunologic parameters in chronic fatigue syndrome, major depression, and multiple sclerosis.	Am J Med 1998 Sep 28;105(3A):43S-49S	The purpose of this study was to evaluate the immune dysfunction hypothesis of chronic fatigue syndrome (CFS) by comparing immunologic data from patients with CFS with data from patients with other fatiguing illnesses--major depression and multiple sclerosis (MS)--and with data from healthy sedentary controls. The subjects were 65 healthy sedentary controls, 71 CFS patients (41 with no axis-I diagnosis), 23 patients with mild MS, and 21 patients with major depression. Blood was sampled and assayed for the following: (1) immunologic serologic variables--circulating immune complexes (i.e., Raji cell and C1q binding), immunoglobulins A, E, G, and M, and IgG subclasses; (2) cell surface activation markers--the proportion of CD4 cells expressing CD45RA and CD45RO and the proportion of CD8 cells expressing CD38, CD11b-, HLA-DR and CD28; and (3) natural killer (NK) total cell count as well as the proportion of lymphocytes expressing NK cell surface markers (i.e., CD3-/CD16 and CD56. Of the 18 variables studied, differences between CFS patients and controls were found only for IgG1 and IgG3. When CFS patients were stratified by the presence or absence of concurrent axis-I disease, it was the group with axis-I disorder that had the lowest IgG1 values-contrary to expectation. When data from patients with MS and major depression were also evaluated, the subclass deficiency was no longer significant. The one group to show evidence for immune activation (i.e., an elevated proportion of CD4 cells expressing the CD45RA activation marker) was the group with mild MS. These data support neither immune dysfunction nor immune

				activation in CFS or in major depression, for the variables studied. The reductions in IgG subclasses may be an epiphenomenon of patient or control subject composition. In contrast, MS, even in the mild and early stages, as in the patients studied here, is associated with immune activation.
Newman ME, Shapira B, Lerer B.	Biological Psychiatry Laboratory, Dept. of Psychiatry, Hadassah - Hebrew University Medical Center.	Evaluation of central serotonergic function in affective and related disorders by the fenfluramine challenge test: a critical review.	Int J Neuropsychopharmcol 1998 Jul;1(1):49-69	Plasma prolactin levels following oral administration of the serotonin (5-HT) releasing agent, fenfluramine hydrochloride, have been extensively used to evaluate central serotonergic function in affective and related disorders. Cortisol responses to fenfluramine have generally been a less informative measure. In healthy subjects, prolactin release by fenfluramine is dose-dependent, blocked by antagonists of serotonin receptors of the 5-HT-2a/2c type, negatively correlated with age and increased in young females. In major depression, a preponderance of studies have found blunted prolactin responses compared to matched normal controls. Although a significant minority of studies have not found blunting, increased prolactin release has not been observed. The blunted prolactin release is not due to a deficient secretory capacity of pituitary lactotrophs and is congruent with other evidence for reduced central serotonergic function in major depression. Blunting of the prolactin response may be associated with severity of depression and with elevated baseline cortisol levels. Treatment with antidepressant drugs and electroconvulsive therapy has been reported to increase the prolactin response but this has not been replicated in all studies. Blunted prolactin responses to fenfluramine have been fairly consistently associated with impulsive aggression in different personality disorders and with severity of suicide attempts in depressed patients. A number of studies employing the fenfluramine challenge test (FCT) have been conducted in obsessive compulsive disorder but their results have been variable. Prolactin responses to fenfluramine may be enhanced in panic disorder and chronic fatigue syndrome but the number of studies in these conditions is small as is the case for seasonal affective disorder. Since the therapeutic administration of fenfluramine as an appetite suppressant has been suspended because of reports of cardiac complications, further use of this compound as a challenge agent is not anticipated. Future studies are likely to employ agents acting on specific serotonin receptors and should apply methodological insights from the use of the FCT, which are considered in this review. Use of concomitant brain imaging to evaluate the central effects of challenge agents directly is likely to become more prevalent and may supplant neuroendocrine challenge paradigms such as the FCT which have been remarkably heuristic but are limited in scope and methodologically complex.
Nicolson GL, Nicolson NL.	Institute for Molecular Medicine, Huntington Beach, CA 92649-1041, USA. gnicimm@ix.netcom.co	Gulf War illnesses: complex medical, scientific and political paradox.	Med Confl Surviv 1998 Apr-Jun;14(2):156-65	Gulf War illnesses are a collection of disorders that for the most part can be diagnosed and treated, if effective programmes exist to assist veterans, and in some cases their immediate family members. Although these illnesses are complex and have multi-organ signs and symptoms, a proportion of these patients can be identified as having Chronic Fatigue Syndrome/Myalgic Encephalomyelitis (CFS/ME)

	m			and/or Fibromyalgia Syndrome (FMS). Although there are many possible causes of CSF/ME/FMS, chronic infections can explain, at least in a subset of patients, the apparent transmission of these illnesses to family members and the appearance of chronic, multi-organ and auto-immune signs and symptoms. Unfortunately, many veterans who have been diagnosed with chronic infections, such as mycoplasmal infections, cannot obtain adequate treatment for their condition, resulting in their reliance on private physicians and clinics for assistance. This lack of response may ultimately be responsible for the transmission of the illness to non-veterans.
Nisenbaum R, Reyes M, Mawle AC, Reeves WC.	Klemm Analysis Group, Atlanta, GA, USA.	Factor analysis of unexplained severe fatigue and interrelated symptoms: overlap with criteria for chronic fatigue syndrome.	Am J Epidemiol 1998 Jul 1;148(1):72-7	The objective of this study was to identify factors explaining the correlations among unexplained severe fatigue of different durations (1-5 months or > or =6 months) and symptoms reported as being significant health problems during a preceding 4-week period. Between June and December of 1994, a cross-sectional, random digit dialing telephone survey was conducted among residents of San Francisco, California. All subjects who reported having severe fatigue lasting for > or =1 month and a random sample of nonfatigued subjects were asked to participate in a detailed telephone interview. Data from 1,510 individuals aged 18-60 years who did not have medical or psychiatric conditions that could explain their severe fatigue were analyzed. Common factor analyses identified three correlated factors (defined as "fatigue-mood-cognition" symptoms, "flu-type" symptoms, and "visual impairment") that explained the correlations among fatigue lasting for > or =6 months and 14 interrelated symptoms. No factor explained the correlations among fatigue lasting for 1-5 months and other symptoms. The combination of fatigue of > or =6 months' duration and selected symptoms overlaps with published criteria used to define cases of chronic fatigue syndrome (CFS). Although symptoms described in this study were reported as appearing within the preceding month, and CFS symptoms must have been present for the previous 6 months, these results provide empirical support for the interrelations among unexplained fatigue of > or =6 months' duration and symptoms included in the CFS case definition.
Ogawa M, Nishiura T, Yoshimura M, Horikawa Y, Yoshida H, Okajima Y, Matsumura I, Ishikawa J, Nakao H, Tomiyama Y, Kanayama Y, Kanakura Y, Matsuzawa Y.	Osaka University Medical School, Osaka, Japan.	Decreased nitric oxide-mediated natural killer cell activation in chronic fatigue syndrome.	Eur J Clin Invest 1998 Nov;28(11):937-43	BACKGROUND: L-Arginine (L-Arg), one of the essential amino acids, has been reported to have an immunomodulatory effect. The precise mechanism of the L-Arg-induced natural killer (NK) cell activation remains unresolved,and the effect of L-Arg on NK cells in chronic fatigue syndrome (CFS) patients has not been estimated. METHODS: NK cell function was evaluated in 20 subjects with CFS and compared with that in 21 healthy individuals. RESULTS: In healthy control subjects, NK activity was significantly increased after treatment with L-Arg, an NK function enhancer, for 24 h, whereas the same treatment failed to enhance NK activity in the CFS patients. We thus focused on L-Arg metabolism, which involves nitric oxide (NO) production through NO synthase (NOS). The expression of inducible NO synthase (iNOS) transcripts in peripheral blood mononuclear cells was not significantly different between healthy control subjects and CFS patients. The L-Arg-mediated NK cell

				activation was abolished by addition of NG-monomethyl-L-arginine, an inhibitor for iNOS. Furthermore, incubation with S-nitroso-N-acetyl-penicillamine, an NO donor, stimulated NK activity in healthy control subjects but not in CFS patients. CONCLUSION: These results demonstrate that the L-Arg-induced activation of NK activity is mediated by NO and that a possible dysfunction exists in the NO-mediated NK cell activation in CFS patients.
Olson LG, Cole MF, Ambrogetti A.	Sleep Disorders Centre, Royal Newcastle Hospital, NSW, Australia. lolson@mail.newcastle.edu.au	Correlations among Epworth Sleepiness Scale scores, multiple sleep latency tests and psychological symptoms.	J Sleep Res 1998 Dec;7(4):248-53	The aim of this study was to identify factors other than objective sleep tendency associated with scores on the Epworth Sleepiness Scale (ESS). There were 225 subjects, of whom 40% had obstructive sleep apnoea (OSA), 16% had simple snoring, and 4.9% had snoring with sleep disruption (upper airway resistance syndrome); 9.3% had narcolepsy and 7.5% had hypersomnolence without REM sleep abnormalities; 12% had chronic fatigue syndrome; 7.5% had periodic limb movement disorder and 3% had diurnal rhythm disorders. ESS, the results of overnight polysomnography and multiple sleep latency test (MSLT) and SCL-90 as a measure of psychological symptoms were recorded. The ESS score and the mean sleep latency (MSL) were correlated (Spearman rho = -0.30, P < 0.0001). The MSL was correlated with total sleep time (TST) and with sleep efficiency but not with apnoea/hypopnoea index. There was no association between the MSL and any aspect of SCL-90 scores, except a borderline significant association with the somatisation subscale. The ESS was correlated with TST but not with sleep efficiency or apnoea/hypopnoea index. The ESS was correlated with all subscales of the SCL-90 except psychoticism. An ESS > or = 10 had poor sensitivity and specificity as a predictor of MSL < 10 min or MSL < 5 min. We conclude that the MSLT and the ESS are not interchangeable. The ESS was influenced by psychological factors by which the MSL was not affected. The ESS cannot be used to demonstrate or exclude sleepiness as it is measured by MSLT.
Ottenweller JE, Natelson BH, Gause WC, Carroll KK, Beldowicz D, Zhou XD, LaManca JJ.	Neurobehavioral Unit, VA Medical Center, East Orange, NJ 07018-1095, USA. jeo@nbunj.jvnc.net	Mouse running activity is lowered by Brucella abortus treatment: a potential model to study chronic fatigue.	Physiol Behav 1998 Mar;63(5):795-801	Chronic fatigue syndrome, which can occur after acute infection and last for years, is characterized by severe and persistent fatigue. Others have reported decreases in mouse running activity following infection and have suggested this may provide an animal model for studying chronic fatigue. Voluntary running is a highly motivated activity in mice, which will often run 5-7 mi/day in our laboratory. Following 2 weeks of acclimation to running wheels with food and water available ad lib, female BALB/c mice received 0.2-mL tail vein injections of killed Brucella abortus (BA) or saline vehicle. Subsequently the effects on voluntary running and grooming behavior were determined. Injection of BA caused an immediate large decrease in running and a lack of grooming. Vehicle injections produced no changes in behavior. After the first several days of reduced running behavior, levels of running and grooming slowly returned back to normal over the next 2-4 weeks, with substantial individual differences in the rate of recovery. The pattern of running during recovery was intriguing in that BA mice first ran at normal levels just after the lights went out, but they stopped after only 1-2 h. As recovery proceeded, they gradually increased the

				duration of the running bout during the night. Because this model uses voluntary exertion and the ability to run for longer periods of time characterizes recovery, the model may be a good one for studying the biologic underpinnings of chronic fatigue.
Panay N, Studd JW.	Academic Department of Obstetrics and Gynaecology, Chelsea and Westminster Hospital, London, UK.	The psychotherapeutic effects of estrogens.	Gynecol Endocrinol 1998 Oct;12(5):353-65	The effect of estrogens on the central nervous system, particularly mood and behavior, remains a controversial area which needs clarification, not just for understanding of depression in women but to ensure that such commonplace problems in women have efficient and appropriate therapy. There is now good evidence that estrogens are rapidly effective in the treatment of depression in many women but this information has not found its way through to those health care personnel, psychiatrists and psychologists who are principally involved in the treatment of depression. There is also strong evidence for the benefits of estrogens on cognitive functioning, not only in preventing the onset of dementia but also in improving the symptoms in the established condition. Recent work has also suggested a benefit for estrogens on mood in women diagnosed as suffering from chronic fatigue syndrome. This article reviews the effect of endogenous estrogen on the female central nervous system and the ever increasing evidence for the diverse psychotherapeutic effects of exogenous estrogens.
Patarca R, Mary Ann Fletcher		Interleukin-6 and Disease Two Case Reports that Point to the Usefulness of Measuring Cytokine Levels in Clinical Settings	Journal of Chronic Fatigue Syndrome 1998: 4(1): 53 - 69	Chronic fatigue syndrome has been associated with patterns of cytokine imbalances whose relevance to disease status remains to be documented. We present here two case reports that illustrate thc relevance of measuring interleukin-6 levels in biological fluids in two clinical entities: hypothermia and Sjögren's syndrome. Further studies of this nature in extended patient populations will allow to discern the relevant contribution among the pleiotropy of roles of each particular cytokine in different clinical settings. It becomes apparent from the cases presented that the clinical manifestation of the imbalance in the expression of a particular cytokine is contingent upon the compartment where it occurs and upon levels of other cytokines. Similar studies will allow to define signature cytokine imbalances for each disease condition and may also shed light on thus far uncharacterized etiological agents.
Peterson PK, Pheley A, Schroeppel J, Schenck C, Marshall P, Kind A, Haugland JM, Lambrecht LJ, Swan S, Goldsmith S.	Department of Medicine, Hennepin County Medical Center, Minneapolis, Minn 55415, USA. peter137@maroon.tc.umn.edu	A preliminary placebo-controlled crossover trial of fludrocortisone for chronic fatigue syndrome.	Arch Intern Med 1998 Apr 27;158(8):908-14Comment in: Arch Intern Med. 1998 Nov 9;158(20):2266-7	OBJECTIVE: To provide a preliminary assessment of the efficacy and safety of fludrocortisone acetate treatment of chronic fatigue syndrome. DESIGN: A placebo-controlled, double-blind, random-allocation crossover trial of 6 weeks of fludrocortisone. SETTING: An outpatient clinical trials unit. PATIENTS: Twenty-five participants with chronic fatigue syndrome (mean age, 40 years; 19 [76%] women; mean duration of illness, 7.0 years) were recruited from a research and clinic registry. Five patients withdrew from the trial. INTERVENTIONS: All participants were scheduled to receive fludrocortisone acetate (0.1-0.2 mg) or a placebo for 6 weeks in each treatment. MAIN OUTCOME MEASURES: Self-administered questionnaires were completed at the beginning and end of each treatment arm that asked patients to rate the severity of their symptoms on a visual analogue scale. The Medical

				Outcomes Study 36-Item Short-Form Health Survey, a reaction time test, and a treadmill exercise test were used to assess functional status. Blood pressure, heart rate, and plasma norepinephrine levels were obtained at baseline. Blood pressure and heart rate were recorded at the end of the exercise test and monitored at all subsequent visits. RESULTS: At baseline, the study participants reported symptom severity greater than 5 for most symptoms, and all had evidence of marked functional impairments. No improvement was observed in the severity of any symptom or in any test of function for the 20 participants who completed both arms of the trial. Blood pressure and heart rate readings were unaffected by treatment, and plasma norepinephrine levels did not differ from those of a healthy control group. The incidence of adverse experiences was similar in the fludrocortisone and placebo arms of the trial. CONCLUSION: Low-dose fludrocortisone does not provide sufficient benefit to be evident in a preliminary blinded trial of unselected patients with chronic fatigue syndrome. Publication Types: Clinical Trial Randomized Controlled Trial
Pollet C, Natelson BH, Lange G, Tiersky L, DeLuca J, Policastro T, Desai P, Ottenweller JE, Korn L, Fiedler N, Kipen H.	Center for Environmental Hazards Research, VA Medical Center, East Orange, NJ 07018, USA.	Medical evaluation of Persian Gulf veterans with fatigue and/or chemical sensitivity.	J Med 1998;29(3-4):101-13	The purpose of this study was to determine if Gulf War veterans with complaints of severe fatigue and/or chemical sensitivity (n = 72) fulfill case definitions for chronic fatigue syndrome (CFS) and/or multiple chemical sensitivity (MCS) and to compare the characteristics of those veterans who received a diagnosis of CFS (n = 24) to a group of non-veterans diagnosed with CFS (n = 95). Thirty-three veterans received a diagnosis of CFS with 14 having MCS concurrently; an additional six had MCS but did not fulfill a case definition for CFS. The group of fatigued veterans receiving a diagnosis of CFS was comprised of significantly fewer women and fewer Caucasians than the civilian group, and significantly fewer veterans reported a sudden onset to their illness. Veterans with CFS had a milder form of the illness than their civilian counterparts based on medical examiner assessment of the severity of the symptoms, reported days of reduced activity, and ability to work. Since CFS in veterans seems less severe than that seen in civilians, the prognosis for recovery of veterans with this disorder may be better.
Poteliakhoff A		Fatigue Syndromes and the Aetiology of Autoimmune Disease	Journal of Chronic Fatigue Syndrome 1998: 4(4): 31 - 49	In the last decade or so, an impairment of HypothalamicPituitary-Adrenal (HPA) axis activity has been observed in fatigue syndromes. Elevated levels of glucocorticoids help to prevent the immune system From over-reacting and generating a damaging autoimmune proccss. The corollary should be that reduced activity of the HPA axis and diminished levels of plasma cortisol could be associated with autoimmune (AI) disease. Experimental work in mice and rats supports this view. Furthermore, plasma levels of cortisol have been found to be low in the early stages of rheumatoid arthritis. There is some clinical evidence that connective tissue disorders (many of which are regarded as autoimmune diseases) occur approximately one year after the onset of prolonged or chronic fatigue, with the implication that fatigue is not merely a symptom of these disorders but precedes them. Many workers have found changes

				in the immune system of subjects suffering from CFS (mainly immune activation) which could be conducive to the development of AI disease. It has recently been found that there is, in the CFS, some deficiency of another adrenal steroid, namely that of dehydroepiandrosterone. This steroid exerts a regulatory activity on the immune system and a deficiency may well be an additional factor in the genesis of AI disease. If an association can be established between fatigue syndromes and autoimmune disease then these syndromes will need to be addressed in a more concerned manner and prophylactic measures undertaken to to forestall AI disease.
Richardson J, Durval Campos Costa		Relationship Between SPECT Scans and Buspirone Tests in Patients with ME/CFS	Journal of Chronic Fatigue Syndrome 1998: 4(3): 23 - 38	The purpose of this exercise was to study the relationship between the detail shown on the SPECT brain scans with those seen in the buspirone tests. Thirty-nine patients are included in this study. These patients were selected from a large number who had been referred to Dr. Richardson from various parts of the country by their doctors because of a tentative diagnosis of ME/CFS. All the selected patients were confirmed by Dr. Richardson as suffering from ME/CFS taking into account the subjective scoring methods, clinical examination, virology and buspirone tests. This study is an attempt to link together the results of the previously described techniques to investigate possible areas of impaired cellular function in brain which may have purely neuroncural effects or possibly neurohormonal effects. All patients within this study displayed hypoperfusion in some brain area as shown by their SPECT scans (see Appendix, Table 1.1). Thirty-five (90%) showed hypoperfusion in the regions comprising: Twenty-four (62%) in the Brain Stem Twenty (51%) in tlic Caudate Nuclei Nine (23%) showed hypoperfusion in both Brain Stem and Caudate Nuclei regions Thirty (77%) cased demonstrated hypoperfusion in the regions comprising: Tweny-four (62%) in the Temporal Lobes Twelve (31%) in the Parietal Lobes Nine (23%) in the Frontal Lobes. The significance of these results is to confirm that there is actual evidence of neurological dysfunction which results in the continuing morbidity in these ME/CFS patients. The completion of this buspirone test and SPECT scan can be deemed to be basic complementary evidence for the positive diagnosis of ME/CFS.
Rowbottom D, David Keast, , Zhukov Pervan, Carmel Goodman, Chotoo Bhagat Byron Kakulas Alan Morton		The Role of Glutamine in the Aetiology of the Chronic Fatigue Syndrome A Prospective Study	Journal of Chronic Fatigue Syndrome 1998: 4(2): 3 - 22	Background: Recent studies have observed low plasma glutamine concentrations in chronic fatigue syndrome (CFS) subjects. Glutamine has been shown to be essential for immune function and a key substrate in brain neurochemistry. A dysfunctional immune response to infection and/or neurotransmitter dysfunction may be associated with CFS. Objective: To compare the glutamine status of CFS subjects to matched controls and to test the effect of L-glutamine supplementation on the symptoms associated with CFS. Design: A 26-week, randomised, double-blind, placebo-controlled trial. Patients: Sixteen subjects diagnosed with CFS and 16 ageand sex-matched, healthy controls. Intervention: L-glutamine or placebo (2000 mg/day for 26 weeks). Measurements: Plasma and muscle glutamine concentrations, complete haematology counts, lymphocyte surface marker analysis, serum cortisol and testosterone concentrations, and self-reported symptomatic status. Results:

				Plasma and muscle glutamine concentrations were lower in CFS subjects than controls (P < 0.001 and P = 0.027, respectively). Significant increases in plasma (P = 0.020) and muscle (P = 0.037) glutamine concentration were observed following L-glutamine, but not placebo (P > 0.05), supplementation. However, improvements in symptomatic status were not observed in the L-glutamine group. Although six subjects showed clinical improvements during the trial, there was no change in their plasma or muscle glutamine concentrations. Conclusions: These data suggest that while low plasma glutamine concentrations may occur coincident with CFS, they may not be directly causative of fatigue or other symptoms.
Rowbottom D, David Keast, Zhukov Pervan, Alan Morton		The Physiological Response to Exercise in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(2): 33 - 49	Background: The chronic fatigue syndrome (CFS) is characterised by a limited exercise capacity. Studies have reported reduced muscle oxidative capacity in CFS, evidenced by abnormal acidosis during exercise and reduced aerobic capacity and exercise endurance. Objective: To compare physiological responses to walking exercise in CFS subjects, sedentary controls, and clinically improved CFS subjects. Design: Ageand sex-matched pairs, with repeated measures. Subjects: Sixteen subjects diagnosed with CFS and 16 ageand sex-matched sedentary controls. Measurements: Heart rate (HR), oxygen uptake (VO2), ventilation (VE) and relative perceived exertion (RPE) responses to incremental walking exercise to volitional exhaustion. Results: CFS subjects reached significantly lower HRpeak (P = 0.023) and achieved nonsignificantly (P > 0.05) lower VO2peak than control subjects. Despite no differences in submaximal exercise responses, CFS subjects reported higher RPE scores than controls (P = 0.003) at submaximal workloads. RPE scores correlated with symptomatic scores for emotionality (r = 0.642) and general fatigue (r = 0.568). Symptomatic recovery in six CFS subjects was associated with nonsignificant increases in HRpeak, VO2peak and VEpeak, and nonsignificant decreases in RPE scores at submaximal workloads. Conclusions: These data suggested that the limited exercise capacity in CFS subjects may be explained by deconditioning due to the sedentary lifestyle necessitated bv the condition. coupled with an increased perception of exertion, potentially linked to psychological symptoms associated with CFS.
Rowbottom DG, Keast D, Green S, Kakulas B, Morton AR.	Department of Human Movement, University of Western Australia, Nedlands, Australia.	The case history of an elite ultra-endurance cyclist who developed chronic fatigue syndrome.	Med Sci Sports Exerc 1998 Sep;30(9):1345-8	An elite ultra-endurance athlete, who had previously undergone physiological and performance testing, developed chronic fatigue syndrome (CFS). An incremental cycling exercise test conducted while he was suffering from CFS indicated decreases in maximum workload achieved (Wmax; -11.3%), the maximum oxygen uptake (VO2max; -12.5%), and the anaerobic threshold (AT; -14.3%) compared to pre-CFS data. A third test conducted after the athlete had shown indications of significant improvement in his clinical condition revealed further decreases in Wmax (-7.9%), VO2max (-10.2%) and AT (-8.3%). These data, along with submaximal exercise data and muscle biopsy electron microscopic analyses, suggest that the performance decrements were the result of detraining, rather than an impairment of aerobic metabolism due to CFS per se. These data may be indicative of central, possibly

				neurological, factors influencing fatigue perception in CFS sufferers.
Rowe PC, Calkins H.	Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA.	Neurally mediated hypotension and chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):15S-21S	A substantial body of clinical evidence now supports an association between various forms of hypotension and both idiopathic chronic fatigue and the chronic fatigue syndrome (CFS). Patients with CFS have a high prevalence of neurally mediated hypotension, and open treatment of this autonomic dysfunction has been associated with improvements in CFS symptoms. Randomized trials are now in progress to evaluate the efficacy of treatments directed at neurally mediated hypotension in those with CFS patients, and the results of these trials should help guide more basic inquiries into the mechanisms of orthostatic intolerance in affected individuals.
Russo J, Katon W, Clark M, Kith P, Sintay M, Buchwald D.	Department of Psychiatry & Behavioral Sciences, Harborview Medical Center, University of Washington, Seattle 98104, USA. jerusso@u.washington.edu	Longitudinal changes associated with improvement in chronic fatigue patients.	J Psychosom Res 1998 Jul;45(1 Spec No):67-76	Tertiary care patients with chronic fatigue were followed for 2.5 years to determine if changes in physical and psychological status were associated with improvements in chronic fatigue, physical functioning, and return to work. Results indicated that improvement in psychological symptoms, DSM-III-R disorders, physical examination signs, and changes in whether the patient continued to meet criteria for chronic fatigue syndrome (CFS) were associated with recovery from fatigue, improved functioning, and return to work. Patients who never met CFS criteria or only met criteria at the initial assessment, reported improved physical functioning. Patients whose psychiatric disorders and physical examination signs were still present at a mean follow-up time of 2.5 years were more likely to have persistent fatigue and work disability. Loss of physical examination signs was a significant independent predictor of improved functioning and return to work. These results suggest that psychiatric status, as well as physical status, are associated with recovery from chronic fatigue.
Saggini R, Pizzigallo E, Vecchiet J, Macellari V, Giacomozzi C.	Institute of Medical Pathophysiology, University G. D'Annunzio, Chieti, Italy.	Alteration of spatial-temporal parameters of gait in Chronic Fatigue Syndrome patients.	J Neurol Sci 1998 Jan 21;154(1):18-25	Chronic Fatigue Syndrome (CFS) has been widely studied and a lot of information is available in the literature regarding the immunological, virological, neuroendocrinal and psychiatric aspects of the disease, but its aetiology is still poorly understood. Great attention has also been paid to the alteration of the muscular function caused by CFS. The aim of the present work was to study CFS patients' gait in order to find out objective measures which can better characterize the pathology. Spatial and temporal parameters of gait were collected from a group of 12 CFS informed volunteers by using the typical instrumentation of movement analysis, and raw data were statistically elaborated. Comparisons with reference data from a population of healthy subjects revealed significant abnormalities in the symmetry indices of the bilateral parameters and in the linear relationships among parameters, and between these parameters and the physical characteristics of the patients. Interestingly, the abnormalities were present as from the beginning of the gait, which indicates that they are unlikely to be caused by the rapid increasing fatigue. This strengthens the hypothesis of a direct involvement of the central nervous system (CNS) in the onset of the disease.
Saltzstein BJ, Wyshak	Harvard Medical	A naturalistic study of	Gen Hosp Psychiatry	Chronic fatigue syndrome (CFS), a controversial illness without clear etiology, causes

G, Hubbuch JT, Perry JC.	School, Boston, MA, USA.	the chronic fatigue syndrome among women in primary care.	1998 Sep;20(5):307-16	profound debilitation in its sufferers. This study explored subjects' perceptions of the variables that mediated the course of their illness and identified coping strategies in 15 women with CFS referred from the practice of a primary care physician. Exploratory semistructured interviews were adapted from Kleinman's Illness Narratives. Four instruments were used: the Beck Depression Inventory, the Sickness Impact Profile, a modified Karnofsky scale, and the Defense Mechanism Rating Scale. Of the 15 women, 60% reported improvement and/or recovery at the time of the interview. Improvement was associated with social support and lower levels of depressive symptoms. Health status was influenced by how subjects perceived their illness, their future, and the doctor's prognosis; and by the physician's early diagnosis, validation of the CFS, and intensive medical follow-up. Obsessional and healthy neurotic defense levels predominated, which differs from historical comparison groups with dysthymia and panic disorder. Psychological adaptation to CFS is similar to adaptive coping in other chronic illnesses: subjective perceptions of health status can predict functional status. Physician validation is particularly important given the controversial status of CFS. Maintaining relationships with others--doctor, work, family, and group/spiritual activities reflected healthy coping strategies that promoted hope and attitudinal shifts. The finding of a mixture of neurotic and healthy defenses and a low proportion of defenses associated with personality disorders has not been previously reported in the CFS literature and warrants further investigation.
Schmaling KB, Daniel L. Hamilos Jeannie D. DiClementi, James F. Jones		Pain Perception in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(3): 13 - 22	Pain complaints (myalgia, arthralgia, headache, sore throat) are commonly associated with chronic fatigue syndrome (CFS), yet to date, these patients' responses to standardized measures of pain perception have not been investigated. Pain perception was measured by pressure dolorimeter and ice water cold pressor tests, and the McGill Pain Questionnaire among 15 female subjects with CFS, 11 suhjects with Major Depression and 11 healthy controls. No differences were found between the groups for pain threshold or intolerance levels on the pressure dolorimeter and cold pressor tests. CFS and depressed subjects endorsed significantly more self-reported pain complaints than did control subjects. Although more pain complaints were predicted by greater somatization and lower health perceptions, pain threshold and intolerance were not associated with psychiatric symptoms or functional status. The study yielded some interesting preliminary observations related to variability in pain tolerance among CFS patients. These preliminary observations are discussed in terms of the need for future research and their potential implications for treatment and coping with the illness.
Scott LV, Burnett F, Medbak S, Dinan TG.	Department of Psychological Medicine, St Bartholomew's and the	Naloxone-mediated activation of the hypothalamic-pituitary-adrenal axis in chronic	Psychol Med 1998 Mar;28(2):285-93	BACKGROUND: Opioidergic pathways have an inhibitory regulatory influence on the hypothalamic-pituitary-adrenal axis (HPA) in man. Previous studies have suggested impairment of pituitary-adrenal activation in chronic fatigue syndrome (CFS). We, therefore, decided to investigate the extent of opioid inhibition of HPA activity in CFS

	Royal London School of Medicine.	fatigue syndrome.		as a possible explanation for the reputed HPA hypofunctioning in patients with CFS. METHOD: Thirteen patients with CFS, diagnosed according to CDC criteria, were compared with thirteen healthy subjects. Adrenocorticotropin (ACTH) and cortisol (CORT) responses were measured following the administration of the opiate antagonist naloxone. RESULTS: Baseline ACTH and cortisol levels did not differ between the two groups. The release of ACTH (but not cortisol) was significantly blunted in the CFS subjects compared with controls. CONCLUSIONS: Naloxone mediated activation of the HPA is attenuated in CFS. Excessive opioid inhibition of the HPA is thus an unlikely explanation for the HPA dysregulation in this disorder.
Scott LV, Dinan TG.	Department of Psychological Medicine, St. Bartholomew's Hospital and the Royal London School of Medicine, West Smithfield, UK.	Urinary free cortisol excretion in chronic fatigue syndrome, major depression and in healthy volunteers.	J Affect Disord 1998 Jan;47(1-3):49-54	Urinary free cortisol excretion (UFC) was compared in 21 patients with chronic fatigue syndrome (CFS), in 10 melancholic depressives and in 15 healthy controls. Patients with depression had UFC values which were significantly higher than healthy comparison subjects, whereas UFC excretion of CFS patients was significantly lower than the comparison group. These findings are in keeping with currently held hypotheses of hyperactivity and hypoactivity of the hypothalamic-pituitary-adrenal (HPA) axis in depression and chronic fatigue syndrome respectively. Five of the 21 CFS patients had a co-morbid depressive illness. This sub-group retained the profile of UFC excretion of those with CFS alone, suggesting a different pathophysiological basis for depressive symptoms in CFS.
Scott LV, Medbak S, Dinan TG.	Department of Psychological Medicine, St Bartholomew's and the Royal London School of Medicine, West Smithfield, UK.	Blunted adrenocorticotropin and cortisol responses to corticotropin-releasing hormone stimulation in chronic fatigue syndrome.	Acta Psychiatr Scand 1998 Jun;97(6):450-7	Hypofunctioning of the pituitary-adrenal axis has been suggested as the pathophysiological basis for chronic fatigue syndrome (CFS). Blunted adrenocorticotropin (ACTH) responses but normal cortisol responses to exogenous corticotropin-releasing hormone (CRH), the main regulator of this axis, have been previously demonstrated in CFS patients, some of whom had a comorbid psychiatric disorder. We wished to re-examine CRH activation of this axis in CFS patients free from concurrent psychiatric illness. A sample of 14 patients with CDC-diagnosed CFS were compared with 14 healthy volunteers. ACTH and cortisol responses were measured following the administration of 100 microg ovine CRH. Basal ACTH and cortisol values did not differ between the two groups. The release of ACTH was significantly attenuated in the CFS group ($P < 0.005$), as was the release of cortisol ($P < 0.05$). The blunted response of ACTH to exogenous CRH stimulation may be due to an abnormality in CRH levels with a resultant alteration in pituitary CRH receptor sensitivity, or it may reflect a dysregulation of vasopressin or other factors involved in HPA regulation. A diminished output of neurotrophic ACTH, causing a reduced adrenocortical secretory reserve, inadequately compensated for by adrenoceptor upregulation, may explain the reduced cortisol production demonstrated in this study.
Scott LV, Medbak S, Dinan TG.	Department of Psychiatry, Trinity College Medical	The low dose ACTH test in chronic fatigue syndrome and in	525: Clin Endocrinol (Oxf) 1998 Jun;48(6):733-	OBJECTIVE: A number of dynamic tests of the hypothalamic-pituitary-adrenal axis provide evidence for a mild central adrenal insufficiency in chronic fatigue syndrome (CFS). The 1 microgram adrenocorticotropin (ACTH) test has been proposed to be

	School, Dublin, Eire.	health.	7Comment in: Clin Endocrinol (Oxf). 2000 Jun;52(6):797-9	more sensitive than the standard 250 micrograms ACTH test in the detection of subtle pituitary-adrenal hypofunctioning. We aimed to establish whether the 1 microgram ACTH test would support such a dysregulation in CFS, and also, given the relative novelty of this test in clinical practice and the uncertainty with regard to appropriate cut-off values for normality, to compare our healthy volunteer data with those of previous studies. PATIENTS AND DESIGN: Twenty subjects with CFS, diagnosed according to Centres for Disease Control and Prevention criteria, were compared with 20 healthy volunteer subjects. All participants underwent a 1 microgram ACTH test beginning at 1400 h. Plasma samples for cortisol estimation were drawn at 0, and min. RESULTS: Baseline cortisol values did not differ between CFS patients and healthy subjects. The delta cortisol (maximum increment from baseline) value was significantly lower in the CFS than the volunteer group ($P < 0.05$). Comparison of the min cortisol values revealed no significant differences. Using an incremental cortisol of > 250 nmol/l as an arbitrary cutoff point, two (10%) of the healthy subjects and nine (45%) of the CFS subjects failed the test on this basis ($chi 2 = 4.3$, $df = 38$, $P < 0.05$). CONCLUSIONS: This study provides further evidence for a subtle pituitary-adrenal insufficiency in subjects with chronic fatigue syndrome compared to healthy volunteers. Disparities between our healthy volunteer data and those of other groups using the 1 microgram ACTH test suggest that the test may not be as reliable as previously indicated.
See DM, Cimoch P, Chou S, Chang J, Tilles J.	University of California, Irvine, Department of Medicine, Orange 92668, USA.	The in vitro immunomodulatory effects of glyconutrients on peripheral blood mononuclear cells of patients with chronic fatigue syndrome.	Integr Physiol Behav Sci 1998 Jul-Sep;33(3):280-7	In humans, eight monosaccharides are required for the synthesis of glycoproteins. Dietary supplements that supply these crucial sugars are known as glyconutrients. A glyconutrient compound was added to Peripheral Blood Mononuclear Cells (PBMC) isolated from normal controls and patients with the Chronic Fatigue Syndrome (CFS), a disease associated with immune dysregulation. The in vitro immunomodulatory effects were investigated. Cell surface expression of the glycoproteins CD5, CD8, and CD11a were significantly lower in patients with CFS compared to normal controls. Addition of glyconutrient homogenate to PBMC from patients with CFS stimulated with phytohemagglutinin significantly increased the expression of each glycoprotein. Furthermore, natural killer (NK) cell function was reduced in CFS patients. The glyconutrient preparation significantly enhanced NK cell activity versus human herpes virus 6 (HHV-6)-infected H9 cells in an 8 h 51Cr release assay compared to placebo for PBMC from patients with CFS ($p< .01$). Finally, apoptosis was significantly higher in patients with CFS. The percentage of apoptotic cells was significantly decreased in PBMC from patients with CFS that had been incubated for 48 h with glyconutrients. Thus, glyconutrients improved abnormal immune parameters in vitro in patients with CFS.
Seelig M		Review and Hypothesis Might Patients with the Chronic Fatigue	Journal of Chronic Fatigue Syndrome 1998: 4(2): 77 - 108	The latent tetany syndrome (LTS) parallels CFS in its neuromuscular and psychiatric manifestations, as well as in inner ear disturbances: vestibular in CFS and FM, as well as in LTS, and increased vulnerability to noise-induced deafness in LTS. Microvascular

		Syndrome Have Latent Tetany of Magnesium Deficiency		damage to the cochlea is seen in Mg deficiency, noise-induced deafness, and might be a factor in migraine and other severe headaches in both LTS and in CFS and FM. Abnormal sleep patterns occur in both LTS and CFS; impaired cognition more in CFS than in LTS. However, some brain and neurotransmitter dysfunctions seen with Mg deficiency might be contributory to cognitive disorders of CFS. Mg loss caused by enhanced catecholamine release produced by stress may well be contributory to stress-induced acute episodes of CFS. Malfunctions of the cellular and humoral immunological systems are caused by experimental Mg deficiency. Whether allergies in CFS patients and abnormal response to antigenic challenge are results of low Mg remains to be proven. Mitral valve prolapse is seen in many LTS and CFS patients; whether a putative Mg deficiency predisposes to this abnormality is not known. Clinical improvement with Mg treatment has been proven in LTS, and seemed helpful in the rare cases of CFS and FM in whom it has been tried. The Mg status should be determined in patient with CFS and FM, but methodology is a handicap. Serum Mg is an inaccurate index. Three methods show promise. Percentage retention of a Mg load is accurate but requires patient's cooperation. Free ionic Mg measurement requires ion-selective electrodes. Blood cell Mg is reliable in a little more than half the patients; sublingual cell Mg seems more accurate. More intensive, and controlled studies of the Mg status of CFS and FM patients, and of their response to Mg therapy is desirable.
Servatius RJ, Tapp WN, Bergen MT, Pollet CA, Drastal SD, Tiersky LA, Desai P, Natelson BH.	New Jersey Medical School, Department of Neuroscience, East Orange 07019, USA.	Impaired associative learning in chronic fatigue syndrome.	Neuroreport 1998 Apr 20;9(6):1153-7	Patients with chronic fatigue syndrome (CFS) report cognitive difficulties (impaired attention, memory and reasoning). Neuropsychological tests have failed to consistently find cognitive impairments to the degree reported by CFS patients. We tested patients with CFS and sedentary controls in protocols designed to measure sensory reactivity and acquisition of the classically conditioned eyeblink response. Patients with CFS exhibited normal sensitivity and responsivity to acoustic stimuli. However, CFS patients displayed impaired acquisition of the eyeblink response using a delayed-type conditioning paradigm. Sensitivity and responsivity to the airpuff stimulus were normal. In the absence of sensory/motor abnormalities, impaired acquisition of the classically conditioned eyeblink response indicates an associative deficit. These data suggest organic brain dysfunction within a defined neural substrate in CFS patients.
Sharpe M.		Doctors' diagnoses and patients' perceptions. Lessons from chronic fatigue syndrome.	Gen Hosp Psychiatry 1998 Nov;20(6):335-8	
Sharpe M.		Cognitive behavior therapy for chronic fatigue syndrome.	Am J Psychiatry 1998 Oct;155(10):1461-2 Comment on: Am J Psychiatry. 1997	

			Mar;154(3):408-14	
Sharpe M.	University of Edinburgh Department of Psychiatry, Royal Edinburgh Hospital, United Kingdom.	Cognitive behavior therapy for chronic fatigue syndrome: efficacy and implications.	Am J Med 1998 Sep 28;105(3A):104S-109S	Cognitive behavior therapy (CBT) is a form of non-pharmacologic treatment. It is based on a model of chronic fatigue syndrome (CFS) that hypothesizes that certain cognitions and behavior may perpetuate symptoms and disability--that is, act as obstacles to recovery. Treatment emphasizes self-help and aims to help the patient to recover by changing these unhelpful cognitions and behavior. There is now good evidence from 2 independent randomized clinical trials to support the efficacy of CBT in patients with CFS. The treatment effect is substantial, although few patients are cured. The urgent clinical need is to make this form of treatment available to patients with CFS. One approach is to incorporate the principles of CBT into routine clinical practice. The preliminary evaluation of these simpler forms of CBT are promising, although the results of controlled trials are awaited. At present, intensive individual CBT administered by a skilled therapist remains the treatment of choice for patients with CFS.
Sibbald B.		Chronic fatigue syndrome comes out of the closet.	CMAJ 1998 Sep 8;159(5):537-41Comment in: CMAJ. 1999 Mar 9;160(5):636, 638 CMAJ. 1999 Mar 9;160(5):638	An Alberta court ruling and new guidelines for physicians issued by the Quebec medical college are giving chronic fatigue syndrome a legitimacy it never before enjoyed. What will this mean for physicians?
Sisto SA, Tapp WN, LaManca JJ, Ling W, Korn LR, Nelson AJ, Natelson BH.	NJCFS Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA. sueann@nbunj.jvnc.net	Physical activity before and after exercise in women with chronic fatigue syndrome.	QJM 1998 Jul;91(7):465-73	We measured physical activity after strenuous exercise in 20 women with chronic fatigue syndrome (CFS), compared to 20 sedentary healthy volunteers who exercised no more than once per week. Activity was measured for 2 weeks using a portable waist-worn vertical accelerometer. After the first week of activity monitoring, all participants returned for a maximal treadmill test, followed by continued activity monitoring for the second week. Five activity measures were derived from the data: (i) average activity; (ii) total activity; (iii) duration of waking day; (iv) duration; and (v) number of daily rests. A repeated measures ANCOVA was used to determine post-treadmill group differences accounting for pre-treadmill differences. There was a significant reduction in overall average activity after the treadmill test, with the greatest decrease on days 12 through 14. This reduction was accompanied by a significant increase in the duration of the waking day and number of daily rests. Thus, marked exertion does produce changes in activity, but later than self-report would suggest, and are apparently not so severe that CFS patients cannot compensate.
Smit AA, Bolweg NM, Lenders JW, Wieling W.	Academisch Medisch Centrum, afd. Interne Genceskunde, Amsterdam.	[No strong evidence of disturbed regulation of blood pressure in chronic fatigue syndrome].[article in	Ned Tijdschr Geneeskd 1998 Mar 21;142(12):625-8	Recent medical publications postulate a connection between the Chronic Fatigue Syndrome (CFS) and disturbed regulation of the circulation, manifesting itself during orthostatic stress testing. Four studies were published on the circulatory response on prolonged head up tilt testing. Numerous CFS patients displayed postural tachycardia or syncope during the test. However, many CFS patients examined had had

		Dutch]		orthostatic symptoms prior to the examination. It is not certain that cardiovascular dysregulation is present in CFS patients without orthostatic symptoms. It is also not clear whether such a dysregulation would be the effect of physical inactivity or a manifestation of a subtle form of autonomic neuropathy.
Speight AN.		Increased illness experience preceding chronic fatigue syndrome.	J R Coll Physicians Lond 1998 May-Jun;32(3):274Comment in: J R Coll Physicians Lond. 1998 Jul-Aug;32(4):389 and 1998 Jan-Feb;32(1):44-8	
Steele L, Dobbins JG, Fukuda K, Reyes M, Randall B, Koppelman M, Reeves WC.	Viral Exanthems and Herpesvirus Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, US Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.	The epidemiology of chronic fatigue in San Francisco.	Am J Med 1998 Sep 28;105(3A):83S-90S	Despite considerable research on chronic fatigue syndrome (CFS) and conditions associated with unexplained chronic fatigue (CF), little is known about their prevalence and demographic distribution in the population. The present study describes the epidemiology and characteristics of self-reported CF and related conditions in a diverse urban community. The study used a cross-sectional telephone screening survey of households in San Francisco, followed by interviews with fatigued and nonfatigued residents. Respondents who appeared to meet case definition criteria for CFS, based on self-reported fatigue characteristics, symptoms, and medical history, were classified as CFS-like cases. Subjects who reported idiopathic chronic fatigue (ICF) that did not meet CFS criteria were classified as ICF-like cases. Screening interviews were completed for 8,004 households, providing fatigue and demographic information for 16,970 residents. Unexplained CF was extremely rare among household residents <18 years of age, but was reported by 2% of adult respondents. A total of 33 adults (0.2% of the study population) were classified as CFS-like cases and 259 (1.8%) as ICF-like cases. Neither condition clustered within households. CFS- and ICF-like illnesses were most prevalent among women and persons with annual household incomes below $40,000, and least prevalent among Asians. The prevalence of CFS-like illness was elevated among African Americans, Native Americans, and persons engaged in clerical occupations. Although CFS-like cases were more severely ill than those with ICF-like illness, a similar symptom pattern was observed in both groups. In conclusion, conditions associated with unexplained CF occur in all sociodemographic groups but appear to be most prevalent among women, persons with lower income, and some racial minorities.
Stewart J, Weldon A, Arlievsky N, Li K, Munoz J.	Department of Pediatrics, New York Medical College, Valhalla 10595, USA. stewart@nymc.edu	Neurally mediated hypotension and autonomic dysfunction measured by heart rate variability during head-	Clin Auton Res 1998 Aug;8(4):221-30	Recent investigations suggest a role for neurally mediated hypotension (NMH) in the symptomatology of chronic fatigue syndrome (CFS) in adults. Our previous observations in children with NMH and syncope (S) unrelated to CFS indicate that the modulation of sympathetic and parasympathetic tone measured by indices of heart rate variability (HRV) is abnormal in children who faint during head-up tilt (HUT). In

		up tilt testing in children with chronic fatigue syndrome.		order to determine the effects of autonomic tone on HUT in children with CFS we performed measurements of HRV during HUT in 16 patients aged 11-19 with CFS. Data were compared to 26 patients evaluated for syncope and with 13 normal control subjects. After 30 minutes supine, patients were tilted to 80 degrees for 40 minutes or until syncope occurred. Time domain indices included RR interval, SDNN, RMSSD, and pNN50. An autoregressive model was used to calculate power spectra. LFP (.04-.15 Hz), HFP (.15-.40Hz), and TP (.01-.40Hz). Data were obtained supine (baseline) and after HUT. Thirteen CFS patients fainted (CFS, 5/13 pure vasodepressor syncope) and three patients did not (CFS-). Sixteen syncope patients fainted (S, all mixed vasodepressor-cardioinhibitory) and 10 did not (S-). Four control patients fainted (Control, all mixed vasodepressor-cardioinhibitory) and nine did not (Control-). Baseline indices of HRV were not different between Control and S, and between Control- and S-, but were depressed in S compared to S-. HRV indices were strikingly decreased in CFS patients compared to all other groups. With tilt, SDNN, RMSSD, and pNN50 and spectral indices decreased in all groups, remaining much depressed in CFS compared to S or control subjects. With HUT, sympathovagal indices (LFP/HFP, nLFP, and nHFP) were relatively unchanged in CFS, which contrasts with the increase in nLFP with HUT in all other groups. With syncope RMSSD, SDNN, LFP, TP, and HFP increased in S (and Control), suggesting enhanced vagal heart rate regulation. These increases were not observed in CFS patients. CFS is associated with NMH during HUT in children. All indices of HRV are markedly depressed in CFS patients, even when compared with already low HRV in S or Control patients. Sympathovagal balance does not shift toward enhanced sympathetic modulation of heart rate with HUT and there is blunting in the overall HRV response with syncope during HUT. Taken together these data may indicate autonomic impairment in patients with CFS.
Stores G, Fry A, Crawford C.	University Section, Park Hospital for Children, Oxford, UK.	Sleep abnormalities demonstrated by home polysomnography in teenagers with chronic fatigue syndrome.	J Psychosom Res 1998 Jul;45(1 Spec No):85-91	To provide objective information about sleep physiology in young people with chronic fatigue syndrome (CFS), home polysomnography (PSG) was performed on 18 teenagers, aged 11-17 years, in whom CFS had been diagnosed according to internationally accepted criteria. The results were compared with those for healthy controls matched individually for gender and age. Compared with controls, CFS subjects showed significantly higher levels of sleep disruption by both brief and longer awakenings. Disruption of sleep in this way could at least contribute to the daytime symptoms of young people with CFS. The underlying cause of the disruption needs to be considered in each individual case. Further research is required to clarify the relative contribution of this neurobiological aspect of CFS in young people.
Streeten DH, Anderson GH Jr.	Department of Medicine, SUNY Health Science Center, Syracuse, NY 13210, USA.	The role of delayed orthostatic hypotension in the pathogenesis of chronic fatigue.	Clin Auton Res 1998 Apr;8(2):119-24	Past studies have shown that severe fatigue was the presenting symptom in six of seven patients with delayed orthostatic hypotension and that tilt table-induced hypotension was found in 22 of 23 patients with the chronic fatigue syndrome. We have determined the prevalence of fatigue, volunteered in response to a nonspecific pre-examination questionnaire used in 431 patients, each subsequently diagnosed as

				having one of eight neurological or endocrine disorders. The results show that fatigue is a very common symptom in patients with delayed orthostatic hypotension (n = 21), as well as both primary (n = 30) and secondary (n = 106) hypocortisolism: 70-83% in all groups. In contrast, fatigue was an uncommon complaint in patients with multiple system atrophy (MSA) (n = 30), pituitary disorders without hypocortisolism (n = 106) or idiopathic hirsutism (n = 96): 7-33% in all groups, and was intermediate in prevalence in patients with acute hyperadrenergic orthostatic hypotension (n = 32): 41%. It is concluded that fatigue commonly results from delayed orthostatic hypotension and all forms of hypocortisolism but is less common in patients with acute orthostatic hypotension, both idiopathic and due to MSA, which more commonly present with lightheadedness or syncope.
Streeten DH, David S. Bell		Original ResearchCirculating Blood Volume in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(1): 3 - 11	Chronic fatigue syndrome (CFS) is an illness associated with severe activity limitation and a characteristic pattern of symptoms despite a relatively normal physical examination and routine laboratory evaluation. The recent description of delayed orthostatic hypotension in patients with CFS, and previous findings of reduced red blood cell (RBC) mass in other patients with orthostatic hypotension not known to have CFS, led us to measure RBC mass and plasma volume in 19 individuals (15 female, four male) with well characterized, severe CFS. RBC mass was found to be significantly reduced ($p < 0.001$) below the published normal range in the 16 women, being subnormal in 15 (93.8%) of them as well as in two of the four men. Plasma volume was subnormal in 10 (52.6%) patients and total blood volume was below normal in 12 (63.2%). The high prevalence and frequent severity of the low RBC mass suggest that this abnormality might contribute to the symptoms of CFS by reducing the oxygen-carrying power of the blood reaching the brain in many of these patients.
Strickland P, Morriss R, Wearden A, Deakin B.	University of Manchester and (Guild NHS Trust), Department of Community Psychiatry, Royal Preston Hospital, Fulwood, UK.	A comparison of salivary cortisol in chronic fatigue syndrome, community depression and healthy controls.	J Affect Disord 1998 Jan;47(1-3):191-4	BACKGROUND: Previous studies reporting cortisol hyposecretion in chronic fatigue syndrome may have been confounded by venepuncture, fasting and hospitalisation. METHODS: Morning and evening salivary cortisol were obtained on consecutive days in the first 3 days of the menstrual cycle and compared in three samples of women taking no medication and matched for age: 14 patients with chronic fatigue syndrome, 26 community cases of ICD-10 current depressive episodes and 131 healthy community controls. RESULTS: The mean evening cortisol was significantly lower in the chronic fatigue syndrome patients compared to controls with depression ($P = 0.02$) and healthy controls ($P = 0.005$). Chronic fatigue syndrome patients without psychiatric disorder had significantly lower morning salivary cortisols compared to controls ($P = 0.009$). CONCLUSION: Chronic fatigue syndrome patients display cortisol hyposecretion in saliva as well as plasma compared to patients with depression and healthy controls. LIMITATIONS: Small samples of female patients with cortisol estimated at only two time points in the day. Cortisol secretion may be secondary to other neurotransmitter abnormalities or other physiological or lifestyle factors in chronic fatigue syndrome patients. CLINICAL RELEVANCE: Chronic fatigue

				syndrome is biochemically distinct from community depression.
Swanink CM, Stolk-Engelaar VM, van der Meer JW, Vercoulen JH, Bleijenberg G, Fennis JF, Galama JM, Hoogkamp-Korstanje JA.	Department of Medical Microbiology, University Hospital Nijmegen, The Netherlands.	Yersinia enterocolitica and the chronic fatigue syndrome.	J Infect 1998 May;36(3):269-72	OBJECTIVES: To investigate the potential role of Yersinia enterocolitica in patients with chronic fatigue syndrome (CFS). METHODS: An immunoblot technique was used to detect antibodies to various Yersinia outer membrane proteins (YOPs) in serum samples from 88 patients with CFS and 77 healthy neighbourhood controls, matched for gender and age. RESULTS: The prevalence of IgG and IgA antibodies to various Yersinia outer membrane proteins (YOPs) did not differ between patients with CFS and healthy controls. Twenty-four patients (27%) and nineteen controls (25%) had IgG antibodies to one or more YOPs. Four patients and two controls had both serum IgG and IgA antibodies to at least two different YOPs, compatible with a recent or persistent infection. Although all patients with positive IgG and IgA reactions to two or more YOPs had symptoms that could point to persistent Yersinia infection, these symptoms were also found frequently in patients without antibodies to YOPs. CONCLUSIONS: We conclude that Y. enterocolitica is unlikely to play a major role in the aetiology of CFS.
Terman M, Levine SM, Terman JS, Doherty S.	Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York State Psychiatric Institute, New York 10032, USA.	Chronic fatigue syndrome and seasonal affective disorder: comorbidity, diagnostic overlap, and implications for treatment.	Am J Med 1998 Sep 28;105(3A):115S-124S	This study aimed to determine symptom patterns in patients with chronic fatigue syndrome (CFS), in summer and winter. Comparison data for patients with seasonal affective disorder (SAD) were used to evaluate seasonal variation in mood and behavior, atypical neurovegetative symptoms characteristic of SAD, and somatic symptoms characteristic of CFS. Rating scale questionnaires were mailed to patients previously diagnosed with CFS. Instruments included the Personal Inventory for Depression and SAD (PIDS) and the Systematic Assessment for Treatment Emergent Effects (SAFTEE), which catalogs the current severity of a wide range of somatic, behavioral, and affective symptoms. Data sets from 110 CFS patients matched across seasons were entered into the analysis. Symptoms that conform with the Centers for Disease Control and Prevention (CDC) case definition of CFS were rated as moderate to very severe during the winter months by varying proportions of patients (from 43% for lymph node pain or enlargement, to 79% for muscle, joint, or bone pain). Fatigue was reported by 92%. Prominent affective symptoms included irritability (55%), depressed mood (52%), and anxiety (51%). Retrospective monthly ratings of mood, social activity, energy, sleep duration, amount eaten, and weight change showed a coherent pattern of winter worsening. Of patients with consistent summer and winter ratings (n = 73), 37% showed high global seasonality scores (GSS) > or = 10. About half this group reported symptoms indicative of major depressive disorder, which was strongly associated with high seasonality. Hierarchical cluster analysis of wintertime symptoms revealed 2 distinct clinical profiles among CFS patients: (a) those with high seasonality, for whom depressed mood clustered with atypical neurovegetative symptoms of hypersomnia and hyperphagia, as is seen in SAD; and (b) those with low seasonality, who showed a primary clustering of classic CFS symptoms (fatigue, aches, cognitive disturbance), with depressed mood most closely

				associated with irritability, insomnia, and anxiety. It appears that a subgroup of patients with CFS shows seasonal variation in symptoms resembling those of SAD, with winter exacerbation. Light therapy may provide patients with CFS an effective treatment alternative or adjunct to antidepressant drugs.
Thompson D, Hylan TR, McMullen W, Romeis ME, Buesching D, Oster G.	Policy Analysis, Inc., Indianapolis, USA. dthompson@pai2.com	Predictors of a medical-offset effect among patients receiving antidepressant therapy.	Am J Psychiatry 1998 Jun;155(6):824-7	OBJECTIVE: Characteristics of patients receiving antidepressant therapy were examined to identify factors that may be associated with a medical-offset effect. METHOD: In a retrospective study, the authors analyzed claims data from a large health insurer in New England. The study subjects included 1,661 persons initiating treatment for depression with selective serotonin reuptake inhibitors or tricyclic antidepressants between July 1991 and June 1993. RESULTS: Patients with anxiety disorders, coronary heart disease, cancer, and chronic fatigue syndrome and those remaining on their initial regimens of antidepressant therapy for at least 6 months were more likely to experience significant reductions in the costs of medical care services. The number of visits to mental health providers had no effect on the costs of medical services. CONCLUSIONS: Specific comorbid conditions and sustained use of antidepressant drugs may be associated with a medical-offset effect for patients receiving treatment for depression.
Timothy K. Roberts , Neil R. McGregor, R. Hugh Dunstan, Mark Donohoe, Raymond N. Murdoch , D. Hope , DipEd, S. Zhang BMed, Henry L. Butt , Jennifer A. Watkins , Warren G. Taylor		Immunological and Haematological Parameters in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(4): 51 - 65	Red and white blood cell parameter profiles and pokeweed mitogen responses were investigated in 57 CDC-defined CFS patients and 34 age-and sex-matched controls. CFS patients had significantly different red and white blood cell profiles compared with controls. Red cell distribution width (RDW) was the primary regression factor differentiating the groups. RDW was positively associated with mean platelet volume (MPV) in control subjects, but negatively correlated with MPV in CFS patients, indicating a reversal of the functional relationship between these parameters in CFS patients. Hematological parameters, and not the immunological parameters studied, were more important in differentiating CFS patients from healthy control subjects. Female CFS patients had significant increases in RDW and mean platelet volume, and decreases in the numbers of T-helper cells, T-cells and lymphocytes compared with control females. These alterations were not observed in corresponding male comparisons. There were no differences in the pokeweed mitogen (PWM) response between the CFS and control groups. However, in control subjects, a significant association was observed between pokeweed mitogen responses and Rh(D) antigen status, whereas no similar association was measured in CFS patients. Rh(D)-negative control subjects had a significantly increased mitogen response compared with Rh(D)-positive subjects, whereas in CFS patients, no difference was found. It was concluded that future blood parameter and lymphocyte mitogen response studies in CFS patients should bc controlled for sex and Rh status, respectively.
Tirelli U, Chierichetti F, Tavio M, Simonelli C, Bianchin G, Zanco P,	Division of Medical Oncology and Acquired Immunodeficiency	Brain positron emission tomography (PET) in chronic fatigue	Am J Med 1998 Sep 28;105(3A):54S-58S	Chronic fatigue syndrome (CFS) has been widely studied by neuroimaging techniques in recent years with conflicting results. In particular, using single-photon emission computed tomography (SPECT) and perfusion tracers, hypoperfusion has been found

Ferlin G.	Syndrome, Centro di Riferimento Oncologico, Aviano, Italy.	syndrome: preliminary data.		in several brain regions, although the findings vary across research centers. The objective of this study was to investigate brain metabolism of patients affected by CFS, using [18F]fluorine-deoxyglucose (18FDG) positron emission tomography (PET). We performed 18FDG PET in 18 patients who fulfilled the criteria of the working case definition of CFS. Twelve of the 18 patients were females; the mean age was 34 15 years (range, 15-68) and the median time from CFS diagnosis was 16 months (range, 9-138). Psychiatric diseases and anxiety/neurosis were excluded in all CFS patients. CFS patients were compared with a group of 6 patients affected by depression (according to DSM IV-R) and 6 age-matched healthy controls. The CFS patients were not taking any medication at the time of PET, and depressed patients were drug-free for at least 1 week before the PET examination. The PET images examined 22 cortical and subcortical areas. CFS patients showed a significant hypometabolism in right mediofrontal cortex (P = 0.010) and brainstem (P = 0.013) in comparison with the healthy controls. Moreover, comparing patients affected by CFS and depression, the latter group showed a significant and severe hypometabolism of the medial and upper frontal regions bilaterally (P = 0.037-0.001), whereas the metabolism of brain stem was normal. Brain 18FDG PET showed specific metabolism abnormalities in patients with CFS in comparison with both healthy controls and depressed patients. The most relevant result of our study is the brain stem hypometabolism which, as reported in a perfusion SPECT study, seems to be a marker for the in vivo diagnosis of CFS.
Treib J, Fernandez A, Haass A, Grauer MT, Holzer G, Woessner R.	Department of Neurology, University of the Saarland, Homburg, Germany.	Clinical and serologic follow-up in patients with neuroborreliosis.	Neurology 1998 Nov;51(5):1489-91Comment in: Neurology. 1999 Sep 11;53(4):895-6	The authors performed a clinical and serologic follow-up study after 4.2 1.2 years in 44 patients with clinical signs of neuroborreliosis and specific intrathecal antibody production. All patients had been treated with ceftriaxone 2 g/day for 10 days. Although neurologic deficits decreased significantly, more than half the patients had unspecific complaints resembling a chronic fatigue syndrome and showed persisting positive immunoglobulin M serum titers for Borrelia in the Western blot analysis.
Tuck I, Human N.	Department of Nursing Systems, Community and Psychiatric Mental Health Nursing, School of Nursing, Virginia Commonwealth University, Richmond 23298-0567, USA.	The experience of living with chronic fatigue syndrome.	J Psychosoc Nurs Ment Health Serv 1998 Feb;36(2):15-9	1. Chronic fatigue syndrome (CFS) is a condition that affects the total person, body, mind, and spirit. 2. CFS sufferers describe the experience as being in the illness, remembering life before the illness, and living with the symptoms. 3. Empathy and compassion are essential components of providing nursing care for clients with CFS.
van de Luit L, van der Meulen J, Cleophas TJ, Zwinderman AH.	Department of Medicine, Merwede Hospital Dordrecht, The Netherlands.	Amplified amplitudes of circadian rhythms and nighttime hypotension in patients with chronic fatigue	Angiology 1998 Nov;49(11):903-8	Fatigue is an important symptom of a disturbed circadian rhythm. To date, no studies of circadian rhythms in patients with chronic fatigue syndrome (CFS) have been published. The objectives of the study were to study rhythms of heart rate and systolic and diastolic blood pressure in patients with chronic fatigue syndrome compared with age-matched normotensive controls and to study the effects of

		syndrome: improvement by inopamil but not by melatonin.		melatonin and inopamil on such rhythms. Ambulatory blood pressure (ABP) measurements (Space Lab, Inc, validated) of 18 patients with CFS were made according to the 1987 U.S. Center for Disease Control Criteria, and measurements of 12 age-matched normotensive controls were used in a cosinor analysis of the two groups. The effects of melatonin and inopamil on ABP were studied subsequently in four patients in an 8-week open-label evaluation. One patient was hypertensive (diastolic blood pressure > 90 mm Hg at least once every 4 hours), and was, therefore, excluded. The data of the remaining 17 patients (15 women, 2 men) revealed a significant 12-hour rhythm in heart rate and 24-hour rhythm in systolic and diastolic blood pressure with 95% confidence intervals not significantly different from sinusoidal patterns. Although these rhythms were synchronous with the control group rhythms, their amplitudes were not and showed, respectively, 2.8, 2.8, and 9.0 times the size of the control group rhythms ($p < 0.001$, $p < 0.001$, and $p < 0.0001$, respectively). Systolic blood pressures in the patients with CFS were consistently below 100 mm Hg during the nighttime. In a subsequent pilot study of four patients from the study population treated with melatonin 4 mg daily and inopamil 200 mg daily for 4 weeks, inopamil reduced nighttime hypotension ($p < 0.05$), whereas melatonin increased nighttime hypotension ($p < 0.02$). Patients with CFS have increased amplitudes of circadian rhythms and systolic blood pressures consistently below 100 mm Hg during the nighttime. Positive inotropic compounds may be beneficial in such patients, but melatonin may not be.
Vercoulen JH, Bazelmans E, Swanink CM, Galama JM, Fennis JF, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands. j.vercoulen@cksmps.kun.nl	Evaluating neuropsychological impairment in chronic fatigue syndrome.	J Clin Exp Neuropsychol 1998 Apr;20(2):144-56	This study was designed to provide an estimate of the prevalence of neuropsychological impairment in chronic fatigue syndrome (CFS), to evaluate the concordance between impairment found on standardized tests and self-reported neuropsychological problems, and to study the relationship between neuropsychological functioning and fatigue severity and psychological processes. We adopted an individual approach to determine neuropsychological impairment as contrasted with the group-comparisons approach used in previous studies. Also, correction for premorbid functioning and confounders was done on an individual basis. The results show that a minority of participants were impaired in neuropsychological functioning. There was no relationship between neuropsychological impairment on standardized tests and self-reported memory and concentration problems. Neuropsychological functioning was not related to fatigue or depression. Slowed speed of information processing and motor speed were related to low levels of physical activity.
Vercoulen JH, Swanink CM, Galama JM, Fennis JF, Jongen PJ, Hommes OR, van der Meer JW, Bleijenberg	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	The persistence of fatigue in chronic fatigue syndrome and multiple sclerosis: development of a	J Psychosom Res 1998 Dec;45(6):507-17	The cause of chronic fatigue syndrome (CFS) is unknown. With respect to factors perpetuating fatigue, on the other hand, a model has been postulated in the literature in which behavioral, cognitive, and affective factors play a role in perpetuating fatigue. In the present study, this hypothesized model was tested on patients with CFS and on fatigued patients with multiple sclerosis (MS). The model

G.		model.		was formulated in terms of cause-and-effect relationships and an integral test of this model was performed by the statistical technique, "structural equation modeling," in 51 patients with chronic fatigue syndrome and 50 patients with multiple sclerosis matched for age, gender, and education. Attributing complaints to a somatic cause produced low levels of physical activity, which in turn had a causal effect on fatigue severity. Depression had to be deleted from the model. Sense of control over symptoms and focusing on bodily symptoms each had a direct causal effect on fatigue. The model showed an excellent fit for CFS patients, but was rejected for MS patients. Therefore, a new model for MS patients had to be developed in which sense of control had a causal effect on fatigue. In the MS model, no causal relationship was found between the physical state as measured by the Expanded Disability Status Score (EDSS) and fatigue or functional impairment. The present study shows that cognitive and behavioral factors are involved in the persistence of fatigue. Treatment should be directed at these factors. The processes involved in the subjective experience of fatigue in CFS were different from the processes related to fatigue in MS.
Vilikus Z, Mareckova H, Janatkova I, Krystufkova O, Barackova M, Boudova L, Brandejsky P, Fucikova T.	Ustav telovychovneho lekarstvi a Ustav klinicke imunologie 1. lekarske fakulty Univerzity Karlovy, Praha, Czech Republic. zdenek vilikus@medicom.cz	[Risk factors for ischemic heart disease in patients with chronic fatigue syndrome].[article in Czech]	Sb Lek 1998;99(1):53-61	Risk factors of coronary artery disease (CAD) between a group of patients suffering of chronic fatigue syndrome (CFS) and a control group of healthy persons (whose exercise activity was not health-limited) were compared. Thirty three patients (27 women, 6 men, average age 39.9 11.7 years) and the same number of controls matched in age (39.8 10.3 years), gender and body weight. The Minnesota Questionnaire (by Taylor) and the Compendium of Physical Activities (by Ainsworth) were used to estimate total energetic expenditure in exercise activity as well as in job. The risk factors of CAD in the patients with CFS were not higher than in the control group. Aerobic physical fitness, basic anthropometric data, blood pressure, spectrum of blood lipoproteins, blood uric acid and smoking habits were not different between the compared groups. Patients suffering from CFS had lower total energetic expenditure in exercise activity. Nevertheless, this significant difference in sports activity was not large enough to cause any difference in risk factors of CAD between the CFS patients and the control group.
Visser J, Blauw B, Hinloopen B, Brommer E, de Kloet ER, Kluft C, Nagelkerken L.	Division of Immunological and Infectious Diseases, TNO Prevention and Health, Leiden Amsterdam Center for Drug Research, The Netherlands.	CD4 T lymphocytes from patients with chronic fatigue syndrome have decreased interferon-gamma production and increased sensitivity to dexamethasone.	607: J Infect Dis 1998 Feb;177(2):451-4	A disturbed hypothalamus-pituitary-adrenal gland axis and alterations at the immune system level have been observed in patients with chronic fatigue syndrome (CFS). Glucocorticoids are known to modulate T cell responses; therefore, purified CD4 T cells from CFS patients were studied to determine whether they have an altered sensitivity to dexamethasone (DEX). CD4 T cells from CFS patients produced less interferon-gamma than did cells from controls; by contrast, interleukin-4 production and cell proliferation were comparable. With CD4 T cells from CFS patients (compared with cells from controls), a 10- to 20-fold lower DEX concentration was needed to achieve 50% inhibition of interleukin-4 production and proliferation, indicating an increased sensitivity to DEX in CFS patients. Surprisingly, interferon-

				gamma production in patients and controls was equally sensitive to DEX. A differential sensitivity of cytokines or CD4 T cell subsets to glucocorticoids might explain an altered immunologic function in CFS patients.
Vojdani A, Choppa PC, Tagle C, Andrin R, Samimi B, Lapp CW.	Immunosciences Laboratory, Beverly Hills, CA 90211, USA. immunsi@ix.netcom.com	Detection of Mycoplasma genus and Mycoplasma fermentans by PCR in patients with Chronic Fatigue Syndrome.	FEMS Immunol Med Microbiol 1998 Dec;22(4):355-65	Mycoplasma fermentans and other Mycoplasma species are colonizers of human mucosal surfaces and may be associated with human immunodeficiency virus infection. While many infectious agents have been described in different percentages of patients with Chronic Fatigue Syndrome (CFS), little is known about the prevalence of mycoplasmas and especially M. fermentans in CFS patients. A polymerase chain reaction (PCR)-based assay was used to detect Mycoplasma genus and M. fermentans genomes in peripheral blood mononuclear cells (PBMC) of CFS patients. Blood was collected from 100 patients with CFS and 50 control subjects. The amplified products of 717 bp of Mycoplasma genus, and 206 bp of M. fermentans were detected in DNA purified from blood samples in 52% and 34% of CFS samples, respectively. In contrast, these genomes were found in only 14% and 8% of healthy control subjects respectively ($P < 0.0001$). All samples were confirmed by Southern blot with a specific probe based on internal sequences of the expected amplification product. Several samples, which were positive for Mycoplasma genus, were negative for M. fermentans indicating that other Mycoplasma species are involved. A quantitative PCR was developed to determine the number of M. fermentans genome copies present in 1 microg of DNA for controls and CFS patients. Mycoplasma copy numbers ranging from 130 to 880 and from 264 to 2400 were detected in controls and CFS positive subjects, respectively. An enzyme immunoassay was applied for the detection of antibodies against p29 surface lipoprotein of M. fermentans to determine the relationship between M. fermentans genome copy numbers and antibody levels. Individuals with high genome copy numbers exhibited higher IgG and IgM antibodies against M. fermentans specific peptides. Isolation of this organism by culture from clinical specimens is needed in order to demonstrate specificity of signal detected by PCR in this study.
Vollmer-Conna U, Lloyd A, Hickie I, Wakefield D.	Inflammation Research Unit, School of Pathology, University of New South Wales, Sydney, Australia.	Chronic fatigue syndrome: an immunological perspective.	Aust N Z J Psychiatry 1998 Aug;32(4):523-7	OBJECTIVE: The aim of this study is to review research examining an immunological basis for chronic fatigue syndrome (CFS) and to discuss how a disturbance in immunity could produce central nervous system (CNS)-mediated symptoms. METHOD: Data relevant to the hypothesis that abnormal cytokine release plays a role in the pathogenesis of CFS are reviewed as well as recent evidence relating to potential mechanisms by which immune products may enter the brain and produce a disturbance in CNS processes. RESULTS: Examinations of cytokine levels in patients with CFS have produced inconclusive results. Recent evidence suggests that abnormal release of cytokines within the CNS may cause neural dysfunction by a variety of complex mechanisms. CONCLUSION: Neuropsychiatric symptoms in patients with CFS may be more closely related to disordered cytokine production by glial cells within the CNS than to circulating cytokines. This possibility is discussed in

				the context of unresolved issues in the pathogenesis of CFS. Review Literature
Ware NC.	Department of Social Medicine, Harvard Medical School, Boston, Massachusetts 02115, USA. nware@warren.med.harvard.edu	Sociosomatics and illness in chronic fatigue syndrome.	Psychosom Med 1998 Jul-Aug;60(4):394-401Comment in: Psychosom Med. 1999 Mar-Apr;61(2):256	OBJECTIVE: This study examines social processes that construct the course of chronic illness. Specifically, it identifies and describes mechanisms that constitute the process of role constriction in employment for individuals with chronic illness. METHOD: Sixty-six persons meeting the Centers for Disease Control case definition of chronic fatigue syndrome (CFS) participated in a longitudinal study involving three waves of data collection over 3 years. Qualitative and quantitative methods were combined in the research, which included face-to-face semistructured interviews, telephone interviews, and self-report questionnaires. Materials presented in this study are drawn principally from the Year 1 face-to-face and telephone interviews. RESULTS: When patterns of symptoms and of the illness course in CFS intersect with work requirements, they impede performance and place ill individuals at risk for job loss. Persons with CFS devise and implement specific strategies to resist role constriction and remain in the work force. CONCLUSIONS: Role constriction is a social process of marginalization in chronic illness. Opposing forces of marginalization and resistance define the social course in chronic illness and suggest that chronicity can be thought of as a marginalized position in social space.
Watson WS, Donald C. McMillan, Abhijit Chaudhuri, Peter O. Behan		Increased Resting Energy Expenditure in the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1998: 4(4): 3 - 14	It has been suggested that resting energy expenditure may be raised in chronic fatigue syndrome due to an upregulation of transmembrane ion transport. We measured resting energy expenditure by indirect calorimetry in 11 women with chronic fatigue and in 11 healthy women. Total body potassium, by whole body counting, and total body water, extracellular water and intracellular water, by a bioelectrical impedance method, were also measured. When individual resting energy expenditure was predicted on the basis of total body potassium values for the chronic fatigue group, 5 out of 11 of these subjects had resting energy expenditure above the upper limit of normal as defined by the control group data. This is consistent with the hypothesis that there is upregulation of the sodium-potassium pump in chronic fatigue syndrome.
Wearden AJ, Morriss RK, Mullis R, Strickland PL, Pearson DJ, Appleby L, Campbell IT, Morris JA.	University of Manchester, Department of Psychiatry, Withington Hospital.	Randomised, double-blind, placebo-controlled treatment trial of fluoxetine and graded exercise for chronic fatigue syndrome. Erratum in: Br J Psychiatry 1998 Jul;173:89Comment in: Br J Psychiatry. 1998 Jun;172:491-2 Br J Psychiatry. 1998	Br J Psychiatry 1998 Jun;172:485-90	BACKGROUND: The Joint Working Group of the Royal Colleges of Physicians, Psychiatrists and General Practitioners (1996) recommended graded exercise and antidepressants for patients with chronic fatigue syndrome. We assessed efficacy and acceptability of these treatments. METHOD: Six-month prospective randomised placebo and therapist contact time controlled trial with allocation to one of four treatment cells: exercise and 20 mg fluoxetine, exercise and placebo drug, appointments only and 20 mg fluoxetine, appointments and placebo drug. Drug treatment was double blind and patients were blind to assignment to exercise or appointments. RESULTS: Ninety-six (71%) of 136 patients completed the trial. Patients were more likely to drop out of exercise than non-exercise treatment (P = 0.05). In an intention to treat analysis, exercise resulted in fewer patients with case level fatigue than appointments only at 26 weeks (12 (18%) v. 4 (6%) respectively P =

		Oct;173:353 Br J		0.025) and improvement in functional work capacity at 12 (P = 0.005) and 26 weeks (P = 0.03). Fluoxetine had a significant effect on depression at week 12 only (P = 0.04). Exercise significantly improved health perception (P = 0.012) and fatigue (P = 0.028) at 28 weeks. CONCLUSIONS: Graded exercise produced improvements in functional work capacity and fatigue, while fluoxetine improved depression only.
Weiss B.	Department of Environmental Medicine, University of Rochester Medical Center, NY 14642, USA.	Neurobehavioral properties of chemical sensitivity syndromes.	Neurotoxicology 1998 Apr;19(2):259-68	Chemical sensitivity Syndromes refers to aggregations of symptoms marked by largely subjective neurobehavioral complaints and hypothesized links to immune system dysfunction. The entities reviewed here consist of the Multiple Chemical Sensitivity Syndrome, the Sick Building Syndrome, the Chronic Fatigue Syndrome, and the Gulf War Syndrome. Except for the Chronic Fatigue Syndrome, toxic chemical exposures are accorded a significant role in their etiology. The connections are ambiguous because of the variety of chemical agents cited and, for the most part, the relatively low levels at which exposures occur. Conventional clinical signs are also typically lacking. Explanatory mechanisms include psychiatric diagnoses such as somatization, behavioral mechanisms such as conditioning and generalization, neuropharmacological mechanisms such as sensitization, and psychoneuroimmunological mechanisms such as those involving the hypothalamic-pituitary-adrenal axis. Laboratory animal experimentation and controlled clinical trials, especially with inhaled material, provide the means for exploring the proffered explanations.
Wessely S.		The epidemiology of chronic fatigue syndrome.	Epidemiol Psichiatr Soc 1998 Jan-Apr;7(1):10-24	
White PD, Thomas JM, Amess J, Crawford DH, Grover SA, Kangro HO, Clare AW.	St Bartholomew's, London.	Incidence, risk and prognosis of acute and chronic fatigue syndromes and psychiatric disorders after glandular fever.	Br J Psychiatry 1998 Dec;173:475-81	BACKGROUND: The role of viruses in the aetiology of both chronic fatigue syndrome (CFS) and depressive illness is uncertain. METHOD: A prospective cohort study of 250 primary care patients, presenting with glandular fever or an ordinary upper respiratory tract infection (URTI). RESULTS: The incidence of an acute fatigue syndrome was 47% at onset, after glandular fever, compared with 20% with an ordinary URTI (relative risk 2.3, 95% CI 1.3-4.1). The acute fatigue syndrome lasted a median (interquartile range) of eight weeks (4-16) after glandular fever, but only three weeks (2-4) after an URTI. The prevalence of CFS was 9-22% six months after glandular fever, compared with 0-6% following an ordinary URTI, with relative risks of 2.7-5.1. The most conservative measure of the incidence of CFS was 9% after glandular fever, compared with no cases after an URTI. A conservative estimate is that glandular fever accounts for 3113 (95% CI 1698-4528) new cases of CFS per annum in England and Wales. New episodes of major depressive disorder were triggered by infection, especially the Epstein-Barr virus, but lasted a median of only three weeks. No psychiatric disorder was significantly more prevalent six months after onset than before. CONCLUSIONS: Glandular fever is a significant risk factor for both acute and chronic fatigue syndromes. Transient new major depressive disorders

				occur close to onset, but are not related to any particular infection if they last more than a month.
Whiteside TL, Friberg D.	University of Pittsburgh Cancer Institute, Pennsylvania 15213-2582, USA.	Natural killer cells and natural killer cell activity in chronic fatigue syndrome.	Am J Med 1998 Sep 28;105(3A):27S-34S	Chronic fatigue syndrome (CFS) is associated with insidious and persistent immunologic abnormalities that have proved difficult to reproduce. The heterogeneity of CFS, the variable quality of immunologic assays and their performance, along with an almost complete absence of longitudinal studies of cellular immune abnormalities in CFS may explain this difficulty. However, in a significant proportion of cases, low levels of natural killer (NK) cell activity have been reported. This article will explore the mechanisms responsible for low NK cell activity, discuss the relation between levels of NK cell activity and health/disease, describe new findings on NK cell-brain interactions, and put forth a specific hypothesis for the role of NK cells in the pathogenesis of CFS.
Wilke WS, Fouad-Tarazi FM, Cash JM, Calabrese LH.	Department of Rheumatic and Immunologic Disease, Cleveland Clinic Foundation, OH 44195, USA.	The connection between chronic fatigue syndrome and neurally mediated hypotension.	Cleve Clin J Med 1998 May;65(5):261-6	Research from several groups of investigators indicates that some patients with chronic fatigue syndrome have abnormal vasovagal or vasodepressor responses to upright posture. If confirmed, these findings may explain some of the symptoms of chronic fatigue syndrome. There is also speculation that neurally mediated hypotension may be present in fibromyalgia. This article discusses the original research in this area, the results of follow-up studies, and the current approach to treating patients with chronic fatigue syndrome in whom neurally mediated hypotension is suspected.
Wood B, Wessely S, Papadopoulos A, Poon L, Checkley S.	Institute of Psychiatry, London, UK.	Salivary cortisol profiles in chronic fatigue syndrome.	Neuropsychobiology 1998;37(1):1-4	Salivary cortisol profiles (hourly sampling over a 16-hour period) of 10 patients with chronic fatigue syndrome (CFS) but without concurrent depressive disorder were compared with those of 10 healthy volunteers matched for age, sex and menstrual cycle. The mean saliva cortisol concentration over the 16-hour period was slightly but significantly greater in the patients than the controls ($p < 0.05$). These findings are at variance with earlier reports that CFS is a hypocortisolaemic state and suggest that in CFS the symptom of fatigue is not caused by hypocortisolaemia.
Wright JB, Beverley DW.	Lime Trees Child and Family Unit, York, UK.	Chronic fatigue syndrome.	Arch Dis Child 1998 Oct;79(4):368-74	
Young AH, Sharpe M, Clements A, Dowling B, Hawton KE, Cowen PJ.	University Department of Psychiatry, Warneford Hospital, Oxford, United Kingdom.	Basal activity of the hypothalamic-pituitary-adrenal axis in patients with the chronic fatigue syndrome (neurasthenia).	Biol Psychiatry 1998 Feb 1;43(3):236-7	BACKGROUND: Impairments in both basal activity and activation of the hypothalamic-pituitary-adrenal axis (HPA) have been reported in chronic fatigue syndrome (CFS; neurasthenia). We sought to replicate these findings and examined basal activity of the HPA in a carefully selected sample of patients with CFS. METHODS: Basal activity of the HPA was assessed using salivary and urinary cortisol collection over a 24-hour period in 22 (12 male; 10 female) patients meeting criteria for CFS and appropriate controls. RESULTS: Salivary and urinary cortisol measures did not differ between CFS patients and controls. CONCLUSIONS: Basal activity of the HPA was not reduced in CFS patients. Reasons for the failure to replicate previous findings are discussed.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Albus C.	Institut und Poliklinik fur Psychosomatik und Psychotherapie, Universitat zu Koln.	[Chronic fatigue syndrome--a disease entity or an unspecified psychosomatic disorder]?[article in German]	Z Arztl Fortbild Qualitatssich 1997 Dec;91(8):717-21	In spite of its nature as an often severe and disabeling disease, it is still unclear, whether the Chronic Fatigue Syndrome (CFS) is an entire disease of its own right or not. Moreover, there is a growing evidence that patients with CFS belong to an inhomogeneous group with different etiologic constellations. Specific somatic factors, e.g. viruses, seem to be less important for onset than certain personality-traits like depressiveness and workaholism. These traits lead to an increased vulnerability to unspecific psychological or biological stressors that may cause chronic fatigue by complex psychosomatic interferences. Concerning diagnosis, there are no specific methods or results available, the same is true for pharmacological treatment. As a consequence, practitioners should be aware not to miss a somatic disease causing fatigue, and, parallel to this, start right from the beginning talking about the psychosomatic background of CFS. Furthermore, psychotherapy has shown to be effective in CFS.
Allain TJ, Bearn JA, Coskeran P, Jones J, Checkley A, Butler J, Wessely S, Miell JP.	Department of Medicine, Kings College School of Medicine and Dentistry, London, United Kingdom.	Changes in growth hormone, insulin, insulinlike growth factors (IGFs), and IGF-binding protein-1 in chronic fatigue syndrome.	Biol Psychiatry 1997 Mar 1;41(5):567-73	Chronic fatigue syndrome (CFS) is characterized by severe physical and mental fatigue of central origin. Similar clinical features may occur in disorders of the hypothalamopituitary axis. The aim of the study was to determine whether patients with CFS have abnormalities of the growth hormone/insulinlike growth factor (GH-IGF) axis basally or following hypothalamic stimulation with insulin-induced hypoglycemia. We compared levels of GH, IGF-I, IGF-II, IGF-binding protein-1 (IGFBP-1), insulin, and C-peptide in nondepressed CFS patients and normal controls. We found attenuated basal levels of IGF-I (214 +/- 17 vs. 263.4 +/- 13.4 micrograms/L, p = .036) and IGF-II (420 +/- 19.8 vs. 536 +/- 24.3 micrograms/L, p = .02) in CFS patients and a reduced GH response to hypoglycemia (peak GH; 41.9 +/- 11.5 vs. 106.0 +/- 25.6 mU/L, p = .017). Insulin levels were higher (7.6 +/- 1.0 vs. 4.3 +/- 0.8 mU/L, p = .02) and IGFBP-1 levels were lower (19.7 +/- 4.6 vs. 43.2 +/- 2.7 mg/L, p = .004) in CFS patients compared with controls. This study provides preliminary data abnormalities of the GH-IGF axis in CFS. It is not apparent whether these changes are components of a primary pathological process or are acquired secondary to behavioral aspects of CFS such as reduced physical activity.
Anderson JS, Ferrans CE.	University of Illinois at Chicago Medical Center, Department of Psychiatry 60612, USA.	The quality of life of persons with chronic fatigue syndrome.	J Nerv Ment Dis 1997 Jun;185(6):359-67	This descriptive study used a between-methods triangulation design to analyze the multiple dimensions of quality of life in persons with chronic fatigue syndrome (CFS). This method, which refers to the combination of both quantitative and qualitative methods in the same study, allowed the authors to obtain more comprehensive and robust data than could be obtained by either method alone. A convenience sample of 110 persons with CFS completed the quality of life index and CFS questionnaire, and a subset of 22 persons were interviewed regarding their lived experience with CFS. Overall scores on the

				quality of life index were significantly lower in CFS than for other chronic illness groups. Subjects reported the lowest quality of life scores in health and functioning domain. Indepth interviews provided a more complete understanding of the quality of life in CFS and further explained the low ratings that were found on the quality of life index. The findings suggest that quality of life is particularly and uniquely disrupted in CFS.
Ax S, Gregg VH, Jones D.	Birkback College, University of London, England.	Chronic fatigue syndrome: sufferers' evaluation of medical support.	J R Soc Med 1997 May;90(5):250-4	In response to reports of negative cooperation between sufferers of chronic fatigue syndrome (CFS) and their doctors, semi-structured interviews were conducted with sufferers from two different patient samples. Satisfaction with support received and with medical professionals in general was low. Sufferers complained about insufficient informational as well as emotional support from their doctors, and as a consequence most opted for alternative or complementary forms of treatment. In addition, disagreements over illness aetiology and treatment precluded effective cooperation. If satisfaction and compliance are to improve, sufferers will need more information about CFS and more support.
Baschetti R.		Etiology of chronic fatigue syndrome.	Am J Med 1997 Apr;102(4):422-3 Comment on: Am J Med. 1996 May;100(5):548-54	
Baschetti R.		Lung function test findings in patients with chronic fatigue syndrome (CFS)	Aust N Z J Med 1997 Jun;27(3):346 Comment on: Aust N Z J Med. 1996 Aug;26(4):563-4	
Baschetti R.		Similarity of symptoms in chronic fatigue syndrome and Addison's disease.	Eur J Clin Invest 1997 Dec;27(12):1061-2 Comment on: Eur J Clin Invest. 1997 Apr;27(4):257-67	
Baschetti R.		Chronic fatigue syndrome.	QJM 1997 Nov;90(11):723 Comment on: QJM. 1997 Mar;90(3):223-33	
Bazelmans E, Vercoulen JH, Galama JM, van Weel C, van der Meer JW, Bleijenberg G.	Afd. Medische Psychologie, Academisch Ziekenhuis, Nijmegen.	[Prevalence of chronic fatigue syndrome and primary fibromyalgia syndrome in The Netherlands].[article in Dutch] Erratum in: Ned	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1520-3	OBJECTIVE: To determine the prevalence of chronic fatigue syndrome (CFS) and of primary fibromyalgia syndrome (PFS) in the Netherlands. DESIGN: Questionnaire. SETTING: Department of Medical Psychology, University Hospital Nijmegen, the Netherlands. METHOD: A questionnaire was mailed to all the 6657 general practitioners in the Netherlands in order to inform them of the existence of CFS and to ask them if they had any CFS or PFS patients in their practices.

		Tijdschr Geneeskd 1997 Sep 13;141(37):2686		RESULTS: Sixty percent (n = 4027) of the general practitioners returned the questionnaire. Of all the general practitioners, 27% said they had no CFS patients, 23% said they had 1 CFS patient, while 21% had 2 CFS patients, and 29% said they had 3 or more CFS patients in their practice. Concerning PFS the results were 17% (no PFS patients), 18%, 18% and 47%, respectively. With a mean practice of 2486 patients per general practice, the estimated prevalence of CFS was 112 per 100,000 and that of PFS 157 per 100,000 persons. Of the CFS patients 81% were women and 55% were 25-44 years old; for PFS these figures were 87% and 48% respectively. CONCLUSION: Extrapolation of the study results indicates that there are at least 17,000 CFS patients and 24,000 PFS patients in the Netherlands. The found prevalence is probably an under-estimation.
Beh HC.	Department of Psychology, University of Sydney, New South Wales, Australia.	Effect of noise stress on chronic fatigue syndrome patients.	J Nerv Ment Dis 1997 Jan;185(1):55-8	
Bell DS		Illness Onset Characteristics in Children with Chronic Fatigue Syndrome and Idiopathic Chronic Fatigue	Journal of Chronic Fatigue Syndrome 1997: 3(2): 43 - 51	Twenty-three children and adolescents with unexplained chronic fatigue were evaluated with emphasis upon illness-onset characteristics. Ten subjects had an acute, "flu-like" onset, and four of these subjects had episodes of mild fatigue in the year prior to onset. The thirteen remaining subjects had a gradual onset of chronic fatigue, the majority describing increasing episodes of apparent infectious illnesses associated with fatigue. In these subjects, the fatigue eventually became constant, causing reduction in overall activity levels. In a comparison of subjects who did and did not meet diagnostic criteria for chronic fatigue syndrome, there were no differences in onset characteristics, but differences were noted in illness severity. The majority of children and adolescents with unexplained chronic fatigue had a gradual onset of debilitating symptoms
Bell IR, Michele E. Walsh, Anita Gross, Jane Gersmeyer, Gary E. Schwartz, Philip Kanof		Cognitive Dysfunction and Disability in Geriatric Veterans with Self-Reported Intolerance to Environmental Chemicals	Journal of Chronic Fatigue Syndrome 1997: 3(3): 15 - 42	The symptom of sensitivity or intolerance to low levels of environmental chemicals (CI) is a characteristic of several clinical conditions, such as multiple chemical sensitivity (MCS), chronic fatigue syndrome (CFS), fibromyalgia (FM), and the "Persian Gulf Syndrome." Lesser degrees of CI also occur in 15-30% of non-clinical populations. The present study examined the prevalence and concomitant health patterns of CI in elderly veterans in a VA primary care medical clinic (N = 160, primarily men). Thirty-seven percent of the sample endorsed the screening question asking whether or not they considered themselves "especially sensitive to certain chemicals." The group with CI reported a significantly higher rate of physical disability and increased susceptibility to becoming sick. The CI group reported significantly decreased rates of current cigarette smoking and alcohol use. Those with and those without CI did not differ in level of depression or in past occupational chemical exposures.

				However, the CI group scored significantly lower on a screening test for cognitive dysfunction, including a verbal memory performance pattern consistent with early dementia. When the groups were subdivided into individuals high and low in depression, the depressives without CI reported the highest rate of prior occupational exposure to pesticides. The subgroup who had both CI and depression performed most poorly on the attention/concentration screening test. Taken together, the data suggest that CI as a symptom is extremely common in older male veterans and may be a marker for increased risk of further cognitive decline and/or loss of functional independence. However, the role of occupational chemical exposures in initiating CI in these non-MCS patients is unclear and requires additional study.
Bennett A.		A view of the violence contained in chronic fatigue syndrome.	J Anal Psychol 1997 Apr;42(2):237-51	In this paper I ask whether there might be any one particular psychopathology likely to be linked specifically with the physical illness known as chronic fatigue syndrome (CFS) or myalgic encephalomyelitis (ME), and whether CFS/ME aids and abets and "fits' an original mental state. I think the question cannot yet be answered. However it is my hypothesis that in some personality structures the onset of CFS/ ME following a physical illness exacerbates negativity and is an aspect of ordinary depression where there is a lowering of energy levels and a loss of zest for life, or it may reveal the pathological aspect of unresolved rage. Depending on the degree of pathological disturbance, working with and through the rage may or may not result in a resolution of the symptoms of ME. In this paper I consider some of the problems in the transference and countertransference relationship, which make it extremely difficult to separate out reality from phantasy. There is then the further problem of the denial of the psyche by the patient as part of the violence inherent in the illness. One case is presented, an example of ME in a borderline male patient in whom resolution could not be achieved.
Bennett AL, Chao CC, Hu S, Buchwald D, Fagioli LR, Schur PH, Peterson PK, Komaroff AL.	Chronic Fatigue Syndrome Cooperative Research Center, Brigham and Women's Hospital, Boston, Massachusetts, USA.	Elevation of bioactive transforming growth factor-beta in serum from patients with chronic fatigue syndrome.	J Clin Immunol 1997 Mar;17(2):160-6	The level of bioactive transforming growth factor-beta (TGF-beta) was measured in serum from patients with chronic fatigue syndrome (CFS), healthy control subjects, and patients with major depression, systemic lupus erythematosis (SLE), and multiple sclerosis (MS) of both the relapsing/remitting (R/R) and the chronic progressive (CP) types. Patients with CFS had significantly higher levels of bioactive TGF-beta levels compared to the healthy control major depression, SLE, R/R MS, and CP MS groups ($P < 0.01$). Additionally, no significant differences were found between the healthy control subjects and any of the disease comparison groups. The current finding that TGF-beta is significantly elevated among patients with CFS supports the findings of two previous studies examining smaller numbers of CFS patients. In conclusion, TGF-beta levels were significantly higher in CFS patients compared to patients with various diseases known to be associated with immunologic abnormalities and/or pathologic fatigue. These

				findings raise interesting questions about the possible role of TGF-beta in the pathogenesis of CFS.
Bennett AL, Mayes DM, Fagioli LR, Guerriero R, Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Boston, MA 02115, USA.	Somatomedin C (insulin-like growth factor I) levels in patients with chronic fatigue syndrome.	J Psychiatr Res 1997 Jan-Feb;31(1):91-6	Chronic fatigue syndrome is a disorder clinically quite similar to fibromyalgia syndrome, and it is of interest to examine if these two syndromes have pathogenetic as well as clinical features in common. Somatomedin C levels have been found to be lower in patients with fibromyalgia syndrome than in healthy controls. An attractive hypothesis relating sleep disturbance, altered somatotropic neuroendocrine function and fibromyalgia symptoms has been put forward as a plausible pathogenic mechanism for fibromyalgia syndrome. We therefore sought to investigate the level of somatomedin C in patients with chronic fatigue syndrome. Somatomedin C levels were determined by radioimmunoassay in frozen serum specimens from 49 patients with CFS and 30 healthy blood donor control subjects of similar age and gender. Somatomedin C levels were higher in patients with CFS than in healthy control subjects (255.3 +/- 68.5 vs 211.9 +/- 76.2, P = 0.01). There was no effect of gender, use of nonsteroidal anti-inflammatory drugs or tricyclic drugs on levels of somatomedin C. There was a tendency for somatomedin C levels to fall with age. In contrast to patients with fibromyalgia, in whom levels of somatomedin C have been found to be reduced, levels in patients with CFS were found to be elevated. Thus, despite the clinical similarities between these two conditions, they may be associated with different abnormalities of sleep and/or of the somatotropic neuroendocrine axis.
Berlin B.		Confronting AIDS in older adults.	N J Med 1997 Nov;94(11):39-41	A 57-year-old corporate executive, married with three grown children, began suffering from severe flu-like symptoms and weight loss. Hospitalized for a week, he was tested for chronic fatigue syndrome and mononucleosis. Finally, with no change in his symptoms, his physician recommended an HIV test. The results were positive.
Bertolin JM, Calvo J.		[Chronic fatigue syndrome. To be or not to be]?[article in Spanish]	Med Clin (Barc) 1997 Apr 19;108(15):577-9 Comment on: Med Clin (Barc). 1997 Apr 19;108(15):561-5	
Bleijenberg G.	Academisch Ziekenhuis, afd. Medische Psychologie, Nijmegen.	[Attributions and chronic fatigue].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1510-2Comment in: Ned Tijdschr Geneeskd. 1997 Nov 29;141(48):2360 Ned Tijdschr Geneeskd. 1997 Nov	It was recently suggested that chronic fatigue is merely a question of attribution. Attribution clearly contributes to the course of chronic fatigue syndrome (CFS) but is not its sole determinant. The presence of strong somatic attributions appears to be one of the perpetuating factors in CFS but not the only one. Many CFS patients present a self-diagnosis, e.g. myalgic encephalomyelitis. Communication problems between patient and doctor easily arise because of different attributions of the complaints. At the start of fatigue somatic attributions are of less importance than later on in the course of the complaints.

			29;141(48):2360-1	In this process an iatrogenic factor might be involved. On the other hand doctors are able to influence these attributions actively in a favourable direction.
Bowman MA, Kirk JK, Michielutte R, Preisser JS. Controlled Clinical Trial Letter		Use of amantadine for chronic fatigue syndrome.	Arch Intern Med 1997 Jun 9;157(11):1264-5	
Bruno RL		Chronic Fatigue, Fainting and Autonomic Dysfunction: Further Similarities Between Post-Polio Fatigue and Chronic Fatigue Syndrome?	Journal of Chronic Fatigue Syndrome 1997: 3(3): 109 - 116	To test the hypothesis that fatigue and fainting occur together, 1,047 polio survivors and 419 non-disabled control subjects were asked about the frequency and cause of fainting and asked to rate their typical daily fatigue severity. Fatigue severity was significantly higher in polio survivors as compared to controls, and in both polio survivors and controls who had fainted, as compared to those who had not. Daily fatigue severity also increased in both groups as the number of lifetime faints increased. Fatigue was significantly higher in controls who fainted one time and three times as compared to controls who had never fainted. Daily fatigue severity was significantly higher in polio survivors who had fainted three, four and five times as compared to those who had never fainted. These findings suggest a physiological relationship between fatigue and fainting, possibly attributable to the close proximity of cardiovascular regulation and brain activation centers within the brain stem. Fatigue and hypotension in patients with chronic fatigue syndrome and in polio
Buchwald D, Pearlman T, Kith P, Katon W, Schmaling K.	Department of Medicine, University of Washington, Seattle, USA.	Screening for psychiatric disorders in chronic fatigue and chronic fatigue syndrome.	J Psychosom Res 1997 Jan;42(1):87-94	Psychiatric disorders are common in chronic fatigue (CF) and chronic fatigue syndrome (CFS). To determine the usefulness of the General Health Questionnaire (GHQ), a self-report measure of psychological distress, in identifying those with psychiatric illnesses, a structured psychiatric interview and the GHQ were administered to 120 CF and 161 CFS patients seen in a referral clinic. Overall, 87 (35%) patients had a current and 210 (82%) a lifetime psychiatric disorder. Compared to patients without psychiatric disorders, GHQ scores above the threshold (> or = 12) were more frequent among patients with current ($p < 0.001$) and lifetime ($p < 0.05$) diagnoses; scores among patients with CF and CFS were similar. Longer illness duration, greater fatigue severity, and current psychiatric disorders were significant predictors of the GHQ score. In CF and CFS, the best sensitivity (0.69-0.76) and specificity (0.51-0.62) were achieved for current psychiatric diagnoses using a threshold score of > or = 12. Thus, patients scoring < 12 on the GHQ are significantly less likely to have a psychiatric disorder.
Buchwald D, Wener MH, Pearlman T, Kith P.	Department of Medicine, University of Washington, Seattle, USA.	Markers of inflammation and immune activation in chronic fatigue and chronic fatigue	J Rheumatol 1997 Feb;24(2):372-6	OBJECTIVE: Chronic fatigue syndrome (CFS) has been hypothesized to result from immune activation. We examined the role of serum markers of inflammation and immune activation among patients with CFS and in those with chronic fatigue (CF) not meeting the case definition. METHODS: Assays for soluble interleukin 2 (IL-2) receptor, IL-6, C-reactive protein, beta 2-microglobulin, and neopterin were

		syndrome.		performed in 153 fatigued patients in a referral clinic. Patients were classified according to whether they met criteria for CFS, reported onset of illness with a viral syndrome or had a temperature > 37.5 degrees C on examination. RESULTS: Compared to control subjects, mean concentrations of C-reactive protein, beta 2-microglobulin, and neopterin were higher in patients with CFS (p < or = 0.01) and CF (p < or = 0.01). Results did not distinguish CFS from CF. IL-6 was elevated among febrile patients compared to those without this finding (p < or = 0.001), but other consistent differences between patient subgroups were not observed. The presence of several markers was highly correlated (p < 0.01). CONCLUSION: Our findings that levels of several markers were significantly correlated points to a subset of patients with immune system activation. Whether this phenomenon reflects an intercurrent, transient, common condition, such as an upper respiratory infection, or is the result of an ongoing illness associated process is unknown. Overall, serum markers of inflammation and immune activation are of limited diagnostic usefulness in the evaluation of patients with CSF and CF.
Cannon JG, Angel JB, Abad LW, Vannier E, Mileno MD, Fagioli L, Wolff SM, Komaroff AL.	Department of Medicine, Tufts University-New England Medical Center, Boston, Massachusetts 02111, USA.	Interleukin-1 beta, interleukin-1 receptor antagonist, and soluble interleukin-1 receptor type II secretion in chronic fatigue syndrome.	J Clin Immunol 1997 May;17(3):253-61	Chronic fatigue syndrome is a condition that affects women in disproportionate numbers, and that is often exacerbated in the premenstrual period and following physical exertion. The signs and symptoms, which include fatigue, myalgia, and low-grade fever, are similar to those experienced by patients infused with cytokines such as interleukin-1. The present study was carried out to test the hypotheses that (1) cellular secretion of interleukin-1 beta (IL-1 beta), interleukin-1 receptor antagonist (IL-1Ra), and soluble interleukin-1 receptor type II (IL-1sRII) is abnormal in female CFS patients compared to age- and activity-matched controls; (2) that these abnormalities may be evident only at certain times in the menstrual cycle; and (3) that physical exertion (stepping up and down on a platform for 15 min) may accentuate differences between these groups. Isolated peripheral blood mononuclear cells from healthy women, but not CFS patients, exhibited significant menstrual cycle-related differences in IL-1 beta secretion that were related to estradiol and progesterone levels (R2 = 0.65, P < 0.01). IL-1Ra secretion for CFS patients was twofold higher than controls during the follicular phase (P = 0.023), but luteal-phase levels were similar between groups. In both phases of the menstrual cycle, IL-1sRII release was significantly higher for CFS patients compared to controls (P = 0.002). The only changes that might be attributable to exertion occurred in the control subjects during the follicular phase, who exhibited an increase in IL-1 beta secretion 48 hr after the stress (P = 0.020). These results suggest that an abnormality exists in IL-1 beta secretion in CFS patients that may be related to altered sensitivity to estradiol and progesterone. Furthermore, the increased release of IL-1Ra and sIL-1RII by cells from CFS patients is consistent with the hypothesis that CFS is associated with chronic, low-level activation of the immune system.

Cannon JG, St Pierre BA.	Intercollege Physiology Program, Pennsylvania State University, University Park 16802-6900, USA.	Gender differences in host defense mechanisms.	J Psychiatr Res 1997 Jan-Feb;31(1):99-113	Extensive studies in both humans and animals have shown that females express enhanced levels of immunoreactivity compared to males. Whereas this provides females with increased resistance to many types of infection, it also makes them more susceptible to autoimmune diseases. This review will focus on gender-related differences in non-specific host defense mechanisms with a particular emphasis on monocyte/macrophage function and a primary product of monocytes: interleukin-1 (IL-1). Immunomodulatory cytokines such as IL-1 are influenced by gender-sensitive hormones, and reciprocally, these cytokines influence gender-specific hormones and tissues. Patients with chronic fatigue syndrome (CFS) are predominantly women, therefore it may be useful to look toward gender-specific differences in immune function to find a key for this poorly understood syndrome.
Chaudhuri A, T. Majeed, T. Dinan, P. O. Behan		Chronic Fatigue Syndrome A Disorder of Central Cholinergic Transmission	Journal of Chronic Fatigue Syndrome 1997: 3(1): 3 - 16	No abstract available
Chester AC, Levine PH.	Georgetown University Medical Center, Washington DC, USA.	The natural history of concurrent sick building syndrome and chronic fatigue syndrome.	J Psychiatr Res 1997 Jan-Feb;31(1):51-7	An outbreak of chronic fatigue syndrome linked with sick building syndrome was recently described as a new association. Whether chronic fatigue syndrome acquired in this setting tends to remit or, as sporadic cases often do, persist, is unknown. To clarify the natural history of chronic fatigue syndrome in association with sick building syndrome the 23 individuals involved in the outbreak were interviewed four years after the onset. In the previous interview one year after the onset of symptoms, 15 (including 5 with chronic fatigue syndrome and 10 with idiopathic chronic fatigue) of the 23 noted fatigue. Three years later 10 of the 15 were "fatigue free" or "much improved". Five were only "some better", "the same", or "worse". Three of the five people previously diagnosed with chronic fatigue syndrome were "much improved" (two) or "fatigue free" (one). The remaining two were seriously impaired, homebound and unable to work. The 10 individuals with substantially improved fatigue (three of the five with chronic fatigue syndrome and seven of the 10 with idiopathic chronic fatigue) were more likely to have noted improvement in nasal and sinus symptoms, sore throats, headaches, and tender cervical lymph nodes when compared to those with a lingering significant fatigue ($p < 0.001$). Upper respiratory symptoms and headaches improved in those with reduced fatigue but remained problematic in those with persisting significant fatigue. We conclude that the fatigue related to sick building syndrome, including chronic fatigue syndrome, is significantly more likely to improve than fatigue identified in sporadic cases of chronic fatigue syndrome.
Chester AC.	Georgetown University Medical Center,	Chronic fatigue syndrome criteria in	J Psychiatr Res 1997 Jan-Feb;31(1):45-50	To determine the prevalence of chronic fatigue syndrome (CFS) criteria in other forms of unexplained chronic fatigue, 297 consecutive outpatients under the age

	Washington D.C., USA.	patients with other forms of unexplained chronic fatigue.		of 40 from a general medicine practice were studied. After excluding the three with chronic fatigue syndrome, the remaining 294 individuals were divided into those with unexplained chronic fatigue (64 patients) those without (the remaining 230 patients). Chronic fatigue syndrome criteria noted to be significantly more common in those with unexplained fatigue compared to those without include: fever, painful adenopathy, muscle weakness, myalgia, headache, migratory arthralgia, neuropsychologic symptoms, and sleep disorder. Like chronic fatigue syndrome, unexplained chronic fatigue often started suddenly. I conclude that the CFS criteria are noted more commonly than expected in other forms of unexplained chronic fatigue.
Chester AC.		Neurally mediated hypotension, chronic fatigue syndrome and upper aerodigestive tract reflexes.	Integr Physiol Behav Sci 1997 Apr-Jun;32(2):160-1	
Clauw DJ, Chrousos GP.	Department of Medicine, Georgetown University Medical Center, Washington, D.C. 20007, USA.	Chronic pain and fatigue syndromes: overlapping clinical and neuroendocrine features and potential pathogenic mechanisms.	Neuroimmunomodulation 1997 May-Jun;4(3):134-53	Patients with unexplained chronic pain and/or fatigue have been described for centuries in the medical literature, although the terms used to describe these symptom complexes have changed frequently. The currently preferred terms for these syndromes are fibromyalgia and chronic fatigue syndrome, names which describe the prominent clinical features of the illness without any attempt to identify the cause. This review delineates the definitions of these syndromes, and the overlapping clinical features. A hypothesis is presented to demonstrate how genetic and environmental factors may interact to cause the development of these syndromes, which we postulate are caused by central nervous system dysfunction. Various components of the central nervous system appear to be involved, including the hypothalamic pituitary axes, pain-processing pathways, and autonomic nervous system. These central nervous system changes lead to corresponding changes in immune function, which we postulate are epiphenomena rather than the cause of the illnesses. Review, Academic
Clauw DJ, Schmidt M, Radulovic D, Singer A, Katz P, Bresette J.	Division of Rheumatology, Immunology and Allergy, Georgetown University Medical Center, Washington, D.C., USA.	The relationship between fibromyalgia and interstitial cystitis.	J Psychiatr Res 1997 Jan-Feb;31(1):125-31	Interstitial cystitis (IC) is a relatively uncommon and enigmatic disorder characterized by pain in the bladder and pelvic region, typically accompanied by urinary urgency and frequency. Fibromyalgia is a more common disorder, with the prominent symptoms being diffuse musculoskeletal pain and fatigue, and it has been well established that there is substantial clinical overlap between fibromyalgia and chronic fatigue syndrome (CFS). Although genitourinary and musculoskeletal symptoms predominate in IC and fibromyalgia respectively, both disorders share a number of features, including similar demographics, "allied conditions" (e.g. irritable bowel syndrome, headaches, etc.), natural history, aggravating factors, and efficacious therapy. We hypothesized that there was substantial clinical overlap between fibromyalgia and IC, and examined cohorts of

				individuals with these two disorders in parallel, to compare the spectrum of symptomatology. Sixty fibromyalgia patients, 30 IC patients, and 30 age-matched healthy controls were questioned regarding current symptomatology. A dolorimeter examination was also performed in the three groups to assess peripheral nociception. We found that the frequency of current symptoms was very similar for the fibromyalgia and IC groups. Both the fibromyalgia and IC patients displayed increased pain sensitivity when compared to healthy individuals, at both tender and control points. These data suggest that IC and fibromyalgia have significant overlap in symptomatology, and that IC patients display diffusely increased peripheral nociception, as is seen in fibromyalgia. Although central mechanisms have been suspected to contribute to the pathogenesis of fibromyalgia for some time, we speculate that these same types of mechanisms may be operative in IC, which has traditionally been felt to be a bladder disorder.
Clements A, Sharpe M, Simkin S, Borrill J, Hawton K.	Department of Psychiatry, University of Oxford, Warneford Hospital, UK. alison.clements@psychiatry.ox.ac.uk	Chronic fatigue syndrome: a qualitative investigation of patients' beliefs about the illness.	J Psychosom Res 1997 Jun;42(6):615-24	The chronic fatigue syndrome is a disabling chronic condition of uncertain cause. Previous studies have found that patients seen in hospital clinics with the syndrome often strongly believe that their illness is physical in nature and minimize the role of psychological and social factors. There is also evidence that patients cope by avoiding activity. However, almost all of these studies have assessed illness beliefs only by questionnaire. The aim of this study was to explore the nature and origin of illness beliefs in more detail using in-depth interviews and a qualitative analysis of patient responses. Sixty-six consecutive referrals meeting Oxford criteria for chronic fatigue syndrome were recruited. Analysis of responses indicated that, whereas the most commonly described explanation for the illness was a physical one, more than half the patients also believed "stress" had played a role. Patients believed that they could partially control the symptoms by reducing activity but felt helpless to influence the physical disease process and hence the course of the illness. Patients reported that they had arrived at these beliefs about the illness after prolonged reflection on their own experience combined with the reading of media reports, self help books, and patient group literature. The views of health professionals played a relatively small role. There is potentially a considerable opportunity to help patients arrive at a wider and more enabling explanation of their illness when they first present to primary care.
Cuende JI, Civeira P, Diez N, Prieto J.	Laboratorio de Biologia Molecular, Hospital Provincial San Telmo, Palencia.	[High prevalence without reactivation of herpes virus 6 in subjects with chronic fatigue syndrome].[article in	An Med Interna 1997 Sep;14(9):441-4	INTRODUCTION: Chronic fatigue syndrome (CFS) is a disorder of unknown etiology. Some viruses have been associated with CFS etiology, specially herpesviruses, enteroviruses and retroviruses. Some studies suggest an association between human herpesvirus-6 (HHV-6) and CFS. In order to know if there is an active HHV-6 infection in CFS patients we studied the immunologic and virologic status of HHV-6. MATERIALS AND METHODS: Twenty patients with

		Spanish]		CFS were studied. IgG and IgM anti HHV-6 were determined by indirect immunofluorescence assay. DNA from serum and peripheral blood mononuclear cells (PBMC) were studied by dot- and Southern-blotting and nested-PCR to detect HHV-6 DNA. HHV-6 RNA from PBMC were amplified by RT(retrotranscription)-PCR. RESULTS: Ten patients (50%) had IgG anti-HHV-6 in serum but none had IgM anti-HHV-6. Dot-blotting of DNA from 200 microliters of serum and Southern-blotting of 10 micrograms of PBMC DNA were negative. Nested-PCR from sera were negative. Nested-PCR with 1 microgram PBMC DNA were positive in 8 out 20 (40%) and with 5 micrograms PBMC DNA were positive in 16 out of 20 (80%). No viral RNA were detected in PBMC. CONCLUSIONS: There is a high proportion of CFS patients infected with HHV-6 but with low viral load. Results do not support HHV-6 reactivation in CFS patients.
de Jong LW, Prins JB, Fiselier TJ, Weemaes CM, Meijer-van den Bergh EM, Bleijenberg G.	Afd. Medische Psychologie, Academisch Ziekenhuis, Nijmegen.	[Chronic fatigue syndrome in young persons].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1513-6	The prevalence of chronic fatigue syndrome (CFS) in teenagers is 10-20 per 100,000 inhabitants in the Netherlands. The natural course of the disorder is not favourable according to the literature. Proposed criteria for the diagnosis 'CFS' in adolescence are: absence of a physical explanation for the complaints, a disabling fatigue for at least six months and prolonged school absenteeism or severe motor and social disabilities. Exclusion criterion should be a psychiatric disorder. Factors that attribute to the persistence of fatigue are somatic attributions, illness enhancing cognitions and behaviour of parents as well as physical inactivity. The role of the physician and the role of parents can enhance the problems. The treatment should focus on decreasing the somatic attributions, on reinforcement by the parents of healthy adolescent behaviour, on the gradual increase of physical activity and on decreasing attention (including medical attention) for the somatic complaints.
de Loos WS.	Department of Psychiatry, Utrecht University Hospital, The Netherlands.	Chronic fatigue syndrome: fatigue of unknown origin.	Eur J Clin Invest 1997 Apr;27(4):268-9	
De Lorenzo F, Hargreaves J, Kakkar VV.	Thrombosis Research Institute, London, UK.	Pathogenesis and management of delayed orthostatic hypotension in patients with chronic fatigue syndrome.	Clin Auton Res 1997 Aug;7(4):185-90	The relationship between orthostatic hypotension and chronic fatigue syndrome (CFS) has been reported previously. To study the pathogenesis and management of delayed orthostatic hypotension in patients with CFS, a case comparison study with follow-up of 8 weeks has been designed. A group of 78 patients with CFS (mean age 40 years; 49% men and 51% women), who fulfilled the Centre for Disease Control and Prevention criteria were studied. There were 38 healthy controls (mean age 43 years; 47% men and 53% women). At entry to the study each subject underwent an upright tilt-table test, and clinical and laboratory evaluation. Patients with orthostatic hypotension were offered therapy with sodium chloride (1200 mg) in a sustained-release formulation for 3 weeks, prior to resubmission to the tilt-table testing, and clinical and laboratory evaluation. An

				abnormal response to upright tilt was observed in 22 of 78 patients with CFS. After sodium chloride therapy for 8 weeks, tilt-table testing was repeated on the 22 patients with an abnormal response at baseline. Of these 22 patients, 10 redeveloped orthostatic hypotension, while 11 did not show an abnormal response to the test and reported an improvement of CFS symptoms. However, those CFS patients who again developed an abnormal response to tilt-test had a significantly reduced plasma renin activity (0.79 pmol/ml per h) compared both with healthy controls (1.29 pmol/ml per h) and with those 11 chronic fatigue patients (1.0 pmol/ml per h) who improved after sodium chloride therapy (p = 0.04). In conclusion, in our study CFS patients who did not respond to sodium chloride therapy were found to have low plasma renin activity. In these patients an abnormal renin-angiotensin-aldosterone system could explain the pathogenesis of orthostatic hypotension and the abnormal response to treatment.
Deale A, Chalder T, Marks I, Wessely S.	Academic Department of Psychological Medicine, King's College Hospital, London, United Kingdom.	Cognitive behavior therapy for chronic fatigue syndrome: a randomized controlled trial.	Am J Psychiatry 1997 Mar;154(3):408-14 comment in: Am J Psychiatry. 1998 Oct;155(10):1461-2	OBJECTIVE: Cognitive behavior therapy for chronic fatigue syndrome was compared with relaxation in a randomized controlled trial. METHODS: Sixty patients with chronic fatigue syndrome were randomly assigned to 13 sessions of either cognitive behavior therapy (graded activity and cognitive restructuring) or relaxation. Outcome was evaluated by using measures of functional impairment, fatigue, mood, and global improvement. RESULTS: Treatment was completed by 53 patients. Functional impairment and fatigue improved more in the group that received cognitive behavior therapy. At final follow-up, 70% of the completers in the cognitive behavior therapy group achieved good outcomes (substantial improvement in physical functioning) compared with 19% of those in the relaxation group who completed treatment. CONCLUSIONS: Cognitive behavior therapy was more effective than a relaxation control in the management of patients with chronic fatigue syndrome. Improvements were sustained over 6 months of follow-up. Randomized Controlled Trial
DeLuca J, Johnson SK, Ellis SP, Natelson BH.	UMDNJ-New Jersey Medical School, Newark, USA.	Sudden vs gradual onset of chronic fatigue syndrome differentiates individuals on cognitive and psychiatric measures.	J Psychiatr Res 1997 Jan-Feb;31(1):83-90	To examine the influence of mode of illness onset on psychiatric status and neuropsychological performance, 36 patients with CFS were divided into two groups: sudden vs gradual onset of symptoms. These two CFS subgroups were compared to each other and to sedentary healthy controls on standardized neuropsychological tests of attention/concentration, information processing efficiency, memory, and higher cortical functions. In addition, the distribution of comorbid Axis I psychiatric disease between the two CFS groups was examined. The rate of concurrent psychiatric disease was significantly greater in the CFS-gradual group relative to the CFS-sudden group. While both CFS groups showed a significant reduction in information processing ability relative to controls, impairment in memory was more severe in the CFS-sudden group. Because of the significant heterogeneity of the CFS population, the need for subgroup analysis is

				discussed.
DeLuca J, Johnson SK, Ellis SP, Natelson BH.	University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, USA.	Cognitive functioning is impaired in patients with chronic fatigue syndrome devoid of psychiatric disease.	J Neurol Neurosurg Psychiatry 1997 Feb;62(2):151-5	OBJECTIVE: To examine the effect of the presence or absence of psychiatric disease on cognitive functioning in chronic fatigue syndrome. METHODS: Thirty six patients with chronic fatigue syndrome and 31 healthy controls who did not exercise regularly were studied. Subgroups within the chronic fatigue syndrome sample were formed based on the presence or absence of comorbid axis I psychiatric disorders. Patients with psychiatric disorders preceding the onset chronic fatigue syndrome were excluded. Subjects were administered a battery of standardised neuropsychological tests as well as a structured psychiatric interview. RESULTS: Patients with chronic fatigue syndrome without psychiatric comorbidity were impaired relative to controls and patients with chronic fatigue syndrome with concurrent psychiatric disease on tests of memory, attention, and information processing. CONCLUSION: Impaired cognition in chronic fatigue syndrome cannot be explained solely by the presence of a psychiatric condition. Controlled Clinical Trial
Demitrack MA, Engleberg NC.	Indiana University School of Medicine, Indianapolis, USA.	Chronic fatigue syndrome.	Curr Ther Endocrinol Metab 1997;6:152-60	
Demitrack MA.	Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN 46285, USA.	Neuroendocrine correlates of chronic fatigue syndrome: a brief review.	J Psychiatr Res 1997 Jan-Feb;31(1):69-82	Chronic fatigue syndrome remains one of the more perplexing syndromes in contemporary clinical medicine. One approach to understanding this condition has been to acknowledge its similarities to other disorders of clearer pathophysiology. In this review, a rationale for the study of neuroendocrine correlates of chronic fatigue syndrome is presented, based in part on the clinical observation that asthenic or fatigue states share many of the somatic symptom characteristics seen in recognized endocrine disorders. Of additional interest is the observation that psychological symptoms, particularly disturbances in mood and anxiety, are equally prominent in this condition. At this time, several reports have provided replicated evidence of disruptions in the integrity of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome. It is notable that the pattern of the alteration in the stress response apparatus is not reminiscent of the well-understood hypercortisolism of melancholic depression but, rather, suggests a sustained inactivation od central nervous system components of this system. Recent work also implicates alterations in central serotonergic tone in the overall pathophysiology of this finding. The implications of these observations are far from clear, but they highlight the fact that, though chronic fatigue syndrome overlaps with the well-described illness category of major depression, these are not identical clinical conditions.
Derman W, Schwellnus MP, Lambert MI, Emms M, Sinclair-Smith C,	MRC/UCT Bioenergetics of Exercise Research Unit, University of Cape	The 'worn-out athlete': a clinical approach to chronic fatigue in	J Sports Sci 1997 Jun;15(3):341-51	Chronic fatigue in the athletic population is a common but difficult diagnostic challenge for the sports physician. While a degree of fatigue may be normal for any athlete during periods of high-volume training, the clinician must be able to

Kirby P, Noakes TD.	Town Medical School, Sports Science Institute of South Africa, Newlands, South Africa.	athletes.		differentiate between this physiological fatigue and more prolonged, severe fatigue which may be due to a pathological condition. As chronic fatigue can be the presenting symptom of many curable and harmful diseases, medical conditions which cause chronic fatigue have to be excluded. The clinician must then be able to differentiate between chronic fatigue associated with training or chronic fatigue from other medical causes, and also between the chronic fatigue syndrome and the overtraining syndrome. Once the clinician has excluded all of the above medical conditions which cause chronic fatigue in athletes, a significant proportion of fatigued athletes remain without a diagnosis. Novel data indicate that skeletal muscle disorders may play a role in the development of symptoms experienced by the athlete with chronic fatigue. The histological findings from muscle biopsies of athletes suffering from the 'fatigued athlete myopathic syndrome' are presented. We have designed a clinical approach to the diagnosis and work-up of the athlete presenting with chronic fatigue. The strength of this approach is that it hinges on the participation of a multidisciplinary team in the diagnosis and management of the athlete with chronic fatigue. The athlete, coach, dietician, exercise physiologist and sport psychologist all play an important role in enabling the physician to make the correct diagnosis.
Dickinson CJ.	Wolfson Institute of Preventive Medicine, St. Bartholomew's & Royal London School of Medicine & Dentistry, London, UK.	Chronic fatigue syndrome--aetiological aspects.	Eur J Clin Invest 1997 Apr;27(4):257-67Comment in: Eur J Clin Invest. 1997 Apr;27(4):255-6 Eur J Clin Invest. 1997 Dec;27(12):1061-2	The chronic fatigue syndrome (CFS) has been intensively studied over the last 40 years, but no conclusions have yet been agreed as to its cause. Most cases nowadays are sporadic. In the established chronic condition there are no consistently abnormal physical signs or abnormalities on laboratory investigation. Many physicians remain convinced that the symptoms are psychological rather than physical in origin. This view is reinforced by the emotional way in which many patients present themselves. The overlap of symptoms between CFS and depression remains a source of confusion and difficulty. But even if all CFS patients were rediagnosed as depressives, this would not negate the possibility of an underlying organic cause for the condition, in view of the growing evidence that depression itself has a physical cause and responds best to physical treatments. There is some evidence both for active viral infection and for an immunological disorder in the CFS. Many observations suggest that the syndrome could derive from residual damage to the reticular activating system (RAS) of the upper brain stem and/or to its cortical projections. Such damage could be produced by a previous viral infection, leaving functional defects unaccompanied by any gross histological changes. In animal experiments activation of the RAS can change sleep state and activate or stimulate cortical functions. RAS lesions can produce somnolence and apathy. Studies by modern imaging techniques have not been entirely consistent, but many magnetic resonance imaging (MRI) studies already suggest that small discrete patchy brain stem and subcortical

				lesions can often be seen in CFS. Regional blood flow studies by single photon-emission computerized tomography (SPECT) have been more consistent. They have revealed blood flow reductions in many regions, especially in the hind brain. Similar lesions have been reported after poliomyelitis and in multiple sclerosis--in both of which conditions chronic fatigue is characteristically present. In the well-known post-polio fatigue syndrome, lesions predominate in the RAS of the brain stem. If similar underlying lesions in the RAS can eventually be identified in CFS, the therapeutic target for CFS would be better defined than it is at present. A number of logical approaches to treatment can already be envisaged.
Dimitrov M , Jordan Grafman		Neuropsychological Assessment of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(4): 31 - 42	
Dinan TG, Majeed T, Lavelle E, Scott LV, Berti C, Behan P.	Department of Psychological Medicine, St Bartholomew's Hospital, London, UK. T.G.Dinan@mds.qmw.ac.uk	Blunted serotonin-mediated activation of the hypothalamic-pituitary-adrenal axis in chronic fatigue syndrome.	Psychoneuroendocrinology 1997 May;22(4):261-7	We examined 5HT1a-mediated ACTH release in patients with chronic fatigue syndrome (CFS) using a between-subjects design. Patients attending a specialist outpatient clinic for CFS, who fulfilled CDC criteria, together with age- and sex-matched healthy comparison subjects, were recruited. Subjects had a cannula inserted in a forearm vein at 0830 h and were allowed to relax until 0900 h, when baseline bloods for ACTH and cortisol were drawn. They were then given ipsapirone 20 mg PO and further blood for hormone estimation was taken at +30, +60, +90, +120 and +180 min. Baseline ACTH and cortisol levels did not differ between the two groups. Release of ACTH (but not cortisol) in response to ipsapirone challenge was significantly blunted in patients with CFS. We conclude that serotonergic activation of the hypothalamic-pituitary-adrenal axis is defective in CFS. This defect may be of pathophysiological significance.
Dobbins JG, Bonnie Randall, Michele Reyes , Lea Steele, Elizabeth A. Livens BA, William C. Reeves		The Prevalence of Chronic Fatiguing Illnesses Among Adolescents in the United States	Journal of Chronic Fatigue Syndrome 1997: 3(2): 15 - 27	Objective. To compare the prevalence of unexplained chronic fatigue (CF) and chronic fatigue syndrome (CFS) among adolescents in three studies conducted by the Centers for Disease Control and Prevention and to compare these estimates with those for adults in two of the studies. Design. Thc studies used the following three designs: (i) a physicianbased CFS surveillance system, (ii) a random, cross-sectional community telephone survey and (iii) a cross-sectional survey of school nurses. Setting. Surveillance included all patients with unexplained fatigue seen by participating physicians in four communities over a 2-year period; the community survey was conducted in a defined, urban population; and the survey of nurses included all middle, junior, and high school nurses in two communities. Patients or other participants. Twenty-three adolescent cases of unexplained chronic fatiguing illness were reported to the surveillance system, 7 of whom were classified with CFS. The community survey screened 2,249 persons between the ages of 2 and 17 years and identified 5 with unexplained chronic fatiguing illness, only one of whom might have had CFS. The school nurses identified 22 students with unexplained fatiguing illness, 10 of whom had received a diagnosis

				of CFS. Main outcome measures. The prevalence of unexplained chronic fatiguing illness was estimated in all three studies. The prevalence of CFS was estimated in one study, the prevalence of CFS-like illness was estimated in another, and the prevalence of a reported diagnosis of CFS was estimated in the third. Results. In general, the prevalence estimates of CF, CFS-like illness, and CFS for adolescents were lower than those for adults. One study also included children ages 2 to 11 years and found very little CF and no CFS. Cases of CFS among adolescents were evenly distributed across individual years of age. Conclusions. CFS was clearly present among adolescents, although the prevalence for this group was lower than for most adult age groups: Differences in prevalence estimates among the three studies were consistent with differences in study designs. The validity of adolescent/adult comparisons within each study should not be affected by the study design. Further study of the applicability of the current CFS case definition to adolescents is warranted.
Dowsett EG, Colby J.		Chronic fatigue syndrome in children. Journal was wrong to critizise study in schoolchildren.	BMJ 1997 Oct 11;315(7113):949 Comment on: BMJ. 1997 Jun 7;314(7095):1635-6	
Dowsett EG, Jane Colby		Long-Term Sickness Absence Due to ME/CFS in UK Schools An Epidemiological Study with Medical and Educational Implications	Journal of Chronic Fatigue Syndrome 1997: 3(2): 29 - 42	A study was made to determine whether the recognition of multiple cases of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) in one school is a unique experience. A five-year retrospective period prevalence survey (1991-1995) was collated from sequential reports made in six English Local Education Authority (LEA) areas. By means of a confidential questionnaire circulated to 2,942 school principals via internal mail, 1,098 schools, comprising 27,327 staff and 333,024 pupils, were investigated. Details were obtained on age, gender, location in school sector, work pattern and morbidity. Forty-two percent of all medically certified long-term sickness absence was ascribed to ME/CFS, this figure being well in excess of all other causes. This diagnosis was significantly associated with case clustering, variable geographical prevalence, a marked increase in the female:male case ratio at puberty and prolonged disturbance of educational potential. We conclude that ME/CFS in schools leads to serious economic and career problems. Redirection of research to special educational needs and to early diagnosis of infectious agents which can trigger ME/CFS in schools might prevent, at low cost, much chronic illness and education deficit.
Droge W, Holm E.	Division of Immunochemistry, Deutsches Krebsforschungszentrum, Heidelberg,	Role of cysteine and glutathione in HIV infection and other diseases associated with muscle wasting and	FASEB J 1997 Nov;11(13):1077-89	The combination of abnormally low plasma cystine and glutamine levels, low natural killer (NK) cell activity, skeletal muscle wasting or muscle fatigue, and increased rates of urea production defines a complex of abnormalities that is tentatively called "low CG syndrome." These symptoms are found in patients with HIV infection, cancer, major injuries, sepsis, Crohn's disease, ulcerative

	Germany.	immunological dysfunction.		colitis, chronic fatigue syndrome, and to some extent in overtrained athletes. The coincidence of these symptoms in diseases of different etiological origin suggests a causal relationship. The low NK cell activity in most cases is not life-threatening, but may be disastrous in HIV infection because it may compromise the initially stable balance between the immune system and virus, and trigger disease progression. This hypothesis is supported by the coincidence observed between the decrease of CD4+ T cells and a decrease in the plasma cystine level. In addition, recent studies revealed important clues about the role of cysteine and glutathione in the development of skeletal muscle wasting. Evidence suggests that 1) the cystine level is regulated primarily by the normal postabsorptive skeletal muscle protein catabolism, 2) the cystine level itself is a physiological regulator of nitrogen balance and body cell mass, 3) the cyst(e)ine-mediated regulatory circuit is compromised in various catabolic conditions, including old age, and 4) cysteine supplementation may be a useful therapy if combined with disease-specific treatments such as antiviral therapy in HIV infection. Review, Academic
Durlach J, Bac P, Durlach V, Bara M, Guiet-Bara A.	SDRM, Hopital Saint-Vincent-de-Paul, Paris.	Neurotic, neuromuscular and autonomic nervous form of magnesium imbalance.	Magnes Res 1997 Jun;10(2):169-95	The nervous form of magnesium imbalance represents the best documented experimental and clinical aspects of magnesium disorders. The nervous form of primary magnesium deficit (MD) in the adult appears as the best descriptive model for analysis of the symptomatology, aetiology, physiopathology, diagnosis and therapy of the most frequent form of MD. Nervous hyperexcitability due to chronic MD in the adult results in a non-specific clinical pattern with associated central and peripheral neuromuscular symptoms, analogous to the symptomatology previously described in medical literature as latent tetany, hyperventilation syndrome, spasmophilia, chronic fatigue syndrome, neurocirculatory asthenia and idiopathic Barlow's disease. On encountering this non-specific pattern, the signs of neuromuscular hyperexcitability are of much greater importance. Trousseau's sign is less sensitive than Chvostek's sign, but their sensitivities are increased by hyperventilation (Von Bondsdorff's test). Examination of the precordial area will be conducted in order to search clinical stigmata of mitral valve prolapse (MVP) which is a frequent dyskinesia due to chronic MD (about a quarter to one-third of cases). The electromyogram (EMG) shows one (or several) trains of autorhythmic activities beating for more than 2 min of one of the three tetanic activities (uniplets, multiplets or 'complex tonicoclonic tracings') during one of the three facilitation procedures: tourniquet-induced ischaemia lasting 10 min. post-ischaemia lasting 10 min after the removal of the tourniquet and hyperventilation over 5 min. A repetitive EMG constitutes the principal mark of nervous hyperexcitability (NHE) due to MD. The echocardiogram (ECC) is the best tool for detecting MVP, the 2-dimensional ECC with pulsed Doppler being more accurate than time-motion ECC. The routine

				ionic investigations comprise five static tests: plasma and erythrocyte magnesium, plasma calcium and daily magnesiuria and calciuria. An evaluation of magnesium intake is desirable. Normal concentrations of magnesium in blood do not rule out the diagnosis of the nervous form of primary chronic MD. The histograms of MD group reveal Gaussian type magnesaemias with significantly lower means and the constituent elements can be individually hypo- (one-third of cases), normo- (about two-thirds of cases) and even, exceptionally, hyper-magnesaemic. The diagnosis of MD requires an oral magnesium load test. At physiological dose (5 mg of Mg/kg/day), oral magnesium is totally devoid of the pharmacological effects of parenteral magnesium. Corrections of symptomatology by this oral physiological magnesium load is the best proof that it was due to magnesium deficiency. In particular clinical forms, more sophisticated studies may be useful: standard and quantitative electroencephalograms, electropolygraphic studies of afternoon sleep, electronystagmography, optokinetic test, skin conductance reflex, psychometric inventories, standard or monitoring electrocardiogram, treadmill test, other static and dynamic investigations: e.g. ionized free Mg2+, lymphocyte Mg, brain Mg, cerebrospinal Mg, Mg balance, Mg parenteral load test, glucose load, and even radio-isotope study, the only one able to reveal intestinal magnesium hypersecretion. Nervous primary chronic MD progresses by phases of decompensation against a background of latency. Marginal magnesium deficiency, that is to say an insufficient magnesium intake which merely requires simple oral physiological supplementation, is fundamental in the aetiology of primary magnesium deficit. However a constitutional homeostatic lability of the nervous system or of magnesium metabolism such as belonging to the B35 type of HLA group must be involved. Part of the aetiology of this magnesium deficit is a magnesium depletion, where the disorder which induces magnesium deficit is related to a dysregulation of the control mechanisms of magnesium status which requires a more or less difficult Review, Academic
Egyedi P.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Sep 13;141(37):1790-1	
Elliot DL, Goldberg L, Loveless MO.		Graded exercise testing and chronic fatigue syndrome.	Am J Med 1997 Jul;103(1):84-6 Comment on: Am J Med. 1996 Jun;100(6):634-40	
Evengard B, Lipkin WI.	Institutionen for infektionssjukdomar, mikrobiologi, patologi	[A known virus in animals is suspected in humans. Borna disease	Lakartidningen 1997 Dec 10;94(50):4753-6	Borna disease virus (BDV) is a newly classified non-segmented neurotrophic negative-strand RNA virus with a worldwide distribution and affecting warm-blooded animals ranging from birds to primates. Infection may be asymptomatic

	och immunologi, Huddinge sjukhus.	virus has been detected in human neuropathy].[article in Swedish]		or results in manifest disturbances of movement behaviour. Although BDV has not been unequivocally implicated in any human disease, several reports have suggested relationship to exist between BDV infection and certain neuropsychiatric syndromes including affective disorders, chronic fatigue syndrome, and schizophrenia. Moreover, at least one centre has initiated a trial of antiviral therapy in patients with affective disorders attributable to BDV. The article consists in a review of recent advances in the molecular biology, pathogenesis and epidemiology of BDV, and an outline of anticipated directions for future research.
Fairhurst D, Waterman M, Lynch S.		Cognitive slowing in chronic fatigue syndrome (CFS)	Psychosom Med 1997 Nov-Dec;59(6):638 Comment on: Psychosom Med. 1997 Jan-Feb;59(1):58-66	
Field TM, William Sunshine , Maria Hernandez-Reif , Olga Quintino BS, Saul Schanberg , Cynthia Kuhn , Iris Burman		Massage Therapy Effects on Depression and Somatic Symptoms in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(3): 43 - 51	Subsequent to recent reports of psychomotor retardation in chronic fatigue syndrome (CFS), the present study investigated the relative contributions of cognitive and motor components to psychomotor functioning in CFS. These components were differentiated by means of a reaction time paradigm proposed by Cornell, Suarez and Berent (1). The relationship between the cognitive and motor components of psychomotor performance and subjective cognitive and motor complaints was also investigated. Three groups of subjects participated in the study: an experimental group comprised of ten patients with CFS, and two comparison groups comprised of ten depressed and ten healthy individuals. Although the results of this study are suggestive of minimal functional impairment in CFS, they implicate motor factors in psychomotor slowing in unmedicated CFS patients
Fiore G, Giacovazzo F, Giacovazzo M.	VI Cattedra di Medicina Interna, Universita La Sapienza, Roma, Italy.	Three cases of dermatomyositis erroneously diagnosed as "chronic fatigue syndrome".	Eur Rev Med Pharmacol Sci 1997 Nov-Dec;1(6):193-5	The authors report three cases of dermatomyositis, which ha been erroneously diagnosed as "chronic fatigue syndrome" due to the presence of elevated titers of serum anti-Epstein Barr antibodies.
Fischler B, Cluydts R, De Gucht Y, Kaufman L, De Meirleir K.	Department of Psychiatry, Academic Hospital, Brussels, Balgium.	Generalized anxiety disorder in chronic fatigue syndrome.	Acta Psychiatr Scand 1997 May;95(5):405-13	A structured psychiatric interview, forming part of a global psychopathological approach, revealed higher prevalence rates of current and lifetime psychiatric disorders and a higher degree of psychiatric comorbidity in patients with chronic fatigue syndrome (CFS) than in a medical control group. In contrast to previous studies, a very high prevalence of generalized anxiety disorder (GAD) was found in CFS, characterized by an early onset and a high rate of psychiatric comorbidity. It is postulated that GAD represents a susceptibility factor for the development of CFS. A significantly higher prevalence was also observed for the somatization disorder (SD) in the CFS group. Apart from a higher female-to-male ratio in

				fibromyalgia, no marked differences were observed in sociodemographic or illness-related features, or in psychiatric morbidity, between CFS patients with and without fibromyalgia. CFS patients with SD have a longer illness duration and a higher rate of psychiatric comorbidity. These findings are consistent with the suggestion of Hickie et al. (1) that chronic fatigued subjects with SD should be distinguished from subjects with CFS.
Fischler B, Dendale P, Michiels V, Cluydts R, Kaufman L, De Meirleir K.	Department of Psychiatry, Academic Hospital, Free University of Brussels, Belgium.	Physical fatigability and exercise capacity in chronic fatigue syndrome: association with disability, somatization and psychopathology.	J Psychosom Res 1997 Apr;42(4):369-78	Physical fatigability and avoidance of physically demanding tasks in chronic fatigue syndrome (CFS) were assessed by the achievement or nonachievement of 85% of age-predicted maximal heart rate (target heart rate, THR) during incremental exercise. The association with functional status impairment, somatization, and psychopathology was examined. A statistically significant association was demonstrated between this physical fatigability variable and impairment, and a trend was found for an association with somatization. No association was demonstrated with psychopathology. These results are in accordance with the cognitive-behavioral model of CFS, suggesting a major contribution of avoidance behavior to functional status impairment; however, neither anxiety nor depression seem to be involved in the avoidance behavior. Aerobic work capacity was compared between CFS and healthy controls achieving THR. Physical deconditioning with early involvement of anaerobic metabolism was demonstrated in this CFS subgroup. Half of the CFS patients who did not achieve THR did not reach the anaerobic threshold. This finding argues against an association in CFS between avoidance of physically demanding tasks and early anaerobic metabolism during effort.
Fischler B, Le Bon O, Hoffmann G, Cluydts R, Kaufman L, De Meirleir K.	Department of Psychiatry, Academic Hospital, Free University of Brussels, Belgium.	Sleep anomalies in the chronic fatigue syndrome. A comorbidity study.	Neuropsychobiology 1997;35(3):115-22	Polysomnographic findings were compared between a group of patients with the chronic fatigue syndrome (CFS; n = 49) and a matched healthy control (HC) group (n = 20). Sleep initiation and sleep maintenance disturbances were observed in the CFS group. The percentage of stage 4 was significantly lower in the CFS group. A discriminant analysis allowed a high level of correct classification of CFS subjects and HC. Sleep-onset latency and the number of stage shifts/hour contributed significantly to the discriminant function. The presence of these anomalies as well as the decrease in stage 4 sleep were not limited to the patients also diagnosed with fibromyalgia or with a psychiatric disorder. No association was found between sleep disorders and the degree of functional status impairment. The mean REM latency and the percentage of subjects with a shortened REM latency were similar in CFS and HC.
Fisher L.	Department of Psychological Medicine, King's College Hospital, London. Publication Types: Review Review,	Chronic fatigue syndrome.	Prof Nurse 1997 May;12(8):578-81Comment in: Prof Nurse. 1997 Aug;12(11):827	

	Tutorial			
Fitzgibbon EJ, Murphy D, O'Shea K, Kelleher C.	Department of Health Promotion, University College Galway, Ireland.	Chronic debilitating fatigue in Irish general practice: a survey of general practitioners' experience.	Br J Gen Pract 1997 Oct;47(423):618-22	BACKGROUND: Doctors are called upon to treat chronic debilitating fatigue without the help of a protocol of care. AIMS: To estimate the incidence of chronic debilitating fatigue in Irish general practice, to obtain information on management strategy and outcome, to explore the attitudes of practitioners (GPs) towards the concept of a chronic fatigue syndrome (CFS), and to recruit practitioners to a prospective study of chronic fatigue in primary care. METHOD: A total of 200 names were selected from the database of the Irish College of General Practitioners (ICGP); 164 of these were eligible for the study. RESULTS: Altogether, 118 questionnaires were returned (72%). Ninety-two (78%) responders identified cases of chronic fatigue, giving an estimated 2.1 cases per practice and an incidence of 1 per 1000 population. All social classes were represented, with a male to female ratio of 1:2. Eleven disparate approaches to treatment were advocated. Many (38%) were dissatisfied with the quality of care delivered, and 45% seldom or hardly ever referred cases for specialist opinion. The majority (58%) accepted CFS as a distinct entity, 34% were undecided, and 8% rejected it. Forty-two (35%) GPs volunteered for a prospective study. CONCLUSION: Chronic fatigue is found in Irish general practice among patients of both sexes and all social classes. Doctors differ considerably in their management of patients and are dissatisfied with the quality of care they deliver. Many cases are not referred for specialist opinion. A prospective database is required to accurately assess the scale of this public health problem and to develop a protocol of care.
Fohlman J, Friman G, Tuvemo T.	Infektionskliniken, Akademiska sjukhuset, Uppsala.	[Enterovirus infections in new disguise].[article in Swedish]	Lakartidningen 1997 Jul 9;94(28-29):2555-60	Enteroviruses (Coxsackie A and B, echovirus, poliovirus) belong to a group of small RNA-viruses, picomavirus, which are widespread in nature. Enteroviruses cause a number of wellknown diseases and symptoms in humans, from subclinical infections and the common cold to poliomyelitis with paralysis. The development of polio vaccines is the greatest accomplishment within the field of enterovirus research and the background work was awarded the Nobel prize in 1954. New knowledge implies that enteroviruses play a more important part in the morbidity panorama than was previously thought. Chronic (persistent) enteroviruses were formerly unknown. Serologic and molecular biology techniques have now demonstrated that enteroviral genomes, in certain situations, persist after the primary infection (which is often silent). Persistent enteroviral infection or recurrent infections and/or virus-stimulated autoimmunity might contribute to the development of diseases with hitherto unexplained pathogenesis, such as post polio syndrome, dilated cardiomyopathy, juvenile (type 1) diabetes and possibly some cases of chronic fatigue syndrome.
Franklin AJ.		Graded exercise in chronic fatigue	BMJ 1997 Oct 11;315(7113):947;	

		syndrome. Including patients who rated themselves as a little better would have altered results.	discussion 948 Comment on: BMJ. 1997 Jun 7;314(7095):1635-6 BMJ. 1997 Jun 7;314(7095):1647-52	
Freeman R, Komaroff AL.	Department of Neurology, Beth Israel Deaconess Medical Center, Boston, Massachusetts 02215, USA.	Does the chronic fatigue syndrome involve the autonomic nervous system?	Am J Med 1997 Apr;102(4):357-64	PURPOSE: To investigate the role of the autonomic nervous system in the symptoms of patients with chronic fatigue syndrome (CFS) and delineate the pathogenesis of the orthostatic Intolerance and predisposition to neurally mediated syncope reported in this patient group. PATIENTS AND METHODS: Twenty-three CFS patients and controls performed a battery of autonomic function tests. The CFS patients completed questionnaires pertaining to autonomic and CFS symptoms, their level of physical activity, and premorbid and coexisting psychiatric disorders. The relationship between autonomic test results, cardiovascular deconditioning, and psychiatric disorders was examined with multivariate statistics and the evidence that autonomic changes seen in CFS might be secondary to a postviral, idiopathic autonomic neuropathy was explored. RESULTS: The CFS subjects had a significant increase in baseline ($P < 0.01$) and maximum heart rate (HR) on standing and tilting (both $P < 0.0001$). Tests of parasympathetic nervous system function (the expiratory inspiratory ratio, $P < 0.005$; maximum minus minimum HR difference, $P < 0.05$), were significantly less in the CFS group as were measures of sympathetic nervous system function (systolic blood pressure decrease with tilting, $P < 0.01$; diastolic blood pressure decrease with tilting, $P < 0.05$; and the systolic blood pressure decrease during phase II of a Valsalva maneuver, $P < 0.05$). Twenty-five percent of CFS subjects had a positive tilt table test. The physical activity index was a significant predictor of autonomic test results (resting, sitting, standing, and tilted HR, $P < 0.05$ to $P < 0.009$); and the blood pressure decrease in phase II of the Valvalsa maneuver, $P < 0.05$) whereas premorbid and coexistent psychiatric conditions were not. The onset of autonomic symptoms occurred within 4 weeks of a viral infection in 46% of patients-a temporal pattern that is consistent with a postviral, idiopathic autonomic neuropathy. CONCLUSION: Patients with CFS show alterations in measures of sympathetic and parasympathetic nervous system function. These results, which provide the physiological basis for the orthostatic intolerance and other symptoms of autonomic function in this patient group, may be explained by cardiovascular deconditioning, a postviral idiopathic autonomic neuropathy, or both.
Fukuda K, Dobbins JG, Wilson LJ, Dunn RA, Wilcox K, Smallwood D.	Division of Viral and Rickettsial Diseases, Centers for Disease	An epidemiologic study of fatigue with relevance for the	J Psychiatr Res 1997 Jan-Feb;31(1):19-29	We surveyed households in four rural Michigan communities to confirm a reported cluster of cases resembling chronic fatigue syndrome (CFS) and to study the epidemiology of fatigue in a rural area. Data were collected from 1698

	Control and Prevention, Atlanta, GA 30333, USA.	chronic fatigue syndrome.		households. We did not confirm the reported cluster. The prevalence of households containing at least one fatigued person was similar between communities thought to harbor the cluster and communities selected for comparison. Symptoms and features of generic forms of fatigue were very similar to those often attributed to CFS.
Fulcher KY, White PD.	National Sports Medicine Institute, St Bartholomew's, London.	Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome.	BMJ 1997 Jun 7;314(7095):1647-52Comment in: BMJ. 1997 Jun 7;314(7095):1635-6 BMJ. 1997 Oct 11;315(7113):947-8 BMJ. 1997 Oct 11;315(7113):947; discussion 948 BMJ. 1997 Oct 11;315(7113):948	OBJECTIVE: To test the efficacy of a graded aerobic exercise programme in the chronic fatigue syndrome. DESIGN: Randomised controlled trial with control treatment crossover after the first follow up examination. SETTING: Chronic fatigue clinic in a general hospital department of psychiatry. SUBJECTS: 66 patients with the chronic fatigue syndrome who had neither a psychiatric disorder nor appreciable sleep disturbance. INTERVENTIONS: Random allocation to 12 weeks of either graded aerobic exercise or flexibility exercises and relaxation therapy. Patients who completed the flexibility programme were invited to cross over to the exercise programme afterwards. MAIN OUTCOME MEASURE: The self rated clinical global impression change score, "very much better" or "much better" being considered as clinically important. RESULTS: Four patients receiving exercise and three receiving flexibility treatment dropped out before completion. 15 of 29 patients rated themselves as better after completing exercise treatment compared with eight of 30 patients who completed flexibility treatment. Analysis by intention to treat gave similar results (17/33 v 9/33 patients better). Fatigue, functional capacity, and fitness were significantly better after exercise than after flexibility treatment. 12 of 22 patients who crossed over to exercise after flexibility treatment rated themselves as better after completing exercise treatment 32 of 47 patients rated themselves as better three months after completing supervised exercise treatment 35 of 47 patients rated themselves as better one year after completing supervised exercise treatment. CONCLUSION: These findings support the use of appropriately prescribed graded aerobic exercise in the management of patients with the chronic fatigue syndrome. Randomized Controlled Trial
Galbraith DN, Nairn C, Clements GB.	Regional Virus Laboratory, Ruchill Hospital, Glasgow, UK.	Evidence for enteroviral persistence in humans.	J Gen Virol 1997 Feb;78 (Pt 2):307-12	We have sought evidence of enteroviral persistence in humans. Eight individuals with chronic fatigue syndrome (CFS) were positive for enteroviral sequences, detected by PCR in two serum samples taken at least 5 months apart. The nucleotide sequence of the 5' non-translated region (bases 174-423) was determined for each amplicon. Four individuals had virtually identical nucleotide sequences (> 97%) in both samples. The sequence pairs also each had a unique shared pattern indicating that the virus had persisted. In one individual (HO), it was clear that there had been infection with two different enteroviruses. In the remaining three individuals, the lack of unique shared features suggested that re-infection had occurred, rather than persistence. With the exception of HO, the sequences fell into a subgroup that is related to the Coxsackie B-like viruses.

Gaudino EA, Coyle PK, Krupp LB.	Department of Neurology, State University of New York at Stony Brook, USA.	Post-Lyme syndrome and chronic fatigue syndrome. Neuropsychiatric similarities and differences.	Arch Neurol 1997 Nov;54(11):1372-6	BACKGROUND: Patients with chronic fatigue syndrome (CFS) and post-Lyme syndrome (PLS) share many features, including symptoms of severe fatigue and cognitive difficulty. OBJECTIVE: To examine the neuropsychiatric differences in these disorders to enhance understanding of how mood, fatigue, and cognitive performance interrelate in chronic illness. METHODS: Twenty-five patients with CFS, 38 patients with PLS, and 56 healthy controls participated in the study. Patients with CFS met 1994 criteria for CFS and lacked histories suggestive of Lyme disease. Patients with PLS were seropositive for Lyme disease, had met the Centers for Disease Control and Prevention criteria, or had histories strongly suggestive of Lyme disease and were experiencing severe fatigue that continued 6 months or more following completion of antibiotic treatment for Lyme disease. All subjects completed self-report measures of somatic symptoms and mood disturbance and underwent neuropsychological testing. All patients also underwent a structured psychiatric interview. RESULTS: Patients with CFS and PLS were similar in several somatic symptoms and in psychiatric profile. Patients with CFS reported more flulike symptoms than patients with PLS. Patients with PLS but not patients with CFS performed significantly worse than controls on tests of attention, verbal memory, verbal fluency, and motor speed. Patients with PLS without a premorbid history of psychiatric illness did relatively worse on cognitive tests than patients with PLS with premorbid psychiatric illness compared with healthy controls. CONCLUSIONS: Despite symptom overlap, patients with PLS show greater cognitive deficits than patients with CFS compared with healthy controls. This is particularly apparent among patients with PLS who lack premorbid psychiatric illness.
Gloss TL		The Legal Perspective	Journal of Chronic Fatigue Syndrome 1997: 3(4): 57 - 61	
Goldberg MJ, Ismael Mena, Jacques Darcourt		NeuroSPECT Findings in Children - with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(1): 61 - 67	Background NeuroSPECT studies have described specific abnormalities in cerebral perfusion in adults with criteria for Chronic Fatigue Syndrome. This reports findings in 13 children with criteria for Chronic Fatigue Syndrome. Objective. NeuroSPECT findings in 13 CFS/CFIDS children. Methods. Thirteen children meeting CDC criteria for CFS/CFIDS, were evaluated using NeuroSPECT imaging utilizing Xenon 133 and Tc-99m-HMPAO (1). Results. In 13 children, hypoperfusion was observed at 42 ± 10 ml/min/100g, $p < 0.0001$ in the left temporal lobe and at 45 ± 11, $p < .001$ in right temporal lobe. Statistically significant hypoperfusion was also observed in both parietal lobes and at 50 and 53 ml/ min/100g, $p < 0.05$ in the frontal lobe of the right hemisphere. Quantitatcd HMPAO demonstrated bilateral orbitofrontal and anterior temporal hypoperfusion. There was also hypoperfusion in the dorsal aspects of both frontal lobes and both parietooccipital lobes. Conclusion. NeuroSPECT is

				presented as a quantifiable, reproducible tool that can allow us to document a cohort of children defined as CFS/CFIDS.
Goldenberg DL.		Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol 1997 Mar;9(2):135-43	The diagnosis of fibromyalgia continues to generate heated debate. The presence of multiple lifetime psychiatric diagnoses was not intrinsically related to fibromyalgia but rather to the decision of patients to seek specialty medical care. Better outcome measures in fibromyalgia were tested. Neurally mediated hypotension may be associated with chronic fatigue syndrome (CFS). Treatment of patients with fibromyalgia and CFS continues to be of limited success, although the role of multidisciplinary group intervention appears promising. Two position papers focused on the adverse aspects of the medicolegal issues in fibromyalgia and CFS.
Goudsmit EM.		Graded exercise in chronic fatigue syndrome. Chronic fatigue syndrome is heterogeneous condition.	BMJ 1997 Oct 11;315(7113):948 Comment on: BMJ. 1997 Jun 7;314(7095):1647-52	
Greco A, Tannock C, Brostoff J, Costa DC.	MRI Department, Centre Hospitalier Princesse Grace, Principality of Monaco.	Brain MR in chronic fatigue syndrome.	AJNR Am J Neuroradiol 1997 Aug;18(7):1265-9	PURPOSE: To determine the prevalence of MR white matter abnormalities in patients with chronic fatigue syndrome (CFS). METHODS: Brain MR studies of 43 patients (29 women and 14 men, 22 to 78 years old) with a clinical diagnosis of CFS (n = 15), CFS with associated depression (n = 14), and CFS with associated other psychiatric disorders, namely, anxiety and somatization disorder (n = 14), were compared with brain MR studies in 43 age- and sex-matched control subjects. RESULTS: MR findings were abnormal in 13 (32%) of the patients in the study group (ages 34 to 78 years) and in 12 (28%) of the control subjects (ages 26 to 73 years). One patient with CFS had multiple areas of demyelination in the supratentorial periventricular white matter. Another patient with CFS and associated depression had a single focus of probable demyelination in the supratentorial periventricular white matter. In four patients with CFS (ages 34 to 48 years) MR abnormalities consisted of one or several punctate hyperintense foci in the corona radiata, centrum ovale, and frontal white matter. The remaining seven patients (ages 50 to 78 years) had frontoparietal subcortical white matter foci of high T2 signal. The prevalence of white matter hyperintensities was not different between the patients and the control subjects. CONCLUSIONS: Our findings suggest that no MR pattern of white matter abnormalities is specific to CFS.
Gregg VH.	Department of Psychology, Birkbeck College, London, UK.	Hypnosis in chronic fatigue syndrome.	J R Soc Med 1997 Dec;90(12):682-3	
Gupta S, Aggarwal S,	Department of	Cytokine production by	J Psychiatr Res 1997	It has been suggested that cytokines play a role in certain clinical manifestations

See D, Starr A.	Medicine, University of California, Irvine 92717, USA.	adherent and non-adherent mononuclear cells in chronic fatigue syndrome.	Jan-Feb;31(1):149-56	of chronic fatigue syndrome (CFS). In this study adherent (monocytes) and non-adherent (lymphocytes) mononuclear cells were stimulated in the presence or absence of phytohemagglutinin (PHA) or lipopolysaccharide (LPS), respectively, and supernatants were assayed for IL-6, TNF-alpha, and IL-10 by ELISA. IL-6 was also measured at the mRNA level by polymerase chain reaction. The levels of spontaneously (unstimulated) produced TNF-alpha by non-adherent lymphocytes and spontaneously produced IL-6 by both adherent monocytes and non-adherent lymphocytes were significantly increased as compared to simultaneously studied matched controls. The abnormality of IL-6 was also observed at mRNA level. In contrast, spontaneously produced IL-10 by both adherent and non-adherent cells and by PHA-activated non-adherent cells were decreased. This preliminary study suggests that an aberrant production of cytokines in CFS may play a role in the pathogenesis and in some of the clinical manifestations of CFS.
Harmon DL, McMaster D, McCluskey DR, Shields D, Whitehead AS.	Department of Genetics, Trinity College, Dublin, Ireland.	A common genetic variant affecting folate metabolism is not over-represented in chronic fatigue syndrome.	Ann Clin Biochem 1997 Jul;34 (Pt 4):427-9	
Hedrick TE.		Chronic fatigue syndrome.	QJM 1997 Nov;90(11):723-5 Comment on: QJM. 1997 Mar;90(3):223-33	
Heyll U, Wachauf P, Senger V, Diewitz M.	Gesellschaftsarztliche Abteilung der Deutschen Krankenversicherung, Koln.	[Definition of "chronic fatigue syndrome" (CFS)].[article in German]	Med Klin 1997 Apr 15;92(4):221-7	The definition of "Chronic Fatigue Syndrome" (CFS) in 1988 was an attempt to establish a uniform basis for the previously heterogeneous approaches to research of this severe and inexplicable state of fatigue. At the same time, researchers wished to narrow down a pathogenetically founded disease entity a priori by specifying precise disease criteria. The empirical data gathered in accordance with the CFS definition, however, have failed to confirm the assumption that the disease entity is pathogenetically uniform. Furthermore, the originally selected criteria have proven to be impracticable ore theoretically questionable. In the period that followed, modifications that permitted a more comprehensive and yet more differentiated classification of fatigue states of unclear etiology were proposed. The new research approach avoids postulation of causal entities and puts CFS back in a category with other descriptive states of fatigue.
Holland P.	Psychotherapy Department, Royal Edinburgh Hospital.	Coniunctio--in bodily and psychic modes: dissociation, devitalization and integration in a case of	J Anal Psychol 1997 Apr;42(2):217-36	Three years of analytical psychotherapy with a professional woman in mid-life, suffering from chronic fatigue syndrome (CFS), is described. Gradual recovery merged into mid-life changes; marriage, along with a new balance of maternal and paternal imagos, enabled her to trust enough to become pregnant-coniunctio in the most primal bodily and psychic modes. Her life-long, schizoid

		chronic fatigue syndrome.		type pattern, "the pendulum of closeness and isolation', with its extreme of psycho-physical collapse and devitalization, was replayed in therapy. The analyst's symbolic attitude is emphasized, containing the patient's initial affective explosion and validating the physicality of her condition. Mirroring and steady rhythmic attunement became a new, pre-verbal, source of trust-vitalization; differentiation and separation replaced defensive splitting and dissociation. Then the overwhelmingly powerful bodily/maternal could be counterbalanced by the masculine, and a transitional space emerged for symbolic work. Both the regressive and the dynamic aspects of CFS are located in the earliest undifferentiated, archetypal, bodily/psychic modes, when the frustration of primary needs evokes the defences of the self. It is argued that our psychodynamic understanding can contribute to the stalemate in seeing chronic fatigue syndrome as either an organic illness or depression, and that a new linking of the somatic and psychic calls for a new professional collaboration.
Holmes MJ, Diack DS, Easingwood RA, Cross JP, Carlisle B.	Department of Microbiology, University of Otago, Dunedin, New Zealand. mike.holmes@stonebow.otago.ac.nz	Electron microscopic immunocytological profiles in chronic fatigue syndrome.	J Psychiatr Res 1997 Jan-Feb;31(1):115-22	Structures consistent in size, shape and character with various stages of a Lentivirus replicative cycle were observed by electron microscopy in 12-day peripheral-blood lymphocyte cultures from 10 of 17 Chronic Fatigue Syndrome patients and not in controls. Attempts to identify a lymphoid phenotype containing these structures by immunogold labelling failed and the results of reverse-transcriptase assay of culture supernatants were equivocal. The study was blind and case-controlled, patients being paired with age, sex and ethnically matched healthy volunteers. Prescreening of subjects included the common metabolic and immunological disorders, functional conditions and a virus-screen against hepatitis B and C, Epstein-Barr Virus, Cytomegalovirus and Human Immunodeficiency Virus.
Houde SC, Kampfe-Leacher R.	MGH Institute of Health Professions, Boston, Mass, USA.	Chronic fatigue syndrome: an update for clinicians in primary care.	Nurse Pract 1997 Jul;22(7):30, 35-6, 39-40 passim	Cases of long-standing (6 months or longer) fatigue that are not explained by an existing medical or psychiatric diagnosis are referred to as chronic fatigue syndrome (CFS). CFS is a condition of unknown etiology that presents with a complex array of symptoms in patients with diverse health histories. A diagnosis of CFS is largely dependent upon ruling out other organic and psychologic causes of fatigue. CFS can present the clinician with a unique set of challenges in terms of diagnosis and treatment. A review of recent research suggests that the management of CFS requires an individualized approach for each patient. An historic overview of the condition is presented along with current theories of causation, diagnosis considerations, symptom management, and health promotion strategies. Review Literature
Hume M.		Chronic fatigue syndrome in children. All studies must be subjected to rigorous	BMJ 1997 Oct 11;315(7113):949	

		scrutiny.		
Jacobs G.		Chronic fatigue syndrome in children. Patient organisations are denied a voice.	BMJ 1997 Oct 11;315(7113):949 Comment on: BMJ. 1997 Jun 7;314(7095):1635-6	
Jacobson SK, Daly JS, Thorne GM, McIntosh K.	Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA.	Chronic parvovirus B19 infection resulting in chronic fatigue syndrome: case history and review.	Clin Infect Dis 1997 Jun;24(6):1048-51	The spectrum of disease caused by parvovirus B19 has been expanding in recent years because of improved and more sensitive methods of detection. There is evidence to suggest that chronic infection occurs in patients who are not detectably immunosuppressed. We report the case of a young woman with recurrent fever and a syndrome indistinguishable from chronic fatigue syndrome. After extensive investigation, we found persistent parvovirus B19 viremia, which was detectable by polymerase chain reaction (PCR) despite the presence of IgM and IgG antibodies to parvovirus B19. Testing of samples from this patient suggested that in some low viremic states parvovirus B19 DNA is detectable by nested PCR in plasma but not in serum. The patient's fever resolved with the administration of intravenous immunoglobulin.
Jason LA, Michael T. Ropacki, Nicole B. Santoro, Judith A. Richman , Wendy Heatherly, Renee Taylor, Joseph R. Ferrari , Trina M. Haney-Davis BA, Alfred Rademaker , Josée Dupuis , Jacqueline Golding , Audrius V. Plioplys Sigita Plioplys		A Screening Instrument for Chronic Fatigue Syndrome Reliability and Validity	Journal of Chronic Fatigue Syndrome 1997: 3(1): 39 - 59	Because estimates of the prevalence of Chronic Fatigue Syndrome (CFS) have been quite variable, there is a need for a screening instrument and second stage medical assessment that will produce the most valid estimate of the CFS prevalence. In the present study, four groups of 15 subjects each were recruited: patients diagnosed with (1) CFS, (2) Lupus, (3) Multiple Sclerosis (MS), and (4) a healthy control group. Participants were interviewed twice over a two week period of time with a screening instrument comprising The Fatigue Scale and a newly configured section. The screening instrument had excellent test-retest and interrater reliability. This screening instrument therefore has utility for CFS community-based epidemiologic research. However, while the instrument differentiates with CFS from those who are healthy, it is less likely to distinguish CFS from other autoimmune diseases (especially Lupus). Thus, future community-based CFS prevalence studies should encompass both a screening and a medical examination to adequately differentiate CFS from other illnesses with overlapping symptomatology. We recommend a two-stage research design with (1) a screening instrument with good sensitivity and (2) medical assessments of CFS positives from stage 1 to deal with the specificity problem.
Jason LA, Richman JA, Friedberg F, Wagner L, Taylor R, Jordan KM.	Department of Psychology, DePaul University, Chicago, IL 60614, USA.	Politics, science, and the emergence of a new disease. The case of chronic fatigue syndrome.	Am Psychol 1997 Sep;52(9):973-83Comment in: Am Psychol. 1998 Sep;53(9):1080-2	Chronic fatigue syndrome (CFS) emerged as a diagnostic category during the last decade. Initial research suggested that CFS was a relatively rare disorder with a high level of psychiatric comorbidity. Many physicians minimized the seriousness of this disorder and also interpreted the syndrome as being equivalent to a psychiatric disorder. These attitudes had negative consequences for the treatment of CFS. By the mid-1990s, findings from more representative

				epidemiological studies indicated considerably higher CFS prevalence rates. However, the use of the revised CFS case definition might have produced heterogeneous patient groups, possibly including some patients with pure psychiatric disorders. Social scientists have the expertise to more precisely define this syndrome and to develop appropriate and sensitive research strategies for understanding this disease.
Jason LA, Tryon WW, Frankenberry E, King C.	Department of Psychology, DePaul University, Chicago, IL 60613, USA.	Chronic fatigue syndrome: relationships of self-ratings and actigraphy.	Psychol Rep 1997 Dec;81(3 Pt 2):1223-6	Chronic Fatigue Syndrome is a baffling disease potentially affecting millions of Americans. Self-rating scales were developed to assess this condition but have yet to be validated with objective measures of activity. The present study of a 45-yr.-old man evaluated the relationships between scores on self-rating scales used to measure Chronic Fatigue Syndrome and actigraphy. Measured activity was related to predictors of fatigue but not to fatigue. The implications of these findings are discussed.
Jordan KM, Amy M. Kolak, Leonard A. Jason		Research with Children and Adolescents with Chronic Fatigue Syndrome Methodologies, Designs, and Special Considerations	Journal of Chronic Fatigue Syndrome 1997: 3(2): 3 - 13	Chronic fatigue syndrome (CFS) in children and adolescents presents unique challenges and opportunities to researchers. Issues specific to research conducted on children and adolescents with CFS are discussed. Such issues include the importance of utilizing a consistent definition of CFS and ascertaining that all participants meet the criteria, the need for attention to wading of questions regarding fatigue, and the significance of medical evaluations as part of a research study. Considerations pertaining to research with minors, such as confidentiality and assent, are explored. Finally, suggestions for future research on children are made.
Joyce J, Hotopf M, Wessely S.	Institute of Psychiatry, London, UK.	The prognosis of chronic fatigue and chronic fatigue syndrome: a systematic review.	QJM 1997 Mar;90(3):223-33 comment in: QJM. 1997 Nov;90(11):723 QJM. 1997 Nov;90(11):723-5	The prognosis of chronic fatigue syndrome and chronic fatigue has been studied in numerous small case series. We performed a systematic review of all studies to determine the proportion of individuals with the conditions who recovered at follow-up, the risk of developing alternative physical diagnoses, and the risk factors for poor prognosis. A literature search of all published studies which included a follow-up of patients with chronic fatigue syndrome or chronic fatigue were performed. Of 26 studies identified, four studied fatigue in children, and found that 54-94% of children recovered over the periods of follow-up. Another five studies operationally defined chronic fatigue syndrome in adults and found that < 10% of subjects return to pre-morbid levels of functioning, and the majority remain significantly impaired. The remaining studies used less stringent criteria to define their cohorts. Among patients in primary care with fatigue lasting < 6 months, at least 40% of patients improved. As the definition becomes more stringent the prognosis appears to worsen. Consistently reported risk factors for poor prognosis are older age, more chronic illness, having a comorbid psychiatric disorder and holding a belief that the illness is due to physical causes. Review, Multicase
Kane RL, Gantz NM,	Department of	Neuropsychological and	Neuropsychiatry	Although patients with chronic fatigue syndrome (CFS) typically present

DiPino RK.	Psychology, Veterans Affairs Medical Center, Baltimore, MD 21201, USA.	psychological functioning in chronic fatigue syndrome.	Neuropsychol Behav Neurol 1997 Jan;10(1):25-31	subjective complaints of cognitive and psychological difficulties, studies to date have provided mixed objective support for the existence of specific cognitive deficits. The present study was designed to examine differences in performance between individuals diagnosed with CFS and matched controls with respect to sustained attention, processing efficiency, learning, and memory. Subjects included 17 patients meeting Centers for Disease Control research criteria for CFS and 17 control subjects. Subjects were administered six measures assessing attention, memory, and word-finding ability and two measures assessing psychological distress. For the most part, the two groups did not differ on measures of neurocognitive functioning. Significant group differences were found on a single measure of attention and incidental memory. However, CFS patients differed markedly from controls with respect to reported psychological distress. The results support previous findings of notable levels of psychological distress among CFS patients. They also suggest the need for alternative research paradigms to assess the cognitive abilities of CFS patients.
Kerr JR, Anne-Marie Barrett , Martin D. Curran , Wilhelmina M.H. Behan, Derek Middleton, Peter O. Behan		Brief Communications: Parvovirus B19 and Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(3): 101 - 107	Objective. To investigate the skeletal muscle of patients with chronic fatigue syndrome (CFS) for parvovirus B19. Methods. DNA was extracted from skeletal muscle biopsies from six patients with CFS diagnosed according to thc criteria of the Centers for Disease Control and Prevention and six control cases. Extracted DNA was checked for purity by agarose gel electrophoresis and examined for the presence of B19 DNA by a nested polymerase chain reaction (PCR) method. Results. One of the six biopsies from the CFS group and one of the six from the control group were positive for B19 DNA (Two-tailed P value = 1). Nucleotide sequencing of the PCR product from the CFS patient revealed one silent mutation from A → G at nucleotide 1530 when compared with the published sequence. Nucleotide sequencing of the PCR product from the control patient with mild arthralgia revealed 10 mutations when compared with the published sequence, all silent except the one at nt 1466 (G → C), which resulted in an amino acid change from serine to threonine. Conclusion. The incidence of parvovirus B19 detected in muscle is not increased in patients with CFS compared with controls and the virus in unlikely to play a role in the aetiology of this disorder.
Knepper S.		Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1510-2 [Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2360 Comment on: Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1505-7	
Koehoorn J, Fechter MM, de Vries H.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2362-3	

			Comment on: Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1516-9	
Kroneman H, Croon NH.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Sep 13;141(37):1791	
Kubo K, Fujiyoshi T, Yokoyama MM, Kamei K, Richt JA, Kitze B, Herzog S, Takigawa M, Sonoda S.	Department of Neuropsychiatry, Faculty of Medicine, Kagoshima University, Japan.	Lack of association of Borna disease virus and human T-cell leukemia virus type 1 infections with psychiatric disorders among Japanese patients.	Clin Diagn Lab Immunol 1997 Mar;4(2):189-94	Borna disease virus (BDV) infection has been suspected to be a possible etiological factor in human psychiatric disorders and recently in chronic fatigue syndrome. Evidence of the correlation of BDV infection with these disorders remained unclear. Kagoshima is known to be one of the major areas in which human T-cell leukemia virus type 1 (HTLV-1) is endemic; this is the first isolated human retrovirus that causes adult T-cell leukemia with neurological symptoms. The present study aimed to clarify whether BDV and HTLV-1 infections are associated with psychiatric disorders among Japanese patients. Subjects were 346 patients with psychiatric disorders (schizophrenia, 179; mood disorder, 123; and others, 44) and 70 healthy controls. Anti-BDV antibodies from plasma samples were screened by the indirect immunofluorescence (IF) method using BDV-infected MDCK cells. Results revealed that only three samples were found to be weakly positive for BDV in the IF assay and seronegative by Western blot (immunoblot) assay. Furthermore, BDV-p24 related RNA in peripheral blood mononuclear cells from 106 of 346 psychiatric patients and 12 or 70 healthy controls by p24-reverse transcription PCR was examined. Two mood disorder patients were positive for BDV-p24 RNA but seronegative. To detect anti-HTLV-1 antibodies the plasma samples were screened by the particle agglutination method and no significant difference in seropositivity for anti-HTLV-1 antibody was found between the patients and healthy controls. These results also suggested that there is a lack of association between BDV and HTLV-1 infections with psychiatric disorders among Japanese patients.
Lakein DA, Fantie BD, Grafman J, Ross S, O'Fallon A, Dale J, Straus SE.	American University, USA.	Patients with chronic fatigue syndrome and accurate feeling-of-knowing judgments.	J Clin Psychol 1997 Nov;53(7):635-45	Many Chronic Fatigue Syndrome (CFS) patients complain of memory impairments which have been difficult to document empirically. Subjective complaints of memory impairment may be due to a deficit in metamemory judgment. CFS patients and matched controls were tested with a computerized Trivia Information Quiz that required them to rate their confidence about correctly recognizing an answer in a multiple choice format that they had been unable to remember in a fact-recall format. Even though CFS patients reported significantly greater amounts of fatigue, cognitive, and physical symptoms, the accuracy of their confidence levels and recognition responses were similar to controls. This finding suggests that a metamemory deficit is not the cause of the memory problems reported by CFS patients.
Lapp CW, Hyman HL.		Diagnosis of chronic	Arch Intern Med 1997	

		fatigue syndrome.	Dec 8-22;157(22):2663-4 Comment on: Arch Intern Med. 1997 Mar 10;157(5):491-2	
Lapp CW.		Exercise limits in chronic fatigue syndrome.	Am J Med 1997 Jul;103(1):83-4 Comment on: Am J Med. 1996 Jun;100(6):634-40	
Lawrie SM, MacHale SM, Power MJ, Goodwin GM.		Is the chronic fatigue syndrome best understood as a primary disturbance of the sense of effort?	Psychol Med 1997 Sep;27(5):995-9	
Lawrie SM, Manders DN, Geddes JR, Pelosi AJ.	Edinburgh University Department of Psychiatry, Royal Edinburgh Hospital.	A population-based incidence study of chronic fatigue.	Psychol Med 1997 Mar;27(2):343-53	BACKGROUND: Most research on syndromes of chronic fatigue has been conducted in clinical settings and is therefore subject to selection biases. We report a population-based incidence study of chronic fatigue (CF) and chronic fatigue syndrome (CFS). METHODS: Questionnaires assessing fatigue and emotional morbidity were sent to 695 adult men and women who had replied to a postal questionnaire survey 1 year earlier. Possible CFS cases, subjects with probable psychiatric disorder and normal controls were interviewed. RESULTS: Baseline fatigue score, the level of emotional morbidity and a physical attribution for fatigue were risk factors for developing CF. However, after adjusting for confounding, premorbid fatigue score was the only significant predictor. A minority of CF subjects, all female, had consulted their general practitioner; higher levels of both fatigue and emotional morbidity were associated with consultation. Possible CFS cases reported similar rates of current and past psychiatric disorder to psychiatric controls, but after controlling for fatigue or a diagnosis of neurasthenia the current rates were more similar to those of normal controls. Two new cases of CFS were confirmed. CONCLUSIONS: Both fatigue and emotional morbidity are integral components of chronic fatigue syndromes. The demographic and psychiatric associations of CFS in clinical studies are at least partly determined by selection biases. Given that triggering and perpetuating factors may differ in CFS, studies that examine the similarities and differences between chronic fatigue syndromes and psychiatric disorder should consider both the stage of the illness and the research setting.
Levine PH, Snow PG, Ranum BA, Paul C, Holmes MJ.	Department of Medicine, George Washington University Medical Center,	Epidemic neuromyasthenia and chronic fatigue syndrome in west	Arch Intern Med 1997 Apr 14;157(7):750-4	BACKGROUND: In 1984, an outbreak of an illness characterized by prolonged unexplained fatigue was reported in West Otago, New Zealand. This outbreak resembled other reported outbreaks of epidemic neuromyasthenia in that affected individuals presented with a spectrum of complaints ranging from

	Washington, DC, USA.	Otago, New Zealand. A 10-year follow-up.		transient diarrhea and upper respiratory disorders to chronic fatigue syndrome (CFS). OBJECTIVE: To obtain a perspective on the natural history of CFS not possible in clinic-based studies. METHODS: Twenty-three of the 28 patients in the original report were contacted and asked to complete written questionnaires. Interviews were obtained in person or via telephone. RESULTS: Ten (48%) of the 21 patients with satisfactory interviews appeared to meet the current Centers for Disease Control and Prevention (CDC) case definition of CFS, and 11 were classified as having prolonged or idiopathic fatigue. A return to premorbid activity was seen in most (n = 16) patients, although some reported the need to modify their lifestyle to prevent relapses. A female predominance was noted in those meeting the CDC case definition for CFS, whereas males predominated in patients diagnosed as having prolonged or idiopathic fatigue. CONCLUSIONS: The high proportion of patients recovering from CFS in the West Otago cluster suggests that epidemic-associated CFS has a better prognosis than sporadic cases. Female sex was confirmed as an important risk factor for CFS.
Levine PH.	Department of Medicine, George Washington University Medical Center, Washington, D.C. 20037, USA.	Epidemiologic advances in chronic fatigue syndrome.	J Psychiatr Res 1997 Jan-Feb;31(1):7-18	Epidemiologic studies of chronic fatigue syndrome (CFS) have been hampered by the absence of a specific diagnostic test, but with increasing interest in this disorder there has been a greater understanding of the risk factors, illness patterns, and other aspects of this multisystem disorder. Working case definitions have been developed for research purposes but they have continued to change over time and have not always been utilized precisely by various investigators. This has been a major factor in the widely varying estimates of prevalence rates, but two different studies using the same working definition and including a medical work-up have estimated the prevalence to be approximately 200/100,000. Clusters of CFS cases, which appear to be related to earlier reports of "epidemic neuromyasthenia", have attracted considerable attention and appear to be well documented, although investigated with varying methodology and often with dissimilar case definitions. Risk factors for cases occurring in clusters and sporadically appear to be similar, the most consistent ones being female gender and the co-existence of some form of stress, either physical or psychological. The prognosis of CFS is difficult to predict, although cases occurring as part of clusters appear to have a better prognosis as a group than sporadic cases, and those with an acute onset have a better prognosis than those with gradual onset. It is highly unlikely that there is a single agent, infectious or noninfectious, that is responsible for more than a small proportion of CFS cases and, at the present time, the risk factors for developing CFS appear to lie more prominently in the host rather than the environment.
Lodi R, Taylor DJ, Radda GK.		Chronic fatigue syndrome and skeletal muscle mitochondrial	Muscle Nerve 1997 Jun;20(6):765-6 Comment on: Muscle	

		function.	Nerve. 1996 May;19(5):621-5	
Make B, James F. Jones MD		Impairment of Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(4): 43 - 55	
Malt UF, Nerdrum P, Oppedal B, Gundersen R, Holte M, Lone J.	Department of Psychosomatic and Behavioural Medicine, National Hospital, Oslo, Norway.	Physical and mental problems attributed to dental amalgam fillings: a descriptive study of 99 self-referred patients compared with 272 controls.	Psychosom Med 1997 Jan-Feb;59(1):32-41	OBJECTIVE: The physical and mental symptomatology of 99 self-referred patients complaining of multiple somatic and mental symptoms attributed to dental amalgam fillings were compared with patients with known chronic medical disorders seen in alternative (N = 93) and ordinary (N = 99) medical family practices and patients with dental amalgam fillings (N = 80) seen in an ordinary dental practice. METHOD: The assessments included written self-reports, a 131-item somatic symptom checklist; Eysenck Personality Questionnaire, the General Health Questionnaire, and Toronto Alexithymia Scale. RESULTS: The dental amalgam sample reported significantly more physical symptoms from all body regions. Self-reports suggested that 62% suffered from a chronic anxiety disorder (generalized anxiety disorder or panic). Forty-seven percent suffered from a major depression compared with 14% in the two clinical-comparison samples and none in the dental control sample. Symptoms suggesting somatization disorder were found in 29% of the dental amalgam sample compared with only one subject in the 272 comparison subjects. One third of the dental amalgam patients reported symptoms of chronic fatigue syndrome compared with none in the dental control sample and only 2 and 6%, respectively, in the two clinical comparison samples. The dental amalgam group reported higher mean neuroticism and lower lie scores than the comparison groups. CONCLUSION: Self-referred patients with health complaints attributed to dental amalgam are a heterogeneous group of patients who suffer multiple symptoms and frequently have mental disorders. There is a striking similarity with the multiple chemical sensitivity syndrome.
Manu P		Disablility EvaluationLong-Term Disability for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(4): 19 - 30	To determine the quality of medical evaluations leading to long-term disability payments for chronic fatigue syndrome (CFS) we conducted a structured cross-sectional study of 76 patients receiving such benefits for an average of 2.1 years. Most of the subjects were middle-aged, white (99%), women (87%) who had been previously employed in "white-collar" jobs (96%). In all cases the claim of disability was based on subjective reports of substantial impairment in exercise tolerance and cognitive ability. The quality of disability determinations was judged by the fulfillment of four requirements: correct CFS diagnosis, psychiatric evaluation, neuropsychological testing and physical capacity measurement. The analysis indicated that none of the claims had been fully evaluated and that in 34% of cases none of the requirements had been fulfilled. The diagnosis of CFS was incorrect in 38% of cases. The majority of claimants (84%) had active

				psychiatric disorders, but only 32% had been evaluated by psychiatrists. Only 14% of claimants had their physical capacity objectively assessed and only 11% had formal testing of their cognitive abilities. The data suggest that most medical evaluations resulting in disability payments for CFS are flawed as a result of the overdiagnosis of CFS, the insufficient attention given the comorbid psychiatric disorders, and the infrequent objective testing of physical capacity and cognitive function.
Manu P		Disability Evaluation for Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(4): 9 - 17	
Marcovitch H.		Managing chronic fatigue syndrome in children.	BMJ 1997 Jun 7;314(7095):1635-6Comment in: BMJ. 1997 Oct 11;315(7113):947; discussion 948 BMJ. 1997 Oct 11;315(7113):949 Comment on: BMJ. 1997 Jun 7;314(7095):1647-52	
Marshall PS, Forstot M, Callies A, Peterson PK, Schenck CH.	Department of Psychiatry, Hennepin County Medical Center, Minneapolis, MN 55415, USA.	Cognitive slowing and working memory difficulties in chronic fatigue syndrome.	Psychosom Med 1997 Jan-Feb;59(1):58-66 comment in: Psychosom Med. 1997 Nov-Dec;59(6):638	OBJECTIVE: Patients with chronic fatigue syndrome (CFS) commonly report problems with attention, memory, learning, and speed of cognitive processing. This study attempted to evaluate these complaints using objective test criteria. METHOD: A test battery composed of six tests assessing these cognitive functions was given on two consecutive days. Twenty CFS patients were compared with 20 healthy control subjects and 14 patients with a history of major depression or dysthymia matched by age, intelligence, education level, and sex. RESULTS: Compared with control subjects, CFS patients consistently scored lower on tests in which motor and cognitive processing speeds were a critical factor, eg, reaction-time tasks. They also had more difficulty on working-memory tests in which rapid cognitive processing speed is also an important factor. The effort made on the first day of testing did not result in a decline in cognitive function on the following day. CFS patients did not qualify as having affective disorder by several different diagnostic criteria. Nonetheless, CFS patients' test performances did not differ from patients with a history of major depression or dysthymia. CONCLUSIONS: It is concluded that, although CFS and major depression and dysthymia have distinct clinical features, these disorders have slowed motor and cognitive processing speed in common.
Martin WJ.	Center for Complex	Detection of RNA	Pathobiology	A cytopathic stealth virus was cultured from the cerebrospinal fluid of a nurse

	Infectious Diseases, Rosemead, Calif. 91770, USA. wjmartin@bcf.usc.edu	sequences in cultures of a stealth virus isolated from the cerebrospinal fluid of a health care worker with chronic fatigue syndrome. Case report.	1997;65(1):57-60	with chronic fatigue syndrome. Reverse transcriptase-polymerase chain reaction (RT-PCR) performed on the patient's culture yielded positive results with primer sets based on sequences of a previously isolated African green monkey simian-cytomegalovirus-derived stealth virus. The same primer sets did not yield PCR products when tested directly on DNA extracted from the cultures. The findings lend support to the possibility of replicative RNA forms of certain stealth viruses and have important implications concerning the choice of therapy in this type of patient.
Mawle AC, Nisenbaum R, Dobbins JG, Gary HE Jr, Stewart JA, Reyes M, Steele L, Schmid DS, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.	Immune responses associated with chronic fatigue syndrome: a case-control study.	J Infect Dis 1997 Jan;175(1):136-41	An exploratory case-control study was conducted to assess whether the many reported differences in the immune function of chronic fatigue syndrome (CFS) patients are detectable in rigorously defined cases of CFS. Although many studies have reported differences between cases and controls in various measures of immune function, none of these differences were found in all studies. In this study, no differences were found in white blood cell numbers; immune complex, complement, or serum immunoglobulin levels; delayed type hypersensitivity and allergic responses; NK cell function; and proliferative responses to mitogens and antigens. Marginal differences were detected in cytokine responses and in cell surface markers in the total CFS population. However, when the patients were subgrouped by type of disease onset (gradual or sudden) or by how well they were feeling on the day of testing, more pronounced differences were seen.
Mawle AC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.	Chronic fatigue syndrome.	Immunol Invest 1997 Jan-Feb;26(1-2):269-73	Chronic fatigue syndrome (CFS) has emerged as a public health concern over the past decade. A working case definition was created in 1988 and revised in 1994, and this has been used to establish prevalence estimates using physician-based surveillance and an a random digit dial telephone survey. Although CFS has some characteristics of an infectious disease, so far no infectious agent has been associated with the illness. Studies of immune function in CFS patients failed to detect differences between cases and healthy controls. However, when cases were subgrouped according to whether they had a sudden or gradual onset, differences in immunologic markers were detected between cases and their matched controls.
McGregor NR, R. H. Dunstan, H. L. Butt , T. K. Roberts , I. J. Klineberg , M. Zerbes		A Preliminary Assessment of the Association of SCL-90-R Psychological Inventory Responses with Changes in Urinary Metabolites in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(1): 17 - 37	A previous investigation of a cohort of 20 chronic fatigue syndrome (CFS) patients revealed an increased urinary excretion of an unusual metabolite, tentatively identified as amino-hydroxyN-methyl-pyrrolidine (coded CFSUMl) and ß-alanine, compared with 45 control subjects. The relative abundances of both CFSUM1 and ß-alanine were positively associated with the core diagnostic symptoms of CFS and associated changes in amino and organic acid excretion. The psychological attributes of these CFS patients and controls were assessed in this study by using the Symptom Check List-90-revised (SCL-90-R) psychological inventory. The CFS patients had increases in the SCL-90-R somatization, obsessive compulsive, depression, anxiety and phobic anxiety dimension scores. Nineteen of 20 CFS

				patients had somatization T-scores ≥ 63 (P < 0.0001), suggestive of a somatization disorder. Multiple regression analysis indicated that somatization was the most important SCL-90-R defined dimension discriminating CFS from control subjects. Depression and anxiety were not found to be important inter-group determinants. The dimension scores were each related to specific changes in the urinary excretion of organic and amino acids, suggesting that each is biochemically distinct and has an organic basis. Cluster analysis of dimension profiles revealed that the profile with increased prevalence (P < 0.0001) in CFS patients was associated with increased excretion of CFSUM1 (P < 0.005) and had increases in somatization, obsessive compulsion and depression dimension scores. The PSDI as a measure of SCL-90-R symptom severity was positively correlated with CFSUM1 (model P < 0.003). CFSUM1 was also the primary correlate for the somatization dimension (model P < 0.0008), but was not associated with any other SCL-90-R-defined dimension. Another unidentified urinary metabolite, coded UM15, was the primary correlate for depression (model P < 0.0004) and was associated with multiple dimension elevations by both cluster and logistic regression analysis; the excretion of this compound was unrelated to CFSUM1. These results indicated that, in this CFS cohort, the SCL-90-R defined psychological changes were strongly associated with changes in the biochemical homeostasis of patients, suggestive of an organic basis to CFS.
Miro O, Font C, Fernandez-Sola J, Casademont J, Pedrol E, Grau JM, Urbano-Marquez A.	Servicio de Medicina Interna, Hospital Clinic i Provincial, Universidad de Barcelona.	[Chronic fatigue syndrome: study of the clinical course of 28 cases].[article in Spanish]	Med Clin (Barc) 1997 Apr 19;108(15):561-5Comment in: Med Clin (Barc). 1997 Apr 19;108(15):577-9	BACKGROUND: Chronic fatigue syndrome (CFS) is an entity of unknown etiopathogenesis without specific markers. The diagnosis is based on clinical criteria. There are few studies evaluating the natural evolution and prognosis-related factors in CFS. OBJECTIVES: a) to evaluate the outcome of patients suffering from CFS, and b) to detect predictive factors associated with a better prognosis. MATERIAL AND METHODS: Clinical records of all patients diagnosed of CFS between January 1986 and December 1992 were retrospectively reviewed. Of these patients, we included those fulfilling the CDC criteria for CFS, with a follow-up period greater than one year. We evaluated epidemiological, clinical and evolutive data recorded by their usual physicians. Moreover, the patients were interviewed in order to know their own appreciation with respect to their current clinical status, as well as their present working situation. RESULTS: Twenty-eight patients were included in the present study. Their mean age was 38 +/- 7. Seventy-five percent of them were women. The mean time of clinical follow-up was of 3.2 +/- 1.8 years. According to evaluation, 21% of patients improved or became asymptomatic. A similar percentage (28%) of improvement was obtained from the interview. Forty-eight percent of cases had transitory or definitive laboral incapacity. Regarding to prognostic factors, we could not find any statistical differences among the analyzed variables except for marital status. In this variable, married patients had better outcome than unmarried patients.

				CONCLUSION: CFS is an entity with a poor outcome, since it evolves towards to chronicity in an important number of cases. In addition, strong functional disability may be present, leading frequently to laboral incapacity. Review, Multicase
Moorkens G, Manuel y Keenoy B, Vertommen J, Meludu S, Noe M, De Leeuw I.	Department of Internal Medicine, University Hospital, Antwerp, Belgium.	Magnesium deficit in a sample of the Belgian population presenting with chronic fatigue.	Magnes Res 1997 Dec;10(4):329-37	97 patients (25 per cent males, ages ranging from 14 to 73 years, median 38 years) with complaints of chronic fatigue (chronic fatigue syndrome, fibromyalgia or/and spasmophilia) have been enrolled in a prospective study to evaluate the Mg status and the dietary intake of Mg. An IV loading test (performed following the Ryzen protocol) showed a Mg deficit in 44 patients. After Mg supplementation in 24 patients, the loading test showed a significant decrease (p = 0.0018) in Mg retention. Mean values of serum Mg, red blood cell Mg and magnesuria showed no significant difference between patients with or without Mg deficiency. No association was found between Mg deficiency, CFS or FM. However serum Mg level was significantly lower in the patients with spasmophilia than in the other patients.
Morriss RK, Wearden AJ, Battersby L.	University of Manchester, Department of Community Psychiatry, UK.	The relation of sleep difficulties to fatigue, mood and disability in chronic fatigue syndrome.	J Psychosom Res 1997 Jun;42(6):597-605	The relationship of sleep complaints to mood, fatigue, disability, and lifestyle was examined in 69 chronic fatigue syndrome (CFS) patients without psychiatric disorder, 58 CFS patients with psychiatric disorder, 38 psychiatric out-patients with chronic depressive disorders, and 45 healthy controls. The groups were matched for age and gender. There were few differences between the prevalence or nature of sleep complaints of CFS patients with or without current DSM-IIIR depression, anxiety or somatization disorder. CFS patients reported significantly more naps and waking by pain, a similar prevalence of difficulties in maintaining sleep, and significantly less difficulty getting off to sleep compared to depressed patients. Sleep continuity complaints preceded fatigue in only 20% of CFS patients, but there was a strong association between relapse and sleep disturbance. Certain types of sleep disorder were associated with increased disability or fatigue in CFS patients. Disrupted sleep appears to complicate the course of CFS. For the most part, sleep complaints are either attributable to the lifestyle of CFS patients or seem inherent to the underlying condition of CFS. They are generally unrelated to depression or anxiety in CFS. Randomized Controlled Trial
Mounstephen A, Sharpe M.	University of Edinburgh, Royal Edinburgh Hospital, UK.	Chronic fatigue syndrome and occupational health.	Occup Med (Lond) 1997 May;47(4):217-27	Chronic fatigue syndrome (CFS) is a controversial condition that many occupational physicians find difficult to advise on. In this article we review the nature and definition of CFS, the principal aetiologic hypotheses and the evidence concerning prognosis. We also outline a practical approach to patient assessment, diagnosis and management. The conclusions of this review are then applied to the disability discrimination field. The implications of the new UK occupational health legislation are also examined. Despite continuing controversy about the status, aetiology and optimum management of CFS, we argue that

				much can be done to improve the outcome for patients with this condition. The most urgent needs are for improved education and rehabilitation, especially in regard to employment. Occupational physicians are well placed to play an important and unique role in meeting these needs.
Nakaya T, Kuratsune H, Kitani T, Ikuta K.	Section of Serology, Hokkaido University.	[Demonstration on Borna disease virus in patients with chronic fatigue syndrome].[article in Japanese]	Nippon Rinsho 1997 Nov;55(11):3064-71	Chronic fatigue syndrome (CFS), a recently named heterogeneous disorder, is an illness of unknown etiology. The association between CFS and several viral infection has been suggested. Here, we centered on the possible link between CFS and Borna disease virus (BDV) infection. BDV is a neurotropic, nonsegmented negative-strand (NNS) RNA virus. Recent epidemiological data have suggested that BDV may be closely associated with depression and schizophrenia in humans. In Japanese patients with CFS, the prevalence of BDV infection was 34% (30/89) and 12% (7/57) by immunoblotting and PCR analysis, respectively. Furthermore, anti-BDV antibodies and BDV RNA were detected in a family cluster with CFS. These results suggested that this virus contributes to or initiates CFS, although the single etiologic role of BDV is unlikely. Review Literature
Nishikai M, Kosaka S.		Incidence of antinuclear antibodies in Japanese patients with chronic fatigue syndrome.	Arthritis Rheum 1997 Nov;40(11):2095-7 Comment on: Arthritis Rheum. 1997 Feb;40(2):295-305	
Owens PE, O'Brien ET.	Blood Pressure Unit, Beaumont Hospital, Dublin, Republic of Ireland.	Hypotension: a forgotten illness?.	Blood Press Monit 1997 Dec;2(1):3-14	Low blood pressure is a frequently encountered phenomenon in clinical practice. Few practitioners in the Western world however regard chronic low blood pressure as a genuinely pathological disease state. Evidence is emerging that chronic hypotension is associated with considerable morbidity in the community. It has recently been implicated as the causative mechanism in patients with the chronic fatigue syndrome. Identification of low blood pressure can prove probjlematic, so ambulatory blood pressure monitoring may prove a more reliable method both for determining mean blood pressure levels and for identifying episodes of marked hypotension. Low blood pressure is broadly divided into two categories, chronic constitutional hypotension and hypotension associated with abnormal postural control. The causes are examined and the clinical presentations are discussed. An approach to investigation and diagnosis is outlined, and current options regarding treatment and management are described. The clinical spectrum of low blood pressure is wide. From young patients with vagally mediated syncope or patients with iatrogenic hypotension to elderly patients with autonomic degenerative conditions, there exists a substantial body of patients with potentially avoidable or treatable morbidity. Such a group requires more rigorous scientific investigation and a more sympathetic clinical approach.
Patarca R		Report of the	Journal of Chronic	

		International Meeting on Standardization and Calibration of Cytokine Immunoassays A User's Perspective	Fatigue Syndrome 1997: 3(3): 97 - 99	
Peakman M, Deale A, Field R, Mahalingam M, Wessely S.	Department of Immunology, King's College School of Medicine & Dentistry, London, United Kingdom.	Clinical improvement in chronic fatigue syndrome is not associated with lymphocyte subsets of function or activation.	Clin Immunol Immunopathol 1997 Jan;82(1):83-91	The relationship between markers of immune function and chronic fatigue syndrome (CFS) is controversial. To examine the relationship directly, 43 subjects with CFS entering a randomized controlled trial of a nonpharmacological treatment for CFS gave samples for immunological analysis before and after treatment. Percentage levels of total CD3+ T cells, CD4 T cells, CD8 T cells, and activated subsets did not differ between CFS subjects and controls. Naive (CD45RA+ RO-) and memory (CD45RA- RO+) T cells did not differ between subjects and controls. Natural killer cells (CD16+/CD56+/CD3-) were significantly increased in CFS patients compared to controls, as was the percentage of CD11b+ CD8 cells. There were no correlations between any immune variable and measures of clinical status, with the exception of a weak correlation between total CD4 T cells and fatigue. There was a positive correlation between memory CD4 and CD8 T cells and depression scores and a negative correlation between naive CD4 T cells and depression. No immune measures changed during the course of the study, and there was no link between clinical improvement as a result of the treatment program and immune status. Immune measures did not predict response or lack of response to treatment. In conclusion, we have been unable to replicate previous findings of immune activation in CFS and unable to find any important associations between clinical status, treatment response, and immunological status. Randomized Controlled Trial
Pearn JH.	Department of Paediatrics and Child Health, Royal Children's Hospital, Brisbane, QLD.	Chronic fatigue syndrome: chronic ciguatera poisoning as a differential diagnosis.	Med J Aust 1997 Mar 17;166(6):309-10	
Peterson DL		EditorialsChronic Fatigue Syndrome and Disability	Journal of Chronic Fatigue Syndrome 1997: 3(4): 5 - 7	
Plioplys AV, Plioplys S, Davis JS 4th.	Department of Neurology, University of Illinois College of Medicine at Chicago, USA.	Meeting the frustrations of chronic fatigue syndrome.	Hosp Pract (Off Ed) 1997 Jun 15;32(6):147-50, 153-6, 160-1, passim	Patients face long-term disability, a variable prognosis, and too often, skeptical or misinformed doctors. Physicians lack laboratory markers or definitive treatment. Nevertheless, the diagnosis can be made with confidence by applying established diagnostic criteria- and selected laboratory studies to exclude other disorders- while symptomatic medication can provide support until recovery begins.
Plioplys AV, Plioplys S.	Chronic Fatigue Syndrome Center, Department of	Amantadine and L-carnitine treatment of Chronic Fatigue	Neuropsychobiology 1997;35(1):16-23	Carnitine is essential for mitochondrial energy production. Disturbance in mitochondrial function may contribute to or cause the fatigue seen in Chronic Fatigue Syndrome (CFS) patients. Previous investigations have reported

	Research, Mercy Hospital Chicago, Ill 60616, USA.	Syndrome.		decreased carnitine levels in CFS. Orally administered L-carnitine is an effective medicine in treating the fatigue seen in a number of chronic neurologic diseases. Amantadine is one of the most effective medicines for treating the fatigue seen in multiple sclerosis patients. Isolated reports suggest that it may also be effective in treating CFS patients. Formal investigations of the use of L-carnitine and amantadine for treating CFS have not been previously reported. We treated 30 CFS patients in a crossover design comparing L-carnitine and amantadine. Each medicine was given for 2 months, with a 2-week washout period between medicines. L-Carnitine or amantadine was alternately assigned as fist medicine. Amantadine was poorly tolerated by the CFS patients. Only 15 were able to complete 8 weeks of treatment, the others had to stop taking the medicine due to side effects. In those individuals who completed 8 weeks of treatment, there was no statistically significant difference in any of the clinical parameters that were followed. However, with L-carnitine we found statistically significant clinical improvement in 12 of the 18 studied parameters after 8 weeks of treatment. None of the clinical parameters showed any deterioration. The greatest improvement took place between 4 and 8 weeks of L-carnitine treatment. Only 1 patient was unable to complete 8 weeks of treatment due to diarrhea. L-Carnitine is a safe and very well tolerated medicine which improves the clinical status of CFS patients. In this study we also analyzed clinical and laboratory correlates of CFS symptomatology and improvement parameters. Randomized Controlled Trial
Plioplys AV.	Chronic Fatigue Syndrome Center, Mercy Hospital, Chicago, IL, USA.	Antimuscle and anti-CNS circulating antibodies in chronic fatigue syndrome.	Neurology 1997 Jun;48(6):1717-9	Chronic fatigue syndrome (CFS) patients suffer from disabling physical and mental fatigue. Circulating autoimmune antibodies may produce symptoms of muscular fatigue by reacting with acetylcholine receptors or calcium binding channels. They can also produce mental status changes by reacting with central nervous system (CNS) antigens. We thoroughly investigated the presence of circulating antimuscle and anti-CNS antibodies in 10 CFS patients and 10 controls. We were unable to detect any pathogenic antibodies.
Plioplys AV.	Chronic Fatigue Syndrome Research Center, Mercy Hospital and Medical Center, Chicago, IL 60616, USA.	Chronic fatigue syndrome should not be diagnosed in children.	Pediatrics 1997 Aug;100(2 Pt 1):270-1	
Pourmand R.	Department of Neurology, Indiana University School of Medicine, Indianapolis, USA.	Myasthenia gravis.	Dis Mon 1997 Feb;43(2):65-109	Adult-onset myasthenia gravis is an acquired autoimmune disorder of neuromuscular transmission in which acetylcholine receptor antibodies attack the postsynaptic membrane of the neuromuscular junction. Although the cause of this disease is unknown, the role of immune responses in its pathogenesis is well established. Circulating acetylcholine receptor antibodies are present in 80% to 90% of patients with the generalized form of myasthenia gravis. Most patients

				have ptosis, diplopia, dysarthria and dysphagia. The weakness and fatigue worsen on exertion and improve with rest. Respiratory muscle and limb weakness are rare at the onset of the disease. For the past two decades, there has been considerable progress in understanding the diagnosis and management of myasthenia gravis. The diagnosis is based on clinical presentation, neurologic examination, and confirmation by means of electrophysiologic testing and immunologic studies. Myasthenia gravis mimics many neuromuscular diseases and even illnesses such as depression and chronic fatigue syndrome. One should always exclude drug-induced myasthenia gravis for all patients. With the introduction of new modalities of treatment, particularly immunosuppressive or immunomodulating drugs, plasma exchange and thymectomy, the morbidity and mortality of myasthenia gravis have decreased dramatically to the point that myasthenia gravis should not be considered as serious a disease as it once was. Although the several therapeutic options are usually effective and have meant independence in daily life to many patients with myasthenia gravis, well-designed, controlled, prospective studies are still lacking.
Ray C, Jefferies S, Weir WR.	Department of Human Sciences, Brunel University, Uxbridge, Middlesex, UK.	Coping and other predictors of outcome in chronic fatigue syndrome: a 1-year follow-up.	J Psychosom Res 1997 Oct;43(4):405-15	In this prospective study, 137 patients with chronic fatigue syndrome were followed-up at a 1-year interval to determine factors relating to outcomes. Nearly two thirds reported an improvement on direct ratings of change. In analyses with fatigue and functional impairment at follow-up as the criteria, and controlling for earlier status, poorer outcomes were predicted by illness duration, subjective cognitive difficulty, and somatic symptoms; there was no influence of anxiety, depression, or general emotional distress. Fatigue was also predicted by information-seeking, and impairment by behavioral disengagement and a low internal locus of control. The belief that one's actions can influence outcomes modified the relationship between illness accommodation and both fatigue and impairment; adverse outcomes were associated with accommodating to illness only in the context of lower levels of perceived control. Thus, it is suggested that interventions that either discourage avoidance of activity or enhance perceived control could benefit the course of the illness.
Redmond G.	Women's Hormone Center Beachwood, Ohio, USA.	Mood disorders in the female patient.	Int J Fertil Womens Med 1997 Mar-Apr;42(2):67-72	Disruptive changes in mood and low energy level are among the most common reasons women consult a physician. Usually no clear physiological explantation for these changes can be found. Many physicians feel uncomfortable dealing with patients with these complaints. The purpose of this paper is to discuss a practical approach to helping women with such conditions. A variety of terms have been utilized to refer to the situation in which a female patient has decreased energy or labile mood. Premenstrual Syndrome (PMS) and chronic fatigue syndrome (CFS) are currently popular terms. An association of low mood with menstrual cycle phase is undoubted, with the late luteal-early premenstrual phase most commonly associated with depression and irritability. It seems likely that women

				with PMS and those without it do not differ in circulating hormone levels during their cycles but rather in the brain response to these. Estrogen and progesterone receptors exist in the brain and change during the cycle. Elaborate diagnostic efforts are rarely rewarding in managing mood and energy disorders. Of more value is a careful history particularly concerned with the pattern of mood changes and with life stresses, accompanied by a thorough physical examination and laboratory tests. In most cases, changes in mood and energy are a variant of clinical depression. Changes in energy and sleep may be more evident than low affect. Treatment with an appropriate antidepressant, usually a selective serotonin re-uptake inhibitor (SSRI), benefits most of these patients. Allowing the patient to express concerns about stressful life situations is often of great value.
Regland B, Andersson M, Abrahamsson L, Bagby J, Dyrehag LE, Gottfries CG.	Institute of Clinical Neuroscience, Goteborg University, Sweden.	Increased concentrations of homocysteine in the cerebrospinal fluid in patients with fibromyalgia and chronic fatigue syndrome.	Scand J Rheumatol 1997;26(4):301-7	Twelve outpatients, all women, who fulfilled the criteria for both fibromyalgia and chronic fatigue syndrome were rated on 15 items of the Comprehensive Psychopathological Rating Scale (CPRS-15). These items were chosen to constitute a proper neurasthenic subscale. Blood laboratory levels were generally normal. The most obvious finding was that, in all the patients, the homocysteine (HCY) levels were increased in the cerebrospinal fluid (CSF). There was a significant positive correlation between CSF-HCY levels and fatiguability, and the levels of CSF-B12 correlated significantly with the item of fatiguability and with CPRS-15. The correlations between vitamin B12 and clinical variables of the CPRS-scale in this study indicate that low CSF-B12 values are of clinical importance. Vitamin B12 deficiency causes a deficient remethylation of HCY and is therefore probably contributing to the increased homocysteine levels found in our patient group. We conclude that increased homocysteine levels in the central nervous system characterize patients fulfilling the criteria for both fibromyalgia and chronic fatigue syndrome.
Richmond C.		Mad cows and Englishmen: the aftermath of a BSE scare.	CMAJ 1997 Apr 1;156(7):1043-4	The consumption of prime beef cuts is down, animals have been slaughtered by the thousand and 3 farmers have committed suicide as the mad-cow issue continues to cause concern in the United Kingdom. In this report from London, Caroline Richmond also notes that the royal colleges have published a report stating that chronic fatigue syndrome is a real illness and patients need help.
Robbins JM, Kirmayer LJ, Hemami S.	Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Hospital, Little Rock 72202, USA.	Latent variable models of functional somatic distress.	J Nerv Ment Dis 1997 Oct;185(10):606-15	Latent variable models of functional somatic symptoms were estimated for a sample of 686 family medicine patients. Symptom items from the NIMH Diagnostic Interview Schedule were selected to approximate diagnoses of fibromyalgia syndrome (FMS), chronic fatigue syndrome (CFS), and irritable bowel syndrome (IBS). Confirmatory factor analysis demonstrated that hypothesized latent variables of somatic depression, somatic anxiety, FM-like, CF-like, and IB-like syndromes fit the observed covariations better than models hypothesizing fewer latent variables. Results offer tentative confirmation of functional somatic syndromes as discrete entities and suggest that relaxing the

				diagnostic criteria for somatization may identify individuals with distress limited to a single functional system.
Rosenfeld WD, Walco GA.	Adolescent/Young Adult Center for Health, Morristown Memorial Hospital, 100 Madison Avenue, Morristown, NJ 07962, USA.	One Test Too Many: Toward an Integrated Approach to Psychosomatic Disorders.	Adolesc Med 1997 Oct;8(3):483-487	Conditions such as chronic fatigue syndrome (CFS), fibromyalgia, and several others belong to the group of disorders in which both physiologic and psychologic factors are substantially involved, and in some cases there may be no real distinction between the two. However, primary patient assessment usually employs an array of clinical tools, and only after known physiologic factors are excluded is the patient referred for psychologic or psychiatric evaluation. This chapter suggests that clinical evaluation should initially include both physiologic and psychosocial assessment, which would minimize the division and greatly improve the efficacy of the treatment.
Rowe KS.	Department of Paediatrics, University of Melbourne Royal Children's Hospital, Victoria, Australia.	Double-blind randomized controlled trial to assess the efficacy of intravenous gammaglobulin for the management of chronic fatigue syndrome in adolescents.	J Psychiatr Res 1997 Jan-Feb;31(1):133-47	A double blind randomized controlled trial was conducted in 71 adolescents aged 11-18 years. Inclusion in the trial required fulfilment of the diagnostic criteria, (Fukuda et al., 1994). Three infusions of 1 gm/kg (max 1 litre of 6 gm/100 ml in 10% w/v maltose solution) were given one month apart. The dummy solution was a 10% w/v maltose solution with 1% albumin of equivalent volume for weight. Efficacy was assessed by difference in a mean functional score including school attendance, school work, social activity and physical activity, between baseline, three months and six months after the final infusion. There was a significant mean functional improvement at the six month follow-up of 70 adolescents with Chronic Fatigue Syndrome of average duration 18 months. There was also a significant improvement for both groups from the beginning of the trial to the six month post infusion follow-up. Adverse effects were common with both solutions but not predictive of response. Neither solution could be identified by recipients. Randomized Controlled Trial
Sadler M.		Graded exercise in chronic fatigue syndrome. Patients were selected group.	BMJ 1997 Oct 11;315(7113):947-8 Comment on: BMJ. 1997 Jun 7;314(7095):1647-52	
Salit IE.	Division of Infectious Diseases, Toronto Hospital, Ontario, Canada. irving.salit@utoronto.ca	Precipitating factors for the chronic fatigue syndrome.	728: J Psychiatr Res 1997 Jan-Feb;31(1):59-65	The etiology of the Chronic Fatigue Syndrome (CFS) is unknown but it is usually considered to be postinfectious or postviral. Many infecting agents have been suspected as causative but none has been proven. We investigated precipitating factors in 134 CFS patients through the use of a questionnaire, interview, clinical examination and serology for infecting agents; 35 healthy controls completed a similar questionnaire. CFS started with an apparently infectious illness in 96 (72%) but a definite infection was only found in seven of these 96 (7%). Thirty-eight (28%) had no apparent infectious onset: 15/38 (40%) had noninfectious precipitants (trauma, allergy, surgery). There was no apparent precipitating event in 23/38 (61%). Immunization was not a significant precipitant. Stressful events

				were very common in the year preceding the onset of CFS (114/134, 85%) but these occurred in only 2/35 (6%) of the controls (p < .0001). The onset of CFS may be associated with preceding stressful events and multiple other precipitants. An infectious illness is not uniformly present at the onset and no single infectious agent has been found; CFS is most likely multifactorial in origin.
Sandhaus SH		A Primer for Chronic Fatigue Syndrome Claimants in Applying for Long-Term Disability Policy Benefits	Journal of Chronic Fatigue Syndrome 1997: 3(4): 69 - 73	
Sargent CA, Stuart Anderson, Michael Budek		Psychomotor Functioning in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(3): 53 - 68	
See DM, Broumand N, Sahl L, Tilles JG.	Department of Medicine, U.C. Irvine Medical Center, Orange 92668, USA.	In vitro effects of echinacea and ginseng on natural killer and antibody-dependent cell cytotoxicity in healthy subjects and chronic fatigue syndrome or acquired immunodeficiency syndrome patients.	Immunopharmacology 1997 Jan;35(3):229-35	Extracts of Echinacea purpurea and Panax ginseng were evaluated for their capacity to stimulate cellular immune function by peripheral blood mononuclear cells (PBMC) from normal individuals and patients with either the chronic fatigue syndrome or the acquired immunodeficiency syndrome. PBMC isolated on a Ficoll-hypaque density gradient were tested in the presence or absence of varying concentrations of each extract for natural killer (NK) cell activity versus K562 cells and antibody-dependent cellular cytotoxicity (ADCC) against human herpesvirus 6 infected H9 cells. Both echinacea and ginseng, at concentrations > or = 0.1 or 10 micrograms/kg, respectively, significantly enhanced NK-function of all groups. Similarly, the addition of either herb significantly increased ADCC of PBMC from all subject groups. Thus, extracts of Echinacea purpurea and Panax ginseng enhance cellular immune function of PBMC both from normal individuals and patients with depressed cellular immunity.
Sendrowski DP, Buker EA, Gee SS.	Southern California College of Optometry, Fullerton, USA.	An investigation of sympathetic hypersensitivity in chronic fatigue syndrome.	Optom Vis Sci 1997 Aug;74(8):660-3	BACKGROUND: There are many theories, but the etiology of chronic fatigue syndrome (CFS) remains unknown. Diagnosticians have set guidelines to try to classify the condition, but its clinical definition is one of exclusion rather than defined by specific clinical testing. The primary goal of this investigation was to find a diagnostic key to define CFS. CFS patients and those diagnosed with the sympathetic hypersensitivity condition called fibromyalgia syndrome (FMS) exhibit identical brain single photon emission computerized tomography (SPECT) images. Therefore, this investigation was initiated to see if CFS patients also had denervation hypersensitivity of the sympathetic system. METHODS: A standardized supersensitivity test was performed using an ocular instillation of two drops of 1.0% phenylephrine. Sixty-two subjects (29 CFS patients and 33 normals) participated in the study. Measurements of pupil size were recorded by pupil gauge and flash photography. A pupillary dilation of greater than 2.5 mm would suggest a sympathetic denervation hypersensitivity. RESULTS: For all

				participants, a small, but statistically significant increase in pupil size was found (mean of 0.788 mm in normals and 0.931 mm in CFS patients). The change in pupil size in the CFS patients and controls showed substantial overlap and was not statistically significant (t = 0.83, p = 0.42, dF = 60). CONCLUSION: In conclusion, the results suggest that a denervation hypersensitivity of the pupil does not occur in CFS patients. The use of 1.0% topical phenylephrine had no diagnostic value in detecting CSF patients vs. normals.
Sharpe M, Chalder T, Palmer I, Wessely S.	University of Edinburgh, UK.	Chronic fatigue syndrome. A practical guide to assessment and management.	Gen Hosp Psychiatry 1997 May;19(3):185-99	Chronic fatigue and chronic fatigue syndrome (CFS) have become increasingly recognized as a common clinical problem, yet one that physicians often find difficult to manage. In this review we suggest a practical, pragmatic, evidence-based approach to the assessment and initial management of the patient whose presentation suggests this diagnosis. The basic principles are simple and for each aspect of management we point out both potential pitfalls and strategies to overcome them. The first, and most important task is to develop mutual trust and collaboration. The second is to complete an adequate assessment, the aim of which is either to make a diagnosis of CFS or to identify an alternative cause for the patient's symptoms. The history is most important and should include a detailed account of the symptoms, the associated disability, the choice of coping strategies, and importantly, the patient's own understanding of his/her illness. The assessment of possible comorbid psychiatric disorders such as depression or anxiety is mandatory. When the physician is satisfied that no alternative physical or psychiatric disorder can be found to explain symptoms, we suggest that a firm and positive diagnosis of CFS be made. The treatment of CFS requires that the patient is given a positive explanation of the cause of his symptoms, emphasizing the distinction among factors that may have predisposed them to develop the illness (lifestyle, work stress, personality), triggered the illness (viral infection, life events) and perpetuated the illness (cerebral dysfunction, sleep disorder, depression, inconsistent activity, and misunderstanding of the illness and fear of making it worse). Interventions are then aimed to overcoming these illness-perpetuating factors. The role of antidepressants remains uncertain but may be tried on a pragmatic basis. Other medications should be avoided. The only treatment strategies of proven efficacy are cognitive behavioral ones. The most important starting point is to promote a consistent pattern of activity, rest, and sleep, followed by a gradual return to normal activity; ongoing review of any 'catastrophic' misinterpretation of symptoms and the problem solving of current life difficulties. We regard chronic fatigue syndrome as important not only because it represents potentially treatable disability and suffering but also because it provides an example for the positive management of medically unexplained illness in general.
Sharpe M, Hawton K,	University Department	Increased brain	BMJ 1997 Jul	

Clements A, Cowen PJ.	of Psychiatry, Warneford and Littlemore Hospitals, Oxford.	serotonin function in men with chronic fatigue syndrome.	19;315(7101):164-5	
Sharpe M.	University of Edinburgh, Royal Edinburgh Hospital, United Kingdom.	Cognitive behavior therapy for functional somatic complaints. The example of chronic fatigue syndrome.	Psychosomatics 1997 Jul-Aug;38(4):356-62	Somatic complaints such as pain and fatigue that are unexplained by conventional disease are common in medical practice and are referred to as functional, somatoform, or somatization symptoms. Despite frequent chronicity, disability, and high associated medical costs, patients with these complaints are rarely offered either constructive explanations or effective treatment. In this perspective, a cognitive-behavioral approach to the problem is described, using chronic fatigue syndrome as an example. It is concluded that the utility of the cognitive-behavioral theory and the proven effectiveness cognitive behavior therapy provide the basis for a new evidence-based approach to psychosomatics.
Sharpley A, Clements A, Hawton K, Sharpe M.	Department of Psychiatry, University of Oxford, United Kingdom.	Do patients with "pure" chronic fatigue syndrome (neurasthenia) have abnormal sleep?	Psychosom Med 1997 Nov-Dec;59(6):592-6	OBJECTIVE: To determine whether patients with "pure" chronic fatigue syndrome (neurasthenia) have sleep abnormalities which may contribute to subjective measures of daytime fatigue. METHOD: Sleep characteristics of 20 patients meeting research criteria for chronic fatigue syndrome (CFS) but not depression, anxiety, or sleep disorder were compared with sleep characteristics of 20 healthy subjects matched for age and sex. Measures of sleep included a) subjective interview reports and sleep diaries and b) home-based polysomnography. RESULTS: Patients with CFS complained of poor quality unrefreshing sleep. They also napped during the day. Polysomnograph data showed no difference in actual nocturnal sleep time between the two groups although patients with CFS spent significantly longer in bed ($p < .01$), slept less efficiently ($p < .03$), and spent longer awake after sleep onset ($p < .05$). The polysomnographs of seven patients with CFS and one healthy subject were regarded as significantly abnormal. Five patients and one healthy subject had difficulty maintaining sleep. One patient had a disorder of both initiating and maintaining sleep and one patient woke early. CONCLUSIONS: Patients with "pure" CFS complain of unrefreshing sleep but only a minority have a clearly abnormal polysomnograph. The most common abnormality is of long periods spent awake after initial sleep onset. Although sleep abnormalities may play a role in the etiology of CFS, they seem to be unlikely to be an important cause of daytime fatigue in the majority of patients. However, pharmacological and behavioral methods that improve sleep quality may be an important component of a pragmatically based treatment package for patients who do have abnormal sleep.
Shefer A, Dobbins JG, Fukuda K, Steele L, Koo D, Nisenbaum R, Rutherford GW.	Epidemic Intelligence Service Program, Centers for Disease Control and Prevention,	Fatiguing illness among employees in three large state office buildings, California,	J Psychiatr Res 1997 Jan-Feb;31(1):31-43	The objective was to determine if a cluster of chronic fatigue syndrome (CFS)-like illness had occurred among employees in two large state office buildings in northern California, and to identify risk factors for and features of fatiguing illness in this population. DESIGN: case-control study. POPULATION AND SETTING: Over

	Atlanta, GA 30333, USA.	1993: was there an outbreak?		3300 current employees in two state office buildings and employees in a comparable "control" building. Information was collected on demographic and occupational variables, the occurrence of fatiguing illness for at least one month in the previous year, and the presence of 36 symptoms. A total of 3312 (82%) of 4035 employees returned questionnaires. Overall, 618 (18.7%) persons reported fatigue lasting at least one month; including 382 (11.5%) with fatigue of at least six months' duration and 75 (2.3%) with symptoms compatible with a CFS-like illness. Independent risk factors for fatigue lasting one month or longer were found to be Native American ethnicity (OR 2.4, CI 1.1,5.3), Hispanic ethnicity (OR 1.7, CI 1.3,2.3), female sex (OR 1.5, CI 1.2,1.9), gross household incomes of less than $50,000 (OR 1.3, CI 1.1,1.6), and less than a college education (OR 1.3, CI 1.1,1.6). Similar risks were observed for persons who reported fatigue lasting six months or longer. Female sex (OR 3.2, CI 1.7, 6.4) was the only independent risk factor found for those persons classified as having a CFS-like illness. Case prevalence rates for all three categories of fatigue, as determined by multivariate analysis, were not significantly different among buildings. Despite finding a substantial number of employees with fatiguing illness in the two state office buildings, the prevalence was not significantly different than that for a comparable control building. Previously unidentified risk factors for fatigue of at least one month and at least six months identified in this population included Hispanic ethnicity, not having completed college, and income below $50,000.
Shepherd C, Macintyre A.		Graded exercise in chronic fatigue syndrome. Patients should have initial period of rest before gradual increase in activity.	BMJ 1997 Oct 11;315(7113):947; discussion 948 Comment on: BMJ. 1997 Jun 7;314(7095):1647-52 Erratum in: BMJ 1997 Nov 1;315(7116):1165	
Shepherd C.		Chronic fatigue syndrome.	Lancet 1997 Jan 4;349(9044):57-8 comment on: Lancet. 1996 Nov 16;348(9038):1384-5	
Shepherd C.		Disagreements still exist over the chronic fatigue syndrome.	BMJ 1997 Jan 11;314(7074):146	
Shepherd C.		Chronic fatigue syndrome.	Prof Nurse 1997 Aug;12(11):827 Comment on: Prof	

			Nurse. 1997 May;12(8):578-81	
Sheridan TF		Disability Policy and CFIDS A Washington Perspective	Journal of Chronic Fatigue Syndrome 1997: 3(4): 63 - 67	"Disability Policy and CFIDS: A Washington Perspective" provides a follow-up to Mr. Sheridan's remarks at the American Association for Chronic Fatigue Syndrome's clinical conference in San Francisco on October 16, 1996. In this article, Mr. Sheridan explains that the difficulty for people with CFIDS (PWCs) in obtaining disability benefits stems from the fact that disability determination is based on a person's functional impairments resulting from a particular diagnosis. In other words, the Social Security Administration does not consider a CFIDS diagnosis alone sufficient criteria to win a disability claim. The article also describes the advocacy efforts carried out over the past five years by The CFIDS Association of America and The Sheridan Group and the achievements of that collaboration. Mr. Sheridan concludes his article with advice for PWCs who are considering an application for SSA disability benefits.
Shorter E.	History of Medicine Program, Faculty of Medicine, University of Toronto, Ontario, Canada.	Somatization and chronic pain in historic perspective.	Clin Orthop 1997 Mar;(336):52-60	Practitioners today are confronted with an avalanche of difficult to treat patients with chronic pain for 2 reasons: (1) The culture increasingly encourages patients to conceive vague and nonspecific symptoms as evidence of real disease and to seek specialist help for them; and (2) the rising ascendancy of the media and the breakdown of the family encourage patients to acquire the fixed belief that they have a given illness, often a trendy nondisease such as repetition strain injury or chronic fatigue syndrome. In historic terms, many of these complaints, especially sensory ones featuring chronic pain and chronic fatigue, are relatively new. Patients tend to adopt them on the basis of what the culture considers to be legitimate illness, whereby different patterns exist for men and women.
Simpson M, Bennett A, Holland P.		Chronic fatigue syndrome/myalgic encephalomyelitis as a twentieth-century disease: analytic challenges.	J Anal Psychol 1997 Apr;42(2):191-9	The challenges of chronic fatigue syndrome (often called myalgic encephalomyelitis, especially in the UK) (CFS/ME) to analytical and medical approaches are connected with our inability to understand its distressing somatic symptoms in terms of a single identifiable and understandable disease entity. The evidence for the roles of viral aetiologies remains inconclusive, as does our understanding of the involvement of the immune system. The history and social context of CFS/ME, and its relation to neurasthenia and psychasthenia are sketched. A symbolic attitude to the condition may need to be rooted in an awareness of psychoid levels of operation, and the expression and spread of CFS/ME may sometimes be aided by the ravages of projective identification. Psychic denial, sometimes violent, in sufferers (especially children and adolescents) and their families may be important in the aetiology of CFS/ME. We draw out common threads from psychodynamic work with five cases, four showing some symptomatic improvement, analytic discussions of three cases being presented elsewhere in this issue of JAP.
Simpson M.		A body with chronic	J Anal Psychol 1997	I describe the therapy of a 20-year-old women who believed that her difficulties

		fatigue syndrome as a battleground for the fight to separate from the mother.	Apr;42(2):201-16	in concentrating and remembering were caused by her "ME' (Myalgic encephalomyelitis, Chronic fatigue syndrome, or CFS). She had been fathered by a man who never left his own wife. Work with her dreams revealed a within-body drama in which she was locked in an unspeakable fight to the death with her mother. Her symptoms improved after parallels between a dream and an accident showed her own self-destructive hand in her story. Another dream, reflecting her first 'incestuous' affair, showed her search for her original father-self as someone separate from mother, and a later affair provided a between-body drama, helping her to own the arrogant and abject traits she had before seen only as her mother's. I show how we worked in the area of Winnicott's first 'primitive agony' as experienced by a somatizing patient, stuck in a too-close destructive relationship with her mother-body. I discuss how analytical work can be done with the primitive affects and conflicts against which the ME symptoms may be defending.
Smits MG, Nagtegaal JE, Swart AC.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2359-60	
Sobetzko HM, Stark FM.		["Chronic fatigue syndrome"].[article in German]	Nervenarzt 1997 Nov;68(11):924-5 Comment on: Nervenarzt. 1996 Sep;67(9):711-20	
Spring SB, Eveline Lee Tierney, Heidi M. Jolson		Meeting Reports: Development of Outcome Measures for Therapeutic Trials of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(3): 69 - 95	"The chronic fatigue syndrome (CFS) is a clinically defined condition characterized by severe disabling fatigue and a combination of symptoms that prominently features self-reported impairments in concentration and short-term memory, sleep disturbances and musculoskeletal pain" (1). The variability of the course and severity of CFS combined with slow and infrequent full recovery and the lack of a defined etiology have complicated the implementation of therapeutic clinical trials. The goal of the workshop was to begin a systematic consideration of clinical trials issues and outcome measures that could be used to evaluate CFS therapies in a definitive manner for safety and efficacy. The focus of the workshop was on common issues applicable across therapies rather than on the merits of individual therapies. Careful study design is critical to all trials. New methods and measures of health status will aid in determining the extent of change related to therapeutic interventions. Approaches and methods used in the study and therapy of other chronic illnesses may provide important insights for designing clinical trials and choosing outcome measures for CFS interventions. Short-term outcomes in small groups of patients need to be validated by other research groups, by additional and even larger studies, and by long-term studies. To insure enrollment and compliance, patient concerns need to be considered in

				study design.
Strom SS, Baldwin BJ, Sigurdson AJ, Schusterman MA.	Department of Epidemiology, The University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.	Cosmetic saline breast implants: a survey of satisfaction, breast-feeding experience, cancer screening, and health.	Plast Reconstr Surg 1997 Nov;100(6):1553-7	Saline breast implants have been used for the past 30 years for cosmetic and reconstructive purposes. Data based on a large number of patients are needed to evaluate patient satisfaction, cancer screening practices, problems associated with breast-feeding, and health effects. We conducted a follow-up study of 292 cosmetic saline breast implant patients from Texas and Louisiana who consented to a telephone interview. Using a Likert scale, we measured the patients' degree of satisfaction with the implants. The results indicated that 80.5 percent were satisfied, 73.3 percent would recommend saline breast implants to others, and 65.1 percent felt that implants improved their quality of life. The extent of satisfaction was independent of the number of additional surgeries, age at implant, and follow-up time. Mammography use and breast self-examination were reported with high frequency in this survey. Ninety-one percent of study participants who were between 40 and 49 years of age at time of interview and 94 percent of those 50 or older reported having had at least one mammogram. Breast self-examination was practiced by 75 percent of the women, and 61 percent reported checking their breasts at least once a month. Of the 46 women who had children after augmentation, 28 reported breast-feeding and 8 (28.6 percent) reported having implant-related problems. The patients were asked to provide information regarding a series of conditions for which they sought medical attention. They reported: atypical rheumatoid syndrome (n = 1), Sjogren syndrome (n = 1), atypical autoimmune disorder (n = 1), and chronic fatigue syndrome (n = 2). Overall, women who elected to have saline breast implants were satisfied with their augmentations, had mammograms and performed breast self-examinations more often than nonaugmented women. A few had problems when breast-feeding that could be related to their implants. There were no reports of breast cancer, but five women reported autoimmune conditions.
Suhadolnik RJ, Peterson DL, O'Brien K, Cheney PR, Herst CV, Reichenbach NL, Kon N, Horvath SE, Iacono KT, Adelson ME, De Meirleir K, De Becker P, Charubala R, Pfleiderer W.	Department of Biochemistry, Temple University School of Medicine, Philadelphia, PA, USA.	Biochemical evidence for a novel low molecular weight 2-5A-dependent RNase L in chronic fatigue syndrome.	J Interferon Cytokine Res 1997 Jul;17(7):377-85	Previous studies from this laboratory have demonstrated a statistically significant dysregulation in several key components of the 2',5'-oligoadenylate (2-5A) synthetase/RNase L and PKR antiviral pathways in chronic fatigue syndrome (CFS) (Suhadolnik et al. Clin Infect Dis 18, S96-104, 1994; Suhadolnik et al. In Vivo 8, 599-604, 1994). Two methodologies have been developed to further examine the upregulated RNase L activity in CFS. First, photoaffinity labeling of extracts of peripheral blood mononuclear cells (PBMC) with the azido 2-5A photoaffinity probe, [32P]pApAp(8-azidoA), followed by immunoprecipitation with a polyclonal antibody against recombinant, human 80-kDa RNase L and analysis under denaturing conditions. A subset of individuals with CFS was identified with only one 2-5A binding protein at 37 kDa, whereas in extracts of PBMC from a second subset of CFS PBMC and from healthy controls, photolabeled/immunoreactive 2-

				5A binding proteins were detected at 80, 42, and 37 kDa. Second, analytic gel permeation HPLC was completed under native conditions. Extracts of healthy control PBMC revealed 2-5A binding and 2-5A-dependent RNase L enzyme activity at 80 and 42 kDa as determined by hydrolysis of poly(U)-3'-[32P]pCp. A subset of CFS PBMC contained 2-5A binding proteins with 2-5A-dependent RNase L enzyme activity at 80, 42, and 30 kDa. However, a second subset of CFS PBMC contained 2-5A binding and 2-5A-dependent RNase L enzyme activity only at 30 kDa. Evidence is provided indicating that the RNase L enzyme dysfunction in CFS is more complex than previously reported.
Sykes R.		Chronic fatigue syndrome.	Br J Psychiatry 1997 Oct;171:393	
The chronic fatigue syndrome and hyperventilation. Bazelmans E, Bleijenberg G, Vercoulen JH, van der Meer JW, Folgering H.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	Erratum in: J Psychosom Res 1998 Mar-Apr;44(3-4):517	J Psychosom Res 1997 Oct;43(4):371-7	Chronic fatigue syndrome (CFS) is characterized by severe fatigue, lasting for at least 6 months, for which no somatic explanation can be found. Because hyperventilation can produce substantial fatigue, it seems worthwhile to investigate the relationship between it and CFS. It might be hypothesized that hyperventilation plays a causal or perpetuating role in CFS. CFS patients, non-CFS patients known to experience hyperventilation, and healthy controls were compared on complaints of fatigue and hyperventilation. CFS patients and non-CFS patients known to experience hyperventilation offered substantial complaints of fatigue and hyperventilation, both to a similar degree. Physiological evidence of hyperventilation was found significantly more often in CFS patients than in healthy controls. However, no significant differences between CFS patients with and CFS patients without hyperventilation were found on severity of fatigue, impairment, number of complaints, activity level, psychopathology, and depression. It is concluded that hyperventilation in CFS should probably be regarded as an epiphenomenon.
Tiersky LA, Johnson SK, Lange G, Natelson BH, DeLuca J.	Department of Physical Medicine and Rehabilitation, UMDNJ-New Jersey Medical School, Kessler Institute for Rehabilitation, West Orange 07052, USA.	Neuropsychology of chronic fatigue syndrome: a critical review.	J Clin Exp Neuropsychol 1997 Aug;19(4):560-86	This article provides a comprehensive and critical review of the neuropsychological and related literature on chronic fatigue syndrome (CFS). Despite the methodological limitations observed in several studies, some consistent findings are noted. The most consistently documented neuropsychological impairments are in the areas of complex information processing speed and efficiency. General intellectual abilities and higher order cognitive skills are intact. Emotional factors influence subjective report of cognitive difficulty, whereas their effect on objective performance remains uncertain. Although the neuropathological processes underlying cognitive dysfunction in CFS are not yet known, preliminary evidence suggests the involvement of cerebral white matter. Directions for future research are outlined. Review, Academic
Twemlow SW, Bradshaw SL Jr, Coyne	University of Kansas School of Medicine,	Patterns of utilization of medical care and	Psychol Rep 1997 Apr;80(2):643-58	To what extent do personal constructs affect the relationship between doctor and patient when the ill patient does not readily recover with treatment?

L, Lerma BH.	Wichita, USA.	perceptions of the relationship between doctor and patient with chronic illness including chronic fatigue syndrome.		Questionnaires were returned anonymously by 609 patients with a self-reported diagnosis of chronic fatigue syndrome, who were considered chronically ill. Findings were compared with those of an earlier study of a population of 397 general medical patients. The chronically ill patients lost an average of 65 days of work per year due to illness compared to general medical patients who missed six or fewer days per year because they were ill. The chronically ill patients also reported a 66% higher frequency of iatrogenic illness, spent more money on health care, took more medication, saw more specialists, and were more litigious than the general medical population. Research suggested several patterns of relationships between doctors and patients, and attitudes to health and illness, which may alert doctors to patients' perceptions, beliefs, encoded constructs, and patterns of relating that affect responses to treatment. More attention by doctors to patients who are experiencing the stress of chronic illness is indicated.
Uslan D		Perspectives on CFS and Impairment Proposed Guidelines for Disability Determination	Journal of Chronic Fatigue Syndrome 1997: 3(4): 75 - 85	Chronic Fatigue syndrome (CFS) is a difficult condition for which to determine work limitations and disability. This paper discusses the current problems in the state-of-the-art, and proposes framework standards for multi-disciplinary rehabilitation efforts to assess, prevent or limit disability, and multi-disciplinary standards for disability determination
van der Meer JW, Elving LD.	Academisch Ziekenhuis, afd. Algemeen Interne Geneeskunde, Nijmegen.	[Chronic fatigue--'tired with 23 i's'].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1505-7Comment in: Ned Tijdschr Geneeskd. 1997 Nov 29;141(48):2358-9 Ned Tijdschr Geneeskd. 1997 Nov 29;141(48):2360	Two patients, a woman aged 32 years and a man aged 49, presented with severe chronic fatigue. The woman had chronic fatigue syndrome; she recovered slowly. The man suffered from a pituitary adenoma producing follicle stimulating hormone; he recovered after transsphenoidal hypophysectomy. In patients with chronic fatigue, the history and a thorough physical examination to exclude underlying illness are very important; secondary symptom criteria must not be overemphasized (as is the case with the Holmes and Fukuda criteria), chronic fatigue syndrome should not be diagnosed if the condition has a shorter duration than 6 months, but it should be diagnosed if the clinical picture is compatible. The prognosis is not poor: in patients with a median disease duration of 4.5 years, 20% show significant improvement over an 18-month period.
van der Meer JW, Rijken PM, Bleijenberg G, Thomas S, Hinloopen RJ, Bensing JM.	Afd. Algemeen Interne Geneeskunde, Academisch Ziekenhuis, Nijmegen.	[Indications for management in long-term, physically unexplained fatigue symptoms].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1516-9Comment in: Ned Tijdschr Geneeskd. 1997 Nov 29;141(48):2361-2 Ned Tijdschr Geneeskd. 1997 Nov 29;141(48):2362-3	In meetings arranged by the minister of Public Health, Welfare and Sports between general practitioners and specialists concerning chronic fatigue syndrome (CFS), suggestions for the diagnosis, treatment and assistance and support of patients with protracted physically unexplained fatigue symptoms, were established in the light of current scientific insight. The term 'CFS' is applicable in cases of fatigue complaints, of at least 6 months' standing, reported by the patient himself and evaluated medically, for which no physical explanation has been found and which cause considerable disabilities in professional social and/or personal functioning. The management depends on the duration of the illness. A distinction is made between an acute phase (up to one month after the first consultation; the policy is mostly expectative), a subacute phase (until 6

				months after the onset of the complaints and disabilities; the management is aimed at making the patient accept the condition and persuading him or her to make an effort to promote health) and a chronic phase (from 6 months after the onset of the complaints and disabilities; the management is aimed at health-promoting behaviour and cognitions). Further (laboratory) examinations are useful only if the symptoms have not disappeared after one month (this is the case in approximately 20% of the patients); such examinations may be useful in older patients earlier. It is important that the CFS patient learns to realize that it is useless to continue to spend energy on searching for causes and possible therapies, but that he should try to promote his own health, for instance by means of a quantified programme of activities linked to a time schedule (instead of to a level of fatigue).
van der Meer JW.	Academisch Ziekenhuis, afd. Algemeen Interne Geneeskunde, Nijmegen.	[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1507-9	Chronic fatigue syndrome is a controversial disease entity. Opinions range from non-disease via psychiatric disorder to a somatic disturbance. Somatic pathogenetic hypotheses include persisting infections, intoxications, metabolic or immunologic disturbances, nervous system diseases and endocrine pathology. None of these hypotheses has been substantiated as yet. Psychological factors are important in the course of the disorder and can be used in the therapeutic approach of patients with chronic fatigue syndrome.
van der Meer JW.		Chronic fatigue syndrome.	Eur J Clin Invest 1997 Apr;27(4):255-6 Comment on: Eur J Clin Invest. 1997 Apr;27(4):257-67	
Van Dishoeck EA.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2358-9 Comment on: Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1505-7	
Van Houdenhove B, Fischler B, Neerinckx E.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2360-1 Comment on: Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1510-2	
Vedhara K, Llewelyn MB, Fox JD, Jones M, Jones R, Clements GB, Wang EC, Smith AP,	Department of Medicine, University of Wales College of Medicine, Cardiff, UK.	Consequences of live poliovirus vaccine administration in chronic fatigue	J Neuroimmunol 1997 May;75(1-2):183-95	The effect of live oral polio virus vaccination on chronic fatigue syndrome (CFS) patients was examined in a double-blind study. CFS patients were allocated randomly to placebo (N = 7) or vaccine (N = 7) conditions. All controls subjects received the vaccine (9). Vaccine administration was not associated with clinical

Borysiewicz LK.	k.vedhara@bristol.ac.uk	syndrome.		exacerbation of CFS. However, objective responses to the vaccine revealed differences between patients and controls: increased poliovirus isolation, earlier peak proliferative responses, lower T-cell subsets on certain days post vaccination and a trend for reduced gamma-interferon in the CFS-vaccine group. Polio vaccination was not found to be clinically contraindicated in CFS patients, however, there was evidence of altered immune reactivity and virus clearance. Randomized Controlled Trial
Vercoulen JH, Bazelmans E, Swanink CM, Fennis JF, Galama JM, Jongen PJ, Hommes O, Van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	Physical activity in chronic fatigue syndrome: assessment and its role in fatigue.	J Psychiatr Res 1997 Nov-Dec;31(6):661-73	This paper describes the assessment of physical activity in chronic fatigue syndrome (CFS) and investigated the following questions: Do patients with CFS have low levels of physical activity; is there a relationship between actual level of physical activity and fatigue; can self-report measures adequately assess actual level of physical activity; what is the role of cognitions with respect to physical activity; and are results with respect to physical activity specific to CFS? Three different types of activity measures were used: self-report questionnaires, a 12-day self-observation list, and a motion-sensing device (Actometer) which was used as a reference for actual activity level. Fifty-one patients with CFS, 50 fatigued patients with multiple sclerosis (MS), and 53 healthy subjects participated in this study. Although none of the self-report questionnaires showed high correlations with the Actometer, questionnaires that require simple ratings of specified activities were related to the Actometer and can be used as acceptable substitutes, in contrast to instruments that require general subjective interpretations of activity that had low or non-significant correlations with the Actometer. Actometer results showed that CFS patients and MS patients had similar activity levels and both groups were significantly less active than healthy subjects. Compared to MS patients, CFS patients were more likely to indicate that they had been less active than other persons they knew. Activities which patients expected to result in higher fatigue levels were less frequently performed. Patients with CFS had significantly higher scores on this measure than MS patients and healthy subjects. Low levels of physical activity were related to severe fatigue in CFS but not in MS. In conclusion, although CFS patients have similar low activity levels than MS patients, there are also important differences between both groups: in CFS cognitive factors are more prominently involved in producing the low activity levels than in MS and in CFS patients activity level is related to fatigue but not in MS. Randomized Controlled Trial
Versluis RG, de Waal MW, Opmeer C, Petri H, Springer MP.	Rijksuniversiteit, vakgroep Huisartsgeneeskunde, Leiden.	[Prevalence of chronic fatigue syndrome in 4 family practices in Leiden].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Aug 2;141(31):1523-6	OBJECTIVE: To determine the prevalence of chronic fatigue syndrome (CFS) in general practice. DESIGN: Descriptive. SETTING: General practice and primary health care centres in Leyden region, the Netherlands. METHOD: RNUH-LEO is a computerized database which contains the anonymous patient information of one general practice (with two practitioners) and four primary health care centres. The fourteen participating general practitioners were asked what

				International Classification of Primary Care (ICPC) code they used to indicate a patient with chronic fatigue or with CFS. With these codes and with the code for depression patients were selected from the database. It then was determined whether these patients met the criteria of CFS by Holmes et al. RESULTS: The general practitioners used 10 codes. Including the code for depression a total of 601 patients were preselected from a total of 23,000 patients in the database. Based on the information from the patients' records in the database, 42 of the preselected patients were selected who might fulfill the Holmes' criteria of CFS. According to the patients' own general practitioner, 25 of the 42 patients would fulfil the Holmes' criteria. The men:women ratio was 1:5. The prevalence of CFS in the population surveyed was estimated to be at least 1.1 per 1,000 patients.
Vojdani A, Ghoneum M, Choppa PC, Magtoto L, Lapp CW.	Immunosciences Laboratory Inc., Beverly Hills, California, USA.	Elevated apoptotic cell population in patients with chronic fatigue syndrome: the pivotal role of protein kinase RNA.	J Intern Med 1997 Dec;242(6):465-78Comment in: J Intern Med. 1999 Apr;245(4):409-10	OBJECTIVES: A prominent feature of chronic fatigue syndrome (CFS) is a disordered immune system. Recent evidence indicates that induction of apoptosis might be mediated in a dysregulated immune system by the upregulation of growth inhibitory cytokines. Therefore, the purpose of this study was to evaluate the apoptotic cell population, interferon-alpha (IFN-alpha) and the IFN-induced protein kinase RNA (PKR) gene transcripts in peripheral blood lymphocytes (PBL) of CFS individuals, as compared to healthy controls. SUBJECTS AND METHODS: PBL were isolated from CFS (n = 29) and healthy control individuals (n = 15) and subjected to quantitative analysis of apoptotic cell population and cell cycle progression by flow cytometry. Quantitative competitive polymerase chain reaction (Q/C PCR) and Western blot analysis were used to assess the levels of PKR mRNA and protein in control and CFS individuals. In addition, circulating IFN-alpha was measured by ELISA assay. RESULTS: Increased apoptotic cell population was observed in CFS individuals, as compared to healthy controls (26.6 +/- 12.9% and 9.9 +/- 4.2%, respectively). The increased apoptotic subpopulation in CFS individuals was accompanied by an abnormal cell arrest in the S phase and the G2/M boundary of the cell cycle as compared to the control group (8.6 +/- 1.2 to 22.8 +/- 2.4 and 3.6 +/- 0.82 to 24.3 +/- 3.4, respectively). In addition, CFS individuals exhibited enhanced PKR mRNA and protein levels (mean basal level 3538 +/- 1050 and 2.7 +/- 0.26, respectively) as compared to healthy controls (mean basal level 562 +/- 162 and 0.89 +/- 0.18, respectively). In 50% of the CFS samples (n = 29) treated with 2-aminopurine (2-AP) (a potent inhibitor of PKR) the apoptotic population was reduced by more then 50%. CONCLUSIONS: PKR-mediated apoptosis in CFS individuals may contribute to the pathogenesis and the fatigue symptomatology associated with CFS.
Vollmer-Conna U, Hickie I, Hadzi-Pavlovic D, Tymms K, Wakefield	Inflammation Research Unit, School of Pathology, University of	Intravenous immunoglobulin is ineffective in the	Am J Med 1997 Jul;103(1):38-43	PURPOSE: To determine whether the reported therapeutic benefit of intravenous immunoglobulin in patients with chronic fatigue syndrome (CFS) is dose dependent. PATIENTS AND METHODS: Ninety-nine adult patients, who fulfilled

D, Dwyer J, Lloyd A.	New South Wales, Sydney, Australia.	treatment of patients with chronic fatigue syndrome.		diagnostic criteria for CFS, participated in this double-blind, randomized, and placebo-controlled trial. Patients received intravenous infusions with either a placebo solution (1% albumin) or one of three doses of immunoglobulin (0.5, 1, or 2 g/kg) on a monthly basis for 3 months, followed by a treatment-free follow-up period of 3 months. Outcome was assessed by changes in a series of self-reported measures (quality-of-life visual analog scales, standardized diaries of daily activities, the profile of mood states questionnaire) and the Karnofsky performance scale. Cell-mediated immunity was evaluated by T-cell subset analysis and delayed-type hypersensitivity (DTH) skin testing. RESULTS: No dose of intravenous immunoglobulin was associated with a specific therapeutic benefit. Adverse reactions, typically constitutional symptoms, were reported by 70% to 80% of patients, with no relationship to immunoglobulin treatment. CONCLUSIONS: Intravenous immunoglobulin cannot be recommended as a therapy for the treatment of CFS. A better understanding of the pathophysiology of this disorder is needed before effective treatment can be developed. Randomized Controlled Trial
Vollmer-Conna U, Wakefield D, Lloyd A, Hickie I, Lemon J, Bird KD, Westbrook RF.	Inflammation Research Unit, School of Pathology, University of New South Wales, Sydney, Australia. u.vollmer-conna@unsw.edu.au	Cognitive deficits in patients suffering from chronic fatigue syndrome, acute infective illness or depression.	Br J Psychiatry 1997 Oct;171:377-81	BACKGROUND: Patients with chronic fatigue syndrome (CFS) report neuro-psychological symptoms as a characteristic feature. We sought to assess cognitive performance in patients with CFS, and compare cognitive performance and subjective workload experience of these patients with that of two disease comparison groups (non-melancholic depression and acute infection) and healthy controls. METHOD: A computerized performance battery employed to assess cognitive functioning included tests of continuous attention, response speed, performance accuracy and memory. Severity of mood disturbance and subjective fatigue were assessed by questionnaire. RESULTS: All patient groups demonstrated increased errors and slower reaction times, and gave higher workload ratings than healthy controls. Patients with CFS and non-melancholic depression had more severe deficits than patients with acute infection. All patient groups reported more severe mood disturbance and fatigue than healthy controls, but patients with CFS and those with acute infection reported less severe mood disturbance than patients with depression. CONCLUSIONS: As all patients demonstrated similar deficits in attention and response speed, it is possible that common pathophysiological processes are involved. The differences in severity of mood disturbance, however, suggest that the pathophysiological processes in patients with CFS and acute infection are not simply secondary to depressed mood.
von Mikecz A, Konstantinov K, Buchwald DS, Gerace L, Tan EM.	Institut fur Umwelthygiene, Heinrich Heine Universitat Dusseldorf,	High frequency of autoantibodies to insoluble cellular antigens in patients with	Arthritis Rheum 1997 Feb;40(2):295-305 comment in: Arthritis Rheum. 1997	OBJECTIVE: To elucidate the humoral immune response in patients with chronic fatigue syndrome (CFS), by identification and characterization of autoantibodies. METHODS: Initial immunofluorescence histochemistry studies of sera using human HEp-2 cell substrate were followed by antibody class subtyping and

	Germany.	chronic fatigue syndrome.	Nov;40(11):2095-7	colocalization studies with reference antibodies. Association of CFS autoantigens with insoluble cellular components was determined by in situ extraction of soluble components and subsequent immunofluorescence histochemistry studies on the extracted cell substrate. RESULTS: Of 60 CFS patients, 41 (68%) were positive for antinuclear antibodies. Localization of nuclear staining was found at the nuclear envelope (52%), in reticulated speckles (25%), in nucleoli (13%), and in dense fine speckles (5%). Twenty-eight CFS sera (47%) also had antibodies to cytoplasmic antigens. The major cytoplasmic staining pattern was of the intermediate filament type (35%). The observed nuclear envelope pattern of staining co-localized with lamina-associated polypeptide 2 (an integral nuclear membrane protein), the reticulated speckle pattern co-localized with non-small nuclear RNP splicing factor SC-35, and the intermediate filament pattern co-localized with vimentin. The intermediate filament antigen was shown to be vimentin in immunoblotting experiments using recombinant human vimentin, and one of the nuclear envelope antigens was shown previously to be lamin B1. Fifty of the 60 CFS patients (83%) had antibodies to one or another of these antigens, all of which are relatively insoluble cellular antigens, whereas a control group of patients without chronic fatigue had a significantly lower frequency of such antibodies (17%). CONCLUSION: The high frequency of autoantibodies to insoluble cellular antigens in CFS represents a unique feature which might help to distinguish CFS from other rheumatic autoimmune diseases.
Vooren PH.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2359 Comment on: Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1526-30	
Wagner LI, Jason LA.	Medical College of Wisconsin, Milwaukee, USA.	Outcomes of occupational stressors on nurses: chronic fatigue syndrome--related symptoms.	Nursingconnections 1997 Fall;10(3):41-9	Considering the types and number of occupational stressors involved in caring for patients, nurses may represent a population at high risk for physical illnesses. A sample of 3400 nurses who belong to a statewide or a national nurses organization were randomly chosen for participation. Of this group, 202 reported 6 months or more of debilitating fatigue and completed a three-page questionnaire assessing symptoms related to chronic fatigue syndrome (CFS) and comorbid medical conditions. This group (N = 202) was mailed a follow-up questionnaire 1 year later that reassessed symptoms of CFS and occupational stressors. Many sampled nurses reported a high degree of occupationally related stress but did not report CFS symptoms; however, perceived exposure to the threat of an accident as a nurse and poor physical working conditions were significantly related to symptoms reported. These findings are consistent with previous research.

Watson WS, GT McCreathm A. Chaudhuri, Peter O. Behan		Possible Cell Membrane Transport Defect in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1997: 3(3): 1 - 13	Cardiac thallium-201 single photon emission computerised tomography has been carried out on 10 adult patients with chronic fatigue syndrome. Seven of the patients had defects in the thallium tracer distribution within the left ventricle; this was significantly greater than would be expected in a normal adult population. Similar abnormal scans have been observed in patients with syndrome X, a condition which has a symptom overlap with chronic fatigue syndrome. It has been suggested that an abnormally high efflux of cellular potassium may be the cause of the abnormal scans in syndrome X, and it is proposed that this mechanism may also have a role to play in chronic fatigue syndrome.
Wearden A, Appleby L.	Department of Psychiatry, University Hospital of South Manchester.	Cognitive performance and complaints of cognitive impairment in chronic fatigue syndrome (CFS).	Psychol Med 1997 Jan;27(1):81-90	Patients with chronic fatigue syndrome (CFS) complain that they have difficulties with concentration and memory but studies to date have not found consistent objective evidence of performance deficits. Two groups of CFS patients, depressed and non-depressed, and healthy controls, were asked about concentration problems in general and specifically when reading. CFS subjects were more likely than controls to report that they had concentration problems when reading, that they needed to re-read text and that they failed to take in what they were reading. Subjects then performed a task in which their reading behaviour and text recall was measured. While all CFS subjects complained of general cognitive failures and of difficulties with reading, only depressed CFS subjects recalled significantly less of the text than controls. Severity of complaints about reading problems was not related to amount of text recalled, but was related to severity of depressed mood. However, subjects were able to evaluate accurately their ability to remember the text immediately after reading it and before being tested for recall. Additionally, subjects performed a paired-associate learning task on which no significant differences between the subject groups was found. It is concluded that deficits in cognitive functioning in CFS patients are more likely to be found on naturalistic than on laboratory tasks. Controlled Clinical Trial
Wessely S, Chalder T, Hirsch S, Wallace P, Wright D.	Department of Psychological Medicine, King's College School of Medicine and Dentistry, London, England.	The prevalence and morbidity of chronic fatigue and chronic fatigue syndrome: a prospective primary care study.	Am J Public Health 1997 Sep;87(9):1449-55	OBJECTIVES: This study examined the prevalence and public health impact of chronic fatigue and chronic fatigue syndrome in primary care patients in England. METHODS: There were 2376 subjects, aged 18 through 45 years. Of 214 subjects who fulfilled criteria for chronic fatigue, 185 (86%) were interviewed in the case-control study. Measures included chronic fatigue, psychological morbidity, depression, anxiety, somatic symptoms, symptoms of chronic fatigue syndrome, functional impairment, and psychiatric disorder. RESULTS: The point prevalence of chronic fatigue was 11.3%, falling to 4.1% if comorbid psychological disorders were excluded. The point prevalence of chronic fatigue syndrome was 2.6%, falling to 0.5% if comorbid psychological disorders were excluded. Rates did not vary by social class. After adjustment for psychological disorder, being female

				was modestly associated with chronic fatigue. Functional impairment was profound and was associated with psychological disorder. CONCLUSIONS: Both chronic fatigue and chronic fatigue syndrome are common in primary care patients and represent a considerable public health burden. Selection bias may account for previous suggestions of a link with higher socioeconomic status.
Wessely S.	Institute of Psychiatry, Department of Psychological Medicine, King's College Hospital, London, United Kingdom.	Chronic fatigue syndrome: a 20th century illness?	Scand J Work Environ Health 1997;23 Suppl 3:17-34	The chronic fatigue syndrome has become the fin de siecle illness, now getting similar attention to that of neurasthenia, which dominated medical thinking at the turn of the century. Myalgic encephalomyelitis was an early term introduced in the United Kingdom in 1957 for this state, but it had little or no public or professional prominence. Until then "chronic fatigue had become invisible", with "no name, no known etiology, no case illustrations or clinical accounts in the medical textbook, no ongoing research activity--nothing to relate it to current medical knowledge". The reconstruction of chronic fatigue began in the mid-1980s, with the emergence of "chronic Epstein-Barr virus syndrome", which was later converted to chronic fatigue syndrome. The former term, which first emerged in the mid-1980s, is now regarded as a misnomer and should be abandoned. In the popular American literature the term "chronic fatigue and immune deficiency syndrome" is preferred by the most active of the patient lobbies, while myalgic encephalomyelitis continues to be the usual label in the United Kingdom. The relevant research linking chronic fatigue syndrome with somatization is reviewed in this article. Understanding the nature of somatization can still shed some light on the meaning of chronic fatigue at the end of the 20th century. Review, Academic
White PD, Cleary KJ.	Department of Psychological Medicine, St Bartholomew's and the Royal London Medical School, UK.	An open study of the efficacy and adverse effects of moclobemide in patients with the chronic fatigue syndrome.	Int Clin Psychopharmacol 1997 Jan;12(1):47-52	There is a strong association between the chronic fatigue syndrome and both depressive illness and sleep disturbance, but the efficacy of antidepressants is uncertain. We studied the efficacy and adverse effects of moclobemide in patients with chronic fatigue syndrome, stratifying the sample both by co-morbid major depressive illness and by sleep disturbance. Forty-nine patients with chronic fatigue syndrome were recruited. Patients were given moclobemide up to 600 mg a day for 6 weeks. Four (8%) patients dropped out, three because of adverse effects. Adverse effects wee otherwise mild and transient. On analysing the whole sample, there were significant but small reductions in fatigue, depression, anxiety and somatic amplification, as well as a modest overall improvement. The greatest improvement occurred in those individuals who had a co-morbid major depressive illness, with seven out of 14 (50%) of such individuals rating themselves as "much better" by 6 weeks, compared to six out of 31 (19%) of those who were not depressed (31% difference, 95% CI 1-60%, P = 0.04). Sleep disturbance had no effect on outcome. Moclobemide may be indicated in patients with chronic fatigue syndrome and a co-morbid major depressive disorder. A randomized, placebo-controlled trial is needed to confirm

				this. These results do not support moclobemide as an effective treatment of chronic fatigue syndrome in the absence of a major depressive disorder.
Wijlhuizen T, Hamerslag M.		Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1997 Nov 29;141(48):2361-2 Comment on: Ned Tijdschr Geneeskd. 1997 Aug 2;141(31):1516-9	
Yataco A, Talo H, Rowe P, Kass DA, Berger RD, Calkins H.	Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA.	Comparison of heart rate variability in patients with chronic fatigue syndrome and controls.	615: Clin Auton Res 1997 Dec;7(6):293-7	Recent studies have reported a close association between chronic fatigue syndrome and neurally mediated hypotension. We hypothesized that this association may result from an abnormality in autonomic function among patients with chronic fatigue syndrome, which may be detectable using an analysis of heart rate variability. We prospectively studied 19 patients who fulfilled the Centers for Disease Control criteria for chronic fatigue syndrome and 11 controls. Each subject underwent a two-stage tilt-table test while wearing a Holter monitor. Heart rate variability was assessed in the supine baseline position and during upright tilt using frequency domain parameters. In the baseline supine position, high frequency (HF) power, low frequency (LF) power, and the ratio of low frequency power to high frequency power (LF/HF ratio) were similar. In both patient groups, upright tilt resulted in a similar decrease in HF power, increase in LF power, and increase in the LH/HF ratio. In conclusion, autonomic function, as assessed using an analysis of heart rate variability, does not differ in the baseline supine state, nor in response to upright tilt among patients with chronic fatigue syndrome and healthy controls.
Ziem G, McTamney J.	Occupational and Environmental Medicine, Baltimore, Maryland, USA.	Profile of patients with chemical injury and sensitivity.	Environ Health Perspect 1997 Mar;105 Suppl 2:417-36	Patients reporting sensitivity to multiple chemicals at levels usually tolerated by the healthy population were administered standardized questionnaires to evaluate their symptoms and the exposures that aggravated these symptoms. Many patients were referred for medical tests. It is thought that patients with chemical sensitivity have organ abnormalities involving the liver, nervous system (brain, including limbic, peripheral, autonomic), immune system, and porphyrin metabolism, probably reflecting chemical injury to these systems. Laboratory results are not consistent with a psychologic origin of chemical sensitivity. Substantial overlap between chemical sensitivity, fibromyalgia, and chronic fatigue syndrome exists: the latter two conditions often involve chemical sensitivity and may even be the same disorder. Other disorders commonly seen in chemical sensitivity patients include headache (often migraine), chronic fatigue, musculoskeletal aching, chronic respiratory inflammation (rhinitis, sinusitis, laryngitis, asthma), attention deficit, and hyperactivity (affected younger children). Less common disorders include tremor, seizures, and mitral valve prolapse. Patients with these overlapping disorders should be evaluated for

				chemical sensitivity and excluded from control groups in future research. Agents whose exposures are associated with symptoms and suspected of causing onset of chemical sensitivity with chronic illness include gasoline, kerosene, natural gas, pesticides (especially chlordane and chlorpyrifos), solvents, new carpet and other renovation materials, adhesives/glues, fiberglass, carbonless copy paper, fabric softener, formaldehyde and glutaraldehyde, carpet shampoos (lauryl sulfate) and other cleaning agents, isocyanates, combustion products (poorly vented gas heaters, overheated batteries), and medications (dinitrochlorobenzene for warts, intranasally packed neosynephrine, prolonged antibiotics, and general anesthesia with petrochemicals). Multiple mechanisms of chemical injury that magnify response to exposures in chemically sensitive patients can include neurogenic inflammation (respiratory, gastrointestinal, genitourinary), kindling and time-dependent sensitization (neurologic), impaired porphyrin metabolism (multiple organs), and immune activation.

1996				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Ablashi DV, Levine PH, De Vinci C, Whitman JE Jr, Pizza G, Viza D.	Advanced Biotechnologies Inc., Columbia, MD 21046, USA.	Use of anti HHV-6 transfer factor for the treatment of two patients with chronic fatigue syndrome (CFS). Two case reports.	Biotherapy 1996;9(1-3):81-6	Specific Human Herpes virus-6 (HHV-6) transfer factor (TF) preparation, administered to two chronic fatigue syndrome patients, inhibited the HHV-6 infection. Prior to treatment, both patients exhibited an activated HHV-6 infection. TF treatment significantly improved the clinical manifestations of CFS in one patient who resumed normal duties within weeks, whereas no clinical improvement was observed in the second patient. It is concluded that HHV-6 specific TF may be of significant value in controlling HHV-6 infection and related illnesses.
Anisman H, Baines MG, Berczi I, Bernstein CN, Blennerhassett MG, Gorczynski RM, Greenberg AH, Kisil FT, Mathison RD, Nagy E, Nance DM, Perdue MH, Pomerantz DK, Sabbadini ER, Stanisz A, Warrington RJ.	Department of Psychology, Carloton University, Ottawa, Ont.	Neuroimmune mechanisms in health and disease: 2. Disease.	CMAJ 1996 Oct 15;155(8):1075-82	In the second part of their article on the emerging field of neuroimmunology, the authors present an overview of the role of neuroimmune mechanisms in defence against infectious diseases and in immune disorders. During acute febrile illness, immune-derived cytokines initiate an acute phase response, which is characterized by fever, inactivity, fatigue, anorexia and catabolism. Profound neuroendocrine and metabolic changes take place: acute phase proteins are produced in the liver, bone marrow function and the metabolic activity of leukocytes are greatly increased, and specific immune reactivity is suppressed. Defects in regulatory processes, which are fundamental to immune disorders and inflammatory diseases, may lie in the immune system, the neuro endocrine system or both. Defects in the hypothalamus-pituitary-adrenal axis have been observed in autoimmune and rheumatic diseases, chronic inflammatory disease, chronic fatigue syndrome and fibromyalgia. Prolactin levels are often elevated in patients with systemic lupus erythematosus and other autoimmune diseases, whereas the bioactivity of prolactin is decreased in patients with rheumatoid arthritis. Levels of sex hormones and thyroid hormone are decreased during severe inflammatory disease. Defective neural regulation of inflammation likely plays a pathogenic role in allergy and asthma, in the symmetrical form of rheumatoid arthritis and in gastrointestinal inflammatory disease. A better understanding of neuroimmunoregulation holds the promise of new approaches to the treatment of immune and inflammatory diseases with the use of hormones, neurotransmitters, neuropeptides and drugs that modulate these newly recognized immune regulators.
Anon		Chronic fatigue syndrome: any closer to an answer?	413: Consum Rep 1996 Sep;61(9):60-1	
Arnetz BB.	Department of Medicine, Karolinska Institute, Huddinge University Hospital,	Causes of change in the health of populations: a biopsychosocial viewpoint.	Soc Sci Med 1996 Sep;43(5):605-8	In the current review, a biopsychosocial perspective is applied to current changes in the health of populations. It is proposed that the psychosocial environments either promote health or precipitate disease. Changes in the types of stress that people experience as well as its prevalence over time are discussed. In addition,

	Sweden.			possible biological mechanisms linking the psychosocial environments to health are presented. "Food for thought" is the possible interaction between the physical/chemical and the psychosocial environments and changes in health of individuals. Clearly, our traditional view of disease mechanisms is not sufficient to understand recent phenomena, such as environmental illness and chronic fatigue syndrome. Issues worthy of further discussions are the role of the "just-in-time" society, where individuals increasingly have to change jobs, cope with reorganizations and increased production pressure, and its impact on health and well-being. Further, in what way can we develop better models to truly assess the impact of an increasingly complex interaction between individual and environmental factors on health? A major obstacle to enhancing our understanding of causes of change in the health of populations is the use of inappropriate or outdated statistical analytical models. Finally, it is suggested that prospectively controlled studies of the impact on health of changes in the health and welfare systems are carried out. This would further add to our understanding of factors contributing to changes in the health of population.
Aylward M.		Government's expert group has reached consensus on prognosis of chronic fatigue syndrome.	BMJ 1996 Oct 5;313(7061):885	
Baschetti R.		Chronic fatigue syndrome and neurally mediated hypotension.	JAMA 1996 Feb 7;275(5):359; discussion 360 comment on: JAMA. 1995 Sep 27;274(12):961-7	
Beard TC.		Chronic fatigue syndrome and neurally mediated hypotension.	JAMA 1996 Feb 7;275(5):359; discussion 360 comment on: JAMA. 1995 Sep 27;274(12):961-7	
Bennett AL, Fagioli LR, Schur PH, Schacterle RS, Komaroff AL.	Chronic Fatigue Syndrome Cooperative Research Center, Division of General Medicine and Primary Care, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.	Immunoglobulin subclass levels in chronic fatigue syndrome.	J Clin Immunol 1996 Nov;16(6):315-20	The levels of immunoglobulin subclasses were determined for 46 patients meeting the original Centers for Disease Control case definition of chronic fatigue syndrome and were compared to values obtained for 50 age- and gender-matched healthy volunteer blood donor controls. The levels of immunoglobulin subclasses in these groups were further compared to a third group of additional chronic fatigue syndrome cases from whom samples had been obtained and frozen prospectively over a period of 7 years. These data do not demonstrate significant immunoglobulin subclass deficiencies in patients with chronic fatigue syndrome.

Bombardier CH, Buchwald D.	Department of Rehabilitation Medicine, University of Washington, Seattle, USA.	Chronic fatigue, chronic fatigue syndrome, and fibromyalgia. Disability and health-care use.	795: Med Care 1996 Sep;34(9):924-30	OBJECTIVES: Disabling chronic fatigue that does not meet criteria for chronic fatigue syndrome (CFS) or fibromyalgia (FM) is a condition thought to be associated with substantial disability and an apparently high use of health-care services. The authors compare patients who have chronic fatigue, CFS, FM, or CFS and FM together (CFS+FM) on employment status, self-reported disability, number of medical care visits, type of services obtained, and other diagnoses received. METHODS: The authors studied 402 patients from a university-based chronic fatigue clinic. All patients underwent an initial structured diagnostic assessment. One hundred forty-seven patients met case criteria for CFS, 28 for FM, 61 for CFS+FM, and 166 fell in the residual chronic fatigue group. Of these patients, 388 completed a follow-up questionnaire an average of 1.7 years later. Chi-squared tests and analysis of variance were used to compare groups on follow-up measures of health-care use and disability. RESULTS: Patients with chronic fatigue, CFS, FM, and CFS+FM were similar in terms of disability and health-care use, though those with CFS+FM were significantly more likely to be unemployed and to use more chiropractic and "other" provider services. Rates of unemployment ranged from 26% (chronic fatigue) to 51% (CFS+FM). Overall, patients reported a mean of 21 visits to a wide variety health-care providers during the previous year, with no significant differences between groups. CONCLUSIONS: Chronic fatigue, CFS, and FM are associated with considerable personal and occupational disability and low rates of employment. The potentially large economic burden of these disorders underscores the need for accurate estimates of direct and indirect costs, the relative contribution of individual factors to disability, and the need to develop targeted rehabilitation programs.
Borok G.		Committee to investigate chronic fatigue syndrome.	S Afr Med J 1996 Oct;86(10):1301 comment on: S Afr Med J. 1995 Aug;85(8):780-2	
Brown MT, Sam A. Fleishman, Manuel F. Casanova		Gulf War Syndrome Polysormographic Study of Eight Cases	Journal of Chronic Fatigue Syndrome 1996: 2(1): 41 - 51	Our purpose was to explore whether patients complaining of the "Gulf War Syndrome" might have hidden sleep disorders, or psychiatric disorders, similar to what has been described in patients with chronic fatigue syndrome and fibromyalgia. Eight consecutive Gulf War veterans from the VA Gulf War Registry and Evaluation program complaining of fatigue, as well as other symptoms, were psychiatrically and polysomnographically screened. One was found to have major depression and Post-traumatic Stress Disorder (PTSD), while another had PTSD alone. The sleep diagnoses assigned to the 8 patients were as follows: Three had sleep apnea syndrome, one of whom also had periodic limb movements of sleep disorder. Four others met criteria for periodic limb movements (PLMs) of sleep disorder. Four of the patients had clinically significant sleep state-misperceptions.

				All of the patients' symptoms were reported as occurring subsequent to Gulf War deployment, and not prior to deployment. As with the classic fatigue syndromes such as chronic fatigue syndrome and fibromyalgia, Gulf War Syndrome patients may benefit from a more thorough investigation of their sleep and psychiatric status. In view of these findings, consideration of polysomnographic screening would appear appropriate in Gulf War Veterans with fatigue or sleep-related complaints.
Bruno RL, Nancy M. Frick, Susan Creange, Jerald R. Zimmerman, Todd Lewis		Polioencephalitis and the Brain Fatigue Generator Model of Post-Viral Fatigue Syndromes	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 5 - 27	Fatigue is the most commonly reported and most debilitating Post-Polio Sequelae (PPS), affecting millions of polio survivors world-wide. Post-polio fatigue is associated with: (1) subjective reports of difficulty with attention, cognition, word-finding and maintaining wakefulness; (2) clinically significant deficits on neuropsychological tests of information processing speed and attention; (3) gray and white matter hyperintensities in the reticular activating system on magnetic resonance imaging of the brain; (4) neuroendocrine evidence of impaired activation of the HPA axis. Many of these findings are identical to those documented following a variety of viral encephalitides, including acute poliovirus infection, lethargic encephalitis, Iceland Disease, myalgic encephalomyelitis, and, most recently, Chronic Fatigue Syndrome. The clinical, historic, neuropsychologic, neuroanatomic and physiologic parallels between poliovirus infection, post-polio fatigue and post-viral fatigue syndromes (PVFS) will be explored in an attempt to describe the pathophysiology of PVFS. The disinhibition of a putative Brain Fatigue Generator will be implicated as a cause of the subjective symptoms and objective signs that accompany PVFS. The results of a pilot placebo-controlled study of a dopamine 2 receptor agonist to treat post-polio fatigue will also be described.
Buchwald D, Ashley RL, Pearlman T, Kith P, Komaroff AL.	Department of Medicine, University of Washington, Seattle, USA.	Viral serologies in patients with chronic fatigue and chronic fatigue syndrome.	J Med Virol 1996 Sep;50(1):25-30	Chronic fatigue syndrome (CFS) is an illness characterized by disabling fatigue associated with complaints of fevers, sore throat, myalgia, lymphadenopathy, sleep disturbances, neurocognitive difficulties, and depression. A striking feature of CFS is its sudden onset following an acute, presumably viral, illness and the subsequent recurrent "flu-like" symptoms. It has been speculated that both CFS and debilitating chronic fatigue (CF) that does not meet strict criteria for CFS may be the direct or indirect result of viral infections. We therefore tested 548 chronically fatigued patients who underwent a comprehensive medical and psychiatric evaluation for antibodies to 13 viruses. Our objectives were to compare the seroprevalence and/or geometric mean titer (GMT) of antibodies to herpes simplex virus 1 and 2, rubella, adenovirus, human herpesvirus 6, Epstein-Barr virus, cytomegalovirus, and Cox-sackie B virus, types 1-6 in patients with CF to healthy control subjects. Other goals were to determine if greater rates of seropositivity or higher GMTs occurred among subsets of patients with CFS, fibromyalgia, psychiatric disorders, a self-reported illness onset with a viral

				syndrome, and a documented temperature > 37 degrees C on physical examination. Differences in the seroprevalence or GMTs of antibodies to 13 viruses were not consistently found in those with CF compared with control subjects, or in any subsets of patients including those with CFS, an acute onset of illness, or a documented fever. These particular viral serologies were not useful in evaluating patients presenting with CF.
Buchwald D, Pearlman T, Umali J, Schmaling K, Katon W.	Department of Medicine, University of Washington, Seattle, USA.	Functional status in patients with chronic fatigue syndrome, other fatiguing illnesses, and healthy individuals.	Am J Med 1996 Oct;101(4):364-70	BACKGROUND: Chronic fatigue syndrome (CFS) is a condition that may be associated with substantial disability. The Medical Outcomes Study Short-Form General Health Survey (SF-36) is an instrument that has been widely used in outpatient populations to determine functional status. Our objectives were to describe the usefulness of the SF-36 in CFS patients and to determine if subscale scores could distinguish patients with CFS from subjects with unexplained chronic fatigue (CF), major depression (MD), or acute infectious mononucleosis (AIM), and from healthy control subjects (HC). An additional goal was to ascertain if subscale scores correlated with the signs and symptoms of CFS or the presence of psychiatric disorders and fibromyalgia. DESIGN: Prospectively collected case series. SETTING: Patients with CFS and CF were seen in a university-based referral clinic and had undergone a complete medical and psychiatric evaluation. Other study subjects were recruited from the community to participate in research studies. PARTICIPANTS: The study included 185 patients with CFS, 246 with CF, 111 with AIM, and 25 with MD. There were 99 HC subjects. MEASURES: The SF-36 and a structured psychiatric interview were used. The SF-36 contains 8 subscales: physical, emotional, social, and role functioning, body pain, mental health, vitality, and general health- and a structured psychiatric interview. RESULTS: Performance characteristics (internal reliability coefficients, convergent validity) of the SF-36 were excellent. A strikingly consistent pattern was found for the physical functioning, role functioning, social functioning, general health, and body pain subscales, with the lowest scores in CFS patients, intermediate scores in AIM patients, and the highest scores in the HC subjects. The CFS patients had significantly lower scores than patients with CF alone on the physical functioning ($P < or = 0.01$), role functioning ($P < or = 0.01$), and body pain ($P < or = 0.001$) subscales. The emotional functioning and mental health scores were worst among those with MD. The presence of fibromyalgia, being unemployed, and increasing fatigue severity all were associated with additional functional limitations across multiple functional domains, with increasing fatigue appearing to have the greatest effect. CONCLUSIONS: The SF-36 is useful in assessing functional status in patients with fatiguing illnesses. Patients with CFS and CF have marked impairment of their functional status. The severity and pattern of impairment as documented by the SF-36 distinguishes patients with CFS and CF from those with MD and AIM, and from HC, but does not discriminate between

				CF and CFS.
Buchwald D, Spero M. Manson , Tsilke Pearlman, Jovine Umali, Phalla Kith		Race and Ethnicity in Patients with Chronic Fatigue	Journal of Chronic Fatigue Syndrome 1996: 2(1): 53 - 66	Purpose: Chronic fatigue (CF) is a common complaint in ambulatory settings. Chronic fatigue syndrome (CFS) is characterized by profound fatigue associated with other symptoms that is rarely reported in racial/ethnic minorities. Our objectives were to determine if differences exist between Caucasian and minority patients presenting with CF, particularly in the frequency meeting criteria for CFS. Patients: 690 patients with CF seen in a university-based referral clinic. Design/Methods: Demographic, historical, physical examination, laboratory, and psychosocial information was prospectively collected and compared. Psychosocial assessment consisted of a structured psychiatric interview, the Medical Outcomes Study Short-Form Health Survey to assess functional status, the General Health Questionnaire to ascertain psychological distress, and measures of health locus of control, illness attribution, social support, and coping. Results: With the exception of less social support from friends, no significant race/ethicity-related differences were identified. Minority patients tended less commonly to report a moderate level of fatigue, and to have poorer social function, less social support from families, and lower rates of lifetime major depression and alcohol abuse. Conclusions: Demographic, clinical, and psychosocial factors do not distinguish Caucasian from minority CF patients. Help-seeking behaviors, access to care, and the significance attributed to the central complaints should be examined as potentially competing explanations for these findings.
Buchwald D, Umali J, Pearlman T, Kith P, Ashley R, Wener M.	Department of Medicine, University of Washington, Seattle, USA.	Postinfectious chronic fatigue: a distinct syndrome?	Clin Infect Dis 1996 Aug;23(2):385-7	Chronic fatigue syndrome (CFS) is often preceded by a viral illness and has recurrent "flu-like" symptoms. We compared demographic, clinical, and laboratory features (markers of inflammation and viral infection) among 717 patients with chronic fatigue (CF) with and without a self-reported postinfectious onset to identify associated clinical and biologic findings and to examine the subset of patients with CFS. Only subjective fever, chills, sore throat, lymphadenopathy, poorer functional status, and attribution of illness to a physical condition were significantly associated with a postinfectious onset. The features of patients with CFS were virtually identical to those of the broader category of patients with CF. We conclude that a postinfectious onset was not associated with a pattern of abnormalities across multiple psychosocial and biologic parameters.
Buchwald D, Umali J, Stene M.	Department of Medicine, University of Washington, Seattle, USA.	Insulin-like growth factor-I (somatomedin C) levels in chronic fatigue syndrome and fibromyalgia.	J Rheumatol 1996 Apr;23(4):739-42	OBJECTIVE. Fibromyalgia (FM) and chronic fatigue syndrome (CFS) are similar conditions characterized by substantial fatigue, diffuse myalgias, sleep disturbances and a variety of other symptoms. Many patients with CFS meet strict criteria for FM. Recently, low insulin-like growth factor-I (IGF-I) levels have been demonstrated in patients with FM, suggesting that disruption of the growth hormone-IGF-I axis might explain the link between the muscle pain and poor

				sleep. Our goal was to determine whether IGF-I levels are decreased in CFS, and whether such findings are restricted to patients with concurrent FM. METHODS. Radioimmunoassays were used to determine serum concentrations of IGF-I and its binding protein, (IGFBP-3). Subjects were 3 patients seen in a referral clinic for chronic fatigue: 15 patients with CFS, 15 who met criteria for both CFS and FM (CFS-FM), 27 with FM alone; and 15 healthy control (HC) subjects. RESULTS. Patients and control subjects had similar demographic and clinical characteristics. No significant differences were observed among any of the 3 patient groups and control subjects in the mean concentration of either IGF-I or IGFBP-3. Likewise, the proportion of subjects with values above or below the laboratory's reference range did not differ for IGF-I or IGFBP-3. CONCLUSIONS. These findings suggest the disruption of the growth hormone-IGF-I axis previously demonstrated in FM patients is not evident in a referral population of patients with CFS, CFS-FM, or FM.
Buchwald D.	Department of Medicine, University of Washington, Seattle, USA.	Fibromyalgia and chronic fatigue syndrome: similarities and differences.	Rheum Dis Clin North Am 1996 May;22(2):219-43	CFS and FM are clinical conditions characterized by a variety of nonspecific symptoms including prominent fatigue, myalgia, and sleep disturbances. There are no diagnostic studies or widely accepted, pathogenic, explanatory models for either illness. Despite remarkably different diagnostic criteria, CFS and FM have many demographic and clinical similarities. More specifically, few differences exist in the domains of symptoms, examination findings, laboratory tests, functional status, psychosocial features, and psychiatric disorders. FM appears to represent an additional burden of suffering among those with CFS, however, underscoring the importance of recognizing concurrent CFS and FM. Further clarification of the similarities (and differences) between CFS and FM may be useful in studies of prognosis and help define subsets of patients who may benefit from specific therapeutic interventions.
Bujak DI, Weinstein A, Dornbush RL.	Department of Medicine, New York Medical College, Valhalla 10595, USA.	Clinical and neurocognitive features of the post Lyme syndrome.	J Rheumatol 1996 Aug;23(8):1392-7	OBJECTIVE: To evaluate neurocognitive impairment in patients with persistent arthralgia, fatigue, and subjective memory loss in patients after Lyme disease (post-Lyme syndrome, PLS). METHODS: We compared the clinical, neurocognitive, and psychological features of 23 patients with PLS to 23 age, sex, and education matched recovered patients (REC). All met Centers for Disease Control criteria for Lyme disease, were ELISA positive at onset of Lyme disease and were previously treated with standard antibiotic regimens. RESULTS: Of the patients with PLS, 7 (30%) had fibromyalgia (FM), 3 (13%) had chronic fatigue syndrome, and 10 (43%) had similar but milder symptoms but did not meet the criteria for either. 22 of 23 patients with PLS complained of decreased memory or concentration problems. Patients with PLS had significantly lower scores on the attention/concentration scale ($p = 0.012$) of the Wechsler Memory Scale-Revised (WMS-R), indicating lowered attention/concentration. 52% of patients with PLS and 35% in the REC group had significantly lower ($p < 0.05$) WMS-R verbal

				memory scores than visual memory scores. The PLS group had subjectively more problems with sleep and mood changes and higher scores on several scales of Symptom Check List 90-R ($p < 0.01$), indicating greater physical distress. Beck Depression Inventory scores were also higher for the PLS than the REC group ($p < 0.005$), but were within the normal range. CONCLUSION: Despite antibiotic treatment, a sequelae of Lyme disease may be a PLS characterized by persistent arthralgia, fatigue, and neurocognitive impairment that is probably induced by Lyme disease.
Burnet RB, Yeap BB, Chatterton BE, Gaffney RD.		Chronic fatigue syndrome: is total body potassium important?	Med J Aust 1996 Mar 18;164(6):384 comment on: Med J Aust. 1995 Sep 18;163(6):314-8	
Chagpar A.		Chronic fatigue syndrome: a prodrome to psychosis?	Can J Psychiatry 1996 Oct;41(8):536-7 comment on: Can J Psychiatry. 1996 May;41(4):217-22	
Chilton SA.		Cognitive behaviour therapy for the chronic fatigue syndrome. Evening primrose oil and magnesium have been shown to be effective.	BMJ 1996 Apr 27;312(7038):1096; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
Cleare AJ, O'Keane V.		Re: Endocrine responses to fenfluramine challenge in chronic fatigue syndrome.	Can J Psychiatry 1996 Mar;41(2):129-31 comment on: Can J Psychiatry. 1995 Mar;40(2):93-6	
Cleare AJ, Wessely SC.	Department of Psychological Medicine, Institute of Psychiatry, London. Review Literature	Chronic fatigue syndrome: a stress disorder?	Br J Hosp Med 1996 May 1-14;55(9):571-4	
Cleare AJ, Wessely SC.		Fluoxetine and chronic fatigue syndrome.	Lancet 1996 Jun 22;347(9017):1770; discussion 1771-2	
Conti F, Magrini L, Priori R, Valesini G, Bonini S.	Universita di Roma La Sapienza, I Clinica Medica, Italy.	Eosinophil cationic protein serum levels and allergy in chronic	Allergy 1996 Feb;51(2):124-7	Chronic fatigue syndrome (CFS) is a syndrome of uncertain etiopathogenesis characterized by disabling fatigue associated with a variable number of somatic and/or neuropsychologic symptoms. In patients with CFS, several immunologic

		fatigue syndrome.		abnormalities can be detected, including a higher prevalance of allergy. The aim of this study was to determine whether CFS patients, well studied for their allergy profile, show signs of eosinophil activation, as detectable by the measurement in serum of eosinophil cationic protein (ECP) levels. In 35 consecutive CFS outpatients (diagnosis based on the Centers for Disease Control case definition), ECP was measured in serum by a competitive enzyme immunoassay (ECP-FEIA kit, Kabi Pharmacia Diagnostics, Uppsala, Sweden). Fourteen disease-free subjects with no history of CFS or allergy were selected as controls. ECP serum levels were significantly higher in CFS patients than in controls (18.0 +/- 11.3 micrograms/l vs 7.3 +/- 2.1 micrograms/l; P < 0.01). In the CFS population, the prevalence of RAST positivity to one or more allergens was 77%, while no control showed positive RAST. Twelve of the 14 CFS patients with increased ECP serum levels were RAST-positive. However, CFS RAST-positive patients had no significantly higher ECP serum levels than CFS RAST-negative patients (19.3 +/- 12.4 micrograms/l vs 13.6 +/- 3.7 micrograms/l; P = 0.4). This is the first report of increased serum levels of ECP in CFS. On the basis of the available data, it is discussed whether eosinophil activation has a pathogenetic role in CFS or is linked to the frequently associated allergic condition, or, finally, whether a common immunologic background may exist for both atopy and CFS.
Cope H, David AS.		Neuroimaging in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1996 May;60(5):471-3	
Cope H, Mann A, Pelosi A, David A.	Department of Psychological Medicine, King's College Hospital, London.	Psychosocial risk factors for chronic fatigue and chronic fatigue syndrome following presumed viral illness: a case-control study.	Psychol Med 1996 Nov;26(6):1197-209	This study investigated psychosocial morbidity, coping styles and health locus of control in 64 cases with and without chronic fatigue identified from a cohort of primary care patients recruited 6 months previously with a presumed, clinically diagnosed viral illness. A significant association between chronic fatigue and psychosocial morbidity, somatic symptoms and escape-avoidance coping styles was shown. Chronic fatigue cases were significantly more likely to have a past psychiatric history and a current psychiatric diagnosis based on a standardized clinical interview. Twenty-three of the cases fulfilled criteria for chronic fatigue syndrome (CFS). Such cases were significantly more fatigued than those not fulfilling criteria, but had little excess psychiatric disorder. A principal components analysis provided some evidence for chronic fatigue being separable from general psychosocial morbidity but not from the tendency to have other somatic complaints. Past psychiatric history and psychological distress at the time of the viral illness were risk factors for psychiatric 'caseness' 6 months later, while presence of fatigue, psychologising attributional style and sick certification were significant risk factors for CFS. These findings extend a previous questionnaire study of predictors of chronic 'post-viral' fatigue.
Cordero DL, Sisto SA,	Fatigue Research	Decreased vagal power	Clin Auton Res 1996	The purpose of this study was to determine if patients with the chronic fatigue

Tapp WN, LaManca JJ, Pareja JG, Natelson BH.	Center, DVA Medical Center, East Orange, NJ 07018, USA.	during treadmill walking in patients with chronic fatigue syndrome.	Dec;6(6):329-33	syndrome have less vagal power during walking and rest periods following walking, in comparison to a group of healthy controls. Eleven patients (ten women and one man) who fulfilled the case definition for chronic fatigue syndrome modified to reduce heterogeneity and eleven healthy, but sedentary, age- and sex-matched controls walked on a treadmill at 2.5 mph four times each for 4 min duration. Between each period of walking, subjects were given a 4-min seated rest period. Vagal power, a Fourier-based measure of cardiac, parasympathetic activity in the frequency range of 0.15 to 1.0 Hz, was computed. In each period of walking and in one period of rest, patients had significantly less vagal power than the control subjects despite there being no significant group-wise differences in mean heart rate, tidal volume, minute volume, respiratory rate, oxygen consumption or total spectrum power. Further, patients had a significant decline in resting vagal power after periods of walking. These results suggest a subtle abnormality in vagal activity to the heart in patients with the chronic fatigue syndrome and may explain, in part, their post-exertional symptom exacerbation.
Crofford LJ, Demitrack MA.	Department of Internal Medicine, University of Michigan, Ann Arbor, USA.	Evidence that abnormalities of central neurohormonal systems are key to understanding fibromyalgia and chronic fatigue syndrome.	Rheum Dis Clin North Am 1996 May;22(2):267-84	Fibromyalgia (FM) and chronic fatigue syndrome (CFS) fall into the spectrum of what might be termed stress-associated syndromes by virtue of frequent onset after acute or chronic stressors and apparent exacerbation of symptoms during periods of physical or emotional stress. These illnesses also share perturbation of the hypothalamic-pituitary-adrenal axis and sympathetic stress response systems. In this article, the authors discuss the specific neurohormonal abnormalities found in FM and CFS and potential mechanisms by which dysfunction of neurohormonal stress-response systems could contribute to vulnerability to stress-associated syndromes and to the symptoms of FM and CFS.
Czarnowski D, Panasiuk B, Wiercinska-Drapalo A, Puzanowska B, Prokopowicz D.	Klinika Obscrwacyjno-Zakazna Akademii Medycncj w Bialymstoku.	[Chronic fatigue syndrome].[article in Polish]	Pol Arch Med Wewn 1996 Aug;96(2):161-4	
David A, Wessely S.		Chronic fatigue syndrome.	Lancet 1996 Nov 16;348(9038):1385 comment on: Lancet. 1996 Oct 12;348(9033):971	
De Lorenzo F, Hargreaves J, Kakkar VV.	Thrombosis Research Institute, London, UK.	Possible relationship between chronic fatigue and postural tachycardia syndromes.	Clin Auton Res 1996 Oct;6(5):263-4	Postural tachycardia syndrome refers to the development of symptoms such as light-headedness, visual blurring, palpitations and weakness on assuming an upright posture; these symptoms are relieved by resuming a supine posture. This syndrome is occasionally associated with idiopathic hypovolemia, impaired vasomotor tone, deconditioning and autonomic neuropathy, but has not been reported in association with chronic fatigue syndrome (CFS). We describe five

				patients who satisfied the CFS criteria of the Centres for Disease Control and Prevention. Upright tilt-table testing induced significant hypotension and increased heart rate in all five patients, consistent with clinical and autonomic manifestation of postural tachycardia syndrome.
De Lorenzo F, Hargreaves J, Kakkar VV. Publication Types: Letter		Lung function test findings in patients with chronic fatigue syndrome (CFS)	Aust N Z J Med 1996 Aug;26(4):563-4 comment in: Aust N Z J Med. 1997 Jun;27(3):346	
De Lorenzo F, Kakkar VV.		Twenty-four-hour urine analysis in patients with orthostatic hypotension and chronic fatigue syndrome (CFS)	Aust N Z J Med 1996 Dec;26(6):849-50	
De Vinci C, Levine PH, Pizza G, Fudenberg HH, Orens P, Pearson G, Viza D.	Immunodiagnosis and Immunotherapy Unit, 1st Division of Urology Sant'Orsola-Malpighi Hospital, Bologna, Italy.	Lessons from a pilot study of transfer factor in chronic fatigue syndrome.	Biotherapy 1996;9(1-3):87-90	Transfer Factor (TF) was used in a placebo controlled pilot study of 20 patients with chronic fatigue syndrome (CFS). Efficacy of the treatment was evaluated by clinical monitoring and testing for antibodies to Epstein-Barr virus (EBV) and human herpes virus-6 (HHV-6). Of the 20 patients in the placebo-controlled trial, improvement was observed in 12 patients, generally within 3-6 weeks of beginning treatment. Herpes virus serology seldom correlated with clinical response. This study provided experience with oral TF, useful in designing a larger placebo-controlled clinical trial. Randomized Controlled Trial
Diamantis I.	Department Innere Medizin, Medizinische Universitats-Poliklinik, Basel.	[A case from practice (343). Chronic fatigue syndrome following Lyme borreliosis].[article in German]	Schweiz Rundsch Med Prax 1996 Feb 27;85(9):287-8	
DiPino RK, Kane RL.	Department of Psychology, Veterans Administration Medical Center, Baltimore, Maryland 21201, USA.	Neurocognitive functioning in chronic fatigue syndrome.	Neuropsychol Rev 1996 Mar;6(1):47-60	Although substantial research has been conducted on chronic fatigue syndrome (CFS) over the past decade, the syndrome remains poorly understood. The most recent case definition describes CFS as being characterized both by disabling fatigue and by subjective reports of difficulty with concentration and "short-term" memory. However, research into the neurocognitive and psychological functioning of individuals with CFS has provided mixed objective results. The current paper reviews studies that have examined the neurocognitive and/or psychological functioning of individuals with CFS. Changes in research design and instruments employed to study individuals with CFS are suggested.
Djaldetti R, Ziv I, Achiron A, Melamed E.	Department of Neurology, Beilinson Medical Center, Petah	Fatigue in multiple sclerosis compared with chronic fatigue	Neurology 1996 Mar;46(3):632-5	Fatigue, a common complaint among patients with multiple sclerosis (MS), is poorly characterized. We developed a computerized method that quantitatively measures fatigue, and defined a fatigue index (FI), which is the ratio between the

	Tiqva 49100, Israel.	syndrome: A quantitative assessment.		integral of muscle strength decay over time and maximal voluntary contraction. Thirty patients (mean age, 37.4 +/- 10.3 years) were examined - 20 patients with pyramidal tract involvement and 10 patients with involvement of other neurological systems. We evaluated 10 patients during relapse and 3 months afterwards, and compared their results with those of four patients with chronic fatigue syndrome (CFS) and 13 age-matched health subjects. The FI was significantly higher in the MS patients as compared with the CFS patients and normal controls: 34.2 +/- 6.4% versus 27.5 +/- 1.0% and 23.6 +/- 6.8%, $p < 0.05$. Within the MS group, the FI correlated with the presence of pyramidal signs- 43.5% compared with 33% in patients without pyramidal signs, $p < 0.01$. In MS patients, fatigue worsened during a relapse affecting the pyramidal tract, but not during a relapse in other systems. These results demonstrate that fatigue can be quantitatively measured in MS patients, and that pyramidal dysfunction leads to increased fatigability.
Drago F, Ranieri E, Pastorino A, Casazza S, Crovato F, Rebora A.	Department of Dermatology, University of Genoa, Italy.	Epstein-Barr virus-related primary cutaneous amyloidosis. Successful treatment with acyclovir and interferon-alpha.	Br J Dermatol 1996 Jan;134(1):170-4	Cutaneous lesions related to chronic active Epstein-Barr virus (EBV) infection have been rarely documented in immunocompetent patients. A 30-year-old woman, fulfilling the diagnostic criteria for the chronic fatigue syndrome, had a 10-year history of pruritic brownish macules and papules on her chest and back. Her EBV serology was abnormal; the EBV genome was present in the epidermis of lesions, in oral secretions, and in peripheral mononuclear cells (PMC). Her blood lymphocytes spontaneously outgrew in culture. Histology revealed deposits of amyloid in the papillary dermis. Treatment with acyclovir and interferon-alpha rapidly improved her condition, stopped the lymphocyte outgrowth in culture, and reduced the EBV DNA content in oral secretions and in PMC. These data support an endogenous reactivation of EBV infection and suggest a causal relationship with primary amyloidosis.
Dunstan RH, Donohoe M, Taylor W, Roberts TK, Murdoch RN, Watkins JA, McGregor NR.		Chlorinated hydrocarbons and chronic fatigue syndrome.	Med J Aust 1996 Feb 19;164(4):251 comment on: Med J Aust. 1995 Sep 18;163(6):285-6	
Dyck D, Allen S, Barron J, Marchi J, Price BA, Spavor L, Tateishi S.		Management of chronic fatigue syndrome: case study.	AAOHN J 1996 Feb;44(2):85-92	1. Chronic fatigue syndrome (CFS) is a complex disorder marked by incapacitating fatigue of uncertain etiology which has resulted in a least a 50% reduction in activity and is of at least 6 months' duration. 2. Definitive diagnosis can be very challenging. Because no markers objectively identify the presence of CFS, diagnosis depends heavily on the presence of subjective complaints. 3. The current philosophy of CFS management is to use a multidisciplinary approach incorporating these rehabilitation goals: restore a sense of self efficacy and control; gradually increase physical activity; and decrease the restrictions imposed by CFS.

Eaton KK.		Cognitive behaviour therapy for the chronic fatigue syndrome. Use an interdisciplinary approach.	BMJ 1996 Apr 27;312(7038):1097; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
Euga R, Chalder T, Deale A, Wessely S.	Academic Department of Psychological Medicine, King's College School of Medicine and Dentistry, London.	A comparison of the characteristics of chronic fatigue syndrome in primary and tertiary care.	Br J Psychiatry 1996 Jan;168(1):121-6	BACKGROUND: To evaluated the characteristics of Chronic Fatigue Syndrome (CFS) in primary and tertiary care. METHOD: A comparison of subjects fulfilling criteria for CFS, identified as part of a prospective cohort study in primary care, compared to 79 adults fulfilling the same criteria referred for treatment to a specialist CFS clinic. RESULTS: Hospital cases were more likely to belong to upper socio-economic groups, and to have physical illness attributions. They had higher levels of fatigue and more somatic symptoms, and were more impaired functionally, but had less overt psychological morbidity. Women were over-represented in both primary care and hospital groups. Nearly half of those referred to a specialist clinic did not fulfil operational criteria for CFS. CONCLUSION: The high rates of psychiatric morbidity and female excess that characterise CFS in specialist settings are not due to selection bias. On the other hand higher social class and physical illness attributions may be the result of selection bias and not intrinsic to CFS.
Farmer A, Chubb H, Jones I, Hillier J, Smith A, Borysiewicz L.		Screening for psychiatric morbidity in subjects presenting with chronic fatigue syndrome.	Br J Psychiatry 1996 Mar;168(3):354-8	BACKGROUND. There is a need for a valid self-rating questionnaire to screen for psychiatric morbidity in patients with chronic fatigue syndrome (CFS). This study had the aim of assessing the utility and validity of two commonly used measures. METHOD. Scores obtained on the General Health Questionnaire (GHQ) and the Beck Depression Inventory (BDI) were compared with various diagnostic and severity ratings obtained via a validating clinical interview, the Schedules for the Clinical Assessment of Neuropsychiatry (SCAN) in 95 consecutively referred subjects at a medical out-patient clinic who fulfilled standard criteria for CFS, and 48 healthy controls. Outcome measures were validating coefficients and receiver operating characteristics (ROC) for different thresholds and scoring on GHQ and BDI and index of definition (ID) as measured by SCAN; and Pearson and point by serial correlation coefficients for different diagnostic groups derived via SCAN and defined according to ICD-10 and DSM-III-R. RESULTS. GHQ and BDI perform poorly as screeners of psychiatric morbidity in CFS subjects when compared with various SCAN derived ratings although results for controls are comparable with other studies. CONCLUSIONS. Neither the GHQ nor BDI alone can be recommended as screeners for psychiatric morbidity in CFS subjects.
Few J, Thompson NW, Angelos P, Simeone D, Giordano T, Reeve T.	Department of Surgery, University of Michigan, Ann Arbor, USA.	Riedel's thyroiditis: treatment with tamoxifen.	Surgery 1996 Dec;120(6):993-8; discussion 998-9	BACKGROUND: Riedel's thyroiditis is an often disabling disease with clinical and histologic similarity to several other fibrous inflammatory disorders. Surgical treatment alone is often unsatisfactory in permanently alleviating airway compression, dysphagia, neck immobility, pain, or chronic fatigue syndrome.

				Investigation of drugs shown to be of benefit in the treatment of related fibrous disorders in which hormonal factors or inflammatory deregulation appear to be important is indicated. Tamoxifen has not been previously used in the treatment of Riedel's thyroiditis. METHODS: Four patients with clinical and histologic diagnoses of Riedel's thyroiditis were evaluated before and after treatment with tamoxifen. Each had progressive symptomatic disease of 3 to 16 years' duration despite one or more surgical procedures and steroid therapy. Subjective improvement was noted in all cases, and objective changes were confirmed by periodic physical and computed tomographic examinations. RESULTS: Patients have been monitored for 1 to 4 years with subjective improvement in 100% and objective disease regression ranging from 50% to 100% in all patients. One patient had complete regression within 6 months, and another had more than 50% regression within 3 months. All have returned to predisease activity levels. There were no significant side effects of the therapy. CONCLUSIONS: Tamoxifen has proved to be the most effective drug therapy available for managing Riedel's thyroiditis. Our studies suggest that this is unrelated to antiestrogen activity. Tamoxifen's effectiveness may be caused by a mechanism by which it stimulates the release of transforming growth factor-beta, which may inhibit the fibroblastic proliferation characteristic of Riedel's thyroiditis.
Fiedler N, Kipen H, Natelson B, Ottenweller J.	UMDNJ-Robert Wood Johnson Medical School, Environmental & Occupational Health Sciences Institute, Piscataway 08855, USA.	Chemical sensitivities and the Gulf War: Department of Veterans Affairs Research Center in basic and clinical science studies of environmental hazards.	800: Regul Toxicol Pharmacol 1996 Aug;24(1 Pt 2):S129-38	The purpose of the New Jersey Center for Environmental Hazards Research is to define the illness referred to as Persian Gulf Syndrome (PGS). Our preliminary data indicated that more than half of the Persian Gulf Registry (PGR) veterans reported illness characterized by severe fatigue and symptoms consistent with chemical sensitivities. Therefore, our research approach focuses on investigations of veterans with chronic fatigue syndrome (CFS) and multiple chemical sensitivities (MCS). Project 1 is an epidemiological study of 2800 PGR veterans. Symptoms, indices of Chronic Fatigue (CF) and Chemical Sensitivity (CS), and risk factors will be surveyed with mailed questionnaires. Risk factors include demographics, past medical history, psychosocial variables, Gulf War experiences such as prophylactic medication use, occupational and environmental exposures, and pesticide exposures. Symptoms will be clustered to define Gulf War Syndromes. Significant associations between risk factors and these symptom clusters will also be investigated Subjects identified as CF, CS, or both will be recruited into Projects 2 and 3. In Project 2, healthy veterans will be compared to veterans with CF, CS, and CF concurrent with CS. Veterans will undergo four studies: (1) viral-immunological, (2) psychiatric, psychological, behavioral, and neuropsychological, (3) autonomic dysregulation, and (4) marker of P4501A2 induction resulting from exposure to combusting material. The purpose of Project 3 is to test the autonomic, immunologic, neuropsychologic, and psychologic responses of veterans with CS or CF to two stressors: controlled

				chemical exposure and exercise. CS subjects will undergo chemical exposures in our Controlled Environment Facility (CEF) to assess their biologic and psychologic response to low-level exposure. CF subjects will undergo a maximal treadmill exercise test. Circadian patterns of catecholamines and axillary temperature, viral burden, and cardiovascular and endocrine reactivity will be measured in response to this physical stressor. Project 4 is an animal study evaluating the interaction between stress and pathology/physiology when rats are predisposed to disease by exposure to Soman or to Dioxin. Two strains of rats that differ in stress reactivity will be used to determine the interaction of hereditary factors and chemical exposure.
Fiedler N, Kipen H, Natelson B, Ottenweller J.	Environmental & Occupational Health Sciences Institute, UMDNJ-Robert Wood Johnson Medical School, 681 Frelinghuysen Road, Piscataway, New Jersey, 08855	Chemical Sensitivities and the Gulf War: Department of Veterans Affairs Research Center in Basic and Clinical Science Studies of Environmental Hazards	Regul Toxicol Pharmacol 1996 Aug;24(1):S129-38	The purpose of the New Jersey Center for Environmental Hazards Research is to define the illness referred to as Persian Gulf Syndrome (PGS). Our preliminary data indicated that more than half of the Persian Gulf Registry (PGR) veterans reported illness characterized by severe fatigue and symptoms consistent with chemical sensitivities. Therefore, our research approach focuses on investigations of veterans with chronic fatigue syndrome (CFS) and multiple chemical sensitivities (MCS). Project 1 is an epidemiological study of 2800 PGR veterans. Symptoms, indices of Chronic Fatigue (CF) and Chemical Sensitivity (CS), and risk factors will be surveyed with mailed questionnaires. Risk factors include demographics, past medical history, psychosocial variables, Gulf War experiences such as prophylactic medication use, occupational and environmental exposures, and pesticide exposures. Symptoms will be clustered to define Gulf War Syndromes. Significant associations between risk factors and these symptom clusters will also be investigated. Subjects identified as CF, CS, or both will be recruited into Projects 2 and 3. In Project 2, healthy veterans will be compared to veterans with CF, CS, and CF concurrent with CS. Veterans will undergo four studies: (1) viral-immunological, (2) psychiatric, psychological, behavioral, and neuropsychological, (3) autonomic dysregulation, and (4) marker of P4501A2 induction resulting from exposure to combusting material. The purpose of Project 3 is to test the autonomic, immunologic, neuropsychologic, and psychologic responses of veterans with CS or CF to two stressors: controlled chemical exposure and exercise. CS subjects will undergo chemical exposures in our Controlled Environment Facility (CEF) to assess their biologic and psychologic response to low-level exposure. CF subjects will undergo a maximal treadmill exercise test. Circadian patterns of catecholamines and axillary temperature, viral burden, and cardiovascular and endocrine reactivity will be measured in response to this physical stressor. Project 4 is an animal study evaluating the interaction between stress and pathology/physiology when rats are predisposed to disease by exposure to Soman or to Dioxin. Two strains of rats that differ in stress reactivity will be used to determine the interaction of hereditary factors and

				chemical exposure.
Fiedler N, Kipen HM, DeLuca J, Kelly-McNeil K, Natelson B.	Department of Environmental and Community Medicine, UMDNJ-Robert Wood Johnson Medical School, Piscataway, New Jersey 08855, USA.	A controlled comparison of multiple chemical sensitivities and chronic fatigue syndrome.	Psychosom Med 1996 Jan-Feb;58(1):38-49	The present study had two objectives: 1) to determine the characteristics that differentiated subjects with multiple chemical sensitivities (MCS), chemical sensitivities (CS), and chronic fatigue syndrome (CFS); and 2) to evaluate the psychiatric and neuropsychological complaints of these groups relative to normal controls. A cross-sectional comparison was made of the following groups matched for age, sex, and education: 1) patients whose sensitivities to multiple low level chemical exposures began with a defined exposure (MCS; N = 23); 2) patients with sensitivities to multiple chemicals without a clear date of onset (CS; N = 13); 3) patients meeting CDC criteria for Chronic Fatigue Syndrome (CFS; N = 18); and 4) normal controls (N = 18). Subjects with sensitivities to chemicals (MCS and CS) reported significantly more lifestyle changes due to chemical sensitivities and significantly more chemical substances that made them ill compared with chronic fatigue and normal controls. MCS, CS, and CFS patients had significantly higher rates of current psychiatric disorders than normal controls and reported significantly more physical symptoms with no medical explanation. Seventy-four percent of MCS and 61% of CFS did not qualify for any current Axis I psychiatric diagnosis. Chemically sensitive subjects without a defined date of onset (CS) had the highest rate of Axis I psychiatric disorders (69%). On the MMPI-2, 44% of MCS, 42% of CS, 53% of CFS, and none of the controls achieved clinically significant elevations on scales associated with somatoform disorders. With the exception of one complex test of visual memory, no significant differences were noted among the groups on tests of neuropsychological function. Standardized measures of psychiatric and neuropsychological function did not differentiate subjects with sensitivities to chemicals from those with chronic fatigue. Subjects with sensitivities to chemicals and no clear date of onset had the highest rate of psychiatric morbidity. Standardized neuropsychological tests did not substantiate the cognitive impairment reported symptomatically. Cognitive deficits may become apparent under controlled exposure conditions.
Fischler B, D'Haenen H, Cluydts R, Michiels V, Demets K, Bossuyt A, Kaufman L, De Meirleir K.	Department of Psychiatry, Academic Hospital, Free University of Brussels, Belgium.	Comparison of 99m Tc HMPAO SPECT scan between chronic fatigue syndrome, major depression and healthy controls: an exploratory study of clinical correlates of regional cerebral blood flow.	Neuropsychobiology 1996;34(4):175-83	An explorative analysis of the relationship between symptomatology and cerebral blood flow in the chronic fatigue syndrome (CFS) as assessed with 99mTc HMPAO SPECT scan reveals statistically significant positive correlations between frontal blood flow on the one hand and objectively and subjectively assessed cognitive impairment, self-rating of physical activity limitations and total score on Hamilton Depression Rating Scale on the other. A pathophysiological role of frontal blood flow in the cognitive impairment and physical activity limitations in CFS is hypothesized. A comparison of cerebral blood flow between CFS, major depression (MD) and healthy controls (HC) has been performed. A lower superofrontal perfusion index is demonstrated in MD as compared with both CFS and HC. There is neither a global nor a marked regional hypoperfusion

				in CFS compared with HC. Asymmetry (R > L) of tracer uptake at parietotemporal level is demonstrated in CFS as compared with MD.
Fry AM, Martin M.	University of Oxford Department of Psychiatry, Park Hospital for Children, U.K.. AMFRY@VAX.OX.AC.UK	Cognitive idiosyncrasies among children with the chronic fatigue syndrome: anomalies in self-reported activity levels.	J Psychosom Res 1996 Sep;41(3):213-23	The possibility that children with the chronic fatigue syndrome (CFS) and their parents tend to display idiosyncratic cognitive processing concerning levels of activity was examined by means of subjective and objective measures of current activity, together with subjective and objective measures of desired and expected future activity. The degree to which subjective reports of current activity level reflect objectively measured activity level was examined in a group of children with CFS and a healthy control group. All subjects were assessed over a 3-day period by means of ambulatory activity monitoring, and self-reports and parent-reports of current activity level were collected by means of visual analog scales. Analysis of variance revealed a significant interaction between the method of measurement (objective versus subjective) and the participant group (CFS versus Healthy) with the CFS children and their parents underestimating actual level of activity relative to the healthy group. Desired and expected levels of future activity were also assessed by means of subjective report. Child and parent expected levels of future activity were compared with their desired levels. Although expected levels of future activity were similar in the two groups, the divergence between expected levels and corresponding desired levels was significantly greater in the CFS group. These results are discussed in terms of idiosyncratic cognitive processes, which are hypothesized to be associated with CFS and which may play a role in the maintenance of the disorder.
Fry AM, Martin M.	Department of Experimental Psychology, University of Oxford, UK. AMFRY@VAX.OX.AC.UK	Fatigue in the chronic fatigue syndrome: a cognitive phenomenon?	J Psychosom Res 1996 Nov;41(5):415-26	What is the source of the perception of excessive fatigue in the chronic fatigue syndrome (CFS)? Studies of physiological response to aerobic activity, of muscle pathology and muscle function in CFS, are reviewed, and suggest that the subjective report of fatigue is not due to any peripheral impairment. In addition, current technological methods such as electroencephalography have failed to uncover the nature of any abnormality in the central motor unit. A physiological model which proposes that patients with CFS possess a reduced threshold for sensory fatigue signals is rejected, because it fails to account for recent findings. Instead, it is suggested that the perception of fatigue in CFS is enhanced by idiosyncrasies in cognitive processing. The implications of this view to our understanding of the perpetuation of CFS as a whole are explored. Publication Types: Review Review Literature
Fukazawa T, Sasaki H, Kikuchi S, Hamada T, Tashiro K.	Hokuyukai Neurology Hospital, Sapporo, Japan.	Serum carnitine and disabling fatigue in multiple sclerosis.	Psychiatry Clin Neurosci 1996 Dec;50(6):323-5	The serum concentrations of total, free and acylcarnitine were compared in 25 patients with multiple sclerosis (MS) and among age- and sex-matched normal controls by the new enzymatic cycling method in order to clarify whether the fatigue in MS might be due to possible carnitine-related fatty acid metabolic abnormalities in the mitochondria of skeletal muscles. Patients with MS were divided into those with and those without excessive fatigue. Levels of total and

				free carnitine were not significantly different between MS patients and normal controls. Levels of acylcarnitine, whose decrease in chronic fatigue syndrome has been reported, were also similar between MS patients and normal controls. There was no difference in these carnitine levels between MS patients with and without excessive fatigue. We argue that acylcarnitine deficiency and fatty acid metabolic dysfunction in mitochondria are not relevant to the excessive fatigue in patients with MS, and further explanatory investigations are to be sought.
Gibbons R, Macintyre A, Richards C.		Cognitive behaviour therapy for the chronic fatigue syndrome. Patients were not representative of all patients with the syndrome.	BMJ 1996 Apr 27;312(7038):1096-7; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
Goldenberg DL.	Newton-Wellesley Hospital, Newton, MA 02162, USA.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain.	Curr Opin Rheumatol 1996 Mar;8(2):113-23	The prevalence of fibromyalgia in the general population was found to be 2% and increased with age. Multiple traumatic factors, including sexual and physical abuse, may be important initiating events. The most important pathophysiologic studies in fibromyalgia included evidence of altered blood flow to the brain and hypothalamic-pituitary-adrenal dysfunction. The prevalence of chronic fatigue syndrome is much less than that of fibromyalgia. Epidemiologic studies demonstrated that chronic fatigue and symptoms of fibromyalgia are distributed as continuous variables in the general population. No association between chronic fatigue and initial infections was seen in primary care practices.
Gonzalez MB, Cousins JC, Doraiswamy PM.	Department of Psychiatry, Duke University Medical Center, Durham, NC, USA.	Neurobiology of chronic fatigue syndrome.	Prog Neuropsychopharmacol Biol Psychiatry 1996 Jul;20(5):749-59	1. Chronic fatigue syndrome (CFS) is characterized by a new onset of significant fatigue for a period of six months or longer usually following an infection, injury or period of high stress. 2. The exact etiology of CFS is not known and a diagnostic test is not available. Hence, the diagnosis is made by exclusion of other explanations for the patient's symptoms and by meeting the CDC research case definitions. Early studies supported an infectious or immune dysregulation hypothesis for the pathophysiology of CFS. 3. Subsequent studies documented that neurological, affective and cognitive symptoms also occur at high rates in CFS patients. Neuropsychological, neuroendocrine studies and brain imaging have now confirmed the occurrence of neurobiological abnormalities in most patients with CFS. 4. In this article, the authors review these findings in relation to the clinical neurobiology of CFS and their potential relevance to biological psychiatry.
Goodnick PJ.		Treatment of chronic fatigue syndrome with venlafaxine.	Am J Psychiatry 1996 Feb;153(2):294	
Grant JE, Veldee MS,	University of	Analysis of dietary	J Am Diet Assoc 1996	

Buchwald D.	Washington Medical Center, Seattle, 98104, USA.	intake and selected nutrient concentrations in patients with chronic fatigue syndrome.	Apr;96(4):383-6	
Griffiths RA, Beumont PJ, Moore GM, Touyz SW.	Department of Psychological Medicine, University of Sydney, New South Wales, Australia.	Chronic fatigue syndrome and dieting disorders: diagnosis and management problems.	Aust N Z J Psychiatry 1996 Dec;30(6):834-8	OBJECTIVE: This paper illustrates the importance of conducting an initial and ongoing psychiatric assessment of patients with chronic fatigue syndrome in order to diagnose dieting disorders. The diagnostic issues and management problems of three case vignettes, two with anorexia nervosa and one with bulimia nervosa, are described. METHOD: The treatment response of dieting disordered patients is generally prolonged after a previous diagnosis of chronic fatigue syndrome has been made and the patient and family favour a disease diagnosis. RESULTS: Several management problems arise and family members may also be reluctant to accept a dieting disorder diagnosis. CONCLUSIONS: Early detection of dieting disorders by adequate screening and assessment is necessary so that a significant reduction in morbidity may occur.
Gruber AJ, Hudson JI, Pope HG Jr.	Biological Psychiatry Laboratory, McLean Hospital, Belmont, Massachusetts, USA.	The management of treatment-resistant depression in disorders on the interface of psychiatry and medicine. Fibromyalgia, chronic fatigue syndrome, migraine, irritable bowel syndrome, atypical facial pain, and premenstrual dysphoric disorder.	Psychiatr Clin North Am 1996 Jun;19(2):351-69	We have reviewed studies examining the efficacy of various psychotropic medications, primarily antidepressant agents, in the treatment of a group of disorders that appear to exhibit some phenomenologic and genetic relationship to major depression. These disorders all appear to benefit (albeit to varying degrees) from antidepressant medications of several different chemical families. This observation has important theoretical and clinical implications. From a theoretical perspective, these results invite the hypothesis that these various disorders may share some particular etiologic "step" in common with major depression-and that the various antidepressant classes benefit these various disorders and major depression via a common action at this hypothetical "step". Although there is an appealing parsimony to this hypothesis, several reservations must be considered. First, it must be recognized that the quality of the available studies varies widely. As noted in the text, these studies used numerous different designs, varying diagnostic criteria for the disorders under study, and diverse methods of rating outcome. Interpretation is further complicated by the fact that many studies included other concomitant medications or therapeutic interventions in addition to the psychotropic drugs administered. Also, the dose of antidepressant medications administered in many of these studies, especially those using TCAs, was often much less than that normally administered in the treatment of major depressive disorder itself. Finally, many of the studies did not systematically evaluate improvement in both the physical and psychological symptoms of a given disorder. For all of these reasons, any theoretic discussion of the results must be tentative. Nevertheless, the overall tally of results strongly favors the hypothesis that antidepressant agents, regardless of their chemical class, are generally useful in the treatment of these disorders. At a minimum,

				therefore, we can conclude that antidepressant treatment in these disorders deserves aggressive further investigation in studies with modern, rigorous designs. Second, even allowing that multiple antidepressant agents are effective in these various disorders, it still may be premature to conclude that these disorders are related to major depressive disorder. In particular, many of the studies found little correlation between improvement in psychological symptoms and physical symptoms of a given disorder. This observation would seem to argue against a relationship with major depressive disorder. The alternative hypothesis, however, namely, that these disorders do not share a common etiologic "step," seems even less attractive. It would be a remarkable coincidence if, say, fluoxetine possessed an antidepressant property, an independent antimigraine property, and a third, independent, antipremenstrual dysphoric disorder property. And it would be even more peculiar if various other antidepressant medications chemically unrelated to fluoxetine also, by chance alone, benefited all of these same disorders via still other independent mechanisms. Although we cannot, of course, rule out the possibility of multiple mechanisms and multiple causes, the experience of scientific research often has been that the simpler explanation of a phenomenon has proved to be correct. Therefore, the possibility of a link among these various antidepressant-responsive disorders deserves investigation. From a clinical perspective, too, these results are important. They suggest that trials of antidepressant medications should be strongly considered in patients with these disorders. Furthermore, other types of psychotropic medication appear to have a role in the treatment of individual disorders, as discussed in the corresponding sections.(ABSTRACT TRUNCATED) Review Literature
Gushue J.		Increasing workplace stress means occupational medicine will be a growth area.	CMAJ 1996 Nov 1;155(9):1310-3	Physicians attending a recent annual meeting on occupational medicine heard wide-ranging discussions about chronic fatigue syndrome and the effect of increased stress on workers. They also learned that occupational medicine is likely to be one of the growth specialties in the coming decade.
Hakimi R.	Stabsabteilung arztlicher Dienst der Hallesche-Nationale Krankenversicherung a.G Stuttgart.	[Chronic fatigue syndrome--also an insurance medicine problem].[article in German]	Versicherungsmedizin 1996 Apr 1;48(2):59-61	Not everybody who is chronically tired has a chronic fatigue syndrome. The diagnosis of the chronic fatigue syndrome is still a problem, and is becoming a problem in health insurance medicine too. There is a lack of knowledge concerning the causes, the diagnosis and the therapy of the chronic fatigue syndrome. And there is still the question if the chronic fatigue syndrome is an entity of its own. For these reasons we should apply the few facts we really know about the chronic fatigue syndrome. This is the working case definition of Kaplan et al. from 1988. Otherwise there will be done hundreds of expensive laboratory tests, which are useless for the patient and very costly for the health insurance companies.
Hall SR, Smith AP.	School of Psychology,	Behavioural effects of	Neuropsychobiology	The aim of the present study was to provide preliminary information on the

	University of Birmingham, UK.	infectious mononucleosis.	1996;33(4):202-9	acute and chronic effects of infectious mononucleosis (IM) on memory, attention, psychomotor performance and mood. These issues were examined by comparing individuals with acute IM, those who had the initial illness some months before, and matched healthy controls. Objective measures of memory, attention, motor skills and visual functions were obtained, as were subjective reports of mood. The results showed selective effects of acute IM on performance and mood, with the profile of impairments being very similar to those observed in previous studies of influenza. Different impairments were observed in subjects who had the primary illness several months before, and the effects observed in this group were similar to those observed in recent studies of chronic fatigue syndrome patients. Both acute and chronic IM subjects reported similar levels of symptoms and psychopathology, with both groups having greater scores than the controls. However, the performance impairments did not reflect symptoms or psychopathology. One may conclude that the study of IM will provide important data on both the acute and longer lasting effects of viral infections on the brain and behaviour.
Hamre HJ.		[Chronic fatigue syndrome and cognitive therapy].[article in Norwegian]	Tidsskr Nor Laegeforen 1996 May 10;116(12):1503 comment in: Tidsskr Nor Laegeforen. 1996 May 20;116(13):1615 comment on: Tidsskr Nor Laegeforen. 1996 Mar 10;116(7):861-4	
Hana I, Vrubel J, Pekarek J, Cech K.	Dept. of Immunology, Institute for Clinical and Experimental Medicine, Prague, Czechia.	The influence of age on transfer factor treatment of cellular immunodeficiency, chronic fatigue syndrome and/or chronic viral infections.	Biotherapy 1996;9(1-3):91-5	A group of 222 patients suffering from cellular immunodeficiency (CID), frequently combined with chronic fatigue syndrome (CFS) and/or chronic viral infections by Epstein-Barr virus (EBV) and/or cytomegalovirus (CMV), were immunologically investigated and treated with transfer factor (TF). The age range was 17-77 years. In order to elucidate the influence of aging on the course of the disease and on treatment, 3 subgroups were formed: 17-43 years, 44-53 years, and 54-77 years. Six injections of Immodin (commercial preparation of TF by SEVAC, Prague) were given in the course of 8 weeks. When active viral infection was present, IgG injections and vitamins were added. Immunological investigation was performed before the start of therapy, and subsequently according to need, but not later than after 3 months. The percentages of failures to improve clinical status of patients were in the individual subgroups, respectively: 10.6%, 11.5% and 28.9%. The influence of increasing age on the percentage of failures to normalize low numbers of T cells was very evident: 10.6%, 21.2% and 59.6%. In individuals uneffected by therapy, persistent

				absolute lymphocyte numbers below 1,200 cells were found in 23.1%, 54.5% and 89.3% in the oldest group. Statistical analysis by Pearson's Chi-square test, and the test for linear trend proved that the differences among the individual age groups were significant. Neither sex, nor other factors seemed to influence the results. The results of this pilot study show that age substantially influences the failure rate of CID treatment using TF. In older people, it is easier to improve the clinical condition than CID: this may be related to the diminished number of lymphocytes, however, a placebo effect cannot be totally excluded.
Hausotter W.		[Expert assessment of chronic fatigue syndrome].[article in German]	Versicherungsmedizin 1996 Apr 1;48(2):57-9	The Chronic-Fatigue-Syndrome (CFS) has been first described in 1988 and has been also in Germany recently more frequently diagnosed. It is similar to a lot of other terms, especially to "neurasthenia", which has been introduced 1869 from Beard and is now again content of ICD-10. CFS is defined by primary and secondary criteria, which are however largely subjective. There are no objective signs. It is unknown if this syndrome represents a disease entity of its own. The explanation is either exclusive organic based on immunological and virological findings or exclusive psychogenic as a special form of anxiety psychosis. Possibly are both factors involved as part of "psycho-neuro-immunology". CFS is increased subject of medical certification. It has been tried to give a practical guidance to the assessment of CFS.
Hilgers A, Johannes Frank		Chronic Fatigue Syndrome Evaluation of a 30-Criteria-Score and Correlation with Immune Activation	Journal of Chronic Fatigue Syndrome 1996: 2(4): 35 - 47	Objective: The development of a score for severity of Chronic Fatigue Syndrome (CFS), the correlation of CFS with parameters of immune activation and the association with pathogens. Methods: Five hundred five patients with suspicion of Chronic Fatigue Syndrome and no other definitive diagnosis were checked by a 45-criteria-score, basic laboratory programs and immunological profiles. In most of the patients further tests concerning complement system, immune activation markers, hormones and serology of herpesviruses, Chlamydia and Borrelia could be evaluated. Comparison of the symptoms of CFS patients with healthy controls lead to a 30-criteria-score and this score was correlated with laboratory parameters (Spearman rank-correlation-coefficient rs, ties corrected). Results: Three hundred eighty-five patients fulfilling stronger criteria according to the Centers for Disease Control (CDC) definition showed significant differences to 53 healthy controls in 40 of the 45 criteria ($p < 0.001$, twitches and food allergies $p < 0.05$). Thirteen symptoms corresponding to CDC criteria were all significant ($p < 0.001$), 17 further significant criteria of descending precision were added: respiratory infections, palpitations, dizziness, dyspepsia, dryness of mouth/eyes, allergies, nausea, paresthesia, loss of hair, skin alterations, dyscoordination, chest pain, personality changes, eczema, general infections, twitches, urogenital infections. A correlation between the 30-criteria-score and immunological parameters could be evaluated in 472 of the 505 patients. Significant positive correlation with the 30-criteria-score was found in numbers of CD8+ T-

				lymphocytes, HLA-DR+ T-lymphocytes, gamma globulins, IgM, IgG, and for the number of types of autoantibodies (mainly ANA, ACA, antithyroid and antiparietal cell antibodies). Significant negative correlation was found in albumin-globulin-ratio, eosinophils and IgE. Most of these parameters also correlated with one another. On the other hand, in subgroups of the 505 patients the Frequency of positivity in serological tests for HHV-6 (49.9%), EBV (35.4%), HSV (29.2%), CMV (12.5%) and Chlamydia (35.0%) was striking. Borrelia Western blots showed 3 or more specific IgG-bands in 54 of 131 patients (41.2%). In some cases infection with EBV, HHV-6 and CMV, respectively, was confmed by DNA-PCR-test and antigen detection. Summary: In increasingly larger groups of patients with CFS and related constellations we often see clinical signs and longer anamnesis of other symptoms besides the classical criteria of CFS, especially a high prevalence of local and general susceptibility to infections and hints to prolonged inflammation processes. Together with other results, the data confirm the hypothesis that a reduced or unstable immune control or delayed immune reaction to persisting viruses or bacterial intracellular pathogens, possibly triggered by common infections or other environmental factors, can lead to a chronic neuroimmune activation state and auto-immune disorders. Hypersensitivity symptoms of the patients might not be mediated by classical allergies alone but also result from a type-IV-hypersensitivity.
Ho-Yen DO.		Cognitive behaviour therapy for the chronic fatigue syndrome. Patients' beliefs about their illness were probably not a major factor.	BMJ 1996 Apr 27;312(7038):1097-8 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
Hoffmann A, Linder R, Kroger B, Schnabel A, Kruger GR.	Medizinische Universitatsklinik Lubeck.	[Fibromyalgia syndrome and chronic fatigue syndrome. Similarities and differences].[article in German]	Dtsch Med Wochenschr 1996 Sep 20;121(38):1165-8	
Hotopf M, Noah N, Wessely S.	Institute of Psychiatry, Denmark Hill, London, UK.	Chronic fatigue and minor psychiatric morbidity after viral meningitis: a controlled study.	J Neurol Neurosurg Psychiatry 1996 May;60(5):504-9	OBJECTIVE--To test the hypotheses that patients exposed to viral meningitis would be at an increased risk of developing chronic fatigue syndrome and would have an excess of neurological symptoms and physical impairment. METHODS--Eighty three patients were followed up 6-24 months after viral meningitis and a postal questionnaire was used to compare outcome with 76 controls who had had non-enteroviral, non-CNS viral infections. RESULTS--For the 159 patients and controls the prevalence of chronic fatigue syndrome was 12.6%, a rate higher than previously reported from primary care attenders, suggesting that moderate

				to severe viral infections may play a part in the aetiology of some fatigue states. Those with a history of meningitis showed a slight, non-significant increase in prevalence of chronic fatigue syndrome (OR 1.4; 95% CI 0.5-3.6) which disappeared when logistic regression and analysis was used to correct for age, sex, and duration of follow up (OR 1.0; 95% CI 0.3-2.8). Controls showed marginally higher psychiatric morbidity measured on the general health questionnaire-12 (adjusted OR 0.6; 95% CI 0.3-1.3) Both groups had similar rates of neurological symptoms and physical impairment. The best predictor of chronic fatigue was a prolonged duration time of off work after the illness (OR 4.93, 95% CI 1.3-18.8). The best predictor of severe chronic fatigue syndrome diagnosed by Center for Disease Control criteria was past psychiatric illness (OR 7.82, 95% CI 1.8-34.3). Duration of viral illness, as defined by days in hospital, did not predict chronic fatigue syndrome. CONCLUSIONS--(1) The prevalence of chronic fatigue syndrome is higher than expected for the range of viral illnesses examined; (2) enteroviral infection is unlikely to be a specific risk factor for its development; (3) onset of chronic fatigue syndrome after a viral infection is predicted by psychiatric morbidity and prolonged convalescence, rather than by the severity of the viral illness itself.
Hyams KC, Wignall FS, Roswell R.	U.S. Naval Medical Research Institute, Rockville, Maryland, USA.	War syndromes and their evaluation: from the U.S. Civil War to the Persian Gulf War.	Ann Intern Med 1996 Sep 1;125(5):398-405	PURPOSE: To better understand the health problems of veterans of the Persian Gulf War by analyzing previous war-related illnesses and identifying possible unifying factors. DATA SOURCE: English-language articles and books on war-related illnesses published since 1863 that were located primarily through a manual search of bibliographies. DATA EXTRACTION: Publications were assessed for information on the clinical characteristics of war-related illnesses and the research methods used to evaluate such illnesses. DATA SYNTHESIS: Poorly understood war syndromes have been associated with armed conflicts at least since the U.S. Civil War. Although these syndromes have been characterized by similar symptoms (fatigue, shortness of breath, headache, sleep disturbance, forgetfulness, and impaired concentration), no single recurring illness that is unrelated to psychological stress is apparent. However, many types of illness were found among evaluated veterans, including well-defined medical and psychiatric conditions, acute combat stress reaction, post-traumatic stress disorder, and possibly the chronic fatigue syndrome. No single disease is apparent, but one unifying factor stands out: A unique population was intensely scrutinized after experiencing an exceptional, life-threatening set of exposures. As a result, research efforts to date have been unable to conclusively show causality, have been subject to reporting bias, and have lacked similar control populations. In addition to research limitations, war syndromes have involved fundamental, unanswered questions about the importance of chronic somatic symptoms and the factors that create a personal sense of ill health.

				CONCLUSION: Until we can better understand what constitutes health and illness in all adult populations, we risk repeated occurrences of unexplained symptoms among veterans after each war.
James LC, Folen RA.	Department of Psychology, Tripler Army Medical Center, Honolulu, USA.	EEG biofeedback as a treatment for chronic fatigue syndrome: a controlled case report.	Behav Med 1996 Summer;22(2):77-81	EEG neurofeedback has been identified as a potential diagnostic and treatment protocol with chronic fatigue syndrome (CFS) symptoms. In the present case study, the authors applied an EEG neurofeedback biofeedback paradigm as a treatment modality with a CFS patient. Baseline data were acquired using the Wechsler Adult Intelligence Scale-Revised and qualitative and subjective ratings of cognitive improvement. Test results and clinical findings revealed improvements in the patient's cognitive abilities, functional skill level, and quality of life. The patient showed significant differences in pre- and posttest levels on the Wechsler scale.
Jason LA, Ferrari JR, Taylor RR, Slavich SP, Stenzel CL.	Department of Psychology, DePaul University, Chicago, IL 60614, USA.	A national assessment of the service, support, and housing preferences by persons with chronic fatigue syndrome. Toward a comprehensive rehabilitation program.	Eval Health Prof 1996 Jun;19(2):194-207	Persons with Chronic Fatigue Syndrome (PWCs) completed and returned by mail a brief survey of open- and closed-ended items designed to assess their utilization and preferences for a variety of services. A total of 984 middle-aged adults diagnosed with Chronic Fatique Syndrome (CFS) from across North America returned the survey. During the past 12 months, many of these PWCs reported utilization of a primary care physician, gynecologist, CFS specialist, and self-help group to assist in their recovery from CFS. Most PWCs believed it was important to educate both health-care practitioners and the general public about CFS. In terms of their desire for specific recovery needs, factor analysis of responses indicated that these PWCs preferred self-help/social support services and general advocacy services in the treatment of their illness. The implications of these results for developing rehabilitation programs for PWCs are discussed.
Johnson SK, DeLuca J, Diamond BJ, Natelson BH.	Chronic Fatigue Syndrome Research Center, Research Department, Kessler Institute for Rehabilitation, West Orange, NJ 07052, USA.	Selective impairment of auditory processing in chronic fatigue syndrome: a comparison with multiple sclerosis and healthy controls.	Percept Mot Skills 1996 Aug;83(1):51-62	The most consistent deficit observed in individuals with Chronic Fatigue Syndrome has been in efficiency of information processing. To examine the possibility of a modality-specific impairment, the present study examined subjects with Chronic Fatigue Syndrome, multiple sclerosis, and healthy controls on an auditory-versus visual-paced serial-addition test. 20 subjects with Chronic Fatigue Syndrome, 20 subjects with clinically definite Multiple Sclerosis, and 20 sedentary healthy controls were compared. One-half of the subjects in each group were administered the Paced Auditory Serial Addition Test and the other half were administered the Paced Visual Serial Addition Test. The group with Chronic Fatigue Syndrome was differentially impaired on the auditory relative to the visual processing task. The group with Multiple Sclerosis was equally impaired on both versions of the task. The results are discussed within the framework of Baddeley's model of working memory.
Johnson SK, DeLuca J, Natelson BH.	Research Department, Kessler Institute for Rehabilitation, West	Assessing somatization disorder in the chronic fatigue syndrome.	Psychosom Med 1996 Jan-Feb;58(1):50-7	This study was conducted to examine the rates of somatization disorder (SD) in the chronic fatigue syndrome (CFS) relative to other fatiguing illness groups. It further addressed the arbitrary nature of the judgments made in assigning

	Orange, N.J. 07052, USA.			psychiatric vs. physical etiology to symptoms in controversial illnesses such as CFS. Patients with CFS (N = 42), multiple sclerosis (MS) (N = 18), and depression (N = 21) were compared with healthy individuals (N = 32) on a structured psychiatric interview. The SD section of the Diagnostic Interview Schedule (DIS) III-R was reanalyzed using different criteria sets to diagnose SD. All subjects received a thorough medical history, physical examination, and DIS interview. CFS patients received diagnostic laboratory testing to rule out other causes of fatigue. This study revealed that changing the attribution of SD symptoms from psychiatric to physical dramatically affected the rates of diagnosing SD in the CFS group. Both the CFS and depressed subjects endorsed a higher percentage of SD symptoms than either the MS or healthy groups, but very few met the strict DSM-III-R criteria for SD. The present study illustrates that the terminology used to interpret the symptoms (ie, psychiatric or physical) will determine which category CFS falls into. The diagnosis of SD is of limited use in populations in which the etiology of the illness has not been established.
Johnson SK, DeLuca J, Natelson BH.	Chronic Fatigue Syndrome Research Center, West Orange, NJ 07052, USA.	Personality dimensions in the chronic fatigue syndrome: a comparison with multiple sclerosis and depression.	J Psychiatr Res 1996 Jan-Feb;30(1):9-20 comment in: J Psychiatr Res. 1996 Jan-Feb;30(1):3-7	This study investigated the relative rates of personality disturbance in chronic fatigue syndrome (CFS). Individuals who met the CDC criteria for CFS were compared to two other fatiguing illness groups, mild multiple sclerosis and depression, as well as sedentary healthy controls. Subjects were administered a structured psychiatric interview to determine Axis I psychiatric disorders and two self-report instruments to assess Axis II personality disorders and the personality trait of neuroticism. The depressed group had significantly more personality disorders and elevated neuroticism scores compared with the other three groups. The CFS and MS subjects had intermediary personality scores which were significantly higher than healthy controls. The CFS group with concurrent depressive disorder (34% of the CFS group) was found to account for most of the personality pathology in the CFS sample. The results are discussed in the context of the relationship between personality variables and fatiguing illness.
Johnson SK, DeLuca J, Natelson BH.	Chronic Fatigue Syndrome Center, University of Medicine and Dentistry of New Jersey--New Jersey Medical School, West Orange, USA.	Depression in fatiguing illness: comparing patients with chronic fatigue syndrome, multiple sclerosis and depression.	J Affect Disord 1996 Jun 20;39(1):21-30	Because depression is commonly observed in the chronic fatigue syndrome (CFS), the present study sought to determine whether the symptom pattern is similar to that seen in clinically depressed subjects (DEP). Individuals with multiple sclerosis (MS) were chosen as an additional comparison group because MS is a fatiguing illness of known organic etiology. The Beck Depression Inventory (BDI) was used to compare categories of depressive symptomatology. Absolute scores on the BDI were higher for the depressed group on mood and self-reproach symptoms, but were not higher than the CFS group on somatic and vegetative items. Analysis of symptoms as a percentage of total BDI score revealed no significant differences in mood or vegetative items among the three groups. The CFS and MS groups exhibited a significantly lower percentage of self-reproach symptoms than DEP, whereas the DEP group showed a lower percentage of somatic symptoms

				than the CFS and MS groups.
Josevic M, Nikolic S, Dulovic O, Jovanovic L, Zerjav S, Radivojevic M.	Dr. Kosta Todorovitsh Institute of Infectious and Tropical Diseases, Belgrade.	[Neural manifestations in Lyme disease (Lyme borreliosis of the nervous system)].[article in Serbo-Croatian (Cyrillic)]	Srp Arh Celok Lek 1996 Mar-Apr;124(3-4):87-92	The involvement of the nervous system is common during Lyme's disease, and the term neuroborreliosis has been established. All structures of the nervous system, from meninges to periferial nerves, can be involved. Neurological manifestations are most common in the second stage (dissemination). The article deals with the most important neurological manifestations, as well as with the contemporary pathogenetic considerations and therapy. Eleven patients with neuroborreliosis who were treated at Dr. Kosta Todorovitsh Institute of Infectious and Tropical Diseases, are reviewed. Five of them had acute meningoencephalitis, of whom two had concurrent neuritis; one patient had Banawart's syndrome with arthralgias, arthritis and fatigue syndrome; two patients had neuritis; one had bilateral facial palsy; two had chronic fatigue syndrome.
Joyce E, Blumenthal S, Wessely S.	Academic Department of Psychiatry, Charing Cross and Westminster Medical School, London, UK.	Memory, attention, and executive function in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1996 May;60(5):495-503	OBJECTIVES--To examine cognitive function in chronic fatigue syndrome. METHODS--Twenty patients with chronic fatigue syndrome recruited from primary care and 20 matched normal controls were given CANTAB computerised tests of visuospatial memory, attention, and executive function, and verbal tests of letter and category fluency and word association learning. RESULTS: Patients with chronic fatigue syndrome were impaired, predominantly in the domain of memory but their pattern of performance was unlike that of patients with amnesic syndrome or dementia. They were normal on tests of spatial pattern recognition memory, simultaneous and delayed matching to sample, and pattern-location association learning. They were impaired on tests of spatial span, spatial working memory, and a selective reminding condition of the pattern-location association learning test. An executive test of planning was normal. In an attentional test, eight subjects with chronic fatigue syndrome were unable to learn a response set; the remainder exhibited no impairment in the executive set shifting phase of the test. Patients with chronic fatigue syndrome were also impaired on verbal tests of unrelated word association learning and letter fluency. CONCLUSION--Patients with chronic fatigue syndrome have reduced attentional capacity resulting in impaired performance on effortful tasks requiring planned or self ordered generation of responses from memory.
Kendell R, Turnberg L, Toby J.		Chronic fatigue syndrome.	Lancet 1996 Nov 16;348(9038):1384 comment on: Lancet. 1996 Oct 12;348(9033):971	
Kitani T, Kuratsune H, Fuke I, Nakamura Y, Nakaya T, Asahi S,	Department of Hematology and Oncology, Osaka	Possible correlation between Borna disease virus infection and	Microbiol Immunol 1996;40(6):459-62	Borna disease virus (BDV) is a neurotropic, as yet unclassified, non-segmented, negative-sense, single-strand RNA virus. Natural infection with this virus has been reported to occur in horses and sheep. In addition, antibodies to BDV in plasma

Tobiume M, Yamaguti K, Machii T, Inagi R, Yamanishi K, Ikuta K.	University Medical School, Japan.	Japanese patients with chronic fatigue syndrome.		or BDV RNA in peripheral blood mononuclear cells (PBMCs) were also found in patients with neuropsychiatric diseases. We describe here the possible link between the patients with chronic fatigue syndrome (CFS) and infection with BDV.
Klonoff DC.		Chronic fatigue syndrome and neurally mediated hypotension.	JAMA 1996 Feb 7;275(5):359-60 comment on: JAMA. 1995 Sep 27;274(12):961-7	
Kodama M, Kodama T, Murakami M.	Kodama Research Institute of Preventive Medicine, Nagoya, Japan.	The value of the dehydroepiandrosterone-annexed vitamin C infusion treatment in the clinical control of chronic fatigue syndrome (CFS). I. A Pilot study of the new vitamin C infusion treatment with a volunteer CFS patient.	In Vivo 1996 Nov-Dec;10(6):575-84	A series of publications from our laboratory have indicated that the practice of megadose vitamin C drip infusion treatment enhanced the activity of endogenous glucocorticoids in such a way as to improve the clinical course of allergy and autoimmune disease-a disease entity that is known to respond to the therapeutic effect of glucocorticoids. The present paper represents an extention of our vitamin C studies, and intends to investigate the problem whether or not chronic fatigue syndrome (CFS), an acquired immunodeficiency disease, can also be counted as one of the candidate diseases for the vitamin C infusion treatment. We prepared two kinds of vitamin C infusion sets for the clinical use: the dehydroepiandrosterone-annexed vitamin C infusion set (the new set) and the annex-free vitamin C infusion set (the old set). The new set was expected to enhance the endogenous activities of both glucocorticoids and gonadal steroids. We followed the clinical course of a male CFS patient using the old and new vitamin C infusion sets, and with and without the oral intake of erythromycin and chloramphenico. Results obtained are as follows: a) the observation period of a study subject covered a period of August 1995 to May 1996. Combination of pneumonia signs and dermatomyositis signs marked the onset of his CFS. b) Old infusion treatment together with the short term antibiotics treatment was found effective for the control of pneumonia in the first stage of the disease (from August to October, 1995). c) Signs of pneumonia recurrence gradually became eminent in the second stage of disease (from November, 1995, to January, 1996) in spite of the moderate frequency of the old treatment together with stepwise prolongation of the antibiotics treatment. d) The alternate practice of the old and new infusion treatments together with the long-term antibiotics treatment, as conducted in the 3rd stage of disease (from February to May, 1996) led to substantial extinction of pneumonia signs (leucocytosis, tachycardia etc). e) The practice of the new infusion treatment markedly increased the excretion of both 17-ketosteroids and 17-hydroxycorticosteroids in the urine. Evidence was also available to indicate that the dehydroepiandrosterone annex was converted to testosterone, which in turn made a contribution to the control of CFS. f) The immunological survey of lymphocyte subsets including NK cell percent failed to

				find a coherent change in a study subject with CFS. In conclusion, the above results could be taken as evidence to indicate that the new vitamin C infusion treatment effectuates the clinical control of CFS by fortifying the endogenous activities of both cortisol and testosterone. The significance of parallelism between pulmonary infection and CFS, as observed in the clinical course of the test subject, was discussed in the light of the focal infection theory of nephritis.
Kodama M, Kodama T, Murakami M.	Kodama Research Institute of Preventive Medicine, Nagoya, Japan.	The value of the dehydroepiandrosterone-annexed vitamin C infusion treatment in the clinical control of chronic fatigue syndrome (CFS). II. Characterization of CFS patients with special reference to their response to a new vitamin C infusion treatment.	In Vivo 1996 Nov-Dec;10(6):585-96	This study is a counterpart of the pilot study on the clinical management of chronic fatigue syndrome (CFS) by the combined use of the old (annex-free) and the new (dehydro-epiandrosterone- annexed) vitamin C infusion treatments with and without oral intake of erythromycin and chloramphenicol. We were motivated to start this clinical study by 2 reasons: i) we have made a success in the clinical management of autoimmune disease and allergy by use of the old megadose vitamin C infusion treatment, and we therefore took up CFS as a good candidate for vitamin C infusion treatment; ii) In 1995, we received a total of 313 chronic pneumonia patients whose clinical course showed a good fitness to the criteria of CFS. We assessed the nature of the disease by investigating the clinicoepidemiological aspect of our patients on the one hand and the response of the disease to both the old and new vitamin C infusion treatments with and without the use of 2 antibiotics on the other hand. Results are summarized as follows: a) the analysis of the medical records of our outpatients revealed that chronic type pneumonia epidemic in Nagoya Japan, with its onset of January 1995, showed no sign of its extinction by the end of May 1996. The patient population contained no patients under 15 years of age, and showed a distinct female predominance in the patient number (207 females versus 106 males). In 1995, we also experienced a simple cold epidemic with its onset of January 1995 (162 males and 224 females). The majority of simple cold patients were under 25 years of age in both sexes. b) A chronic type pneumonia patient was distinguished from a simple cold patient in 2 respects: firstly the former required prolonged medical care (over 1 month) resulting in an incomplete cure and return to medical care upon the recurrence of disease, whereas the latter required short-term medical care (mostly within 1 week) ending up with complete cure. Secondly, the former required the long term use of 2 antibiotics (erythromycin and chloramphenicol) together with regular practice of the old and new vitamin C infusion treatments for disease control, whereas the latter recovered from the disease after the short time use of a set of conventional cold remedies. c) The clinical manifestations of our chronic pneumonia patients showed good fitness to the criteria of CFS. d) CFS was distinguished from autoimmune disease-allergy complex by the method of clinical control: the former required the long-term use of 2 antibiotics together with regular practice of the old and new vitamin C infusion treatments, whereas the latter was

				controllable by the single use of the old vitamin C infusion treatment. e) The combined use of the old and new vitamin C infusion treatments rather than the single use of the old vitamin C infusion treatment was more effective for the control of CFS-a finding which suggests that deficient activities of both endogenous glucocorticoid and endogenous androgen in a CFS patient are somehow related to the genesis and further development of CFS. f) Evidence was available to indicate that the sole use of the new vitamin C infusion treatment may induce a state of gonadal steroid excess together with various other problems in the recipient. The maintenance of a good balance between the old vitamin C infusion set (glucocorticoid-inducer) and the new vitamin C infusion set (inducer of both glucocorticoid and gonadal steroids) in their use was of prime importance for the successful control of CFS. g) The historical significance of CFS epidemic in 1995, and in Nagoya-Japan, is discussed in the light of the new infection concept.
Komaroff AL, Fagioli LR, Doolittle TH, Gandek B, Gleit MA, Guerriero RT, Kornish RJ 2nd, Ware NC, Ware JE Jr, Bates DW.	Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115, USA.	Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups.	Am J Med 1996 Sep;101(3):281-90	PURPOSE: To measure the functional status and well-being of patients with chronic fatigue syndrome (CFS), and compare them with those of a general population group and six disease comparison groups. PATIENTS AND METHODS: The subjects of the study were patients with CFS (n = 223) from a CFS clinic, a population-based control sample (n = 2,474), and disease comparison groups with hypertension (n = 2,089), congestive heart failure (n = 216), type II diabetes mellitus (n = 163), acute myocardial infarction (n = 107), multiple sclerosis (n = 25), and depression (n = 502). We measured functional status and well-being using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), which is a self-administered questionnaire in which lower scores are indicative of greater impairment. RESULTS: Patients with CFS had far lower mean scores than the general population control subjects on all eight SF-36 scales. They also scored significantly lower than patients in all the disease comparison groups other than depression on virtually all the scales. When compared with patients with depression, they scored significantly lower on all the scales except for scales measuring mental health and role disability due to emotional problems, on which they scored significantly higher. The two SF-36 scales reflecting mental health were not correlated with any of the symptoms of CFS except for irritability and depression. CONCLUSION: Patients with CFS had marked impairment, in comparison with the general population and disease comparison groups. Moreover, the degree and pattern of impairment was different from that seen in patients with depression.
Komaroff AL, Fagioli LR, Geiger AM, Doolittle TH, Lee J, Kornish RJ, Gleit MA, Guerriero RT.	Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts	An examination of the working case definition of chronic fatigue syndrome.	Am J Med 1996 Jan;100(1):56-64	PURPOSE: Chronic fatigue syndrome (CFS) currently is defined by a working case definition developed under the leadership of the United States Centers for Disease Control and Prevention (CDC) based on a consensus among experienced clinicians. We analyzed the experience from one large center to examine the

	02115, USA.			adequacy of the case definition. PATIENTS AND METHODS: Predefined clinical and laboratory data were collected prospectively from 369 patients with debilitating fatigue, of whom 281 (76%) met the major criteria of the original CDC case definition for CFS: (1) fatigue of at least 6 months' duration, seriously interfering with the patient's life; and (2) without evidence of various organic or psychiatric illnesses that can produce chronic fatigue. The same clinical data were obtained from 311 healthy control subjects and two comparison groups with diseases that can present in a similar fashion; relapsing-remitting multiple sclerosis (n = 25) and major depression (n = 19). RESULTS: All of the minor criteria symptoms from the original CDC case definition distinguished patients with debilitating chronic fatigue from healthy control subjects, and many distinguished the patients with chronic fatigue from the comparison groups with multiple sclerosis and depression: myalgias, postexertional malaise, headaches, and a group of infectious-type symptoms (ie, chronic fever and chills, sore throat, swollen glands in the neck or underarm areas). In addition, two other symptoms not currently part of the case definition discriminated the chronic fatigue patients from the control/comparison groups: anorexia and nausea. Physical examination criteria only infrequently contributed to the diagnosis. Patients meeting the CDC major criteria for CFS also met the minor criteria in 91% of cases. CONCLUSION: Patients meeting the major criteria of the current CDC working case definition of CFS reported symptoms that were clearly distinguishable from the experience of healthy control subjects and from disease comparison groups with multiple sclerosis and depression. Eliminating three symptoms (ie, muscle weakness, arthralgias, and sleep disturbance) and adding two others (ie, anorexia and nausea) would appear to strengthen the CDC case definition of CFS.
Konstantinov K, von Mikecz A, Buchwald D, Jones J, Gerace L, Tan EM.	Autoimmune Disease Center and Department of Cell Biology, The Scripps Research Institute, La Jolla, California 92037, USA.	Autoantibodies to nuclear envelope antigens in chronic fatigue syndrome.	J Clin Invest 1996 Oct 15;98(8):1888-96	We have identified and partially characterized the autoantibodies in sera of 60 patients with chronic fatigue syndrome. Approximately 52% of the sera were found to react with nuclear envelope antigens. The combination of nuclear rim staining observed in immunofluorescence microscopy and immunoblot analysis of highly purified nuclear envelope proteins provided initial characterization of these autoantibodies. Further characterization showed that some sera immunoprecipitated the in vitro transcription and translation product of a human cDNA clone encoding the nuclear envelope protein lamin B1. The autoantibodies were of the IgG isotype. The occurrence of autoantibodies to a conserved intracellular protein like lamin B1 provides new laboratory evidence for an autoimmune component in chronic fatigue syndrome.
Krupp LB, Pollina D.	Department of Neurology, SUNY at Stony Brook 11794-	Neuroimmune and neuropsychiatric aspects of chronic	Adv Neuroimmunol 1996;6(2):155-67	

	8121, USA.	fatigue syndrome.		
Lawrie SM.		Cognitive behaviour therapy for the chronic fatigue syndrome. Essential elements of the treatment must be identified.	BMJ 1996 Apr 27;312(7038):1097; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
Leese G, Chattington P, Fraser W, Vora J, Edwards R, Williams G.	Department of Medicine, University of Liverpool, United Kingdom.	Short-term night-shift working mimics the pituitary-adrenocortical dysfunction in chronic fatigue syndrome.	J Clin Endocrinol Metab 1996 May;81(5):1867-70	The purpose of this study was to determine whether a short period (5 days) of night-shift work affected the pituitary-adrenal responses to CRH. Ten nurses (8 female and 2 male; age 28.1 +/- 1.7 yr: mean +/- SEM) working at the Royal Liverpool University Hospital, and who regularly undertook periods of night and day shift work were enrolled. Measurements were made of basal ACTH and cortisol concentrations, and their responses to iv ovine CRH (1 microgram.kg-1). Basal ACTH concentrations were higher during the night shift than during the day shift (12.9 +/- 5.1 pmol.L-1 vs. 4.7 +/- 1.2 pmol.L-1, P < 0.01) whereas cortisol concentrations were lower (551 +/- 48 nmol.L - 1 vs. 871 +/- 132 nmol.L - 1, P < 0.01). After CRH injection, ACTH concentrations remained consistently higher during the night shift, but the integrated increase in ACTH concentration was lower (P < 0.05) than during the day shift. Conversely, the increase in cortisol concentration was greater during the night shift than the day shift (283 +/- 53 nmol.L-1 vs. 134 +/- 41 nmol.L-1, P < 0.05). We conclude that the pituitary-adrenal responses to CRH are markedly disrupted after only 5 days of nighttime work. These abnormalities mimic those previously observed in patients with chronic fatigue syndrome. Neuroendocrine abnormalities reported to be characteristic of chronic fatigue syndrome may be merely the consequence of disrupted sleep and social routine.
Lemke MR.	Psychiatrische Klinik, Klinikum Ingolstadt.	[Chronic fatigue syndrome--psychiatric aspects].[article in German]	Fortschr Neurol Psychiatr 1996 Apr;64(4):132-41	Diagnosis of the chronic fatigue syndrome depends on various somatic and psychopathological symptoms. Somatic symptoms of the syndrome have been subject of an extensive body of literature. In comparison, psychiatric aspects have caught relatively less attention. Psychiatric aspects of etiological, diagnostic, and therapeutic concepts are essential for evaluation of the syndrome. Application of CDC-criteria to a well known disease does not solve the nosological problem, but may define the syndrome more accurately. In this respect, issues including psychiatric comorbidity and specificity of neuropathological symptoms are discussed. Psychological variables seem to have a high predictor value for time course and outcome of the symptoms. Etiological concepts emphasize on biological or psychosocial factors. Alterations of biological parameters including immune functions, sleep regulation, and hypothalamic-pituary-adrenocortical function have been reported. The role of cultural factors has been discussed extensively. Somatic and psychological stress may result in the same clinical

				syndrome via psychoimmunological mechanisms. An integrated, interdisciplinary approach to further refine diagnostic criteria, understanding of etiology and development of adequate therapeutic measures seems necessary.
Levine PH		The Elusive Gulf War Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 55 - 63	In 1990/1991, approximately 697,000 U.S. service members joined coalition forces in the Middle East for Operations Desert Shield and Desert Storm (ODS/S). Following the military action, a number of service men and women reported a variety of signs and symptoms which they attributed to their participation in the operation; the term Gulf War Syndrome was proposed to facilitate evaluation of what was perceived as a possible new entity. Subsequent studies failed to identify a discrete syndrome, and a series of reports have raised questions as to whether or not Gulf War Syndrome exists or if indeed any of the reported disorders can be attributed to participation in ODS/S. This report reviews the history of U.S. participation in the Gulf War, the medical threats and exposures considered by the U.S. Armed Services, and the U.S. Government's approach to investigating the complaints of the returning servicemen. In the context of the reports from non-U.S. veterans with similar complaints, the elusive Gulf War Syndrome is an important unresolved issue that could provide a model for a number of disorders, including chronic fatigue syndrome.
Levine PH, Dale JK, Benson-Grigg E, Fritz S, Grufferman S, Straus SE.	Division of Cancer Etiology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892-1888, USA.	A cluster of cases of chronic fatigue and chronic fatigue syndrome: clinical and immunologic studies.	Clin Infect Dis 1996 Aug;23(2):408-9	
Levine PH.	Viral Epidemiology Branch, National Cancer Institute, Bethesda, MD, USA.	The use of transfer factors in chronic fatigue syndrome: prospects and problems.	Biotherapy 1996;9(1-3):77-9	Chronic fatigue syndrome (CFS) is a heterogeneous disorder characterized by severe prolonged unexplained fatigue and a variety of associated symptoms such as arthralgias, myalgias, cognitive dysfunction, and severe sleep disturbances. Many patients initially present with an acute onset of apparent infectious origin with either an upper respiratory or gastrointestinal illness, fever, chills, tender lymphadenopathy, and malaise suggestive of a flu-like illness. In some cases, specific viral infections can be identified at the outset, particularly herpes viruses such as Epstein-Barr virus (EBV), human herpes virus-6 (HHV-6), and cytomegalovirus (CMV). Transfer factors (TF) with specific activity against these herpes viruses has been documented. With some studies suggesting that persistent viral activity may play a role in perpetuation of CFS symptoms, there appears to be a rationale for the use of TF in patients with CFS and recent reports have suggested that transfer factor may play a beneficial role in this disorder. This report focuses on the heterogeneity of CFS, the necessity for randomized coded studies, the importance of patient selection and sub-classification in

				clinical trials, and the need to utilize specific end-points for determining efficacy of treatment.
Lieb K, Dammann G, Berger M, Bauer J.	Universitatsklinik fur Psychiatrie und Psychosomatik, Universitat, Freiburg.	[Chronic fatigue syndrome. Definition, diagnostic measures and therapeutic possibilities].[article in German]	Nervenarzt 1996 Sep;67(9):711-20 comment in: Nervenarzt. 1997 Nov;69(11):924-5	This article reviews the chronic fatigue syndrome (CFS), a disorder whose etiology is unknown. The diagnostic criteria proposed in 1994 by the CDC and the International Chronic Fatigue Syndrome Study Group are introduced. In contrast to widespread belief, there are no laboratory tests available to underpin the diagnosis of CFS; the diagnosis is made solely on the basis of clinical criteria. In the differential diagnosis, the exclusion of other conditions that can cause chronic fatigue, such as neuropsychiatric or sleep disorders, is of critical importance. In this context, the question as to whether CFS is a clinical entity that can be differentiated from psychiatric diagnoses, such as depression, somatoform disorder, or neurasthenia, is discussed. At the moment, there is no specific therapy for CFS. Therefore, therapeutic approaches are limited to symptomatic management of the concomitant sleep disturbances, pain, or psychiatric symptoms, such as depression. Patients may benefit from cognitive behavioral therapy, as this may help then to identify and exclude factors contributing to and maintaining chronic fatigue. An integrated medical and psychological approach should be adopted, with the aim of preventing significant secondary negative results of the illness, such as interpersonal conflicts or chronic disability.
Lindal E, Bergmann S, Thorlacius S, Stefansson JG.	Department of Psychiatry, National University Hospital, Reykjavik, Iceland. elindal@rsp.is	The localization of pain in chronic fatigue syndrome on a pain drawing according to grid areas.	Percept Mot Skills 1996 Oct;83(2):508-10	
Lindh G, Samuelson A, Hedlund KO, Evengard B, Lindquist L, Ehrnst A.	Division of Infectious Diseases, Huddinge University Hospital, Karolinska Institutet, Stockholm, Sweden.	No findings of enteroviruses in Swedish patients with chronic fatigue syndrome.	Scand J Infect Dis 1996;28(3):305-7	Enteroviruses have been proposed to cause an immune complex disease in the chronic fatigue syndrome. Altogether 34 patients with the chronic fatigue syndrome, according to criteria of the Centers for Disease Control, USA, were studied evenly over the seasons for the possible presence of a chronic enterovirus infection. In 11 patients, 1-5 faecal samples were collected at about 6 month intervals for virus isolation before and after acid treatment, followed by ultracetrifugation at pH 3 to dissolve possible enterovirus-antibody complexes. Another 14 fecal samples were subjected to routine virus isolation alone. Seven pairs of serum-cerebrospinal fluid samples were analysed for cross-reactive IgG antibody activity to enteroviruses. In 29 patients a muscle biopsy was collected for enterovirus polymerase chain reaction (PCR). We were unable to identify enteroviruses in any of these samples by any of these techniques. Our study does not confirm evidence for persistent enterovirus infection in the chronic fatigue syndrome.
Lohmann K, Prohl A,	Schleswig, Christian-	[Multiple chemical	Gesundheitswesen 1996	The data of 466 subjects suffering from neurologic disorders which are suggested

Schwarz E.	Albrechts-Universitat, Kiel.	sensitivity disorder in patients with neurotoxic illnesses].[article in German]	Jun;58(6):322-31 comment in: Gesundheitswesen. 1997 Jan;59(1):56	to be caused by neurotoxic agents in their environment retrospectively was evaluated and documented. Among these cases there were 151 subjects with symptoms of Multiple Chemical Sensitivity Disorder (MCSD). The relationship between the neurological health impairments and neurotoxic agents in the environment of these patients was characterised using five different categories (probable = A, possible = B, uncertain = C, unclarified = D, not probable = E). From the 466 patients 320 subjects (69%) could be assigned to the categories A and B, respectively. Within theses 320 cases with chronic neurotoxic health impairments 136 subjects (79 females and 57 males) showed signs of MCSD. Age and gender of cases as well as duration and character of exposure to neurotoxic substances retrospectively were assessed from the explicit files of the patients, which had been made anonymous for this purpose. Frequency of characteristic symptoms of neurotoxicity were analysed. Results are given for patients with neurotoxic health impairments with MCSD (n = 136) and without MCSD (n = 184). Neurotoxic substances which were used as indoor wood preservatives (mainly Pentachlorophenol and/or Lindane) were found to be the causative agents in 63% of the cases with neurotoxic health impairments and MCSD. Other important neurotoxic substances to which the patients were mainly exposed were organic solvents (25%), formaldehyde (15%), dental materials (15%), pyrethroides (13%), and other biocides (19%) (multiple exposures were possible). The time of exposure was calculated as being > or = 10 years for 55% of the patients with MCSD and for 50% of the group with neurotoxic health impairments but without MCSD. Out of the 184 cases with neurotoxic health impairments but without MCSD there were 22%, and out of the 136 cases with MCSD there were 39% who showed all symptoms of chronic fatigue syndrome. 53% of the cases with MCSD had an allergic disposition compared to only 20% of the cases without MCSD. This work is not a controlled epidemiological study but a retrospective documentation and evaluation of data related to environmental medicine. With the present documentation in this purely descriptive manner the proof of a causal relationship was not possible or intended. But because corresponding epidemiological studies are lacking, this documentation can give important information on characteristic features of Multiple Chemical Sensitivity Disorder and chronic neurotoxic health impairments. Such information is essential for planning and carrying out epidemiological studies urgently needed in this field.
Lynch S, Seth R.		Fluoxetine and chronic fatigue syndrome.	Lancet 1996 Jun 22;347(9017):1771; discussion 1171-2	
MacDonald KL, Osterholm MT, LeDell	Minnesota Department of Health, Minneapolis,	A case-control study to assess possible triggers	Am J Med 1996 May;100(5):548-54	PURPOSE: To assess possible triggers and cofactors for chronic fatigue syndrome (CFS) and to compare levels of selected cytokines between cases and an

KH, White KE, Schenck CH, Chao CC, Persing DH, Johnson RC, Barker JM, Peterson PK.	55440-9441, USA.	and cofactors in chronic fatigue syndrome.	Comment in: Am J Med. 1997 Apr;102(4):422-3	appropriately matched control group. PATIENTS AND METHODS: We conducted a case-control study of 47 cases of CFS obtained through a regional CFS research program maintained at a tertiary care medical center. One age-, gender-, and neighborhood-matched control was identified for each case through systematic community telephone sampling. Standardized questionnaires were administered to cases and controls. Sera were assayed for transforming growth factor-beta (TGF-beta), interleukin-1 beta, interleukin-6, tumor necrosis factor-alpha, and antibody to Borrelia burgdorferi and Babesia microti. RESULTS: Cases were more likely to have exercised regularly before illness onset than controls (67% versus 40%; matched odds ratio (MOR) = 3.4; 95% CI = 1.2 to 11.8; P = 0.02). Female cases were more likely to be nulliparous prior to onset of CFS than controls (51% versus 31%; MOR = 8.0; 95% CI = 1.03 to 170; P = 0.05). History of other major factors, including silicone-gel breast implants (one female case and one female control), pre-morbid history of depression (15% of cases, 11% of controls) and history of allergies (66% of cases, 51% of controls) were similar for cases and controls. However, cases were more likely to have a diagnosis of depression subsequent to their diagnosis of CFS compared to a similar time frame for controls (MOR = undefined; 95% CI lower bound = 2.5; P < 0.001). Positive antibody titers to B burgdorferi (one case and one control) and B microti (zero cases and two controls) were also similar. CONCLUSIONS: Further investigation into the role of prior routine exercise as a cofactor for CFS is warranted. This study supports the concurrence of CFS and depression, although pre-morbid history of depression was similar for both groups.
MacFarlane JG, Shahal B, Mously C, Moldofsky H.	University of Toronto, Centre for Sleep and Chronobiology, Toronto Hospital (Western Division), Ontario, Canada.	Periodic K-alpha sleep EEG activity and periodic limb movements during sleep: comparisons of clinical features and sleep parameters.	Sleep 1996 Apr;19(3):200-4	The K-alpha sleep electroencephalographic (EEG) phenomenon is characterized by periodic (approximately 20-40 seconds) K-complexes, immediately followed by alpha-EEG activity (7.5-11 Hz) of 0.5- to 5.0-second duration. A group of 14 subjects with the periodic K-alpha anomaly was found to have a similar distribution pattern of interevent intervals as compared with previously published data for sleep-related periodic limb movements during sleep (PLMS). Sleep parameters and somatic symptoms of 30 patients with K-alpha were compared with 30 patients with PLMS. The periodic K-alpha group was predominantly female, younger, exhibiting more slow-wave sleep, gastrointestinal symptoms and muscular complaints and fewer movement arousals on overnight polysomnography. The K-alpha group presented uniformly with complaints of unrefreshing sleep, often associated with fibromyalgia and chronic fatigue syndrome. The PLMS group was predominantly male, showed greater sleep disruption and presented with a variety of sleep-related symptoms.
Manu P, Affleck G, Tennen H, Morse PA, Escobar JI.	Department of Psychiatry, Long Island Jewish Medical Center,	Hypochondriasis influences quality-of-life outcomes in patients	Psychother Psychosom 1996 Mar-Apr;65(2):76-81	BACKGROUND: To determine how hypochondriacal symptoms influence the quality-of-life outcomes of patients with a chief complaint of chronic fatigue. METHODS: Cross-sectional cohort study of a consecutive sample of 71 patients

	New Hyde Park, N.Y., USA.	with chronic fatigue.		(mean duration of fatigue of 4.1 years). Forty-eight (68%) patients met criteria for current major depression and 32 (45%) met criteria for chronic fatigue syndrome (CFS). All patients received a comprehensive medical and psychiatric evaluation. Quality-of-life and physical, depressive and hypochondriacal symptom scores were assessed through reliable self-report questionnaires and a structured interview. A path model expressing the relation between predictor variables (hypochondriasis and depression), intervening variables (physical symptoms) and quality of life was postulated and evaluated using structural equation methods. RESULTS: The paths linking hypochondriasis with physical symptoms and mental health and the path connecting physical symptoms and quality of life were each statistically significant. The model applied especially well to patients who fulfilled CFS criteria. CONCLUSIONS: The quality of life of chronic fatigue patients correlates with the severity of their physical symptoms and their hypochondriacal disposition toward illness.
Marcel B, Komaroff AL, Fagioli LR, Kornish RJ 2nd, Albert MS.	Department of Psychiatry, Massachusetts General Hospital, Charlestown, MA 02129, USA.	Cognitive deficits in patients with chronic fatigue syndrome.	Biol Psychiatry 1996 Sep 15;40(6):535-41	Twenty-nine subjects with chronic fatigue syndrome (CFS) and 25 healthy control subjects were administered a lengthy neuropsychological battery that included standard neuropsychological tests and a computerized set of tasks that spanned the same areas of ability. The primary significant differences between patients and controls were found on tests of learning and memory. These differences remained when the degree of psychiatric symptomatology in the subjects was covaried. Patients on and off psychoactive medications did not differ in their performance on these tasks. These results suggest that at least a subset of CFS patients may experience significant impairments in learning and memory.
Marsh S, Kaplan M, Asano Y, Hoekzema D, Komaroff AL, Whitman JE Jr, Ablashi DV.	Advanced Biotechnologies Inc, Columbia, MD 21046, USA.	Development and application of HHV-6 antigen capture assay for the detection of HHV-6 infections.	J Virol Methods 1996 Sep;61(1-2):103-12	An HHV-6 antigen capture assay measuring gp116/64/54 antigen was developed. This ELISA is specific for HHV-6 Variants A and B, does not cross react with other human herpesviruses, is sensitive, stable, quantitative, and can detect antigen in body fluids and cell cultures. Relative to virus isolation or techniques for measuring HHV-6 nucleic acids, the assay is much simpler and less expensive to perform. Plasmas/sera (413) obtained from healthy donors, children with Exanthem subitum, febrile illnesses, patients with Chronic Fatigue Syndrome, and AIDS patients tested by antigen capture assay demonstrated that the assay is useful in clinical laboratory settings. The capture assay can also be used to monitor cell cultures for virus isolation, production, quantitation, and antiviral agent screening.
Marshall PS, Watson D, Steinberg P, Cornblatt B, Peterson PK, Callies A, Schenck CH.	Department of Psychiatry, Hennepin County Medical Center, Minneapolis, MN 55415, USA.	An assessment of cognitive function and mood in chronic fatigue syndrome.	Biol Psychiatry 1996 Feb 1;39(3):199-206	Data were gathered regarding the associates of chronic fatigue syndrome (CFS) with: (1) speed of cognitive processing, (2) motor speed, (3) ability to sustain attention, and (4) mood. Patients were given a brief neuropsychological test battery before and after double-blind treatment with terfenadine or placebo and completed a daily mood rating scale (Positive and Negative Affect Schedule) during the study. CFS patients exhibited slower cognitive processing and motor

				speed and lower positive affect, as compared to data reported from previous studies of healthy subjects and other patient groups; however, CFS patients did not exhibit deficits in sustained attention in comparison to other groups. The CFS patients' ability to attend to verbal versus figural stimuli and mood ratings were different from those reported in studies of patients with depression. Because of methodological limitations, these findings are preliminary, but they encourage further assessment of cognitive dysfunction and mood in CFS.
Martin WJ.	Center for Complex Infectious Diseases, Rosemead, Calif 91770, USA.	Severe stealth virus encephalopathy following chronic-fatigue-syndrome-like illness: clinical and histopathological features.	Pathobiology 1996;64(1):1-8	The clinical histories and brain biopsy findings of 3 patients with severe stealth virus encephalopathy are reviewed. The patients initially developed symptoms consistent with a chronic fatigue syndrome. One patient has remained in a vegetative state for several years, while the other 2 patients have shown significant, although incomplete, recovery. Histological and electron-microscopic studies revealed vacuolated cells with distorted nuclei and various cytoplasmic inclusions suggestive of incomplete viral expression. There was no significant inflammatory response. Viral cultures provided further evidence of stealth viral infections occurring in these patients.
Martin WJ.	Center for Complex Infectious Diseases, Rosemead, Calif 91770, USA.	Genetic instability and fragmentation of a stealth viral genome.	Pathobiology 1996;64(1):9-17	Partial sequencing was performed on cloned DNA obtained from cultures of a stealth virus isolated from a patient with the chronic fatigue syndrome. The results extend earlier findings showing regions of homology to cytomegalovirus (CMV). Although the virus is much more closely related to simian CMV than to human CMV, many of the cloned viral segments could be aligned with the human CMV genome. The aggregate size of the aligned segments exceeds 100 kilobase pairs (kbp). Undigested viral DNA has a mobility in agarose gel electrophoresis corresponding to approximately 20 kbp. The virus, therefore, apparently exists in multiple fragments. Considerable sequence variation exists between individual clones which overlap to similar regions of the human CMV genome. The fragmented genome and sequence microheterogeneity suggest that both the processivity and the fidelity of replication of the viral genome are defective. An unstable viral genome may provide a potential mechanism of recovery from stealth viral illness.
Martin WJ.	Center for Complex Infectious Diseases, Rosemead, CA 91770, USA.	Simian cytomegalovirus-related stealth virus isolated from the cerebrospinal fluid of a patient with bipolar psychosis and acute encephalopathy.	Pathobiology 1996;64(2):64-6	A cytopathic 'stealth' virus was cultured from the cerebrospinal fluid of a patient with a bipolar psychotic disorder who developed a severe encephalopathy leading to a vegetative state. DNA sequencing of a polymerase chain reaction-amplified product from infected cultures has identified the virus as an African green monkey simian cytomegalovirus (SCMV)-related stealth virus. The virus is similar to the SCMV-related stealth virus isolated from a patient with chronic fatigue syndrome. The findings support the concepts that stealth viruses can account for a spectrum of dysfunctional brain diseases and that some of these viruses may have arisen from live polio viral vaccines.
Mayou R.		Chronic fatigue	Lancet 1996 Nov	

		syndrome.	16;348(9038):1384-5 comment in: Lancet. 1997 Jan 4;349(9044):57-8 comment on: Lancet. 1996 Oct 12;348(9033):971	
McArdle A, McArdle F, Jackson MJ, Page SF, Fahal I, Edwards RH.	Department of Medicine, University of Liverpool, U.K.	Investigation by polymerase chain reaction of enteroviral infection in patients with chronic fatigue syndrome.	Clin Sci (Colch) 1996 Apr;90(4):295-300	1. Chronic fatigue syndrome is characterized by muscle fatigue and pain at rest, symptoms which are usually exacerbated with exercise. Although various studies have shown minor, non-specific morphological and biochemical changes in muscle of patients with chronic fatigue syndrome, no consistent defect has been identified. Some have suggested that an enteroviral infection in muscle may cause the chronic muscle fatigue seen in patients with chronic fatigue syndrome, with acute infection directly and irreversibly impairing mitochondrial function, and persistent infection depressing muscle protein synthesis and metabolism. 2. To clarify the involvement of enterovirus infection in chronic fatigue syndrome, muscle biopsies from a group of patients with chronic fatigue syndrome were examined for the presence of enteroviral RNA by reverse transcriptase-polymerase chain reaction techniques in relation to functional studies of muscle mitochondria and the muscle RNA/DNA ratio. 3. Fifty-eight percent of patients reported an uncharacterized 'viral infection' before the onset of their illness, but none of the muscle samples from 34 patients contained detectable amounts of enteroviral RNA. Muscle tissue had a general reduction in the RNA/DNA ratio and mitochondrial enzyme activities with no specific abnormality in the activity of enzymes encoded partially on the mitochondrial genome (cytochrome-c oxidase) or nuclear genome (citrate synthase, succinate reductase). 4. These data provide no evidence of an enteroviral infection in muscle of patients with chronic fatigue syndrome, although this does not exclude a role of enterovirus in initiating the disease process. The general reduction in RNA/DNA ratio and mitochondrial enzyme activities is consistent with a general reduction in habitual activity.
McCully KK, Natelson BH, Iotti S, Sisto S, Leigh JS Jr.	Department of Medicine, Medical College of Pennsylvania, Philadelphia 19131, USA.	Reduced oxidative muscle metabolism in chronic fatigue syndrome.	Muscle Nerve 1996 May;19(5):621-5 comment in: Muscle Nerve. 1997 Jun;20(6):765-6	The purpose of this study was to determine if chronic fatigue syndrome (CSF) is characterized by abnormalities in oxidative muscle metabolism. Patients with CFS according to Centers for Disease Control (CDC) criteria (n = 22) were compared to normal sedentary subjects (n = 15). CFS patients were also tested before and 2 days after a maximal treadmill test. Muscle oxidative capacity was measured as the maximal rate of postexercise phosphocreatine (PCr) resynthesis using the ADP model (Vmax) in the calf muscles using 31P magnetic resonance spectroscopy. Vmax was significantly reduced in CFS patients (39.6 +/- 2.8 mmol/L/min, mean +/- SE) compared to controls (53.8 +/- 2.8 mmol/L/min). Two days postexercise there was no change in resting inorganic phosphate (Pi)/PCr or

				Vmax in the CFS patients (n = 14). In conclusion, oxidative metabolism is reduced in CFS patients compared to sedentary controls. In addition, a single bout of strenuous exercise did not cause a further reduction in oxidative metabolism, or alter resting Pi/PCr ratios.
McCully KK, Sisto SA, Natelson BH.	Department of Medicine, Medical College of Pennsylvania, USA.	Use of exercise for treatment of chronic fatigue syndrome.	Sports Med 1996 Jan;21(1):35-48	Chronic fatigue syndrome (CFS) is a condition that results in moderate to severe disability, the primary feature of which is fatigue of unknown origin. There is a lot of interest in classifying, characterising and treating patients with CFS. Currently, the two major theories of a medical cause of CFS are viral infection and immune dysregulation. Patients report critical reductions in levels of physical activity, and many experience 'relapses' of severe symptoms following even moderate levels of exertion. Despite this, most studies report CFS patients to have normal muscle strength and either normal or slightly reduced muscle endurance. Histological and metabolic studies report mixed results: CFS patients have either no impairment or mild impairment of mitochondria and oxidative metabolism compared with sedentary controls. Current treatments for CFS are symptom-based, with psychological, pharmacological and rehabilitation treatments providing some relief but no cure. Immunological and nutritional treatments have been tried but have not provided reproducible benefits. Exercise training programmes are thought to be beneficial (if 'relapses' can be avoided), although few controlled studies have been performed. CFS is a long-lasting disorder that can slowly improve with time, but often does not. Further studies are needed to better understand the multiple factors that can cause chronic fatigue illness, as well as the effect that exercise training has on the symptoms of CFS.
McGregor NR, Dunstan RH, Zerbes M, Butt HL, Roberts TK, Klineberg IJ.	Collaborative Pain Research Unit, University of Sydney, Westmead Hospital, NSW, Australia.	Preliminary determination of a molecular basis of chronic fatigue syndrome.	Biochem Mol Med 1996 Apr;57(2):73-80	Chronic fatigue syndrome (CFS/ME) is a debilitating fatigue illness that has an unknown etiology. We studied 20 chronic fatigue syndrome (CFS) patients, who complied with the Oxford and American CDC definitions, and 45 non-CFS subjects. Participants completed questionnaires, were clinically examined, and had first morning urine specimens collected, which were screened by gas chromatography-mass spectrometry for changes in metabolite excretion. Multivariate analysis of the urinary metabolite profiles differed significantly in the CFS patients compared to the non-CFS patients ($P < 0.004$). The CFS patients had increases in aminohydroxy-N-methylpyrrolidine ($P < 0.00003$, referred to as chronic fatigue symptom urinary marker 1, or CFSUM1), tyrosine ($P < 0.02$), beta-alanine ($P < 0.02$), aconitic acid ($P < 0.05$), and succinic acid ($P < 0.05$) and reductions in an unidentified urinary metabolite, CFSUM2 ($P < 0.0007$), alanine ($P < 0.005$), and glutamic acid ($P < 0.02$). CFSUM1, beta-alanine, and CFSUM2 were found by discriminant function analysis to be the first, second, and third most important metabolites, respectively for discriminating between CFS and non-CFS subjects. The abundances of CFSUM1 and beta-alanine were positively correlated with symptom incidence ($P < 0.01$ and $P < 0.001$, respectively), symptom severity,

				core CFS symptoms, and SCL-90-R somatization (P < 0.00001), suggesting a molecular basis for CFS.
McGregor NR, Dunstan RH, Zerbes M, Butt HL, Roberts TK, Klineberg IJ.	Collaborative Pain Research Unit, University of Sydney, Australia.	Preliminary determination of the association between symptom expression and urinary metabolites in subjects with chronic fatigue syndrome.	Biochem Mol Med 1996 Jun;58(1):85-92	Chronic fatigue syndrome (CFS) patients have a urinary metabolite labeled CFSUM1 with increased incidence (P < 0.004) and relative abundance (P < 0.00003). The relative abundances of urinary CFSUM1 and beta-alanine were associated with alterations in metabolite excretion and symptom incidence. In 20 CFS patients and 45 non-CFS subjects, symptom/metabolite associations were investigated by assessing symptom sensitivity and specificity, and symptom indices of total symptom incidence, CFS core symptoms, cognitive, neurological, musculoskeletal, gastrointestinal, infection-related and genitourinary symptom indices, as well as a visual analogue pain scale of average pain intensity. Thirty-three symptoms had significant (P < 0.005) sensitivity and specificity in the CFS patients compared to that in the non-CFS controls. Severe fatigue was the only symptom with 100% sensitivity and specificity and CFSUM1 excretion was the primary metabolite for expression of this symptom. All nine symptom indices had elevated responses in the CFS patients (all P < 0.0000001). Multiple regression analyses indicated that all the symptom indices had significant correlations (R) with changes in the urinary excretion of metabolites (P < 0.0001). CFSUM1 and beta-alanine were the first and second metabolites correlated with the CFS core symptom index and CFSUM1 was primarily associated with infection-related and musculoskeletal indices whereas beta-alanine was primarily associated with gastrointestinal and genitourinary indices. The strong associations of CFSUM1 and beta-alanine with CFS symptom expression provide a molecular basis for developing an objective test for CFS.
Mesch U, Lowenthal RM, Coleman D.		Lead poisoning masquerading as chronic fatigue syndrome.	Lancet 1996 Apr 27;347(9009):1193	
Michiels V, Cluydts R, Fischler B, Hoffmann G, Le Bon O, De Meirleir K.	Department of Psychology, Free University of Brussels (VUB), Belgium.	Cognitive functioning in patients with chronic fatigue syndrome.	J Clin Exp Neuropsychol 1996 Oct;18(5):666-77	A comprehensive battery of neuropsychological tests was administered to 35 outpatients suffering from Chronic Fatigue Syndrome (CFS). They were compared to 33 normal controls matched for age, gender, intelligence, and education. The patients displayed psychomotor slowing and impaired attention. The learning rate of verbal and visual material for patients with CFS was slower, and delayed recall of verbal and visual information was impaired. Because there was a high variability in cognitive impairment within the CFS group, it would be inappropriate to generalize results to the entire CFS population. Two neuropsychological variables indicating aspects of psychomotor performance and verbal memory were found to discriminate best between patients and controls.
Minowa M, Jiamo M.	Department of Epidemiology, National	Descriptive epidemiology of chronic	J Epidemiol 1996 Jun;6(2):75-80	In order to clarify the epidemiological features of chronic fatigue syndrome (CFS), a nationwide survey was conducted using the Japanese version of the CDC

	Institute of Public Health, Tokyo, Japan.	fatigue syndrome based on a nationwide survey in Japan.		Criteria prepared by the CFS Research Group of Japan. All clinical departments of internal medicine, pediatrics, psychiatry and neurology at university hospitals and at ordinary hospitals with 200 or more beds were surveyed. Major results were as follows: (1) Period prevalence adjusted for response rate was 0.85 (0.63 for males and 1.02 for females) per 100,000 population during the year 1992; (2) Based on the first and final dates of hospital visits, the prevalences on January 1 of 1992 and 1993 were 0.40 and 0.60 per 100,000 population, respectively, suggesting an increasing trend; (3) Reported new cases during 1992 were 301, and the response adjusted-incidence was estimated to be 0.46 per 100,000 person-years; (4) The proportion of post-infectious CFS cases was 14.8% for both sexes, and tended to be slightly higher among females than males, but was not related to age. Three clusterings of two cases were reported.
Moss-Morris R, Petrie KJ, Large RG, Kydd RR.		Neuropsychological deficits in chronic fatigue syndrome: artifact or reality?	J Neurol Neurosurg Psychiatry 1996 May;60(5):474-7	
Mulube M.		Myths dispelled about chronic fatigue syndrome.	BMJ 1996 Oct 5;313(7061):839	
Nakaya T, Takahashi H, Nakamura Y, Asahi S, Tobiume M, Kuratsune H, Kitani T, Yamanishi K, Ikuta K.	Section of Serology, Hokkaido University, Sapporo, Japan.	Demonstration of Borna disease virus RNA in peripheral blood mononuclear cells derived from Japanese patients with chronic fatigue syndrome.	FEBS Lett 1996 Jan 8;378(2):145-9	CFS, a recently named heterogeneous disorder, is an illness of unknown etiology. The association of CFS with viral infections has been suggested. A common association between CFS and several viruses examined has not been confirmed. Here, we centered on the possible link between CFS and BDV infection. By nested RT-PCR followed by hybridization, BDV RNA was demonstrated as a clear signal in PBMCs in 3 out of 25 CFS patients. The amplified cDNA fragments were cloned and sequenced. A total of 16 clones were studied. Intra-patients divergencies of the p24 were 2-9%, 3-20%, and 3-11% in the deduced amino acids. Inter-patient divergencies among the 16 clones were 3-24%. Antibodies to recombinant BDV p24 protein were detected in 6 CFS patients including one carrying BDV RNA. Overall, these gave the prevalence of 32% (8/25) in Japanese CFS patients, suggesting that Japanese CFS is highly associated with active infection of BDV, or a related agent.
Natelson BH, Cheu J, Pareja J, Ellis SP, Policastro T, Findley TW.	CFS Center, New Jersey Medical School, East Orange 07018, USA.	Randomized, double blind, controlled placebo-phase in trial of low dose phenelzine in the chronic fatigue syndrome.	Psychopharmacology (Berl) 1996 Apr;124(3):226-30	Because of the striking similarity of the clinical manifestations produced by use of the drug reserpine and seen in patients with the chronic fatigue syndrome (CFS), we theorized that CFS was a disorder of reduced central sympathetic drive. Because of the pharmacology of control of this central sympathetic system, we further postulated that CFS symptoms would respond quickly to low dose treatment with a monamine oxidase inhibitor. To test these hypotheses, we designed a randomized, double blind placebo controlled study using phenelzine. No patient in the trial had a diagnosis of lifetime or current psychiatric disorder

				and none had depressed mood in the range of clinically depressed patients on a paper and pencil test of depression. Patients in the placebo group received placebo for 6 weeks while those in the drug treatment group were treated in three 2-week segments-placebo, 15 mg phenelzine every other day, and then 15 mg daily. This treatment regimen produced a significant pattern of improvement compared to worsening in 20 self report vehicles of CFS symptoms, illness severity, mood or functional status. Thus the data support our hypothesis of reduced sympathetic drive, although an alternative hypothesis of pain alleviation is also possible. The study design also allowed us to evaluate patients for a placebo effect: no evidence for this was found, suggesting that CFS is not an illness due to patients' being overly suggestible. Randomized Controlled Trial
Neri G, Bianchedi M, Croce A, Moretti A.	Clinica Otorinolaringoiatrica, Universita G. d'Annunzio di Chieti.	["Prolonged" decay test and auditory brainstem responses in the clinical diagnosis of the chronic fatigue syndrome].[article in Italian]	Acta Otorhinolaryngol Ital 1996 Aug;16(4):317-23	The chronic fatigue syndrome (CFS) was formally defined to describe disabling fatigue of unknown etiology with immunologic disfunctions. In most cases occur abnormalities of neurophysiological tests. In this paper the Authors use the low (11 pps) and high (51-71 pps) frequency ABR for detecting the electrophysiological function of auditory brainstem responses and propose the "Prolonged Decay Test", a modified impedenzometric technique that explores any alterations of the stapedial contraction, as a new diagnostic test for CFS. Twenty-one patients with suspected CFS, with an age between 17 and 50 years, were examined and the instrumental data were correlated with the clinical findings. The results of the ABR study showed in the examined subjects no many abnormalities in the 11 pps frequency test. The high frequency stimulation trials (with 51 and 71 pps) proved many alterations in 10 patients (absence of the first wave in 6 cases, in 5 many wave latency delay and in 1 patient absence of the first wave and many wave latency delay). The high frequency trials showed no abnormalities in the 11 remaining patients. The clinical-audiological correlation showed a 61.9% of comparison with 33.3% of false negatives and 4.8% of false positives. The Prolonged Decay Test showed a 71.4% of clinical-audiological comparison with 23.8% of false negatives and 4.8% of false positives. The Prolonged Decay Test together with the ABR showed a 81.8% of clinical-audiological comparison with 18.2% of false negatives and 0% of false positives. These preliminary data show that the stapedial reflex together with the ABR test could be useful for the diagnosis of CFS.
Nishikai M, Akiya K, Tojo T, Onoda N, Tani M, Shimizu K.	Department of Internal Medicine, Second Tokyo National Hospital, Japan.	'Seronegative' Sjogren's syndrome manifested as a subset of chronic fatigue syndrome.	Br J Rheumatol 1996 May;35(5):471-4	We determined the extent to which chronic fatigue syndrome (CFS) patients with sicca symptoms fulfil the diagnostic criteria for Sjogren's syndrome (SS). Three sets of diagnostic criteria for SS, formulated by the Japanese, Europeans and Fox, were used. One-third of the CFS patients with sicca symptoms fulfilled the diagnostic criteria for SS. However, they were 'seronegative', differing from the ordinary primary SS.
Oberg K.	Uppsala University,	Interferon-alpha versus	Digestion 1996;57 Suppl	Interferon-alpha (IFN-alpha) has a direct anti-tumour effect and is an

	Sweden.	somatostatin or the combination of both in gastro-enteropancreatic tumours.	1:81-3	immunomodulator. Somatostatin analogues, by contrast, when used to treat neuroendocrine tumours, control the secretion and peripheral effects of hormones, although at high doses they induce apoptosis. We have used IFN-alpha to treat > 350 patients with neuroendocrine tumours, and combining our and published data gives a median 44% biochemical response rate and 11% tumour response rate. Side-effects are mainly flu-like symptoms, then low-grade chronic fatigue syndrome. 15% may develop autoimmune reactions. The side-effects profile of somatostatin analogues is better but patients must take frequent injections and may have bile problems. We combined IFN-alpha and octreotide treatment in 24 patients with malignant carcinoid tumours who did not respond biochemically to high-dose (300 micrograms/day) octreotide alone. Biochemical response occurred in 77% but no significant anti-tumour effect was noted besides disease stabilisation in 4 cases. The combination therapy had an effect on clinical symptoms rather than tumour mass. Interferon was better tolerated when in the combination.
Oughton RA.		Chronic fatigue syndrome (CFS) in Army general practice.	J R Army Med Corps 1996 Jun;142(2):85 comment on: J R Army Med Corps. 1994 Jun;140(2):59-60	
Patarca R, Nancy Klimas Dmitry Sandler, Maria N. Garcia , Mary Ann Fletcher		Interindividual Immune Status Variation Patterns in Patients with Chronic Fatigue Syndrome Association with Gender and the Tumor Necrosis Factor System	Journal of Chronic Fatigue Syndrome 1996: 2(1): 13 - 39	Changes in soluble immune mediator levels in association with the chronic fatigue syndrome (CFS) usually occur within normal ranges and are apparent mainly as changes in the skewness of population distributions. The latter finding undermines the usefulness of cytokine levels as clinical tools at the individual level as has been seen in sepsis syndrome where a similar overlap occurs. Nonetheless, changes in cytokine levels at the population level can contribute to an understanding of the disease process. For example, we reported previously that significant proportions of CFS patients showed elevated serum levels of either soluble tumor necrosis factor-receptor I (sTNF-RI, sCD120a) or TNF-a as compared to controls. The latter results could reflect different disease processes or extremes of a common disease process. Using sera collected over a five-year period, we have now studied an extended cohort of 108 CFS patients and our results are consistent with a common graded disease process. When we assessed the effect of gender on the distributions of serum levels of immune mediators, levels of sTNF-RI, sTNF-RII (sCD 12Ob), sIL-6R (sCDl26), and sICAM-1 were found to be consistently higher among males than females and among CFS patients as compared to controls regardless of gender. Moreover, differences in soluble immune mediator levels between CFS and control individuals were more clearly defined when restricting the analysis to the female gender. These observations are consistent with endocrine influences on immunological changes.

Pearce J.		Cognitive behaviour therapy for the chronic fatigue syndrome. Cognitive behavior therapy should be compared with placebo treatments.	BMJ 1996 Apr 27;312(7038):1097; discussion 1098 comment on: BMJ. 1996 Jan 6;312(7022):22-6	
Pearn J		Chronic Ciguatera One Organic Cause of the Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 29 - 34	Ciguatera is a distressing form of fish poisoning, caused by the ingestion of one or more of a series of ciguatoxins. These poisons, some of the most potent mammalian neurotoxins known, are manufactured in reef-dwelling dinoflagellates and concentrated up the piscine food chain. Human victims, not uncommon in the Pacific, Atlantic and Indian Ocean tropical and subtropical littorals, become poisoned by eating risk species of fish. The acute intoxication is clinically dramatic, resulting in paraesthesiae, dysaesthesiae, prostration, myalgia and arthralgia. In some 20 percent of cases, symptoms of fatigue, reduced exercise tolerance and non-specific aches and pains persist for months and, in a small percentage of cases, for years. Such cases would, in the absence of the prior episode of acute poisoning, satisfy the diagnostic criteria for the chronic fatigue syndrome (CFS). Occasionally, patients are encountered who have been diagnosed as having CFS because of lack of awareness of the ciguatera syndrome, but in whom in retrospect the episode of acute fish poisoning can be established. The fact that at least one potent mammalian toxin can cause a chronic syndrome indistinguishable from CFS opens the way for further research into this enigmatic condition.
Reiffenberger DH, Amundson LH.	Brown Clinic, Watertown, South Dakota, USA.	Fibromyalgia syndrome: a review.	Am Fam Physician 1996 Apr;53(5):1698-712	Fibromyalgia syndrome includes symptoms of widespread, chronic musculoskeletal aching and stiffness and soft tissue tender points. It is frequently accompanied by fatigue and sleep disturbance. Fibromyalgia is more common in women than in men, and it occurs at a mean age of 49 years. Differential diagnosis includes myofascial pain syndrome and chronic fatigue syndrome. Fibromyalgia is a multifactorial problem and no universal treatment guidelines apply to all cases. Pharmacologic therapy may incude tricyclic antidepressants. In addition to commonly used pharmacologic therapies, patient education, reassurance and an exercise program can each play an important role in relieving the symptoms associated with this common musculoskeletal syndrome.
Reyes M, James G. Dobbins , Alison C. Mawle , Lea Steele , Howard E. Gary , Hina Malani , Scott Schmid , Keiji Fukuda John		Risk Factors for Chronic Fatigue Syndrome A Case-Control Study	Journal of Chronic Fatigue Syndrome 1996: 2(4): 17 - 33	Objective: To study various risk factors previously reported to be associated with chronic fatigue syndrome (CFS). Design: Case-control study. Setting: Metropolitan Atlanta CFS surveillance registry consisting of physicians and clinics that evaluate patients with fatiguing illness. Patients: Twenty-five CFS patients identified from the Centers for Disease Control and Prevention, Atlanta CFS study site, were matched by race, sex, and age to two randomly selected controls. Cases were

Stewart Rosane Nisenbaum , William C. Reeves				further subgrouped by type of illness onset-sudden, occurring within a few days, or gradual, occurring over a longer time period. Main outcome measures: A broad panel of risk factors previously associated with CFS. Results: CFS patients were significantly more likely than controls to report a history of stress, persistent nasal symptoms, ear infections, and ingestion of B-complex vitamins during the year prior to the case's onset of illness. In addition, women patients were significantly more likely to have had a hysterectomy. The subset of patients (n = 17) who reported a gradual onset were significantly more likely than patients reporting a sudden onset of illness or controls to report stressful events in the year prior to onset, certain dental procedures, sinusitis, exposures to herbicides, pesticides, or insecticides, and a history of hysterectomy. We could not confirm previously reported associations of CFS with a history of asthma or eczema; exposure to sick animals; exposure to solvents, paint, or other chemicals; ingestion of raw-milk, or travel, occupation, or recreational activity. Conclusions: While no risk factors were identified that effectively distinguish CFS cases from controls, the data do suggest that gradual and sudden onset CFS constitute distinct subclasses of the syndrome. Future studies should subgroup patients based on type of illness onset and further evaluate risk factors of interest, focusing on the role
Ross E.		The history and treatment of chronic fatigue syndrome.	Nurs Times 1996 Oct 30-Nov 5;92(44):34-6	This article looks at chronic fatigue syndrome, a common condition affecting 1-2.5% of the population. The criteria for diagnosis are described and the nurse's role in treatment is discussed.
Rouillon F, Delhommeau L, Vinceneux P.	Service de Psychiatrie, Hopital Louis Mourier, Colombes.	[Chronic fatigue syndrome].[article in French]	Presse Med 1996 Dec 21;25(40):2031-6	Fatigue is one of the most common medical complaints. Sometimes, fatigue is chronic, unexplained and induces significant distress or impairment in social, occupational or other important areas of functioning. This condition was described as neurasthenia by Beard at the end of the 19th Century; more recently the United States Centers for Disease Control and Prevention (CDC) suggested to call it "Chronic Fatigue Syndrome" (SFC). Both are considered as physical diseases and share certain therapeutic measures. Pathophysiology is still unknown and may involve viral agents, immunological processes or psychiatric disorders. Similarly most of the treatments which have been properly evaluated seem to be more or less inefficacious.
Salit IE.	Division of Infection Diseases, The Toronto Hospital, Canada.	The chronic fatigue syndrome: a position paper.	J Rheumatol 1996 Mar;23(3):540-4	
Samii A, Wassermann EM, Ikoma K, Mercuri B, George MS, O'Fallon A, Dale JK, Straus SE, Hallett M.	Human Motor Control Section, National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892-	Decreased postexercise facilitation of motor evoked potentials in patients with chronic fatigue syndrome or	Neurology 1996 Dec;47(6):1410-4	We studied the effects of exercise on motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS) in 18 normal (control) subjects, 12 patients with chronic fatigue syndrome, and 10 depressed patients. Subjects performed repeated sets of isometric exercise of the extensor carpi radialis muscle until they were unable to maintain half maximal force. MEPs were

	1428, USA.	depression.		recorded before and after each exercise set and for up to 30 minutes after the last set. The mean amplitude of MEPs recorded from the resting muscle immediately after each exercise set was 218% of the mean pre-exercise MEP amplitude in normal subjects, 126% in chronic fatigue patients, and 155% in depressed patients, indicating postexercise MEP facilitation in all three groups. The increases in the patient groups, however, were significantly lower than normal. The mean amplitudes of MEPs recorded within the first few minutes after the last exercise sets in all three groups were approximately half their mean pre-exercise MEP amplitudes. This postexercise MEP depression was similar in all groups. We conclude that postexercise cortical excitability is significantly reduced in patients with chronic fatigue syndrome and in depressed patients compared with that of normal subjects.
Scheurlen M.	Medizinische Poliklinik, Universitat, Wurzburg.	[Pathogenicity of fungi in the intestines--current status of the discussion].[article in German]	Fortschr Med 1996 Sep 20;114(26):319-21	The hypothesis that colonization of the intestinal tract by yeasts (e.g. Candida albicans) can lead to disease in immunocompromised individuals is currently being discussed controversially. Proponents assume that toxins produced by the fungi can trigger such complaints as irritable bowel syndrome of the chronic fatigue syndrome, and that such chronic or recurrent infections may be caused by an intestinal reservoir of yeasts. Opponents of the hypothesis, however, point out that no hard data on the pathogenetic significance of an intestinal reservoir of yeasts are available, controlled studies have failed to demonstrate the effectiveness of antifungal treatment. Discussions are however, hampered by a lack of objective data. The postulated pathomechanisms therefore need to be clarified, diagnostic criteria developed, and the efficacy of the proposed therapeutic measures shown by controlled studies. Until this has been done, assumption about the pathogenicity of yeasts in the bowel, cannot be taken as a basis for binding therapeutic recommendations.
Schmaling KB, Jones JF.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle 98105, USA.	MMPI profiles of patients with chronic fatigue syndrome.	J Psychosom Res 1996 Jan;40(1):67-74	Fifty-three patients with chronic fatigue syndrome (CFS) and 43 healthy nonpatient controls completed the Minnesota Multiphasic Personality Inventory (MMPI). All subjects varied in their degree of seropositivity to active Epstein-Barr virus (EBV) as measured by their anti-early antigen titers. EBV titers were higher among CFS patients and were associated with being more symptomatic. Differences in patient status were associated with statistically significant elevations on 8 of 9 clinical scales, 4 of which also showed clinically significant elevations (T scores > or = 70): scales 1, 2, 3, and 8. These results are discussed in terms of their implications for intervention strategies associated with MMPI-based CFS subtypes.
Schnitzer TJ, Penmetcha M.	Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL 60612, USA.	Viral arthritis.	Curr Opin Rheumatol 1996 Jul;8(4):341-5	Viral infections can present with different patterns of joint and soft tissue involvement, and the etiologic role of viruses in various rheumatic diseases is a subject of continued great interest. Recently, new immunoenzymatic assays have brought a better understanding of the relationship between hepatitis C virus

				serotypes and their immunologic manifestations. Our knowledge of the consequences of parvovirus B19 infection has broadened to include the variable clinical spectrum the role of inflammatory cytokine production in parvovirus-induced arthritis, a postulated causative role for B19 in rheumatoid arthritis, and a negative association between parvovirus and Still's disease as well as chronic fatigue syndrome. New, specific antibodies to nonstructural protein NS-1 in parvovirus B19-associated arthritis have been detected. Arthritis related to hepatitis B virus vaccination or measles and mumps vaccination was also reported. The papers reviewed here demonstrate the continuing efforts in defining the etiopathogenesis of virus-induced rheumatic diseases.
Scott LV, T. G. Dinan		The Neuroendocrinology of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(4): 49 - 59	Since the introduction of operationalized criteria, there has been considerable interest in the pathophysiology of chronic fatigue syndrome (CFS). There is an increasing volume of evidence to support the view that patients with this syndrome have unique neuroendocrinology patterns. Central to this endocrine dysfunction is altered hypothalamic-pituitary-adrenal axis (HPA) activity. The cardinal findings include attenuated adrenocorticotrophic hormone (ACTH) responses to corticotropin-releasing hormone (CRH) and low 24-hour urinary cortisol. These are compatible with a mild central adrenal insufficiency. Adrenal steroids have widespread impact in the brain, and of particular importance is their dense concentration on serotonergic and noradrenergic neurotransmitter pathways. Using a variety of different challenge drugs, a supersensitivity of the serotonergic 5-HT 1A receptor has been demonstrated although the results have not been entirely consistent. A blunting of dexamethasone-induced growth hormone release has been described and may reflect a relative subsensitivity of the steroid receptor. It is proposed that the disruption of the HPA, which may be triggered by a number of stressors including infections, may represent a primary phenomenon, and that the neurotransmitter abnormalities described are in fact secondarily heralded by prolonged HPA dysregulation.
See DM, Tilles JG.	Department of Medicine School of Medicine, University of California at Irvine Orange 92668, USA.	alpha-Interferon treatment of patients with chronic fatigue syndrome.	Immunol Invest 1996 Jan-Mar;25(1-2):153-64	Thirty patients who fulfilled clinical criteria defined by the CDC for Chronic Fatigue Syndrome were treated with alfa 2a interferon or placebo in a double-blind crossover study. Outcome was evaluated by Natural Killer (NK) cell function, lymphocyte proliferation to mitogens and soluble antigens, CD4/CD8 counts and a 10 item Quality of Life (QOL) survey. Although mean NK function rose from 87.8 +/- 19.6 to 129.3 +/- 20.7 lytic untis (LU; $p < .05$) with 12 weeks of interferon therapy, there was no significant change in the other immunologic parameters or QOL scores. When the 26 patients who completed the study were stratified according to their baseline NK function and lymphocyte proliferation, 4 groups were identified: 3 patients had normal NK cell function and lymphocyte proliferation when compared to normal, healthy controls, 9 had isolated deficiency in lymphocyte proliferation, 7 had diminished NK function only, and 7

				had abnormalities for both parameters. QOL scores were not significantly different for the four groups at baseline. After 12 weeks of interferon therapy, QOL score significantly improved in each of the seven patients with isolated NK cell dysfunction (mean score, 16.3 +/- 7.9) compared to baseline (39.7 +/- 12.1; p < .05). In these patients the mean NK function increased from 35.1 +/- 11.7 to 91.5 +/- 22.7 LU (p < .01). Significant improvement was not recorded for QOL in the other three groups. Thus, therapy with alpha interferon has a significant effect on the QOL of that subgroup of patients with CFS manifesting an isolated decrease in NK function. Randomized Controlled Trial
Selden SM, Cameron AS.	Communicable Disease Control Unit, South Australian Health Commission, Adelaide, SA.	Changing epidemiology of Ross River virus disease in South Australia.	Med J Aust 1996 Sep 16;165(6):313-7 comment in: Med J Aust. 1997 Aug 18;167(4):229-30 Med J Aust. 1997 Mar 17;166(6):333; discussion 334 Med J Aust. 1997 Mar 17;166(6):334	OBJECTIVE: To investigate changes in epidemiology and symptoms of Ross River virus (RRV) disease in South Australia. DESIGN: Longitudinal questionnaire-based survey of notified cases from one to 36 months after infection. SUBJECTS: All patients with recent serologically confirmed RRV infection notified to the Communicable Disease Control Unit, South Australian Health Commission, between 1 October 1992 and 30 June 1993. OUTCOME MEASURES: Sociodemographic data, source of infection, symptoms and ability to carry out daily activities (at onset of illness and at time of questionnaire, up to 36 months after infection), symptom duration, economic impact of the illness, cases recovery time, factors predictive of delayed recovery. RESULTS: Information was obtained on the acute illness from 698 of the 821 subjects and at 15 months after infection from 436. At 15 months, 51% of respondents still had joint pain and 45% had persistent tiredness and lethargy. Other common symptoms included myalgia (34%), lymphadenopathy (25%), headache (23%) and depression (22%). These symptoms were still common 30 months after infection. Increasing age was the only statistically significant predictor of delayed recovery. Infections were acquired across the State, away from previously recognised RRV-endemic areas. CONCLUSIONS: For many people, RRV disease is debilitating, with long term symptoms similar to those of chronic fatigue syndrome. The geographic range of the infection has expanded in SA.
Sharma A, Kendall MJ, Oyebode F, Jones D.		Fluoxetine and chronic fatigue syndrome.	Lancet 1996 Jun 22;347(9017):1770-1; discussion 1771-2	
Sharpe M, Clements A, Hawton K, Young AH, Sargent P, Cowen PJ.	University Department of Psychiatry, Warneford and Littlemore Hospitals, Oxford, UK.	Increased prolactin response to buspirone in chronic fatigue syndrome.	J Affect Disord 1996 Nov 4;41(1):71-6	We studied the endocrine and subjective responses that followed acute administration of the 5-HT1A receptor agonist buspirone (0.5 mg/kg orally) in 11 male patients with chronic fatigue syndrome (CFS) and a group of matched healthy controls. Patients with CFS had significantly higher plasma prolactin concentrations and experienced more nausea in response to buspirone than did controls. However, the growth hormone response to buspirone did not distinguish CFS patients from controls. Our data question whether the enhancement of buspirone-induced prolactin release in CFS is a consequence of

				increased sensitivity of post-synaptic 5-HT1A receptors. It is possible that the increased prolactin response to buspirone in CFS could reflect changes in dopamine function.
Sharpe M, Hawton K, Simkin S, Surawy C, Hackmann A, Klimes I, Peto T, Warrell D, Seagroatt V.	University Department of Psychiatry, Warneford Hospital, Oxford.	Cognitive behaviour therapy for the chronic fatigue syndrome: a randomized controlled trial.	BMJ 1996 Jan 6;312(7022):22-6 comment in: ACP J Club. 1996 May-Jun;124(3):71 BMJ. 1996 Apr 27;312(7038):1096-7; discussion 1098 BMJ. 1996 Apr 27;312(7038):1096; discussion 1098 BMJ. 1996 Apr 27;312(7038):1097-8 BMJ. 1996 Apr 27;312(7038):1097; discussion 1098	OBJECTIVE--To evaluate the acceptability and efficacy of adding cognitive behaviour therapy to the medical care of patients presenting with the chronic fatigue syndrome. DESIGN--Randomised controlled trial with final assessment at 12 months. SETTING--An infectious diseases outpatient clinic. SUBJECTS--60 consecutively referred patients meeting consensus criteria for the chronic fatigue syndrome. INTERVENTIONS--Medical care comprised assessment, advice, and follow up in general practice. Patients who received cognitive behaviour therapy were offered 16 individual weekly sessions in addition to their medical care. MAIN OUTCOME MEASURES--The proportions of patients (a) who achieved normal daily functioning (Karnofsky score 80 or more) and (b) who achieved a clinically significant improvement in functioning (change in Karnofsky score 10 points or more) by 12 months after randomisation. RESULTS--Only two eligible patients refused to participate. All randomised patients completed treatment. An intention to treat analysis showed that 73% (22/30) of recipients of cognitive behaviour therapy achieved a satisfactory outcome as compared with 27% (8/30) of patients who were given only medical care (difference 47 percentage points; 95% confidence interval 24 to 69). Similar differences were observed in subsidiary outcome measures. The improvement in disability among patients given cognitive behaviour therapy continued after completion of therapy. Illness beliefs and coping behaviour previously associated with a poor outcome changed more with cognitive behaviour therapy than with medical care alone. CONCLUSION--Adding cognitive behaviour therapy to the medical care of patients with the chronic fatigue syndrome is acceptable to patients and leads to a sustained reduction in functional impairment. Randomized Controlled Trial
Sharpe M.	Department of Psychiatry, University of Oxford, United Kingdom.	Chronic fatigue syndrome.	Psychiatr Clin North Am 1996 Sep;19(3):549-73	Chronic fatigue syndrome (CFS) is a medically unexplained illness characterized by chronic, disabling fatigue, impaired concentration, muscle pain, and other somatic symptoms. The conceptual difficulties associated with all medically unexplained illnesses contribute to the controversy surrounding CFS, which has centered around whether it is best regarded as a medical or as a psychiatric condition. Clinically, such an approach is not helpful, and current research suggests that both pathophysiologic changes and psychosocial factors are important. Pragmatic management based on a detailed assessment of the individual is outlined.
Shepherd C.		Cognitive behaviour therapy for the chronic fatigue syndrome. Good general care may offer	BMJ 1996 Apr 27;312(7038):1096; discussion 1098 comment on: BMJ. 1996	

		as much benefit as cognitive behaviour therapy.	Jan 6;312(7022):22-6	
Sisto SA, LaManca J, Cordero DL, Bergen MT, Ellis SP, Drastal S, Boda WL, Tapp WN, Natelson BH.	Department of Neurosciences, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA.	Metabolic and cardiovascular effects of a progressive exercise test in patients with chronic fatigue syndrome.	Am J Med 1996 Jun;100(6):634-40 comment in: Am J Med. 1997 Jul;103(1):83-4 Am J Med. 1997 Jul;103(1):84-6	PURPOSE: To evaluate the aerobic power (as maximum volume of oxygen consumed [VO2 max]) of women with chronic fatigue syndrome (CFS). PATIENTS AND METHODS: Twenty-one women with CFS and 22 sedentary healthy controls (CON) were studied at the CFS Cooperative Research Center Exercise Laboratory at the VA Medical Center, East Orange, New Jersey. Performance was measured on an incremental treadmill protocol walking to exhaustion. Expired gases were analyzed by a metabolic system, heart rate was recorded continuously, and ratings of perceived exertion (RPE) were taken at each workload. The groups were divided into those who achieved VO2 max (CFS-MAX and CON-MAX) and those who stopped at a submaximal level (CFS-NOMAX and CON-NOMAX) by using standard criteria. RESULTS: Seventeen CON and 10 CFS subjects achieved VO2 max. The VO2 max (mL/kg/min) of the CFS-MAX (28.1 +/- 5.1) was lower than that of the CON-MAX (32.1 +/- 4.3, P = 0.05). The CFS-MAX achieved 98 +/- 11% of predicted VO2 max. The CFS group had a higher RPE at the same absolute workloads as controls (P < 0.01) but not the same relative workloads. CONCLUSION: Compared with normal controls, women with CFS have an aerobic power indicating a low normal fitness level with no indication of cardiopulmonary abnormality. Our CFS group could withstand a maximal treadmill exercise test without a major exacerbation in either fatigue or other symptoms of their illness.
Snorrason E, Arni Geirsson, Kari Stefansson		Trial of a Selective Acetylcholinesterase Inhibitor, Galanthamine Hydrobromide, in the Treatment of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1996: 2(2/3): 35 - 54	The purpose of the study was to search for a means of diminishing the plight of patients with chronic fatigue syndrome (CFS) and to test the hypothesis that central to the pathogenesis of CFS is a cholinergic defect. Forty-nine patients who fulfilled consensus criteria for CFS were treated with the acetylcholinesterase inhibitor, galanthamine hydrobromide. Thirty-nine patients finished the study according to the protocol with 43% reporting 50% improvement in fatigue, myalgia and sleep and 70% reporting 30% improvement whereas patients in the placebo group reported only 10% improvement in the same parameters of CFS. The improvement of patients on galanthamine was in most cases gradual and reached significance for the group only after four to eight weeks. The improvement was stable, and no patients who reported over 50% improvement on galanthamine relapsed to a pretrial level of any symptom. One of the most surprising effects was the dramatic improvement of sleep disturbances that occurred in most patients on this medication: more than 60% of the patients who finished the study reported over 70% improvement in sleep deficit. If the subjective report by patients can be proved by objective means, this would be the first demonstration of a drug that can be used to correct a sleep disturbance that also influences a specific stage in normal sleep. The most common adverse

				effect of galanthamine, as given in this study, was nausea that was dose-dependent and reversible. Galanthamine hydrobromide is relatively safe and appears to be an effective medication against many symptoms of CFS. But the positive results of this study have to be interpreted cautiously because of methodological limitations of this trial. First, this study was originally organized as a double-blind, placebo-controlled trial but was changed to an optional crossover after two weeks of treatment. Also, the adverse effects of the active drug in 30% of patients could compromise the double-blind. With these limitations in mind, it is nevertheless tempting to conclude that this study lends an indirect support to our hypothesis that a cholinergic deficit may play a role in the pathogenesis of the syndrome.
St George IM.	Wellington School of Medicine, New Zealand.	Did Cook's sailors have Tapanui 'flu? --chronic fatigue syndrome on the Resolution.	N Z Med J 1996 Jan 26;109(1014):15-7	The 1982 publication of the Resolution journal of Johann George Reinhold Forster provided justification for his recognition as a scientist, and gave a remarkable insight into his character. It also included an account of an illness suffered by many of the sloop's crew, including Forster, after a period ashore at Queen Charlotte Sound. The symptoms of the illness were remarkably similar to those now clustered as the chronic fatigue syndrome.
Steinberg P, McNutt BE, Marshall P, Schenck C, Lurie N, Pheley A, Peterson PK.	Department of Medicine, Hennepin County Medical Center, Minneapolis, MN 55415, USA.	Double-blind placebo-controlled study of the efficacy of oral terfenadine in the treatment of chronic fatigue syndrome.	J Allergy Clin Immunol 1996 Jan;97(1 Pt 1):119-26	BACKGROUND: There is no established treatment for chronic fatigue syndrome (CFS), an illness characterized by disabling fatigue exacerbated by physical activity. A variety of immunologic abnormalities have been reported, including a high incidence of atopy and hypoergy or anergy. OBJECTIVE: Because of anecdotal reports and uncontrolled trials showing antihistamine efficacy in CFS, we evaluated the clinical efficacy of the antihistamine terfenadine (60 mg twice daily) in a placebo-controlled study. METHODS: Thirty patients with CFS were enrolled in a 2-month, double-blind, placebo-controlled trial of terfenadine. Participants underwent a battery of both immediate- and delayed-type hypersensitivity skin tests and completed a self-assessment questionnaire used to measure severity of symptoms, physical and social functioning, health perceptions, and mental health before each of six biweekly visits. RESULTS: Twenty-eight patients completed the trial. History of atopy and positive immediate skin test results were prevalent, 73% and 53%, respectively. No evidence for hypoergy or anergy after delayed-type hypersensitivity skin testing was found. No therapeutic benefit from terfenadine could be detected in terms of symptom amelioration, improved physical or social functioning, health perceptions, or mental health. A high incidence of atopy in patients with CFS was confirmed. CONCLUSION: Although this trial involved a small number of patients, the results suggest that terfenadine is unlikely to be of clinical benefit in treating CFS symptoms. Randomized Controlled Trial
Steinberg P, Pheley A, Peterson PK.	Division of Allergy and Clinical Immunology,	Influence of immediate hypersensitivity skin	J Allergy Clin Immunol 1996 Dec;98(6 Pt	

	Hennepin County Medical Center, Minneapolis 55415, USA.	reactions on delayed reactions in patients with chronic fatigue syndrome.	1):1126-8	
Sterzl I, Zamrazil V.	Endokrinologicky ustav, Praha.	[Endocrinopathy in the differential diagnosis of chronic fatigue syndrome].[article in Czech]	Vnitr Lek 1996 Sep;42(9):624-6	Fatigue is a frequent and sometimes dominant symptom of some endocrinopathies. It may be associated with other symptoms which are included among the criteria of the chronic fatigue syndrome. These units are not always quite distinct and frequently endocrine diseases and chronic fatigue syndrome (CFS) overlap. From this ensue differential diagnostic problems and ideas on possible causal relations. The authors concentrate in articular on autoimmune endocrinopathies and the polyglandular autoimmune syndrome (APS) with emphasis on the necessity of an accurate endocrinological diagnosis, where is some patients with suspected CFS a defined endocrinopathy was revealed. Attention will be also paid to recent views on the possible participation of disorders of the hypothalamus-pituitary-adrenal axis in the etiopathogenesis of CFS where endocrine and immune regulation overlap and condition each other.
Straus SE.		Chronic fatigue syndrome.	BMJ 1996 Oct 5;313(7061):831-2	
Studd J, Panay N.		Chronic fatigue syndrome.	Lancet 1996 Nov 16;348(9038):1384 comment on: Lancet. 1996 Oct 12;348(9033):971	
Swanink CM, Vercoulen JH, Galama JM, Roos MT, Meyaard L, van der Ven-Jongekrijg J, de Nijs R, Bleijenberg G, Fennis JF, Miedema F, van der Meer JW.	Department of General Internal Medicine, University Hospital Nijmegen, Netherlands.	Lymphocyte subsets, apoptosis, and cytokines in patients with chronic fatigue syndrome.	J Infect Dis 1996 Feb;173(2):460-3	Whether immunologic abnormalities correlate with fatigue severity and functional impairment in chronic fatigue syndrome (CFS) was investigated. Blood mononuclear cells were immunophenotyped and circulating ex vivo-produced cytokines were measured in 76 CFS patients and 69 healthy matched controls. Expression of CD11b on CD8 cells was significantly decreased in CFS patients. However, the previously reported increased expression of CD38 and HLA-DR was not confirmed. There was no obvious difference in apoptosis in leukocyte cultures, circulating cytokines, and ex vivo production of interleukin (IL)-1 alpha and IL-1 receptor antagonist. Endotoxin-stimulated ex vivo production of tumor necrosis factor-alpha and IL-beta was significantly lower in CFS. The immunologic test results did not correlate with fatigue severity or psychologic well-being was measured by Checklist Individual Strength, Beck Depression Inventory, and Sickness Impact Profile. Thus, these immunologic tests cannot be used as diagnostic tools in individual CFS patients.
Tripathy BK, Agarwal AK, Sangla KS, Singh CP, Chandra S.	Department of Medicine, Safdarjang Hospital, New Delhi.	Infectious agents and immunological disturbances in relation	J Assoc Physicians India 1996 May;44(5):335-8	

		to chronic fatigue syndrome.		
van Waveren EK.		The rise and fall of the chronic fatigue syndrome as defined by Holmes et al.	Med Hypotheses 1996 Feb;46(2):63-6	This paper is a sequel to my monograph on neurocirculatory asthenia and chronic fatigue syndrome. It pays special attention to the nature of chronic fatigue syndrome, to the forms of neurocirculatory asthenia, and above all to the 6th form in which profound fatigue is the dominant symptom. All forms including the 6th are characterized by the presence of concomitant symptoms due to dysfunction of the autonomic nervous system. Chronic fatigue syndrome as defined by Holmes et al is devoid of these symptoms. Up till the present day no case histories of it have been published. It is argued that chronic fatigue syndrome sensu Holmes et al does not exist, the 6th form of neurocirculatory asthenia having to take up its place.
Vecchiet L, Montanari G, Pizzigallo E, Iezzi S, de Bigontina P, Dragani L, Vecchiet J, Giamberardino MA.	Institute of Medical Pathophysiology, 'G. D'Annunzio' University of Chieti, Italy.	Sensory characterization of somatic parietal tissues in humans with chronic fatigue syndrome.	Neurosci Lett 1996 Apr 19;208(2):117-20	Patients with chronic fatigue syndrome (CFS) mainly complain of symptoms in the musculoskeletal domain (myalgias, fatigue). In 21 CFS patients the deep (muscle) versus superficial (skin, subcutis) sensitivity to pain was explored by measuring pain thresholds to electrical stimulation unilaterally in the deltoid, trapezius and quadriceps and overlying skin and subcutis in comparison with normal subjects. Thresholds in patients were normal in skin and subcutis but significantly lower than normal (hyperalgesia) in muscles ($P < 0.001$) in all sites. The selective muscle hypersensitivity corresponded also to fiber abnormalities at muscle biopsy (quadriceps) performed in nine patients which were absent in normal subjects (four cases): morphostructural alterations of the sarchomere, fatty degeneration and fibrous regeneration, inversion of the cytochrome oxidase/succinate dehydrogenase ratio, pleio/polymorphism and monstruosity of mitochondria, reduction of some mitochondrial enzymatic activities and increments of common deletion of 4977 bp of mitochondrial DNA 150-3000 times the normal values. By showing both sensory (diffuse hyperalgesia) and anatomical (degenerative picture) changes at muscle level, the results suggest a role played by peripberal mechanisms in the genesis of CFS symptoms. They would exclude the heightened perception of physiological signals from all districts hypothesized by some authors, especially as the hyperalgesia is absent in skin/subcutis.
Vercoulen JH, Hommes OR, Swanink CM, Jongen PJ, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	The measurement of fatigue in patients with multiple sclerosis. A multidimensional comparison with patients with chronic fatigue syndrome and healthy subjects.	Arch Neurol 1996 Jul;53(7):642-9	OBJECTIVE: To provide a multidimensional characterization of fatigue in patients with multiple sclerosis (MS). DESIGN: Cross-sectional design. Fifty patients with clinically definite MS were compared on the dimensions of fatigue with 51 patients with chronic fatigue syndrome (CFS) and 53 healthy subjects. RESULTS: Fourty-six percent of the patients with MS reported fatigue to be present at least once a week. Patients with MS and patients with CFS had significantly higher subjective fatigue severity scores than healthy subjects. Patients with MS and patients with CFS had significantly higher scores on measures of psychological well-being than healthy subjects. Patients with MS had scores similar to those of

				patients with CFS, except that patients with CFS had significantly higher somatization scores. High somatization scores reflect strong focusing on bodily sensations. Both groups of patients were significantly less active than the healthy subjects. The Kurtzke Expanded Disability Status Scale (EDSS) and the Beck Depression Inventory scores were not related to subjective fatigue severity. In patients with MS and in patients with CFS, subjective fatigue severity was related to impairment in daily life, low sense of control over symptoms, and strong focusing on bodily sensations. In CFS, but not in MS, evidence was found for a relationship between low levels of physical activity and attributing symptoms to a physical cause and between subjective fatigue severity and physical activity. CONCLUSIONS: Patients with MS experienced significant fatigue, which had a significant impact on daily functioning and was not related to depression on Expanded Disability Status Scale score. Psychological factors, such as focusing on bodily sensations and low sense of control play a role in the experience of fatigue in MS and CFS.
Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital Nijmegen, The Netherlands.	Prognosis in chronic fatigue syndrome: a prospective study on the natural course.	J Neurol Neurosurg Psychiatry 1996 May;60(5):489-94	OBJECTIVE--To determine spontaneous improvement after a follow up interval of 18 months in patients with chronic fatigue syndrome and to identify factors that predict improvement. METHODS--A longitudinal study was used. Of 298 initially assessed self referred patients fulfilling criteria for chronic fatigue syndrome, 246 patients completed self report questionnaires at follow up (response rate 83%). A multidimensional assessment method was used, measuring behavioural, emotional, cognitive, and social functioning. Comparison data from 53 healthy subjects matched for age, sex, and educational level were available. RESULTS--Three per cent of patients reported complete recovery and 17% reported improvement. At follow up, there were considerable problems at work and consumption of medication was high. Subjective improvement was confirmed by dimensional change: at follow up recovered patients had similar scores to healthy subjects and improved patients showed significant improvement on four out of seven outcome measures and had higher scores than healthy subjects in all dimensions. Sociodemographic variables or treatment by specialists and alternative practitioners did not predict improvement. Predictors of improvement were: subjective sense of control over symptoms, less fatigue, shorter duration of complaints, and a relative absence of physical attributions. CONCLUSION--The improvement rate in patients with a relatively long duration of complaints is small. Psychological factors are related to improvement, especially cognitive factors.
Vercoulen JH, Swanink CM, Zitman FG, Vreden SG, Hoofs MP, Fennis JF, Galama JM, van der	Department of Medical Psychology, University Hospital, Nijmegen, The Netherlands.	Randomised, double-blind, placebo-controlled study of fluoxetine in chronic	Lancet 1996 Mar 30;347(9005):858-61	BACKGROUND: No somatic treatment has been found to be effective for chronic fatigue syndrome (CFS). Antidepressant therapy is commonly used. Fluoxetine is recommended in preference to tricyclic agents because it has fewer sedative and autonomic nervous system effects. However, there have been no randomised,

Meer JW, Bleijenberg G.		fatigue syndrome.		placebo-controlled, double-blind studies showing the effectiveness of antidepressant therapy in CFS. We have carried out such a study to assess the effect of fluoxetine in depressed and non-depressed CFS patients. METHODS: In this randomised, double-blind study, we recruited 44 patients to the depressed CFS group, and 52 to the non-depressed CFS group. In each group participants were randomly assigned to receive either fluoxetine (20 mg once daily) or placebo for 8 weeks. The effect of fluoxetine was assessed by questionnaires, self-observation lists, standard neuropsychological tests, and a motion-sensing device (Actometer), which were applied on the day treatment started and on the last day. FINDINGS: The two groups were well matched in terms of age, sex distribution, employment and marital status, and duration of CFS. There were no significant differences between the placebo and fluoxetine-treated groups in the change during the 8-week treatment period for any dimension of CFS. There was no change in subjective assessments of fatigue, severity of depression, functional impairment, sleep disturbances, neuropsychological function, cognitions, or physical activity in the depressed or the non-depressed subgroup. INTERPRETATION: Fluoxetine in a 20 mg daily dose does not have a beneficial effect on any characteristic of CFS. The lack of effect of fluoxetine on depressive symptoms in CFS suggests that processes underlying the presentation of depressive symptoms in CFS may differ from those in patients with major depressive disorder. Randomized Controlled Trial
Wagner M, Gerhard R. F. Krueger, Dharam V. Ablashi, James E. Whitman		Chronic Fatigue Syndrome (CFS): A Critical Evaluation of Testing for Active Human Herpesvirus-6 (HHV-6) Infection Review of Data of 107 Cases	Journal of Chronic Fatigue Syndrome 1996: 2(4): 3 - 16	Aim: To conduct a virologic study in patients with chronic fatigue syndrome (CFS, ICD-10: G 93.3) for identification of reactivated human herpesvirus-6 (HHV-6) infection. Patients and Method: One hundred seven patients (60 women, 47 men, f/m ratio: 1.27/1; age: between 7 and 76 years, medium 41.8 years) with clinical CFS were studied with follow-up periods from 10 months to 7.5 years. Patients were recruited for the study by answering a standard questionnaire and by matching the Holmes' criteria for CFS. This was followed by physical examination, conventional hematological and chemistry testing, lymphocyte phenotyping, and control of other immunologic parameters. Testing for HHV-6 infection included indirect immunofluorescence assays (IFA), antigen capture enzyme linked immunosorbent assay (antigen capture ELISA, ACE), nested polymerase chain reaction (nPCR) on peripheral blood cells, and virus isolation. Results: HHV-6 seroprevalence in CFS patients was 97%. Seventy-two percent of the CFS patients had elevated serum anti-HHV-6 IgG titers, but active HHV-6 infection was detected in only 38.6% of the cases as identified by ACE, nPCR, and virus isolation. In absence of anti-HHV-6-IgM, anti-HHV-6-IgG titers were less reliable for monitoring virus activity. Among other infections EBV was seen in 19.6% of the cases and, less frequently, HSV, Chlamydia, Campylobacter, coxsackie, CMV, Yersinia or Candida. In 46% of the patients there were evident

				signs of immune deficiency. In additional 20% evidence was less clear (e.g., decreased lymphocyte stimulation: PHA/ConA 46%; low NK cell levels: 35%; and low CD4/CD8 cell ratio: 21%). Conclusion: Active HHV-6 infection was prevalent in one third of our CFS patients, much less than expected. Additional testing besides routine IFA is necessary for confirminig virus activity.
Ward MH, DeLisle H, Shores JH, Slocum PC, Foresman BH.	Department of Medicine, University of North Texas Health Science Center, Fort Worth, USA.	Chronic fatigue complaints in primary care: incidence and diagnostic patterns.	J Am Osteopath Assoc 1996 Jan;96(1):34-46, 41	The complaint of chronic fatigue is ubiquitous in the primary care setting. Because of the nonspecific nature of chronic fatigue, practitioners do not focus on this complaint. Furthermore, most physicians use a problem-based approach. Such a prematurely narrowed focus could overlook the chronic fatigue complaint. Omissions in the data collection process would prove this oversight. Therefore, we postulated that a retrospective review of evaluations for chronic fatigue would demonstrate significant categorical deficiencies. These deficiencies would indicate a problem focus different than the chronic fatigue complaint itself. The authors reviewed the current literature to establish historical, physical, and laboratory findings pertinent to the evaluation of chronic fatigue. Six major categories and the associated data elements were identified for use in analyzing patient records. The patient records from the preceding 6 months were reviewed to find those containing a complaint of chronic fatigue. These records were analyzed to determine if a complete data set had been sought and if an associated diagnosis was made. A total of 425 consecutive charts from an academic family practice clinic were retrospectively reviewed; 9.9% (42) mentioned chronic fatigue. Physicians were lax in performing the mental status and physical examinations; taking the patient's psychiatric and sleep history, as well as the history of chief complaint; and ordering laboratory evaluations. The physician diagnoses included: depression (40.4%), nonspecific fatigue (35.7%), general medical disorders (16.6%), chronic fatigue syndrome (2.4%), fibromyalgia (2.4%), and sleep apnea (2.4%). From these data, the investigators conclude that the workup for chronic fatigue is often incomplete or lacks documentation. This oversight is likely due to a problem focus not directed at the chronic fatigue complaints. Also complicating the evaluation process are the multiple associated disorders, the prevalence of the complaint, and cost/benefit issues facing the primary care physician.
Wearden AJ, Appleby L.	Department of Psychiatry, University Hospital of South Manchester, UK. awearden@psy.man.ac.uk	Research on cognitive complaints and cognitive functioning in patients with chronic fatigue syndrome (CFS): What conclusions can we draw?	J Psychosom Res 1996 Sep;41(3):197-211	People with chronic fatigue syndrome (CFS) complain of difficulties with concentration and memory yet studies suggest that they do not suffer gross deficits in cognitive functioning. Depressed patients make similar cognitive complaints, and there is symptomatic overlap between CFS and depression. Cognitive complaints and depressed mood are positively correlated in CFS patients but, except on tasks which are particularly sensitive to depression, cognitive performance and depression are not. The inconsistency between cognitive complaints and results of tests of cognitive functioning resembles that

				found in other subject groups and may be due in part to the inappropriate use of laboratory memory tests for assessing "everyday" cognitive functioning. Even when cognitive capacity is intact, cognitive performance may be affected by factors such as arousal, mood, and strategy. In CFS patients, everyday cognitive tasks may require excessive processing resources leaving patients with diminished spare attentional capacity or flexibility.
Wessely S, Chalder T, Hirsch S, Wallace P, Wright D.	Department of Psychological Medicine, King's College School of Medicine and Dentistry, London.	Psychological symptoms, somatic symptoms, and psychiatric disorder in chronic fatigue and chronic fatigue syndrome: a prospective study in the primary care setting.	Am J Psychiatry 1996 Aug;153(8):1050-9	OBJECTIVE: This study assessed relationships among psychological symptoms, past and current psychiatric disorder, functional impairment, somatic symptoms, chronic fatigue, and chronic fatigue syndrome. METHOD: A prospective cohort study was followed by a nested case-control study. The subjects, aged 18-45 years, had been in primary care for either clinical viral infections or a range of other problems. Questionnaire measures of fatigue and psychological symptoms were completed by 1,985 subjects 6 months later; 214 subjects with chronic fatigue were then compared with 214 matched subjects without fatigue. Assessments were made with questionnaires, interviews, and medical records of fatigue, somatic symptoms, psychiatric disorder, and functional impairment. RESULTS: Subjects with chronic fatigue were at greater risk than those without chronic fatigue for current psychiatric disorder assessed by standardized interview (60% versus 19%) or by questionnaire (71% versus 31%). Chronic fatigue subjects were more likely to have received psychotropic medication or experienced psychiatric disorder in the past. There was a trend for previous psychiatric disorder to be associated with comorbid rather than noncomorbid chronic fatigue. Most subjects with chronic fatigue syndrome also had current psychiatric disorder when assessed by interview (75%) or questionnaire (78%). Both the prevalence and incidence of chronic fatigue syndrome were associated with measures of previous psychiatric disorder. The number of symptoms suggested as characteristics of chronic fatigue syndrome was closely related to the total number of somatic symptoms and to measures of psychiatric disorder. Only postexertion malaise, muscle weakness, and myalgia were significantly more likely to be observed in chronic fatigue syndrome than in chronic fatigue. CONCLUSIONS: Most subjects with chronic fatigue or chronic fatigue syndrome in primary care also meet criteria for a current psychiatric disorder. Both chronic fatigue and chronic fatigue syndrome are associated with previous psychiatric disorder, partly explained by high rates of current psychiatric disorder. The symptoms thought to represent a specific process in chronic fatigue syndrome may be related to the joint experience of somatic and psychological distress.
Wessely S.	King's College School of Medicine and Dentistry, London.	Chronic fatigue syndrome. Summary of a report of a joint committee of the Royal	J R Coll Physicians Lond 1996 Nov-Dec;30(6):497-504	Chronic Fatigue Syndrome (CFS) is not a single diagnostic entity. It is a symptom complex which can be reached by many different routes. The conceptual model of CFS needs to be changed from one determined by a single cause/agent to one in which dysfunction is the end stage of a multifactorial process. Although it is

		Colleges of Physicians, Psychiatrists and General Practitioners.		important to recognise the role of factors that precipitate the condition, greater understanding is required of factors that predispose individuals to develop the illness, and those that perpetuate disability.
Wiebe E.	Department of Family Practice, University of British Columbia, Vancouver.	N of 1 trials. Managing patients with chronic fatigue syndrome: two case reports.	Can Fam Physician 1996 Nov;42:2214-7	Chronic fatigue syndrome is a heterogeneous condition with as proves effective treatment. I present two case reports in which N of 1 trials helped me make management decisions. High-dose vitamin B12 injections were ineffective in one case; nimodipine was very effective in the other case.
Wilhelmsen I, Bodtker J.		[Chronic fatigue syndrome and cognitive therapy].[article in Norwegian]	Tidsskr Nor Laegeforen 1996 May 20;116(13):1615 comment on: Tidsskr Nor Laegeforen. 1996 Mar 10;116(7):861-4 Tidsskr Nor Laegeforen. 1996 May 10;116(12):1503	
Williams DC.	Virginia-Carolina Sleep Disorders Center in Danville, USA.	Periodic limb movements of sleep and the restless legs syndrome.	Va Med Q 1996 Fall;123(4):260-5	Periodic limb movements of sleep and the restless legs syndrome are not diagnoses but rather an indication that there is some CNS disturbance and are associated with an ever-growing number of conditions. They are very common, exist in many forms and are often overlooked by physicians. It is the author's opinion that they are parts of what has been called an akathisia syndrome in the most severe situations and may include the same mechanisms that underlie attention disorders, chronic fatigue syndrome and "sun-downing." They are likely parts of a syndrome caused by dysfunction in a complex brainstem center. This center's normal function is to maintain a smooth electrical template on which discrete neuronal impulses sculpture the rich repertoire we recognize as sensory and motor function awake and to effect a smooth "switching" mechanism allowing sleep to occur without motor and sensory input invading consciousness (awakening). While the DA-ergic CNS pathways have been thought to be the primary neurotransmitter involved, the opioids secondary, there is mounting evidence that the situation is far more complicated, that many neurotransmitter, including stimulating and inhibiting amino acids, play a part. These patients agonize with their indisposition but can be helped by various treatments. Treatment alleviates not only the distress caused by the symptoms but also the devastating insomnia and excessive daytime sleepiness associated with it.
Williams G, Pirmohamed J, Minors D, Waterhouse J, Buchan I, Arendt J, Edwards RH.	Department of Medicine, University of Liverpool, UK.	Dissociation of body-temperature and melatonin secretion circadian rhythms in patients with chronic	Clin Physiol 1996 Jul;16(4):327-37	Many patients with chronic fatigue syndrome (CFS) display features of hypothalamic dysfunction. We have investigated aspects of circadian rhythmicity, an important hypothalamic function, in 20 CFS patients and in 17 age- and sex-matched healthy control subjects. There were no differences between the two groups in the amplitude, mesor (mean value) or timing of the peak (acrophase) of

		fatigue syndrome.		the circardian rhythm of core temperature, or in the timing of the onset of melatonin secretion. However, the CFS patients showed no significant correlation between the timing of the temperature acrophase and the melatonin onset ($P < 0.5$), whereas the normal significant correlation was observed in the controls ($P < 0.05$). Dissociation of circadian rhythms could be due to the sleep deprivation and social disruption, and/or the reduction in physical activity which typically accompany CFS. By analogy with jet-lag and shift-working, circadian dysrhythmia could be an important factor in initiating and perpetuating the cardinal symptoms of CFS, notably tiredness, impaired concentration and intellectual impairment.
Zorzenon M, Gull Rukh, Giuseppe A. Botta, Roberto Colle, Laura A. Barsanti , Luca Ceccherini-Nelli		Active HHV-6 Infection in Chronic Fatigue Syndrome Patients from Italy New Data	Journal of Chronic Fatigue Syndrome 1996: 2(1): 3 - 12	Primary Human Herpesvirus-6 (HHV-6) infection has been related to different clinical pictures and, notably, to Chronic Fatigue Syndrome (CFS). We studied 52 patients fulfilling the criteria of Centers for Disease Control (CDC) for CFS and a control group of 51 matched healthy blood donors. HHV-6 was recovered by culture and confirmed by immunofluorescence assay (IFA) and by PCR in 30/52 patients (57.7%) and in 6/51 (11.7%) of blood donors.

1995				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Ablashi DV, Kristine L. Ablashi, Bernhard Kramarsky, John Bernbaum, James E. Whitman , Gary R. Pearson		Viruses and Chronic Fatigue Syndrome Current Status	Journal of Chronic Fatigue Syndrome 1995: 1(2): 4 - 22	Because of the sudden onset of "flu-like" symptoms in he vast majority of cases, followed by persistent illness and fatigue over several years, bolh RNA (retroviruses) and DNA (herpesviruses and enteroviruses) viruses have been suspected to be implicated in the pathogenesis of CFS. In recent years, evidence of the association of some viruses wilh CFS has progressed, whereas, with some others it has weakened considerably. Thus far, no single virus has been found to be the causative agent of CFS. Reactivation, however, of latent virus or viruses could contribute to the symptomatology of CFS by damaging the immune system either directly or indirectly. In this report we have provided a comprehensive review of the status of research on viral agents which have been investigated for their role in the pathogenesis of CFS.
Arav-Boger R, Spirer Z.	Department of Pediatrics, Dana Children's Hospital, Tel Aviv Sourasky Medical Center, Israel.	Chronic fatigue syndrome: pediatric aspects.	988: Isr J Med Sci 1995 May;31(5):330-4	
Ash-Bernal R, Wall C 3rd, Komaroff AL, Bell D, Oas JG, Payman RN, Fagioli LR.	Department of Otology and Laryngology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, USA.	Vestibular function test anomalies in patients with chronic fatigue syndrome.	Acta Otolaryngol 1995 Jan;115(1):9-17	Chronic fatigue syndrome (CFS) is distinguished by the new onset of debilitating fatigue that lasts at least 6 months, concomitant with other symptoms to be described later. Many CFS patients complain of disequilibrium, yet the exact type of the balance dysfunction and its function and its location (peripheral vs. central) have not been described. Herein we report results of vestibular function testing performed on 11 CFS patients. These results revealed no predominant pattern of abnormalities. Patients typically performed below average in dynamic posturography testing, with a significant number of falls in the tests requiring subjects to depend heavily on the vestibular system. One patient had abnormal caloric testing, while 3 had abnormally low earth vertical axis rotation (EVA) gains at the higher frequencies tested. As a group, the average gain of EVA was significantly lower than normals in the 0.1 - 1.0 Hz range ($p < 0.05$). In earth horizontal axis rotation, the CFS group had a higher than normal bias value for the optokinetic (OKN) and eyes open in the dark conditions ($p < 0.05$), but had normal scores during visual vestibular reflex testing. Five of the 11 subjects had an abnormal OKN bias build up over the course of the run, equal to or actually exceeding the 60 degrees/s target velocity by as much as 14 degrees/s. Altogether, these results are more suggestive of central nervous system deficits than of peripheral vestibular disfunction.
Baschetti R.		Chronic fatigue syndrome and liquorice.	993: N Z Med J 1995 Apr 26;108(998):156-7 comment in: N Z Med J.	

			1995 Jun 14;108(1001):234-5	
Baschetti R.		Liquorice and chronic fatigue syndrome.	968: N Z Med J 1995 Jun 28;108(1002):259 comment in: N Z Med J. 1995 Aug 11;108(1005):324-5 comment on: N Z Med J. 1995 Jun 14;108(1001):234-5	
Baschetti R.		Viral illness and chronic fatigue (syndrome)	952: Lancet 1995 Jul 1;346(8966):47 comment on: Lancet. 1995 May 27;345(8961):1333-8	
Bates DW, Buchwald D, Lee J, Kith P, Doolittle T, Rutherford C, Churchill WH, Schur PH, Wener M, Wybenga D, et al.	Department of Medicine, Brigham and Women's Hospital, Boston, Mass.	Clinical laboratory test findings in patients with chronic fatigue syndrome.	Arch Intern Med 1995 Jan 9;155(1):97-103 comment in: Arch Intern Med. 1995 Jun 26;155(12):1332	BACKGROUND: Results of readily available clinical laboratory tests in patients with chronic fatigue syndrome were compared with results in healthy control subjects. METHODS: Cases consisted of all 579 patients who met either the Centers for Disease Control and Prevention, Atlanta, Ga, British, or Australian case definition for chronic fatigue syndrome. They were from chronic fatigue clinics in Boston, Mass, and Seattle, Wash. Control subjects consisted of 147 blood donors who denied chronic fatigue. Outcome measures were the results of 18 clinical laboratory tests. RESULTS: Age- and sex-adjusted odds ratios of abnormal results, comparing cases with control subjects, were as follows: circulating immune complexes, 26.5 (95% confidence interval [CI] 3.4-206), atypical lymphocytosis, 11.4 (95% CI, 1.4-94); elevated immunoglobulin G, 8.5 (95% CI, 2.0-37); elevated alkaline phosphatase, 4.2 (95% CI, 1.6-11); elevated total cholesterol, 2.1 (95% CI, 1.2-3.4); and elevated lactic dehydrogenase, 0.30 (95% CI, 0.16-0.56). Also, antinuclear antibodies were detected in 15% of cases vs 0% in the control subjects. The results of these tests were generally comparable for the cases from Seattle and Boston. Although these tests served to discriminate the population of patients from healthy control subjects, at the individual level they were not as useful. CONCLUSIONS: Patients with chronic fatigue syndrome who were located in two geographically distant areas had abnormalities in the results of several readily available clinical laboratory tests compared with healthy control subjects. The immunologic abnormalities are in accord with a growing body of evidence suggesting chronic, low-level activation of the immune system in chronic fatigue syndrome. While each of these laboratory findings supports the diagnosis of chronic fatigue syndrome, each lacks sufficient sensitivity to be a diagnostic test. Furthermore, the specificity of

				these findings relative to other organic and psychiatric conditions that can produce fatigue remains to be established.
Bearn J, Allain T, Coskeran P, Munro N, Butler J, McGregor A, Wessely S.	Department of Psychiatry, Institute of Psychiatry, London, UK.	Neuroendocrine responses to d-fenfluramine and insulin-induced hypoglycemia in chronic fatigue syndrome.	Biol Psychiatry 1995 Feb 15;37(4):245-52	Chronic fatigue syndrome (CFS) is a disorder characterized by severe physical and mental fatigue and fatiguability of central rather than peripheral origin. We hypothesized that CFS is mediated by changes in hypothalamopituitary function and so measured the adrenocorticotrophic hormone (ACTH), cortisol, growth hormone, and prolactin responses to insulin-induced hypoglycemia, and the ACTH, cortisol, and prolactin responses to serotoninergic stimulation with dexfenfluramine in nondepressed CFS patients and normal controls. We have shown attenuated prolactin responses to hypoglycemia in CFS. There was also a greater ACTH response and higher peak ACTH concentrations (36.44 +/- 4.45 versus 25.60 +/- 2.78 pg ml), whereas cortisol responses did not differ, findings that are compatible with impaired adrenal cortical function. This study provided evidence for both pituitary and adrenal cortical impairment in CFS and further studies are merited to both confirm and determine more precisely their neurobiological basis so that rational treatments can be evolved.
Bell DS		Chronic Fatigue Syndrome in Children	Journal of Chronic Fatigue Syndrome 1995: 1(1): 9 - 33	Chronic fatigue syndrome (CFS), formerly called chronic Epstein-Barr virus syndrome, chronic mononucleosis, and numerous other names, is a symptom complex characterized by marked functional limitation which affects children as well as adults. The symptom complex, physical examination, laboratory evaluation, clinical course, and differential diagnosis are reviewed with particular emphasis upon CFS in children. Management consists of a comprehensive treatment plan including medical, educational, and psychosocial support wiih the aim of reducing both symptom and activity limitation. While etiology is unknown, the use of the term "chronic fatigue syndrome" is appropriate for children with marked functional limitation due to unexplained fatigue who have the associated symptom complex and physical examination findings characteristic of this condition.
Bell DS		Diagnosis of Chronic Fatigue Syndrome in Children and Adolescents: Special Considerations	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 29 - 36	It has been a common occurrence that children with chronic, unexplained fatigue receive no specific diagnosis because of difficulties posed by the 1988 research criteria for chronic fatigue syndrome (CFS). The lack of a specific diagnosis creates medical uncertainty and may lead to increased psychosocial and educational disruption. With the recent publication of new research criteria these problems may be improved as the new criteria are less restrictive. In the process of developing new research criteria, data was collected for children who presented for evaluation of chronic unexplained fatigue over a two year period. Diagnosis of CFS was based upon the 1988 CDC criteria or clinical criteria based upon activity limitation and the associated symptom complex. Comparison of these two groups showed differences in symptom severity and degree of activity limitation, while demographics, psychosocial variables, and symptom pattern were similar. These

				results would suggest that chronic fatigue syndrome exists in a continuum of severity and that definition based solely upon severity of fatigue is arbitrary. While severe and debilitating fatigue should remain the basis of any research definition, clinical criteria based upon the symptom pattern of CFS may improve long term management by providing a working clinical diagnosis.
Berelowitz GJ, Burgess AP, Thanabalasingham T, Murray-Lyon IM, Wright DJ.	Department of Psychiatry, Charing Cross Hospital, London, UK.	Post-hepatitis syndrome revisited.	J Viral Hepat 1995;2(3):133-8	To examine the role of acute hepatitis A and B infection in the aetiology of chronic fatigue syndrome and psychiatric morbidity we studied 40 patients with acute viral hepatitis A or B consecutively admitted to an infectious diseases unit and studied at least 6 months after recovery. Liver function tests (LFT) had returned to normal in each case. Forty-seven patients with other infectious diseases, of which 12 were presumed viral, admitted immediately after each hepatitis patient during the same period acted as controls. The main outcome measures were scores on a fatigue and muscle pain questionnaire, general health questionnaire (GHQ-12) and supplementary questions. The hepatitis cases scored significantly higher fatigue scores, GHQ-12 scores and muscle pain scores. Length of time since recovery from illness, age and sex were not confounding factors. Hepatitis cases were also less energetic, had greater weight change, had altered alcohol tolerance, had less exercise tolerance and felt less fit than the control group and compared with their premorbid state. Hence fatigue is more common after recovery in patients hospitalized for hepatitis A and B up to 30 months post-infection compared with matched controls hospitalized for other infectious diseases. Hepatitis A and B infection is a risk factor for post-infection fatigue, intermittent fatigue, as well as for psychiatric morbidity.
Berman BM		Alternative Medicine: Part of the Mainstream	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 41 - 45	
Bianchedi M, Croce A, Moretti A, Neri G, Barberio A, Iezzi A, Pizzigallo E.	Clinica Otorinolaringoiatrica, Universita, G. D'Annunzio di Chieti.	[Auditory brain stem evoked potentials in the evaluation of chronic fatigue syndrome].[article in Italian]	908: Acta Otorhinolaryngol Ital 1995 Dec;15(6):403-10	The Chronic Fatigue Syndrome (CFS) was formally defined to describe disabling fatigue of multifactorial ethology with depression and immunologic dysfunctions linked to some currently recognized infectious agents. In most cases neurophysiological tests reveal abnormalities. In this paper the Authors use low (11 pps) and high (51-71 pps) frequency ABR to evaluate the electrophysiological function of auditory brainstem responses. Eighteen patients with suspected CFS, between the ages of 17 and 63, were examined. Eleven subjects had clinically diagnosed "true" CFS (CDC criteria modified by Fukuda). The 11 pps frequency test did not reveal a high number of abnormalities in the patients in question. However, the high frequency stimulation test (with 51 and 71 pps) which was statistically significant (P = 0.009) revealed numerous aberrations in 7 patients; absence of the first wave in 1 case, in 5 numerous wave gap delays and in 1 patient absence of the first wave and numerous wave gap delays. The high frequency test did not show many abnormalities for the 4 remaining patients. For

				the 7 "non CFS" subjects, the clinical-audiological comparison showed no statistical significance (P = 0.920). The Authors hypothesize that the absence of the first wave in the CFS Subject may well indicate a cyto-neural junction disease in the organ of Corti. The combined analysis of clinical and audiological data showed that the described tests are more reliable when employed in dealing with patients with clinically assessed "true" CFS.
Boda WL, Natelson BH, Sisto SA, Tapp WN.	Department of Physical Medicine and Rehabilitation, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, East Orange, USA.	Gait abnormalities in chronic fatigue syndrome.	948: J Neurol Sci 1995 Aug;131(2):156-61	To evaluate our clinical impression that patients with the chronic fatigue syndrome (CFS) did not walk normally, we assessed gait kinematics at slow walking speeds (i.e., 0.45, 0.89 and 1.34 m/sec) and 30 m run time speeds on CFS patients and on a comparison group of sedentary controls. Run time was significantly slower for CFS than control subjects ($p < 0.001$). There was a significant interaction ($p < 0.01$) between group and speed for maximum hip angle during stance and swing phase with hip angle being significantly larger at 1.34 m/sec for CFS than controls subjects for both cases ($p < 0.05$). Knee flexion during stance and swing phases was significantly larger for controls than CFS subjects at 0.45 m/sec ($p < 0.01$). Ratio of stride length divided by leg length was significantly larger for the control subjects than for the CFS subjects with differences occurring at 0.45 and 0.89 m/sec ($p < 0.01$) but not 1.34 m/sec. The data indicate that CFS patients have gait abnormalities when compared to sedentary controls. These could be due to balance problems, muscle weakness, or central nervous system dysfunction; deciding which will require further research. Evaluation of gait may be a useful tool to measure outcome following therapeutic interventions.
Bohr TW.	Department of Neurology, Loma Linda University School of Medicine, California, USA.	Fibromyalgia syndrome and myofascial pain syndrome. Do they exist?	991: Neurol Clin 1995 May;13(2):365-84	"It is in the healing business that the temptations of junk science are the strongest and the controls against it the weakest." Despite their subjective nature, these syndromes (particularly MPS) have little reliability and validity, and advocates paint them as "objective." Despite a legacy of poor-quality science, enthusiasts continue to cite small, methodologically flawed studies purporting to show biologic variables for these syndromes. Despite a wealth of traditional pain research, disciples continue to ignore the placebo effect, demonstrating a therapeutic hubris despite studies showing a dismal natural history for FS. In reviewing the literature on MPS and FS, F.M.R. Walshe's sage words come to mind that the advocates of these syndromes are "better armed with technique than with judgment." A sympathic observer might claim that labeling patients with monikers of nondiseases such as FS and MPS may not be such a bad thing. After all, there is still a stigma for psychiatric disease in our society, and even telling a sufferer that this plays only a partial role may put that patient on the defensive. Labeling may have iatrogenic consequences, however, particularly in the setting of the work place. Furthermore, review of a typical support group newsletter gives ipso facto proof of this noxious potential. The author of a flyer

				stuffed inside the newsletter complains that getting social security and disability benefits for "the invisible disability" can be "an uphill battle. But don't loose (sic) hope." Apparently the "seriousness of the condition" is not appreciated by the medical community at large, and "clinician bias may well be the largest threat," according to Boston epidemiologist Dr. John Mason. Sufferers are urged to trek to their local medical library and pull four particular articles claiming FS patients have more "stress," "daily hassles," and difficulty working compared with arthritis patients. If articles can't be located, patients are told to ask their lawyers for help. Although "Chronic Fatigue Syndrome" and FS are not considered by everyone to be the same malady, the "National Institute of Health (sic) has lumped these two conditions together. This could work in your favor." (A U.S. political advocacy packet is available for $8, but a list of U.S. senators with Washington, DC addresses is freely provided.) These persons see themselves as victims worthy of a star appearance on the Oprah Winfrey show. A sense of bitterness emerges; one literally bed-bound Texas homemaker writes in Parents magazine that "Some doctors may give up and tell you that you are a hypochondriac."(ABSTRACT TRUNCATED AT 400 WORDS)
Bombardier CH, Buchwald D.	Department of Rehabilitation Medicine, University of Washington School of Medicine, Seattle, USA.	Outcome and prognosis of patients with chronic fatigue vs chronic fatigue syndrome.	920: Arch Intern Med 1995 Oct 23;155(19):2105-10	BACKGROUND: There are few data on the natural history and prognosis of persons with chronic fatigue (CF) or CF syndrome (CFS). Therefore, we compared functional outcomes in patients with each condition and tested the validity of various prognostic indicators. METHODS: Four hundred forty-five (89%) of 498 consecutive referral patients were surveyed an average of 1.5 years after an initial evaluation. Data from the initial evaluation were used to predict outcomes. RESULTS: Sixty-four percent of all patients reported improvement, but only 2% reported complete resolution of symptoms. Patients initially diagnosed as having CFS reported greater symptom severity and lower level of functioning at follow-up than did patients with CF. Major depression predicted unemployment in the CF group. Older age, longer duration of illness, and a lifetime history of dysthymia predicted less improvement in the CF group. Current dysthymia predicted less improvement for the CFS group. CONCLUSIONS: The case definition of CFS according to the Centers for Disease Control and Prevention identifies chronically fatigued patients with poorer prognosis. In a tertiary care setting, recovery from CF or CFS is rare, but improvement is common. Prognostic indicators vary for the two groups, but the coexistence of dysthymia suggests poorer outcomes generally.
Bou-Holaigah I, Rowe PC, Kan J, Calkins H.	Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Md, USA.	The relationship between neurally mediated hypotension and the chronic fatigue syndrome.	931: JAMA 1995 Sep 27;274(12):961-7 comment in: JAMA. 1996 Feb 7;275(5):359-60 JAMA. 1996 Feb	OBJECTIVE--To compare the clinical symptoms and response evoked by upright tilt-table testing in healthy individuals and in a sample of those satisfying strict criteria for chronic fatigue syndrome. DESIGN--Case-comparison study with mean (SD) follow-up of 24 (5) weeks. SETTING--Tertiary care hospital. PATIENTS AND OTHER PARTICIPANTS--A sample of 23 patients with chronic fatigue syndrome

			7;275(5):359; discussion 360	(five men and 18 women; mean age, 34 years), each of whom fulfilled the strict diagnostic criteria of the Centers for Disease Control and Prevention, was recruited from regional chronic fatigue support groups and from the investigators' clinical practices. There were 14 healthy controls (four men and 10 women; mean age, 36 years). INTERVENTIONS--Each subject completed a symptom questionnaire and underwent a three-stage upright tilt-table test (stage 1, 45 minutes at 70 degrees tilt; stage 2, 15 minutes at 70 degrees tilt with 1 to 2 micrograms/min of isoproterenol; and stage 3, 10 minutes at 70 degrees with 3 to 4 micrograms/min of isoproterenol). Patients were offered therapy with fludrocortisone, beta-adrenergic blocking agents, and disopyramide, alone or in combination, directed at neurally mediated hypotension. MAIN OUTCOME MEASURES--Response to upright tilt and scores on symptom questionnaires prior to and during follow-up. RESULTS--An abnormal response to upright tilt was observed in 22 of 23 patients with chronic fatigue syndrome vs four of 14 controls ($P < .001$). Seventy percent of chronic fatigue syndrome patients, but no controls, had an abnormal response during stage 1 ($P < .001$). Nine patients reported complete or nearly complete resolution of chronic fatigue syndrome symptoms after therapy directed at neurally mediated hypotension. CONCLUSIONS--We conclude that chronic fatigue syndrome is associated with neurally mediated hypotension and that its symptoms may be improved in a subset of patients by therapy directed at this abnormal cardiovascular reflex.
Buchwald D, Umali P, Umali J, Kith P, Pearlman T, Komaroff AL.	University of Washington, Seattle, USA.	Chronic fatigue and the chronic fatigue syndrome: prevalence in a Pacific Northwest health care system.	951: Ann Intern Med 1995 Jul 15;123(2):81-8	OBJECTIVES: To investigate the point prevalence of the chronic fatigue syndrome and unexplained debilitating chronic fatigue in a community-based sample of persons and to describe demographic, clinical, and psychosocial differences among those with the chronic fatigue syndrome, those with chronic fatigue, and healthy controls. DESIGN: Prospective cohort study. SETTING: A health maintenance organization in Seattle, Washington. PARTICIPANTS: A random sample of 4000 members of the health maintenance organization was surveyed by mail for the presence of chronic fatigue. MEASUREMENTS: Persons with chronic fatigue were evaluated using a questionnaire that requested information about medical history and fatigue and related symptoms; validated measures of functional status and psychological distress; a physical examination; and standardized blood tests. A structured psychiatric interview was done in persons who appeared to meet the original Centers for Disease Control and Prevention (CDC) criteria for the chronic fatigue syndrome. Participants completed self-report measures at 12 and 24 months. Those with chronic fatigue were reevaluated in person 1 year after study enrollment. RESULTS: 3066 (77%) of the 4000 members surveyed responded. Chronic fatigue was reported by 590 persons (19%). Of these, 388 (66%) had a medical or psychiatric condition that could account for the fatigue. Of the 74 persons (37%) with chronic fatigue who

				were enrolled in the study, only 3 met the CDC criteria for the chronic fatigue syndrome. The remaining 71 persons were designated as having chronic fatigue alone. Seventy-four healthy, age- and sex-matched controls who were drawn from the same sample but who denied having chronic fatigue were also studied. Demographic characteristics were similar in persons with the chronic fatigue syndrome, persons with chronic fatigue alone, and controls. Those with the chronic fatigue syndrome or chronic fatigue alone had more frequent cervical and axillary adenopathy, poorer functional status, and greater psychological distress than controls. Women and minorities were not overrepresented among cases with chronic fatigue. CONCLUSIONS: Using different assumptions about the likelihood that persons who did not participate in the study had the chronic fatigue syndrome, the estimated crude point prevalence of the syndrome in this community ranged from 75 to 267 cases per 100,000 persons. The point prevalence of chronic fatigue alone was strikingly higher; it ranged from 1775 to 6321 cases per 100,000 persons.
Campion PD, Dowrick CF, Edwards RH.		Illness behaviour in the chronic fatigue syndrome and multiple sclerosis. Choice of multiple sclerosis as comparison condition was inappropriate.	922: BMJ 1995 Oct 21;311(7012):1092-3 comment on: BMJ. 1995 Jul 1;311(6996):15-8	
Cater RE 2nd.		Chronic intestinal candidiasis as a possible etiological factor in the chronic fatigue syndrome.	984: Med Hypotheses 1995 Jun;44(6):507-15	The chronic candidiasis syndrome, also known as the Candida-related complex, putatively caused by the overgrowth of Candida albicans in the gastrointestinal tract and secondarily in the genital organs, is briefly described. Patients with this disorder have many of the same symptoms as those with the chronic fatigue syndrome, except for the recurrent flu-like symptoms of the latter disorder. The positive response of a large number of patients with the chronic fatigue syndrome (CFS) to an oral antifungal agent and a diet for intestinal candidiasis has been described by another clinician. There is evidence that Candida albicans infection of the mucous membranes depresses T cell and natural killer (NK) cell function. Similar abnormalities of immune function are found in the CFS. The function of cytotoxic T cells, T helper cells, and NK cells is important in preventing reactivation of infections from Epstein-Barr virus, cytomegalovirus, and other herpesviruses. Reactivation of one or more of these viruses could lead to the expression of the flu-like symptoms in the CFS. Yet the immune dysfunction found in this disorder has been considered the primary underlying causal factor. It is proposed that chronic intestinal candidiasis may be an agent which leads to immune depression in many CFS patients and therefore that it could be a causal factor in CFS.

Chalder T, Deale A, Wessely S, Marks I.		Cognitive behavior therapy for chronic fatigue syndrome.	996: Am J Med 1995 Apr;98(4):419-20; discussion 421-2 comment on: Am J Med. 1993 Feb;94(2):197-203	
Chalder T, Deale A, Wessely S.		Cognitive behavioral therapy for chronic fatigue syndrome.	Clin Infect Dis 1995 Mar;20(3):717-8 comment on: Clin Infect Dis. 1994 Jan;18 Suppl 1:S105-10	
Chalder T, Wessely S, Wallace P, Hirsch S, Wright D.		Viral illness and chronic fatigue (syndrome)	941: Lancet 1995 Aug 12;346(8972):449 comment on: Lancet. 1995 Jul 1;346(8966):47 Lancet. 1995 Jul 1;346(8966):47-8 Lancet. 1995 Jul 1;346(8966):48	
Chalder T.		Chronic fatigue syndrome.	924: Br J Psychiatry 1995 Oct;167(4):549-50 comment on: Br J Psychiatry. 1995 Jun;166(6):798-801	
Clark MR, Katon W, Russo J, Kith P, Sintay M, Buchwald D.	Department of Psychiatry and Behavioral Sciences, Johns Hopkins Hospital, Baltimore, Maryland 21287-5371.	Chronic fatigue: risk factors for symptom persistence in a 2 1/2-year follow-up study.	Am J Med 1995 Feb;98(2):187-95	BACKGROUND: The prolonged disability of patients suffering from chronic fatigue may be due to sustaining factors that are independent of the cause and subject to intervention. This study reexamined a cohort of patients with chronic fatigue to define medical and psychiatric predictors of persistent symptoms. METHODS: Seventy-eight patients with chronic fatigue present for 6 months or more (not required to meet the Centers for Disease Control case definition for chronic fatigue syndrome [CFS]) completed a self-report, follow-up questionnaire to measure the overall improvement or worsening of their condition at a mean of 2.5 years after their initial examination. At the time of initial evaluation, patients underwent a structured psychiatric examination, physical examination, laboratory studies, and self-report measures of psychological distress and functional disability. The psychiatric examination queried the patient about 28 somatic symptoms that are separate from those associated with CFS. Discriminant analysis was used to determine which variables present at the initial examination were significant predictors of persistent symptoms and disability at 2.5 years. RESULTS: The factors most important at the time of initial presentation in predicting persistent illness were: (1) more than eight medically unexplained

				physical symptoms separate from those associated with CFS case definition; (2) lifetime history of dysthymia; (3) duration of chronic fatigue symptoms greater than 1.5 years; (4) less than 16 years of formal education; and (5) age older than 38 years. None of the results of the initial physical examination, or immunologic, general laboratory, or viral antibody measurements were significant in predicting persistence of symptoms. Recovery rates for those who met the criteria for CFS by either of two case definitions were lower than the rate of noncases, but the differences were not statistically significant. The five aforementioned variables formed a significant discriminative function, correctly classifying 78% of those who recovered and 74% of those with persistent symptoms. CONCLUSIONS: At initial examination, patients with chronic fatigue, more than eight medically unexplained physical symptoms (excluding symptoms in the case criteria for CFS), a lifetime history of dysthymic disorder, longer than 1.5 years of chronic fatigue, less than 16 years of formal education, and who were older than 38 years were the most likely to have persistence of symptoms of chronic fatigue at the 2.5-year follow-up.
Clauw DJ.	Georgetown University Medical Center, Washington, DC 20007, USA.	The pathogenesis of chronic pain and fatigue syndromes, with special reference to fibromyalgia.	987: Med Hypotheses 1995 May;44(5):369-78	Syndromes characterized by chronic pain and fatigue have been described in the medical literature for centuries. Fibromyalgia is the term currently used to describe this symptom complex, and considerable research has been performed in the last decade to delineate the epidemiology, pathophysiology, and genesis of this entity. Although fibromyalgia is defined by its musculoskeletal features, it is clear that there are a large number of non-musculoskeletal symptoms, such that we now understand that there is considerable overlap with allied conditions such as the chronic fatigue syndrome, migraine and tension headaches, irritable bowel syndrome, and affective disorders. This article will review our current state of knowledge regarding fibromyalgia and these allied conditions, and present a unifying hypothesis that describes both the pathophysiology of symptoms and the genesis of these disorders.
Cleare AJ, Bearn J, Allain T, McGregor A, Wessely S, Murray RM, O'Keane V.	Maudsley Hospital, Denmark Hill, London, UK.	Contrasting neuroendocrine responses in depression and chronic fatigue syndrome.	940: J Affect Disord 1995 Aug 18;34(4):283-9	Hypothalamic-pituitary-adrenal (HPA) axis and central 5-HT function were compared in chronic fatigue syndrome (CFS), depression and healthy states. 10 patients with CFS and 15 patients with major depression were matched for age, weight, sex and menstrual cycle with 25 healthy controls. Baseline-circulating cortisol levels were highest in the depressed, lowest in the CFS and intermediate between the two in the control group (P = 0.01). Prolactin responses to the selective 5-HT-releasing agent d-fenfluramine were lowest in the depressed, highest in the CFS and intermediate between both in the healthy group (P = 0.01). Matched pair analysis confirmed higher prolactin responses in CFS patients than controls (P = 0.05) and lower responses in depressed patients than controls (P = 0.003). There were strong inverse correlations between prolactin and cortisol responses and baseline cortisol values. These data confirm that depression is

				associated with hypercotisolaemia and reduced central 5-HT neurotransmission and suggest that CFS may be associated with hypocortisolaemia and increased 5-HT function. The opposing responses in CFS and depression may be related to reversed patterns of behavioural dysfunction seen in these conditions. These findings attest to biological distinctions between these disorders.
Committee for Science and Education, Medical Association of South Africa.		Chronic fatigue syndrome.	946: S Afr Med J 1995 Aug;85(8):780-2 comment in: S Afr Med J. 1996 Oct;86(10):1301	OBJECTIVE: To acknowledge the clinical syndrome chronic fatigue syndrome (CFS) and outline the diagnostic criteria and reasonable management. OUTCOMES: Attempt at containment of treatment cost and improvement of the quality of care of patients with CFS. EVIDENCE: Delphi-type commentary from 20 expert clinicians and appropriate organisations. Limited literature survey. VALUES: To clarify the reasonable management of CFS amid conflicting clinical opinion on a condition of concern to patients, funders and doctors. An adaptation of an existing guideline was sent to organisations and individuals for comment. Comments received were included in this guideline where possible. BENEFITS, HARMS AND COSTS. To acknowledge a clinical syndrome with a reasonable approach to management considering the cost implications. No cost analysis was done. RECOMMENDATIONS: To recommend the following: (i) diagnostic criteria for CFS; (ii) potential differential diagnoses and possible investigations; and (iii) management protocol. VALIDATION: The draft guidelines were subjected to external review by individual doctors who are acknowledged CFS treaters, doctor groups and the patient support group. There were major disputes about the content, with the responses falling into two groups: those who do not believe CFS is a distinguishable illness, and those who do. DEVELOPER AND FUNDING: The Committee for Science and Education, Medical Association of South Africa. ENDORSEMENTS: Medical Association of South Africa and national health care organisations (see list at the end of the document).
Cope H, David A, Pelosi A, Mann A.		Chronic fatigue syndrome.	Lancet 1995 Jan 14;345(8942):131 comment on: Lancet. 1994 Nov 26;344(8935):1514	
Cope H, Pernet A, Kendall B, David A.	Section of Neuropsychiatry, Institute of Psychiatry, London.	Cognitive functioning and magnetic resonance imaging in chronic fatigue.	965: Br J Psychiatry 1995 Jul;167(1):86-94	BACKGROUND. This study examines whether cognitive dysfunction in chronic fatigue may be accounted for by depression and anxiety or is due to brain pathology evident on magnetic resonance imaging (MRI). METHOD. Twenty-six subjects with chronic fatigue, with and without coexisting depression, and 18 age-matched normal controls were recruited from primary care following a presumed viral illness six months previously. Comparison was made with 13 psychiatric controls with depressive illness on standardised cognitive tests. MRI determined the presence of cerebral white-matter lesions. RESULTS. No substantial differences in performance were shown between subjects with

				chronic fatigue, most of whom met the criteria for chronic fatigue syndrome, and controls. Subjective cognitive dysfunction increased with psychopathology. White-matter lesions were found in a minority from all groups. Improvement in fatigue and depression coincided with improved performance on cognitive measures. CONCLUSIONS. Subjective complaints of cognitive impairment are a prominent feature of chronic fatigue, but objective cognitive and MRI abnormalities are not. Such complaints probably reflect psychopathology rather than a post-viral process.
Costa DC, Tannock C, Brostoff J.	Department of Psychiatry, UCL Medical School, London, UK.	Brainstem perfusion is impaired in chronic fatigue syndrome.	918: QJM 1995 Nov;88(11):767-73 comment in: QJM. 1996 Feb;89(2):163-4	We looked for brain perfusion abnormalities in patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). An initial pilot study revealed widespread reduction of regional brain perfusion in 24 ME/CFS patients, compared with 24 normal volunteers. Hypoperfusion of the brainstem (0.72 +/- 0.05 vs. 0.80 +/- 0.04, $p < 0.0001$) was marked and constant. We then tested whether perfusion to the brainstem in ME/CFS patients differs from that in normals, patients with major depression, and others with epilepsy. Data from a total of 146 subjects were included in the present study: 40 normal volunteers, 67 patients with ME/CFS (24 in the pilot study, 16 with no psychiatric disorders, 13 with ME/CFS and depression, 14 with ME/CFS and other psychiatric disorders), 10 epileptics, 20 young depressed patients and 9 elderly depressed individuals. Brain perfusion ratios were calculated using 99Tcm-hexamethylpropylene amine oxime (99Tcm-HMPAO) and single-photon emission tomography (SPET) with a dedicated three-detector gamma camera computer/system (GE Neurocam). Brain-stem hypoperfusion was confirmed in all ME/CFS patients. Furthermore, the 16 ME/CFS patients with no psychiatric disorders and the initial 24 patients in the pilot study showed significantly lower brainstem perfusion (0.71 +/- 0.03) than did depressed patients (0.77 +/- 0.03; ANOVA, $p < 0.0001$). Patients with ME/CFS have a generalized reduction of brain perfusion, with a particular pattern of hypoperfusion of the brainstem.
Cuellar ML, Gluck O, Molina JF, Gutierrez S, Garcia C, Espinoza R.	Department of Medicine, LSU Medical Center at New Orleans, USA.	Silicone breast implant--associated musculoskeletal manifestations.	915: Clin Rheumatol 1995 Nov;14(6):667-72	Three hundred consecutive women with silicone breast implants (SBI), referred to the arthritis clinic with a variety of musculoskeletal complaints, were evaluated for the presence of underlying connective tissue disease. A complete history and physical examination were performed, as well as laboratory testing for C-reactive protein, rheumatoid factor; and autoantibody determination by indirect immunofluorescence and immunodiffusion. The group mean age was 44.4 years (range 25-69), the mean time from initial implant surgery to appearance of symptoms was 6.8 years (range: 6m-19y) and 83.3% of women studied had clinical manifestations highly suggestive of an underlying connective tissue disorder. Fifty-four percent met criteria for fibromyalgia and/or chronic fatigue syndrome, distinct connective tissue diseases was detected in 11%, undifferentiated connective tissue disease or human adjuvant disease was found

				in 10.6%, and a variety of disorders such as angioneurotic oedema, frozen shoulder, multiple sclerosis-like syndrome were present. Several other miscellaneous conditions including recurrent unexplained low grade fever, hair loss, skin rash, sicca symptoms, Raynaud's phenomenon, carpal tunnel syndrome, memory loss, headaches, chest pain, and shortness of breath were also seen accompanying specific and non-specific conditions. Seventy percent of patients who underwent explanation of the implants reported improvement of their systemic symptomatology. A significant proportion of SBI patients referred for rheumatic evaluation have clinical manifestations highly suggestive of an underlying connective tissue disease. Furthermore, improvement of their symptomatology follows explanation of the implants in over half of the patients.
David A, Cope H, Pelosi A, Mann A.		Viral illness and chronic fatigue (syndrome)	964: Lancet 1995 Jul 1;346(8966):47 comment in: Lancet. 1995 Aug 12;346(8972):449 comment on: Lancet. 1995 May 27;345(8961):1333-8	
DeLuca J, Johnson SK, Beldowicz D, Natelson BH.	Department of Research and Psychology, Kessler Institute for Rehabilitation, West Orange, New Jersey.	Neuropsychological impairments in chronic fatigue syndrome, multiple sclerosis, and depression.	J Neurol Neurosurg Psychiatry 1995 Jan;58(1):38-43	To examine the degree and nature of cognitive impairments in chronic fatigue syndrome, a comprehensive neuropsychological battery was given to patients with chronic fatigue syndrome, multiple sclerosis, depressed patients, and healthy controls. The battery included tests of attention and concentration, information processing speed, verbal and visual memory, intellectual ability, and concept formation. Measures of depression and anxiety were also obtained. The chronic fatigue syndrome group did not differ from the depressed group in overall neuropsychological performance, but differed from the multiple sclerosis and control groups. The most significant impairment was in information processing speed in the chronic fatigue syndrome group. Depression and anxiety were not related to neuropsychological performance. The influence of reduced information processing on other areas of cognition is discussed.
DeLuca J, Karen B. Schmaling		Neurocognitive Testing in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 21 - 26	
Di Luca D, Zorzenon M, Mirandola P, Colle R, Botta GA, Cassai E.	Institute of Microbiology, University of Ferrara, Italy.	Human herpesvirus 6 and human herpesvirus 7 in chronic fatigue syndrome.	976: J Clin Microbiol 1995 Jun;33(6):1660-61	We analyzed lymphocytes of patients with chronic fatigue syndrome (CFS) for the presence of human herpesvirus 6 (HHV-6) and HHV-7 DNA. HHV-7 was present in over 80% of CFS patients and healthy controls, while the prevalence of HHV-6 variant A increased significantly in CFS cases (22 versus 4%; P = 0.05).
Dobbins JG, Benjamin Natelson, Ira Brassloff,		Physical, Behavioral, and Psychological Risk	Journal of Chronic Fatigue Syndrome 1995:	In spite of the distinct epidemiologic features of chronic fatigue syndrome, its cause remains unknown and no risk factors for the illness have been identified. In

Susan Drastal, Sue-Ann Sisto		Factors for Chronic Fatigue Syndrome A Central Role for Stress?	1(2): 43 - 58	order to better characterize CFS, we conducted a case-control study of well-defined CFS cases to identify physical, behavioral, and psychological factors related to the occurrence of CFS. The study, conducted in the metropolitan area surrounding Newark, New Jersey, USA, included 20 patients who fulfilled the CFS case definition and 20 matched controls. All subjects completed a self-administered questionnaire. The greatest difference between cases and controls was the reported level of stress from any of five sources in the 5 years prior to onset of illness (95% vs. 55%; P = 0.01 1). In addition, the risk of CFS was significantly related to the number of sources of stress, especially
Dodge JH, Kita MW.		The chronic fatigue syndrome.	960: Ann Intern Med 1995 Jul 1;123(1):75; discussion 76 comment on: Ann Intern Med. 1994 Dec 15;121(12):953-9	
Dunstan RH, Donohoe M, Taylor W, Roberts TK, Murdoch RN, Watkins JA, McGregor NR.	Department of Biological Sciences, University of Newcastle, NSW.	A preliminary investigation of chlorinated hydrocarbons and chronic fatigue syndrome.	934: Med J Aust 1995 Sep 18;163(6):294-7	OBJECTIVE: To determine whether serum levels of chlorinated hydrocarbons are elevated in patients with chronic fatigue syndrome. METHODS: Chlorinated hydrocarbon levels were measured in 22 patients with chronic fatigue syndrome (CFS) (as defined by the Centers for Disease Control [CDC]); in 17 patients with CFS symptoms whose history of exposure to toxic chemicals excluded them from the research definition of CFS; and in 34 non-CFS control subjects matched for age and sex. RESULTS: DDE (1,1-dichloro-2,2-bis (p-chlorophenyl) ethene) was detected in all serum samples at levels over 0.4 ppb. The incidence of hexachlorobenzene (HCB) contamination (> 2.0 ppb) was 45% in the CFS group, compared with 21% in the non-CFS control group (P < 0.05). The CFS group had a significantly higher total organochlorine level (15.9 ppb; SEM, 4.4) than the control group (6.3 ppb; SEM, 1.1; P < 0.05). The toxic exposure group also had a higher mean organochlorine level (13.6 ppb; SEM, 6.2) than the control group, but the difference was not statistically significant. DDE and HCB comprised more than 90% of the total organochlorines measured in each of the groups. CONCLUSION: The results suggest that recalcitrant organochlorines may have an aetiological role in CFS. There were no significant differences in serum organochlorine concentrations between CFS patients and chronic fatigue patients with a history of toxic chemical exposure. Therefore, exclusion of patients from the CDC research definition of CFS on the basis of a reported history of known exposure to toxic chemicals is not valid. The role of low-level organochlorine bioaccumulation in the development of CFS symptoms requires further investigation.
Farmer A, Jones I, Hillier J, Llewelyn M,	Department of Psychological Medicine,	Neuraesthenia revisited: ICD-10 and DSM-III-R	925: Br J Psychiatry 1995 Oct;167(4):503-6	BACKGROUND: Different definitions of chronic fatigue syndrome (CFS) have different psychiatric exclusion criteria and this affects the type and frequency of

Borysiewicz L, Smith A.	University of Wales College of Medicine, Heath Park, Cardiff.	psychiatric syndromes in chronic fatigue patients and comparison subjects.		associated psychiatric morbidity found. The operational criteria for neuraesthenia in ICD-10 vary in this and other respects from the Centers for Disease Control and Prevention (CDC) criteria for CFS. Neuraesthenia and associated psychiatric morbidity in CDC-defined CFS are evaluated. METHOD: CFS subjects and controls were interviewed with the Schedule for the Clinical Assessment of Neuropsychiatry (SCAN). The computerised scoring program for SCAN (CATEGO5) facilitates the assignment of operational definitions according to DSM-III-R and ICD-10. Subjects were re-interviewed with SCAN an average of 11 months later. No specific treatments or interventions were given during this period. RESULTS: The majority of subjects fulfilled ICD-10 operational criteria for neuraesthenia and had two and a half times the rate of psychiatric morbidity as the healthy comparison group according to the CATEGO5 Index of Definition (ID). Approximately 80% of subjects fulfilled both DSM-III-R and ICD-10 criteria for sleep disorders. There was a significant fall in the number of subjects fulfilling criteria for depression and anxiety disorders and a significant increase in the number of subjects with no diagnosis for DSM-III-R criteria over time. There were no significant changes over time for any diagnosis according to ICD-10 criteria or for overall levels of psychopathology as reflected in CATEGO5 ID levels. CONCLUSIONS: The ICD-10 'neuraesthenia' definition identifies almost all subjects with CDC-defined CFS. Fifty percent of CFS subjects also had depressive or anxiety disorders, some categories of which remit spontaneously over time.
Farrar DJ, Locke SE, Kantrowitz FG.	Department of Psychiatry, Beth Israel Hospital, Harvard Medical School, Boston, USA.	Chronic fatigue syndrome. 1: Etiology and pathogenesis.	Behav Med 1995 Spring;21(1):5-16	Chronic fatigue syndrome (CFS) is a disorder of unknown etiology characterized by debilitating fatigue and other somatic and neuropsychiatric symptoms. A range of heterogeneous clinical and laboratory findings have been reported in patients with CFS. Various theories have been proposed to explain the underlying pathophysiologic processes but none has been proved. Research findings of immunologic dysfunction and neuroendocrine changes suggest the possible dysregulation of interactions between the nervous system and the immune system. Without a clear understanding of its etiopathogenesis, CFS has no definitive treatment. Management approaches have been necessarily speculative, and they have evolved separately in a number of medical and nonmedical disciplines. The results of several controlled treatment studies have been inconclusive. An accurate case definition identifying homogeneous subtypes of CFS is needed. The integration of medical and psychologic treatment modalities and the use of both biologic and psychologic markers to evaluate treatment response will enhance future treatment strategies.
Fennell PA		CFS Sociocultural Influences and Trauma: Clinical Considerations	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 159 - 173	An integrated model of the assessment and treatment of the CFS population needs to include the sociocultural influences that affect CFS patients as well as their treating clinicians. These sociocultural factors include: (1) the pre-existing cultural climate toward disease, (2) cultural intolerance of ambiguity, (3) cultural

				intolerance of chronic vs. acute illness, (4) the ongoing psyche-soma duality among health care providers, and (5) initial disease illegitimacy and subsequent enculturation. These specific influences, as well as the patient's medical status, need to be carefully considered in the assessment and treatment of CFS patients and their families. The traumatogenic effects of these sociocultural influences on CFS patients will be discussed and specific treatment strategies will be suggested
Fennell PA		The Four Progressive Stages of the CFS Experience: A Coping Tool for Patients	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 69 - 79	The CFS experience may be construed as a series of adaptations and adjustments that begin at the onset of symptoms. The ability of the CFS-affected individual to cope with symptoms and disabilities is strongly influenced by sociocultural factors. The purpose of this paper is to present a comprehensive multistage model of the CFS experience that recognizes the influences of cultural, psychosocial and medical factors in CFS assessment and treatment. The patient's awareness of these stages of adjustment can be an important coping tool in reconstructing the illness experience.
Fisk JW.		Chronic fatigue syndrome.	932: N Z Med J 1995 Sep 22;108(1008):393 comment on: N Z Med J. 1995 Jul 28;108(1004):301	
Flanigan MJ, Morehouse RL, Shapiro CM.	Department of Psychiatry, University of Toronto, Ontario, Canada.	Determination of observer-rated alpha activity during sleep.	927: Sleep 1995 Oct;18(8):702-6	Patients suffering from chronic fatigue syndrome (CFS) have been described as having alpha intrusion into sleep. In a separate study of the relationship between depression and CFS, we investigated the sleep of CFS patients. We could not detect any observable alpha anomaly in our group of CFS patients. It is possible that there is a subgroup of CFS patients in whom no alpha anomaly is present. However, the sleep electroencephalogram (EEG) montage used in our study was different to that employed by previous researchers. This paper investigates the influence of electrode derivations on the outcome of observable alpha ratings. We compared simultaneous recordings of sleep EEG using three commonly employed montages. Our results indicate that use of the mastoid reference (montage 1) results in the highest observer-related alpha. This may suggest that data regarding alpha intrusion should always be collected using montage 1. However, there is a possibility that the mastoid electrode is not electrically silent and is contaminating the data of the referenced channels. The implications of these findings are discussed in relation to the validity of alpha intrusion measurement of CFS and fibromyalgia.
Friedberg F		The Stress/Fatigue Link in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 147 - 152	This paper cites preliminary evidence for the relationship between fatigue and stress in chronic fatigue syndrome. Stress may intensify symptoms of CFS and erode positive mood and affect. A model of the stress/fatigue link in CFS will be presented and a specific coping technique will be described as a tool to interrupt the stress/symptom interaction in CFS.

Friedberg F		Clinical Assessment of Coping in CFS Patients	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 53 - 58	The controversy regarding psychosocial factors in the onset and maintenance of chronic fatigue syndrome (CFS) is briefly outlined. The primary purpose of this presentation is to describe coping assessments and possible cognitive-behavioral interventions for CFS patients.
Furst G		Occupational Therapy	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 91 - 94	
Galbraith DN, Nairn C, Clements GB.	Regional Virus Laboratory, Ruchill Hospital, Glasgow, UK.	Phylogenetic analysis of short enteroviral sequences from patients with chronic fatigue syndrome.	953: J Gen Virol 1995 Jul;76 (Pt 7):1701-7	This study used phylogenetic analysis based on a region of the 5' non-translated region (5'NTR) of a variety of enteroviral sequences to compare sequences associated with chronic fatigue syndrome (CFS) and those from enteroviruses causing acute infections. Direct sequencing of PCR products was used to obtain the nucleic acid sequences from CFS patients. The inferred phylogenetic tree identified three groupings, one correlating with the diagnosis of CFS. The analysis identified a close relationship between the chronic fatigue enteroviral sequences, and showed that 19/20 were distinct from previously described enteroviruses. These results suggest there is persistence of enterovirus infection in some CFS patients and indicate the presence of distinct novel enterovirus sequences.
Gantz NM.	Department of Medicine, Polyclinic Medical Center, Harrisburg, Pa., USA.	10 key questions answered on chronic fatigue syndrome.	971: Contemp Intern Med 1995 Jul;7(7):15-6, 21-4, 27-8	
Gascon J, Marcos T, Vidal J, Garcia-Forcada A, Corachan M.	Seccion Medicina Tropical, Hospital Clinic, Provincial de Barcelona, Spain.	Cytomegalovirus and Epstein-Barr Virus Infection as a Cause of Chronic Fatigue Syndrome in Travelers to Tropical Countries.	J Travel Med 1995 Mar 1;2(1):41-44	
Gascon J, Marcos T, Vidal J, Garcia-Forcada A, Corachan M.	Seccion Medicina Tropical, Hospital Clinic, Provincial de Barcelona, Spain.	Cytomegalovirus and Epstein-Barr Virus Infection as a Cause of Chronic Fatigue Syndrome in Travelers to Tropical Countries.	470: J Travel Med 1995 Mar 1;2(1):41-44	
Ghahramani M, Gooriah V.	Trenton Forensic Psychiatric Hospital, NJ 08628, USA.	Chronic fatigue syndrome associated with a psychotic state resulting in multiple murders.	Bull Am Acad Psychiatry Law 1995;23(4):613-6	A 28-year-old, ambitious, academically successful Asian man with a zeal for hard work develops infectious mononucleosis and its resultant lethargy and fatigue. He becomes depressed, then develops symptoms of mania before turning floridly psychotic. In his psychotic state he develops grandiose delusions about being the second son of God after Christ and takes it upon himself to rid the world of all evil by defeating the anti-Christ. He kills four people and seriously injures a fifth. He is arrested and found not guilty by reason of insanity. He remains a diagnostic

				puzzle for a long time before starting to respond to neuroleptic medication.
Glover DM.	Virginia Mason Clinic East, 13014 120th Avenue, N.E., Kirkland, WA 98034, USA.	Chronic Fatigue Syndrome.	Adolesc Med 1995 Feb;6(1):101-114	Despite its new name, chronic fatigue syndrome is not a new disease. This chapter reviews current definitions, emphasizing that chronic fatigue syndrome is a diagnosis of exclusion. The author also discusses viral infections that are associated with CFS, including Epstein-Barr virus, cytomegalovirus, herpesvirus type 6, enteroviruses, and retroviruses.
Gold PW, Licinio J, Wong ML, Chrousos GP.	Clinical Neuroendocrinology Branch, NIMH, Bethesda, Maryland 20892, USA.	Corticotropin releasing hormone in the pathophysiology of melancholic and atypical depression and in the mechanism of action of antidepressant drugs.	906: Ann N Y Acad Sci 1995 Dec 29;771:716-29	Hypercortisolism in depression seems to preferentially reflect activation of hypothalamic CRH secretion. Although it has been postulated that this hypercortisolism is an epiphenomenon of the pain and stress of major depression, our data showing preferential participation of AVP in the hypercortisolism of chronic inflammatory disease suggest specificity for the pathophysiology of hypercortisolism in depression. Our findings that imipramine causes a down-regulation of the HPA axis in experimental animals and healthy controls support an intrinsic role for CRH in the pathophysiology of melancholia and in the mechanism of action of psychotropic agents. Our data suggest that hypercortisolism is not the only form of HPA dysregulation in major depression. In a series of studies, commencing in patients with Cushing's disease, and extending to hyperimmune fatigue states such as chronic fatigue syndrome and examples of atypical depression such as seasonal affective disorder, we have advanced data suggesting hypofunction of hypothalamic CRH neurons. These data raise the question that the hyperphagia, hypersomnia, and fatigue associated with syndromes of atypical depression could reflect a central deficiency of a potent arousal-producing anorexogenic neuropeptide. In the light of data presented elsewhere in this symposium regarding the role of a hypofunctioning hypothalamic CRH neuron in susceptibility to inflammatory disease, these data also raise the question of a common pathophysiological mechanism in syndromes associated both with inflammatory manifestations and atypical depressive symptoms. This concept of hypofunctioning of hypothalamic CRH neurons in these disorders also raises the question of novel forms of neuropharmacological intervention in both inflammatory diseases and atypical depressive syndromes. Review, Academic
Golden HE.		Clinical laboratory test findings in patients with chronic fatigue syndrome.	969: Arch Intern Med 1995 Jun 26;155(12):1332 comment on: Arch Intern Med. 1995 Jan 9;155(1):97-103	
Goldenberg DL.	Newton-Wellesley and Tufts University School of Medicine,	Fibromyalgia, chronic fatigue syndrome, and myofascial pain	Curr Opin Rheumatol 1995 Mar;7(2):127-35	Two important studies in which nuclear magnetic resonance spectroscopy was used convincingly demonstrated that muscle is not the primary pathologic factor in fibromyalgia. There were further studies reporting that fibromyalgia-chronic

	Massachusetts, USA.	syndrome.		fatigue syndrome may follow well treated Lyme disease or mimic Lyme disease. The longest therapeutic trial to date in fibromyalgia demonstrated an initial modest effect of tricyclic medications, but at 6 months that efficacy was no longer evident. Investigation in both fibromyalgia and chronic fatigue syndrome now focuses on the central nervous system. The use of new technology, eg, neurohormonal assays and imaging such as single-photon emission computed tomography scan, may be important in understanding these elusive conditions.
Goldstein JA, Ismael Mena, Eugenio Jouanne, Ira Lesser		The Assessment of Vascular Abnormalities in Late Life Chronic Fatigue Syndrome by Brain SPECT: Comparison with Late Life Major Depressive Disorder	Journal of Chronic Fatigue Syndrome 1995: 1(1): 55 - 79	We report on brain SPECT analysis of regional cerebral blood flow (rCBF) in late life chronic fatigue syndrome (CFS) patients and compare their results with patients with late life depression and elderly normal controls 45 years and older. We attempted to distinguish CFS from normals and patients with depression and applied the findings to understand the pathophysiology of the illness. We studied 33 patients with CFS (55 ± 10 years), 26 patients with late life depression (62 ± 8 years), and 19 normal controls (66 ± 8 years); 43 other normal controls had only ^{133}Xe rCBF measurements (66 ± 8 years). We evaluated rCBF quantitatively with ^{133}Xe images and qualitatively with high resolution imaging using 99mTc-HMPAO. We found that rCBF in CFS measured by ^{133}Xe varied between 35 and 41 ml/min/l00g in both hemispheres, $p < 0.0001$ and 0.05; similar findings were observed in depression. In CFS 99mTc-HMPAO imagain demonstrated right orbitofrontal and marked right dorsofrontal hypoperfusion at 58% to 66% of the maximal activity in the brain, p , 0.001. In late life depression, hypoperfusion was primarily limited to the right orbitofrontal lobe, 42% and 57%, p , 0.001. In depression, the abnormalities were most striking in the left temporal lobe and particularly in the left anterior frontal lobes. CFS patients with major depressive disorder by DMS-III-R criteria did not differ in regional cerebral hypoperfusion from those without major depression. The pathophysiology of the illness may involve the dysregulation of a neural network which includes circuits between the hippocampus (located in the anterior temporal lobe) and the dorsolateral prefrontal cortex.
Hamre HJ.		[Chronic fatigue syndrome--a review of the literature].[article in Norwegian]	923: Tidsskr Nor Laegeforen 1995 Oct 10;115(24):3042-5	Chronic fatigue syndrome is a clinical condition characterized by abnormal fatigue, subfebrile body temperature, sore throat, lymphadenopathy, arthralgia, myalgia and neuropsychiatric symptoms. Typically, the syndrome develops after a flu-like illness and is markedly exacerbated by exercise. The etiology is unknown and there is no single diagnostic test. The patients may have cognitive dysfunction, immunological and endocrinological abnormalities and abnormal mitochondria. Magnetic resonance imaging scans may show increased uptake of signals in the brain, and single photon emission computerized tomography reveals regional hypoperfusion of the brain. The author discusses similarities and distinctions between the syndrome and depression.
Hamre HJ.		[Chronic fatigue	914: Tidsskr Nor	

		syndrome].[article in Norwegian]	Laegeforen 1995 Nov 10;115(27):3419 comment on: Tidsskr Nor Laegeforen. 1995 Oct 10;115(24):3017-22	
Harrison AL		Development and Evaluation of Claims Involving Chronic Fatigue Syndrome (CFS) Under the Social Security Disability Provisions	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 131 - 133	
Heiman TH		Chronic Fatigue Syndrome and Vocational Rehabilitation: Unserved and Unmet Needs	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 105 - 118	Individuals with chronic fatigue syndrome (CFS) are largely unserved by the health care and rehabilitation professions. Their numbers are growing and their needs are complex and extensive. Some persons with CFS (PWCs), who have the least functional impairment, may benefit from vocational rehabilitation services. While employment options or accommodations, as well as support services, may be available to PWCs, their disabilities are gravely misunderstood, requiring long-term, intermittent, knowledgeable, professional counseling, and support. Given the frequency of reports by consumers and advocates concerning unserved, unmet needs of PWCs, a survey was conducted among PWCs throughout Wisconsin to identify their needs both for independent living support services and for employment accommodations. A weighted scale was developed based upon self-reports of 119 respondents regarding importance and satisfaction levels for such services. Results provided rankings of PWC needs, to the degree that such needs were perceived as unserved and unmet. Furthermore, subjects reported the number of good days and bad days experienced monthly, describing dfferential levels of symptoms and function for these days on a CFIDS Disability Scale, created by David Bell, M.D. Results indicated the devastating impact of CFS upon health, daily activities, personal relationships, income, and work. PWC's reported significantly-unmet or highly-unmet needs for the great majority of the selected support services and employment accomodations.
Hickie I, Lloyd A, Hadzi-Pavlovic D, Parker G, Bird K, Wakefield D.	School of Psychiatry, University of New South Wales, Australia.	Can the chronic fatigue syndrome be defined by distinct clinical features?	937: Psychol Med 1995 Sep;25(5):925-35	To determine whether patients diagnosed as having chronic fatigue syndrome (CFS) constitute a clinically homogeneous class, multivariate statistical analyses were used to derive symptom patterns and potential patient subclasses in 565 patients. The notion that patients currently diagnosed as having CFS constitute a single homogeneous class was rejected. An alternative set of clinical subgroups was derived. The validity of these subgroups was assessed by sociodemographic, psychiatric, immunological and illness behaviour variables. A two-class statistical solution was considered most coherent, with patients from the smaller class (27%

				of the sample) having clinical characteristics suggestive of somatoform disorders. The larger class (73% of sample) presented a more limited combination of fatigue and neuropsychological symptoms, and only moderate disability but remained heterogeneous clinically. The two patient groups differed with regard to duration of illness, spontaneous recovery, severity of current psychological morbidity, utilization of medical services and CD8 T cell subset counts.The distribution of symptoms among patients was not unimodal, supporting the notion that differences between the proposed subclasses were not due simply to differences in symptom severity. This study demonstrated clinical heterogeneity among patients currently diagnosed as CFS, suggesting aetiological heterogeneity. In the absence of discriminative clinical features, current consensus criteria do not necessarily reduce the heterogeneity of patients recruited to CFS research studies.
Hickie I, Lloyd A.	School of Psychiatry, University of New South Wales, Sydney, Australia.	Are cytokines associated with neuropsychiatric syndromes in humans?	943: Int J Immunopharmacol 1995 Aug;17(8):677-83	Traditional aetiological models in neuropsychiatry have placed little emphasis on the abnormal behavioural responses (decreased psychomotor activity, anorexia, weight loss, decreased social exploration and sexual behaviour, impaired cognitive function and increased somnolence) that are common to both psychiatric syndromes, notably depression, and the illness behaviour of sick animals. In recent years, the possible role of cytokines, as mediators of not only the immunological and metabolic responses to infection and inflammation but also a co-ordinated behavioural response, has been described. Further, a range of possible mechanisms for these effects has been postulated, notably involving corticotropin releasing factor (CRF) and prostaglandins of the E series (PgE) with the central nervous system (CNS). Here we outline a series of human clinical conditions where neuropsychiatric syndromes co-occur with a host response to infection or inflammation. These may be characterized by cytokine production (e.g. acute, recurrent and chronic viral illness, systemic autoimmune diseases and chronic fatigue syndrome). Other clinical situations characterized by exposure to or in vivo production of cytokines (e.g. treatment of chronic infections and malignancies, progression and/or recurrence of malignancies) are also discussed. We postulate that the stereotyped behavioural repertoire observed is mediated by cytokine-dependent mechanisms within the CNS. Systematic studies of the behavioural responses of such patient groups are suggested, noting specifically correlations between the time course and severity of immune and neuroendocrine and behavioural responses and dose-response effects.
Hickie IB, Lloyd AR, Wakefield D.	University of New South Wales, Sydney.	Chronic fatigue syndrome: current perspectives on evaluation and management.	933: Med J Aust 1995 Sep 18;163(6):314-8 comment in: Med J Aust. 1996 Mar 18;164(6):384	OBJECTIVE: To describe clinical and laboratory guidelines for assessment and management of patients presenting with chronic fatigue syndrome (CFS). DATA SOURCES: Relevant international consensus diagnostic criteria and research literature on the epidemiology, pathophysiology, concurrent medical and psychological disturbance and clinical management of CFS. CONCLUSIONS:

				Medical and psychiatric morbidity should be carefully assessed and actively treated, while unnecessary laboratory investigations and extravagant treatment regimens should be avoided. No single infective agent has been demonstrated as the cause of CFS, and immunopathological hypotheses remain speculative. The aetiological role of psychological factors is debated, but they do predict prolonged illness. The rate of spontaneous recovery appears to be high. Effective clinical management requires a multidisciplinary approach, with consideration of the medical, psychological and social factors influencing recovery.
Hicks JE		General Approaches to the Rehabilitation of Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 85 - 90	
Hilden J.		[Chronic fatigue syndrome--a psychosocial syndrome]?[article in Danish]	Ugeskr Laeger 1995 Feb 6;157(6):757 comment on: Ugeskr Laeger. 1994 Nov 14;156(46):6832-6	
Hutchison AS.		Exercise responses in the chronic fatigue syndrome. Objective assessment of study is difficult without knowledge of data.	913: BMJ 1995 Nov 11;311(7015):1304 comment on: BMJ. 1995 Aug 26;311(7004):544-5	
Ilaria RL Jr, Komaroff AL, Fagioli LR, Moloney WC, True CA, Naides SJ.	Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA.	Absence of parvovirus B19 infection in chronic fatigue syndrome.	989: Arthritis Rheum 1995 May;38(5):638-41	OBJECTIVE. To evaluate the presence of infection with parvovirus B19 in patients with chronic fatigue syndrome (CFS) who also had rheumatologic symptoms and mild hematologic abnormalities. METHODS. Seven patients meeting the Centers for Disease Control and Prevention working case definition for CFS who also had mild leukopenia, thrombocytopenia, or anemia were studied. Bone marrow was aspirated from each patient, and examined for morphologic abnormalities, including features seen in marrow infections with parvovirus B19, as well as for parvoviral DNA, using polymerase chain reaction (PCR) amplification. Serum obtained at the time of marrow aspiration was also evaluated for parvoviral DNA, using the PCR method, and was examined for the presence of IgM and IgG antibodies to the virus. RESULTS. No evidence of marrow involvement with parvovirus B19 was found in any patient. One patient had antibody evidence of a transient parvoviral infection, during which time an underlying thrombocytopenia worsened. CONCLUSION. Despite examining a selected group of patients thought most likely to have parvoviral infection, based on clinical and hematologic measures, no evidence of clinically important parvoviral infection was noted. Thus, it seems unlikely that parvovirus B19 plays a role in CFS, even though it has

				been associated with fibromyalgia, a clinically similar syndrome.
Izquierdo Clemente C, Ibanez Estella JA, Sanchez Ibanez A.		[Chronic fatigue syndrome].[article in Spanish]	912: Aten Primaria 1995 Dec;16(10):647 comment on: Aten Primaria. 1995 May 31;15(9):587-8	
Jason LA, Taylor R, Wagner L, Holden J, Ferrari JR, Plioplys AV, Plioplys S, Lipkin D, Papernik M.	Department of Psychology, DePaul University, Chicago, Illinois 60614, USA.	Estimating rates of chronic fatigue syndrome from a community-based sample: a pilot study.	947: Am J Community Psychol 1995 Aug;23(4):557-68	Most of the Chronic Fatigue Syndrome (CFS) epidemiological studies have relied on physicians who refer patients having at least six months of chronic fatigue and other symptoms. However, there are a number of potential problems when using this method to derive prevalence statistics. For example, some individuals with CFS might not have the economic resources to access medical care. Other individuals with CFS might be reluctant to use medical personnel, particularly if they have encountered physicians skeptical of the authenticity of their illness. In addition, physicians that are skeptical of the existence of CFS might not identify cases. In the present pilot study, a random community sample (N = 1,031) was interviewed by telephone in order to identify and comprehensively evaluate individuals with symptoms of CFS and those who self-report having CFS. Different definitions of CFS were employed, and higher rates (0.2%) of CFS were found than in previous studies. Methodological benefits in using more rigorous epidemiological methods when estimating CFS prevalence rates are discussed.
Jenzer G.		[Clinical aspects and neurologic expert assessment in sequelae of whiplash injury to the cervical spine].[article in German]	929: Nervenarzt 1995 Oct;66(10):730-5	Whiplash injury to the cervical spine and its possible long-term sequelae, the late (or chronic) whiplash syndrome, are analysed based on a clearly defined accident mechanism and an initial battery of investigations to exclude lesions other than those affecting the soft tissue of the neck region (i.e. the consequences of strain and sprain). Predictors are discussed that may point to a delayed and complicated recovery, with development of a complex array of symptoms. The pattern of this symptomatology, as reviewed on the basis of different neuropsychological investigations, appears inhomogeneous. Comparison with other non-traumatic conditions, such as the chronic fatigue syndrome, the fibromyalgia syndrome and chronic daily headache, as well as with chronic disturbances of cervical origin, reveals striking similarities. In cases of litigation, these circumstances require careful assessment of the patient's previous history and an extensive differential diagnosis. Whiplash injury to the cervical spine rarely results in disability and, if so, is only minor.
Jonas WB		How Useful Are the Alternative Therapies for Chronic Fatigue Syndrome?	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 47 - 50	
Jovanovic J, Cvjetkovic D, Brkic S, Madle-	Medicinski fakultet, Novi Sad.	[The Epstein-Barr virus and chronic fatigue	Med Pregl 1995;48(11-12):391-3	Lately discovered chronic fatigue syndrome is associated with Epstein-Barr virus infection. The objective of this paper was to detect this syndrome in our patients.

Samardzija N.		syndrome].[article in Serbo-Croatian (Roman)]		31 patients with cured acute infective mononucleosis were examined by questionnaire, physical check-up and laboratory analyses in order to detect disorders characteristic for chronic fatigue syndrome. Six months after they had been cured, out of 7 patients 5 patients complained of frequent sore throat, fatigue and exhaustion, and a year later, all 5 patients were sleepy and tired all the time. More than a year after the acute illness 19 patients were examined and in 5.6% frequent sore throat and enlarged neck lymph nodes occurred. The gathered results point to disorders characteristic for chronic fatigue syndrome in a high percentage. This pilot study should only be the beginning of examinations of this kind.
Kantrowitz FG, Farrar DJ, Locke SE.	Department of Psychiatry, Beth Israel Hospital, Harvard Medical School in Boston, USA.	Chronic fatigue syndrome. 2: Treatment and future research.	Behav Med 1995 Spring;21(1):17-24	
Kelly R.		Myalgic encephalomyelitis and chronic fatigue syndrome.	999: N Z Med J 1995 Mar 22;108(996):110 comment on: N Z Med J. 1995 Feb 8;108(993):44-5	
Kermode-Scott B.		Don't worry about the label. Diagnose underlying perpetuating factors in chronic fatigue syndrome.	972: Can Fam Physician 1995 Jun;41:1126-8	
Kerr JR, Curran MD, Moore JE, Murphy PG.	Department of Bacteriology, Belfast City Hospital, Northern Ireland.	Parvovirus B19 infection--persistence and genetic variation.	Scand J Infect Dis 1995;27(6):551-7	53 patients with acute B19 infection were studied; symptoms at acute infection were rash and arthralgia (n = 26), rash (n = 7), arthralgia (n = 16), aplastic crisis (n = 3), and intrauterine fetal death (n = 1). These patients were followed for 26-85 months (mean 57 months) and re-assessed for persistent symptoms, anti-B19 antibodies, and B19 DNA. At follow-up, 7 individuals were positive for serum B19 DNA, compared with none of the controls (2-tailed p value = 0.016). All 7 of those persistently infected were women, 3 of whom had symptoms; 1 had a chronic haemolytic anaemia (initial presentation was aplastic crisis); 1 had persistent arthralgia in both knees (initial presentation was bilateral knee arthralgia); and 1 had arthralgia in one knee and chronic fatigue syndrome (initial presentation was bilateral arthralgia in knees and shoulders). For the 7 persistently infected patients, serum from the time of diagnosis of acute B19 infection was available for 4, all of which contained B19 DNA. With single-stranded conformational polymorphism (SSCP) assay of these 11 PCR products, identical SSCP types were demonstrated in 5 of 7 follow-up isolates. In 2 of the 4 cases for which both acute

				and follow-up PCR product was available, the SSCP type of the follow-up product was different from that of the acute product. Two B19 virus types were demonstrated in one patient (with persistent arthralgia and chronic fatigue syndrome) at follow-up assessment.
Klebanova VA.		[Chronic fatigue syndrome (Review)].[article in Russian]	Gig Sanit 1995 Jan-Feb;(1):35-8	
Klein R, Berg PA.	Department of Internal Medicine, University of Tubingen, Germany.	High incidence of antibodies to 5-hydroxytryptamine, gangliosides and phospholipids in patients with chronic fatigue and fibromyalgia syndrome and their relatives: evidence for a clinical entity of both disorders.	619: Eur J Med Res 1995 Oct 16;1(1):21-6	The fibromyalgia syndrome (FMS) is one of the most frequent rheumatic disorders showing a wide spectrum of different symptoms. An association with the chronic fatigue syndrome (CFS) has been discussed. Recently, a defined autoantibody pattern consisting of antibodies to serotonin (5-hydroxytryptamine, 5-HT), gangliosides and phospholipids was found in about 70% of the patients with FMS. We were therefore interested in seeing whether patients with CFS express similar humoral immunoreactivity. Sera from 42 CFS patients were analysed by ELISA for these antibodies, and the results were compared with those previously observed in 100 FMS patients. 73% of the FMS and 62% of the CFS patients had antibodies to serotonin, and 71% or 43% to gangliosides, respectively. Antibodies to phospholipids could be detected in 54% of the FMS and 38% of the CFS patients. 49% of FMS and 17% of the CFS patients had all three antibodies in parallel, 70% and 55%, respectively had at least two of these antibody types. 21% of FMS and 29% of CFS patients were completely negative for these antibodies. Antibodies to 5-HT were closely related with FMS/CFS while antibodies to gangliosides and phospholipids could also be detected in other disorders. The observation that family members of CFS and FMS patients also had these antibodies represents an argument in favour of a genetic predisposition. These data support the concept that FMS and CFS may belong to the same clinical entity and may manifest themselves as 'psycho-neuro-endocrinological autoimmune diseases'.
Krilov LR.	Department of Pediatrics, Cornell University Medical College, Manhasset, New York, USA.	Chronic fatigue syndrome.	975: Pediatr Ann 1995 Jun;24(6):290-2, 294	
Lane RJ, Burgess AP, Flint J, Riccio M, Archard LC.	Academic Unit of Neuroscience, Charing Cross and Westminster Medical School, London.	Exercise responses and psychiatric disorder in chronic fatigue syndrome.	939: BMJ 1995 Aug 26;311(7004):544-5 comment in: BMJ. 1995 Nov 11;311(7015):1304	
Lapp CW, Cheney PR.		The chronic fatigue syndrome.	956: Ann Intern Med 1995 Jul 1;123(1):74-5	

			comment on: Ann Intern Med. 1994 Dec 15;121(12):953-9	
LaRosa JH		NIH and the Women's Health Agenda	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 137 - 143	
Lawrie SM, Pelosi AJ.	Edinburgh University Department of Psychiatry, Royal Edinburgh Hospital.	Chronic fatigue syndrome in the community. Prevalence and associations.	974: Br J Psychiatry 1995 Jun;166(6):793-7	BACKGROUND. Chronic fatigue syndrome (CFS) is a poorly understood condition, apparently related to both psychiatric disturbance and infectious illness. Little progress has been made in identifying aetiology, owing to a lack of epidemiological studies using case-definition criteria. METHOD. A community postal survey of a random sample of over 1000 patients registered at a local health centre comprised a fatigue questionnaire and the 12-item General Health Questionnaire (GHQ). RESULTS. Total fatigue scores were modestly higher in women than men. Fatigue was most frequently attributed to psychosocial factors. Fatigue and GHQ scores were strongly correlated. Two men and two women satisfied British criteria for CFS, a prevalence of 0.56% (95% Cl 0.16-1.47%); three were probable psychiatric cases. CONCLUSIONS. Previously reported sociodemographic associations of CFS may reflect medical referral patterns. A strong association exists with psychological morbidity, but relabelling CFS as a psychiatric disorder is not justified.
Leitch AG.	Royal Victoria Chest Clinic, Chalmers Hospital, RIE NHS Trust, Edinburgh, UK.	Neurasthenia, myalgic encephalitis or cryptogenic chronic fatigue syndrome?	977: QJM 1995 Jun;88(6):447-50	
Lemke MR.		[Chronic fatigue syndrome. The necessity for an integrated, interdisciplinary approach].[article in German]	Dtsch Med Wochenschr 1995 Jan 5;120(1-2):47	
Lesniak OM, Belikov ES.		[The classification of Lyme borreliosis (Lyme disease)].[article in Russian]	Ter Arkh 1995;67(11):49-51	A new version of Lyme's disease classification based on the authors' experience and other classifications is proposed. It distinguishes periods of the disease (acute, subacute, chronic) and stages (I--isolated erythema migrans, II--local disseminated infection, III--generalized disseminated infection) as well as the signs which are significant in Lyme's disease diagnosis: erythematous and nonerythematous form, seropositivity or seronegativity against Borrelia burgdorferi. Subclinical (latent) infection, complications of Lyme's disease (fibromyalgia syndrome, chronic fatigue syndrome, etc.) and mixed-infection with tick-borne viral encephalitis are included as well.

Lipkin DM, Robin R, Vasquez L, Plioplys AV, Plioplys S.		Chronic fatigue syndrome.	979: J Neurol Neurosurg Psychiatry 1995 Jun;58(6):764-5 comment on: J Neurol Neurosurg Psychiatry. 1994 May;57(5):617-21	
Loblay RH.		Chronic fatigue syndrome: what's in a name?	935: Med J Aust 1995 Sep 18;163(6):285-6 comment in: Med J Aust. 1996 Feb 19;164(4):251	
Lutgendorf S, Nancy G. Klimas, Michael Antoni , Andrew Brickman, Mary Ann Fletcher		Relationships of Cognitive Difficulties to Immune Measures, Depression and Illness Burden in Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(2): 23 - 41	Objective. We related the subjective assessment of cognitive difficulties with lymphocyte phenotypes, cellmediated immunity (CMI), cytokine and neopterin levels in patients with chronic fatigue syndrome (CFS), in order to determine if CFS patients complaining of greater cognitive difficulties would show greater impairments in cell-mediated immunity and a greater degree of immune system dysregulation, and to determine if these cognitive difficulties would correlate with the other non-affective measures of CFS associated illness burden. We also assessed whether these relationships would hold independent of depression in two ways, by statistically covarying depression severity scores and by comparing subsets of CFS patients with and without a concurrent diagnosis of major depressive disorder. Design. A case series of CFS patients. Setting. Outpatient tertiary referral clinic at the University of Miami School of Medicine, Miami, FL. Patienrs. Consecutive sample of 65 patients who were referred as CFS to the University of Miami Diagnostic Immunology Clinic, who met the Centers for Disease Control and Prevention (CDC) criteria for diagnosis of CFS and consented to participate. Main Measures. Self-assessment of cognitive difficulties, depression and illness burden, clinician-assessed depression and CFS symptoms, lymphocyte phenotype, proliferative response to mitogens, serum levels of cytokines and neopterin. Results. Among CFS patients, high Cognitive Difficulty Scale (CDS) scores were significantly related to lower lymphocyte proliferative responses to mitogens, higher neopterin levels, and higher CD4 and lower CD8 lymphocyte counts. These relationships, with the exception of T cell subset percentages, were maintained when depression severity was used as a co-variate. High CDS scores were also significantly related to lower Karnofsky scores, and greater illness burden as measured by the Sickness Impact Profile. Conclusions. Evidence is presented that CFS patients with higher cognitive difficulty scores have more immune and clinical dysfunction than those patients with less cognitive difficulty, and that these relationships are independent of depression. These observations provide support for the concept that although

				both cognitive difficulties and immunologic abnormalities, such as immune activation and impaired cell-mediated immunity, may represent secondary sequence to the same event(s), they are not likely to be secondary sequence to depression.
Lutgendorf SK, Antoni MH, Ironson G, Fletcher MA, Penedo F, Baum A, Schneiderman N, Klimas N.	Department of Psychology, University of Miami, Coral Gables, FL 33124, USA.	Physical symptoms of chronic fatigue syndrome are exacerbated by the stress of Hurricane Andrew.	967: Psychosom Med 1995 Jul-Aug;57(4):310-23	This study examined the effects of Hurricane Andrew on physical symptoms and functional impairments in a sample of chronic fatigue syndrome (CFS) patients residing in South Florida. In the months after Hurricane Andrew (September 15-December 31, 1992), 49 CFS patients were assessed for psychosocial and physical functioning with questionnaires, interviews, and physical examinations. This sample was made up of 25 CFS patients living in Dade county, a high impact area, and 24 patients in Broward and Palm Beach counties, areas less affected by the hurricane. Based on our model for stress-related effects on CFS, we tested the hypothesis that the patients who had the greatest exposure to this natural disaster would show the greatest exacerbation in CFS symptoms and related impairments in activities of daily living (illness burden). In support of this hypothesis, we found that the Dade county patients showed significant increases in physician-rated clinical relapses and exacerbations in frequency of several categories of self-reported CFS physical symptoms as compared to the Broward/Palm Beach county patients. Illness burden, as measured on the Sickness Impact Profile, also showed a significant increase in the Dade county patients. Although extent of disruption due to the storm was a significant factor in predicting relapse, the patient's posthurricane distress response was the single strongest predictor of the likelihood and severity of relapse and functional impairment. Additionally, optimism and social support were significantly associated with lower illness burden after the hurricane, above and beyond storm-related disruption and distress responses. These findings provide information on the impact of environmental stressors and psychosocial factors in the exacerbation of CFS symptoms.
Macintyre A.		Viral illness and chronic fatigue (syndrome)	963: Lancet 1995 Jul 1;346(8966):47 comment in: Lancet. 1995 Aug 12;346(8972):449 comment on: Lancet. 1995 May 27;345(8961):1333-8	
Martin WJ, Glass RT.	Department of Pathology, University of Southern California School of Medicine, Los	Acute encephalopathy induced in cats with a stealth virus isolated from a patient with	Pathobiology 1995;63(3):115-8	A simian cytomegalovirus-related stealth virus, isolated from a patient with the chronic fatigue syndrome, induced an acute neurological illness when inoculated into cats. Histological examination of brain tissue showed foci of cells with cytoplasmic vacuolization and an absence of any inflammatory reaction. Electron

	Angeles 90033, USA.	chronic fatigue syndrome.		microscopy confirmed the presence of herpes-like viral particles and viral-like products in the brain of an inoculated animal. These findings support the role of stealth viruses in the pathogenesis of human neurological diseases and provide an animal model to evaluate potential antiviral therapy.
Mawle AC, Nisenbaum R, Dobbins JG, Gary HE Jr, Stewart JA, Reyes M, Steele L, Schmid DS, Reeves WC.	Division of Viral and Rickettsial Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333, USA.	Seroepidemiology of chronic fatigue syndrome: a case-control study.	907: Clin Infect Dis 1995 Dec;21(6):1386-9	We performed serological testing for a large number of infectious agents in 26 patients from Atlanta who had chronic fatigue syndrome (CFS) and in 50 controls matched by age, race, and sex. We did not find any agent associated with CFS. In addition, we did not find elevated levels of antibody to any of a wide range of agents examined. In particular, we did not find elevated titers of antibody to any herpesvirus, nor did we find evidence of enteroviral exposure in this group of patients.
Mayberg H		Functional Neuroimaging in CFS: Applications and Limitations	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 9 - 20	
McComas AJ, Miller RG, Gandevia SC.	Department of Biomedical Sciences, McMaster University, Hamilton, Canada.	Fatigue brought on by malfunction of the central and peripheral nervous systems.	Adv Exp Med Biol 1995;384:495-512	Increased fatigability necessarily occurs in every patient with muscle weakness, regardless of whether the latter is due to a central or peripheral neurological disorder. The tendency for disuse to increase fatigability, as a secondary phenomenon, must also be considered; disuse affects both motoneuron recruitment and the biochemical and physiological properties of the muscle fibers. In recent studies impaired recruitment has been observed in postpolio patients, while patients with multiple sclerosis or spinal cord injury have shown, in addition, altered neuromuscular function. Findings are also presented in ALS and the chronic fatigue syndrome. In general, the most dramatic increases in fatigability take place in disorders of the peripheral nervous system and almost any cell component can be incriminated. There is a need to study fatigability systematically in neurology and rehabilitation.
McKenzie M, Lucy Dechene , Fred Friedberg , Robert Fontanetta		Coping Reports of Patients with Long-Term Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 59 - 67	Two hundred sixty-five patients with chronic fatigue syndrome, who had been ill for a minimum of 10 years, responded to an open-ended questionnaire with detailed descriptions of major illness issues and coping techniques. Their predominant illness concerns and personal accounts of coping strategies as well as an analysis of style of coping and illness progression will be presented.
McKenzie R, Straus SE.	Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA.	Chronic fatigue syndrome.	Adv Intern Med 1995;40:119-53	
Mitterer M, Pescosta N,	Department of	Chronic active Epstein-	958: Br J Haematol 1995	Persistent polyclonal B-cell lymphocytosis (PPBL) is a rare haematological

Fend F, Larcher C, Prang N, Schwarzmann F, Coser P, Huemer HP.	Haematology, General Hospital, Bozen, Italy.	Barr virus disease in a case of persistent polyclonal B-cell lymphocytosis.	Jul;90(3):526-31	disorder. It is characterized by activated and morphologically atypical B lymphocytes and polyclonal IgM production and has been associated with female sex, cigarette smoking, and HLA-DR7 expression. We report a case of PPBL with intermitting symptoms compatible with a chronic fatigue syndrome, recurrent erythema nodosum and multiforme. Serological findings suggested a chronic active Epstein-Barr virus (EBV) infection. Messenger RNA of EBV immediate early gene transactivation BZLF1 was detected in peripheral blood lymphocytes by reverse transcriptase PCR indicating a persistent replication of the virus. Over 2 years of observation we detected varying numbers of atypical lymphocytes. These cells hybridized with a probe specific for the EBV internal repeat region (BamHI W) which indicates a productive infection. Of interest, no reaction was observed with a probe specific for the latency-associated small RNAs (EBERs). The immunological phenotype of the polyclonal B cells was similar to B-cell lines immortalized by EBV in vitro, expressing a number of activation molecules (CD23, CD25, CD54) and the bcl-2 protein. In summary, our findings suggest that persistent EBV replication might be crucial in the development of lymphoproliferative disorders such as PPBL.
Moldofsky H.	Centre for Sleep and Chronobiology, Toronto Hospital, Western Division, Canada.	Sleep, neuroimmune and neuroendocrine functions in fibromyalgia and chronic fatigue syndrome.	Adv Neuroimmunol 1995;5(1):39-56	The justification for disordered chronobiology for fibromyalgia and chronic fatigue syndrome (CFS) is based on the following evidence: The studies on disordered sleep physiology and the symptoms of fibromyalgia and CFS; the experimental studies that draw a link between interleukin-1 (IL-1), immune-neuroendocrine-thermal systems and the sleep-wake cycle; studies and preliminary data of the inter-relationships of sleep-wakefulness, IL-1, and aspects of peripheral immune and neuroendocrine functions in healthy men and in women during differing phases of the menstrual cycle; and the observations of alterations in the immune-neuroendocrine functions of patients with fibromyalgia and CFS (Moldofsky, 1993b, d). Time series analyses of measures of the circadian pattern of the sleep-wake behavioural system, immune, neuroendocrine and temperature functions in patients with fibromyalgia and CFS should determine whether alterations of aspects of the neuro-immune-endocrine systems that accompany disordered sleep physiology result in nonrestorative sleep, pain, fatigue, cognitive and mood symptoms in patients with fibromyalgia and CFS. Review, Academic
Moss SE		Cognitive/Linguistic Deficits Associated with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 95 - 100	
Murdoch JC.		Chronic fatigue syndrome.	950: N Z Med J 1995 Jul 28;108(1004):301 comment in: N Z Med J.	

			1995 Sep 22;108(1008):393 comment on: N Z Med J. 1995 Jun 14;108(1001):234-5	
Murtagh J.	Department of Community Medicine, Monash University.	Patient education. Chronic fatigue syndrome.	957: Aust Fam Physician 1995 Jul;24(7):1297	
Naik SR, Ghoshal UC		Low grade pyrexia: is chronic fatigue syndrome a safe and justified diagnosis? .	926: J Assoc Physicians India 1995 Oct;43(10):725-6 comment on: J Assoc Physicians India. 1994 Aug;42(8):606-8	
Nairn C, Galbraith DN, Clements GB.	Regional Virus Laboratory, Ruchill Hospital, Glasgow, Scotland.	Comparison of coxsackie B neutralisation and enteroviral PCR in chronic fatigue patients.	949: J Med Virol 1995 Aug;46(4):310-3	Coxsackie B enteroviruses have been implicated repeatedly as agents associated with chronic fatigue syndrome (CFS). The objective of this study was to compare the serological evidence for the presence of Coxsackie B virus neutralising antibody, with the polymerase chain reaction (PCR) detecting a portion of the 5' nontranslated region (NTR) of the enterovirus genome. Serum samples from 100 chronic fatigue patients and from 100 healthy comparison patients were used in this study. In the CFS study group, 42% patients were positive for enteroviral sequences by PCR, compared to only 9% of the comparison group. Using the neutralisation assay, 34% of study patients were positive, compared to 41% of comparison patients. In the study group, 66/100 patient results correlated, i.e., they were either positive/positive or negative/negative for both tests. Of those that did not correlate, the majority were PCR-positive/Coxsackie B antibody-negative (21/34). In the comparison group, 58/100 patient results correlated. Of those that did not, the majority were PCR-negative/Coxsackie B antibody-positive (37/42). The Coxsackie B antibody neutralisation assay was not able to differentiate the CFS study group from the healthy comparison group, and thus the clinical relevance of this assay may be questioned. The PCR assay did differentiate the two groups with significantly more CFS patients having evidence of enterovirus than the comparison group.
Natelson BH, Ellis SP, Braonain PJ, DeLuca J, Tapp WN.	CFS Center, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark 07103.	Frequency of deviant immunological test values in chronic fatigue syndrome patients.	Clin Diagn Lab Immunol 1995 Mar;2(2):238-40	Of 11 immunological tests done on chronic fatigue syndrome patients and on fatigued controls, 3 tests (protein A binding, Raji cell, or C3 or C4 [deviant values in either complement component were counted as positive]) with deviant results discriminated best among the groups. Other tests, including immunoglobulin G subclasses, complement component CH50, interleukin-2, and anticardiolipin antibodies, did not discriminate well among the groups.
Natelson BH, Johnson	Department of	Reducing heterogeneity	916: Clin Infect Dis 1995	Chronic fatigue syndrome (CFS) is a heterogeneous illness characterized by a high

SK, DeLuca J, Sisto S, Ellis SP, Hill N, Bergen MT.	Neurosciences, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark, USA.	in chronic fatigue syndrome: a comparison with depression and multiple sclerosis.	Nov;21(5):1204-10	prevalence of psychiatric problems. We reasoned that we could reduce heterogeneity by excluding patients with psychiatric problems preceding CFS. We compared the functional status, mood, fatigue level, and psychiatric status of this more homogeneous group of CFS patients with the same parameters in patients with mild multiple sclerosis and in patients with major depression or dysthymia. Patients with CFS and those with multiple sclerosis were similar in terms of level of anger, severity of depression, level of anxiety, and frequency of current psychiatric diagnoses. Patients with CFS resembled depressed patients in having impaired vigor and experiencing substantial fatigue and confusion--problems constituting part of the case definition of CFS. The group with CFS was not psychologically vulnerable before the development of this condition and maintained adequate networks of social support despite disabling illness. Stratification to exclude patients with prior psychiatric disease and those with mild CFS allowed us to define a group of patients with CFS who more resembled patients with mild MS than patients with major depression or dysthymia and thus were more likely to have illness with an infectious or immunologic cause. Use of such a stratification strategy should prove important in testing of the viral/immunologic hypothesis of the etiology of CFS.
Nixon PG.		Hyperventilation and chronic fatigue syndrome.	QJM 1995 Jan;88(1):73-4 Erratum in: QJM 1995 Apr;88(4):299	
Nixon PG.		Chronic fatigue syndrome in Army general practice.	981: J R Army Med Corps 1995 Jun;141(2):112-3	
Pankow W, Feddersen CO, von Wichert P.	Abteilung Poliklinik, Zentrum fur Innere Medizin, Klinikum, Philipps-Universitat, Marburg.	[Differential therapy of chronic fatigue syndrome].[article in German]	911: Internist (Berl) 1995 Dec;36(12):1156-61	
Patarca R, Nancy G. Klimas Maria N. Garcia, Michael J. Walters, Derek Dombroski, Hector Pons , Mary Ann Fletcher		Dysregulated Expression of Soluble Immune Mediator Receptors in a Subset of Patients with Chronic Fatigue Syndrome: Cross-Sectional Categorization of Patients by Immune Status	Journal of Chronic Fatigue Syndrome 1995: 1(1): 81 - 96	Individuals with chronic fatigue syndrome (CFS) have significantly increased proportions of activated CD8+T cells, decreased natural killer (NK) cell cytotoxic and lymphoproliferative activities, elevated serum levels of tumor necrosis factor (TNF)-α and detectable TNF-β, interleukin (IL)-lβ, and IL-6 mRNA in peripheral blood mononuclear cells (PBMC). We report here that CFS patients as a group also have significantly higher levels, as compared to controls, of soluble TNF receptor type I (sTNF-RI or sCDl20a), sIL-6R (sCD126) and β2-microglobulin (β2-m), but not of IL-1 receptor antagonist (IL-1Ra). Correlative and population distribution studies that included lymphoid phenotypic distributions and function as well as soluble immune mediator expression levels revealed the existence of at least two mainly nonoverlapping immunological categories among CFS patients

				with either: (1) dysregulaled TNF-α/β expression in association with changes in the serum levels of IL-lα, IL-4, sIL-2R and IL-lRa, PBMC-associated expression of IL-1β, IL-6 and TNF-β mRNA, and T cell activation; or, (2) interrelated and dysregulated expression of sTNF-RI, sIL-6R, and β2-m and significantly decreased lymphoproliferative and NK cell cytotoxic activities. This preliminary systematization is of usefulness in the diagnosis, follow-up, and characterization of possible etiological agents for CFS.
Patnaik M, Komaroff AL, Conley E, Ojo-Amaize EA, Peter JB.	Specialty Laboratories, Inc., Santa Monica, California 90404-3900, USA.	Prevalence of IgM antibodies to human herpesvirus 6 early antigen (p41/38) in patients with chronic fatigue syndrome.	919: J Infect Dis 1995 Nov;172(5):1364-7 Erratum in: J Infect Dis 1995 Dec;172(6):1643	To evaluate the association between human herpesvirus 6 (HHV-6) and chronic fatigue syndrome (CFS), 2 geographically separate groups of CFS patients (125 and 29 patients, respectively) and healthy controls (150 and 15 controls, respectively) were compared, using an EIA, for antibodies to HHV-6 early antigen p41/38 (EA). Sixty percent (93/154) of CFS patients were were positive for HHV-6 EA IgM, 40% (61/154) were positive for IgG, and 23% (35/154) were positive for both. A total of 119 (77%) of the CFS patients were positive for HHV-6 EA IgG or IgM (or both); only 12% (20/165) of the controls had IgG or IgM to HHV-6 EA. These data demonstrate that more CFS patients than controls had elevated levels of HHV-6 EA-specific IgM, perhaps indicating active replication of HHV-6 in CFS.
Pelcovitz D, Septimus A, Friedman SB, Krilov LR, Mandel F, Kaplan S.	Department of Psychiatry, North Shore University Hospital, Manhasset, NY 11030, USA.	Psychosocial correlates of chronic fatigue syndrome in adolescent girls.	928: J Dev Behav Pediatr 1995 Oct;16(5):333-8	Behavior problems and family functioning were investigated in a sample of 10 adolescent girls with chronic fatigue syndrome (CFS), 10 matched healthy adolescent girls, and 10 adolescents with childhood cancer in remission. Based on the adolescent girls' reports, the CFS group had significantly higher scores than the cancer and healthy comparison adolescent girls on somatic complaints and also significantly higher scores than the cancer controls on internalizing symptoms and depression. Parent reports resulted in significantly higher scores in the CFS group than the adolescent girls from the healthy comparison groups on internalizing scores and somatic complaints. There were no significant differences on any family variables.
Petrie K, Moss-Morris R, Weinman J.	Department of Psychiatry and Behavioural Science, University of Auckland Medical School, New Zealand.	The impact of catastrophic beliefs on functioning in chronic fatigue syndrome.	J Psychosom Res 1995 Jan;39(1):31-7	This study investigated the association between catastrophic beliefs and disability in the context of Chronic fatigue syndrome (CFS). A sample of 282 CFS sufferers were asked about the consequences of pushing themselves beyond their present physical state. Responses were coded into catastrophic or non-catastrophic categories. While not differing on the length of illness or psychological adjustment, subjects demonstrating catastrophic responses evidenced significantly higher levels of fatigue and were more disabled in terms of their ability to work both in their normal occupation and around the house. Catastrophizers also showed greater disability in terms of their sleep and rest, social communication, and recreational activities. The role of catastrophic beliefs and personal perceptions of CFS in maintaining the illness is discussed.
Plioplys AV, Plioplys S.	Chronic Fatigue Syndrome Center,	Serum levels of carnitine in chronic	Neuropsychobiology 1995;32(3):132-8	Carnitine is essential for mitochondrial energy production. Disturbance in mitochondrial function may contribute to or cause the fatigue seen in chronic

	Mercy Hospital and Medical Center, Chicago, Ill. 60616, USA.	fatigue syndrome: clinical correlates.		fatigue syndrome (CFS) patients. One previous investigation has reported decreased acylcarnitine levels in 38 CFS patients. We investigated 35 CFS patients (27 females and 8 males); our results indicate that CFS patients have statistically significantly lower serum total carnitine, free carnitine and acylcarnitine levels, not only lower acylcarnitine levels as previously reported. We also found a statistically significant correlation between serum levels of total and free carnitine and clinical symptomatology. Higher serum carnitine levels correlated with better functional capacity. These findings may be indicative of mitochondrial dysfunction, which may contribute to or cause symptoms of fatigue in CFS patients.
Plioplys AV, Plioplys S.	Chronic Fatigue Syndrome Center, Mercy Hospital and Medical Center, Chicago, IL 60616, USA.	Electron-microscopic investigation of muscle mitochondria in chronic fatigue syndrome.	Neuropsychobiology 1995;32(4):175-81	Patients with chronic fatigue syndrome (CFS) suffer from disabling physical and mental fatigue. Abnormalities in mitochondrial function can lead to fatigue and weakness. Ultrastructural mitochondrial abnormalities have been reported to be present in CFS patients. We obtained percutaneous needle muscle biopsies from 15 CFS patients and 15 age- and sex-matched controls. We investigated previously reported ultrastructural abnormalites in CFS: subsarcolemmal mitochondrial aggregates, intermyofibrillar mitochondrial aggregates, mitochondrial circumference, area, pleomorphism and the presence of compartmentalization of the inner mitochondrial membrane. All of the steps of tissue processing, electron microscopy and data abstracting and analysis were performed in a totally blinded fashion. All of our data were rigorously quantified. We found no difference in any of these studied parameters between CFS patients and controls. Although there is no ultrastructural mitochondrial abnormality in CFS patients, other lines of evidence suggest the presence of a possible functional mitochondrial abnormality.
Plioplys S, Plioplys AV.	Chronic Fatigue Syndrome Center, Mercy Hospital and Medical Center, Chicago, IL 60616, USA.	Chronic fatigue syndrome (myalgic encephalopathy).	930: South Med J 1995 Oct;88(10):993-1000	Chronic fatigue syndrome is associated with many misconceptions. In this review, we attempt to summarize various pathogenic hypotheses for this disease and discuss new lines of insight into causes and treatments of this baffling and most frustrating condition.
Polich J, Moore AP, Wiederhold MD.	Department of Neuropharmacology, Scripps Research Institute, La Jolla, California 92037, USA.	P300 assessment of chronic fatigue syndrome.	J Clin Neurophysiol 1995 Mar;12(2):186-91	The P3(00) event-related brain potential (ERP) was elicited with an auditory tone-discrimination paradigm in 25 patients diagnosed with chronic fatigue syndrome (CFS) and 25 matched normal control subjects. Target stimulus probability was varied systematically (0.20, 0.50, 0.80) in different task conditions. No differences between the CFS and control subjects were found for either P3 amplitude or latency. No group effects were observed for the N1, P2, and N2 components. Despite the attentional and immediate memory deficits reported in CFS, the P3 ERP from auditory stimuli does not reliably discriminate CFS from matched control subjects.
Pollark RJ, Komaroff AL,		Borrelia burgdorferi	Clin Infect Dis 1995	

Telford SR 3rd, Gleit, Fagioli L, Brunet LR, Spielman A.		infection is rarely found in patients with chronic fatigue syndrome.	Feb;20(2):467-8	
Priest RG, Gimbrett R, Roberts M, Steinert J.	Department of Psychiatry, St Mary's Hospital Medical School, Imperial College of Science, Technology and Medicine, University of London, United Kingdom.	Reversible and selective inhibitors of monoamine oxidase A in mental and other disorders.	Acta Psychiatr Scand Suppl 1995;386:40-3	The clinically tested reversible inhibitors of monoamine oxidase A (RIMAs) include brofaromine, moclobemide and toloxatone. Moclobemide has shown unequivocal antidepressant activity against serious depressive illness in 4 placebo-controlled double-blind trials. It has been compared with amitriptyline, imipramine, clomipramine, desipramine, maprotiline, fluoxetine, fluvoxamine, tranylcypromine, toloxatone, mianserin and amineptine in the treatment of depressive disorders. Meta-analysis showed convincing evidence of moclobemide efficacy, comparable with the most potent antidepressants available. The efficacy of moclobemide has been demonstrated in psychotic and non-psychotic depression, in depression with and without melancholia, in endogenous depression (both unipolar and bipolar), in retarded depression and in agitated depression. The efficacy of moclobemide, allied to the unusually benign side effect profile, has led to exploration of its use in other disorders. Two small studies have given encouraging results in the treatment of attention-deficit hyperactivity disorder. Large placebo-controlled studies have shown the activity of moclobemide in the depression that accompanies dementia (such as senile dementia of Alzheimer type). The results also suggested that, in this patient population, cognitive ability improved in parallel. Social phobia has also been shown to improve on treatment with either moclobemide or brofaromine. Clinical trials are in progress on the effect of moclobemide in chronic fatigue syndrome. Moreover, there are encouraging results with the use of brofaromine and moclobemide in panic disorder. Other disorders in which treatment with RIMA is of interest include agoraphobia, bulimia, borderline personality disorder, post-traumatic stress disorder, compulsive hair pulling (trichotillomania), dysmorphophobia, kleptomania as well as various anxiety syndromes.
Ray C, Jefferies S, Weir WR.	Department of Human Sciences, Brunel University, Uxbridge, London.	Coping with chronic fatigue syndrome: illness responses and their relationship with fatigue, functional impairment and emotional status.	936: Psychol Med 1995 Sep;25(5):937-45	The implications of patients' approaches to managing chronic fatigue syndrome were examined in a cross-sectional study. With severity of fatigue controlled, attempting to maintain activity was associated with less functional impairment, while accommodating to the illness was positively related to impairment; behavioural disengagement was related not only to higher levels of impairment but also to greater emotional disturbance. Fatigue itself was positively associated with focusing on symptoms and with behavioural disengagement; it was associated also with illness accommodation, but only for illness of longer duration. The causal direction of relationships between coping and fatigue severity is ambiguous, and a follow-up study will address the effects of coping on changes in the illness over time.
Ray C, Jefferies S, Weir	Department of Human	Life-events and the	910: Br J Med Psychol	Life-events have been implicated in the onset and course of various illnesses. The

WR.	Sciences, Brunel University, Middlesex, UK.	course of chronic fatigue syndrome.	1995 Dec;68 (Pt 4):323-31	present study examined their role in chronic fatigue syndrome, in the context of the ongoing illness. Using the PERI list, events experienced during the past year were elicited in interviews with 130 patients. The analyses were restricted to those events implying moderate or major life change, and separate analyses were carried out for positive and negative events. Positive events were found to be associated with lower scores for fatigue, impairment, anxiety and depression, as assessed at the time of the life-events interview, and these relationships were also significant when prior scores at the beginning of the year were statistically controlled. Negative life-events were associated with higher anxiety, but were unrelated to the other measures. It was concluded that positive life-events and experiences may contribute to the process of recovery in chronic fatigue syndrome, though their occurrence may also be facilitated by a preceding lifting of symptoms.
Reilly PA.	Frimley Park NHS Trust Hospital, Camberley, Surrey, UK.	'Repetitive strain injury': from Australia to the UK.	944: J Psychosom Res 1995 Aug;39(6):783-8	The UK is now experiencing an epidemic of upper limb pain similar to that which affected Australia in the 1980s. The pain is often non-specific, and does not conform to the pattern of various well-recognized rheumatological entities. The syndrome is known by a number of terms, some of which imply an aetiological link to workplace activities unsubstantiated by hard evidence. The syndrome may well be largely psychosocial, and analogous to the chronic fatigue syndrome. It is currently the cause of many contentious and well-publicized medico-legal cases. Possible factors behind the epidemic will be discussed, and an approach to management suggested.
Rest J.		The chronic fatigue syndrome.	955: Ann Intern Med 1995 Jul 1;123(1):75; discussion 76 comment on: Ann Intern Med. 1994 Dec 15;121(12):953-9	
Richardson JR		Disturbance of Hypothalamic Function and Evidence for Persistent Enteroviral Infection in Patients with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(2): 59 - 66	It has been suggested that one of the major effects of persistent virus infections in the production of disorders such as the chronic fatigue syndrome/myalgic encephalomyelitis (CFSFIE) is on the hypothalamus (1). Buspirone, which is one of the anxiolytic drugs of the azapyrone group, causes a release of prolactin by stimulation of serotonin 5-hydroxytryptamine (5-HT) receptors. The buspironeprolactin response was studied in a subgroup of patients with CFS/ME and evidence of persistent enteroviral infection, as shown by the repealed detection of the groupspecific protein of enteroviruses, VPI, in the blood. Family controls who were asymptomatic were studied at the same time. In addition to the response to buspirone, diurnal variations in cortisol and prolactin levels were studied. It was found that the patients with CFS/ME had much greater rises in prolactin levels one hour after buspirone compared to controls. Cortisol levels

				were elevated in the patients, but the rise was not signiftcantly different between the two groups. There was a significant association between the pattern of sleep disturbance, which we speak of as the OWL syndrome, and the ratio of preand post-buspirone prolactin levels. This study shows that there is a hypothalamic disturbance in the patients who also had evidence of enteroviral infection as part of the disorder of CFSME. It represents a quantifiable biochemical alteration to be found in this group of patients
Romer FK.		[Chronic fatigue syndrome and angiotensin-converting enzyme].[article in Danish]	Ugeskr Laeger 1995 Feb 6;157(6):756-7 comment on: Ugeskr Laeger. 1994 Nov 14;156(46):6832-6 Ugeskr Laeger. 1994 Nov 14;156(46):6836-40	
Roser Galard C, Juncadella Garcia E, Hernandez Hernandez A, Maymo Pijuan N.		[Chronic fatigue syndrome: is it ignored in primary care]?[article in Spanish]	985: Aten Primaria 1995 May 31;15(9):587-8 comment in: Aten Primaria. 1995 Dec;16(10):647	
Rotheram EB Jr.		The chronic fatigue syndrome.	954: Ann Intern Med 1995 Jul 1;123(1):75; discussion 76 comment on: Ann Intern Med. 1994 Dec 15;121(12):953-9	
Rowe PC, Bou-Holaigah I, Kan JS, Calkins H.	Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD 21287.	Is neurally mediated hypotension an unrecognised cause of chronic fatigue?	Lancet 1995 Mar 11;345(8950):623-4 comment in: Lancet. 1995 Apr 29;345(8957):1112; discussion 1112-3 Lancet. 1995 Apr 29;345(8957):1113	Neurally mediated hypotension is now recognised as a common cause of otherwise unexplained recurrent syncope, but has not been reported in association with chronic fatigue. We describe seven consecutive non-syncopal adolescents with chronic post-exertional fatigue, four of whom satisfied strict criteria for chronic fatigue syndrome. Upright tilt-table testing induced significant hypotension in all seven (median systolic blood pressure 65 mm Hg, range 37-75), consistent with the physiology of neurally mediated hypotension. Four had prompt improvement in their chronic fatigue when treated with atenolol or disopyramide. These observations suggest an overlap in the symptoms of chronic fatigue syndrome and neurally mediated hypotension.
Sairenji T, Yamanishi K, Tachibana Y, Bertoni G, Kurata T.	Department of Pathology, National Institute of Health, Tokyo, Japan.	Antibody responses to Epstein-Barr virus, human herpesvirus 6 and human herpesvirus 7 in patients with	Intervirology 1995;38(5):269-73	To test for an association between chronic fatigue syndrome (CFS) and infections with Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6) and human herpesvirus 7 (HHV-7), antibodies to these viruses were tested in the serum from three groups of individuals: (1) 10 CFS patients with chronic fatigue beginning with a clinical pattern of acute infectious mononucleosis [IM; true chronic IM

		chronic fatigue syndrome.		(CIM)]; (2) 10 CFS patients whose illness did not start with acute IM (non-CIM), and (3) healthy controls. High EBV antibody titers were demonstrated in most patients. Antibodies to ZEBRA, a product of the immediate early EBV gene BZLF1, were detected in the serum of CFS patients at a higher frequency than in healthy controls. Antibody titers to HHV-6 and HHV-7 were also higher in the patients with CFS than in the controls. These results are consistent with the view that CFS patients may have reactivations of EBV, HHV-6 and HHV-7.
Schaefer KM.	Allentown College of St. Francis de Sales, Center Valley, PA 18034, USA.	Sleep disturbances and fatigue in women with fibromyalgia and chronic fatigue syndrome.	J Obstet Gynecol Neonatal Nurs 1995 Mar-Apr;24(3):229-33	OBJECTIVE: To determine the relationship between sleep disturbances and fatigue in women with fibromyalgia (FM) and those with chronic fatigue syndrome (CFS) and to assess whether any differences existed between the two groups. DESIGN: Descriptive comparative. SETTING: Community program on chronic fatigue syndrome and related disorders. PARTICIPANTS: Sixty-three women who attended the program; 13 had CFS, and 50 had FM. MAIN OUTCOME MEASURES: A moderately strong relationship between fatigue and sleepiness was found ($r = .63$, $p < .01$). Trouble staying asleep was the highest rated sleep disturbance, and fatigue was the most common subjective feeling reported. Women with CFS reported significantly more trouble staying asleep than women with FM, $t(61) = 1.81$, $p < .03$. CONCLUSIONS: Data from this study support that women with FM and CFS encounter problems sleeping. Clinicians are encouraged to assess women with FM and CFS for their quality of sleep rather than amount of sleep. Researchers are encouraged to continue study of sleep disturbances in women with FM and CFS to improve understanding of the disturbances and to test the effectiveness of sleep interventions.
Schlech WF 3rd.	Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada.	The practice of infectious diseases in the 1990s: the Canadian experience.	Clin Infect Dis 1995 Feb;20(2):291-5	A survey of the members of the Canadian Infectious Disease Society was carried out to determine the content of an infectious diseases consultative practice in the 1990s. Respondents were asked to identify all new inpatient, outpatient, and telephone consultations during a 1-week period in 1990. Consultations were categorized by the infectious disease syndrome of the patient and by the microorganism that was identified. Bacterial infections were the most common cause of inpatient consultations, while viral infections were more common in outpatients. Consultations for parasitic infections were primarily for Pneumocystis carinii pneumonia related to infection with the human immunodeficiency virus (HIV). "Newer" infectious disease syndromes such as chronic fatigue syndrome, toxic shock syndrome, and Lyme disease were all represented in the responses for the 1-week study period. The significant impact of HIV infection on the overall consultative load suggests that there will be a continuing need for newly trained infectious disease consultants into the 21st century.
Schmaling KB, Jeannie D. DiClementi		Interpersonal Stressors in Chronic Fatigue	Journal of Chronic Fatigue Syndrome 1995:	This paper reports two preliminary studies on interpersonal influences in CFS. The first study explored histories of abuse in patients with CFS and the second

		Syndrome: A Pilot Study	1(3/4): 153 - 158	report assessed fatigue activity level and relationship satisfaction in CFS patients. The results of the first study indicated that the patients with CFS reported high levels of prior abuse compared to prior experiences of healthy controls. In the second study, higher levels of fatigue were moderately correlated with inactivity for CFS individuals in satisfied relationships, but not among patients in dissatisfied relationships. These findings suggested that solicitous partners may be inadvertently reinforcing disability. The results of the two studies support a biopsychosocial model of CFS.
Schonfeld U.		[Chronic fatigue syndrome].[article in German]	994: Med Monatsschr Pharm 1995 Apr;18(4):90-6	
Schweitzer R, Kelly B, Foran A, Terry D, Whiting J.	Queensland University of Technology, Australia.	Quality of life in chronic fatigue syndrome.	917: Soc Sci Med 1995 Nov;41(10):1367-72	Whilst the debilitating fatigue experienced in patients suffering from Chronic Fatigue Syndrome (CFS) results in a subjective marked impairment in functioning, little research has investigated the impact of this disorder on quality of life. Forty-seven subjects with a confirmed diagnosis of CFS and 30 healthy controls were compared using the Sickness Impact Profile (SIP). A subgroup of subjects were interviewed regarding the impact CFS has had on their social and family relationships, work and recreational activities. Results from both the SIP and the interview revealed that CFS subjects had significantly impaired quality of life, especially in areas of social functioning. These findings highlight the importance of addressing the social isolation and loss of role functioning experienced by CFS sufferers.
Secchiero P, Carrigan DR, Asano Y, Benedetti L, Crowley RW, Komaroff AL, Gallo RC, Lusso P.	Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.	Detection of human herpesvirus 6 in plasma of children with primary infection and immunosuppressed patients by polymerase chain reaction.	J Infect Dis 1995 Feb;171(2):273-80	A sensitive and specific polymerase chain reaction method for the detection of human herpesvirus 6 (HHV-6) DNA in serum or plasma has been developed. In total, 157 human serum or plasma samples were studied. HHV-6 DNA was detected in 6 (85.7%) of 7 children with exanthem subitum, 3 (23.1%) of 13 bone marrow transplant (BMT) recipients, 4 (22.2%) of 18 human immunodeficiency virus (HIV)-infected patients, 1 (2.6%) of 39 patients with chronic fatigue syndrome, and none of 37 healthy adults. In the HHV-6-positive BMT recipients, HHV-6 plasma DNA was transiently detected during episodes of fever and respiratory infection. In children with exanthem subitum and in 1 HIV-infected patient, the HHV-6 strains were characterized as variant B, whereas variant A was detected in all other patients. Detection of viral DNA in serum or plasma is a marker of active infection that can be used to investigate the role of HHV-6 in human disease.
Shanks MF, Ho-Yen DO.	Royal Cornhill Hospital, Aberdeen.	A clinical study of chronic fatigue syndrome.	973: Br J Psychiatry 1995 Jun;166(6):798-801 comment in: Br J Psychiatry. 1995 Oct;167(4):549-50	BACKGROUND. This study examines the hypothesis that more recently ill patients with chronic fatigue syndrome (CFS) might have different characteristics from more chronic patients in tertiary referral centres. METHOD. Sixty-four patients who fulfilled strict diagnostic criteria for CFS had detailed medical, viral, immunological and psychiatric assessment. Patients were advised to remain

				within their energy limits. Patient and doctor monitored progress using a scoring system. RESULTS. Using the Schedule for Affective Disorders and Schizophrenia, patients were placed into four groups: group A (no psychiatric disorder, 35 patients), group B (psychiatric disorder before onset of CFS, 7 patients), group C (coincident psychiatric disorder and CFS, 11 patients), and group D (psychiatric disorder after onset of CFS, 11 patients). There were no viral or immunological differences between the groups. Patients in groups B, C and D had more severe illness than those in group A ($P < 0.05$), but patients in group A had more muscle pain ($P < 0.05$) than patients in group C. Counselling resulted in 52 patients becoming better; nine remained the same and three became worse. CONCLUSIONS. A lower incidence of psychiatric disorder may characterise patients who are more recently ill, as may the type of associated emotional disorder and better outcome.
Sharpe M.		Cognitive behavior therapy for chronic fatigue syndrome.	995: Am J Med 1995 Apr;98(4):420-1; discussion 421-2 comment on: Am J Med. 1993 Feb;94(2):197-203	
Shepherd C.		Viral illness and chronic fatigue (syndrome)	962: Lancet 1995 Jul 1;346(8966):47-8 comment on: Lancet. 1995 Aug 12;346(8972):449 Lancet. 1995 May 27;345(8961):1333-8	
Shepherd C.		Illness behaviour in the chronic fatigue syndrome and multiple sclerosis. Disentangling common characteristics is not so easy.	921: BMJ 1995 Oct 21;311(7012):1093 comment on: BMJ. 1995 Jul 1;311(6996):15-8	
Simpson LO.		Myalgic encephalomyelitis and chronic fatigue syndrome.	N Z Med J 1995 Feb 8;108(993):44-5 comment in: N Z Med J. 1995 Mar 22;108(996):110	
Sisto SA		Rehabilitation of the Patient with Chronic Fatigue Syndrome	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 101 - 104	
Sisto SA, Tapp W,	Neurobehavioral Unit,	Vagal tone is reduced	982: Clin Auton Res	Patients with chronic fatigue syndrome (CFS) often complain of an inability to

Drastal S, Bergen M, DeMasi I, Cordero D, Natelson B.	VA Medical Center, E. Orange, NJ 07018-1095, USA.	during paced breathing in patients with the chronic fatigue syndrome.	1995 Jun;5(3):139-43	maintain activity levels and a variety of autonomic-like symptoms that make everyday activity intolerable at times. The purpose of the study was to determine if there were differences in vagal activity at fixed breathing rates in women with CFS. Twelve women with the diagnosis of CFS between the ages of 32 and 59 years volunteered for the study. Healthy women, who were between the ages of 30 and 49, served as controls. Full signal electrocardiograph and respiratory signals were collected during a paced breathing protocol of three fixed breathing rates (8, 12 and 18 breaths/min) performed in the sitting and standing postures. Vagal activity was analyzed by means of heart rate spectral analysis to determine the subject's response to specific breathing rates and postures. Heart rate variability was used as a non-invasive method of measuring the parasympathetic component of the autonomic nervous system. Using this method, although there was significantly less vagal power in the sitting versus the standing postures for both groups, the overall vagal power was significantly lower ($p < 0.034$) in the CFS group versus healthy controls. Vagal power was also significantly lower ($p < 0.01$ to $p < 0.05$) at all breathing rates in both postures except while standing and breathing at 18 breaths/min. Knowledge of the differences in vagal activity for CFS patients may allow stratification for the analysis of other research variables.
Smets EM, Garssen B, Bonke B, De Haes JC.	University of Amsterdam, Department of Medical Psychology, The Netherlands.	The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue.	997: J Psychosom Res 1995 Apr;39(3):315-25	The Multidimensional Fatigue Inventory (MFI) is a 20-item self-report instrument designed to measure fatigue. It covers the following dimensions: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity. This new instrument was tested for its psychometric properties in cancer patients receiving radiotherapy, patients with the chronic fatigue syndrome, psychology students, medical students, army recruits and junior physicians. We determined the dimensional structure using confirmatory factor analyses (LISREL's unweighted least squares method). The hypothesized five-factor model appeared to fit the data in all samples tested (AGFIs > 0.93). The instrument was found to have good internal consistency, with an average Cronbach's alpha coefficient of 0.84. Construct validity was established after comparisons between and within groups, assuming differences in fatigue based on differences in circumstances and/or activity level. Convergent validity was investigated by correlating the MFI-scales with a Visual Analogue Scale measuring fatigue ($0.22 < r < 0.78$). Results, by and large, support the validity of the MFI.
Solomon GF		Psychoneuroimmunology and Chronic Fatigue Syndrome: Toward New Models of Disease	Journal of Chronic Fatigue Syndrome 1995: 1(1): 3 - 7	
Stevens SR		Using Exercise Testing to Document Functional Disability in CFS	Journal of Chronic Fatigue Syndrome 1995: 1(3/4): 127 - 129	

Strayer DR, William Carter Kenneth I. Strauss, Isadore Brodsky, Robert Suhadolnik, Dharam Ablashi, Berch Henry , William M. Mitchell , Sheila Bastien , Daniel Peterson		Long Term Improvements in Patients with Chronic Fatigue Syndrome Treated with Ampligen	Journal of Chronic Fatigue Syndrome 1995: 1(1): 35 - 53	Fifteen patients who fit the CDC definition of chronic fatigue syndrome (CFS) and had evidence of severe reduction in performance levels by low Kamofsky performance scores (KPS) of 20-60 were treated with Ampligen. At baseline most patients showed evidence of cerebral dysfunction by neuropsychological testing, were antigen positive by cell culture assay for human herpesvirus-6 (HHV-6), and displayed reduced performance during exercise tolerance testing, as measured by oxygen consumption. These patients represented a subset of CFS patients with especially severe and sustained symptomatology. Following 1248 weeks of Ampligen therapy, sustained improvements were noted in KPS ($p < 0.01$). Cognitive function improved including IQ and memory. Oxygen uptake and treadmill duration during exercise tolerance testing was also improved after 24 weeks of treatment ($p < 0.01$). Reduction in HHV-6 expression as measured by the giant cell assay was significant ($p < 0.001$). Patients continued to show significant improvement late in therapy, taking 8 to 12 weeks as baseline. It was concluded that while receiving Ampligen, the severely afflicted patients studied here derived long-lasting clinical benefit from the Ampligen therapy.
Surawy C, Hackmann A, Hawton K, Sharpe M.	University Department of Psychiatry, Warneford Hospital, Oxford, England.	Chronic fatigue syndrome: a cognitive approach.	980: Behav Res Ther 1995 Jun;33(5):535-44	Observations concerning the characteristics of patients who presented to a medical clinic with a principal complaint of chronic medically unexplained fatigue (Chronic Fatigue Syndrome or CFS) are described, including the cognitions (thoughts and assumptions) elicited from a sample of these patients who were treated using cognitive behavioural therapy. On the basis of these observations a cognitive theory of the aetiology of CFS is proposed. These observations have implications for the treatment of patients with CFS.
Swanink CM, van der Meer JW, Vercoulen JH, Bleijenberg G, Fennis JF, Galama JM.	Department of Medical Microbiology, University Hospital Nijmegen, The Netherlands.	Epstein-Barr virus (EBV) and the chronic fatigue syndrome: normal virus load in blood and normal immunologic reactivity in the EBV regression assay.	992: Clin Infect Dis 1995 May;20(5):1390-2	The etiology of chronic fatigue syndrome (CFS) is unknown. Some patients have high antibody titers to viral capsid antigen (VCA) and early antigen (EA) of Epstein-Barr virus (EBV), suggesting that reactivation of EBV is involved. We investigated virus load (spontaneous transformation) and immunologic regression of EBV-induced transformation in peripheral blood mononuclear cells (PBMCs) from 10 selected patients with CFS who had high antibody titers to VCA and EA. The outcome was compared with that for nine healthy controls and one patient with severe chronic active EBV infection (SCAEBV). There were no significant differences in viral load between patients and healthy controls. Immunologic regression of in vitro-transformed PBMCs was also equally efficient in patients and controls. The SCAEBV-infected patient and two controls, who were all seronegative for EBV, showed impaired regression. In conclusion, we were unable to demonstrate a role for reactivation of EBV in CFS, even in selected patients with high titers of antibody to VCA and EA of EBV.
Swanink CM, Vercoulen JH, Bazelmans E, Fennis JF, Bleijenberg G, van		Viral antibodies in chronic fatigue syndrome.	938: Clin Infect Dis 1995 Sep;21(3):708-9 comment on: Clin Infect	

der Meer JW, Galama JM.			Dis. 1994 Sep;19(3):448-53	
Swanink CM, Vercoulen JH, Bleijenberg G, Fennis JF, Galama JM, van der Meer JW.	Department of Medical Microbiology, University Hospital, Nijmegen, Netherlands.	Chronic fatigue syndrome: a clinical and laboratory study with a well matched control group.	990: J Intern Med 1995 May;237(5):499-506	OBJECTIVE. To investigate the relation between severity of complaints, laboratory data and psychological parameters in patients with chronic fatigue syndrome (CFS). SUBJECTS. Eighty-eight patients with CFS and 77 healthy controls matched for age, sex and geographical area. METHODS. Patients and controls visited our outpatient clinic for a detailed medical history, physical examination and psychological tests: Checklist Individual Strength (CIS). Beck Depression Inventory (BDI) and Sickness Impact Profile (SIP). Venous blood was drawn for a complete blood cell count, serum chemistry panel, C-reactive protein and serological tests on a panel of infectious agents. RESULTS. All patients fulfilled the criteria for CFS as described by Sharpe et al. (J R Soc Med 1991; 84: 118-21), only 18 patients (20.5%) fulfilled the CDC criteria. The outcome of serum chemistry tests and haematological tests were within the normal range. No significant differences were found in the outcome of serological tests. Compared to controls, significant differences were found in the results on the CIS, the BDI, and the SIP. These results varied with the number of complaints (CDC criteria). When the number of complaints was included as the covariate in the analysis, there were no significant differences on fatigue severity, depression, and functional impairment between patients who fulfilled the CDC criteria and patients who did not. CONCLUSION. It is concluded that the psychological parameters of fatigue severity, depression and functional impairment are related to the clinical severity of the illness. Because the extensive panel of laboratory tests applied in this study did not discriminate between patients and controls, it was not possible to investigate a possible relation between the outcomes of psychological and laboratory testing.
Tedeschi R, Foong YT, Cheng HM, dePaoli P, Lehtinen T, Elfborg T, Dillner J.	Microbiology and Tumor Biology Center, Karolinska Institute, Stockholm, Sweden.	The disease associations of the antibody response against the Epstein-Barr virus transactivator protein ZEBRA can be separated into different epitopes.	983: J Gen Virol 1995 Jun;76 (Pt 6):1393-400	The BamHI-Z-encoded Epstein-Barr virus (EBV) replication activator (ZEBRA) is a key mediator of the switch from latency to productive cycle in EBV virus. Antibodies against ZEBRA are a marker of EBV reactivation and are regularly found among patients with infectious mononucleosis (IM) or nasopharyngeal carcinoma (NPC), but are only rarely found among healthy EBV-seropositive donors. In order to define the serologically reactive epitopes in the ZEBRA protein, we synthesized a set of overlapping peptides and tested them for reactivity with serum samples from EBV-seronegative persons, patients with NPC, IM, chronic fatigue syndrome, lymphoma or from healthy donors. Three major EBV-specific epitopes were found. These epitopes were further defined and optimized using substitution or truncation analogues of the peptides. Reactivity with epitope number 22 was found in 63% of NPC patients' sera, with < 2% of healthy donors' sera being positive. Serological reactivity with epitope number 19 was associated with IM (57% positive, 5% healthy donors positive). Serum

				antibodies against epitope 1 were found among healthy donors, but were significantly elevated among patients with NPC, IM or lymphomas. In conclusion, different serologically reactive epitopes in the ZEBRA protein associate with different EBV-associated diseases.
Trigwell P, Hatcher S, Johnson M, Stanley P, House A.	High Royds Hospital, Menston, Leeds.	"Abnormal" illness behaviour in chronic fatigue syndrome and multiple sclerosis.	961: BMJ 1995 Jul 1;311(6996):15-8 comment in: BMJ. 1995 Oct 21;311(7012):1092-3 BMJ. 1995 Oct 21;311(7012):1093	OBJECTIVE--To investigate the presence of abnormal illness behaviour in patients with a diagnosis of chronic fatigue syndrome. DESIGN--A cross sectional descriptive study using the illness behaviour questionnaire to compare illness behaviour scores and illness behaviour profiles of patients with chronic fatigue syndrome and patients with multiple sclerosis. SETTING--A multidisciplinary fatigue clinic and a teaching hospital neurology outpatient clinic. SUBJECTS--98 patients satisfying the Oxford criteria for chronic fatigue syndrome and 78 patients with a diagnosis of multiple sclerosis. MAIN OUTCOME MEASURE--Responses to the 62 item illness behaviour questionnaire. RESULTS--90 (92%) patients in the chronic fatigue syndrome group and 70 (90%) in the multiple sclerosis group completed the illness behaviour questionnaire. Both groups had significantly high scores on the general hypochondriasis and disease conviction subscales and significantly low scores on the psychological versus somatic concern subscale, as measured in relation to normative data. There were, however, no significant differences in the subscale scores between the two groups and the two groups had identical illness behaviour profiles. CONCLUSION--Scores on the illness behaviour questionnaire cannot be taken as evidence that chronic fatigue syndrome is a variety of abnormal illness behaviour, because the same profile occurs in multiple sclerosis. Neither can they be taken as evidence that chronic fatigue and multiple sclerosis share an aetiology. More needs to be known about the origins of illness beliefs in chronic fatigue syndrome, especially as they are important in determining outcome.
Van Houdenhove B, Onghena P, Neerinckx E, Hellin J.	Department of Psychiatry, Katholieke Universiteit Leuven, Belgium.	Does high 'action-proneness' make people more vulnerable to chronic fatigue syndrome? A controlled psychometric study.	966: J Psychosom Res 1995 Jul;39(5):633-40	Degree of premorbid 'action-proneness' was measured, using a self-administered questionnaire, in 35 patients suffering from chronic fatigue syndrome (CFS), all the members of 'ME'-self help groups and all those meeting CDC-criteria of CFS. The results were compared with those of 30 chronic idiopathic musculoskeletal pain patients, 34 patients with a chronic organic condition, and 34 neurotic patients without primary somatic complaints. Statistical analysis showed that CFS patients described themselves as significantly more 'action-prone' than the last two groups, and to a degree which was comparable with the chronic pain group. The results could not be explained by concomitant depression and are in accordance with anecdotal reports of premorbid hyperactive lifestyle in CFS patients. Further investigations seem worthwhile to test the hypothesis that hyperactivity might be a predisposing factor for chronic illness behaviour in CFS patients.
Wahlstrom L.	Psykiatrisk konsult till	[Does chronic fatigue	Lakartidningen 1995 Jan	

	infektionskliniken, Huddinge sjukhus.	syndrome have physiological or psychological causes? A wrongly formulated question may result in information].[article in Swedish]	18;92(3):150-3	
Welch JC.		Chronic fatigue syndrome and liquorice.	970: N Z Med J 1995 Jun 14;108(1001):234-5 comment in: N Z Med J. 1995 Aug 11;108(1005):324-5 N Z Med J. 1995 Jul 28;108(1004):301 N Z Med J. 1995 Jun 28;108(1002):259 comment on: N Z Med J. 1995 Apr 26;108(998):156-7	
Wessely S, Chalder T, Hirsch S, Pawlikowska T, Wallace P, Wright DJ.	Department of Psychological Medicine, King's College School of Medicine and Dentistry, London, UK.	Postinfectious fatigue: prospective cohort study in primary care.	986: Lancet 1995 May 27;345(8961):1333-8 comment in: Lancet. 1995 Jul 1;346(8966):47 Lancet. 1995 Jul 1;346(8966):47-8 Lancet. 1995 Jul 1;346(8966):48	The idea that chronic fatigue has an infectious origin has become popular, but the main evidence for such an association has come from retrospective case-control studies, which are subject to ascertainment bias. We report a prospective study of the outcome of clinically diagnosed infections in patients presenting to UK general practitioners. Questionnaires assessing fatigue and psychiatric morbidity were sent to all patients aged 18-45 years in the study practices. The prevalence of chronic fatigue and chronic fatigue syndrome was then ascertained among 1199 people aged 18-45 who presented to the general practitioners with symptomatic infections and in 1167 people who attended the surgeries for other reasons. 84% were followed up at 6 months. 9.9% of cases and 11.7% of controls reported chronic fatigue (odds ratio 1.0 [95% CI 0.6-1.1]). There were no differences in the proportions who met various criteria for chronic fatigue syndrome. No effect of infection was noted when we excluded subjects who reported fatigue or psychological morbidity at the baseline screening. The strongest independent predictors of postinfectious fatigue were fatigue assessed before presentation with clinical infection (3.0 [1.9-4.7]) and psychological distress before presentation (1.8 [1.2-2.9]) and at presentation with the acute infection (1.8 [1.1-2.8]). There was no effect of sex or social class. Our study shows no evidence that common infective episodes in primary care are related to the onset of chronic fatigue or chronic fatigue syndrome.
Wessely S.	Department of	The epidemiology of	Epidemiol Rev	

	Psychological Medicine, King's College School of Medicine, London, England. Review, Multicase	chronic fatigue syndrome.	1995;17(1):139-51	
Westin J, Rodjer S, Turesson I, Cortelezzi A, Hjorth M, Zador G.	Department of Medicine/Haematology, University of Lund, Sweden.	Interferon alfa-2b versus no maintenance therapy during the plateau phase in multiple myeloma: a randomized study. Cooperative Study Group.	Br J Haematol 1995 Mar;89(3):561-8	This clinical trial was designed to investigate if maintenance therapy with alfa-interferon could prolong the plateau phase in patients with multiple myeloma. In addition, the tolerability of interferon treatment and its effect on survival were evaluated. From September 1987 to September 1989 a total of 314 patients were accrued to a multi-institutional randomized clinical trial. All patients entered into the protocol received standard melphalan-prednisone (MP) induction therapy. Response was noted in 184 (59%) and a plateau phase achieved in 155 (49%). From the latter group, 125 eligible patients were randomized to either interferon alfa-2b or no maintenance. The patients were followed for an average of 51 months (minimum 36 months) from the time of randomization. The plateau phase was significantly prolonged in the group of patients treated with interferon (median 13.9 v 5.7 months from the time of randomization; $P < 0.0001$). The interferon therapy was tolerated fairly well, moderate granulocytopenia and a chronic fatigue syndrome being the most frequent side-effects (22% v 18% W.H.O. grade 3 toxicity). The median survival from randomization was almost identical in both groups (36 v 35 months). The study shows that interferon maintenance therapy given to multiple myeloma patients who have achieved a response to initial treatment with MP prolongs the plateau phase duration with tolerable toxicity. The clinical value of this finding should be interpreted with caution, because survival was not prolonged. Further studies are required to clarify the role of interferon in the treatment of multiple myeloma. Multicenter Study Randomized Controlled Trial
Wilson A, Hickie I, Lloyd A, Hadzi-Pavlovic D, Wakefield D.	Department of Psychiatry, Prince Henry Hospital, Little Bay, NSW, Australia.	Cell-mediated immune function and the outcome of chronic fatigue syndrome.	942: Int J Immunopharmacol 1995 Aug;17(8):691-4	This study examined the importance of cell-mediated immunity in determining the long-term outcome of patients diagnosed with chronic fatigue syndrome (CSF). A total of 103 patients (74%) of 139 previously enrolled in one of two treatment trials conducted within a university hospital referral center was reviewed a mean of 3.2 yr after trial entry. Ongoing symptom severity, levels of disability and immunological function were assessed at follow-up. The relationship between immunological function at trial entry and measures of outcome was also evaluated. Sixty-five patients (63%) had improved, while only 6 (6%) reported no current symptoms. Thirty-one subjects (30%) were unable to perform any form of work and 26 (25%) were on a disability benefit directly attributable to CFS. Cell-mediated immune function, as measured at trial entry or follow-up, did not appear to affect outcome. Whilst improvement occurred in the majority of patients with CFS, a substantial proportion (37%) remained

				functionally impaired. Impairment of cell-mediated immunological function measured during the course of the illness may not be an important factor in determining long-term outcome.
Wong MT, Dolan MJ, Lattuada CP Jr, Regnery RL, Garcia ML, Mokulis EC, LaBarre RA, Ascher DP, Delmar JA, Kelly JW, et al.	Department of Infectious Diseases/PSMI, Wilford Hall Medical Center, Lackland Air Force Base, Texas 78236-5300, USA.	Neuroretinitis, aseptic meningitis, and lymphadenitis associated with Bartonella (Rochalimaea) henselae infection in immunocompetent patients and patients infected with human immunodeficiency virus type 1.	945: Clin Infect Dis 1995 Aug;21(2):352-60	Bartonella (Rochalimaea) henselae causes a variety of diseases, including bacillary angiomatosis, peliosis hepatis, lymphadenitis, aseptic meningitis with bacteremia, and cat-scratch disease (CSD). Cases of B. henselae-related disease were collected from September 1991 through November 1993. Patients with suspected CSD, unexplained fever and lymphadenitis, or suspected B. henselae infection who were seen in the Infectious Diseases Clinic at Wilford Hall Medical Center (Lackland Air Force Base, TX) underwent physical and laboratory examinations. In addition to three previously described cases, 23 patients with R. henselae-related infection were identified. The patients included 19 immunocompetent individuals presenting with lymphadenitis (11), stellate neuroretinitis (5), Parinaud's oculoglandular syndrome with retinitis (1), chronic fatigue syndrome-like disease (1), and microbiologically proven adenitis without the presence of immunofluorescent antibodies to B. henselae (1) and four patients infected with human immunodeficiency virus type 1 presenting with isolated lymphadenitis (1), diffuse upper-extremity adenitis (1), neuroretinitis (1), and aseptic meningitis (1). A couple with neuroretinitis and their pet cat, a persistently fatigued patient, and a patient with Parinaud's oculoglandular syndrome were shown to have bacteremia. Tissue cultures were positive for B. henselae in three recent cases of adenitis. Twenty-two patients were exposed to cats. This series further demonstrates the similarities between B. henselae-related diseases and CSD and identifies several new syndromes due to B. henselae.
Woodward RV, Broom DH, Legge DG.	National Centre for Epidemiology and Population Health, Australian National University, Canberra.	Diagnosis in chronic illness: disabling or enabling--the case of chronic fatigue syndrome.	978: J R Soc Med 1995 Jun;88(6):325-9 comment in: J R Soc Med. 1995 Dec;88(12):723	This paper examines doctors' and patients' views on the consequences of an increasingly common symptomatic diagnosis, chronic fatigue syndrome (CFS). Two studies were conducted: the first comprised interviews with 20 general practitioners; the second was a longitudinal study, comprising three interviews over a period of 2 years with 50 people diagnosed with CFS. Contrasts were apparent between doctors' practical and ethical concerns about articulating a diagnosis of CFS and patients' experiences with and without such a diagnosis. Seventy per cent of the doctors were reluctant to articulate a diagnosis of CFS. They felt constrained by the scientific uncertainty regarding its aetiology and by a concern that diagnosis might become a disabling self-fulfilling prophecy. Patients, by contrast, highlighted the enabling aspects of a singular coherent diagnosis and emphasized the negative effects of having no explanation for their problems.
Wookey C.		Viral illness and chronic fatigue (syndrome)	959: Lancet 1995 Jul 1;346(8966):48 comment in: Lancet.	

			1995 Aug 12;346(8972):449 comment on: Lancet. 1995 May 27;345(8961):1333-8	
Yatham LN, Morehouse RL, Chisholm BT, Haase DA, MacDonald DD, Marrie TJ.	Dalhousie University, Nova Scotia Hospital, Dartmouth.	Neuroendocrine assessment of serotonin (5-HT) function in chronic fatigue syndrome.	Can J Psychiatry 1995 Mar;40(2):93-6 comment in: Can J Psychiatry. 1996 Mar;41(2):129-31	Prolactin and cortisol responses to dl-fenfluramine challenge were examined in 11 patients with chronic fatigue syndrome and in 11 healthy controls who were age and gender matched. After obtaining two baseline samples, each subject was given 60 mg of dl-fenfluramine orally and further blood samples were drawn hourly during the following five hours in order to measure prolactin and cortisol levels. There was no difference in either baseline or fenfluramine-induced hormonal responses between patients with chronic fatigue syndrome and controls. There was also no correlation between depression scores on HAM-D and hormonal responses in patients with chronic fatigue syndrome. The findings of this study do not support a role for 5-HT in chronic fatigue syndrome.
Zannolli R, Morgese G.	Paediatric Clinic, Chieti University, Italy.	New pathogens, and diseases old and new. I) Afipia felis and Rochalimaea. II) Parvovirus B 19. III) herpesvirus 6.	909: Panminerva Med 1995 Dec;37(4):238-47	The paper describes events that in the last fifteen years, have led to the identification of the aetiological agents of three widely known diseases: cat scratch disease, erythema infectiosum and exanthem subitum. The particular features of Afipia felis and Rochalimaea, Parvovirus B 19 and Herpesvirus 6 are presented. The paternity of new diseases (i.e. bacillary angiomatosis, bacillary peliosis hepatitis, LES-like syndrome, chronic fatigue syndrome, petechial glove and sock syndrome, etc.) has also been attributed to some of these pathogens as has the paternity of some older ones (i.e. aplastic crisis, erythroblastosis fetalis, trench fever, hepatitis, opportunistic infection, etc.). It has been argued that the same pathogen can cause different diseases depending on the immunogenic state of the subject. To date, persisting difficulties in isolating the pathogen or differentiating between latent or active infection, still in some cases raises doubts concerning the attribution of the disease to a specific agent. New immunological or molecular techniques, allowing the direct detection of in vivo replication, are still needed in order to establish a sure connection between some of these agents and some of these diseases. Progress here will both give more accurate data about the epidemiology of some diseases and allow us to apply more appropriate treatment and prevention techniques. Review, Academic
Zhang C, Baumer A, Mackay IR, Linnane AW, Nagley P.	Department of Biochemistry, Monash University, Clayton, Victoria, Australia.	Unusual pattern of mitochondrial DNA deletions in skeletal muscle of an adult human with chronic fatigue syndrome.	998: Hum Mol Genet 1995 Apr;4(4):751-4	

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Abbot NC, Spence VA, Lowe JG, Potts RC, Hassan AH, Belch JJ, Beck JS.		Chronic fatigue syndrome. Immunological findings vary between populations.	BMJ 1994 May 14;308(6939):1299 comment on: BMJ. 1994 Mar 19;308(6931):756-9	
Ablashi DV, Berneman ZN, Kramarsky B, Asano Y, Choudhury S, Pearson GR.	Georgetown University School of Medicine, Washington, DC 20007.	Human herpesvirus-7 (HHV-7).	In Vivo 1994 Jul-Aug;8(4):549-54	HHV-7 first isolated in 1990 from a healthy individual, is a ubiquitous agent. The second independent isolation of HHV-7 from a chronic fatigue syndrome patient was reported in 1992. The seroepidemiology of HHV-7 suggested that its prevalence rate in the U.S.A. population is > 85%; however, in Japan a low prevalence rate has been reported. HHV-7 can be more readily isolated from the saliva than HHV-6. The primary infection of HHV-7 appears later in life than HHV-6. No disease has been reported that is etiologically linked to HHV-7. HHV-7 is more closely related to HHV-6 and the human cytomegalovirus than other members of the human herpesvirus family.
Ablashi DV.	National Cancer Institute, Bethesda, Maryland.	Viral studies of chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S130-3	
Agut H, Aubin JT.	Laboratoire de virologie, CNRS EP 57, CERVI, hopital Pitie-Salpetriere, Paris.	[A new virus: the human herpesvirus 6].[article in French]	Rev Prat 1994 Apr 1;44(7):871-4	Human herpesvirus 6 (HHV-6) was discovered in 1986. This novel virus is genetically related to cytomegalovirus. HHV-6 mainly infects T lymphocytes but its tropism appears to be much wider and probably involves some epithelial cells. Two HHV-6 variants, designated as A and B, can be distinguished by genetical and immunological analysis. HHV-6 infection is ubiquitous and widespread; it occurs most often during infancy and it is life-long. During primary infection, HHV-6 is the causative agent of exanthem subitum and fever episodes without rash in infants. HHV-6 is suspected to be the causative agent of opportunistic infections such as pneumonitis and retinitis in immunocompromised subjects. Its role in human immunodeficiency virus infection, lymphomas and chronic fatigue syndrome is controversial. In vitro, HHV-6 is sensitive to ganciclovir and foscarnet.
Altura BT, Burack JL, Cracco RQ, Galland L, Handwerker SM, Markell MS, Mauskop A, Memon ZS, Resnick LM, Zisbrod Z, et al.	Department of Physiology, State University of New York, Health Science Center at Brooklyn 11203.	Clinical studies with the NOVA ISE for IMg2+.	Scand J Clin Lab Invest Suppl 1994;217:53-67	The Nova ISE for IMg2+ was utilized to examine IMg2+ in plasma and serum of patients with a variety of pathophysiologic and disease syndromes (e.g., long-term renal transplants [LTRT], during and before cardiac surgery, migraine headaches, head trauma, pregnancy, chronic fatigue syndrome [CFS], non-insulin dependent diabetes mellitus [NIDDM], asthma and after excessive dietary intake of Mg). The results indicate that LTRT treated with cyclosporin A, migraine, head trauma, pregnancy, NIDDM, diseased pregnant, and asthmatic patients all on the average, exhibit significant depression in IMg2+ but not total Mg (TMg). Patients with CFS failed to exhibit changes in serum IMg2+ or TMg levels. Increased

				dietary load of Mg, for only 6 days, resulted in significant elevations of serum IMg2+ but not TMg. Correlations between the clinical course of several of these syndromes and the fall in IMg2+ were found. The Ca2+/Mg2+ ratio appears to be an important guide for signs of peripheral vasoconstriction and or spasm and possibly enhanced atherogenesis. Overall, the data point to important uses for ISE's for IMg2+ in the diagnosis and treatment of disease states.
Ambrogetti A, Olson LG.	Sleep Disorders Centre, John Hunter Hospital, New Lambton, NSW.	Consideration of narcolepsy in the differential diagnosis of chronic fatigue syndrome.	Med J Aust 1994 Apr 4;160(7):426-9	OBJECTIVE: To justify the inclusion of narcolepsy in the differential diagnosis of patients with chronic fatigue. CLINICAL FEATURES: We report three patients aged 17 (two women and one man) and one woman aged 45 who had been diagnosed as having chronic fatigue syndrome (CFS). They had no psychiatric illness. Their main problem was severe daytime sleepiness, presenting as "tiredness and fatigue". The history, sleep study and multiple sleep latency test suggested a diagnosis of narcolepsy. INTERVENTION: Treatment with methylphenidate resulted in complete resolution of symptoms in two patients and significant improvement in the other two. CONCLUSIONS: The differential diagnosis of CFS requires the exclusion of other conditions. If daytime sleepiness is a major complaint, other symptoms of narcolepsy should be sought and the diagnosis confirmed with sleep study and a multiple sleep latency test.
Anand AC, Kumar R, Rao MK, Dham SK.	AFMC, Pune.	Low grade pyrexia: is it chronic fatigue syndrome?	J Assoc Physicians India 1994 Aug;42(8):606-8 comment in: J Assoc Physicians India. 1995 Oct;43(10):725-6	Eighty seven consecutive patients presenting with prolonged low grade pyrexia (99 degrees-101 +/- F) during 1984-93 were followed up for a mean duration of 2.9 years. Mean age was 37.55 years (SD + 10.16) and 66 (75.8%) were females. Onset of pyrexia was acute in 57 patients and was associated with chilly sensation (42), Fatigue (69), Arthralgias (61), myalgias (55) and several other non specific symptoms. Clinical examination showed paucity of physical signs with 7 patients showing tender lymphadenopathy, 7 showing splenomegaly, 5 hepatomegaly, and 1 phylctenular conjunctivitis. Psychiatric examination was within normal limits. Extensive investigations for any viral or other infection, autoimmune disorder or malignancy were unrewarding. Patients were followed up for an average of 2.9 (2 to 5 years). Thirteen patients had become asymptomatic within one year of onset of symptoms, 38 by two years and 45 by the end of three years. This syndrome may be a variant of chronic fatigue syndrome.
Anderson N.		Chronic fatigue syndrome. ...and study them separately.	BMJ 1994 May 14;308(6939):1298 comment on: BMJ. 1994 Mar 19;308(6931):732-3	
Antoni MH, Brickman A, Lutgendorf S, Klimas N, Imia-Fins A, Ironson G, Quillian R, Miguez	Department of Psychology, University of Miami, Coral Gables, Florida 33124.	Psychosocial correlates of illness burden in chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S73-8	We related reported physical symptoms, cognitive appraisals (e.g., negative style of thinking), and coping strategies (e.g., denial/disengagement strategies) with illness burden across several functional domains separately in subsets of chronic fatigue syndrome (CFS) patients with (n = 26) and without (n = 39) concurrently

MJ, van Riel F, Morgan R, et al.				diagnosed major depressive disorder (MDD). In regard to cognitive appraisal measures, automatic thoughts and dysfunctional attitudes were strongly associated with a higher illness burden, as indicated in sickness impact profile (SIP) scores. Active-involvement coping strategies measured on COPE scales (active coping, planning, and positive reinterpretation and growth) were not associated with SIP scores, while other coping strategies (mental disengagement, behavioral disengagement, and denial) were positively correlated with psychosocial and physical SIP scales, especially those pertaining to interpersonal life-style arenas. After we accounted for the number of different CFS-specific physical complaints reported and DSM-III-R depression diagnosis status, cognitive appraisals and coping strategies predicted a substantial proportion of the variance in the severity of illness burden. For the most part, the magnitude of these relationships between our predictor model variables and illness burden severity was similar in the MDD and non-MDD subgroups.
Arber M, Macintyre A.		Chronic fatigue syndrome or myalgic encephalitis.	Lancet 1994 Jan 22;343(8891):242-3 comment on: Lancet. 1993 Nov 13;342(8881):1247-8	
Artsimovich NG, Chugunov VS, Kornev AV, Ivanova TM, Chugunov AV, Oprishchenko MA.		[The chronic fatigue syndrome].[article in Russian]	Zh Nevropatol Psikhiatr Im S S Korsakova 1994;94(5):47-50	CFIDS (chronic fatigue and immune disfunction syndrome) is also known as CFS (chronic fatigue syndrome), CEBV (chronic Epstein-Barr virus), M.E. (myalgic encephalomyelitis), yuppie flu and by other names. It is a complex illness characterized by incapacitating fatigue (experienced as exhaustion and extremely poor stamina), neurological problems and a constellation of symptoms that can resemble many disorders, including; mononucleosis, multiple sclerosis, fibromyalgia, AIDS-related complex (ARC) and autoimmune diseases such as lupus. These symptoms tend to wax and wane, but any often severely debilitating and may last for many months or years. All sections of the population (including children) are at risk, but women under 45 seem to be most susceptible. The investigators suggest that CFIDS results from dysfunction of the immune system. The exact nature of this dysfunction is not yet well defined, but it can generally be viewed as an unregulated or overactive state which is responsible for most of the symptoms. There is also evidence of some immune suppression in CFIDS. None of the treatments is consistently satisfactory, but some may be helpful: psychotherapy, physiotherapy, exercise programs, acupunctures, small doses of antidepressants, etc.
Barker E, Fujimura SF, Fadem MB, Landay AL, Levy JA.	Department of Medicine, University of California, San Francisco 94143-0128.	Immunologic abnormalities associated with chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S136-41	Several aspects of cellular immunity in patients with clinically defined chronic fatigue syndrome (CFS) were evaluated and compared with those in healthy individuals. Flow cytometric analyses revealed normal expression of total T (CD3+), B (CD19+), and NK (natural killer) (CD16+, CD56+) markers on the surface

				of peripheral blood mononuclear cells (PMC) from patients with CFS. However, compared with those of healthy individuals, patients' CD8+ T cells expressed reduced levels of CD11b and expressed the activation markers CD38 and HLA-DR at elevated levels. In many of the individuals in whom expression of CD11b was reduced the expression of CD28 was increased. These findings indicate expansion of a population of activated CD8+ cytotoxic T lymphocytes. A marked decrease in NK cell activity was found in almost all patients with CFS, as compared with that in healthy individuals. No substantial abnormalities in monocyte activity or T cell proliferation were observed. The results of this study suggest that immune cell phenotype changes and NK cell dysfunction are common manifestations of CFS.
Bates DW, Buchwald D, Lee J, Kith P, Doolittle TH, Umali P, Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts 02115.	A comparison of case definitions of chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S11-5	We compared three case definitions of chronic fatigue syndrome (CFS) applied to patients followed in CFS clinics at two institutions. All patients had debilitating fatigue without apparent etiology; patients with medical conditions associated with chronic fatigue and with major psychiatric disorders were stratified and presented separately. Patients were classified according to whether they met case definitions developed by a Centers for Disease Control and Prevention (CDC) Working Group, a British group, or an Australian group. When findings for 805 patients followed at the two clinics were combined, 61% met the CDC criteria, 55% met the British criteria, and 56% met the Australian criteria; these proportions were relatively similar at both sites. In addition, similar laboratory abnormalities were found for all case groups and for fatigued patients who met none of the three case definitions. These data suggest that more inclusive case definitions may be superior.
Bearn J, Wessely S.	Bethlem Royal Hospital, London, UK.	Neurobiological aspects of the chronic fatigue syndrome.	Eur J Clin Invest 1994 Feb;24(2):79-90	
Bell DS, Bell KM, Cheney PR.	Department of Pediatrics, Cambridge Hospital, Massachusetts 02139.	Primary juvenile fibromyalgia syndrome and chronic fatigue syndrome in adolescents.	Clin Infect Dis 1994 Jan;18 Suppl 1:S21-3	Chronic fatigue syndrome (CFS) and primary juvenile fibromyalgia syndrome (PJFS) are illnesses with a similar pattern of symptoms of unknown etiology. Twenty-seven children for whom CFS was diagnosed were evaluated for fibromyalgia by the presence of widespread pain and multiple tender points. Eight children (29.6%) fulfilled criteria for fibromyalgia. Those children who met fibromyalgia criteria had a statistically greater degree of subjective muscle pain, sleep disturbance, and neurological symptoms than did those who did not meet the fibromyalgia criteria. There was no statistical difference between groups in degree of fatigue, headache, sore throat, abdominal pain, depression, lymph node pain, concentration difficulty, eye pain, and joint pain. CFS in children and PJFS appear to be overlapping clinical entities and may be indistinguishable by current diagnostic criteria.
Bell DS.	Harvard Medical School, Boston, Massachusetts.	Chronic fatigue syndrome update.	Postgrad Med 1994 Nov 1;96(6):73-6, 79-81	Neither Epstein-Barr virus nor human herpesvirus 6 appears to play a causative role in chronic fatigue syndrome. The possibility that a novel human retrovirus

		Findings now point to CNS involvement.		may be present in patients with the syndrome needs further study. A number of abnormalities found in patients with chronic fatigue syndrome point to central nervous system (CNS) involvement. These include immunologic abnormalities, indications of pituitary and hypothalamic involvement, abnormal basal plasma levels of certain neurotransmitter metabolites, and cerebral perfusion abnormalities. The symptom pattern of chronic fatigue syndrome may eventually be explainable in terms of CNS dysfunction.
Bellanti JA.		[Chronic fatigue syndrome].[article in Spanish]	612: Rev Alerg Mex 1994 May-Jun;41(3):65-8	
Bennett AL, Fagioli L, Komaroff AL, Raoult D.		Persistent infection with Bartonella (Rochalimaea) henselae or Afipia felis is unlikely to be a cause of chronic fatigue syndrome.	Clin Infect Dis 1994 Oct;19(4):804-5	
Bertolin Guillen JM, Bedate Villar J.	Centro de Salud Mental, Diputacion Provincial-Servicio Valenciano de Salud.	[Therapeutic guidelines in chronic fatigue syndrome].[article in Spanish]	Actas Luso Esp Neurol Psiquiatr Cienc Afines 1994 May-Jun;22(3):127-30	The treatment of CFS is not definitive up till now and it is limited both by ignorance of its causes and by different applicable operative case definitions. It has been etiopathologically related to infectious agents, neuromuscular illnesses, neuro-endocrinous-immunologic alterations and to different psychiatric disorders, particularly depressive disorders. Consequently, a great variety of therapeutic strategies have been tried, most of them with insufficient results. Among the medicamentous ones: immunity activator agents such as recombinant interleukin-2, nonspecific immunitary modulators such as seric gamma globulin, antivirus drugs such as acyclovir, muscular relaxants such as ciclobenzaprine, H2 receptor blockers and steroid and nonsteroid anti-inflammatory drugs such as ibuprofen, naproxen and fulbiprofen. Better results seem to have been obtained with antidepressants, and amfebutamone and serotonin-reuptake selective inhibitors are specially promising. Among the nonmedicamentous strategies, cognitive behavioural treatment can be effective and the so called "psychiatric management of the patient with CFS" has been proposed as a global, pragmatic, individualized, comprehensive approach which must be completed with other interdisciplinary interventions on the patient and his environment.
Blatch C, Blatt T.		Chronic fatigue syndrome. Role of psychological factors overemphasised.	BMJ 1994 May 14;308(6939):1297 comment in: BMJ. 1994 Jul 23;309(6949):275 comment on: BMJ. 1994 Mar 19;308(6931):756-9	
Bonner D, Ron M,	Maudsley Hospital,	Chronic fatigue	J Neurol Neurosurg	Forty-six of 47 patients diagnosed as having chronic fatigue and offered

Chalder T, Butler S, Wessely S.	London, UK.	syndrome: a follow up study.	Psychiatry 1994 May;57(5):617-21 comment in: J Neurol Neurosurg Psychiatry. 1995 Jun;58(6):764-5	treatment four years previously were followed up. Twenty-nine patients were interviewed, three patients refused an interview, and information on the remaining 14 was obtained from their general practitioners. All the instruments used at interview had been used in the initial study. The long-term prognosis for patients with chronic fatigue syndrome who have initially responded to treatment is good. Spontaneous recovery in those who declined or who did not benefit from treatment is unlikely. Patients who continue to fulfil the criteria for chronic fatigue syndrome four years after they were initially diagnosed are likely to have had more somatic disorders, to have been more fatigued, and to have had a previous psychiatric history when they were initially assessed.
Branco JC, Tavares V, Abreu I, Humbel RL.	Unidade de Reumatologia, Hospital de Egas Moniz, Lisboa.	[Viral infection and fibromyalgia].[article in Portuguese]	Acta Med Port 1994 Jun;7(6):337-41	Fibromyalgia (FM) is a very frequent syndrome of unknown cause, characterized by generalized pain, fatigue and a number of tender points to palpation. Among the several etiopathogenic hypotheses discussed, the association of FM with some viral infections has been the object of multiple studies due to its relation and similarity with the chronic fatigue syndrome, acknowledges as being related, although not exclusively, with the chronic infection by the Epstein-Barr virus. Many individual descriptions of association between infection with the human parvovirus B19 and FM led us to carry out this study, comparing the serology for that virus in 52 patients with FM and 39 healthy controls. The titers of specific IgG anti-parvovirus B19 antibodies, indicating previous infection with that virus, were determined in all 91 individuals through ELISA method and at the same laboratory. Results revealed, though not significantly, a greater prevalence of positive titers, of which the mean was also higher, in patients than in controls. When comparing the women from both groups, this tendency was even less perceptible. These data imply that there is no etiologic association between infection with the human parvovirus B19 and FM.
Briggs NC, Levine PH.	Viral Epidemiology Branch, NCI/NIH, Bethesda, Maryland 20892.	A comparative review of systemic and neurological symptomatology in 12 outbreaks collectively described as chronic fatigue syndrome, epidemic neuromyasthenia, and myalgic encephalomyelitis.	Clin Infect Dis 1994 Jan;18 Suppl 1:S32-42	Outbreaks of illnesses of unknown etiology typified by a chronic relapsing course of constitutional symptoms and nervous system involvement have collectively been referred to as chronic fatigue syndrome, epidemic neuromyasthenia, and myalgic encephalomyelitis. To examine heterogeneity of clinical presentation, a comparative review was undertaken for 12 well-documented outbreaks reported since 1934. A systemic syndrome characterized by excessive fatigue, myalgias, headache, low-grade fever, and other constitutional symptoms was common to cases in all outbreaks. However, marked heterogeneity in the range of neurological features was apparent. On the basis of predominant neurological manifestations, outbreaks could be grouped into four levels of increasing neurological involvement: affective neuropsychological changes (level I); prominent cutaneous sensory symptoms with both affective and cognitive neuropsychological changes (level II); marked objective paresis with cutaneous sensory as well as affective and cognitive neuropsychological changes (level III);

				and cutaneous sensory, affective and cognitive neuropsychological, posterior column, cranial nerve, and mixed upper and lower motor neuron changes (level IV). Groups with the most prominent objective neurological findings (levels III and IV) comprised exclusively outbreaks reported between the 1930s and 1950s. All but one outbreak in groups with less prominent neurological findings (levels I and II) were reported between the 1960s and 1980s; a range of neurological features was observed for these groups. Because a complete neurological examination is not emphasized as part of the diagnostic workup in current outbreaks, it is possible that less obvious neurological findings may be overlooked. Careful evaluation of neurological features in epidemic and endemic cases of what is now called chronic fatigue syndrome may be one approach to distinguishing subtypes of what has been described in the past as a nosological entity. Review Review, Tutorial
Brouwer B, Packer T.	School of Rehabilitation Therapy, Division of Occupational Therapy, Queen's University, Kingston, Ontario, Canada.	Corticospinal excitability in patients diagnosed with chronic fatigue syndrome.	Muscle Nerve 1994 Oct;17(10):1210-2	
Buchwald D, Garrity D.	Department of Medicine, Harborview Medical Center, Seattle.	Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities.	Arch Intern Med 1994 Sep 26;154(18):2049-53 comment in: Arch Intern Med. 1995 Sep 25;155(17):1913	BACKGROUND: Chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivities (MCS) are conditions associated with fatigue and a variety of other symptoms that appear to share many clinical and demographic features. Our objectives were to describe the similarities and differences among patients with CFS, FM, and MCS. Additional objectives were to determine how frequently patients with MCS and FM met the criteria for CFS and if they differed in their health locus of control. METHODS: Demographic, clinical, and psychosocial measures were prospectively collected in 90 patients, 30 each with CFS, FM, and MCS. Patients were recruited from a university-based referral clinic devoted to the evaluation and treatment of chronic fatigue and three private practices. Variables included demographic features, symptoms characteristic of each condition, psychological complaints, a measure of health locus of control, and information on health care use. RESULTS: Overall, the three patient groups were remarkably similar in demographic characteristics and the presence of specific symptoms. Patients with CFS and FM frequently reported symptoms compatible with MCS. Likewise, 70% of patients with FM and 30% of those with MCS met the criteria for CFS. Health care use was substantial among patients with CFS, FM, and MCS, with an average of 22.1, 39.7, and 23.3 visits, respectively, to a medical provider during the prior year. Health locus of control did not differ among the three populations. CONCLUSIONS: In general, demographic and clinical factors and health locus of control do not clearly distinguish patients with CFS, FM, and

				MCS. Symptoms typical of each disorder are prevalent in the other two conditions.
Buchwald D, Pascualy R, Bombardier C, Kith P.	Department of Medicine, University of Washington, Seattle.	Sleep disorders in patients with chronic fatigue.	Clin Infect Dis 1994 Jan;18 Suppl 1:S68-72	This prospective, cohort study examined the prevalence of sleep disorders among highly selected patients with chronic fatigue. On the basis of responses suggestive of sleep pathology on a screening questionnaire, 59 patients from a university-based clinic for chronic fatigue who had undergone a medical and psychiatric evaluation underwent polysomnography. Criteria for chronic fatigue syndrome (CFS) were met by 64% of patients and those for a current psychiatric disorder were met by 41%. Overall, 41% of patients had abnormal results for a multiple sleep latency test and 81% had at least one sleep disorder, most frequently sleep apnea (44%) and idiopathic hypersomnia (12%). In comparing patients who did and did not meet CFS criteria, no significant differences were found in individual sleep symptoms or sleep disorders. Likewise, symptoms and sleep disorders were unrelated to psychiatric diagnoses. In conclusion, chronically fatigued patients with suggestive symptoms may have potentially treatable coexisting sleep disorders that are not associated with meeting criteria for CFS or a current psychiatric disorder.
Buchwald D, Pearlman T, Kith P, Schmaling K.	Department of Medicine, University of Washington, Seattle.	Gender differences in patients with chronic fatigue syndrome.	J Gen Intern Med 1994 Jul;9(7):397-401	OBJECTIVE: To determine whether there are differences between men and women patients who have chronic fatigue syndrome (CFS) and, if so, to ascertain whether a gender-related pattern exists. DESIGN: A descriptive study of demographic, clinical, and psychosocial measures, the results of which were prospectively collected for patients who had CFS. SETTING: A university-based referral clinic devoted to the evaluation and management of chronic fatigue. PATIENTS: 348 CFS patients who had undergone complete medical evaluations. MEASURES: Clinical variables included symptoms, physical examination findings, and laboratory results. Psychosocial assessment consisted of a structured psychiatric interview, the Medical Outcomes Study Short-form General Health Survey to assess functional status, the General Health Questionnaire to ascertain psychological distress, the Multidimensional Health Locus of Control, and measures of attribution, social support, and coping. MAIN RESULTS: Overall, few gender-related differences were identified. Women had a higher frequency of tender or enlarged lymph nodes (60% versus 33%, p < or = 0.01) and fibromyalgia (36% versus 12%, p < or = 0.001) and lower scores on the physical functioning subscale of the Medical Outcomes Study Short-form General Health Survey (37.6 versus 52.2, p < 0.01); men more often had pharyngeal inflammation (42% versus 22%, p < or = 0.001) and reported a higher lifetime prevalence of alcoholism (20% versus 9%, p < or = 0.01). CONCLUSIONS: In general, demographic, clinical, and psychosocial factors do not distinguish men from women CFS patients.
Caffery BE, Josephson JE, Samek MJ.		The ocular signs and symptoms of chronic	J Am Optom Assoc 1994 Mar;65(3):187-91	BACKGROUND: Chronic Fatigue syndrome (CFS) is a relatively newly defined clinical entity that affects multiple systems including the ocular system. These

		fatigue syndrome.		effects have not been well documented. METHODS: 25 consecutive CFS patients were evaluated and the ocular signs and symptoms were described. RESULTS: Significant ocular symptoms were present in all 25 patients. The most common clinical findings were abnormalities of the preocular tear film and ocular surface (19 patients) and reduced accommodation for age (18 patients). CONCLUSIONS: CFS affects the ocular system in many ways. Eye care practitioners should pay particular attention to accommodative needs, ocular surface disease and tear film dysfunction when examining these patients. Further research into the pathophysiology of these ocular findings may lead to a better understanding of the pathophysiology of CFS.
Calabrese LH, Davis ME, Wilke WS.	Department of Rheumatic and Immunologic Disease, Cleveland Clinic Foundation, Ohio 44195-5028.	Chronic fatigue syndrome and a disorder resembling Sjogren's syndrome: preliminary report.	Clin Infect Dis 1994 Jan;18 Suppl 1:S28-31	Chronic fatigue syndrome (CFS), as currently described in the working criteria proposed by the Centers for Disease Control and Prevention (Atlanta), may be associated with multiple, distinct, and possibly unique clinical and/or etiopathogenic subsets. Sjogren's syndrome (SS) is a disease of unknown etiology that is characterized by dryness of the mucous membranes and a variety of autoimmune phenomena and conditions. Subjective manifestations of SS such as neurocognitive dysfunction and fatigue have been stressed by some observers. We have detected a large number of patients with unrecognized SS-like illness in a clinical specializing in CFS and believe the relationship to be more than casual. From January 1991 through April 1992, 172 patients were evaluated for CFS; the SS cohort consisted of 27 females (mean age, 41.9 years). Sixteen of these patients had previously been found to have CFS by a physician, and 11 were self-referred. All patients complained of severe, dominating, chronic fatigue. Complaints of myalgia were prominent; 20 of 27 patients met the criteria for fibromyalgia. Neurocognitive complaints and/or a history of neuropsychiatric disease was frequent. Results of Schirmer's test were abnormal for 16 of 27, and results of minor salivary-gland biopsy were abnormal for 20 of 25. Antibodies to nuclear antigen were present in 16 of 27, but anti-Ro was present in only 1 of 21. In the SS group, 13 of 27 patients met eight or more CDC minor criteria for CFS, and 18 of 27 met six or more of the criteria.(ABSTRACT TRUNCATED AT 250 WORDS)
Carver LA, Connallon PF, Flanigan SJ, Crossley-Miller MK.	159th MASH, Louisiana Army National Guard, Jackson Barracks, New Orleans 70146.	Epstein-Barr virus infection in Desert Storm reservists.	Mil Med 1994 Aug;159(8):580-2	Approximately 150 U.S. Army reservists from Indiana reported symptoms consistent with chronic fatigue syndrome after returning stateside from the tour of duty in Saudi Arabia. A psychiatric team confirmed the diagnosis, evaluated possible etiology, and treated the service members when appropriate. Those available service members who met the study's diagnostic criteria for chronic fatigue syndrome (n = 37) received an Epstein-Barr virus panel. Seventy-three percent of these selected service members were positive either for an acute or reactivated Epstein-Barr viral infection. These data suggest that service members who suffer from chronic fatigue syndrome may have their symptoms increased

				and prolonged by secondary viral infections.
Chester AC, Levine PH.	Georgetown University Medical Center, Washington, D.C.	Concurrent sick building syndrome and chronic fatigue syndrome: epidemic neuromyasthenia revisited.	Clin Infect Dis 1994 Jan;18 Suppl 1:S43-8	Sick building syndrome (SBS) is usually characterized by upper respiratory complaints, headache, and mild fatigue. Chronic fatigue syndrome (CFS) is an illness with defined criteria including extreme fatigue, sore throat, headache, and neurological symptoms. We investigated three apparent outbreaks of SBS and observed another more serious illness (or illnesses), characterized predominantly by severe fatigue, that was noted by 9 (90%) of the 10 teachers who frequently used a single conference room at a high school in Truckee, California; 5 (23%) of the 22 responding teachers in the J wing of a high school in Elk Grove, California; and 9 (10%) of the 93 responding workers from an office building in Washington, D.C. In those individuals with severe fatigue, symptoms of mucous membrane irritation that are characteristic of SBS were noted but also noted were neurological complaints not typical of SBS but quite characteristic of CFS. We conclude that CFS is often associated with SBS.
Conference proceedings. Albany New York,		Chronic Fatigue Syndrome: Current Concepts. Conference proceedings. Albany New York, 3-4 October 1992. Overall	Clin Infect Dis 1994 Jan;18 Suppl 1:S1-167	
Connolly S, Fowler CJ.		Single fibre EMG studies in chronic fatigue syndrome: a reappraisal.	J Neurol Neurosurg Psychiatry 1994 Sep;57(9):1157 comment on: J Neurol Neurosurg Psychiatry. 1994 Mar;57(3):375-6	
Conti F, Priori R, De Petrillo G, Rusconi AC, Arpino C, Valesini G.	Istituto di Clinica Medica I, Universita degli Studi La Sapienza di Roma.	Prevalence of chronic fatigue syndrome in Italian patients with persistent fatigue.	Ann Ital Med Int 1994 Oct-Dec;9(4):219-22	Our study was carried out to determine the prevalence of chronic fatigue syndrome (CFS) within a selected population of patients suffering from persistent fatigue. We studied subjects with recurrent or persistent fatigue lasting 6 months and fulfilling at least four minor Center for Disease Control (CDC) criteria for the diagnosis of CFS. Evaluation included both clinical examination and laboratory testing. All subjects filled out a questionnaire specifically designed to gain information about the length and severity of symptoms, and patients with a previously diagnosed illness associated with fatigue were excluded. The study was carried out at the Fatigue Clinic of an internal medicine unit (Clinica Medica I) of the University of Rome "La Sapienza". Sixty-three subjects, residents of the Lazio region (central Italy), completed the diagnostic assessment. Alternative diagnoses were established in 37 (59%) of the 63 patients. A diagnosis of CFS based on the CDC criteria was established in only 6 cases. In 2 subjects, CFS had appeared following infectious mononucleosis, and no definitive diagnosis could

				be formulated for 18 patients. In Italy, CFS seems to be an infrequent cause of severe and persistent fatigue in a selected population. Numerous morbid conditions may be responsible for a clinical picture closely resembling CFS. We recommend that patients suffering from fatigue be thoroughly evaluated.
Cox D, Findley L.		Chronic fatigue syndrome in adolescence.	Br J Hosp Med 1994 Jun 1-14;51(11):614 comment on: Br J Hosp Med. 1994 Feb 2-15;51(3)::110-2	
Dantzer R.	INRA-INSERM U 176, Bordeaux.	[Current studies on the neurobiology of chronic fatigue syndrome].[article in French]	Encephale 1994 Nov;20 Spec No 3:597-602	Cytokines are soluble mediators which are released by activated immune cells during infection and inflammation. The possibility that fatigue is mediated by the effects of cytokines on the central nervous system is supported by several converging lines of evidence: 1) infusions of cytokines to immunocompromised patients induce flu-like symptoms including fatigue and malaise; 2) peripheral and central injection of cytokines to laboratory rodents induce sickness behaviour; 3) symptoms of sickness behaviour occurring during experimental infections can be abrogated by administration of anti-cytokine treatments; 4) although many pitfalls in the detection of cytokines still exist, patients afflicted with the chronic fatigue syndrome have been found in some studies to display instances of excessive production of cytokines. Experimental studies have confirmed that cytokines are interpreted by the brain as internal signals for sickness. Furthermore, there is evidence that sickness is a motivation which reorganizes the organism's priorities in face of this particular threat which is represented by infectious pathogens. The elucidation of the mechanisms that are involved in these effects and in particular, the role of the cytokines which are produced in the brain in response to peripheral immune stimuli and to stressors, should give new insight on the way sickness and recovery processes are organized in the brain.
Deale A, David AS.	Department of Psychological Medicine, King's College Hospital, London, United Kingdom.	Chronic fatigue syndrome: evaluation and management.	J Neuropsychiatry Clin Neurosci 1994 Spring;6(2):189-94	
Deluca J, Johnson SK, Natelson BH.	Kessler Institute for Rehabilitation, Department of Research, West Orange, New Jersey 07052, USA.	Neuropsychiatric status of patients with chronic fatigue syndrome: an overview.	Toxicol Ind Health 1994 Jul-Oct;10(4-5):513-22	Chronic fatigue syndrome (CFS) is an illness that results in debilitating fatigue as well as rheumatological, infectious, and neuropsychiatric symptoms. The present paper is a brief overview of the neuropsychological and psychiatric research on CFS. Studies from our laboratory contrasting CFS with patients with multiple sclerosis, depression, and healthy controls are detailed. Our hypothesis of neuropsychological impairments in CFS is discussed.
Demitrack MA,	University of Michigan	Chronic fatigue	Curr Ther Endocrinol	

Engleberg NC.	Medical School, Ann Arbor.	syndrome.	Metab 1994;5:135-42	
Demitrack MA. Review Review, Tutorial		Chronic fatigue syndrome: a disease of the hypothalamic-pituitary-adrenal axis?	Ann Med 1994 Feb;26(1):1-5	
Dworkin HJ, Lawrie C, Bohdiewicz P, Lerner AM.	William Beaumont Hospital, Nuclear Medicine Department, Royal Oak, MI 48073.	Abnormal left ventricular myocardial dynamics in eleven patients with chronic fatigue syndrome.	Clin Nucl Med 1994 Aug;19(8):675-7	Eleven patients diagnosed with chronic fatigue syndrome were found to have abnormal left ventricular myocardial dynamics as indicated on MUGA studies. Among the abnormalities noted were abnormal wall motion at rest and stress, dilatation of the left ventricle, and segmental wall motion abnormalities.
Eicosanoids and essential fatty acid modulation in chronic disease and the chronic fatigue syndrome.	Gray JB, Martinovic AM.	Erratum in: Med Hypotheses 1995 Aug;45(2):219	Med Hypotheses 1994 Jul;43(1):31-42	Abnormalities of Essential Fatty Acid (EFA) incorporation into phospholipid are found in chronic diseases. More recently changes in circulating EFA metabolites (EFAM) together with EFAM hypo-responsiveness of immune cells and EFAM production from cells have been found associated with disease. We hypothesize that changes in ratio of EFAMs are the normal physiological responses to stressors, but when stressors are excessive or prolonged, EFAM systems may become unpredictably hypo-responsive owing to factors such as receptor down regulation and substrate depletion. In time, many homeostatic system become deranged and held in that state by minor stressors. Literature review of chronic fatigue syndrome (CFS) shows hyper and hypo-responsiveness in immune function, several Hypothalamo-Pituitary (HP) axes and sympathetic nervous system, all relatable to dysfunctional changes in EFA metabolism. For the first time, we explain chronic immune system activation and hypo-responsive immune function in CFS; through EFAMs. Dietary EFA modulation (DEFA) can alter ratios of both membrane EFAs and produced EFAMs, and if maintained can restore hypo-responsive function. We discuss dietary strategies and relevance in CFS, and a case series of CFS patients applying DEFA with other titrated published managements which saw 90% gaining improvement within 3 months and more than 2/3 fit for full time duties. This hypothesis and DEFA may have relevance in other chronic conditions. Review, Academic
Fenske TK, Davis P, Aaron SL.	Department of Medicine, University of Alberta, Edmonton, Canada.	Human adjuvant disease revisited: a review of eleven post-augmentation mammoplasty patients.	Clin Exp Rheumatol 1994 Sep-Oct;12(5):477-81	OBJECTIVES: We have reviewed 11 women post-augmentation mammoplasty who were referred to our clinic with diffuse rheumatic complaints. All patients had undergone mammoplasty with silicone gel-filled implants prior to the onset of their locomotor symptoms (mean latency time 7.8 years). One physician interviewed and examined each of these patients following a standardized format for clinical retrieval. RESULTS: Of the patients reviewed, 6 patients had clinical fibromyalgia based on the ACR criteria, and the remaining 5 patients had symptoms consistent with the "chronic fatigue syndrome." None of our patients were found to have evidence of a defined connective tissue disease. Antinuclear

				antibodies were detected in 4 (36%) patients and low level titres of extractable nuclear antigens in only 2 (18%). CONCLUSIONS: Previously a causal relationship between the use of silicone gel-filled breast implants and the subsequent development of symptoms referred to as human adjuvant disease (HAD) has been proposed. On the basis of currently accepted criteria we have preferred to diagnose our post-mammoplasty patients without specific connective tissue disease, as having chronic fatigue syndrome (CFS), or when tender points are present, as having fibromyalgia (FMS), rather than implying that such cases represent a separate and unique rheumatological disease entity. In the light of our current understanding of CFS and FMS, a relationship between them and the previous silicone mammoplasty seems possible.
Fiedler N, Kipen H, Deluca J, Kelly-McNeil K, Natelson B.	UMDNJ-Robert Wood Johnson Medical School, Environmental and Occupational Health Sciences Institute, Piscataway 08855, USA.	Neuropsychology and psychology of MCS.	Toxicol Ind Health 1994 Jul-Oct;10(4-5):545-54	Neurological symptoms are frequently reported by patients with multiple chemical sensitivities (MCS). Methods to compare the psychiatric, personality, and neuropsychological function of patients with MCS, chronic fatigue syndrome (CFS), and normal controls are described. Increased rates of Axis I psychiatric diagnoses are observed in the literature for MCS and CFS subjects relative to controls. Findings on the MMPI-2 and the Toronto Alexithymia Scale reveal profiles consistent with the tendency to report somatic rather than emotional symptoms in response to stress. However, many of the reported somatic symptoms also coincide with those found in neurologic disorders. The overall neuropsychological profile for MCS subjects does not reflect cognitive impairment. Relative to normal controls, the only difference in neuropsychological performance observed is reduced recognition of nontarget designs on a visual memory task. More fruitful areas for future psychological research will include measurement of the interaction between behavioral response styles and attentional processes in cognition, as well as observations under controlled challenge conditions.
Fox DS.		Chronic fatigue syndrome: a review and practical guide.	J Am Acad Nurse Pract 1994 Dec;6(12):565-70	Diagnosis and management of chronic fatigue syndrome (CFS) is a difficult challenge for nurse practitioners. The syndrome is widespread, poorly-defined, and problematic. Despite extensive etiologic research, no cause has been identified. Each case should be carefully evaluated for possible organic, psychiatric, and other factors reported as potential causes. Clinical manifestations, possible causes, and options for management are reviewed.
Friedberg F, Krupp LB.	Department of Psychiatry, State University of New York at Stony Brook.	A comparison of cognitive behavioral treatment for chronic fatigue syndrome and primary depression.	Clin Infect Dis 1994 Jan;18 Suppl 1:S105-10 comment in: Clin Infect Dis. 1995 Mar;20(3):717-8	To evaluate the effect of cognitive behavioral intervention on chronic fatigue syndrome (CFS), we studied three patient groups: a CFS-treatment group (n = 22), a primary depression-treatment group (n = 20), and a no-treatment control group of subjects with CFS (n = 22). For the CFS-treatment group, a trend toward reduced depression-symptom scores was noted, but there were no significant changes in stress-related symptoms or fatigue severity. For the most depressed treated subjects with CFS, significant score reductions were observed in

				measures of depression, stress, fatigue severity, and fatigue-related thinking. In the depression group, significant reductions in depression, stress, and fatigue severity scores were found. No significant changes in any measure were observed in the CFS control group. A new fatigue-related cognitions scale, developed to assess cognitive and emotional reactions to fatigue, showed a significant reduction in such reactions in the CFS-treatment group, a finding suggesting that depression in this group was mediated by maladaptive thinking. The results suggest that a subset of CFS patients with cognition-related depressive symptomatology may respond to short-term behavioral intervention.
Fudenberg NH.		Treatment for chronic fatigue syndrome.	Am J Med 1994 Nov;97(5):493-4 comment on: Am J Med. 1993 Feb;94(2):197-203	
Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A.	Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30333.	The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group.	Ann Intern Med 1994 Dec 15;121(12):953-9 comment in: Ann Intern Med. 1995 Jul 1;123(1):74-5 Ann Intern Med. 1995 Jul 1;123(1):75; discussion 76	The complexities of the chronic fatigue syndrome and the methodologic problems associated with its study indicate the need for a comprehensive, systematic, and integrated approach to the evaluation, classification, and study of persons with this condition and other fatiguing illnesses. We propose a conceptual framework and a set of guidelines that provide such an approach. Our guidelines include recommendations for the clinical evaluation of fatigued persons, a revised case definition of the chronic fatigue syndrome, and a strategy for subgrouping fatigued persons in formal investigations.
Gardner W.		Hyperventilation and chronic fatigue syndrome.	QJM 1994 Jul;87(7):443	
Goldenberg DL.	Newton-Wellesley Hospital, Massachusetts.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol 1994 Mar;6(2):223-33	No major pathophysiologic or therapeutic findings have appeared over the past year regarding fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome, three poorly understood, controversial, and overlapping syndromes. The frequent prevalence of these disorders in association with Lyme disease and other medical and psychiatric illness was emphasized. New studies demonstrated the potential role for central nervous system activation in fibromyalgia and chronic fatigue syndrome.
Goudsmit EM.		Chronic fatigue syndrome. Distinguish between syndromes...	BMJ 1994 May 14;308(6939):1297-8 comment in: BMJ. 1994 Jul 23;309(6949):275 comment on: BMJ. 1994 Mar 19;308(6931):756-9	
Gow JW, Behan WM, Simpson K, McGarry F, Keir S, Behan PO.	Department of Neurology, University of Glasgow, Scotland,	Studies on enterovirus in patients with chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S126-9	A large study on 121 patients with the chronic fatigue syndrome (CFS) that examined muscle biopsy samples for enterovirus by means of polymerase chain reaction analysis was carried out. The results were compared with those

	United Kingdom.			obtained from 101 muscle biopsy specimens from patients with a variety of other neuromuscular disorders (OND), including neurogenic atrophies, dystrophies, and mitochondrial, metabolic, and endocrine myopathies. Thirty-two (26.4%) of the biopsy specimens from the group of patients with CFS were positive, compared with 20 (19.8%) from the group of patients with OND, a difference that was not significant. This finding is in contrast to those of our previous smaller study in which significantly more patients with CFS than control subjects (53% [32 of 60] vs. 15% [6 of 41]) had enterovirus RNA sequences in their muscle. It was concluded that it is unlikely that persistent enterovirus infection plays a pathogenetic role in CFS, although an effect in initiating the disease process cannot be excluded.
Hauben M.		Quinacrine and chronic fatigue syndrome.	Am Fam Physician 1994 May 1;49(6):1354	
Henderson DA.	Executive Office of the President, Office of Science and Technology Policy, Washington, D.C.	Reflections on epidemic neuromyasthenia (chronic fatigue syndrome).	Clin Infect Dis 1994 Jan;18 Suppl 1:S3-6; discussion S7-9	Personal Name as Subject: Henderson DA
Heneine W, Woods TC, Sinha SD, Khan AS, Chapman LE, Schonberger LB, Folks TM.	Retrovirus Diseases Branch, Centers for Disease Control and Prevention, Atlanta, Georgia 30333.	Lack of evidence for infection with known human and animal retroviruses in patients with chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S121-5	We investigated 21 patients with chronic fatigue syndrome who were identified through the surveillance system of the Centers for Disease Control and Prevention (CDC) in Atlanta for the presence of several human and animal retroviruses. In addition, we evaluated 21 CDC employee controls matched with the patients for age (+/- 5 years), gender, and race. The viruses tested included human T-lymphotropic viruses types I and II; human spuma retrovirus; simian T-lymphotropic virus type I; simian retroviruses types 1, 2, and 3; bovine leukemia virus; feline leukemia virus; and gibbon ape leukemia virus. Samples of peripheral blood lymphocytes and leukocytes from patients and controls were analyzed in a blinded fashion for retroviral sequences; polymerase chain reaction (PCR) amplification assays and Southern blot hybridization to 32P-labeled internal oligoprobes were used. All PCR assays were optimized for maximal sensitivity on respective infected cell lines or plasmids, and sensitivity controls were included in each experiment. All samples from patients and controls were negative for the tested retroviral sequences. Our data indicate that none of these retroviruses plays an etiologic role or is a cofactor in the chronic fatigue syndrome illnesses of our study population.
Hilgers A, Frank J.	Institut fur angewandte Immunologie und Umweltmedizin, Dusseldorf.	[Chronic fatigue syndrome: immune dysfunction, role of pathogens and toxic agents and neurological and cardial	Wien Med Wochenschr 1994;144(16):399-406	375 patients with chronic fatigue syndrome (CFS) were examined using a standardized questionnaire and subsequent interview on 11 risk factors and 45 symptoms. Additionally immunologic, serologic, toxicologic, neuroradiologic, neurophysiologic and cardiologic investigations were performed. Immunologic tests showed cellular immunodeficiences particularly in functional regard (pathological lymphocyte stimulation in 50% of the patients, disorders of

		changes].[article in German]		granulocyte function in 44%). Furthermore variable deviations were found in the lymphocyte subpopulations (CD3, CD4, CD8, CD19, DR, Leu 11 + 19). In the humoral part tendencies to low IgG-3- and IgG-1-subclass-levels occurred (59% respectively 11% of the patients) also as decreases in complement system (CH50, C3, C4, C1-esterase-inhibitor). In the group of activation markers and cytokines 42% of the investigated patients had circulating immune complexes (CIC), 47% increases of tumor-necrosis-factor (TNF-a) and 21% increases of soluble interleukin-2-receptor (IL-2-R). The increased occurrence of autoantibodies in the CFS-patients (specially antinuclear anti-bodies [ANA], microsomal thyroid antibodies) suggest, that CFS is associated with or the beginning of manifest autoimmune disease. Under the pathogens 78% of the patients had a striking serological constellation of Epstein-Barr-Virus (EBV-EA positive, low EBNA-titers), in the HHV-6-Virus 47% showed increased antibody-titers. Tests on further herpes viruses and on Borreliae, Chlamydiae, Candida and Amoebae were positive in 8 to 36% of the examined patients. Furthermore there were found variable deficits of vitamins and trace elements also as hormonal disturbances.(ABSTRACT TRUNCATED AT 250 WORDS)
Hinds G, Bell NP, McMaster D, McCluskey DR.	Department of Medicine, Queen's University of Belfast, Northern Ireland, UK.	Normal red cell magnesium concentrations and magnesium loading tests in patients with chronic fatigue syndrome.	Ann Clin Biochem 1994 Sep;31 (Pt 5):459-61	Red blood cell magnesium concentrations were measured in samples from 89 patients who fulfilled the diagnostic criteria for chronic fatigue syndrome and the results compared to those found in an age and sex matched group selected from the normal population. No significant difference was found. Six patients were further investigated using a magnesium loading test to determine if there was any evidence of magnesium deficiency associated with this disorder. None was found. There is therefore no indication for the use of magnesium therapy in the management of this condition.
Hoey M.		Chronic fatigue syndrome. What is happening to M.E.?	Aust Nurs J 1994 Oct;2(4):18-20	
Howes S.		Chronic fatigue syndrome. ME Association is honest about prognosis.	BMJ 1994 May 14;308(6939):1299-300 comment on: BMJ. 1994 Mar 19;308(6931):732-3	
Howes S.		Chronic fatigue syndrome or myalgic encephalitis.	Lancet 1994 Jan 22;343(8891):243 comment on: Lancet. 1993 Nov 13;342(8881):1247-8	
Ho-Yen DO, Grant A.		Chronic fatigue syndrome. Self help groups give valuable	BMJ 1994 May 14;308(6939):1298-9	

		support.		
Ho-Yen DO, Shanks M.		Chronic fatigue syndrome. Prevalence study overlooked.	BMJ 1994 May 14;308(6939):1299 comment on: BMJ. 1994 Mar 19;308(6931):732-3	
Ho-Yen DO.		Chronic fatigue syndrome and fibromyalgia.	BMJ 1994 Dec 3;309(6967):1515 comment on: BMJ. 1994 Sep 17;309(6956):696-9	
Jason LA, Taylor SL.	Department of Psychology, DePaul University, Chicago, Illinois 60614, USA.	Monitoring chronic fatigue syndrome.	J Nerv Ment Dis 1994 Apr;182(4):243-4	
Jefferies WM.	Case-Western Reserve University School of Medicine, Cleveland, Ohio.	Mild adrenocortical deficiency, chronic allergies, autoimmune disorders and the chronic fatigue syndrome: a continuation of the cortisone story.	Med Hypotheses 1994 Mar;42(3):183-9	The possibility that patients with disorders that improve with administration of large, pharmacologic dosages of glucocorticoids, such as chronic allergies and autoimmune disorders, might have mild deficiency of cortisol production or utilization has received little attention. Yet evidence that patients with rheumatoid arthritis improved with small, physiologic dosages of cortisol or cortisone acetate was reported over 25 years ago, and that patients with chronic allergic disorders or unexplained chronic fatigue also improved with administration of such small dosages was reported over 15 years ago, suggesting that these disorders might be associated with mild adrenocortical deficiency. The apparent reasons for the failure of these reports to be confirmed or mentioned in medical textbooks and the facts needed to restore perspective are reviewed, and the need for further studies of the possible relationship of a mild deficiency of the production or utilization of cortisol and possibly other normal adrenocortical hormones to the development of these disorders is discussed.
Johnson SK, DeLuca J, Fiedler N, Natelson BH.	Department of Physical Medicine, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark.	Cognitive functioning of patients with chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S84-5	Neuropsychological problems are a distressing and frequent component of the symptom complex associated with chronic fatigue syndrome. Objective assessment of these difficulties is essential to understanding the nature of this illness. Results of the studies discussed in this paper suggest that impaired information processing, rather than primary memory dysfunction, may be at the root of the cognitive problems that afflict so many patients with CFS.
Johnston JH.		Chronic fatigue syndrome in Army general practice.	J R Army Med Corps 1994 Jun;140(2):59-60 comment in: J R Army Med Corps. 1996 Jun;142(2):85	
Khoury PB.		Chronic fatigue syndrome (CFS) and	Am J Med 1994 May;96(5):485-6	

		psychiatric disorders.	comment on: Am J Med. 1991 Oct;91(4):335-44 Am J Med. 1992 Jun;92(6):710	
Kim E.	University of South Florida College of Medicine.	A brief history of chronic fatigue syndrome.	JAMA 1994 Oct 5;272(13):1070-1	
King JC, Goddard MJ.	University of Texas Health Science Center, San Antonio 78284.	Pain rehabilitation. 2. Chronic pain syndrome and myofascial pain	Arch Phys Med Rehabil 1994 May;75(5 Spec No):S9-14.	This article highlights chronic pain syndrome and myofascial pain. It is part of the chapter on pain rehabilitation in the Self-Directed Medical Knowledge Program for practitioners and trainees in physical medicine and rehabilitation. This article discusses behavioral maladaptations to chronic pain which lead to global physical, psychologic, social, and vocational impairments--the chronic pain syndrome. The spectrum of myofascial pain syndromes, contributing factors, and interventions are detailed. New advances that are covered in this section include controversies in long-term use of opioids and muscle relaxants; differentiating fibromyalgia, myofascial pain syndromes, and chronic fatigue syndrome; pathophysiology of myofascial pain; and beneficial treatments.
Kohler D.		[Sleep apnea as the cause of chronic fatigue syndrome].[article in German]	Med Klin 1994 Aug 15;89(8):457	
Krueger GR, Klueppelberg U, Hoffmann A, Ablashi DV.	Immunopathology Section, University of Cologne, Germany.	Clinical correlates of infection with human herpesvirus-6.	In Vivo 1994 Jul-Aug;8(4):457-85	Human herpesvirus-6 is a lymphotropic virus which infects susceptible individuals during the first year of life and usually causes life-long latency. In a variable percentage primary infections are followed by a short acute disease, exanthema subitum. Older individuals may suffer from infectious mononucleosis-like illnesses or from Kikuchi-Fujimoto's disease. In addition, there is a fairly wide spectrum of lymphoid and hematopoietic diseases or autoimmune disorders, which are associated with elevated titers of HHV-6 antibody, and from which replicating virus may be isolated. Such diseases include atypical polyclonal lymphoproliferation, Hodgkin's disease, chronic fatigue syndrome and systemic lupus erythematosus. The present article reviews the current knowledge of such associations. Review, Academic
Krupp LB, Sliwinski M, Masur DM, Friedberg F, Coyle PK.	Department of Neurology, State University of New York-Stony Brook.	Cognitive functioning and depression in patients with chronic fatigue syndrome and multiple sclerosis.	Arch Neurol 1994 Jul;51(7):705-10	OBJECTIVE: To assess cognitive function in patients with chronic fatigue syndrome (CFS) and multiple sclerosis (MS) and to evaluate the role of depressive symptoms in cognitive performance. DESIGN: Case-control. All subjects were given a neuropsychological battery, self-report measures of depression and fatigue, and a global cognitive impairment rating by a neuropsychologist "blinded" to clinical diagnosis. Patients with MS and CFS were additionally evaluated with a Structured Clinical Interview for DSM-III-R (Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition) disorders. SETTING:

				Institutional and private neurological practices and the community at large. PATIENTS: Twenty patients with CFS diagnosed in accord with the Centers for Disease Control and Prevention-revised criteria who had cognitive complaints; 20 patients with clinically definite MS who were ambulatory and were matched for fatigue severity, age, and education to CFS subjects; and 20 age- and education-matched healthy controls. RESULTS: Patients with CFS had significantly elevated depression symptoms compared with patients with MS and healthy controls (P < .001) and had a greater lifetime prevalence of depression and dysthymia compared with MS subjects. Patients with CFS, relative to controls, performed more poorly on the Digit Symbol subtest (P = .023) and showed a trend for poorer performance on logical memory (P = .087). Patients with MS compared with controls had more widespread differences of greater magnitude on the Digit Span (P < .004) and Digit Symbol (P < .001), Trail Making parts A (P = .022) and B (P = .037), and Controlled Oral Word Association (P = .043) tests. Patients with MS also showed a trend of poorer performance on the Booklet Category Test (P = .089). When patients with CFS and MS were directly compared, MS subjects had lower scores on all measures, but the differences reached significance only for the Digit Span measure of attention (P = .035). CONCLUSIONS: Patients with CFS compared with MS have more depressive symptoms but less cognitive impairment. Relative to controls, a subset of CFS subjects did poorly on tests of visuomotor search and on the logical memory measure of the Wechsler Memory Scale-revised. Poor performance of logical memory in CFS appears to be related to depression, while visuomotor deficits in CFS are unrelated. Cognitive deficits in patients with MS are more widespread compared with those in patients with CFS and are independent of depressive symptoms.
Kuratsune H, Yamaguti K, Takahashi M, Misaki H, Tagawa S, Kitani T.	Osaka University Medical School, Japan.	Acylcarnitine deficiency in chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S62-7	One of the characteristic complaints of patients with chronic fatigue syndrome (CFS) is the skeletal muscle-related symptom. However, the abnormalities in the skeletal muscle that explain the symptom are not clear. Herein, we show that our patients with CFS had a deficiency of serum acylcarnitine. As carnitine has an important role in energy production and modulation of the intramitochondrial coenzyme A (CoA)/acyl-CoA ratio in the skeletal muscle, this deficiency might induce an energy deficit and/or abnormality of the intramitochondrial condition in the skeletal muscle, thus resulting in general fatigue, myalgia, muscle weakness, and postexertional malaise in patients with CFS. Furthermore, the concentration of serum acylcarnitine in patients with CFS tended to increase to the normal level with the recovery of general fatigue. Therefore, the measurement of acylcarnitine would be a useful tool for the diagnosis and assessment of the degree of clinical manifestation in patients with CFS.
Lane RJ, Woodrow D, Archard LC.		Lactate responses to exercise in chronic	J Neurol Neurosurg Psychiatry 1994	

		fatigue syndrome.	May;57(5):662-3 comment on: J Neurol Neurosurg Psychiatry. 1993 Sep;56(9):993-8	
Lanham RJ.	Division of General Medicine, University at Buffalo, Erie County Medical Center, New York 14215, USA.	Chronic fatigue syndrome: a diagnostic challenge for the laboratory.	Clin Lab Sci 1994 Sep-Oct;7(5):279-82	OBJECTIVE: To review the literature and current research about the causes of chronic fatigue syndrome (CFS). DATA SOURCES: Recent research articles about CFS and data gathered by the author. STUDY SELECTION: Performed by the author. DATA EXTRACTION: Performed by the author. DATA SYNTHESIS: Chronic fatigue syndrome (CFS) is a disease of pain, excessive fatigue after minor exertion, cognitive difficulties, and other symptoms-all occurring in cycles. While its etiology is unclear, CFS is associated with abnormal results of immune system tests. There is no specific marker for the illness. Treatment is symptomatic, and the long-term outlook for recovery is good. CONCLUSION: A rational, symptomatic approach to treating CFS patients can be made using the model developed at the author's institution. Research into the causes of CFS must continue.
Lawrie SM, MacHale SM.		Chronic fatigue syndrome.	Lancet 1994 Nov 26;344(8935):1514 comment in: Lancet. 1995 Jan 14;345(8942):131 comment on: Lancet. 1994 Sep 24;344(8926):864-8	
Lawrie SM, Pelosi AJ.		Chronic fatigue syndrome and myalgic encephalomyelitis.	BMJ 1994 Jul 23;309(6949):275 comment on: BMJ. 1994 May 14;308(6939):1297 BMJ. 1994 May 14;308(6939):1297-8	
Lawrie SM, Pelosi AJ. Editorial		Chronic fatigue syndrome: prevalence and outcome.	BMJ 1994 Mar 19;308(6931):732-3 comment in: BMJ. 1994 May 14;308(6939):1298 BMJ. 1994 May 14;308(6939):1299 BMJ. 1994 May 14;308(6939):1299-300 comment on: BMJ. 1994 Mar 19;308(6931):776-7	

Levine PH, Atherton M, Fears T, Hoover R.	Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892.	An approach to studies of cancer subsequent to clusters of chronic fatigue syndrome: use of data from the Nevada State Cancer Registry.	Clin Infect Dis 1994 Jan;18 Suppl 1:S49-53	Chronic fatigue syndrome (CFS) has been increasingly associated with immune dysregulation, including depressed natural killer cell activity; this phenomenon is associated with increased susceptibility to cancer. Although anecdotal reports have suggested an association between CFS and cancer, particularly non-Hodgkin's lymphoma and brain cancer, there has been no a priori justification for evaluating such an association and no consideration of relevant parameters, such as length of latent period vs. tumor type. We reviewed data from the Nevada State Cancer Registry subsequent to a reported outbreak of a CFS-like illness in Nevada that occurred during 1984-1986. We concentrated on non-Hodgkin's lymphoma and brain/CNS tumors, with particular emphasis on persons 15-34 and 35-54 years of age. An upward trend in the incidence of brain/CNS tumors, which could be related to a national upward trend for this disease, was noted. No consistent trends were noted for non-Hodgkin's lymphoma. Because of the difficulties inherent in studies of cancer subsequent to various exposures, we evaluated the methodology for determining an association between outbreaks of CFS-like disease and cancer. We propose several approaches that should be considered in future studies for investigation of possible associations between CFS and cancer, including expected latent periods for specific tumors.
Levine PH.	Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892.	Epidemiology of chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S57-60	
Levine PH.	Viral Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20892.	Epidemic neuromyasthenia and chronic fatigue syndrome: epidemiological importance of a cluster definition.	Clin Infect Dis 1994 Jan;18 Suppl 1:S16-20	Outbreaks of illness variously identified by a number of terms, including epidemic neuromyasthenia, myalgic encephalomyelitis, Iceland disease, and atypical poliomyelitis, have been reported from many countries during the past 45 years. Since the first well-described outbreak occurring in 1934, > 60 outbreaks have been reported, but few of these have been described in considerable detail. These outbreaks are usually cited in historical reports of chronic fatigue syndrome (CFS) since each of these outbreaks appears to contain a number of cases meeting the current case definition of CFS. There has been inadequate attention given to the fact that epidemic neuromyasthenia and related clusters characterized by various complaints, including fatigue, do not have an accepted epidemiological or clinical definition, and only rarely have descriptions of these clusters included a specific case definition. When such case definitions have been applied, the occurrence of cases meeting the current case definition for CFS appears to be both variable and infrequent. This report utilizes examples of several well-documented outbreaks to emphasize specific aspects that should be considered in the investigation of future clusters.
Levy JA.	Department of Medicine, University of	Viral studies of chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S117-20	Chronic fatigue syndrome (CFS) has many characteristics suggesting persistent fatigue following a viral illness. At least nine different RNA and DNA viruses have

	California School of Medicine, San Francisco.			been considered to be associated with this disease, but none of these viruses has been found to be the etiologic agent. Immunologic studies have demonstrated activated CD8+ cells and reduced function of natural killer cells suggesting a host response to an infection that has led to persistent immune disorders. Some of the symptoms of CFS may be due to cytokines produced by this hyperactive immune response to a virus that is still present in the host or that has been eliminate but leaves abnormal immunologic sequelae. These possibilities offer directions for future studies of CFS and therapeutic approaches to this condition.
Lewis S, Cooper CL, Bennett D.	Department of Psychology and Speech Pathology, Manchester Metropolitan University.	Psychosocial factors and chronic fatigue syndrome.	Psychol Med 1994 Aug;24(3):661-71	This study investigated the number and severity of life events, Type A behaviour, coping strategies and social support differences between chronic fatigue and irritable bowel syndrome patients prior to illness and between these groups and healthy controls. Although few differences were found between the groups for life events, a number of interesting results emerged with regard to different aspects of Type A behaviour, various coping strategies and social support. These findings are discussed with respect to existing research in the field.
Lloyd A, Gandevia S, Brockman A, Hales J, Wakefield D.	Department of Infectious Diseases, Prince Henry Hospital, Little Bay, New South Wales, Australia.	Cytokine production and fatigue in patients with chronic fatigue syndrome and healthy control subjects in response to exercise.	Clin Infect Dis 1994 Jan;18 Suppl 1:S142-6	We have studied the relationship between the cytokine production induced in vivo by prolonged isometric exercise and the symptom complex marked by fatigue in patients with chronic fatigue syndrome (CFS). Twelve male patients and 13 matched male control subjects undertook an isometric hand-grip exercise protocol utilizing dynamometers. Subjects undertook 30 minutes of exercise, for which the target force was set at 40% of the maximal voluntary contraction and the duty cycle was 50%. Prior to, during, and for 24 hours following the exercise, blood samples were collected and assayed for the presence of cytokines, including interferon-gamma and interferon-alpha, interleukin-1 beta, and tumor necrosis factor-alpha. At those times subjects also completed the Profile of Mood States (POMS) questionnaire, which served as a measure of changes in subjective fatigue. No significant alteration in the level of any of the cytokines in the plasma of patients or control subjects was detected before, during, or after exercise. Surprisingly, the patients' levels of fatigue, depression, and confusion, as measured by the POMS, decreased in response to the exercise. These data do not confirm the presence of an immunologic process correlating with the exacerbation of fatigue after exercise experienced by patients with CFS. Limitations in the study design and in the sensitivity of the cytokine assays may have affected our results.
Lloyd A, Pender H.		Chronic fatigue syndrome: does it need more healthcare resources?	Pharmacoeconomics 1994 Jun;5(6):460-4	
Lund-Olesen LH, Lund-Olesen K.	Department of Radiology, Svendborg	The etiology and possible treatment of	Med Hypotheses 1994 Jul;43(1):55-8	It is suggested that chronic fatigue syndrome/fibromyalgia is caused by virus injury to the calcium channels leading to larger quantities than usual of calcium

	Hospital, Denmark.	chronic fatigue syndrome/fibromyalgia.		ions entering the striated muscle cells. Should this be true, then treatment with a calcium antagonist (CA) may possibly be of value.
MacLean G, Wessely S.	Academic Department of Psychological Medicine, King's College School of Medicine and Dentistry, London.	Professional and popular views of chronic fatigue syndrome.	BMJ 1994 Mar 19;308(6931):776-7 comment in: BMJ. 1994 Mar 19;308(6931):732-3 BMJ. 1995 Jul 29;311(7000):329	OBJECTIVE--To study the coverage of the chronic fatigue syndrome in the popular and professional press. DESIGN--Search of all original research papers on the chronic fatigue syndrome published in British journals from 1980 onwards and of professional trade papers, national newspapers, and women's magazines. Interviews with six medical journalists. SETTING--British scientific, medical, and popular press. RESULTS--37 (49%) articles in research journals did not favour organic causes and 23 (31%) favoured organic causes. By contrast 31 (55%) articles in the medical trade press and 118 (69%) in national newspapers and women's magazines favoured organic causes. CONCLUSIONS--Press coverage of chronic fatigue syndrome has amplified and distorted divisions in the research community concerning the chronic fatigue syndrome. Articles in the press concentrate on a simple medical model of illness reinforcing the stigma of psychological illness and dissatisfaction with traditional medical authority. Review Literature
Makela EH.		Understanding chronic fatigue syndrome.	Am Pharm 1994 Apr;NS34(4):45-54; quiz 55-6	
Manian FA.	Division of Infectious Diseases, St. John's Mercy Medical Center, St. Louis, Missouri.	Simultaneous measurement of antibodies to Epstein-Barr virus, human herpesvirus 6, herpes simplex virus types 1 and 2, and 14 enteroviruses in chronic fatigue syndrome: is there evidence of activation of a nonspecific polyclonal immune response?	Clin Infect Dis 1994 Sep;19(3):448-53 comment in: Clin Infect Dis. 1995 Sep;21(3):708-9	As a test of the hypothesis that elevated titers of viral antibodies in patients with chronic fatigue syndrome (CFS) are due to a nonspecific polyclonal immune response, antibodies to Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), and 14 enteroviruses in 20 patients with CFS and 20 age- and gender-matched controls were simultaneously measured. Similarly, titers of IgG to herpes simplex virus (HSV) types 1 and 2 were measured in 18 of these cases and in the respective controls. IgG to EBV viral capsid antigen (VCA) was present at titers > or = 1:320 in 55% of cases vs. 15% of controls (P = .02). The geometric mean titers of early antigen antibody to EBV, HHV-6 IgG, and HSV-1 and HSV-2 IgG were not significantly different among cases and controls. Of the 14 enteroviral antibodies tested for, only those to coxsackieviruses B1 and B4 were present at significant titers (> or = 1:8) in cases vs. controls (P = .02 and P = .001, respectively). Of the cases, 19 (95%) had either an EBV VCA IgG titer > or = 1:320 or a coxsackievirus B1 or B4 antibody titer > or = 1:8, a percentage significantly higher than that of controls (40%; P = .0004). Titers of EBV VCA IgG and coxsackievirus B1 and B4 antibodies were simultaneously elevated in only 20% of cases. There was no correlation between elevated titers of EBV VCA IgG and IgG to HHV-6, HSV-1, and HSV-2 or antibody to coxsackieviruses B1 and B4 in the cases. The prevalence of reported allergies to medications or other substances was identical in both groups (60%). These findings suggest that in the majority of cases of CFS, elevation of viral antibody titers is not due to a nonspecific polyclonal immune

				response.
Mann AH, Mc Donald E, Cope H, Pelosi A, David A.	Section of Epidemiology & General Practice, Institute of Psychiatry, London, United Kingdom.	[Epidemiologic study of chronic fatigue in primary care (general practice)].[article in French]	Encephale 1994 Nov;20 Spec No 3:575-9	The results of a cross sectional study of fatigue in two large samples of patients attending primary care physicians are reported. The level of complaint of fatigue was higher in the prospective sample, which consisted of patients who had been diagnosed as suffering from a viral infection six months earlier. Duration and frequency of experience of fatigue correlated with severity in both samples. Severity, duration and frequency were continuously distributed in these populations. Attribution of fatigue in these two samples was mixed: social stresses, current physical illness and psychological problems all being offered as explanations. 11% of the cross sectional sample and 17% of the prospective sample met study operational criteria for a possible chronic fatigue state. These patients were assessed in greater detail. The majority had a diagnosable psychiatric disorder, predominantly depression. Physical illnesses were not adequate to explain these fatigue states. These studies in primary care do not support a clinical entity of a "chronic fatigue syndrome". Some patients in primary care settings have complaints of fatigue that are both disabling and long lasting, but they do not form a distinct group although the majority are likely however to be suffering from a concurrent psychiatric disorder. In contrast to similar patients with chronic fatigue syndromes attending hospital clinics, primary care patients with complaints of fatigue are much more varied in their ideas of causation with considerable less evidence of disease conviction.
Mant D.	University of Southhampton, UK.	Chronic fatigue syndrome.	Lancet 1994 Sep 24;344(8926):834-5 comment on: Lancet. 1994 Sep 24;344(8926):864-8	
Manu P, Lane TJ, Matthews DA, Castriotta RJ, Watson RK, Abeles M.	Department of Medicine, University of Connecticut School of Medicine, Farmington.	Alpha-delta sleep in patients with a chief complaint of chronic fatigue.	South Med J 1994 Apr;87(4):465-70 comment in: South Med J. 1994 Dec;87(12):1289-90	Our prospective, standardized cohort study was designed to assess the presence of alpha wave intrusions during non-rapid eye movement sleep (alpha-delta sleep) and its relationship to fibromyalgia, major depression, and chronic fatigue syndrome (CFS) in patients with a chief complaint of chronic fatigue. The study group comprised 30 consecutive patients seen at a university hospital referral clinic for evaluation of chronic fatigue. All patients had nocturnal polysomnography, dolorimetric tender point assessment for fibromyalgia, a comprehensive history, physical, and laboratory evaluation, and a structured psychiatric interview. Alpha-delta sleep was identified in 8 of the 30 patients (26%), major depression in 20 (67%), CFS in 15 (50%), and fibromyalgia in 4 (13%). Ten of the 30 patients (33%) had a primary sleep disorder (sleep apnea, periodic limb movements, or narcolepsy). Alpha-delta sleep was not significantly correlated with fibromyalgia, CFS, major depression, or primary sleep disorders, but was significantly more common among patients who had chronic fatigue

				without major depression. We conclude that primary sleep disorders are relatively common among patients with chronic fatigue and must be diligently sought and treated. Alpha-delta sleep is not a marker of fibromyalgia or CFS, but may contribute to the illness of nondepressed patients with these conditions.
Martin WJ, Zeng LC, Ahmed K, Roy M.	Department of Pathology, USC School of Medicine, Los Angeles 90033.	Cytomegalovirus-related sequence in an atypical cytopathic virus repeatedly isolated from a patient with chronic fatigue syndrome.	Am J Pathol 1994 Aug;145(2):440-51	An atypical virus, cytopathic for human and animal fibroblasts, was repeatedly cultured from a patient with chronic fatigue syndrome. Viral particles, suggestive of cytomegalovirus (CMV) were seen by electron microscopy. Infected cells did not, however, stain with antisera specific for CMV, herpes, simplex virus, or human herpes-virus-6. Polymerase chain reaction (PCR) assays for these viruses were also negative. Two distinct products of approximately 1.5 kilobase pairs were amplified from virally infected cells using the human T lymphotropic virus-II tax gene reactive primer, SK44, in low stringency PCR. Sequencing of one of the amplified products showed a region of highly significant partial homology with the UL34 gene of CMV. The sequence of the other PCR product did not correspond with CMV or any other virus. DNA was extracted from the material pelleted by ultracentrifugation of filtered culture supernatants. It migrated in agarose gels as a single band of approximately 20 kpb. The banded DNA was digested with EcoRI and cloned. A 2.2 kbp plasmid containing the CMV-related sequence identified within the PCR product was recovered. Sequencing of this plasmid extended the region of partial sequence homology with CMV to include a portion of the UL35 gene of CMV. Initial sequencing of additional plasmids has confirmed the partial relatedness to CMV. The data indicate a novel type of CMV-related "stealth" virus that is able to establish a clinically persistent human infection.
Martin WJ.	University of Southern California School of Medicine, Los Angeles 90033, USA.	Stealth viruses as neuropathogens.	CAP Today 1994 Oct;8(10):67-70	Neuropsychiatric diseases viewed as multifaceted expression of a dysfunctional brain in which atypical responses are evoked by various sensory inputs. Disease entities have traditionally been classified according to the predominant manifestation ( ) without regard to the overlapping features of many of the diseases (+/-). Thus, mild to moderate pain, mood, cognitive, and neurosomatic symptoms are frequently present in chronic fatigue syndrome (CFS) patients. Fibromyalgia syndrome (FMS) is listed as an example of a predominantly chronic pain syndrome. Affect (mood) disorders include depression (Depress.), anxiety, panic reactions, blunted affect, mania, etc. Schizophrenia (Schizo.) is listed as an example of a major cognitive psychosis. Autism as well as various forms of dementia would be included in this category. Irritable bowel syndrome (IBS) is an example of a neurosomatic disease.
Masuda A, Nozoe SI, Matsuyama T, Tanaka H.	First Department of Internal Medicine, Faculty of Medicine, Kagoshima University,	Psychobehavioral and immunological characteristics of adult people with chronic	Psychosom Med 1994 Nov-Dec;56(6):512-8	The psychobehavioral responses and cellular immune function were investigated in healthy people (control, N = 21), adult people with chronic fatigue (fatigue-non-CFS group, N = 24), and patients with chronic fatigue syndrome (CFS, N = 10). Based on psychobehavioral responses, the fatigue-non-CFS group had low

	Japan.	fatigue and patients with chronic fatigue syndrome.		general activity levels ($p < .05$) and slightly depressive tendencies ($p < .01$) compared with the control. They had many life event stresses ($p < .05$) and sleep disturbances ($p < .01$), and they could not cope appropriately with stresses. The fatigue-non-CFS group also showed significantly lower natural killer (NK) cell activity ($p < .01$) and decreased numbers of CD16+ and CD56+ cells ($p < .05$). Compared with the fatigue-non-CFS group, patients with CFS had higher degrees of physical fatigue ($p < .01$) and more life event stresses ($p < .05$). They had lower general activity levels and social introversion. They were also in a depressive state. NK cell activity and the numbers of CD16+ and CD56+ cells were significantly reduced in patients with CFS ($p < .01$). These findings suggest that adult people with chronic fatigue may be in an intermediate state between the healthy control and patients with CFS in terms of psychobehavioral responses and low NK cell activity. We observed three cases in such an intermediate state in whom CFS subsequently developed. Randomized Controlled Trial
Matsuda J, Gohchi K, Gotoh N.		Serum concentrations of 2',5'-oligoadenylate synthetase, neopterin, and beta-glucan in patients with chronic fatigue syndrome and in patients with major depression.	J Neurol Neurosurg Psychiatry 1994 Aug;57(8):1015-6	
Matsuda J.		[Chronic fatigue syndrome: fictious or true disease]?[article in Japanese]	Ryumachi 1994 Oct;34(5):921-8	
Matsuno T, Hikita K, Matsuo T.	Department of Neuropsychiatry, Faculty of Medicine, Kyushu University.	[Chronic fatigue syndrome and psychiatric diseases].[article in Japanese]	Nippon Rinsho 1994 May;52(5):1339-44	The chronic fatigue syndrome consists of a combination of non-specific symptoms. Some believe that the CFS is subcategory of major depression, because the symptoms are similar to those of major depression. We believe that the CFS is quite different from major depression or neurotic depression, since the CFS has no lack of initiative and effort, no inhibition which is seen in endogenous depression, and sharp fluctuations in general fatigue, anxiety, and various persisting somatic symptoms, such as, malaise and mild fever. CFS seems to be similar to the neurasthenia. It is harmful, at least, in aetiology and treatment, to neglect the diagnosis of the CFS.
McGarry F, Gow J, Behan PO.		Enterovirus in the chronic fatigue syndrome.	Ann Intern Med 1994 Jun 1;120(11):972-3	
Millner L, Widerman E.	Temple University, School of Social	Women's health issues: a review of the current	Soc Work Health Care 1994;19(3-4):145-72	To assess the ways in which social work is addressing issues in women's health care, the profession's journals from 1985-1992 were searched, yielding 36

	Administration, Philadelphia, PA 19122.	literature in the social work journals, 1985-1992.		articles. Over half addressed issues of reproduction and sexuality including pregnancy, family planning, abortion, substance abuse in pregnancy, and fetal protection policies. Remaining articles addressed medical diagnoses; including AIDS/HIV/STDs, cancer, illnesses associated with aging, PMS, Turner's Syndrome, and chronic fatigue syndrome. Foci, methodologies, and recommendations are discussed and the authors critically analyze the articles' reflections of the status of women's health as a social work concern.
Moutschen M, Triffaux JM, Demonty J, Legros JJ, Lefebvre PJ.	Department of Internal Medicine, CHU Sart-Tilman, Liege, Belgium.	Pathogenic tracks in fatigue syndromes.	Acta Clin Belg 1994;49(6):274-89	This review analyses the recent literature devoted to two related fatigue syndromes: chronic fatigue syndrome (CFS) and acute onset postviral fatigue syndrome (PVFS). The articles are grouped into five pathogenic tracks: infectious agents, immune system, skeletic muscle, hypothalamo-pituitary-adrenal (HPA) axis and psychiatric factors. Although a particular infectious agent is unlikely to be responsible for all CFS cases, evidence is shown that host-parasite relationships are modified in a large proportion of patients with chronic fatigue. Antibody titres against infectious agents are often elevated and replication of several viruses could be increased. Chronic activation of the immune system is also observed and could be due to the reactivation of persistent or latent infectious agents such as herpes viruses (i.e. HHV-6) or enteroviruses. It could also be favorised by an impaired negative feedback of the HPA axis on the immune system. A model is proposed where the abnormalities of the HPA axis are primary events and are mainly responsible for a chronic activation of the immune system which in turn induces an increased replication of several viruses under the control of cellular transcription factors. These replicating viruses together with cytokines such as TNF-alpha would secondarily induce functional disorders of muscle and several aspects of asthenia itself.
Natelson BH, Ye N, Moul DE, Jenkins FJ, Oren DA, Tapp WN, Cheng YC.	Chronic Fatigue Syndrome Center, UMDNJ-New Jersey Medical School, Newark.	High titers of anti-Epstein-Barr virus DNA polymerase are found in patients with severe fatiguing illness.	J Med Virol 1994 Jan;42(1):42-6	Forty-one patients with chronic fatigue syndrome (CFS), 76 healthy controls matched with the patient group for age range, sex, race, and socioeconomic class, and 22 symptomatic patients with seasonal affective disorder (SAD) had serum sampled for antibodies against 2 Epstein-Barr virus (EBV) replicating enzymes. Abnormal titers of antibodies were found twice as often in CFS patients as controls (34.1% vs. 17.1%), with SAD patients having an intermediate frequency (27.3%). Stratifying for disease severity sharpened the differences considerably, with the sicker CFS and SAD patients having 52% and 50% abnormal tests, respectively; more mildly afflicted CFS and SAD patients had a frequency of abnormal tests in the normal range. Antibodies to EBV DNA polymerase (DNAP) were the more sensitive of the two tests in that they were positive in all cases but one. These findings suggest that antibodies against EBV DNAP may be a useful marker in delineating a subset of patients with severe fatiguing illness for appropriate treatment trials and for monitoring their outcomes.
Neutra RR.	Special Epidemiological	Some preliminary	Public Health Rev	Epidemiology has played a role in clarifying mysterious symptom complexes such

	Studies Program, California Department of Health Services, Albany 94706.	thoughts on the potential contribution of epidemiology to the question of multiple chemical sensitivity.	1994;22(3-4):271-8	as AIDS, Chronic Fatigue Syndrome, and Psychiatric Disease. Is Multiple Chemical Sensitivity a new environmental disease or another in the parade of psychosomatic syndromes which have come and gone in history. It is proposed that epidemiology can: (1) Describe quantitatively the relative frequency of presenting symptoms and natural history. (2) Work with experimental psychologists to develop double-blind protocols for the "environmental unit" where chemical challenges are said to reveal chemical etiology. (3) Develop an epidemiological definition in a clinical series. (4) Develop an epidemiological definition in cohorts recently exposed to chemicals. (5) Apply the epidemiological definitions in descriptive studies and around hazardous waste sites.
Nixon PG.	Charing Cross Hospital, London, England.	Effort syndrome: hyperventilation and reduction of anaerobic threshold.	Biofeedback Self Regul 1994 Jun;19(2):155-69	Effort syndrome is an entity in danger of being subsumed into "chronic fatigue syndrome" and lost to sight. Its distinctive feature is the reduction of the anaerobic threshold for work by depletion of the body's alkaline buffering systems through hyperventilation. This article describes the history and clinical features of effort syndrome and reports a study in which capnography is used to identify the anaerobic threshold by registering the respiratory response to the onset of metabolic acidosis. The patients' thresholds are low, and provide a goal for rehabilitation. In other forms of chronic fatigue syndrome, the pathogenesis and logic of therapy are unclear.
Packer TL, Sauriol A, Brouwer B.	Division of Occupational Therapy, School of Rehabilitation Therapy, Queen's University, Kingston, Ontario, Canada.	Fatigue secondary to chronic illness: postpolio syndrome, chronic fatigue syndrome, and multiple sclerosis.	Arch Phys Med Rehabil 1994 Oct;75(10):1122-6	Estimates of the percentage of patients with postpolio syndrome, chronic fatigue syndrome, and multiple sclerosis who experience fatigue range from approximately 75% to 100%. In this study we describe the severity of fatigue and its impact on subjects with these three diagnoses. The Fatigue Severity Scale, the Human Activity Profile, and the Nottingham Health Profile were used to measure fatigue, activity, and health status respectively of each diagnostic group as well as a control group. Using a Kruskal-Wallis one-way analysis of variance followed by a Bonferroni-adjusted Mann Whitney U test all diagnostic groups reported significantly higher levels ($p = .0000$ to $p = .002$) of fatigue and lower perceived health status than the control group. Subjects with chronic fatigue and multiple sclerosis also had significantly reduced activity levels ($p = .002$ to $p = .01$) compared with the control group. Further attention should be directed toward understanding the relationship between fatigue and ability to engage in activities as well as strategies for remediation and/or compensation of the fatigue.
Pagani M, Lucini D, Mela GS, Langewitz W, Malliani A.	Centro Ricerche Cardiovascolari, CNR, Ospedale L Sacco, University of Milano, Italy.	Sympathetic overactivity in subjects complaining of unexplained fatigue.	Clin Sci (Colch) 1994 Dec;87(6):655-61	1. Theoretical and practical considerations suggest that in subjects complaining of fatigue, in the absence of evident organ dysfunction, an alteration in the autonomic nervous system might be present as a functional correlate. 2. Autoregressive spectral analysis of R-R interval variability from a surface ECG, was used in healthy control subjects (n = 24, age 45 +/- 4 years) and in subjects complaining of unexplained fatigue (n = 53, age 46 +/- 9 years) to obtain quantitative indices of the state of the sympathovagal balance, both at rest and

				during a mental stimulus (mental arithmetic), capable of enhancing sympathetic drive. Sympathetic and vagal modulations were inferred from the normalized powers of the low frequency and high frequency spectral components respectively. 3. We observed in patients, at rest, a prevailing low frequency component of R-R variability (patients low frequency = 73 +/- 11, control subjects 51 +/- 10 normalized units, P < 0.05). The responsiveness to mental arithmetic was reduced in patients as compared with controls. Systolic blood pressure variability did not differ. This suggested a selective imbalance in autonomic control of the sinoatrial node, characterized by sympathetic predominance as well as by vagal withdrawal, at rest. 4. The possibility of discriminating patients from control subjects on the basis of simple non-invasive functional markers might provide a better understanding of the mechanisms, clinical evolution and outcome of conditions such as the chronic fatigue syndrome, which lack ordinary evidence of disease, but comprise, as physiopathological correlate, a quantitative alteration of autonomic control.
Patarca R, Klimas NG, Lugtendorf S, Antoni M, Fletcher MA.	E. M. Papper Laboratory of Clinical Immunology, University of Miami School of Medicine, Florida.	Dysregulated expression of tumor necrosis factor in chronic fatigue syndrome: interrelations with cellular sources and patterns of soluble immune mediator expression.	Clin Infect Dis 1994 Jan;18 Suppl 1:S147-53	Among a group of 70 individuals who met the criteria established by the Centers for Disease Control and Prevention (Atlanta) for chronic fatigue syndrome (CFS), 12%-28% had serum levels exceeding 95% of control values for tumor necrosis factor (TNF) alpha, TNF-beta, interleukin (IL) 1 alpha, IL-2, soluble IL-2 receptor (sIL-2R), or neopterin; overall, 60% of patients had elevated levels of one or more of the nine soluble immune mediators tested. Nevertheless, only the distributions for circulating levels of TNF-alpha and TNF-beta differed significantly in the two populations. In patients with CFS--but not in controls--serum levels of TNF-alpha, IL-1 alpha, IL-4, and sIL-2R correlated significantly with one another and (in the 10 cases analyzed) with relative amounts (as compared to beta-globin or beta-actin) of the only mRNAs detectable by reverse transcriptase-coupled polymerase chain reaction in peripheral-blood mononuclear cells: TNF-beta, unspliced and spliced; IL-1 beta, lymphocyte fraction; and IL-6 (in order of appearance). These findings point to polycellular activation and may be relevant to the etiology and nosology of CFS.
Pawlikowska T, Chalder T, Hirsch SR, Wallace P, Wright DJ, Wessely SC.	Department of General Practice, St Mary's Hospital Medical School, London.	Population based study of fatigue and psychological distress.	BMJ 1994 Mar 19;308(6931):763-6 comment in: BMJ. 1995 Jul 29;311(7000):329 BMJ. 2000 Feb 19;320(7233):515-6 BMJ. 2000 May 13;320(7245):1343	OBJECTIVES--To determine the prevalence of fatigue in the general population and the factors associated with fatigue. DESIGN--Postal survey. SETTING--Six general practices in southern England. SUBJECTS--31,651 men and women aged 18-45 years registered with the practices. MAIN OUTCOME MEASURES--Responses to the 12 item general health questionnaire and a fatigue questionnaire which included self reported measures of duration, severity, and causes of fatigue. RESULTS--15,283 valid questionnaires were returned, giving a response rate of 48.3%, (64% after adjustment for inaccuracies in the practice registers). 2798 (18.3%) of respondents reported substantial fatigue lasting six months or longer. Fatigue and psychological morbidity were moderately

				correlated (r = 0.62). Women were more likely to complain of fatigue than men, even after adjustment for psychological distress. The commonest cited reasons for fatigue were psychosocial (40% of patients). Of 2798 patients with excessive tiredness, only 38 (1.4%) attributed this to the chronic fatigue syndrome. CONCLUSION--Fatigue is distributed as a continuous variable in the community and is closely associated with psychological morbidity.
Peterson PK, Sirr SA, Grammith FC, Schenck CH, Pheley AM, Hu S, Chao CC.	Department of Medicine, Hennepin County Medical Center, Minneapolis, MN 54415, USA.	Effects of mild exercise on cytokines and cerebral blood flow in chronic fatigue syndrome patients.	Clin Diagn Lab Immunol 1994 Mar;1(2):222-6	Chronic fatigue syndrome (CFS) is an idiopathic disorder characterized by fatigue that is markedly exacerbated by physical exertion. In the present study, we tested the hypothesis that mild exercise (walking 1 mph [1 mile = 1.609 km] for 30 min) would provoke serum cytokine and cerebral blood flow abnormalities of potential pathogenic importance in CFS. Interleukin-1 beta, interleukin-6, and tumor necrosis factor alpha were nondetectable in sera of CFS patients (n = 10) and healthy control subjects (n = 10) pre- and postexercise. At rest, serum transforming growth factor beta (TGF-beta) levels were elevated in the CFS group compared with the control group (287 +/- 18 versus 115 +/- 5 pg/ml, respectively; P < 0.01). Serum TGF-beta and cerebral blood flow abnormalities, detected by single-photon emission-computed tomographic scanning, were accentuated postexercise in the CFS group. Although these findings were not significantly different from those in the control group, the effect of exercise on serum TGF-beta and cerebral blood flow appeared magnified in the CFS patients. Results of this study encourage future research on the interaction of physical exertion, serum cytokines, and cerebral blood flow in CFS that will adopt a more rigorous exercise program than the one used in this study.
Pichot P.		[Neurasthenia, yesterday and today].[article in French]	Encephale 1994 Nov;20 Spec No 3:545-9	Neurasthenia was described and explained in very mechanistic terms, at the end of the 19th century, by G.M. Beard to account for physical and mental exhaustion and for varied somatic troubles imputed to failure of too much solicited nervous resources. This concept was then universally adopted and gave rise to diverse interpretations, among which was the Freud's one. Later, in Occident, came a deterioration, the diagnostic of neurasthenia giving way to those of anxious or affective disorders. In the same time, at least for ideological and cultural reasons, the concept remained lively in Russia and in Asia. During the last decade the western psychiatry has been led to accept that there are clinical situations focussed on fatigue and fatigability, even if it coined for them new terminologies (post-infectious fatigue, chronic fatigue syndrome, etc.) and while DSMs keep on ignoring neurasthenia, the ICD 10 gives it an important place.
Priori R, Conti F, Luan FL, Arpino C, Valesini G.	Istituto di Clinica Medica I, Universita La Sapienza, Roma, Italy.	Chronic fatigue: a peculiar evolution of eosinophilia myalgia syndrome following treatment with L-	Eur J Pediatr 1994 May;153(5):344-6	We describe four Italian adolescents in whom a persistent, debilitating fatigue appeared after therapeutic ingestion of products containing L-tryptophan and subsequent to the development of a transient rise in eosinophil count and severe myalgia (Eosinophilia Myalgia Syndrome-EMS). Their clinical picture was indistinguishable from that of the so-called Chronic Fatigue Syndrome. A chronic

		tryptophan in four Italian adolescents.		fatigue may occur after diverse triggering agents and its represents the peculiar clinical evolution of these four paediatric cases of EMS.
Przewlocka M.	Katedry i Kliniki Kardiologii AM we Wroclawiu.	[Chronic fatigue syndrome].[article in Polish]	Pol Tyg Lek 1994 Jun 20-27;49(25-26):593-5	
Raanani P, Martinowitz U.		[Chronic fatigue syndrome].[article in Hebrew]	Harefuah 1994 Dec 1;127(11):467-71	
Raik E.		Chronic fatigue syndrome and the medical referee.	Med J Aust 1994 Jan 3;160(1):47-8 comment on: Med J Aust. 1993 Sep 20;159(6):432	
Rasmussen AK, Andersen V, Nielsen H, Wiik A.	Medicinsk afdeling TTA, Rigshospitalet, Kobenhavn.	[Chronic fatigue syndrome--a defined unity]?[article in Danish]	Ugeskr Laeger 1994 Nov 14;156(46):6832-6 comment in: Ugeskr Laeger. 1995 Feb 6;157(6):756-7 Ugeskr Laeger. 1995 Feb 6;157(6):757	Chronic fatigue syndrome (CFS) is characterized by a sudden onset of an influenza-like illness followed by marked chronic fatigue and abnormal exercise-induced exhaustion. The precise pathogenesis of this disorder is unknown, but viral infection triggering immune imbalance has been suggested. The literature on CFS is reviewed. We find no consistent support for chronic viral infection or immunological dysfunction. The data in the published studies are rather conflicting, and further research in order to identify parameters that differentiate CFS from other disorders is necessary.
Rasmussen AK, Nielsen H, Andersen V, Barington T, Bendtzen K, Hansen MB, Nielsen L, Pedersen BK, Wiik A.	Medicinsk afdeling TTA og infektionsmedicinsk afdeling M, Rigshospitalet, Kobenhavn.	[Chronic fatigue syndrome--a controlled cross-sectional study].[article in Danish]	Ugeskr Laeger 1994 Nov 14;156(46):6836-40 comment in: Ugeskr Laeger. 1995 Feb 6;157(6):756-7	Twenty-one patients fulfilling the Center for Disease Control criteria for chronic fatigue syndrome (CFS) were examined in a controlled study. Viral antibodies and tests evaluating the immune system were investigated in the patients and in a control group of 21 sex- and age-matched individuals. Production in vitro of the predominantly T-cell-derived cytokines interleukin-2 and interferon-gamma was significantly higher in patients with CFS compared the control group. Furthermore, the serum concentrations of IgA and IgE were significantly lower in patients with CFS; however, the values were within the normal reference range. All other variables were similar in the two groups. This study does not suggest a clearly disordered immune system or a chronic viral infection as a major pathogenetic factor in CFS. Longitudinal studies of immunological and virological parameters in CFS are warranted as are studies on patients that are severely handicapped.
Rasmussen AK, Nielsen H, Andersen V, Barington T, Bendtzen K, Hansen MB, Nielsen L, Pedersen BK, Wiik A.	Medical Department TTA M. Rigshospitalet, Copenhagen, Denmark.	Chronic fatigue syndrome--a controlled cross sectional study.	J Rheumatol 1994 Aug;21(8):1527-31	OBJECTIVE. To look for signs of immunodeficiencies and/or longstanding infections underlying chronic fatigue syndrome (CFS). METHODS. Twenty-one patients fulfilling the Centers for Disease Control criteria for CFS were compared to 21 age and sex matched controls. A number of viral antibodies as well as the following tests evaluating the immune system were studied: autoantibody profile, cell surface markers on isolated blood mononuclear cells, cytokine production, lymphocyte proliferative responses, natural killer cell activity and

				quantitation of immunoglobulin secreting cells. RESULTS. Production in vitro of the predominantly T cell derived cytokines interleukin 2 and interferon gamma was significantly higher in patients with CFS compared to the control group. Furthermore, the serum concentrations of IgA and IgE were lower in patients with CFS; however, this difference was caused by a larger number with values of IgA and IgE above the upper limit of the normal range among the controls than among the patients with CFS. All other variables were similar in the 2 groups. CONCLUSION. A pathogenically significant imbalance of the immune system in patients with CFS cannot be excluded. However, evidence of a causal link between abnormal immunity and CFS was not obtained.
Rebora A, Drago F.	Department of Dermatology, University of Genoa, Italy.	Chronic fatigue syndrome: a novel disorder with cutaneous manifestations.	Dermatology 1994;188(1):3-5	Persistent and disabling fatigue associated with low-grade fever and other constitutional symptoms, without any known disorder that accounts for it, is recognized as chronic fatigue syndrome (CFS). Skin lesions occur in 10-35% of patients, but their description is inaccurate. Recurrent aphthous stomatitis or persistent Epstein-Barr virus (EBV)-related erythema multiforme have also been reported. Patients may be diagnosed as having CFS only when they fulfill at least 2 major and 8 minor criteria. Major criteria are the presence of debilitating fatigue persisting or recurring for at least 6 months and the absence of any other medical disorder that may explain it. Although different viral or nonviral etiologies have been documented, evidence implicating EBV is gaining support.
Rest J.		The chronic fatigue syndrome.	955: Ann Intern Med 1995 Jul 1;123(1):75; discussion 76 comment on: Ann Intern Med. 1994 Dec 15;121(12):953-9	
Richman JA, Flaherty JA, Rospenda KM.	Department of Psychiatry, University of Illinois at Chicago 60612.	Chronic fatigue syndrome: have flawed assumptions been derived from treatment-based studies?	Am J Public Health 1994 Feb;84(2):282-4	Chronic fatigue syndrome is a disabling disorder that has been studied primarily in clinical settings. In the absence of an adequate epidemiological database, cultural stereotypes have influenced the characterization of chronic fatigue syndrome as "the yuppie flu," similar to the 19th century characterization of neurasthenia as a disease of the affluent. The limited epidemiological data available and the overall medical-sociological literature call this assumption into question. Only a community "true" prevalence study that is unbiased by help seeking and access to health care can provide an accurate assessment of the risk factors for and the public health ramifications of this disease.
Roberts L, Byrne E.	Department of Neurology, St Vincent's Hospital, Fitzroy, Melbourne, Australia.	Single fibre EMG studies in chronic fatigue syndrome: a reappraisal.	J Neurol Neurosurg Psychiatry 1994 Mar;57(3):375-6 comment in: J Neurol Neurosurg Psychiatry.	Single fibre EMG studies were carried out on the right extensor digitorum communis muscle in 30 subjects with chronic fatigue syndrome and in 30 age and sex matched controls. Abnormal jitter was seen in five patients with chronic fatigue syndrome. Slight but significant differences between the mean consecutive differences in the remainder of the chronic fatigue subjects and the

			1994 Sep;57(9):1157	control subjects were recorded. Overall the differences were so minor that it seems unlikely that a disturbance of neuromuscular function as reflected by jitter measurement has a pathogenetic role. It is suggested that the increased jitter seen may be explained by the effects of the variability of motor unit firing rates on the myogenic component of the jitter.
Rosen SD.		Hyperventilation and the chronic fatigue syndrome.	Q J Med 1994 Jun;87(6):373-4 comment on: Q J Med. 1994 Jan;87(1):63-7	
Saisch SG, Deale A, Gardner WN, Wessely S.	Department of Thoracic Medicine, Kings College School of Medicine and Dentistry, London, UK.	Hyperventilation and chronic fatigue syndrome.	Q J Med 1994 Jan;87(1):63-7 comment in: Q J Med. 1994 Jun;87(6):373-4	We studied the link between chronic fatigue syndrome (CFS) and hyperventilation in 31 consecutive attenders at a chronic fatigue clinic (19 females, 12 males) who fulfilled criteria for CFS based on both Oxford and Joint CDC/NIH criteria. All experienced profound fatigue and fatigability associated with minimal exertion, in 66% developing after an infective episode. Alternative causes of fatigue were excluded. Hyperventilation was studied during a 43-min protocol in which end-tidal PCO2 (PETCO2) was measured non-invasively by capnograph or mass spectrometer via a fine catheter taped in a nostril at rest, during and after exercise (10-50 W) and for 10 min during recovery from voluntary overbreathing to approximately 2.7 kPa (20 mmHg). PETCO2 < 4 kPa (30 mmHg) at rest, during or after exercise, or at 5 min after the end of voluntary overbreathing, suggested either hyperventilation or a tendency to hyperventilate. Most patients were able voluntarily to overbreathe, but not all were able to exercise. Twenty-two patients (71%) had no evidence of hyperventilation during any aspect of the test. Only four patients had unequivocal hyperventilation, in one associated with asthma and in three with panic. Only one patient with severe functional disability and agoraphobia had hyperventilation with no other obvious cause. A further five patients had borderline hyperventilation, in which PETCO2 was < 4 kPa (30 mmHg) for no more than 2 min, when we would have expected it to be normal. There was no association between level of functional impairment and degree of hyperventilation. There is only a weak association between hyperventilation and chronic fatigue syndrome.(ABSTRACT TRUNCATED AT 250 WORDS)
Schmaling KB, DiClementi JD, Cullum CM, Jones JF.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle 98105.	Cognitive functioning in chronic fatigue syndrome and depression: a preliminary comparison.	Psychosom Med 1994 Sep-Oct;56(5):383-8	This study used a brief battery of neuropsychological measures to examine the performance of patients with chronic fatigue syndrome (CFS) (N = 16) and patients in a major depressive episode (N = 23). The overall neuropsychological performance of the CFS group was not significantly different from depressed patients, and both groups scored within normal limits on most measures. Variability of neuropsychologic performance was in general unrelated to level of depressive symptoms. The results are discussed in terms of the validity of the cognitive criterion for the CFS diagnosis. Subjective complaints of cognitive

				dysfunction by CFS patients in light of the lack of objective evidence for the same are considered in terms of a somatic vigilance hypothesis.
Schmidley JW, Hines J.		Folate and chronic fatigue syndrome.	Neurology 1994 Nov;44(11):2214-5 comment on: Neurology. 1993 Dec;43(12):2645-7	
Schmitz S, Tesch H, Bohlen H, Engert A, Diehl V.	Klinik I fur Innere Medizin, Universitat zu Koln.	[Chronic fatigue syndrome].[article in German]	Med Klin 1994 Mar 15;89(3):154-9	
Schwartz RB, Garada BM, Komaroff AL, Tice HM, Gleit M, Jolesz FA, Holman BL.	Department of Radiology, Brigham and Women's Hospital, Boston, MA 02115.	Detection of intracranial abnormalities in patients with chronic fatigue syndrome: comparison of MR imaging and SPECT.	AJR Am J Roentgenol 1994 Apr;162(4):935-41	OBJECTIVE. Chronic fatigue syndrome is a recently characterized condition of unknown origin that is manifested by fatigue, flulike complaints, and neurologic signs and symptoms, including persistent headache, impaired cognitive abilities, mood disorders, and sensorimotor disturbances. This syndrome can be difficult to diagnose clinically or by standard neuroradiologic tests. We performed MR imaging and single-photon emission computed tomography (SPECT) in patients with chronic fatigue syndrome to compare the usefulness of functional and anatomic imaging in the detection of intracranial abnormalities. SUBJECTS AND METHODS. Sixteen patients who fulfilled the Centers for Disease Control, British, and/or Australian criteria for chronic fatigue syndrome had MR and SPECT examinations within a 10-week period. Axial MR and SPECT scans were analyzed as to the number and location of focal abnormalities by using analysis of variance with the Student-Newman-Keuls option. MR imaging findings in patients with chronic fatigue syndrome were compared with those in 15 age-matched control subjects, and SPECT findings in the patients with chronic fatigue syndrome were compared with those in 14 age-matched control subjects by using Fisher's exact test. The findings on MR and SPECT scans in the same patients were compared by using the Wilcoxon matched-pairs signed-ranks test. RESULTS. MR abnormalities consisted of foci of T2-bright signal in the periventricular and subcortical white matter and in the centrum semiovale; there were 2.06 foci per patient, vs 0.80 foci per control subject. MR abnormalities were present in eight (50%) of 16 patients, compared with three (20%) of 15 age-matched control subjects. Neither of these differences reached significance, although the power of the study to detect differences between groups was small. Patients with chronic fatigue syndrome had significantly more defects throughout the cerebral cortex on SPECT scans than did normal subjects (7.31 vs 0.43 defects per subject, $p < .001$). SPECT abnormalities were present in 13 (81%) of 16 patients, vs three (21%) of 14 control subjects ($p < .01$). SPECT scans showed significantly more abnormalities than did MR scans in patients with chronic fatigue syndrome ($p < .025$). In the few patients who had repeat SPECT and MR studies, the number of SPECT

				abnormalities appeared to correlate with clinical status, whereas MR changes were irreversible. CONCLUSION. SPECT abnormalities occur more frequently and in greater numbers than MR abnormalities do in patients with chronic fatigue syndrome. SPECT may prove to be useful in following the clinical progress of patients with this syndrome.
Schwartz RB, Komaroff AL, Garada BM, Gleit M, Doolittle TH, Bates DW, Vasile RG, Holman BL.	Department of Radiology, Brigham and Women's Hospital, Boston, MA 02215.	SPECT imaging of the brain: comparison of findings in patients with chronic fatigue syndrome, AIDS dementia complex, and major unipolar depression.	AJR Am J Roentgenol 1994 Apr;162(4):943-51	OBJECTIVE. Chronic fatigue syndrome is an illness of unknown origin that begins abruptly with a flulike state and has symptoms suggesting both a chronic viral encephalitis and an affective disorder. We compared single-photon emission computed tomography (SPECT) scans of patients with chronic fatigue syndrome with those of patients with AIDS dementia complex and unipolar depression. SUBJECTS AND METHODS. We used 99mTc-hexamethylpropyleneamine oxime to examine 45 patients with chronic fatigue syndrome, 27 patients with AIDS dementia complex, and 14 patients with major unipolar depression. Scans of 38 healthy persons were used as controls. Comparison of regional defects between groups, as well as midcerebral uptake indexes (an objective measure of global radionuclide uptake), was performed by using analysis of variance with the Student-Newman-Keuls option. Correlation between the number of regional defects and the midcerebral uptake index was determined by using the Spearman rank-correlation test. RESULTS. Patients with AIDS dementia complex had the largest number of defects (9.15 per patient) and healthy patients had the fewest defects (1.66 per patient). Patients with chronic fatigue syndrome and depression had similar numbers of defects per patient (6.53 and 6.43, respectively). In all groups, defects were located predominantly in the frontal and temporal lobes. The midcerebral uptake index was found to be significantly lower ($p < .002$) in the patients with chronic fatigue syndrome (.667) and patients with AIDS dementia complex (.650) than in patients with major depression (.731) or healthy control subjects (.716). Also, a significant negative correlation was found between the number of defects and midcerebral uptake index in patients with chronic fatigue syndrome and AIDS dementia complex, but not in depressed patients or control subjects. CONCLUSION. These findings are consistent with the hypothesis that chronic fatigue syndrome may be due to a chronic viral encephalitis; clinical similarities between chronic fatigue syndrome and depression may be due to a similar distribution and number of defects in the two disorders.
Schweitzer R, Robertson DL, Kelly B, Whiting J.	Department of Psychology, University of Queensland, Australia.	Illness behaviour of patients with chronic fatigue syndrome.	J Psychosom Res 1994 Jan;38(1):41-9	The study examines the illness behaviour of patients with Chronic Fatigue Syndrome (CFS). The Illness Behaviour Questionnaire (IBQ), the twenty-eight version of the General Health Questionnaire (GHQ-28), and the Beck Depression Inventory (BDI) were administered to forty patients with a diagnosis of CFS. The results revealed that CFS patients in comparison with general practice patients, scored significantly higher on the IBQ sub-scales of General Hypochonriasis,

				t(188) = 5.2, p < 0.001 and Disease Conviction, t(188) = 13.28, p < 0.001 but lower on the Psychological/Somatic sub-scale, t(188) = -5.88, p < 0.001. The CFS and psychiatric patients did not differ significantly on the general hypochondriasis sub-scale. Results of the GHQ-28 revealed 66.7% of the CFS patients scored above the cut-off for psychiatric morbidity. In comparison to a previous study of CFS patients [1], the current findings indicate a significantly higher score on general hypochondriasis. The implications of these findings are discussed.
Secchiero P, Berneman ZN, Gallo RC, Lusso P.	Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.	Biological and molecular characteristics of human herpesvirus 7: in vitro growth optimization and development of a syncytia inhibition test.	Virology 1994 Jul;202(1):506-12	Two isolates of human herpesvirus 7 (HHV-7) were recovered from phytohemagglutinin-activated peripheral blood mononuclear cells of a patient with chronic fatigue syndrome and of a healthy blood donor. A genetic polymorphism between the two isolates was detected by Southern blot analysis using a novel HHV-7 genomic clone (pVL8) as a probe. We developed optimized conditions for the in vitro propagation of HHV-7 by using enriched populations of activated CD4+ T lymphocytes derived from normal peripheral blood, resulting in the production of high-titered extracellular virus (> 10(6) cell culture infectious doses/ml). Bona fide syncytia formation was documented both in normal CD4+ T lymphocytes and in the Sup-T1 CD4+ T-cell line following infection with high-titered HHV-7. To identify neutralizing antibodies to HHV-7, a syncytia-inhibition test was developed. Variable titers of syncytia-neutralizing antibodies were detected in all the human sera tested, thus confirming the high prevalence of HHV-7 in the human population.
Shepherd C.		Chronic fatigue syndrome or myalgic encephalitis.	Lancet 1994 Jan 22;343(8891):243 comment on: Lancet. 1993 Nov 13;342(8881):1247-8	
Sidebotham PD, Skeldon I, Chambers TL, Clements S, Culling J.		Refractory chronic fatigue syndrome in adolescence.	Br J Hosp Med 1994 Feb 2-15;51(3):110-2 comment in: Br J Hosp Med. 1994 Jun 1-14;51(11):614	
Steere AC.	Division of Rheumatology/Immunology, Tufts University School of Medicine, New England Medical Center, Boston, MA 02111.	Lyme disease: a growing threat to urban populations.	Proc Natl Acad Sci U S A 1994 Mar 29;91(7):2378-83	Lyme disease or Lyme borreliosis, which is caused by three groups of the spirochete Borrelia burgdorferi, is transmitted in North America, Europe, and Asia by ticks of the Ixodes ricinus complex. The primary areas around the world that are now affected by Lyme disease are near the terminal moraine of the glaciers 15,000 years ago. The emergence of Lyme disease in the United States in this century is thought to have occurred because of ecological conditions favorable for deer. From 1982 through 1991, 40,195 cases occurring in 47 states were reported to the Centers for Disease Control, but enzootic cycles of B. burgdorferi have been identified in only 19 states. During the last several decades, the

				disease has spread to new areas and has caused focal outbreaks, including locations near Boston, New York, and Philadelphia. Lyme disease is like syphilis in its multisystem involvement, occurrence in stages, and mimicry of other diseases. Diagnosis of late neurologic abnormalities of the disorder has created the most difficulty. A recent phenomenon is that a number of poorly understood conditions, such as chronic fatigue syndrome or fibromyalgia, are misdiagnosed as "chronic Lyme disease." Part of the reason for misdiagnosis is due to problems associated with diagnostic tests. The various manifestations of Lyme disease can usually be treated successfully with oral doxycycline or amoxicillin, except for objective neurologic manifestations, which seem to require intravenous therapy. Vector control of thick-borne diseases has been difficult and, therefore, reduction of the risk of infection has been limited primarily to personal protection measures.
Sternon J, Decaux G, Hoffmann G.	Service de Medecine Interne, Hopital Erasme.	[Chronic fatigue syndrome].[article in French]	Rev Med Brux 1994 Sep-Oct;15(5):311-5	The major and minor diagnostic criteria of the chronic fatigue syndrome are described. The stages of the differential diagnosis, the diagnostic strategies and the controversies, while insisting on certain sleeping disorders are discussed. The cause of the syndrome may be a viral infection, and an anxious-depressive state may increase somatic complaints. Patients with chronic fatigue syndrome did not demonstrate a specific response to therapy. Spontaneous remission after a few years is a typical feature of this syndrome.
Straus SE, Komaroff AL, Wedner HJ.	Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892.	Chronic fatigue syndrome: point and counterpoint.	J Infect Dis 1994 Jul;170(1):1-6	Two clinical investigators with divergent views on chronic fatigue syndrome (CFS) were invited to debate their positions at the 1993 annual meeting of The Infectious Disease Society of America. Major points of the discourse focused on the value of the US Centers for Disease Control and Prevention case definition of CFS, the potential roles of infectious and allergic problems in the syndrome, the confounding problem of concurrent psychiatric problems, and the utility of diagnostic tests.
Strayer DR, Carter WA, Brodsky I, Cheney P, Peterson D, Salvato P, Thompson C, Loveless M, Shapiro DE, Elsasser W, et al.	School of Medicine, Hahnemann University, Philadelphia, Pennsylvania 19102.	A controlled clinical trial with a specifically configured RNA drug, poly(I).poly(C12U), in chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S88-95	Chronic fatigue syndrome (CFS) is a physically debilitating illness associated with immunologic abnormalities, viral reactivation, and impairment of cognition. In a randomized, multicenter, placebo-controlled, double-blind study of 92 patients meeting the CFS case definition of the Centers for Disease Control and Prevention, the response of several laboratory and clinical variables to an antiviral and immunomodulatory drug, poly(I).poly(C12U), was determined. Measures of clinical response included Karnofsky performance score, a cognition scale derived from a self-administered instrument assessing symptomatology (SCL-90-R), an activities of daily living scale, and exercise treadmill performance. After 24 weeks, patients receiving poly(I).poly(C12U) had higher scores for both global performance and perceived cognition than did patients receiving placebo. In particular, patients given poly(I).poly(C12U) had increased Karnofsky performance scores ($P < .03$), exhibited a greater ability to do work during

				exercise treadmill testing (P = .01), displayed an enhanced capacity to perform the activities of daily living (P < .04), had a reduced cognitive deficit (P = .05), and required less use of other medications (P < .05). Multicenter Study Randomized Controlled Trial
Suhadolnik RJ, Reichenbach NL, Hitzges P, Adelson ME, Peterson DL, Cheney P, Salvato P, Thompson C, Loveless M, Muller WE, et al.	Department of Biochemistry, Temple University School of Medicine, Philadelphia, Pennsylvania 19140.	Changes in the 2-5A synthetase/RNase L antiviral pathway in a controlled clinical trial with poly(I)-poly(C12U) in chronic fatigue syndrome.	In Vivo 1994 Jul-Aug;8(4):599-604	Latent 2', 5'-oligoadenylate (2-5A) synthetase activity, bioactive 2-5A and RNase L activity were measured in extracts of peripheral blood mononuclear cells (PMBC) before and during a randomized, multicenter, placebo-controlled, double-blind study of poly(I)-poly(C12U) in individuals with chronic fatigue syndrome (CFS) as defined by the Centers for Disease Control and Prevention. The mean values for bioactive 2-5A and RNase L activity were significantly elevated at baseline compared to controls (p < .0001 and p = .001, respectively). In individuals that presented with elevated RNase L activity at baseline, therapy with poly(I)-poly(C12U) resulted in a significant decrease in both bioactive 2-5A and RNase L activity (p = .09 and p = .005, respectively). Decrease in RNase L activity in individuals treated with poly(I)-poly(C12U) correlated with cognitive improvement (p = .007). Poly(I)-poly(C12U) therapy resulted in a significant decrease in bioactive 2-5A and RNase L activity in agreement with clinical and neuropsychological improvements (Strayer DR, et al., Clin. Infectious Dis. 18:588-595, 1994). The results described show that poly(I)-poly(C12U) is a biologically active drug in CFS. Multicenter Study Randomized Controlled Trial
Suhadolnik RJ, Reichenbach NL, Hitzges P, Sobol RW, Peterson DL, Henry B, Ablashi DV, Muller WE, Schroder HC, Carter WA, et al.	Department of Biochemistry, Temple University School of Medicine, Philadelphia, Pennsylvania 19140.	Upregulation of the 2-5A synthetase/RNase L antiviral pathway associated with chronic fatigue syndrome.	Clin Infect Dis 1994 Jan;18 Suppl 1:S96-104	Levels of 2',5'-oligoadenylate (2-5A) synthetase, bioactive 2-5A, and RNase L were measured in extracts of peripheral blood mononuclear cells (PBMCs) from 15 individuals with chronic fatigue syndrome (CFS) before and during therapy with the biological response modifier poly(I).poly(C12U) and were compared with levels in healthy controls. Patients differed significantly from controls in having a lower mean basal level of latent 2-5A synthetase (P < .0001), a higher pretreatment level of bioactive 2-5A (P = .002), and a higher level of pretherapy RNase L activity (P < .0001). PBMC extracts from 10 persons with CFS had a mean basal level of activated 2-5A synthetase higher than the corresponding control value (P = .009). All seven pretherapy PBMC extracts tested were positive for the replication of human herpesvirus 6 (HHV-6). Therapy with poly(I).poly(C12U) resulted in a significant decrease in HHV-6 activity (P < .01) and in downregulation of the 2-5A synthetase/RNase L pathway in temporal association with clinical and neuropsychological improvement. The upregulated 2-5A pathway in CFS before therapy is consistent with an activated immune state and a role for persistent viral infection in the pathogenesis of CFS. The response to therapy suggests direct or indirect antiviral activity of poly(I).poly(C12U) in this situation.
Swanink CM, Melchers WJ, van der Meer JW,	Department of Medical Microbiology, University	Enteroviruses and the chronic fatigue	Clin Infect Dis 1994 Nov;19(5):860-4	The possible role of enteroviral persistence in the etiology of the chronic fatigue syndrome (CFS) was investigated by serological testing, VP-1 antigen testing, and

Vercoulen JH, Bleijenberg G, Fennis JF, Galama JM.	Hospital Nijmegen, The Netherlands.	syndrome.		polymerase chain reaction (PCR) analysis of stool specimens as well as by viral cultures of stool--both direct and after acid treatment. No differences between 76 patients with disabling unexplained fatigue and 76 matched controls were found by serological or antigen testing. Furthermore, no enteroviruses were isolated from any stool culture. Enterovirus was detected by PCR in one stool specimen from a patient with CFS but was not detectable in a second sample obtained from the same patient 3 months later. All stool specimens from controls were PCR-negative. These results argue against the hypothesis that enteroviruses persist in patients with CFS and that their persistence plays a role in the pathogenesis of this syndrome.
Swanink CM, Vercoulen JH, Bazelmans E, Fennis JF, Bleijenberg G, van der Meer JW, Galama JM.		Viral antibodies in chronic fatigue syndrome.	938: Clin Infect Dis 1995 Sep;21(3):708-9 comment on: Clin Infect Dis. 1994 Sep;19(3):448-53	
Taerk G, Gnam W.	Department of Psychiatry, Toronto Hospital, Ontario, Canada.	A psychodynamic view of the chronic fatigue syndrome. The role of object relations in etiology and treatment.	Gen Hosp Psychiatry 1994 Sep;16(5):319-25 comment in: Gen Hosp Psychiatry. 1998 Nov;20(6):382-4	The chronic fatigue syndrome (CFS) is a constellation of physical and psychological symptoms including incapacitating fatigue associated with a marked reduction in activity. Although the etiology of CFS is unclear, reports in the literature suggest the presence of both physical and psychological dysfunction in this patient population. These findings have led to a debate between those who consider CFS to be primarily organic in origin and those who view CFS as a primary psychiatric disorder characterized by somatic preoccupations. This debate led the authors to develop a working model for CFS designed to integrate the psychological and physiological findings, based on the hypothesis that early object relations have an etiologic relationship to CFS. This hypothesis then formed the rationale for a psychoanalytic treatment approach which will be described. There are no published case reports describing psychoanalytic psychotherapy as a primary treatment modality for this patient population. The current paper attempts to fill a void. Two case reports of long-term (> 18 months), intensive (2-3 times per week) psychoanalytic psychotherapy with CFS patients referred by infectious disease specialists at a university teaching hospital will be presented. The following aspects of the treatment will be highlighted: 1) the unique opportunity afforded by this treatment to view the nature of CFS, namely, the intimate relationship over time of fatigue symptoms to disturbances in object relationships, particularly within the transference; (2) the improvement in symptoms when this relationship is seen and understood by the patient; (3) the importance of the patient-therapist bond as a facilitating medium for clinical improvement; (4) the challenges involved in treating CFS patients with psychotherapy.
Tannock C, Costa DC,		Chronic fatigue	BMJ 1994 May	

Brostoff J.		syndrome. Preliminary report misrepresented.	14;308(6939):1298 comment in: BMJ. 1994 Jun 25;308(6945):1716-7	
Tirdei G, Ruta SM, Popescu AE.	Institut de Virologie, Stefan S. Nicolau, Bucarest, Roumanie.	[Human herpesvirus 6. General overview].[article in French]	Rev Roum Virol 1994 Jan-Jun;45(1-2):83-95	Human herpesvirus 6 (HHV6) was first isolated in 1985 and included in the Herpesviridae family and the beta-herpes virinae subfamily, mainly due to its genomic similarities to the human cytomegalic virus (HCMV). HHV6 is largely disseminated in the population. The contamination takes place very early, most frequently before the age of three. In some very rare cases, a benign illness is produced, known since 1911 as Roseolum infantum or Exanthemum subitum. Seroepidemiological surveys showed that anti-HHV6 IgG antibodies were present in more than 60% of the adult population. By now, there are good information about in vitro cultivability of the virus, viral genome and proteins, epidemiology of the infection and etiopathogenic relation between virus and Exanthemum subitum. Relations between virus and lymphoproliferative diseases, some auto-immune diseases, chronic fatigue syndrome and some other diseases are less clear. Relation between this virus and HIV-infection is another problem requiring more research.
Tirelli U, Marotta G, Improta S, Pinto A.	CFS Unit, Division of Medical Oncology and AIDS, Centro di Riferimento Oncologico (CRO), Aviano, Italy.	Immunological abnormalities in patients with chronic fatigue syndrome.	Scand J Immunol 1994 Dec;40(6):601-8	Between January 1991 and January 1993, 265 patients who fulfilled the CDC criteria of the working case definition of Chronic Fatigue Syndrome (CFS) have been observed at our Institution and submitted for clinical and laboratory evaluation. One hundred and sixty-three patients were females and 102 males, the median age was 35 years (range 4-55 years); all patients reported profound and prolonged fatigue, lasting for a median of 3 years (range 6 months-10 years), preceded or accompanied at appearance by fever in 185 cases, and neuropsychologic problems including inability to concentrate, difficulty in thinking, confusion, irritability, forgetfulness, and depression. The fatigue was so severe that it required 102 patients to stop their working activities for a period of time ranging from 3 months to 2 years (range 7 months). In 40 consecutive patients a comprehensive immunologic testing by single and two-colour flow cytometry was performed and results compared with a group of 35 healthy, age- and sex-matched controls. Whilst no significant differences were found in the absolute numbers of circulating total T cells (CD3+) and of total helper/inducer (CD4+) or suppressor/cytotoxic (CD8+) T cells, an evident reduction in CD3-/CD16+ and CD57+/CD56+ NK lymphocytes along with an expansion of the CD8+/CD56+ and CD16-/CD56+ NK subsets, were found in the CFS group. In addition, CD56+ NK cells from CFS subjects were found to express an increased amount of cell adhesion molecules (CD11b, CD11c, CD54) and activation antigens (CD38). Both the percentage and absolute numbers of CD4+ T cells bearing the CD45RA antigen appeared significantly reduced in CFS patients, and CD4+ T

				lymphocytes from CFS subjects displayed an increased expression of the intercellular adhesion molecule-1 (ICAM-1/CD54). Finally, the total numbers of circulating (CD19+) B lymphocytes, were significantly higher in CFS cases than in controls, and in 11 out of 30 CFS patients the increase in circulating B cells was sustained by the expansion of the CD5+/CD19+ subset of B lymphocytes. We conclude that CFS is a syndrome not previously described in Italy, with already known clinical characteristics and appears to be associated with several immunologic abnormalities, including those reported previously in cohort of patients from different countries. We also show for the first time that CD56- NK cell subsets from CFS patients display an abnormally increased expression of cell adhesion molecules and activation markers.
Trevor A.		Chronic fatigue syndrome: what's in a name?	Can Fam Physician 1994 Jun;40:1088-9 comment on: Can Fam Physician. 1993 Dec;39:2586-92, 2595-7	
Trinidad EE, Ramirez-Ronda C.	Programa de Enfermedades Infecciosas Universidad de Puerto Rico, San Juan.	[Chronic fatigue syndrome].[article in Spanish]	Bol Asoc Med P R 1994 Jul-Sep;86(7-9):56-61	The Chronic Fatigue Syndrome is a disease that originates in the 18th Century of unknown etiology. The chronic fatigue is a common complain with an estimate prevalence of 24%. In 1988 the Chronic Fatigue Syndrome was define by the experts due to an increase in the recognition of the disease. Is a disease that possess similar characteristics to other conditions for which the diagnosis is one of exclusion. Cases has been reported around the world been most common in women between 20-50 years of age. The treatment is mostly supportive.
Trojani FT.		[The chronic fatigue syndrome].[article in Italian]	Clin Ter 1994 Apr;144(4):373-6	
Trojani FT.		[Chronic fatigue syndrome].[article in Italian]	Clin Ter 1994 Mar;144(3):269-72	
Trojani FT.		[Chronic fatigue syndrome].[article in Italian]	Clin Ter 1994 Feb;144(2):163-6	
Valesini G, Conti F, Priori R. Review Review, Tutorial		Chronic fatigue syndrome: what factors trigger it off?	Clin Exp Rheumatol 1994 Sep-Oct;12(5):473-6	
Vercoulen JH, Swanink CM, Fennis JF, Galama JM, van der Meer JW, Bleijenberg G.	Department of Medical Psychology, University Hospital, Nijmegen, The Netherlands.	Dimensional assessment of chronic fatigue syndrome.	J Psychosom Res 1994 Jul;38(5):383-92	The absence of laboratory tests and clear criteria to identify homogeneous (sub)groups in patients presenting with unexplained fatigue, and to assess clinical status and disability in these patients, calls for further assessment methods. In the present study, a multi-dimensional approach to the assessment of chronic fatigue syndrome (CFS) is evaluated. Two-hundred and ninety-eight patients with

				CFS completed a set of postal questionnaires that assessed the behavioural, emotional, social, and cognitive aspects of CFS. By means of statistical analyses nine relatively independent dimensions of CFS were identified along which CFS-assessment and CFS-research can be directed. These dimensions were named: psychological well-being, functional impairment in daily life, sleep disturbances, avoidance of physical activity, neuropsychological impairment, causal attributions related to the complaints, social functioning, self-efficacy expectations, and subjective experience of the personal situation. A description of the study sample on these dimensions is presented.
Wassif WS, Sherman D, Salisbury JR, Peters TJ.	Department of Clinical Biochemistry, Kings College School of Medicine and Dentistry, London, UK.	Use of dynamic tests of muscle function and histomorphometry of quadriceps muscle biopsies in the investigation of patients with chronic alcohol misuse and chronic fatigue syndrome.	Ann Clin Biochem 1994 Sep;31 (Pt 5):462-8	Ischaemic lactate/ammonia tests, serum carnosinase and creatine kinase assays and percutaneous needle muscle biopsies were performed on 10 patients with chronic fatigue syndrome (CFS), and 10 with chronic alcohol misuse complaining of muscular symptoms. Basal serum lactate levels were significantly elevated in the alcohol misusers compared to the CFS patients, but all were within the reference range. Lactate profiles after ischaemic forearm exercise did not differ significantly for the two patient groups. In one patient previously diagnosed as having CFS, myoadenylate deaminase deficiency was identified on the basis of a flat ammonia response to ischaemia and absent muscle adenosine monophosphate deaminase activity. In addition, two further patients in the CFS group were subsequently shown to have other disorders: one had polymyositis and one had myopathy with mild type II fibre atrophy of unknown cause. Histomorphometric examination of muscle needle biopsy in the alcohol misusers showed features of chronic alcohol-induced skeletal myopathy in six patients and polymyositis in one patient. Type II fibre atrophy factors were significantly elevated in the alcohol group but were within the reference range in CFS patients. Dynamic tests of muscle function and muscle histology are valuable tools in excluding alternative pathology in CFS, whereas muscle histomorphometry is of the greatest value in the diagnosis of chronic alcoholic myopathy.
Wessely S.	Academic Dpt of Psychologic, King's College Hospital, London, United Kingdom.	[Chronic fatigue syndrome. Clinical, social psychological problems and management].[article in French]	Encephale 1994 Nov;20 Spec No 3:581-95	Fatigue chronic syndrome (SFC) is the heir-at-law of neurasthenia. Both are seen like physical diseases and share certain therapeutic measures, such as sleep; they have the same symbolic function and enable patients as well as doctors reluctant to psychological dimensions of pathology, to get and express sympathy and attention. A strong controversy developed these last years concerning the SFC physiopathology particularly concerning the responsibility of viral infectious agents or psychiatric troubles. The SFC fatigue is unlikely hysterical or neuromuscular but it probably depends on several associated factors; cerebral neurobiochemistry anomalies (possibly induced by an infection or immune reactions), effort perception trouble, affective trouble, lack of physical activity. The handicap seems to be worse on account of unsuitable care and inefficacious

				treatment. Especially sleep, which is often beneficial in a short term, is source of ulterior chronicisation. Antidepressants are the only justified pharmacological treatment for SFC at the moment. Referring to the existence and the nature of cognitive distortions, the author suggests a cognitivo-behavioural therapy, whose aim is a progressive activity resumption.
Wilborn F, Schmidt CA, Brinkmann V, Jendroska K, Oettle H, Siegert W.	Universitatsklinikum Rudolf Virchow, Innere Medizin und Poliklinik mit Schwerpunkt Hamatologie und Onkologie, Berlin, Germany.	A potential role for human herpesvirus type 6 in nervous system disease.	J Neuroimmunol 1994 Jan;49(1-2):213-4	Human herpesvirus type 6 (HHV-6) is a new representative of the herpesvirus family which was associated with a spectrum of diseases, including myalgic encephalitis, meningitis and the chronic fatigue syndrome. We set out to study the potential role of HHV-6 in multiple sclerosis (MS) (n = 21), facial palsy (FP) (n = 19) and Guillain-Barre-syndrome (GBS) (n = 7). Results were compared with a control group (CG) (n = 16). We analyzed paired samples of serum and cerebrospinal fluid (CSF) with the polymerase chain reaction (PCR) for the presence of HHV-6 DNA. The studies were complemented by ELISA determination of serum antibodies against HHV-6. In the MS group we detected HHV-6 DNA in the CSF from three of 21 (14.3%) patients but not in the corresponding serum samples. In FP, GBS and controls CSF and serum PCRs were negative in all cases. HHV-6 serum antibody titers were significantly higher in MS compared with FP, GBS and controls. These findings suggest that HHV-6 may play a role in MS.
Wilson A, Hickie I, Lloyd A, Hadzi-Pavlovic D, Boughton C, Dwyer J, Wakefield D.	Department of Psychiatry, Prince Henry Hospital, Little Bay, NSW, Australia.	Longitudinal study of outcome of chronic fatigue syndrome.	BMJ 1994 Mar 19;308(6931):756-9 comment in: BMJ. 1994 May 14;308(6939):1297 BMJ. 1994 May 14;308(6939):1297-8 BMJ. 1994 May 14;308(6939):1299	OBJECTIVE--To examine the predictors of long term outcome for patients with the chronic fatigue syndrome. DESIGN--Cohort study. SUBJECTS--139 subjects previously enrolled in two treatment trials; 103 (74%) were reassessed a mean of 3.2 years after start of the trials. SETTING--University hospital referral centre. MAIN OUTCOME MEASURES--Age at onset, duration of illness, psychological and immunological status at initial assessment. Ongoing symptom severity, levels of disability, and immunological function at follow up. RESULTS--65 subjects had improved but only six reported no current symptoms. An alternative medical diagnosis had been made in two and psychiatric illness diagnosed in 20. The assignment of a primary psychiatric diagnosis at follow up and the strength of the belief that a physical disease process explained all symptoms at entry to the trials both predicted poor outcome. Age at onset of illness, duration of illness, neuroticism, premorbid psychiatric diagnoses, and cell mediated immune function did not predict outcome. CONCLUSION--Though most patients with the chronic fatigue syndrome improve, a substantial proportion remain functionally impaired. Psychological factors such as illness attitudes and coping style seem more important predictors of long term outcome than immunological or demographic variables.
Wilson A, Hickie I, Lloyd A, Wakefield D.	Department of Psychiatry, Prince Henry Hospital, Little Bay NSW, Australia.	The treatment of chronic fatigue syndrome: science and speculation.	Am J Med 1994 Jun;96(6):544-50	The chronic fatigue syndrome (CFS) is a heterogeneous disorder characterized by fatigue, neuropsychiatric symptoms, and various other somatic complaints. Treatment studies to date reflect both the diversity of medical disciplines involved in the management of patients with CFS and the multiple

				pathophysiologic mechanisms proposed. There have been few attempts to study integrated treatment programs, and although several controlled studies have been reported, no treatment has been shown clearly to result in long-term benefit in the majority of patients. Good clinical care integrating medical and psychologic concepts, together with symptomatic management, may prevent significant secondary impairment in the majority of patients. Future treatment studies should examine differential response rates for possible subtypes of the disorder (eg, documented viral onset, concurrent clinical depression), evaluate the extent of any synergistic effects between therapies (ie, medical and psychologic), and employ a wide range of biologic and psychologic parameters as markers of treatment response.
Yalcin S, Kuratsune H, Yamaguchi K, Kitani T, Yamanishi K.	Department of Virology, Osaka University Medical School, Japan.	Prevalence of human herpesvirus 6 variants A and B in patients with chronic fatigue syndrome.	Microbiol Immunol 1994;38(7):587-90	Peripheral blood mononuclear cells collected from 13 patients with chronic fatigue syndrome and 13 healthy controls were analyzed for the presence of human herpesvirus 6 (HHV-6) DNA by variant-specific polymerase chain reaction and dot blot hybridization. HHV-6 DNA was detected in 7 of 13 (53%) patients, and of those 7 patients, 4 were positive for HHV-6 variant A DNA and 3 were for variant B. No HHV-6 DNA was detected in the controls. Serum antibody titers to the late antigen and antibody prevalence to the early antigen of HHV-6 were significantly higher in the patient group. These results suggest active replication of HHV-6 in patients with chronic fatigue syndrome.
Zavalishin IA, Zakharova MN.		[The chronic fatigue syndrome].[article in Russian]	Zh Nevropatol Psikhiatr Im S S Korsakova 1994;94(5):44-6	
Zubieta JK, Engleberg NC, Yargic LI, Pande AC, Demitrack MA.	Department of Psychiatry, University of Michigan Medical Center, Ann Arbor 48109-0116.	Seasonal symptom variation in patients with chronic fatigue: comparison with major mood disorders.	J Psychiatr Res 1994 Jan-Feb;28(1):13-22	The psychobiology of idiopathic fatigue has received renewed interest in the medical literature in recent years. In order to examine the relation between chronic, idiopathic fatigue and specific subtypes of depressive illness, we characterized the pattern and severity of seasonal symptom variation in 73 patients with chronic, idiopathic fatigue, compared to patients with major depression (n = 55), atypical depression (n = 35), and seasonal affective disorder (n = 16) Fifty of the fatigued subjects also met the specific Centers for Disease Control and Prevention case criteria for chronic fatigue syndrome, though this definition was unable to discriminate a distinct subgroup of patients, based on their seasonality scores alone. As a group, the fatigued subjects reported the lowest levels of symptom seasonality of any of the study groups. Further, even in those fatigued subjects with scores in the range of those seen in patients with seasonal affective disorder, seasonality was not reported to be a subjectively distressing problem. These findings lend support to the idea that although chronic fatigue shares some clinical features with certain mood disorders, they are not the same illnesses. These data are also consistent with the emerging view that chronic fatigue represents a heterogeneously determined clinical condition.

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Abbey SE.	Department of Psychiatry, Toronto Hospital, Ontario, Canada.	Somatization, illness attribution and the sociocultural psychiatry of chronic fatigue syndrome.	Ciba Found Symp 1993;173:238-52; discussion 252-61	In addition to epidemiological and neurobiological perspectives on the relationship between chronic fatigue syndrome (CFS) and psychiatric disorders there has been increasing interest in the role of cognitive-behavioural, psychological, psychodynamic and social factors in the psychiatric aspects of this syndrome. These factors may be important in the initiation and/or maintenance of CFS and play important roles in the misdiagnosis of primary psychopathology as CFS. They may be important targets for intervention and treatment. This paper examines the relevance of the following issues for better understanding the relationship between CFS and the results of psychiatric studies: (1) the concepts of somatization and abnormal illness behaviour; (2) the role of patients' illness attributions; (3) psychological and psychodynamic constructs such as depressive vulnerability occurring in individuals dependent upon achievement for the maintenance of self-esteem and euthymic mood, perfectionism, and helplessness; (4) the role of personality characteristics and styles; (5) the potential iatrogenic role of the health care system in producing disability in individuals with a diagnosis of CFS; (6) the role of the media and other sociocultural forces in the patient's choice of the CFS label; and (7) the impact of the CFS label on the patient. The importance of differentiating between initiating and maintaining or perpetuating factors is emphasized.
Anon		Inability of retroviral tests to identify persons with chronic fatigue syndrome, 1992.	MMWR Morb Mortal Wkly Rep 1993 Mar 19;42(10):183, 189-90	Chronic fatigue syndrome (CFS) is characterized by prolonged, debilitating fatigue. Although the cause of CFS unknown, CDC and researchers in other organizations have been investigating whether infection with a previously unidentified retrovirus might be an etiologic factor. Based on reports suggesting that retroviral infection with a human T-lymphotropic virus type 2 (HTLV-II)-like retrovirus or a spumavirus might be associated with CFS, some research and commercial laboratories developed assays to test specimens from persons with CFS. Even though the hypothesized association between infection with retroviruses and CFS has not been confirmed, these tests are used commonly to evaluate patients with CFS. This report summarizes the findings of a controlled, blinded study conducted in 1992 to determine whether three retroviral tests can distinguish serologically between patients with CFS (i.e., case-patients) and healthy controls.
Aoki T, Miyakoshi H, Usuda Y, Herberman RB.	Department of Internal Medicine, Shinrakuen Hospital, Niigata, Japan. Review, Academic	Low NK syndrome and its relationship to chronic fatigue syndrome.	Clin Immunol Immunopathol 1993 Dec;69(3):253-65	
Barnes CL, Fleming CA, Poinsett-Holmes K,		Chronic fatigue syndrome: what are the	J Pract Nurs 1993 Sep;43(3):24-31; quiz	

Kennedy LD.		facts?	32-4	
Barnes PR, Taylor DJ, Kemp GJ, Radda GK.	MRC Biochemical and Clinical Magnetic Resonance Unit, John Radcliffe Hospital, Oxford, UK.	Skeletal muscle bioenergetics in the chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1993 Jun;56(6):679-83	Skeletal muscle bioenergetics and control of intracellular pH have been investigated in 46 patients with chronic fatigue syndrome by phosphorus magnetic resonance spectroscopy. The results have been compared with those from healthy controls and from a group of patients with mitochondrial cytopathies affecting skeletal muscle. No consistent abnormalities of glycolysis, mitochondrial metabolism or pH regulation were identified in the group when taken as a whole, although in 12 of the 46 patients the relationship between pH and phosphocreatine utilisation during exercise fell outside the normal range. Of these, 6 patients showed increased acidification relative to phosphocreatine depletion while 6 showed reduced acidification. These findings do not support the hypothesis that any specific metabolic abnormality underlies fatigue in this syndrome although abnormalities may be present in a minority of patients.
Bates DW, Schmitt W, Buchwald D, Ware NC, Lee J, Thoyer E, Kornish RJ, Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Boston, Mass.	Prevalence of fatigue and chronic fatigue syndrome in a primary care practice.	Arch Intern Med 1993 Dec 27;153(24):2759-65	BACKGROUND: Our goals were to determine the prevalence of unusual, debilitating fatigue and the frequency with which it was associated with the chronic fatigue syndrome (CFS) or other physical or psychological illness in an outpatient clinic population. METHODS: We prospectively evaluated a cohort of 1000 consecutive patients in a primary care clinic in an urban, hospital-based general medicine practice. The study protocol included a detailed history, physical examination, and laboratory and psychiatric testing. RESULTS: Five patients who came because of CFS studies were excluded. Of the remaining 995, 323 reported fatigue, and 271 (27%) complained of at least 6 months of unusual fatigue that interfered with their daily lives. Of the 271, self-report or record review revealed a medical or psychiatric condition that could have explained the fatigue in 186 (69%). Thus, 85 (8.5%) of 995 patients had a debilitating fatigue of at least 6 months' duration, without apparent cause. Of these patients, 48 refused further evaluation, and 11 were unavailable for follow-up; 26 completed the protocol. Three of the 26 were hypothyroid, and one had a major psychiatric disorder. Of the remaining 22 patients, three met Centers for Disease Control and Prevention criteria for CFS, four met British criteria, and 10 met the Australian case definition. The point prevalences of CFS were thus 0.3% (95% confidence interval [CI], 0% to 0.6%), 0.4% (95% CI, 0% to 0.8%), and 1.0% (95% CI, 0.4% to 1.6%) using the Centers for Disease Control and Prevention, British, and Australian case definitions, respectively. These estimates were conservative, because they assumed that none of the patients who refused evaluation or were unavailable for follow-up would meet criteria for CFS. CONCLUSIONS: While chronic, debilitating fatigue is common in medical outpatients, CFS is relatively uncommon. Prevalence depends substantially on the case definition used.
Behan WM, Behan PO.	Department of Pathology, Western	The role of viral infection in	Baillieres Clin Neurol 1993 Nov;2(3):637-57	

	Infirmary, Glasgow, UK.	polymyositis, dermatomyositis and chronic fatigue syndrome.		
Bentall RP, Wood GC, Marrinan T, Deans C, Edwards RH.	Department of Clinical Psychology, University of Liverpool, UK.	A brief mental fatigue questionnaire.	Br J Clin Psychol 1993 Sep;32 (Pt 3):375-9	A brief mental fatigue questionnaire was administered to normal subjects and muscle-diseased, Chronic Fatigue Syndrome (CFS), recovered CFS and depressed patients. The questionnaire was found to have excellent internal consistency and discriminated effectively between CFS and depressed patients on the one hand and recovered CFS, normal and muscle-diseased patients on the other. However, the scale failed to discriminate between CFS and depressed subjects, who were found to experience qualitatively and quantitatively similar mental fatigue symptoms.
Bertolin JM, Bertolin V.	Centro de Salud Mental, Servicio Valenciano de Salud. Review, Academic	[Chronic fatigue syndrome: biologic and psychopathologic investigations].[article in Spanish]	Med Clin (Barc) 1993 Jun 5;101(2):67-75	
Bialyszewski A.	IV Kliniki Psychiatrycznej Instytutu Psychiatrii i Neurologii, Warszawie.	[The chronic fatigue syndrome].[article in Polish]	Psychiatr Pol 1993 Nov-Dec;27(6):601-11	The chronic fatigue syndrome (CFS) including myalgic encephalomyelitis and the postviral syndrome is a term used today to describe a not fully recognized disease characterized primarily by chronic or recurrent debilitating fatigue and various combinations of neuromuscular and neuropsychological symptoms. The term CFS has been introduced and defined by the Centers for Disease Control (CDC) in Atlanta. Fatigue is one of the most common symptoms in medicine, but CFS as defined by CDC has appeared to be quite rare in the general population. Researchers have suggested that the syndrome is a heterogenous immunologic disorder that follows viral infection, but despite numerous studies on the subject the etiologic factor of the syndrome is unknown. CFS is a controversial diagnosis. In a very high percentage of patients with the CFS depression, phobias or anxiety disorders have frequently preceded the onset of the chronic fatigue. There are many overlapping symptoms between CFS and major depression. Some clinicians suggest that it is not obvious that CFS can be distinguished from neurasthenia.
Blondel-Hill E, Shafran SD.	Department of Medicine, University of Alberta, University of Alberta Hospitals, Walter Mackenzie Health Sciences Centre, Edmonton, Canada.	Treatment of the chronic fatigue syndrome. A review and practical guide.	Drugs 1993 Oct;46(4):639-51	The chronic fatigue syndrome (CFS) was formally defined in 1988 to describe a syndrome of severe and disabling fatigue of uncertain aetiology associated with a variable number of somatic and/or psychological symptoms. CFS has been reported in most industrialised countries and is most prevalent in women aged between 20 and 50 years. Despite occasional claims to the contrary, the aetiology of CFS remains elusive. Although abnormalities in tests of immune function and cerebral imaging have been described in variable numbers of CFS patients, such findings have been inconsistent and cannot be relied upon, either to establish or exclude the diagnosis. Thus, diagnosis rests on fulfillment of the Centers for

				Disease Control case definition which was revised in 1992. This case definition remains somewhat controversial, largely due to its subjectiveness. The mainstay of treatment is establishing the diagnosis and educating the patient about the illness. An empathetic clinician can stop further consultations elsewhere ('doctor shopping') and subsequent excessive investigations, which frequently occur in such patients. Most patients should undertake a trial of antidepressant therapy, even if major depression is not present. The choice of antidepressant drug should tailor the tolerability profile to relief of particular CFS symptoms, such as insomnia or hypersomnia. Failure to improve within 12 weeks warrants an alternative antidepressant agent of another class. Many other drugs have been reported anecdotally to be beneficial, but no therapy has been demonstrated to be reproducibly useful in double-blind, placebo-controlled clinical trials with an adequate duration of follow-up.
Bojic I, Mijuskovic P, Lilic D, Kuljic-Kapulica N, Mijuskovic Z, Berger S, Mitrovic D.	Vojnomedicinska akademija, Klinika za infektivne i tropske bolesti, Institut za medicinska istrazivanja.	[The chronic fatigue syndrome associated with Epstein-Barr virus infection].[article in Serbo-Croatian (Roman)]	Vojnosanit Pregl 1993 May-Jun;50(3):304-7	
Bond PA.		A role for herpes simplex virus in the aetiology of chronic fatigue syndrome and related disorders.	Med Hypotheses 1993 May;40(5):301-8	
Bowles NE, Bayston TA, Zhang HY, Doyle D, Lane RJ, Cunningham L, Archard LC.	Department of Biochemistry, Charing Cross and Westminster Medical School, London, England.	Persistence of enterovirus RNA in muscle biopsy samples suggests that some cases of chronic fatigue syndrome result from a previous, inflammatory viral myopathy.	J Med 1993;24(2-3):145-60	Molecular hybridization using an enterovirus group specific probe detected virus RNA in muscle biopsy samples from 25 of 96 cases of inflammatory muscle disease and similarly from 41 of 158 cases of postviral fatigue syndrome (PFS). Enterovirus RNA was detected in only two of 152 samples of control muscle. The inflammatory myopathy group comprised patients with polymyositis (PM), juvenile dermatomyositis (JDM) or adult dermatomyositis (DM), and all showed the presence of an inflammatory infiltrate and fiber necrosis on histological examination of a muscle biopsy sample. In contrast, muscle samples from the PFS group were histologically normal except for non-specific changes such as occasional single fiber atrophy. By analogy with enteroviral myocarditis, which can progress to a post-inflammatory disease with persistence of virus in myocardium and disposes to the rapid development of dilated cardiomyopathy, we propose that PFS syndrome may be a sequela of a previous inflammatory viral myopathy.
Brook MG, Bannister BA, Weir WR. Letter		Interferon-alpha therapy for patients	J Infect Dis 1993 Sep;168(3):791-2	

		with chronic fatigue syndrome.		
Burdge DR, O'Hanlon DP.	Department of Medicine, University of British Columbia, Vancouver, Canada.	Experience at a referral center for patients with suspected Lyme disease in an area of nonendemicity: first 65 patients.	Clin Infect Dis 1993 Apr;16(4):558-60	A multidisciplinary referral center was established at a university hospital for prospectively assessing patients with possible Lyme disease. Borrelia burgdorferi is not known to be endemic in this region, but considerable anxiety about Lyme disease has developed among the general public. Sixty-five patients were referred for suspected Lyme borreliosis. Detailed histories were obtained and physical examinations were performed; patients were investigated aggressively in accordance with their symptom complexes. Strict diagnostic criteria consistent with published standards were applied. Only two of the 65 patients were judged to have probable Lyme disease. Definite major alternate diagnoses were made for 50 patients (77%); firm medical diagnoses (11 dermatologic, 9 rheumatologic, 9 infectious disease, 6 gastrointestinal, 4 neurological, and 2 miscellaneous) were made for 41 patients (63%); and major psychiatric diagnoses were made for 9 patients (14%). Probable diagnoses of chronic fatigue syndrome and fibromyalgia were made for 11 patients (17%). The conditions of four patients (6%) were undiagnosed. A referral center for patients with suspected Lyme disease can be useful even in an area of nonendemicity, and careful clinical assessment will reveal treatable alternate diagnoses for many patients with suspected Lyme disease.
Cathebras P, Bouchou K, Charmion S, Rousset H.	Service de Medecine Interne, Hopital Nord, Saint-Etienne.	[Chronic fatigue syndrome: a critical review].[article in French]	Rev Med Interne 1993 Apr;14(4):233-42	The term "chronic fatigue syndrome" (CFS) applies to a condition of unknown aetiology characterized clinically by an association of subjective symptoms, the most constant being an invalidating tiredness. The diagnostic criteria in current use do not permit to isolate an homogeneous subgroup among patients consulting for chronic asthenia. In the present state of research no infectious or immunological cause has been demonstrated conclusively, although a persistent enterovirus or herpesvirus type 6 infection or a state of chronic immune activation seem to play a role in some cases. Patients who fulfill the criteria of CFS present with psychiatric overmorbidity, essentially depressive, and in 50% of the cases with the mental disorders preceding CFS. The various theoretical models linking CFS to psychopathology are discussed, and finally the syndrome is regarded as a social construction reproducing or renovating the neurasthenia of the late 19th century. There is no specific treatment of CFS, but antidepressants, cognitive-behavioural therapy and perhaps certain immuno-modulators can be useful. The future lines of research should endeavour to isolate a subgroup of patients with prolonged asthenia after a recognized episode of infection and to identify the immunological, psychological and behavioral characteristics of this particular group as well as their reciprocal interactions. Review, Academic
Centers for Disease Control and Prevention		From the Centers for Disease Control and	JAMA 1993 Apr 14;269(14):1779, 1782	

		Prevention. Inability of retroviral tests to identify persons with chronic fatigue syndrome, 1992.		
Chester AC.		Hypothesis: the nasal fatigue reflex.	Integr Physiol Behav Sci 1993 Jan-Mar;28(1):76-83	Natural selection results in adaptations. I suggest that unexplained fatigue may be an adaptive response to nasal impairment. For macrosmatic animals, intact olfaction is necessary to detect predators. In such animals, any reflex (e.g., fatigue) triggered by nasal dysfunction that limited exposure would offer great survival advantage. The "fatigued" animal would remain in its protected environment, unexposed to hungry carnivores, while the nose healed. In humans, clinical syndromes associated with unexplained fatigue (chronic fatigue syndrome, tension fatigue syndrome, allergic fatigue, neurasthenia, etc.) are characterized by symptoms that, in part, are nasal in origin. The older medical literature does describe the resolution of fatigue in neurasthenia after nasal treatments. Nasal reflexes in animals do cause significant systemic effects, including an inhibition of muscle action potentials that is, perhaps, analogous to the "heavy-limbed" sensation of those with fatigue. Furthermore, reflexes similar to the one proposed do exist in humans: the diving reflex presumably served our amphibian ancestors well as an oxygen conserving technique with submersion, but serves no known useful function now. Other human nasopharyngeal reflexes with profound cardiovascular and systemic effects are well described but only occasionally studied. The proposed nasal fatigue reflex should be examined as a possible ancient adaptive response to nasal malfunction.
Clee MD, McLaughlin K.		Complications of sarcoidosis. Chronic fatigue syndrome.	Sarcoidosis 1993 Sep;10(2):138 comment on: Sarcoidosis. 1993 Mar;10(1):1-3	
Cox DL, Findley LJ.		Chronic fatigue syndrome.	BMJ 1993 Jul 31;307(6899):328 comment on: BMJ. 1993 Jun 12;306(6892):1557-8	
Dechene L.	Fitchburg State College, Fitchburg, Massachusetts 01420.	Chronic fatigue syndrome: influence of histamine, hormones and electrolytes.	Med Hypotheses 1993 Jan;40(1):55-60	The chronic fatigue syndrome is poorly understood. We believe the underlying causes in many atopics and women are a persistent infection and hypersensitivity to the immune-suppressive effects of histamine and certain pathogens. We believe much to the symptomatology can be explained by all four types of hypersensitivity (Gell and Coombs classification) in reaction to a pathogen, electrolyte disturbances which include sometimes permanent changes in cell membranes' ability to pass electrolytes, sometimes permanent biochemical

				changes in mitochondrial function, and disturbances of insulin and T3-thyroid hormone functions. We also explain in detail what 'fatigue' means for these patients. We present evidence from the medical literature for the plausibility of our hypotheses.
Delage G, Salit I, Pennie R, Alary M, Duval B, Ward B.		[The possible relation between hepatitis B vaccination and chronic fatigue syndrome].[article in French]	Union Med Can 1993 Jul-Aug;122(4):278-9	
DeLuca J, Johnson SK, Natelson BH.	Department of Physical Medicine and Rehabilitation, University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark.	Information processing efficiency in chronic fatigue syndrome and multiple sclerosis.	Arch Neurol 1993 Mar;50(3):301-4	OBJECTIVE--To compare the cognitive performance of subjects with chronic fatigue syndrome (CFS), multiple sclerosis (MS), and healthy controls. All subjects were matched for age, education, and verbal intelligence, as previous neuropsychological studies of CFS had not used appropriate control groups. DESIGN--Case-control design. All subjects were given a neuropsychological battery and the test scores were compared among the groups. SETTING--Subjects with CFS and subjects with MS were recruited from private and institutional practice and from the community. Healthy subjects were recruited from the community. PATIENTS/OTHER PARTICIPANTS--Twelve subjects (all female) with CFS participated in the study. Chronic fatigue syndrome was diagnosed in these patients in accordance with the requirements outlined by the Centers for Disease Control as modified subsequently to not exclude patients with concurrent depression and/or anxiety. All subjects with CFS were referred for a neuropsychological examination to assess persistent cognitive complaints. Eleven subjects (10 female, one male) with the diagnosis of clinically stable MS were chosen from clinics and the community because of complaints of mild to moderate cognitive impairment. The subjects with MS and 11 healthy volunteers (10 female, one male) were matched to the group with CFS by age, education, and estimated verbal intelligence (based on the Vocabulary subtest of the Wechsler Adult Intelligence Scale-Revised). The subjects with MS had a mean Kurtzke Expanded Disability Status Scale score of 4.95 (SD, 1.95; range, 2.0 to 7.5). As a result of the matching procedure, there were no differences among the three groups in age ($F[2,31] = 0.32$), education ($F[2,31] = 0.80$), and verbal intelligence ($F[2,31] = 0.31$). INTERVENTIONS--None. MAIN OUTCOME MEASURES--These measures included the Beck Depression Inventory (BDI), the Paced Auditory Serial Addition Test (PASAT), Digit Span Test, and the Similarities Test of Verbal Abstract Reasoning. RESULTS--The mean number of correctly identified responses collapsed across the four PASAT trials was significantly different across groups ($F[2,31] = 4.03$; $P < .05$). While the CFS and MS groups did not differ from each other, subjects with CFS (SEM, 124.2 +/- 6.4) and subjects

				with MS (SEM, 112.9 +/- 10.9) scored significantly below controls (SEM, 146.4 +/- 6.4) (Fisher's Protected Least Significant Difference test; P < .05). There were significant differences among the three groups on mean Digit Span Test performance (F[2,31] = 5.5; P < .01). While the CFS and MS group did not differ significantly from each other, only the CFS group was significantly lower than control (Fisher's Protected Least Significant Difference test; P < .05). Mean performance on the Similarities test did not differ among the three groups (F = 0.58). In addition, there were significant differences among the three groups in mean BDI scores (F[2,31] = 7.6; P < .01). The CFS and MS groups did not differ significantly from each other, and both groups showed a statistically significantly elevated mean BDI score relative to the control group (Fisher's Protected Least Significant Difference test; P < .05). No significant correlations were found between BDI scores and PASAT total scores (CFS, r = -.21; MS, r = .13; control, r = .27), or between BDI and Digit Span Test (CFS, r = -.32; MS, r = -.40; control, r = -.19). Results of the PASAT and Digit Span Test were significantly correlated in the CFS group (r = .71; P < .01), but not in the MS (r = .06) or control groups (r = .49). CONCLUSIONS--These results indicate that subjects with CSF and subjects with MS show significant impairment on a test of complex concentration when compared with appropriate controls. The data suggest that subjects with CFS and subjects with MS have difficulty on tasks that require the simultaneous processing of complex cognitive information. Selective impairment in information processing efficiency may lie at the
Denz-Penhey H, Murdoch JC.	Department of General Practice, University of Otago Medical School, Dunedin.	General practitioners acceptance of the validity of chronic fatigue syndrome as a diagnosis.	N Z Med J 1993 Apr 14;106(953):122-4	AIM. To identify whether general practitioners accept the validity of a diagnosis of chronic fatigue syndrome (CFS). METHOD. An anonymous questionnaire was sent out to 98 general practitioners in Otago. RESULTS. The clinical validity of chronic fatigue syndrome was accepted by 74 (90%); 57 believed they had sufficient knowledge about the condition to make a differential diagnosis; 72 indicated they had had patients with chronic fatigue syndrome in the past; 62 currently had patients; there is a minimum prevalence rate of 167/100,000 in the general practice population; 83 replies were received. CONCLUSION. The 90% acceptance rate of chronic fatigue syndrome as a clinically valid diagnosis suggests that amongst the Otago general practitioners the controversy had receded. The low numbers suggest that they are on the conservative end of the diagnostic spectrum.
Denz-Penhey H, Murdoch JC.	Department of General Practice, Otago Medical School, Dunedin, New Zealand.	Service delivery for people with chronic fatigue syndrome: a pilot action research study.	Fam Pract 1993 Mar;10(1):14-8	Chronic fatigue syndrome (CFS) is a symptom complex which while mild in some cases is severely debilitating in others. Long-term ill health leads to greater use of resources but in the case of long-term CFS the anecdotal evidence suggested a low compliance with the available options and a high level of both patient and general practitioner dissatisfaction. This pilot study sought through repeated action research cycles to start to identify culturally and contextually sensitive

				forms of language and models for service delivery suitable for people with CFS in a general practice setting. It worked through a number of action research cycles, to initiate the identification of conceptual models acceptable to both doctors and to patients suffering from CFS, self-management options which encouraged the body's ability to heal itself and services and delivery mechanisms which met patient needs within health provider options.
Edwards RH, Gibson H, Clague JE, Helliwell T.	Department of Medicine, University of Liverpool, UK.	Muscle histopathology and physiology in chronic fatigue syndrome.	Ciba Found Symp 1993;173:102-17; discussion 117-31	Chronic fatigue syndrome (CFS) is characterized by fatigue at rest which is made worse by exercise. Previous biopsy studies on small numbers of CFS patients have shown a range of morphological changes to which have been attributed fatigue and myalgia. We have now studied 108 patients with CFS or muscle pain and 22 normal volunteers by light and electron microscopy. There was no consistent correlation between symptoms and changes in fibre type prevalence, fibre size, degenerative or regenerative features, glycogen depletion, or mitochondrial abnormalities. Physiological contractile properties of quadriceps (maximal isometric force generation, frequency: force characteristics and relaxation rate) were also examined before and for up to 48 hours after a symptom-limited incremental cycle ergometer exercise test in 12 CFS patients and 12 normal volunteers. Voluntary and stimulated force characteristics were normal at rest and during recovery. Exercise duration was similar in the two groups although CFS patients had higher perceived exertion scores in relation to heart rate during exercise, indicating a reduced effort sensation threshold. On physiological and pathological grounds it is clear that CFS is not a myopathy. Psychological/psychiatric factors appear to be of greater importance in this condition.
Fohlman J, Friman G.	Department of Infectious Diseases, University Hospital of Uppsala, Sweden.	Is juvenile diabetes a viral disease?	Ann Med 1993 Dec;25(6):569-74	The purpose of this review is to discuss recent literature data concerning the etiology and pathobiology in insulin-dependent diabetes mellitus as well as present our own experience from all children up to 15 years of age in Uppsala County, Sweden presenting with juvenile (type I) diabetes since 1976. Chronic enterovirosis is an emerging concept in apparently immunologically competent patients. By means of new serological and DNA-based methods, a persistent enteroviral (Coxsackie virus A, B and ECHO virus) infection can sometimes be demonstrated after an acute primary infection, which is often subclinical. There are several indications that these viruses can contribute to the development of illnesses with a pathogenesis as yet not fully understood, e.g. dilated cardiomyopathy, type I diabetes, and possibly some cases of the so-called chronic fatigue syndrome. In type I diabetes, many pieces of evidence including epidemiology, genetic analysis of the host susceptibility genes, cytokine analysis and new seriological evaluation suggest an infection to be the starting point for the beta cell destruction. These etiological agents most likely belong to the enteroviral group of picornaviruses. Later events may well involve all parts of the

				immune system launching a selective autoimmune 'suicidal attack' on the cells necessary for glucose homeostasis.
Folks TM, Heneine W, Khan A, Woods T, Chapman L, Schonberger L.	Division of Viral and Rickettsial Diseases, Centers for Disease Control, Atlanta, GA 30333.	Investigation of retroviral involvement in chronic fatigue syndrome.	Ciba Found Symp 1993;173:160-6; discussion 166-75	Within the last few years significant efforts have been made to identify objective reliable diagnostic markers from individuals with chronic fatigue syndrome (CFS). We report the absence of a previously described retroviral marker (HTLV-II gag) in a blinded study of CFS cases. Even with excellent reproducible sensitivities, this marker failed in repeated attempts to distinguish cases from controls. In addition, four other retroviruses (simian T cell leukaemia virus, human spumavirus, bovine leukaemia virus and simian retrovirus) were examined for their presence in these CFS cases and found to be absent. Our findings suggest that these agents, at least as markers, are non-distinguishing for CFS and that other factors may be confounding the resolution of an aetiology to this syndrome.
Fucikova T, Petanova J.	Oddeleni klinicke imunologie 1. Lekarske fakulty Univerzity Karlovy, Praha.	[Chronic fatigue syndrome].[article in Czech]	Vnitr Lek 1993 Oct;39(10):995-1002	The authors followed up for a period of 1-14 years 52 patients with CFS who met the criteria outlined by Holmes. The group comprised 10 men and 42 women. In 15% of these patients after a mean period of 5.5 years thyroiditis was diagnosed. Complete recovery was recorded in 20%, improvement in 32% of the patients, on average after 7 years. In the course of treatment mainly immunomodulating preparations were used. Indication of these drugs was individual based on immunological examinations. The success was only partial. The clinical condition of the patients did not correlate with serological findings of IgM, IgA and IgG antibodies against VCA nor with antibodies against EA of the EBV virus.
Gibson H, Carroll N, Clague JE, Edwards RH.	Department of Medicine, University of Liverpool, UK.	Exercise performance and fatiguability in patients with chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1993 Sep;56(9):993-8 comment in: J Neurol Neurosurg Psychiatry. 1994 May;57(5):662-3	To examine the role of delay in recovery of peripheral muscle function following exercise in the fatigue experienced by patients with the chronic fatigue syndrome (CFS) and to examine the influence of effort perception in limiting exercise performance in these patients, a study was carried out on a group of twelve patients with chronic fatigue syndrome and 12 sex and age-matched sedentary control subjects. Symptom limited incremental cycle exercise tests including measurements of perceived exertion were performed followed by examination of the contractile properties of the quadriceps muscle group for up to 48 hours. Muscle function was assessed by percutaneous electrical stimulation and maximum voluntary contractions. Muscle function at rest and during recovery was normal in CFS patients as assessed by maximum isometric voluntary contraction, 20:50 Hz tetanic force ratio and maximum relaxation rate. Exercise duration and the relationship between heart rate and work rate during exercise were similar in both groups. CFS patients had higher perceived exertion scores in relation to heart rate during exercise representing a reduced effort sensation threshold of 3.2 units on an unmodified Borg scale in CFS patients. Patients with chronic fatigue syndrome show normal muscle physiology before and after exercise. Raised perceived exertion scores during exercise suggest that central factors are limiting exercise capacity in these patients.

Goldenberg DL.	Newton-Wellesley Hospital, Massachusetts.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol 1993 Mar;5(2):199-208	Operational diagnostic criteria for fibromyalgia were applied to most clinical studies during the past year. Similar diagnostic criteria for chronic fatigue syndrome are being revised, but criteria for myofascial pain have not been agreed on or tested. Intense research efforts focused on the role of neurohormones and the hypothalamic-pituitary-adrenal axis in fibromyalgia and chronic fatigue syndrome over the past year.
Goodnick PJ, Sandoval R.	Department of Psychiatry, University of Miami, FL 33136.	Psychotropic treatment of chronic fatigue syndrome and related disorders.	J Clin Psychiatry 1993 Jan;54(1):13-20	BACKGROUND: Chronic fatigue syndrome (CFS) and fibromyalgia frequently are associated with symptoms of major depression. For this reason, antidepressants have been used in treatment of these disorders; however, little direction has been provided into this application in psychopharmacology. METHOD: First, nine studies were reviewed regarding the relationship of the symptoms of fatigue and depression. Next, 23 reports (12 double-blind studies, 7 open studies, and 4 case reports) were reviewed for the effectiveness of therapy as assessed by global response and improvement of both depression and pain. Studies were differentiated by type of controls, as well as by alleged mechanism of action of the pharmacologic agent. RESULTS: Disturbances in brain neurochemistry shared by CFS and major depression may serve as a basis for the effectiveness of some antidepressants in CFS. Response to some antidepressants in patients with CFS or fibromyalgia may occur at doses lower than those used in major depression, e.g., amitriptyline 25-75 mg/day. We further found that the more serotonergic treatments (e.g., clomipramine) were more successful in alleviating pain than depression, whereas catecholaminergic agents (e.g., maprotiline, bupropion) seemed particularly effective for symptoms of associated depression. CONCLUSION: To maximize response of the physiologic and psychological consequences of the disorder, more investigation is needed to replicate the apparent findings that relate the neurochemical impairment underlying CFS and fibromyalgia to the type of antidepressant mechanism.
Grafman J, Schwartz V, Dale JK, Scheffers M, Houser C, Straus SE.	Cognitive Neuroscience Section, NINDS, NIH, Bethesda, MD 20892.	Analysis of neuropsychological functioning in patients with chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1993 Jun;56(6):684-9	Memory impairment dominates the cognitive complaints of patients with chronic fatigue syndrome (CFS). Twenty CFS patients were available for studies with a clinical and experimental battery composed of memory and cognitive tests. The results on objective testing indicated that the CFS patients had some mild memory impairment, but only on tasks requiring conceptually driven encoding and retrieval processes. There were no associations between the nature of the precipitating illness, self ratings of fatigue, physical findings, or laboratory determination and objective memory performance or self report of memory functioning. These generally negative results indicate that memory impairment in CFS patients is typically mild and involves memory processes that participate in conceptualising information.
Gunn WJ, Connell DB, Randall B.	Division of Viral and Rickettsial Diseases,	Epidemiology of chronic fatigue syndrome: the	Ciba Found Symp 1993;173:83-93;	The US Centers for Disease Control initiated physician-based chronic fatigue syndrome (CFS) surveillance systems in four cities in September 1989 to

	Centers for Disease Control, Atlanta, GA 30333.	Centers for Disease Control Study.	discussion 93-101	determine the prevalence, incidence, course and impact of the illness. The participating physicians have referred to our surveillance system 590 patients who were ill during the first two years of surveillance with severe, debilitating, unexplained fatigue for at least the preceding six months. Referred patients were screened for psychiatric disorders preceding, concurrent with, and subsequent to the onset of their fatigue by specially trained nurses using a modified Diagnostic Interview Schedule. Complete health histories were obtained by interview and review of medical records and a basic panel of standard laboratory diagnostic tests were conducted. Four physicians have independently reviewed the health information of 337 of the patients for classification. Approximately 26% of patients referred to the surveillance system met the CFS case definition in all regards, 14% lacked one or more of the required eight symptom criteria, 15% were judged to have another possible or known medical illness which could account for the severe fatigue, and the remaining 45% did not meet the case definition because of histories of psychiatric disorders preceding the onset of fatigue. Minimum prevalence rates for the period 1 September 1989 to 1 September 1991 ranged from 2.0 to 7.3 per 100,000 of the general population across the four study sites and rates based on prorated data ranged from 4.6 to 11.3 per 100,000. More than 80% of the CFS cases were female, most were white, and their average age at onset was approximately 30 years.
Hashimoto N.	Third Department of Internal Medicine, Jikei University, School of Medicine. Review, Multicase	[Chronic fatigue syndrome].[article in Japanese]	Nippon Rinsho 1993 Jan;51 Suppl:1107-14	
Heuft L, Bravenboer B, Ziekenhuis C.		Functional hypoglycaemia postulated as cause of chronic fatigue syndrome.	BMJ 1993 Sep 18;307(6906):735 comment on: BMJ. 1993 Jun 12;306(6892):1557-8	
Honda M, Kitamura K, Nakasone T, Fukushima Y, Matsuda S, Nishioka K, Matsuda J, Hashimoto N, Yamazaki S.	Laboratory of Immunology, National Institute of Health, Tokyo, Japan.	Japanese patients with chronic fatigue syndrome are negative for known retrovirus infections.	Microbiol Immunol 1993;37(10):779-84	Although chronic fatigue syndrome (CFS) is known to be the syndrome that begins with an acute flu-like illness that may be due to the exposure to an infectious agent, there has been no convincing evidence on the causative agents. Recently, human T-lymphotropic virus type II (HTLV-II)-like virus has been reported to be associated with the CFS by using HTLV Western blot analysis and polymerase chain reaction. However, some investigators could not detect HTLV-II by indirect immunofluorescence analysis. Lately, CFS patients have been reported in Japan. We detected all 30 tested patients with CFS were seronegative for HTLV-II, HTLV-I and HIV by specific peptide ELISA and Western blot. Further, PCR analysis was negative for HTLV-II and retrovirus was not detected by coculture

				method with patients' PBMC. Thus, known human retrovirus infections do not cause a CFS in Japan.
Izquierdo Clemente C, Ibanez Estella JA, Sanchez Ibanez A, Rubio Montanes ML, Malumbres Juarros P.		[Chronic fatigue syndrome. Diagnostic strategy in primary care].[article in Spanish]	An Med Interna 1993 Dec;10(12):622-3	
Jacobson W, Saich T, Borysiewicz LK, Behan WM, Behan PO, Wreghitt TG.	University Department of Paediatrics, Addenbrooke's Hospital, Cambridge, UK.	Serum folate and chronic fatigue syndrome.	Neurology 1993 Dec;43(12):2645-7 comment in: Neurology. 1994 Nov;44(11):2214-5	We assayed serum folate levels of 60 patients with chronic fatigue syndrome (CFS) and found that 50% had values below 3.0 micrograms/l. Some patients with CFS are deficient in folic acid.
James DG.		Complications of sarcoidosis. Chronic fatigue syndrome.	Sarcoidosis 1993 Mar;10(1):1-3 comment in: Sarcoidosis. 1993 Sep;10(2):138	Well-recognised complications are pulmonary fibrosis, cor pulmonale, glaucoma, cataract and nephrocalcinosis causing failure of lungs, heart, vision and kidneys. Less well-recognised is the post-sarcoidosis chronic fatigue syndrome. The afflicted join sarcoidosis patients' associations because of their profound symptoms of myalgia, fatigue, sleep reversal and low-spiritedness. The symptoms are out of proportion to the lack of physical signs and the absence of objective evidence of sarcoidosis. Management includes unremitting sympathy and replenishment of essential neurochemicals.
Jason LA, Taylor SL, Johnson S, Goldston SE, Salina D, Bishop P, Wagner L.	Department of Psychology, DePaul University, Chicago, IL 60614.	Prevalence of chronic fatigue syndrome-related symptoms among nurses.	Eval Health Prof 1993 Dec;16(4):385-99	Chronic Fatigue Syndrome is an illness that is characterized by debilitating fatigue and a group of other related symptoms. Few epidemiological studies have been conducted, and none have focused on a nursing population. The present study is the first to assess the prevalence of Chronic Fatigue Syndrome-related symptoms in a sample of nurses. Demographic characteristics, symptoms, and possible prevalence rates are presented and discussed. When using both narrow and more inclusive criteria to define this symptom complex, higher rates of this disorder were found than in previous epidemiological studies. The implications of these findings are discussed.
Kent-Braun JA, Sharma KR, Weiner MW, Massie B, Miller RG.	Department of Neurology, University of California, San Francisco.	Central basis of muscle fatigue in chronic fatigue syndrome.	Neurology 1993 Jan;43(1):125-31 comment in: Neurology. 1993 Sep;43(9):1866-7	We studied whether muscle fatigue, metabolism, or activation are abnormal in the chronic fatigue syndrome (CFS). Subjects performed both an intermittent submaximal and a sustained maximal voluntary isometric exercise protocol of the tibialis anterior muscle. The extent of fatigue, metabolic response, and changes in both M-wave amplitude and twitch tension during exercise were similar in patients and controls. The response to systemic exercise was also normal in the patients. However, voluntary activation of the tibialis was significantly lower in the patients during maximal sustained exercise. The results indicate that patients with CFS have (1) normal fatigability and metabolism at both the intracellular and systemic levels, (2) normal muscle membrane function and excitation-contraction coupling, and (3) an inability to fully activate skeletal muscle during intense, sustained exercise. This failure of activation was well in excess of that found in

				controls, suggesting an important central component of muscle fatigue in CFS.
Khan AS, Heneine WM, Chapman LE, Gary HE Jr, Woods TC, Folks TM, Schonberger LB.	Centers for Disease Control and Prevention, Atlanta, Georgia.	Assessment of a retrovirus sequence and other possible risk factors for the chronic fatigue syndrome in adults.	Ann Intern Med 1993 Feb 15;118(4):241-5	OBJECTIVE: To assess whether the human T-lymphotropic virus type II (HTLV-II) gag gene sequence, a purportedly new laboratory marker of the chronic fatigue syndrome (CFS), and other possible risk factors for CFS, particularly those associated with retroviral transmission, are associated with well-characterized CFS. DESIGN: Two matched case-control studies. SETTING: The metropolitan Atlanta area. PATIENTS: Twenty-one patients with CFS who were identified by the Centers for Disease Control and Prevention CFS surveillance system; 21 CDC employee controls (laboratory study) and 42 neighborhood controls (risk-factor study) who were matched to patients by age, race, and gender. MEASUREMENTS: Peripheral blood lymphocytes and leukocytes were assayed for the HTLV-II gag gene sequence by polymerase chain reaction and specific Southern blot hybridization. Questionnaires elicited demographic and clinical information and a history of exposures associated with retrovirus transmission (for example, blood transfusions, sexual practices, intravenous drug use). RESULTS: All patients were white and 86% were female. The median age at illness onset was 34 years (range, 16 to 51 years). The HTLV-II gag gene sequence was not identified in the blood of any patient or control under conditions in which the appropriate assay controls were positive. No statistical differences were observed between patients and controls in frequency of blood transfusions (10% compared with 7%), median number of sex partners before illness (3 compared with 3), bisexual or homosexual behavior (14% compared with 7%), intravenous drug use (0% compared with 0%), and other factors associated with retroviral infection. CONCLUSIONS: The HTLV-II gag gene sequence was not a marker for CFS in this small study of well-defined patients, nor did other characteristics of the patients and controls support the hypothesis that a retrovirus, transmitted by usual modes, was a cause of CFS.
Kiener S.	Departement Innere Medizin, Universitatspoliklinik Basel.	[A case from practice (279). 1. Chronic fatigue syndrome (CFS). 2. Psychosocial problems].[article in German]	Schweiz Rundsch Med Prax 1993 Oct 12;82(41):1142-3	
Kilburn KH.		Symptoms, syndrome, and semantics: multiple chemical sensitivity and chronic fatigue syndrome.	Arch Environ Health 1993 Sep-Oct;48(5):368-9	
Kitani T.		[Chronic fatigue syndrome].[article in	Nippon Naika Gakkai Zasshi 1993 Sep	

		Japanese]	10;82(9):1571-6	
Komaroff AL, Bell DS, Cheney PR, Lo SC.		Absence of antibody to Mycoplasma fermentans in patients with chronic fatigue syndrome.	Clin Infect Dis 1993 Dec;17(6):1074-5	
Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115.	Clinical presentation of chronic fatigue syndrome.	Ciba Found Symp 1993;173:43-54; discussion 54-61	Chronic fatigue syndrome (CFS) is a chronic illness of uncertain aetiology characterized by at least six months of debilitating fatigue and associated symptoms. The symptoms of the syndrome are all non-specific and some (but not all) are also seen in psychiatric illness. The symptomatology suggesting an organic component to the illness includes its abrupt onset with an 'infectious-like' illness, intermittent unexplained fevers, arthralgias and 'gelling' (stiffness), sore throats, cough, photophobia, night sweats, and post-exertional malaise with systemic symptoms. The illness can last for years and is associated with marked impairment of functional health status.
Krupp LB, Jandorf L, Coyle PK, Mendelson WB.	Dept of Neurology, State University of New York, Stony Brook 11794-8121.	Sleep disturbance in chronic fatigue syndrome.	J Psychosom Res 1993 May;37(4):325-31	Sleep and fatigue characteristics were evaluated in 72 patients who met major criteria for the chronic fatigue syndrome (CFS), 57 multiple sclerosis (MS) patients preselected for fatigue complaints, and 40 healthy controls. Using previously validated rating scales, CFS patients had significant elevations in fatigue and sleep disturbance compared to the MS and healthy control groups. To confirm these subjective measures, polysomnography was carried out in a subgroup of CFS patients who included sleep disturbance as one of their symptoms on initial clinical interview. In 10 of 16 (62.5%) polysomnography revealed clinically significant and potentially treatable sleep abnormalities. Their sleep disorders included periodic movement disorder (4), excessive daytime sleepiness (3), apnea (2), and narcolepsy (1). We conclude that subjective sleep disturbance is common in CFS and some CFS patients may have objective sleep disorders.
Langsjoen PH, Langsjoen PH, Folkers K.		Isolated diastolic dysfunction of the myocardium and its response to CoQ10 treatment.	Clin Investig 1993;71(8 Suppl):S140-4	Symptoms of fatigue and activity impairment, atypical precordial pain, and cardiac arrhythmia frequently precede by years the development of congestive heart failure. Of 115 patients with these symptoms, 60 were diagnosed as having hypertensive cardiovascular disease, 27 mitral valve prolapse syndrome, and 28 chronic fatigue syndrome. These symptoms are common with diastolic dysfunction, and diastolic function is energy dependent. All patients had blood pressure, clinical status, coenzyme Q10 (CoQ10) blood levels and echocardiographic measurement of diastolic function, systolic function, and myocardial thickness recorded before and after CoQ10 replacement. At control, 63 patients were functional class III and 54 class II; all showed diastolic dysfunction; the mean CoQ10 blood level was 0.855 micrograms/ml; 65%, 15%, and 7% showed significant myocardial hypertrophy, and 87%, 30%, and 11% had elevated blood pressure readings in hypertensive disease, mitral valve prolapse

				and chronic fatigue syndrome respectively. Except for higher blood pressure levels and more myocardial thickening in the hypertensive patients, there was little difference between the three groups. CoQ10 administration resulted in improvement in all; reduction in high blood pressure in 80%, and improvement in diastolic function in all patients with follow-up echocardiograms to date; a reduction in myocardial thickness in 53% of hypertensives and 36% of the combined prolapse and fatigue syndrome groups; and a reduced fractional shortening in those high at control and an increase in those initially low.(ABSTRACT TRUNCATED AT 250 WORDS)
Lerner AM, Lawrie C, Dworkin HS.	Wayne State University School of Medicine, Royal Oak, Mich.	Repetitively negative changing T waves at 24-h electrocardiographic monitors in patients with the chronic fatigue syndrome. Left ventricular dysfunction in a cohort.	Chest 1993 Nov;104(5):1417-21	This study surveys the occurrence of repetitively negative to flat T waves, alternating with normal upright T waves in 24-h electrocardiographic recordings from a subspecialty infectious diseases outpatient practice during the years 1982 to 1990. Patients with normal resting electrocardiogram in the assayed leads, but with repetitively inverted to isoelectric abnormal T waves at Holter monitors, were considered to have abnormal readings. A total of 300 patients had undergone a 24-h Holter monitor. This group included 24 individuals with chronic fatigue syndrome (CFS). This population was restricted to individuals 50 years old or younger, and the patients with CFS are compared with the patients without CFS. One of the more striking differences between the two groups was the difference in abnormal Holter readings. The patients with CFS all had abnormal Holter readings, while 22.4 percent patients without CFS had abnormal readings ($p < 0.01$). We further report the occurrence of mild left ventricular dysfunction in 8 of 60 patients in continuing studies of this population with CFS, younger than 50 years old, and with no risk factors for coronary artery disease. All 60 patients with CFS showed repetitively flat to inverted T waves alternating with normal T waves. Stress multiple gated acquisitions (MUGAs) (labeled erythrocytes with stannous pyrophosphate) were abnormal in eight patients with CFS. Although resting ejection fractions (EFs) were normal (mean, 60 percent), with increasing work loads (Kilopon meters [Kpms]), gross left ventricular dysfunction occurred. The fatigue of patients with CFS may be related to subtle cardiac dysfunction occurring at work loads common to ordinary living.
Levine PH, Komaroff AL.		Human herpesvirus type 6 and chronic fatigue syndrome.	Arch Intern Med 1993 Mar 8;153(5):661 comment on: Arch Intern Med. 1992 Aug;152(8):1611-6	
Lloyd AR, Hickie I, Brockman A, Hickie C, Wilson A, Dwyer J, Wakefield D.	Department of Immunology, Prince Henry Hospital, Sydney, Australia.	Immunologic and psychologic therapy for patients with chronic fatigue syndrome: a	Am J Med 1993 Feb;94(2):197-203 comment in: Am J Med. 1994 Nov;97(5):493-4	PURPOSE: To evaluate the potential benefit of immunologic therapy with dialyzable leukocyte extract and psychologic treatment in the form of cognitive-behavioral therapy (CBT) in patients with chronic fatigue syndrome (CFS). PATIENTS AND METHODS: Immunologic and psychologic treatments were

		double-blind, placebo-controlled trial.	Am J Med. 1995 Apr;98(4):419-20; discussion 421-2 Am J Med. 1995 Apr;98(4):420-1; discussion 421-2	administered to 90 adult patients who fulfilled diagnostic criteria for CFS in a double-blind, randomized, and placebo-controlled study. A four-cell trial design allowed the assessment of benefit from immunologic and psychologic treatment individually or in combination. Outcome was evaluated by measurement of global well-being (visual analogue scales), physical capacity (standardized diaries of daily activities), functional status (Karnofsky performance scale), and psychologic morbidity (Profile of Mood States questionnaire), and cell-mediated immunity was evaluated by peripheral blood T-cell subset analysis and delayed-type hypersensitivity skin testing. RESULTS: Neither dialyzable leukocyte extract nor CBT (alone or in combination) provided greater benefit than the nonspecific treatment regimens. CONCLUSIONS: In this study, patients with CFS did not demonstrate a specific response to immunologic and/or psychologic therapy. The improvement recorded in the group as a whole may reflect both nonspecific treatment effects and a propensity to remission in the natural history of this disorder. Randomized Controlled Trial
Lloyd AR, Wakefield D, Hickie I.	Laboratory of Molecular Immunoregulation, National Cancer Institute, Frederick, MD 21702-1201.	Immunity and the pathophysiology of chronic fatigue syndrome.	Ciba Found Symp 1993;173:176-87; discussion 187-92	The pathophysiology of chronic fatigue syndrome (CFS) remains unknown. The syndrome often follows a recognized or presumed infection and the disorder may therefore result from a disordered immune response to a precipitating infection or antigenic challenge. Abnormalities of both humoral and cellular immunity have been demonstrated in a substantial proportion of patients with CFS. The most consistent findings are of impaired lymphocyte responses to mitogen and reduced natural killer cell cytotoxicity. Cutaneous anergy and immunoglobulin G subclass deficiencies have also been found. Further studies are needed examining cytokine levels in serum and cerebrospinal fluid, and cytokine production in vitro in patients with CFS. Interpretation of the findings of published studies of immunity is limited by probable heterogeneity in the patient groups studied, and by the lack of standardization and reproducibility in the assays used. The pattern of abnormalities reported in immunological testing in patients with CFS is consistent with the changes seen during the resolving phases of acute viral infection. These data provide circumstantial support for the hypothesis that CFS results from a disordered immune response to an infection. Longitudinal studies of immunity in patients developing CFS after defined infectious illnesses will provide the best means of further examining this hypothesis.
Lusso P, Malnati MS, Garzino-Demo A, Crowley RW, Long EO, Gallo RC.	Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892.	Infection of natural killer cells by human herpesvirus 6.	Nature 1993 Apr 1;362(6419):458-62	Natural killer (NK) cells are a functionally defined subset of non-T, non-B lymphocytes of bone marrow origin, which induce lysis of selected target cells, including neoplastic and virus-infected cells. The NK cell function provides an important mechanism of primary defence against viruses in vivo, as demonstrated by the occurrence of multiple herpesvirus infections in patients congenitally lacking NK cells. Here we show that functionally competent CD3- NK clones can be productively infected by human herpesvirus 6 (HHV-6), a T-

				lymphotropic DNA virus that may play a role in the acquired immunodeficiency syndrome (AIDS) and in the chronic fatigue syndrome, two disorders associated with a defective NK cell activity. The infection is cytopathic and induces de novo expression of CD4, an antigen not expressed within the NK lineage, thereby predisposing NK cells to infection by human immunodeficiency virus type 1 (HIV-1). These results provide evidence that a herpesvirus can directly target and kill NK cells, a potential strategy to suppress the natural anti-viral immunity of the host.
Macintyre A, Hume MC.		The chronic fatigue syndrome.	Postgrad Med J 1993 Feb;69(808):164	
Manu P, Lane TJ, Matthews DA.	Department of Medicine, University of Connecticut School of Medicine, University of Connecticut Health Center, Farmington 06032.	Chronic fatigue and chronic fatigue syndrome: clinical epidemiology and aetiological classification.	Ciba Found Symp 1993;173:23-31; discussion 31-42	To determine the medical and psychiatric diagnoses that have an aetiological role in chronic fatigue we conducted a prospective study of 405 (65% women) patients who presented for evaluation with this chief complaint to an academic medical centre. The average age was 38.1 years and the average duration of fatigue at entry in the study was 6.9 years. All patients were given comprehensive physical and laboratory evaluations and were administered a highly structured psychiatric interview. Psychiatric diagnoses explaining the chronic fatigue were identified in 74% of patients and physical disorders were diagnosed in 7% of patients. The most common psychiatric conditions in this series were major depression, diagnosed in 58% of patients, panic disorder, diagnosed in 14% of patients, and somatization disorder, diagnosed in 10% of patients. Primary sleep disorders, diagnosed in 2% patients, and chronic infections, confirmed in 1.6% patients, explained the majority of cases whose chronic fatigue was attributed to a physical disorder. Thirty per cent of patients met the criteria used to define the chronic fatigue syndrome (CFS). Compared with age- and gender-matched control subjects with chronic fatigue, CFS patients had a similarly high prevalence of current psychiatric disorders (78% versus 82%), but were significantly more likely to have somatization disorder (28% versus 5%) and to attribute their illness to a viral infection (70% versus 33%). We conclude that most patients with a chief complaint of chronic fatigue, including those exhibiting the features of CFS, suffer from standard mood, anxiety and/or somatoform disorders. Careful research is still needed to determine whether CFS is a distinct entity or a variant of these psychiatric illness.
Matsunaga K.	1st Department of Internal Medicine, Urafune Hospital Yokohama City University School of Medicine.	[The "anti-Ki" syndrome: major clinical features].[article in Japanese]	Rinsho Byori 1993 Aug;41(8):882-7	OBJECTIVE. To describe the major clinical features of patients with high titers of anti-Ki antibodies. METHOD AND RESULTS. Four of 172 patients with connective tissue diseases showed high titers (> 1/256) of anti-Ki antibodies. In these four patients, (1) the common clinical findings were alopecia, disabling chronic fatigue, muscle weakness, tenosynovitis, dry mouth, and abnormal glucose tolerance test; (2) anti-Ki antibodies were positive not only in patients with sicca lupus, but also in those with nonsicca lupus. In this case, anti-insulin receptor

				antibody was positive and there was a regulatory insufficiency of the pituitary. (3) Symptoms of anti-Ki antibodies share many clinical and laboratory features of chronic fatigue syndrome and fibromyalgia, that is, they may share either a common etiologic agents or a common pathogenetic pathway or both. CONCLUSION. "Anti-Ki antibody" syndrome may be a subset of sicca lupus.
Mawle AC, Reyes M, Schmid DS.	Viral Exanthems and Herpes Branch, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333.	Is chronic fatigue syndrome an infectious disease?	Infect Agents Dis 1993 Oct;2(5):333-41	
McCluskey DR.	Department of Medicine, Queen's University of Belfast, UK.	Pharmacological approaches to the therapy of chronic fatigue syndrome.	Ciba Found Symp 1993;173:280-7; discussion 287-97	Although a variety of pharmacological agents have been used to treat patients with chronic fatigue syndrome none has been shown to effect a complete resolution of symptoms. Data obtained from a retrospective study and from an objective assessment of the aerobic work capacity of patients with this disorder suggest that the underlying pathophysiological abnormality is a disorder of sleep regulation. This results not only in profound fatigue and lethargy but also reduced sensory threshold for pain, disordered temperature regulation, cardiovascular abnormalities, disturbed higher cerebral function and mental depression. Drugs which modulate sleep, such as tricyclic antidepressants, have a limited effect in improving the symptoms that CFS patients experience. We suggest that other agents which affect central nervous system neurotransmitters, particularly serotonin, may have potential in the management of this condition and need to be evaluated in large controlled clinical trials.
McDonald E, David AS, Pelosi AJ, Mann AH.	Department of Epidemiology, Institute of Psychiatry, London.	Chronic fatigue in primary care attenders.	Psychol Med 1993 Nov;23(4):987-98	From 686 patients attending primary care physicians, 77 were identified by a screening procedure as having chronic fatigue. Of these, 65 were given a comprehensive psychological, social and physical evaluation. Seventeen cases (26%) met criteria for the chronic fatigue syndrome. Forty-seven (72%) received an ICD-9 diagnosis of whom 23 had neurotic depression, with a further 5 meeting criteria for neurasthenia. Forty-nine were 'cases' as defined by the revised Clinical Interview Schedule (CIS-R), and 42 if the fatigue item was excluded. Psychiatric morbidity was more related to levels of social stresses than was severity of fatigue. The main difference between these subjects and those examined in hospital settings is that the former are less liable to attribute their symptoms to wholly physical causes, including viruses, as opposed to social or psychological factors. Identification and management of persistent fatigue in primary care may prevent the secondary disabilities seen in patients with chronic fatigue

				syndromes.
McSherry J.	Department of Family Medicine, University of Western Ontario, London.	Chronic fatigue syndrome. A fresh look at an old problem.	Can Fam Physician 1993 Feb;39:336-40 comment in: Can Fam Physician. 1993 May;39:1022-4	Chronic fatigue syndrome (CFS), an organic disease of unexplained origin, affects about three people in 100,000. Symptoms last approximately 2 1/2 years, and most CFS patients return to normal health. Diagnosis of CFS is by exclusion. No single remedy has yet proven consistently beneficial. Family physicians can help by providing medical validation of disability to persons who might otherwise be seen as malingerers.
Mechanic D.	Institute for Health, Health Care Policy and Aging Research, Rutgers University, New Brunswick, NJ 08903.	Chronic fatigue syndrome and the treatment process.	Ciba Found Symp 1993;173:318-27; discussion 327-41	Fatigue is a common complaint in general practice and is often associated with psychiatric and psychosocial problems and demoralization. Although the Centers for Disease Control definition of chronic fatigue syndrome (CFS) excludes pre-existing psychiatric illness, common psychosocial problems short of a clinical disorder (such as irritability, difficulty in thinking, inability to concentrate, depression and sleep disturbance) overlap with the criteria for CFS. Psychological states can affect the course of CFS or become confused in the patient's and doctor's mind with the course of infection. The core dilemma in practice is how aggressively to pursue a possible basis for CFS when it persists in the absence of an identifiable external cause. Possibilities for exploration are numerous and potentially expensive. In practice, the persistence of doctors depends on the patient's illness behaviour, on financial and organizational factors, and on the culture of medical care and practice styles. It is essential to differentiate the appropriate management of CFS from scientific study where intensive investigation may be warranted. In practice doctors should proceed in a manner that conveys concern, supports function, and avoids dysfunctional illness behaviour and inadvertent legitimization and reinforcement of disability.
Medizinische Universitatsklinik, Bonn.		[The chronic fatigue syndrome].[article in German] Ewig S.	Dtsch Med Wochenschr 1993 Sep 24;118(38):1373-80	
Meyers DH.		Chronic fatigue syndrome and the medical referee.	Med J Aust 1993 Sep 20;159(6):432 comment in: Med J Aust. 1994 Jan 3;160(1):47-8	
Moldofsky H.	Centre for Sleep and Chronobiology, Toronto Hospital, Canada.	Fibromyalgia, sleep disorder and chronic fatigue syndrome.	Ciba Found Symp 1993;173:262-71; discussion 272-9	Various research studies show that the amalgam of disordered sleep physiology, chronic fatigue, diffuse myalgia, and cognitive and behavioural symptoms constitutes a non-restorative sleep syndrome that may follow a febrile illness, as in the chronic fatigue syndrome. Where rheumatic complaints are prominent such a constellation of disturbed sleep physiology and symptoms also characterizes the fibromyalgia disorder. In contrast to the chronic fatigue syndrome, fibromyalgia is associated with a variety of initiating or perpetuating factors such as psychologically distressing events, primary sleep disorders (e.g. sleep apnoea, periodic limb movement disorder) and inflammatory rheumatic

				disease, as well as an acute febrile illness. The chronic fatigue syndrome and fibromyalgia have similar disordered sleep physiology, namely an alpha rhythm disturbance (7.5-11 Hz) in the electroencephalogram (EEG) within non-rapid eye movement (NREM) sleep that accompanies increased nocturnal vigilance and light, unrefreshing sleep. Aspects of cytokine and cellular immune functions are shown to be related to the sleep-wake system. The evidence suggests a reciprocal relationship of the immune and sleep-wake systems. Interference either with the immune system (e.g. by a viral agent or by cytokines such as alpha-interferon or interleukin 2) or with the sleeping-waking brain system (e.g. by sleep deprivation) has effects on the other system and will be accompanied by the symptoms of the chronic fatigue syndrome.
Morris DH, Stare FJ.	Department of Nutrition, Harvard School of Public Health, Boston, Mass.	Unproven diet therapies in the treatment of the chronic fatigue syndrome.	Arch Fam Med 1993 Feb;2(2):181-6	This report is a review of the unproven diet therapies recommended for individuals with chronic fatigue syndrome (CFS). Diet therapies promoted for the relief of CFS symptoms by the authors of five CSF self-help books were evaluated on the basis of nutritional adequacy and scientific rationale. Unproven diet therapies for patients with CFS include megavitamin/mineral supplements; royal jelly and other dietary supplements; and elimination, avoidance, and rotation diets. Claims that these therapies relieve CFS symptoms and promote recovery are anecdotal and have not been substantiated by clinical research. The yeast-avoidance and sugar-free diets, both promoted to combat Candida albicans overgrowth, are of questionable value in treating patients with CFS. The rotation diet is not balanced and does not meet the current recommended dietary intake levels. Diet strategies that call for the avoidance of food additives, preservatives, sweeteners, and other ingredients are not supported by available evidence and are not practical for patients with CFS. A diet plan for patients with CFS should be based on sound nutritional principles and common sense. Until the results of studies demonstrating the benefits of particular diet therapies in the management of CFS are available, patients with CFS are advised to eat a varied diet selected from among and within the basic food groups to ensure an adequate nutrient intake and to reach and maintain a reasonable body weight.
Morriss R, Sharpe M, Sharpley AL, Cowen PJ, Hawton K, Morris J.	MRC Clinical Pharmacology Unit, Littlemore Hospital, Oxford.	Abnormalities of sleep in patients with the chronic fatigue syndrome.	BMJ 1993 May 1;306(6886):1161-4	OBJECTIVE--To determine whether patients with the chronic fatigue syndrome have abnormalities of sleep which may contribute to daytime fatigue. DESIGN--A case-control study of the sleep of patients with the chronic fatigue syndrome and that of healthy volunteers. SETTING--An infectious disease outpatient clinic and subjects' homes. SUBJECTS--12 patients who met research criteria for the chronic fatigue syndrome but not for major depressive disorder and 12 healthy controls matched for age, sex, and weight. MAIN OUTCOME MEASURES--Subjective reports of sleep from patients' diaries and measurement of sleep patterns by polysomnography. Subjects' anxiety, depression, and functional impairment were assessed by interview. RESULTS--Patients with the chronic fatigue syndrome

				spent more time in bed than controls (544 min v 465 min, p < 0.001) but slept less efficiently (90% v 96%, p < 0.05) and spent more time awake after initially going to sleep (31.9 min v 16.6 min, p < 0.05). Seven patients with the chronic fatigue syndrome had a sleep disorder (four had difficulty maintaining sleep, one had difficulty getting to sleep, one had difficulty in both initiating and maintaining sleep, and one had hypersomnia) compared with none of the controls (p = 0.003). Those with sleep disorders showed greater functional impairment than the remaining five patients (score on general health survey 50.4% v 70.4%, p < 0.05), but their psychiatric scores were not significantly different. CONCLUSIONS--Most patients with the chronic fatigue syndrome had sleep disorders, which are likely to contribute to daytime fatigue. Sleep disorders may be important in the aetiology of the syndrome.
Morriss R.		Insomnia in the chronic fatigue syndrome.	BMJ 1993 Jul 24;307(6898):264	
Natelson BH, Cohen JM, Brassloff I, Lee HJ.	Department of Neurosciences, UMDNJ-New Jersey Medical School, Newark 07103.	A controlled study of brain magnetic resonance imaging in patients with the chronic fatigue syndrome.	J Neurol Sci 1993 Dec 15;120(2):213-7	Two neuroradiologists compared the brain MR scans of 52 patients with the CDC criteria for the chronic fatigue syndrome (CFS) with those of 52 age and sex matched controls who had undergone imaging because of histories of head trauma or headache. CFS patients had significantly more abnormal scans than controls--27% vs 2%. Abnormalities seen were foci of increased white matter T2 signal in 9 CFS patients and one control and ventricular or sulcal enlargement in 5 CFS patients. Follow up of patients with subcortical signal hyperintensities revealed 3 who had symptoms suggestive of other known medical causes of what appeared to be CFS. The data indicate that some CFS patients have some organic problem manifesting itself on neuroimaging. But, finding MR abnormalities should warn the physician that the patient's symptoms may be secondary to some other medical illness and not simply primary CFS.
Nixon PG.	Charing Cross Hospital, London.	The grey area of effort syndrome and hyperventilation: from Thomas Lewis to today.	J R Coll Physicians Lond 1993 Oct;27(4):377-83	Lewis used the diagnosis 'effort syndrome' for subjects whose ability to make and sustain effort had been reduced by homeostatic failure. A major element was depletion of the body's capacity for buffering the acids produced by exercise. In his view this systems disorder was not to be regarded as a specific organ disease, and losing sight of the metabolic element would foster the invention of fanciful, unphysiological diagnoses. His views were dismissed because normal resting plasma bicarbonate levels were considered by others in that era to exclude serious depletion of the body's total capacity for buffering the effects of exertion. Today, effort syndrome is still a useful diagnosis for a condition of exhaustion and failure of performance associated with depletion of the body's buffering systems. Other elements associated with homeostatic failure are now recognised, principally emotional hyperarousal and hyperventilation. Their physiological interrelationships are described. Effort syndrome is amenable to recovery through rehabilitation, and it may be a mistake to treat chronic fatigue syndrome

				and unspecific illness without including it in the differential diagnosis.
Norregaard J, Bulow PM, Prescott E, Jacobsen S, Danneskiold-Samsoe B.	Department of Rheumatology C, Frederiksberg Hospital, Copenhagen, Denmark.	A four-year follow-up study in fibromyalgia. Relationship to chronic fatigue syndrome.	Scand J Rheumatol 1993;22(1):35-8	The primary objectives of this study were to examine to what extent fibromyalgia patients later on developed presumpted causative somatic diseases and to examine symptoms and muscle strength some years after the diagnosis of fibromyalgia was established. A secondary objective was to describe the overlap between fibromyalgia and chronic fatigue syndrome. Only in two of 91 the muscle pain was found to be caused by another somatic disease during the median 4 year follow-up period. In one of the 83 attending subjects a somatic disease associated with muscle symptoms was established at the follow-up visit. 60 out of 83 reported increased pain, 8 reported improvement of pain. The 83 subjects showed no significant fall in muscle strength during the follow-up period. The majority reported severe fatigue but only one fifth fulfilled the proposed chronic fatigue syndrome criteria.
Pepper CM, Krupp LB, Friedberg F, Doscher C, Coyle PK.	Department of Psychology, State University of New York, Stony Brook 11794.	A comparison of neuropsychiatric characteristics in chronic fatigue syndrome, multiple sclerosis, and major depression.	J Neuropsychiatry Clin Neurosci 1993 Spring;5(2):200-5	Chronic fatigue syndrome (CFS), a controversial clinical entity characterized by severe fatigue and constitutional symptoms, has been associated with a variety of psychiatric disorders. To further understand the psychiatric profile of CFS, the authors compared patients with CFS, multiple sclerosis (MS), and major depression by using diagnostic interviews and self-report measures of Axis I disorders and personality disorders. CFS patients differed from patients with major depression, with significantly less depression and fewer personality disorders. Compared with MS patients, CFS patients did not differ with regard to personality disorders. However, they did have significantly more frequent current depression than MS patients, particularly following onset of their illness.
Ray C, Phillips L, Weir WR.	Department of Human Sciences, Brunel University, Uxbridge, Middlesex, UK.	Quality of attention in chronic fatigue syndrome: subjective reports of everyday attention and cognitive difficulty, and performance on tasks of focused attention.	Br J Clin Psychol 1993 Sep;32 (Pt 3):357-64	Patients with chronic fatigue syndrome (also known as post-viral fatigue syndrome or myalgic encephalomyelitis) commonly report cognitive difficulties concerning attention, concentration and memory. In this study, patients were compared with matched controls on two questionnaires which assess subjective difficulties with attention and general cognitive functioning, and on two tasks requiring focused attention. Patients reported significantly greater difficulty with attention on the Everyday Attention Questionnaire and more cognitive symptoms on the Profile of Fatigue-Related Symptoms. The objective tests did not clearly indicate a deficit in patients' focused attention; patients tended to perform less well on the Embedded Figures Test and the Stroop Colour-Word Interference Test, but these differences were not significant. There was, however, evidence of psychomotor retardation, with patients having longer response times for word reading and colour naming in the Stroop test. Difficulties in interpreting findings for both subjective and objective cognitive measures are discussed.
Ray C, Weir W, Stewart D, Miller P, Hyde G.	Department of Human Sciences, Brunel University, Uxbridge,	Ways of coping with chronic fatigue syndrome: development	Soc Sci Med 1993 Aug;37(3):385-91	Chronic fatigue syndrome (CFS) is a disorder of uncertain aetiology, and there is uncertainty also about the appropriate way in which patients should manage the illness. An illness management questionnaire (IMQ) was designed to assess

	Middlesex, U.K.	of an illness management questionnaire.		coping in CFS. This was completed by 207 patients, in parallel with the COPE scales (a general measure of coping that can be applied situationally), and measures of functional impairment, anxiety and depression. The IMQ yielded four factors: maintaining activity, accommodating to the illness, focusing on symptoms and information-seeking. Scales based upon these factors together predicted 26, 27 and 22% of the variance in functional impairment, anxiety and depression, respectively, and each scale had significant relationships with relevant scales of the COPE, supporting the interpretation of the factors. It is suggested that the IMQ may be employed to relate ways of coping to outcomes in CFS, and to assess coping as a mediator of change in cognitive-behavioural interventions.
Robin R, Lipkin DM, Hume GW.		Taking exception to chronic fatigue syndrome prevalence findings by Price, et al.	Public Health Rep 1993 Jan-Feb;108(1):135-7 comment on: Public Health Rep. 1992 Sep-Oct;107(5):514-22	
Sharpe M.	University of Oxford Department of Psychiatry, Warneford Hospital, UK.	Non-pharmacological approaches to treatment.	Ciba Found Symp 1993;173:298-308; discussion 308-17	Chronic fatigue syndrome (CFS) as currently defined overlaps with other syndromes including chronic pain, fibromyalgia, anxiety and depression. It also resembles historical descriptions of neurasthenia. The role of psychological (cognitive) and behavioural therapies in CFS is examined. There are both pragmatic and theoretical arguments for their application to CFS. It is pragmatic to target obvious and treatable factors including inactivity and depression. A theoretical model in which psychological, physiological and social factors interact offers a plausible rationale for such treatment but is not yet empirically proven. While there is evidence for the efficacy of this type of therapy in related syndromes, the evidence in CFS is inconclusive. A randomized controlled trial of combined cognitive and behavioural therapy currently in progress is described. Initial results suggest that most patients receiving cognitive behaviour therapy improve, especially in terms of functional impairment. It remains to be seen whether this therapy will prove to be more effective than standard general practitioner care. In the meantime cognitive behaviour therapy offers a pragmatic and rational therapy for patients with CFS. Randomized Controlled Trial Review Review, Tutorial
Shaw T.		Chronic fatigue syndrome.	Aust Fam Physician 1993 Apr;22(4):635 comment on: Aust Fam Physician. 1992 Mar;21(3):278-9, 283-5	
Shorter E.	History of Medicine Program, Faculty of	Chronic fatigue in historical perspective.	Ciba Found Symp 1993;173:6-16;	Chronic fatigue as a presenting complaint, in the absence of other evident organic illness, was seldom reported historically before the second half of the

	Medicine, University of Toronto, Ontario, Canada.		discussion 16-22	19th century. Its first eruption was the so-called 'bed cases' or 'sofa cases' among middle-class females in the period from 1860 to about 1910. 'Neurasthenia' does not necessarily represent an early forerunner of chronic fatigue. Many patients receiving that diagnosis did not complain of fatigue. Others with functional fatigue did not receive the diagnosis 'neurasthenia'. Both medical-anecdotal and quantitative sources make it clear that by the time of the First World War, chronic fatigue was a common complaint in Europe and North America. Medical concepts of chronic fatigue since the 1930s have run along four separate lines: (1) 'postinfectious neuromyasthenia', going back to an atypical 'poliomyelitis' epidemic in 1934; (2) 'chronic Epstein-Barr virus' infection, an illness attribution that increased in frequency after the discovery in 1968 that this virus caused mononucleosis; (3) 'myalgic encephalomyelitis', dating from an epidemic at the Royal Free Hospital in London in 1955; and (4) 'fibrositis', or 'fibromyalgia', used as a rheumatological description since the turn of the century. Recently, these four separate paths have tended to converge into the diagnosis of 'chronic fatigue syndrome'.
Simpson LO.		Chronic fatigue syndrome.	N Z Med J 1993 May 26;106(956):211-2	
Smith AP, Behan PO, Bell W, Millar K, Bakheit M.	Health Psychology Research Unit, School of Psychology, University of Wales College of Cardiff.	Behavioural problems associated with the chronic fatigue syndrome.	Br J Psychol 1993 Aug;84 (Pt 3):411-23	Disturbances of memory, concentration and motor function are often reported by patients with the chronic fatigue syndrome (CFS). The present study objectively evaluated these behavioural problems using a computerized test battery measuring memory, attention and motor skills. Fifty-seven CFS patients were compared with 19 matched controls and all subjects completed the performance test battery and filled in questionnaires measuring psychopathology and mood. The patients reported significantly higher levels of depression, anxiety, physical symptoms and cognitive failures than the controls. Similarly, they reported more negative affect at the time of testing. The patients were slower on psychomotor tasks, showed increased visual sensitivity and impaired attention. Digit span and free recall were not impaired but retrieval from semantic memory and logical reasoning were slower. None of the performance differences between patients and controls could be attributed to differences in psychopathology. These results agree with recent findings from other laboratories, and it is now time to consider the nature of the neurological dysfunction underlying these effects.
Smith RD, Scott A.		The economic impact of chronic fatigue syndrome.	Med J Aust 1993 Feb 15;158(4):286-7 comment on: Med J Aust. 1992 Nov 2;157(9):599-601	
Steere AC, Taylor E,	Division of	The overdiagnosis of	JAMA 1993 Apr	OBJECTIVE--To analyze the diagnoses, serological test results, and treatment

McHugh GL, Logigian EL.	Rheumatology/Immunology, New England Medical Center, Boston, MA 02111.	Lyme disease.	14;269(14):1812-6 comment in: JAMA. 1993 Dec 8;270(22):2682-3 JAMA. 1993 Dec 8;270(22):2682; discussion 2683 JAMA. 1993 Dec 8;270(22):2683	results of the patients evaluated in a Lyme disease clinic, both prior to referral and from current evaluation. DESIGN--Retrospective case survey of prescreened patients. SETTING--Research and diagnostic Lyme disease clinic in a university hospital. PATIENTS--All 788 patients referred to the clinic during a 4.5-year period who were thought by the referring physician or the patient to have a diagnosis of Lyme disease. MAIN OUTCOME MEASUREMENTS--Symptoms and signs of disease, immunodiagnostic tests of Lyme disease, and tests of neurological function. RESULTS--Of the 788 patients, 180 (23%) had active Lyme disease, usually arthritis, encephalopathy, or polyneuropathy. One hundred fifty-six patients (20%) had previous Lyme disease and another current illness, most commonly chronic fatigue syndrome or fibromyalgia; and in 49 patients, these symptoms began soon after objective manifestations of Lyme disease. The remaining 452 patients (57%) did not have Lyme disease. The majority of these patients also had the chronic fatigue syndrome or fibromyalgia; the others usually had rheumatic or neurological diseases. Of the patients who did not have Lyme disease, 45% had had positive serological test results for Lyme disease in other laboratories, but all were seronegative in our laboratory. Prior to referral, 409 of the 788 patients had been treated with antibiotic therapy. In 322 (79%) of these patients, the reason for lack of response was incorrect diagnosis. CONCLUSIONS--Only a minority of the patients referred to the clinic met diagnostic criteria for Lyme disease. The most common reason for lack of response to antibiotic therapy was misdiagnosis.
Steere AC.	Tufts University School of Medicine, Boston.	Current understanding of Lyme disease.	Hosp Pract (Off Ed) 1993 Apr 15;28(4):37-44	It is now the most common vector-borne disease in the United States. But because of misdiagnosis, the spread of this disease may also be more apparent than real. Lack of standardized serologic tests and varying clinical presentations do create confusion. Nevertheless, it is possible to distinguish Lyme disease from look-alike disorders, such as chronic fatigue syndrome and fibromyalgia.
Stern K.		Chronic fatigue syndrome: signs and symptoms.	CDS Rev 1993 Aug;86(7):26-9	
Stockdale T.		Chronic fatigue syndrome (ME)	Nutr Health 1993;9(1):59-60	
Straus SE, Fritz S, Dale JK, Gould B, Strober W.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.	Lymphocyte phenotype and function in the chronic fatigue syndrome.	J Clin Immunol 1993 Jan;13(1):30-40	Lymphocytes of 18 patients meeting the Centers for Disease Control (CDC) case definition for the chronic fatigue syndrome (CFS), 10 similar, chronically fatigued patients not fully conforming to the CDC case definition, and 17 matched, healthy individuals were studied to determine the presence of abnormalities of peripheral cell phenotype and function. Extensive phenotypic analyses of B- and T-cell subsets, natural killer (NK) cells, and macrophages were performed using single-, dual-, and three-color flow cytometry. Compared to controls, in CFS patients the percentage of CD4 T cells and CD4,CD45RA, or naive T cells, was

				reduced. The CD4,CD45RO, or memory T-cell, subset was numerically normal but expressed increased levels of adhesion markers (CD29, CD54, and CD58). CFS patient lymphocytes showed reduced proliferative responses to phytohemagglutinin, concanavalin A, and staphylococcal enterotoxin B. Lymphocytes from fatigue patients not meeting the CDC definition showed similar abnormalities. These data indicate that peripheral T cells manifest an increased state of differentiation in CFS and related conditions. This may arise as a consequence of an underlying neuropsychiatric and/or neuroendocrine disorder or because of exposure to antigens or superantigens of an infectious agent.
Straus SE.	Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD 20892.	Studies of herpesvirus infection in chronic fatigue syndrome.	Ciba Found Symp 1993;173:132-9; discussion 139-45	The relationship of herpesviruses to chronic fatigue syndrome has received considerable attention over the past decade. Data suggesting an association fall into three major categories. First, among acute precipitants of the syndrome are primary infections with some herpesviruses, most notably Epstein-Barr virus and cytomegalovirus. Second, a series of studies have detailed elevations of antibodies to most herpesviruses in selected chronic fatigue syndrome populations, with Epstein-Barr virus and human herpes type 6 being the objects of most scrutiny. Third, one recent study reported a greater ease of recovery of human herpes virus type 6 from chronic fatigue syndrome patients. This review article critically examines the cumulative data regarding an association between one or more herpesviruses and the chronic fatigue syndrome in the context of the known biology and epidemiology of these agents. In view of these, and additional considerations regarding study methodologies, the conclusion is drawn that herpesviruses are not dominant causes of the chronic fatigue syndrome and may not even be necessary to the perpetuation of the illness, but it is premature to dismiss entirely this latter possibility.
Symposium proceedings		Chronic Fatigue Syndrome. Symposium proceedings. London, 12-14 May 1992. Overall	Ciba Found Symp 1993;173:1-357	
Thomas PK. Historical Article		The chronic fatigue syndrome: what do we know?	BMJ 1993 Jun 12;306(6892):1557-8 comment in: BMJ. 1993 Jul 31;307(6899):328 BMJ. 1993 Sep 18;307(6906):735	
Tirelli V, Pinto A, Marotta G, Crovato M, Quaia M, De Paoli P, Galligioni E, Santini G.		Clinical and immunologic study of 205 patients with chronic fatigue	Arch Intern Med 1993 Jan 11;153(1):116-7, 120	

		syndrome: a case series from Italy.		
Valesini G, Conti F, Priori R, Balsano F.		Gilbert's syndrome and chronic fatigue syndrome.	Lancet 1993 May 1;341(8853):1162-3 comment on: Lancet. 1993 Mar 27;341(8848):842	
Walford GA, Nelson WM, McCluskey DR.	Department of Child and Adolescent Psychiatry, Royal Belfast Hospital for Sick Children, Northern Ireland.	Fatigue, depression, and social adjustment in chronic fatigue syndrome.	Arch Dis Child 1993 Mar;68(3):384-8	The aims of this study were to determine the characteristics and perceived levels of fatigue and the prevalence of depression in children with chronic fatigue syndrome and to assess the effects of illness on schooling and social functioning. Twelve children with chronic fatigue syndrome were compared with a matched group of children with cystic fibrosis and matched healthy controls. Levels of fatigue (fatigue questionnaire), depression (children's depression inventory), and social adjustment (semistructured interview with parents) were compared between groups. Children with chronic fatigue syndrome had significantly higher median scores for physical and mental fatigue and depressive symptomatology than either comparison group and five children scored as depressed on the children's depression inventory. Schooling and social functioning were seriously disrupted. Children with chronic fatigue syndrome reported high levels of fatigue affecting both physical and mental functioning, the association with depression found in adult studies was confirmed, and social adjustment was poor.
Ware NC.	Department of Social Medicine, Harvard Medical School, Boston, MA 02115.	Society, mind and body in chronic fatigue syndrome: an anthropological view.	Ciba Found Symp 1993;173:62-73; discussion 73-82	An anthropological view of chronic fatigue syndrome places the study of illness in social context. Data from an interview study of 50 chronically fatigued patients demonstrate the relation of local social worlds--families, workplaces, communities--to the meaning and experience of illness. Negative life events and difficulties, multiple commitments, and a hectic pace are among prominent themes in the subjects' local worlds. These themes are reflected in: (1) attributions of illness onset to social sources, (2) the symbolism of the core complaint of fatigue, and (3) an illness-induced, positively valued lifestyle transformation suggesting the rejection of culturally prescribed 'busyness'. Dichotomous definitions of the relation of mind and body are shown to be part of culture, not Nature, in the paper's second section. The 'mind-body dichotomy' and the differing values attached to physical and psychological disorders by a naturalistic scientific paradigm explain the delegitimizing experiences of sufferers, who find their illness dismissed as psychosomatic and therefore 'not real'. A conceptualization of chronic fatigue syndrome which links local social worlds to psychological distress, felt bodily sensation and biological changes is proposed. Collaborative teams of social scientists and medical researchers might fruitfully pursue aspects of social context in relation to psychiatric, immunological and viral dimensions of the illness.

Weiger WA.		Chronic fatigue syndrome.	Neurology 1993 Sep;43(9):1866-7 comment on: Neurology. 1993 Jan;43(1):125-31	
Wessely S.	Department of Psychological Medicine, Institute of Psychiatry, De Crespigny Park, London, UK.	The neuropsychiatry of chronic fatigue syndrome.	Ciba Found Symp 1993;173:212-29; discussion 229-37	This paper explores the relationship between chronic fatigue syndrome (CFS) and psychiatric disorder, with special reference to neuropsychiatry, Topics reviewed include (1) epidemiological evidence of central disorder in CFS; (2) evidence from longitudinal studies of an interaction between vulnerability to CFS and psychiatric disorder; and (3) evidence from neuroimaging, neuropsychology, neurophysiology and neuroendocrinology of disordered CNS function in CFS. The most impressive evidence of CNS disturbance comes from neuroendocrinological studies, which suggest a role of hypothalamic disorder as a final common pathway for CFS. It is concluded that the equal and opposite tendencies of psychiatry to be 'brainless' and neurology to be 'mindless' have led to needless controversy over the nature of CFS. Now that the contributions of psychiatric disorder to CFS, and of neurobiological dysfunction to psychiatric disorder, are both established, it will be possible to make real advances in understanding the nature of CFS.
working group		Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome.	CMAJ 1993 Aug 1;149(3):314-9	
working group		Report of the working group on the possible relationship between hepatitis B vaccination and the chronic fatigue syndrome.	Can Commun Dis Rep 1993 Feb 28;19(4):25-8	
Young A.		Amma therapy: a holistic approach to chronic fatigue syndrome.	J Holist Nurs 1993 Jun;11(2):172-82	A significant number of people suffering with chronic fatigue syndrome have become more and more discouraged by the traditional medical approach, which seems to lack the proper perspective on the disease. Unfortunately, very little published information is available about specific holistic health management practices used for these patients. It is the purpose of this article to examine a specific holistic practice, called Amma Therapy, as an alternative approach for the management of this syndrome.

1992				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Alexander EL, Kumar AJ, Kozachuk WE.		The chronic fatigue syndrome controversy.	Ann Intern Med 1992 Aug 15;117(4):343-4 comment on: Ann Intern Med. 1992 Jan 15;116(2):103-13	
Apfelbaum B.		Taking chronic fatigue syndrome seriously.	Am J Psychiatry 1992 Dec;149(12):1754; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Bauermeister CD, Wagner C, Brede HD.		[What is the relation of human herpesvirus 6 to chronic fatigue syndrome]?[article in German]	Med Monatsschr Pharm 1992 Jun;15(6):165-8	
Bell DS.		Taking chronic fatigue syndrome seriously.	Am J Psychiatry 1992 Dec;149(12):1753; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Bell DS.	Harvard Medical School, Boston, Massachusetts.	Chronic fatigue syndrome. Recent advances in diagnosis and treatment.	Postgrad Med 1992 May 1;91(6):245-52	Chronic fatigue syndrome is a chronic debilitating illness that is marked in the majority of cases by sudden onset of fatigue and flulike symptoms. Symptoms subsequently relapse and remit and may persist for years. Physical examination typically reveals relatively minor, nonspecific abnormalities in an apparently well patient. Although immunologic abnormalities are associated with chronic fatigue syndrome, tests for these features are expensive, nonspecific, and generally reserved for research purposes. The diagnosis is made on the basis of new onset of severe fatigue, a characteristic pattern of symptoms, and exclusion of other illnesses. Treatment is aimed at alleviating symptoms and helping patients adjust to the debilitating and chronic nature of the illness. Review Literature
Berger RM.		"Chronic fatigue syndrome and women: can therapy help?".	Soc Work 1992 Sep;37(5):477-8 comment on: Soc Work. 1992 Jan;37(1):35-9	
Berman DS, Wenglin BD.		Chronic fatigue syndrome and	Am J Med 1992 Jun;92(6):710 comment	

		psychiatric disorders.	in: Am J Med. 1994 May;96(5):485-6 comment on: Am J Med. 1991 Oct;91(4):335-44	
Berneman ZN, Ablashi DV, Li G, Eger-Fletcher M, Reitz MS Jr, Hung CL, Brus I, Komaroff AL, Gallo RC.	Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.	Human herpesvirus 7 is a T-lymphotropic virus and is related to, but significantly different from, human herpesvirus 6 and human cytomegalovirus.	Proc Natl Acad Sci U S A 1992 Nov 1;89(21):10552-6	An independent strain (JI) of human herpesvirus 7 (HHV-7) was isolated from a patient with chronic fatigue syndrome (CFS). No significant association could be established by seroepidemiology between HHV-7 and CFS. HHV-7 is a T-lymphotropic virus, infecting CD4+ and CD8+ primary lymphocytes. HHV-7 can also infect SUP-T1, an immature T-cell line, with variable success. Southern blot analysis with DNA probes scanning 58.8% of the human herpesvirus 6 (HHV-6) genome and hybridizing to all HHV-6 strains tested so far revealed homology to HHV-7 with only 37.4% of the total probe length. HHV-7 contains the GGGTTA repetitive sequence, as do HHV-6 and Marek's disease chicken herpesvirus. DNA sequencing of a 186-base-pair fragment of HHV-7(JI) revealed an identity with HHV-6 and human cytomegalovirus of 57.5% and 36%, respectively. Oligonucleotide primers derived from this sequence (HV7/HV8, HV10/HV11) amplified HHV-7 DNA only and did not amplify DNA from other human herpesviruses, including 12 different HHV-6 strains. Southern blot analysis with the p43L3 probe containing the 186-base-pair HHV-7 DNA fragment hybridized to HHV-7 DNA only. The molecular divergence between human cytomegalovirus, on the one hand, and HHV-6 and HHV-7, on the other, is greater than between HHV-6 and HHV-7, which, in turn, is greater than the difference between HHV-6 strains. This study supports the classification of HHV-7 as an additional member of the human beta-herpesviruses.
Bode L, Komaroff AL, Ludwig H.		No serologic evidence of borna disease virus in patients with chronic fatigue syndrome.	Clin Infect Dis 1992 Dec;15(6):1049	
Bryan CS. Editorial		The chronic fatigue syndrome: caveat emptor.	J S C Med Assoc 1992 Feb;88(2):79-81 comment on: J S C Med Assoc. 1992 Feb;88(2):51-7	
Buchwald D, Garrity D, Pascualy R, Kith P, Ashley RL, Wener MH, Kidd PG, Katon WJ, Russo JE.	Department of Medicine, School of Medicine, University of Washington, Seattle.	Chronic fatigue syndrome.	Toxicol Ind Health 1992 Jul-Aug;8(4):157-73	
Burke SG.	School of Social Work, Loyola University of	Chronic fatigue syndrome and women:	Soc Work 1992 Jan;37(1):35-9 comment	This article presents current research on chronic fatigue syndrome, which currently afflicts mostly females between the ages of 25 and 55. Because

	Chicago, IL 60614.	can therapy help?	in: Soc Work. 1992 Sep;37(5):477-8 Soc Work. 1992 Sep;37(5):478	depression is a common symptom of chronic fatigue syndrome, mental health practitioners are often involved with the victims and must formulate an appropriate treatment strategy that considers the physiological, intrapsychic, interpersonal, and environmental aspects of the client. This article includes case material focusing on a woman who was medically diagnosed with the Epstein-Barr virus and was in psychotherapy with the author. The difficulty of managing the interplay of the real health problems and the emotional issues presented by the client is highlighted.
Calabrese L, Danao T, Camara E, Wilke W.	Cleveland Clinic Foundation, Ohio.	Chronic fatigue syndrome.	Am Fam Physician 1992 Mar;45(3):1205-13	Fatigue is one of the most common complaints among patients seen in the primary care setting. Chronic fatigue syndrome, which has recently been called chronic fatigue immune dysfunction syndrome, is distinctive, with an abrupt onset of symptoms that wax and wane for at least six months. Usually there is low-grade fever, pharyngitis and tender, but not enlarged, lymph nodes. The fatigue can be disabling and is often made worse by physical activity. Some patients with this disorder have also been found to have highly characteristic immunologic abnormalities. Treatment can be rewarding and is based on patient education and support, exercise and symptomatic therapies for abnormal sleep patterns, musculoskeletal pain and other symptoms.
Castilla A, Subira ML, Civeira MP, Cuende JI.		[Surface T-lymphocyte markers and monocyte dysfunction in the chronic fatigue syndrome].[article in Spanish]	An Med Interna 1992 Apr;9(4):207-8	
Chao CC, DeLaHunt M, Hu S, Close K, Peterson PK.	Neuroimmunobiology and Host Defense Laboratory, Minneapolis Medical Research Foundation, Minnesota 55404.	Immunologically mediated fatigue: a murine model.	Clin Immunol Immunopathol 1992 Aug;64(2):161-5	Chronic fatigue syndrome (CFS) is an idiopathic disorder in which the chief symptoms is profound fatigue. To explore the relationship between immune stimulation and fatigue, we developed a murine model for quantifying fatigue: reduction in voluntary running and delayed initiation of grooming after swimming. Inoculation of female BALB/c mice with Corynebacterium parvum antigen or the relatively avirulent Me49 strain of Toxoplasma gondii induced fatigue: baseline running reduced to less than 50 and 30% for 8 and 14 days, respectively, and delayed initiation of grooming after swimming in both immunologically stimulated groups. A threefold evaluation of serum transforming growth factor-beta levels, a cytokine increased in CFS patients, was found in fatigued C. parvum- and T. gondii-inoculated mice. This murine model appears promising for investigation of the pathogenesis of immunologically mediated fatigue.
Cho WK, Stollerman GH.	Yale University School of Medicine, New Haven.	Chronic fatigue syndrome.	Hosp Pract (Off Ed) 1992 Sep 15;27(9):221-4, 227-30, 233-6 passim	

Clague JE, Edwards RH, Jackson MJ.		Intravenous magnesium loading in chronic fatigue syndrome.	Lancet 1992 Jul 11;340(8811):124-5 comment in: Lancet. 1992 Aug 15;340(8816):426 comment on: Lancet. 1991 Mar 30;337(8744):757-60	
Coovadia HM.	University of Natal Medical School, Durban, Congella, South Africa.	Rheumatic fever and disorders of the musculoskeletal system.	Curr Opin Rheumatol 1992 Oct;4(5):718-24	New information provided on the pathogenesis and management of rheumatic fever is of current interest. Invasive disease by group A streptococci has been shown to be due to production of toxin A. The natural history and immunopathologic basis for chronic Lyme arthritis are reported. Attention is drawn to pyomyositis and clinical presentation of chronic fatigue syndrome in children. Patients with Sweet's syndrome often have antineutrophil cytoplasmic autoantibodies. Biopsy specimens of panniculitis should be taken to aid treatment. Long-term outcome in chronic osteomyelitis is favorable; recommendations on the rational use of imaging have been reported.
Cope H, David AS.		Outcome in the chronic fatigue syndrome.	BMJ 1992 Aug 8;305(6849):365 comment on: BMJ. 1992 Jul 18;305(6846):147-52	
Crimson crescents--a possible association with the chronic fatigue syndrome.	Cunha BA.	Erratum in: Ann Intern Med 1992 May 1;116(9):779	Ann Intern Med 1992 Feb 15;116(4):347	
Dale JK, Straus SE.	Medical Virology Section, National Institute of Allergy and Infectious Disease, National Institutes of Health, Bethesda, Maryland. Review, Academic	The chronic fatigue syndrome: considerations relevant to children and adolescents.	Adv Pediatr Infect Dis 1992;7:63-83	
Demitrack MA, Gold PW, Dale JK, Krahn DD, Kling MA, Straus SE.	Department of Psychiatry, University of Michigan Medical Center, Ann Arbor 48109-0116.	Plasma and cerebrospinal fluid monoamine metabolism in patients with chronic fatigue syndrome: preliminary findings.	Biol Psychiatry 1992 Dec 15;32(12):1065-77	The syndrome of chronic fatigue, feverishness, diffuse pains, and other constitutional complaints, often precipitated by an acute infectious illness and aggravated by physical and emotional stressors, has a lengthy history in the medical literature. The Centers for Disease Control (CDC) recently formulated a case definition, renaming the illness "chronic fatigue syndrome." Nevertheless, there remain few biological data that can validate the existence of this syndrome as distinct from a wide variety of other, largely psychiatric disorders, and little

				understanding of its pathogenesis. In the present study, basal plasma and cerebrospinal fluid levels of the monoamine metabolites, 3-methoxy-4-hydroxyphenylglycol (MHPG), 5-hydroxyindoleacetic acid (5-HIAA), and homovanillic acid (HVA) were determined in 19 patients meeting CDC research case criteria for chronic fatigue syndrome and in 17 normal individuals. Patients with chronic fatigue syndrome showed a significant reduction in basal plasma levels of MHPG and a significant increase in basal plasma levels of 5-HIAA. Although the functional significance of these findings has not been definitively elucidated, they are compatible with the clinical presentation of a syndrome associated with chronic lethargy and fatigue, and with evidence of persistent immune stimulation, and lend support to the idea that chronic fatigue syndrome represents a clinical entity with potential biological specificity.
Digon A, Goicoechea A, Moraza MJ.		Chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1992 Jan;55(1):85 comment on: J Neurol Neurosurg Psychiatry. 1991 Aug;54(8):669-71	
Dooley DP.		Commercial laboratory testing for chronic fatigue syndrome.	JAMA 1992 Aug 19;268(7):873-4	
Downey DC.	Oregon Health Sciences University, School of Dentistry, Portland 97201.	Fatigue syndromes: new thoughts and reinterpretation of previous data.	Med Hypotheses 1992 Oct;39(2):185-90	Recently, the author has identified 19 patients who have complained of marked fatigue that had abnormal responses to copper test bracelets or necklaces. At this time, 8 have been shown to have at least one enzyme deficiency in the heme pathway. These patients have been diagnosed with multiple sclerosis, chronic fatigue syndrome and other non-specific diagnoses. A lengthy but still limited review of the literature was performed regarding the following conditions: multiple sclerosis (MS), hepatic porphyria (HP), chronic fatigue syndrome (CFS) and paralytic polio (PP). The text will focus on similar epidemiologies, laboratory findings and clinical courses. Copper as a common but not unique etiologic agent will be discussed; as will the heme pathway, a biologic process that may be disordered in all.
Drago F, Romagnoli M, Loi A, Rebora A.	Department of Dermatology, University of Genoa, Italy.	Epstein-Barr virus-related persistent erythema multiforme in chronic fatigue syndrome.	Arch Dermatol 1992 Feb;128(2):217-22	BACKGROUND--Erythema multiforme (EM) has been rarely reported in Epstein-Barr virus (EBV)-associated diseases; this includes patients with chronic fatigue syndrome who have chronic or recurrent and disabling illness and an abnormal antibody reactivity to EBV. We describe a patient fulfilling the chronic fatigue syndrome diagnostic criteria who had developed an unusually persistent EM resistant to corticosteroids therapy. The EBV DNA was studied in skin EM lesions, throat washings, peripheral mononuclear cells, and plasma. The EBV antigens were studied in skin EM lesions and in mononuclear cells. The patient was

				followed up to 2 years. OBSERVATIONS--The patient had abnormal titers of antibodies against various EBV antigens and by immunofluorescence she disclosed the EBV nuclear antigen and the viral capsid antigen in the blood vessels of the affected skin. The dot blot hybridization assay detected viral DNA in throat washings and mononuclear cells, but not in plasma. The presence of the viral genomic content in lesional skin is suggested by the autoradiographic signal and by the difference from appropriate control specimens. Skin lesions and constitutional symptoms cleared after acyclovir sodium therapy and recurred after discontinuation of this therapy. CONCLUSIONS--This is the first EM case in which evidence of the EBV causal role has been provided. The association with chronic fatigue syndrome suggests the EBV role in selected cases of this syndrome.
Durlach J.	International Society for the Development of Research on Magnesium, Neuilly/Seine, France. Randomized Controlled Trial	Chronic fatigue syndrome and chronic primary magnesium deficiency (CFS and CPMD).	Magnes Res 1992 Mar;5(1):68	
Englander K.		"Chronic fatigue syndrome and women: can therapy help?".	Soc Work 1992 Sep;37(5):478 comment on: Soc Work. 1992 Jan;37(1):35-9	
Faas RJ.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1992 Oct 10;136(41):2037-8	
Fallon BA, Liebowitz MR, Klein DF.		Taking chronic fatigue syndrome seriously.	Am J Psychiatry 1992 Dec;149(12):1756; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Flugel RM, Mahnke C, Geiger A, Komaroff AL.		Absence of antibody to human spumaretrovirus in patients with chronic fatigue syndrome.	1409: Clin Infect Dis 1992 Feb;14(2):623-4	
Fuchs D, Weiss G, Wachter H.		Pathogenesis of chronic fatigue syndrome.	J Clin Psychiatry 1992 Aug;53(8):296 comment on: J Clin Psychiatry. 1991 Oct;52(10):403-10	

Gerow G, Poierier MB, Alt R.	Department of Diagnosis, National College of Chiropractic, Lombard, IL 60148-4583.	Chronic fatigue syndrome.	J Manipulative Physiol Ther 1992 Oct;15(8):529-35 Erratum in: J Manipulative Physiol Ther 1992 Nov-Dec;15(9):followi	A 36-yr-old white female presented with severe fatigue and symptoms consistent with immune deficiency, but was later found to be suffering from chronic fatigue syndrome. This article discusses the diagnostic criteria for this condition. Chiropractic manipulation afforded relief of some symptoms for this patient.
Ginsburg KS, Kundsin RB, Walter CW, Schur PH.	Department of Rheumatology and Immunology, Brigham and Women's Hospital, Boston, MA 02115.	Ureaplasma urealyticum and Mycoplasma hominis in women with systemic lupus erythematosus.	Arthritis Rheum 1992 Apr;35(4):429-33	OBJECTIVE. To determine the prevalence of genitourinary mycoplasma infection in women with systemic lupus erythematosus (SLE). METHODS. Urine specimens from 49 patients with SLE and 22 patients with chronic fatigue syndrome (CFS) were cultured for mycoplasma. Patient records were reviewed for medical history and SLE disease activity. RESULTS. Sixty-three percent of the SLE patients were culture positive, compared with 4.5% of the CFS patients (P less than 0.001). Neither corticosteroid treatment, SLE activity, nor age accounted for this difference. CONCLUSION. Genitourinary mycoplasma colonization occurs significantly more frequently in SLE than in CFS.
Goldenberg DL.	Newton-Wellesley Hospital, Massachusetts.	Fibromyalgia, chronic fatigue, and myofascial pain syndromes.	Curr Opin Rheumatol 1992 Apr;4(2):247-57	During the past year many studies have been published on fibromyalgia and chronic fatigue syndromes. Randomized clinical trials using current operational diagnostic criteria were reported, but no single therapy has been highly effective in either condition. The working case definition of chronic fatigue syndrome has been criticized and suggestions for a new case definition have been made. Further understanding of the overlap of these three common disorders will also require that uniform diagnostic criteria be tested in chronic fatigue syndrome and myofascial pain syndrome.
Goodnick PJ, Sandoval R, Brickman A, Klimas NG.	Department of Psychiatry, University of Miami, Florida 33136.	Bupropion treatment of fluoxetine-resistant chronic fatigue syndrome.	Biol Psychiatry 1992 Nov 1;32(9):834-8	Chronic fatigue syndrome (CFS) includes many symptoms of major depression. For this reason, many antidepressants have been used to treat the symptoms of this disorder. Among the more recently released antidepressants are fluoxetine and bupropion. In this open study, nine CFS patients who either could not tolerate or did not respond to fluoxetine showed significant response when administered 300 mg/day of bupropion for an 8-week period in both rating of HDRS ($t = 4.80$, $p < 0.01$) and BDI ($t = 2.48$, $p < 0.05$). Furthermore, bupropion improvement in Hamilton Depression Rating Scale correlated significantly with change in plasma homovanillic acid (HVA) ($r = 0.96$, $p < 0.01$). Plasma total methylhydroxyphenolglycol (MHPG) also increased significantly during bupropion treatment ($t = 2.37$, $p = 0.05$). Measures of T1 microsomal antibodies also decreased over treatment time; increases in natural killer cell numbers correlated inversely with change in plasma levels of free MHPG ($r = -0.88$, $p < 0.05$). Bupropion responders were more likely to have trough blood levels above 30 ng/ml (chi 2 = 3.6, $p = 0.05$).
Goodrich W.		Taking chronic fatigue	Am J Psychiatry 1992	

		syndrome seriously.	Dec;149(12):1753; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Goudsmit EM, Macintyre A.		Chronische-moeheidsyndroom. [Chronic fatigue syndrome.	Ned Tijdschr Geneeskd 1992 Apr 4;136(14):708-9	
Goudsmit EM, Shepherd C.		Chronic fatigue syndrome.	Br J Psychiatry 1992 Jan;160:127-8 comment on: Br J Psychiatry. 1991 Sep;159:439-40	
Gow JW, Simpson K, Schliephake A, Behan WM, Morrison LJ, Cavanagh H, Rethwilm A, Behan PO.	Department of Neurology, University of Glasgow, UK.	Search for retrovirus in the chronic fatigue syndrome.	J Clin Pathol 1992 Dec;45(12):1058-61	AIM: To examine peripheral blood and skeletal muscle from patients with chronic fatigue syndrome for exogenous retrovirus. METHODS: Blood samples from 30 patients and muscle biopsy specimens of 15 patients were examined for retroviral sequences by DNA extraction, polymerase chain reaction (PCR), and Southern blotting hybridisation. Sera were examined for human foamy virus by western immunoblotting and indirect immunofluorescence techniques. RESULTS: No differences between the patient and control populations was found for any of the PCR primer sets used (gag, pol, env, and tax regions of HTLV I/II). An endogenous gag band was observed in both the patient and control groups. All sera were negative for antibody to human foamy virus. CONCLUSION: The results indicate that there is no evidence of retroviral involvement in the chronic fatigue syndrome.
Grau JM, Casademont J, Pedrol E, Fernandez-Sola J, Cardellach F, Barros N, Urbano-Marquez A.	Department of Internal Medicine, Hospital Clinic i Provincial, Barcelona, Spain.	Chronic fatigue syndrome: studies on skeletal muscle.	Clin Neuropathol 1992 Nov-Dec;11(6):329-32	Chronic fatigue syndrome represents a poorly defined disease with protean clinical manifestations, the majority of them expressed as a muscle fatigue or as inability to maintain the expected muscle strength. In the present work we studied muscle function and muscle histopathology in 20 patients fulfilling the proposed criteria for chronic fatigue syndrome. Special interest is directed towards the immunoreactive expression of class I MHC molecules comparing some inflammatory and virus-related myopathies with muscles from chronic fatigue syndrome. Only minor morphological changes were detected in 9 out of 20 patients of the series. The nonspecific morphological changes in muscle tissue and the lack of class I MHC expression does not support the viral etiology of muscle fatigue in chronic fatigue syndrome. In contrast with the reported clinical improvement with high doses of essential fatty acids, our patients' clinical condition did not improve after three months of L-carnitine therapy.
Hashimoto N, Kuraishi Y, Yokose T, Tajima N,	3rd Dept. Internal Medicine, Jikei Univ.	[Chronic fatigue syndrome--51 cases in	Nippon Rinsho 1992 Nov;50(11):2653-64	Between April 1991 and August 1992, we diagnosed 51 cases of CFS who met definition of CFS designated by CDC, 1988. They are 41 female and 11 male, and

Mochio S, Shimizu M, Yokoyama J, Kobayashi N, Nohara A, Taniguchi I, et al.	School of Medicine.	the Jikei University School of Medicine].[article in Japanese]		78% are women. At first visit, their ages are ranged from 16 to 64 years old, and approximately 45% is 20 to 30 years old. In periods of illness from onset, 39.2% of the patients are in period of 6 month to 1 year, 19.6% within 2 years, and 15.6% within 3 years, respectively. The sufferer who have symptoms of CFS over 10 years long are in 6 cases. Most of patients have already been examined by many other clinics and hospitals. They have been told as no abnormal medical condition, or often as neurosis, depressive state and autonomous imbalance etc. Interesting things are trigger of CFS. 77.5% of patients have onset of flu-like symptom, including 5 cases of acute infectious mononucleosis. In many female patients, symptoms of CFS begun after hand work in addition to psychological factors. Specific laboratory results are not shown in CBC, urinalysis, biochemical studies and inflammatory marhers. 6 cases hare positive Rheumatoid factor and positive ANF are shown in 16 cases (31.3%). Specific patterns of anti EBV antibodies are not shown. Lymphocyte subsets used by monoclonal antibodies are not specific. At the present, prognosis is good and 56.8% of CFS patients are generally improved. For severe cases, NSAID, Sulpiride, Amitryptiline and minor tranquilizer are used.
Hashimoto N.	3rd Dept. Internal Medicine, Jikei Univ. School of Medicine.	[Definition of the chronic fatigue syndrome and its issues].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2591-9	This article reviewed Definition of CFS proposed by CDC 1988. There are several issues in Definition for CFS of CDC. It is presented that other chronic clinical conditions have been satisfactorily excluded, including preexisting psychiatric diseases in (2) of major criteria. However, fibromyalgia can not be excluded from the fifth symptom of minor criteria, myalgia, and also depression from the ninth symptom. It is practically difficult to define impairment of average daily activity below 50% of the patient's premorbid activity level for a period of at least 6 months, as shown in (1) of major criteria, and it is not adapted for a first visit patient. Definition for CFS of CDC has been discussed on EBV infection, but not written on postviral fatigue syndrome and myalgic encephalomyelitis. Especially whether epidemic type of CFS is present or not was not discussed. Diagnostic criteria of CFS is necessary for clinical practice. Review Literature
Hickie I, Lloyd A, Wakefield D.	Mood Disorders Unit, Prince Henry Hospital, Little Bay, NSW.	Immunological and psychological dysfunction in patients receiving immunotherapy for chronic fatigue syndrome.	Aust N Z J Psychiatry 1992 Jun;26(2):249-56	Associations between immunological and psychological dysfunction in 33 patients with Chronic Fatigue Syndrome (CFS) were examined before and in response to treatment in a double blind, placebo-controlled trial of high dose intravenous immunoglobulin. Only those patients who received active immunotherapy demonstrated a consistent pattern of correlations between improvement in depressive symptoms and markers of cell-mediated immunity (CMI). This finding lends some support to the hypothesis that depressive symptoms in patients with CFS occur secondary to, or share a common pathophysiology with, immunological dysfunction. This pattern and the lack of strong associations between depression and immunological disturbance prior to treatment are less supportive of the view that CFS is primarily a form of

				depressive disorder or that immunological dysfunction in patients with CFS is secondary to concurrent depression.
Hickie I, Lloyd A, Wilson A, Wakefield D.		Taking chronic fatigue syndrome seriously.	Am J Psychiatry 1992 Dec;149(12):1755-6; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Higgins ES.	Department of Family Medicine, Medical University of South Carolina, Charleston 29425-5820.	Chronic fatigue syndrome: a depressive disorder.	J S C Med Assoc 1992 Feb;88(2):51-7 comment in: J S C Med Assoc. 1992 Feb;88(2):79-81	
Hissink Muller W.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1992 Jan 18;136(3):147	
Holmwood C, Shannon C.	Family Medicine Programme, South Australia.	Chronic fatigue syndrome. A review from the general practice perspective.	Aust Fam Physician 1992 Mar;21(3):278-9, 283-5 comment in: Aust Fam Physician. 1993 Apr;22(4):635	There is no doubt that the chronic fatigue syndrome exists. It is a condition that is debilitating and of unknown cause. Research into chronic fatigue syndrome demonstrates possible psychiatric or organic causes. The truth may be somewhere in between. Evidence for the existence of an ongoing chronic infection is now not convincing. Treatment should be based on supportive counselling, explanation, psychiatric help (both pharmacological and non pharmacological) and a graded programme of increased activity with the eventual aim of resumption of full functioning.
Hooge J.	There is much controversy as to whether chronic fatigue syndrome is a physical or a psychological illness. This article reviews the literature, explains where nursing stands in the controversy and makes suggestions for nursing care.	Chronic fatigue syndrome: cause, controversy and care.	Br J Nurs 1992 Sep 10-23;1(9):440-1, 443, 445-6	
Horstink MW, Gonera EG, Berger HJ, van Weel C.		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1992 Jan 18;136(3):148 comment on: Ned Tijdschr Geneeskd. 1991	

			Oct 26;135(43):2005-9	
House A.		Alleged link between hepatitis B vaccine and chronic fatigue syndrome.	CMAJ 1992 Apr 1;146(7):1145 comment on: Can Med Assoc J. 1992 Jan 1;146(1):37-8	
Howard JM, Davies S, Hunnisett A.		Magnesium and chronic fatigue syndrome.	Lancet 1992 Aug 15;340(8816):426 comment on: Lancet. 1992 Jul 11;340(8811):124-5	
Hudson JI, Goldenberg DL, Pope HG Jr, Keck PE Jr, Schlesinger L.	Biological Psychiatry Laboratory, McLean Hospital, Belmont, Massachusetts 02178.	Comorbidity of fibromyalgia with medical and psychiatric disorders.	Am J Med 1992 Apr;92(4):363-7	PURPOSE: Patients with fibromyalgia have been reported to display high rates of several concomitant medical and psychiatric disorders, including migraine, irritable bowel syndrome, chronic fatigue syndrome, major depression, and panic disorder. To test further these and other possible associations, we assessed the personal and family histories of a broad range of medical and psychiatric disorders in patients with fibromyalgia. PATIENTS AND METHODS: Subjects were 33 women (mean age 42.1 years) who each met American College of Rheumatology criteria for fibromyalgia and presented to a rheumatologist at a tertiary referral center. They received the Structured Clinical Interview for DSM-III-R (SCID); a supplemental interview, in SCID format, for other medical and psychiatric disorders, including migraine, irritable bowel syndrome, and chronic fatigue syndrome; and an interview for family history of medical and psychiatric disorders. RESULTS: Patients with fibromyalgia displayed high lifetime rates of migraine, irritable bowel syndrome, chronic fatigue syndrome, major depression, and panic disorder. They also exhibited high rates of familial major mood disorder. CONCLUSIONS: The finding that migraine, irritable bowel syndrome, chronic fatigue syndrome, major depression, and panic disorder are frequently comorbid with fibromyalgia is consistent with the hypothesis that these various disorders may share a common physiologic abnormality.
Ichise M, Salit IE, Abbey SE, Chung DG, Gray B, Kirsh JC, Freedman M.	Department of Radiology (Division of Nuclear Medicine), University of Toronto, Canada.	Assessment of regional cerebral perfusion by 99Tcm-HMPAO SPECT in chronic fatigue syndrome.	Nucl Med Commun 1992 Oct;13(10):767-72	Chronic fatigue syndrome (CFS) is a severely disabling illness of uncertain aetiology. It is characterized by a chronic, sustained or fluctuating sense of debilitating fatigue without any other known underlying medical conditions. It is also associated with both somatic and neuropsychological symptoms. Both physical and laboratory findings are usually unremarkable. Regional cerebral blood flow (rCBF) was assessed in 60 clinically defined CFS patients and 14 normal control (NC) subjects using 99Tcm-hexamethylpropyleneamine oxime (99Tcm-HMPAO) single photon emission computed tomography (SPECT). Compared with the NC group, the CFS group showed significantly lower cortical/cerebellar rCBF ratios, throughout multiple brain regions ($P < 0.05$). Forty-eight CFS subjects (80%) showed at least one or more rCBF ratios

				significantly less than normal values. The major cerebral regions involved were frontal (38 cases, 63%), temporal (21 cases, 35%), parietal (32 cases, 53%) and occipital lobes (23 cases, 38%). The rCBF ratios of basal ganglia (24 cases, 40%) were also reduced. 99Tcm-HMPAO brain SPECT provided objective evidence for functional impairment of the brain in the majority of the CFS subjects. The findings may not be diagnostic of CFS but 99Tcm-HMPAO SPECT may play an important role in clarifying the pathoaetiology of CFS. Further studies are warranted.
James DG, Brook MG, Bannister BA.	Academic Department of Medicine, Royal Free Hospital, London, UK.	The chronic fatigue syndrome.	Postgrad Med J 1992 Aug;68(802):611-4	
Kanayama Y.	Second Department of Internal Medicine, Osaka University Medical School.	[Chronic fatigue syndrome--symptoms, signs, laboratory tests, and prognosis].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2586-90	Chronic fatigue syndrome (CFS) is an undefined clinical problem and is perceived as a complex of multiple symptomatology with an unexplained persistent fatigue. Major symptoms include fatigue lasting for more than 6 months, low-grade fever, moderate lymphadenopathy, muscle and joint pain, and various psychological presentations. Since no specific laboratory tests are available, clinical diagnosis demands that known causes of chronic fatigue should be excluded. The pathogenesis is at present unknown, but it is suspected that CFS is a physical and psychological condition associated with some unrecognized infectious agent. Further study is needed to clarify the precise pathophysiology of this newly recognized entity. Review Literature
Kaplan KH, Goldenberg DL, Galvin-Nadeau M.		Taking chronic fatigue syndrome seriously.	Am J Psychiatry 1992 Dec;149(12):1754; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Karetzky MS. Editorial		Chronic fatigue syndrome.	N J Med 1992 Mar;89(3):191-2 comment on: N J Med. 1992 Mar;89(3):211-6	
Kato Y, Kamijima S, Kashiwagi A, Oguri T.	Second Department of Internal Medicine, Aichi Medical College.	[Chronic fatigue syndrome, a case of high anti-HHV-6 antibody titer and one associated with primary hyperaldosteronism].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2673-8	Two cases of chronic fatigue syndrome (CFS) were reported which were suggestive for the study of the etiology and a cure for CFS. Case 1: A 31-year-old woman was admitted for chronic fatigue syndrome. Examination revealed a high titer of anti HHV-6 antigen of x2560 and an increased percentage of suppressor T lymphocytes in the peripheral blood. HHV-6 was speculated to be reactivated and stimulating the immune system in CFS. Case 2: A 46-year-old woman suffering from CFS had been in remission for 6 years. She was admitted for hypertension associated with right adrenal adenoma and hyperaldosteronism. After right adrenalectomy, there was a recurrence of high fever and other CFS symptoms. It

				was suggested that CFS symptoms may be ameliorated by aldosterone.
Katon W, Russo J.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle 98195.	Chronic fatigue syndrome criteria. A critique of the requirement for multiple physical complaints.	Arch Intern Med 1992 Aug;152(8):1604-9 comment in: Arch Intern Med. 1992 Aug;152(8):1569-70	OBJECTIVE. The purpose of this study was to test the hypothesis that the patients with chronic fatigue who have the highest number of medically unexplained physical symptoms over their lifetime would also have the highest prevalence of current and lifetime affective and anxiety disorders, lifetime affective symptoms, and the most functional disability. A further goal was to use this information to modify the current case definition to better identify a subgroup of patients with chronic fatigue syndrome who are less likely to have psychiatric illness. DESIGN. Two hundred eighty-five consecutive patients with chronic fatigue were interviewed with the National Institute of Mental Health Diagnostic Interview Schedule and completed four self-rating questionnaires measuring psychologic distress, functional disability, and the tendency to amplify symptoms. Based on previously published data, patients were divided into four groups with a progressively higher number of lifetime medically unexplained physical symptoms. The prevalence of current and lifetime psychiatric disorders, lifetime psychologic symptoms, and extent of functional impairment was then compared in these four groups of patients. MAIN RESULTS. The prevalence of current and lifetime psychiatric diagnosis and lifetime depressive symptoms increased linearly with the number of lifetime physical symptoms that the patient experienced. The extent of impairment in activities of daily living and the tendency to amplify symptoms also increased linearly with the number of medically unexplained physical symptoms. CONCLUSION. The patients with the highest numbers of medically unexplained physical symptoms had extraordinarily high rates of current and lifetime psychiatric disorders. These data suggest that the current case definition for chronic fatigue syndrome inadvertently selects for patients with the highest prevalence of lifetime psychiatric diagnoses. A recommendation based on these results is to modify the case criteria for chronic fatigue syndrome to include patients with fatigue and few physical symptoms and to identify and consider excluding patients with high numbers of physical complaints.
Kawa K.	Dept. Pediatrics, Osaka Medical Center.	[Chronic fatigue syndrome in school children].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2606-11	Chronic fatigue syndrome (CFS) is characterized by persistent or relapsing debilitating fatigue for at least 6 months without any apparent medical diagnosis that would explain the clinical presentation. Although, most of the reported patients are over age 30, CFS also affects school children. To better understand CFS, the network of the central nervous-endocrine-immune systems should be considered, and one must be careful to distinct CFS from school absenteeism and other psychosomatic disorders often seen among them. Review Literature
Kawai K, Kawai A.	Kawai Internal Medicine Clinic, Tokyo, Japan.	Studies on the relationship between chronic fatigue syndrome and Epstein-	Intern Med 1992 Mar;31(3):313-8	Among 1,153 consecutive patients, 22 patients (1.9%) who complained of chronic fatigue for a period of over 6 months without detectable causes were studied. Ten patients (0.86%) satisfied the criteria of chronic fatigue syndrome (CFS) and were classified to be definite cases of CFS. The other patients were classified as

		Barr virus in Japan.		probable cases. In order to clarify the role of Epstein-Barr virus (EBV) as a cause of CFS, we measured various antibodies for EBV. The definite cases had significantly higher titers of early antigen complex (EA)-IgG than both the probable cases and controls. We proposed the EA-IgG/EBNA ratio as the indicator of activation of EBV and attempted to estimate the degree of fatigue by the EA-IgG/EBNA ratio. The highest ratio value (16.0) of the 22 patients ratios was the most serious case. In general, the ratio correlated with the degree of fatigue. Based on these results, it was concluded that a relationship does exist between CFS and EBV.
Kitani T, Kuratsune H, Yamaguchi K.	Dep. of Internal Medicine, Osaka University.	[Diagnostic criteria for chronic fatigue syndrome by the CFS Study Group in Japan].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2600-5	Much interest recently has been given to chronic fatigue syndrome (CFS) in Japan as other countries. The CFS Study Group sponsored by the Ministry of Health and Welfare has been developed since April 1991, A diagnostic criteria for CFS was newly proposed by this group. The criteria is substantially based upon the working case definition, which was made by Holmes and colleagues in 1988. There are some modification from CDC working case definition; the criteria of probable cases of CFS was defined, and postinfectious CFS was also given. Review Literature
Kitani T, Kuratsune H.		[Chronic fatigue syndrome].[article in Japanese]	Nippon Naika Gakkai Zasshi 1992 Apr 10;81(4):573-82	
Kitani T.	Department of Internal Medicine, Osaka University.	[Chronic fatigue syndrome: the present concept and historical perspective].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2581-5	
Klonoff DC.	Department of Medicine, University of California, San Francisco.	Chronic fatigue syndrome.	Clin Infect Dis 1992 Nov;15(5):812-23	Chronic fatigue syndrome (CFS) is defined by symptoms and diagnosed without any objective diagnostic tests. Risk factors for developing CFS may include infection, psychiatric disorders, and allergies. Modest dysfunction of multiple organ systems, including the immune, central nervous, endocrine, and muscular systems, have been identified in cases of CFS. Symptoms of various organic, psychiatric, and poorly understood disorders overlap those of CFS. There is no known cure for CFS; however, exercise, counseling, and medications may provide symptomatic relief.
Kminek A.	Klinika detskeho a dorostoveho lekarstvi I. LF UK, Praha.	[Chronic fatigue syndrome].[article in Czech]	Cesk Pediatr 1992 Apr;47(4):226-9	
Komaroff AL, Wang SP, Lee J, Grayston JT.		No association of chronic Chlamydia pneumoniae infection with chronic fatigue	J Infect Dis 1992 Jan;165(1):184	

		syndrome.		
Kuratsune H, Yamaguti K, Hattori H, Tazawa H, Takahashi M, Yamanishi K, Kitani T.	Department of Clinical Research, Osaka University.	[Symptoms, signs and laboratory findings in patients with chronic fatigue syndrome].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2665-72	This review summarizes the symptoms, signs and laboratory abnormalities seen in 59 patients with chronic fatigue syndrome (CFS), 2 patients with post-infectious CFS and in 26 patients with possible CFS whose illnesses fulfill the criteria proposed by the study group of the Ministry of Welfare, Japan. The characteristic symptoms and signs of CFS are prolonged generalized fatigue following exercise, headache, neuropsychological symptoms, sleep disturbance and mild fever. In possible CFS patients, the frequency of mild fever, muscle weakness, myalgia and headache is low. Our standard hematologic and laboratory tests revealed a few abnormality in patients with CFS. The characteristic abnormality in CFS patients is the low values of 17-Ketosteroid-Sulfates/creatinine in morning urine and the acylcarnitine deficiency. It seems likely that this deficiency of acylcarnitine induces an energy deficit in the skeletal muscle, resulting in general fatigue, myalgia, muscle weakness and postexertional malaise in CFS patients. Virologic studies revealed no evidence of retrovirus infection with HTLV-1, HTLV-2 and HIV, but the reactivation of HHV-6 infection was apparent.
Kyle DV, deShazo RD.	University of Alabama, School of Medicine, Department of Medicine, Birmingham.	Chronic fatigue syndrome: a conundrum.	Am J Med Sci 1992 Jan;303(1):28-34	Chronic fatigue syndrome (CFS) is a multi-faceted disorder for which no etiology has been determined. This paper discusses the implications of the new clinical case definition of CFS on previous and future studies of this illness. The authors' own management approach is also discussed.
Levine PH, Jacobson S, Pocinki AG, Cheney P, Peterson D, Connelly RR, Weil R, Robinson SM, Ablashi DV, Salahuddin SZ, et al.	Environmental Epidemiology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892.	Clinical, epidemiologic, and virologic studies in four clusters of the chronic fatigue syndrome.	Arch Intern Med 1992 Aug;152(8):1611-6 comment in: Arch Intern Med. 1993 Mar 8;153(5):661	BACKGROUND. The purpose of this study is to provide a case definition of chronic fatigue syndrome in an outbreak occurring in the Nevada-California region to evaluate candidate etiologic agents and observe the natural history of the illness. METHODS. Patients diagnosed as having chronic fatigue syndrome were studied by repeated interviews, questionnaires, and blood collection over a 3-year period. Serum samples were tested for antibodies to Epstein-Barr virus, human herpesvirus-6, and human T-lymphotropic viruses I and II. Leukocytes from typical cases were also assayed for human T-lymphotropic viruses I and II. RESULTS. Cases were defined as persons who had: (1) severe persistent fatigue following an acute illness appearing in an individual with no previous physical or psychological symptoms; (2) presenting signs and symptoms of an acute infection; (3) severe and persistent headache and/or myalgias; and (4) abrupt change in cognitive function or the appearance of a new mood disorder. After 3 years of follow-up, almost all study subjects were able to return to pre-illness activity. None of the viruses evaluated--human T-lymphotropic viruses I and II, Epstein-Barr virus, or human herpesvirus-6--could be etiologically linked to these outbreaks. CONCLUSION. Clinical features of outbreaks of chronic fatigue syndrome differ sufficiently to suggest different etiologic agents. Giardiasis appears to have precipitated one of the four clusters in this study but the

				cause(s) of the other three outbreaks is as yet uncertain. The overall prognosis of chronic fatigue syndrome is usually favorable.
Levine PH, Peterson D, McNamee FL, O'Brien K, Gridley G, Hagerty M, Brady J, Fears T, Atherton M, Hoover R.	Epidemiology and Biostatistics Program, National Cancer Institute, NIH, Bethesda, Maryland 20892.	Does chronic fatigue syndrome predispose to non-Hodgkin's lymphoma?	Cancer Res 1992 Oct 1;52(19 Suppl):5516s-5518s; discussion 5518s-5521s	Chronic fatigue syndrome, an illness that frequently is associated with abnormalities of cellular immunity, has been reported anecdotally to be associated with an increased incidence of lymphoid hyperplasia and malignancy. This report describes an initial analysis of population-based cancer incidence data in Nevada, focusing on the patterns of non-Hodgkin's lymphoma prior to and subsequent to well described, documented outbreaks of chronic fatigue syndrome during 1984-1986. In a study of time trends in four age groups, the observed time trends were consistent with the national trends reported in the Surveillance, Epidemiology, and End Results Program. No statistically significant increase attributable to the chronic fatigue syndrome outbreak was identified at the state level. Additional studies are in progress analyzing the data at the country level, reviewing patterns in other malignancies, and continuing to monitor the cancer patterns over subsequent years.
Linde A, Andersson B, Svenson SB, Ahrne H, Carlsson M, Forsberg P, Hugo H, Karstorp A, Lenkei R, Lindwall A, et al.	Department of Virology, National Bacteriological Laboratory, Stockholm.	Serum levels of lymphokines and soluble cellular receptors in primary Epstein-Barr virus infection and in patients with chronic fatigue syndrome.	J Infect Dis 1992 Jun;165(6):994-1000	The immunopathology in primary Epstein-Barr virus (EBV) infections and in chronic fatigue syndrome was studied by examining serum levels of interleukins (IL) and of soluble T cell receptors in serum samples. Serum samples were from patients during and 6 months after primary EBV-induced infectious mononucleosis and from patients with chronic fatigue syndrome and serologic evidence of EBV reactivation. Markers for T lymphocyte activation (soluble IL-2 and CD8) and for monocyte activation (neopterin) were significantly elevated during acute infectious mononucleosis but not in patients with chronic fatigue syndrome. Interferon-alpha, IL-1 beta, and IL-6 levels were not significantly increased in any patient group but inferferon-gamma levels were significantly increased during the acute phase of infectious mononucleosis. The levels of IL-1 alpha were significantly higher than in controls both in patients with infectious mononucleosis and in those with chronic fatigue syndrome. In the latter, the lack of most markers for lymphocyte activation found in patients with infectious mononucleosis makes it less likely that EBV reactivation causes symptoms.
Lloyd A, Hickie I, Hickie C, Dwyer J, Wakefield D.	Department of Immunology, Prince Henry Hospital, Sydney, Australia.	Cell-mediated immunity in patients with chronic fatigue syndrome, healthy control subjects and patients with major depression.	Clin Exp Immunol 1992 Jan;87(1):76-9	The chronic fatigue syndrome (CFS) is characterized by severe persistent fatigue and neuropsychiatric symptoms. It has been proposed that the abnormalities in cell-mediated immunity which have been documented in patients with CFS may be attributable to a clinical depression, prevalent in patients with this disorder. Cell-mediated immune status was evaluated in patients with carefully defined CFS and compared with that of matched subjects with major depression (non-melancholic, non-psychotic) as well as healthy control subjects. Patients with CFS demonstrated impaired lymphocyte responses to phytohaemagglutinin (PHA) stimulation, and reduced or absent delayed-type hypersensitivity (DTH) skin responses when compared either with subjects with major depression or with

				healthy control subjects (P less than 0.05 for each analysis). Although depression is common in patients with CFS, the disturbances of cell-mediated immunity in this disorder differ in prevalence and magnitude from those associated with major depression. These observations strengthen the likelihood of a direct relationship between abnormal cell-mediated immunity and the etiology of CFS.
Lloyd AR, Pender H.	Department of Infectious Diseases, Prince Henry Hospital, Little Bay, NSW.	The economic impact of chronic fatigue syndrome.	Med J Aust 1992 Nov 2;157(9):599-601 comment in: Med J Aust. 1993 Feb 15;158(4):286-7	OBJECTIVE: To estimate the economic impact of chronic fatigue syndrome (CFS) on the individual, the government, and the community. DESIGN: The financial burden produced by CFS was studied by calculating the direct and indirect costs arising from the disorder. Data regarding use of health resources, income and employment were obtained by questionnaire from patients with CFS. In addition, aggregate Medicare data on the incidence and fees charged for each Schedule item for these patients was obtained. SETTING: The Richmond Valley, New South Wales. PARTICIPANTS: Forty-two patients with CFS identified in our population-based prevalence study. RESULTS: The conservative estimate of the per annum costs of CFS in the Richmond Valley, with a prevalence of 37.1 cases per 100,000, was $396,000. If extrapolated to the Australian population, we estimate CFS would generate an annual cost of at least $59 million. CONCLUSION: This disorder constitutes a large but neglected area of health resource utilisation and economic burden.
Lozano de Leon F, Gutierrez Fernandez J, Martin Mazuelos E, Garcia-Bragado F.	Unidad de Enfermedades Infecciosas, Hospital Universitario de Valme, Sevilla.	[Infection by human herpesvirus type 6: epidemiology, immunopathology and clinical implications].[article in Spanish]	Rev Clin Esp 1992 Jan;190(1):37-42	The human herpesvirus type 6 has been discovered recently and is the object of numerous investigations. Even though, its morphology is very close to the cytomegalovirus, its epidemiologic, immunopathologic and clinic characteristics are similar to the Epstein-Barr virus. Like the latter, HHV-6 persists latent in the host during all his live, frequently relapsed and is ubiquitous. Exanthema subitum in children and mononucleosis-like syndrome in adults have been attributed to acute HHV-6 infection. Under certain conditions, the development of chronic fatigue syndrome, some lymphoproliferative disorders and, perhaps, others diseases can be influenced by the persistent activity of this infection furthermore, HHV-6 can be a cofactor in infection with HIV and provokes a faster evolution and more severe illness.
Lynch S, Montgomery S, Seth R.		Chronic fatigue syndrome.	Br J Gen Pract 1992 Jan;42(354):39-40 comment on: Br J Gen Pract. 1991 Nov;41(352):479-80	
Lynch SP, Seth RV, Main J.	St James University Hospital, Leeds.	Monospot and VP1 tests in chronic fatigue syndrome and major depression.	1348: J R Soc Med 1992 Sep;85(9):537-40	Thirty-four patients with chronic fatigue syndrome (CFS) were compared with controls with DSM-III-R major depression on the Monospot and VP1 antigen tests. There was no significant difference in the numbers initially VP1 positive in the groups (11/34 and 7/34 positive in the chronic fatigue and major depression group respectively). Four CFS but no depressed patients were Monospot positive

				initially. No patient was both Monospot and VP1 positive. Patients positive on the tests were offered a repeat 6 months later. Eight of the 11 VP1 positive patients in the CFS group were retested and four remained positive, but none of the four depressed patients retested remained positive. No patient retested remained Monospot positive. The Monospot and VP1 tests appear to have little discriminating ability between these groups as screening tests and their predictive validity is unclear.
Mahnke C, Kashaiya P, Rossler J, Bannert H, Levin A, Blattner WA, Dietrich M, Luande J, Lochelt M, Friedman-Kien AE, et al.	Projektgruppe Humane Retroviren, DKFZ, Heidelberg, Federal Republic of Germany.	Human spumavirus antibodies in sera from African patients.	Arch Virol 1992;123(3-4):243-53	Serum samples collected from patients with a wide variety of diseases from African and other countries were tested for antibodies to the human spumaretrovirus (HSRV). A spumaviral env-specific ELISA was employed as screening test. Out of 3020 human sera screened, 106 were found to be positive (3.2%). While the majority of patients' sera from Europe (1581) were negative, 26 were positive (1.6%). Sera from healthy adult blood donors (609), from patients with multiple sclerosis (48), Graves' disease (45), and chronic fatigue syndrome (41) were negative or showed a very low prevalence for spumaviral env antibodies. A higher percentage of seropositives (6.3%) were found among 1338 African patients from Tanzania, Kenya, and Gabon. Out of 1180 patients from Tanzania, 708 suffered from tumors, 75 from AIDS, and 128 had gynecological problems; 51 of the Tanzanian patients were HSRV seropositive (4.3%). A particularly high percentage of 16.6% seropositives were identified among nasopharyngeal carcinoma patients (NPC) from Kenya and Tanzania consistent with results reported 10 years ago. However, 20 nasopharyngeal carcinoma patients from Malaysia were HSRV-seronegative. In selected cases, sera from seropositive individuals were reacted with proteins from HSRV-infected cells in vitro. HSRV env- and gag-specific antibodies were specifically detected by these sera in Western blots. The results indicate spumavirus infections in human patients with various diseases at a relatively low prevalence worldwide; in African patients, however, the prevalence of spumavirus infections is markedly higher.
Manu P, Lane TJ, Matthews DA.	Department of Psychiatry, University of Connecticut Health Center, Farmington 06032.	The pathophysiology of chronic fatigue syndrome: confirmations, contradictions, and conjectures.	Int J Psychiatry Med 1992;22(4):397-408	OBJECTIVE: To examine published data regarding patient cohorts with the recently defined chronic fatigue syndrome. METHOD: Review of thirty-two peer-assessed research publications that included full disclosure of the methodology employed; classification of the findings as confirmed, contradictory, or non-duplicated. RESULTS: Research studies have confirmed that the majority of patients with the chronic fatigue syndrome: 1) are white middle-aged women, 2) have a high prevalence of current major depression and somatization disorder, 3) have abnormal personality traits, 4) believe that their fatigue has a physical cause, and 5) show mild abnormalities of humoral immunity. Contradictory data have been presented with regard to: 1) the time of onset of depressive disorders, 2) the etiologic role of herpetic and enteroviral infections, 3) the presence of abnormal cellular immunity, and 4) the clinical utility of immunoglobulin therapy.

				Non-duplicated research has indicated 1) hypothalamic-pituitary-adrenal axis dysfunction, 2) abnormalities on magnetic resonance images of the brain, 3) altered cytokine production, and 4) the possibility of retroviral infection. CONCLUSIONS: As presently defined, the chronic fatigue syndrome has many of the clinical and biological features associated with depressive and somatoform disorders. A specific etiologic role for infections or immune dysfunction has not been confirmed.
Martin WJ.		Chronic fatigue syndrome.	Science 1992 Feb 7;255(5045):663 comment on: Science. 1991 Dec 20;254(5039):1726-8	
Matsuda J, Gohchi K.	Department of Medicine, Teikyo University School of Medicine.	[Overview of our patients with chronic fatigue syndrome (CFS) from the pathoetiological aspects].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2635-40	We interviewed 285 patients who visited our department claiming with a complaint of chronic fatigue syndrome (CFS) and subsequently diagnosed 55 as having CFS, according to the criteria for CFS of the centers for disease control (CDC). We measured various virus antibody titers, 2-5, adenylate synthetase levels in the serum lymphocyte subset in blood, employing a double staining technique with monoclonal antibodies. In this paper, we pathoetiology of CFS, based on our findings and other researchers' is discussed.
Matsuda J.	Department of Medicine, Teikyo University School of Medicine.	[Chronic fatigue syndrome].[article in Japanese]	Nippon Rinsho 1992 Apr;50(4):887-91	Chronic fatigue syndrome (CFS), which is characterized by devastating fatigue, mild fever, lymphadenopathy, headache, myalgia, insomnia and neuropsychiatric disorders, now has drawn much attentions from many physicians, researchers and even peoples in general society world wide. The pathogenesis of CFS is still remains to be clarified and clinico-pathological difference between CFS and mood disorder is controversial. In this paper, CFS would be reviewed in detail.
Matsumoto Y, Ninomiya S.	Second Department of Internal Medicine, Nagoya City University Medical School.	[Allergy among Japanese patients with chronic fatigue syndrome].[article in Japanese]	Arerugi 1992 Dec;41(12):1722-5	Allergy is a common feature of patients with chronic fatigue syndrome (CFS). Because of this strong association, we attempted to explore the prevalence of allergies among Japanese patients with CFS. Of the present 18 patients, 78% had allergies during their premorbid and/or postmorbid conditions. Their allergies were mainly cutaneous reactions including drug allergies and 43% of the patients had 2 or more allergic reactions. In the case of a premorbid condition, allergies improved spontaneously after onset of CFS. Clinical manifestations of CFS, however, became worse during the period of an association with allergies. Immunologic tests, including peripheral blood lymphocyte-subsets, blastogenesis, natural killer-cell functions and cytokine-assays, were not any correlation between both patients with and without allergies.
McCluskey DR, Riley MS.	Department of Medicine, Royal Victoria Hospital, Belfast, Ireland.	Chronic fatigue syndrome.	Compr Ther 1992 Apr;18(4):13-6	Chronic Fatigue Syndrome appears to represent a spectrum of disorders in which a variety of pathophysiological mechanisms may operate. While the initiating event in the majority of patients is a pyrexial illness, possibly due to enterovirus infection, evidence of persisting infection or inflammatory changes in muscle

				and/or brain remain unconvincing. CFS patients display a definite reduced aerobic work capacity compared to normal control subjects, but this may reflect a state of deconditioning resulting from prolonged physical inactivity. They also have an altered perception of their level of exertion and premorbid fitness. The characteristic fluctuation in symptoms, with periods of relapses and partial remissions, may indicate that some central disorder of sensory perception is operational. It may be that a primary sleep disorder results in a reduced sensory threshold for afferent stimuli from muscle. This could well account for many of the subjective symptoms which patients experience. Much more research is clearly necessary if we are to achieve a better understanding of this distressing and at present enigmatic disorder.
Moyer HL Jr.		"Chronic fatigue syndrome and women: can therapy help?".	Soc Work 1992 Sep;37(5):478 comment on: Soc Work. 1992 Jan;37(1):35-9	
Murdoch JC.	University of Otago, Dunedin, New Zealand.	Chronic fatigue syndrome. A review from the general practice perspective.	Aust Fam Physician 1992 Aug;21(8):1205-6	
Murray JB.	Psychology Department, St. John's University, Jamaica, NY 11439.	Psychological aspects of chronic fatigue syndrome.	Percept Mot Skills 1992 Jun;74(3 Pt 2):1123-36	
Nishikai M.	Department of Internal Medicine, Second Tokyo National Hospital.	[Chronic fatigue syndrome--study of 51 cases treated at the Second Tokyo National Hospital].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2641-7	Fifty-one patients with chronic fatigue syndrome (CFS) were studied. Tender points, which are a characteristic clinical feature of fibromyalgia, were found in all but two of the patients at 11.4 points (mean) per patient. IgG antibody titers to EB virus viral capsid antigen were more elevated in the CFS patient group compared to that of the control ($p < 0.0015$). IgG antibody titers to HHV-6 were not higher in the patient group. NK cell activity was not more decreased in the patient group, whereas, the mean number of NK cells was lower ($p < 0.005$) in the patient group, when CD57 was used as the NK cell marker. Viral infections and/or disorders in cellular immunity may be important factors in the pathogenesis of CFS.
Ogawa R, Toyama S, Matsumoto H.	Department of Internal Medicine, Kanebo Memorial Hospital.	[Chronic fatigue syndrome--cases in the Kanebo Memorial Hospital].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2648-52	In our hospital, 134 patients (28 male, 106 female, 10-82 years of age) were diagnosed as having chronic fatigue syndrome (CFS). Some patients had mild elevation of antibodies against Epstein-Barr Virus and immunologic abnormalities (natural killer cell dysfunction and high rates of skin reactivity to house dust, pollen, drugs and common food). In the patients with immunologic abnormalities, we found decreases in serum concentrations of arachidonic acid and dihomogamma-linolenic acid. A Kampo medicine, Ren-Shen-Yang-Rong-Tang was used in the management of 134 patients and 98 patients returned to work or

				school.
Okano M.	Department of Pediatrics, Hokkaido University School of Medicine.	[Viral infection and its causative role for chronic fatigue syndrome].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2617-24	Patients with chronic fatigue syndrome (CFS), of unknown etiology, have been increasingly reported. This syndrome is characterized by debilitating fatigue, lymphadenopathy, and fever. Herein, I focus on and review this syndrome from the view point of the causative role of viral infection. Since the symptoms of CFS are similar to those of chronic infectious mononucleosis (CIM) or chronic Epstein-Barr virus infection (CEBV), the role of EBV has been intensively studied. The etiological relationship between EBV and CFS, however, is questioned, like other lymphotropic viruses, including human retroviruses, adenoviruses and human herpesvirus 6. Additionally, severe chronic active EBV infection syndrome (SCAEBV) is also discussed in this review because symptoms of this disorder are similar to those of CFS but more severe in degree. Currently, the cause(s) and treatment of CFS are enigmatic and require further research and multidisciplinary study. Review Literature
O'Sullivan SJ.		Alleged link between hepatitis B vaccine and chronic fatigue syndrome.	CMAJ 1992 Jan 1;146(1):37-8 comment in: Can Med Assoc J. 1992 Apr 1;146(7):1145	
O'Sullivan SJ.		Alleged link between hepatitis B vaccine and chronic fatigue syndrome.	CMAJ 1992 Aug 15;147(4):399, 402	
Pamphlett R, O'Donoghue P.		Antibodies against Sarcocystis and Toxoplasma in humans with the chronic fatigue syndrome.	Aust N Z J Med 1992 Jun;22(3):307-8	
Peterson PK, Schenck C.		Chronic fatigue syndrome as a "real" disease?	J Gen Intern Med 1992 Jan-Feb;7(1):119-20 comment on: J Gen Intern Med. 1991 Jul-Aug;6(4):378-9	
Phillips N.		Chronic fatigue syndrome.	Aust N Z J Psychiatry 1992 Jun;26(2):329-30 comment on: Aust N Z J Psychiatry. 1992 Mar;26(1):64-72	
Price RK, North CS, Wessely S, Fraser VJ.	Department of Psychiatry, Washington University School of	Estimating the prevalence of chronic fatigue syndrome and	Public Health Rep 1992 Sep-Oct;107(5):514-22 comment in: Public	Chronic fatigue syndrome is a poorly understood disease characterized by debilitating fatigue and neuromuscular and neuropsychological symptoms. Despite numerous studies on the subject, the epidemiology of the syndrome in

	Medicine, St. Louis, MO 63110.	associated symptoms in the community.	Health Rep. 1993 Jan-Feb;108(1):135-7	the community remains largely unexplored. An estimate of the prevalence in the population is presented, approximating the Centers for Disease Control criteria as well as the prevalence estimates of the fatigue symptom complex that include fatigue, disability, and neuromuscular and neuropsychological symptoms. The study population consisted of a very large, multicenter, stratified, and random sample of a general population health survey known as the Epidemiologic Catchment Area Program. Data used for this study were gathered between 1981 and 1984. The Diagnostic Interview Schedule, a highly structured mental health interview, was used to assess the lifetime prevalence of medical and psychological symptoms. Chronic fatigue was common. A total of 23 percent of the subjects reported having experienced the symptom of persistent fatigue sometime during their lives. Chronic fatigue syndrome, however, as defined by the Centers for Disease Control, appeared to be quite rare in the general population. Only 1 of 13,538 people examined was found to meet a diagnosis of the syndrome with an approximation of the CDC criteria. Fatigue symptom complex was frequently related to medical or psychiatric illness or substance abuse; thus, persons meeting partial criteria of chronic fatigue syndrome were also found to be rare when psychiatric or medical exclusions were applied.
Ray C, Weir WR, Cullen S, Phillips S.	Department of Human Sciences, Brunel University, Uxbridge, Middlesex, U.K.	Illness perception and symptom components in chronic fatigue syndrome.	J Psychosom Res 1992 Apr;36(3):243-56	Two-hundred and eight patients with chronic fatigue syndrome (post-viral fatigue syndrome) completed a questionnaire which dealt both with their illness in general and with the extent to which they experienced specific symptoms. A factor analysis of the symptom data yielded four components: emotional distress; fatigue; somatic symptoms; and cognitive difficulty. Emotional disturbance is a common feature of the disorder and its role has been widely debated. When the symptom components were considered independently, fatigue, somatic symptoms and cognitive difficulty were associated with questionnaire items relating to general illness severity, but emotional distress was not. Thus negative emotions did not contribute directly to patients' perception of illness severity. They were, however, correlated with the other symptom components. It is argued that this correlation reflects a reciprocal influence, with negative emotions exacerbating fatigue and other key symptoms and the debilitating nature of these symptoms enhancing emotional vulnerability.
Ray C.	Department of Human Sciences, Brunel University, Uxbridge, Middlesex, United Kingdom.	Positive and negative social support in a chronic illness.	Psychol Rep 1992 Dec;71(3 Pt 1):977-8	A measure of social support was developed and administered to 207 patients with chronic fatigue syndrome. Positive social support was related to anxiety, and negative social support was related to both anxiety and depression.
Reeves WC, Pellett PE, Gary H Jr.		The chronic fatigue syndrome controversy.	Ann Intern Med 1992 Aug 15;117(4):343; discussion 344	

			comment on: Ann Intern Med. 1992 Jan 15;116(2):103-13	
Rikard-Bell CJ, Waters BG.	Arndell Children's Unit, North Ryde, New South Wales.	Psychosocial management of chronic fatigue syndrome in adolescence.	Aust N Z J Psychiatry 1992 Mar;26(1):64-72 comment in: Aust N Z J Psychiatry. 1992 Jun;26(2):329-30	The state of chronic fatigue syndrome (CFS) as abnormal illness behaviour or as biologically determined disease is undecided. The ensuing, often public, debate has confused the community and has led to sharp differences in the therapeutic approach to individual patients. These challenges are compounded when the patient is an adolescent and intergenerational issues enter the picture. Two adolescent cases with different outcomes are presented and the principles of a rehabilitation approach to treatment are outlined which attempt to avoid being drawn into unproductive debates about aetiology.
Saltzstein B, Gurwitt A, Webster W, Barrett SN.		Taking chronic fatigue syndrome seriously.	Am J Psychiatry 1992 Dec;149(12):1755; discussion 1756-7 comment on: Am J Psychiatry. 1991 Dec;148(12):1638-46	
Scheffers MK, Johnson R Jr, Grafman J, Dale JK, Straus SE.	Cognitive Neurophysiology Unit, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD 20892.	Attention and short-term memory in chronic fatigue syndrome patients: an event-related potential analysis.	Neurology 1992 Sep;42(9):1667-75	We recorded event-related brain potentials (ERPs) from 13 patients with chronic fatigue syndrome (CFS) and 13 matched normal controls. To assess attentional and memory deficits in CFS patients, we used a short-term memory task in which events occurred in different spatial locations and the patients made a rapid-response (RT) when a letter in a relevant location matched a letter in the prememorized set (Attention paradigm). Time-on-task effects on the ERP and behavioral measures were assessed over the 2 1/4-hour duration of this task. Both groups also performed a visual Oddball paradigm, with an RT, before and after the Attention paradigm. The patients' RTs were much more variable and, in nine of 13 cases, slower than the mean RT of the controls in both paradigms. The patients' memory performance was not significantly different from that of the controls and there were no group differences in the overall amplitude, latency, or scalp distribution of the N1, P2, N2, or P300 components of the ERP in either paradigm. The ERP and performance data from both paradigms suggest that perceptual, attentional, and short-term memory processes were unaffected in CFS patients and that the differences were limited to response-related processes.
Schluederberg A, Straus SE, Peterson P, Blumenthal S, Komaroff AL, Spring SB, Landay A, Buchwald D.	National Institute of Allergy and Infectious Diseases, Bethesda, MD.	NIH conference. Chronic fatigue syndrome research. Definition and medical outcome assessment.	Ann Intern Med 1992 Aug 15;117(4):325-31	A workshop was held 18 to 19 March 1991 at the National Institutes of Health to address critical issues in research concerning the chronic fatigue syndrome (CFS). Case definition, confounding diagnoses, and medical outcome assessment by laboratory and other means were considered from the perspectives of key medical specialties involved in CFS research. It was recommended that published Centers for Disease Control (CDC) case-definition criteria be modified to exclude fewer patients from analysis because of a history of psychiatric disorder. Specific

				recommendations were made concerning the inclusion or exclusion of other major confounding diagnoses, and a standard panel of laboratory tests was specified for initial patient evaluation. The workshop emphasized the importance of recognizing other conditions that could explain the patient's symptoms and that may be treatable. It was viewed as essential for the investigator to screen for psychiatric disorder using a combination of self-report instruments followed by at least one structured interview to identify patients who should be excluded from studies or considered as a separate subgroup in data analysis. Because CFS is not a homogeneous abnormality and because there is no single pathogenic mechanism, research progress may depend upon delineation of these and other patient subgroups for separate data analysis. Despite preliminary data, no physical finding or laboratory test was deemed confirmatory of the diagnosis of CFS. For assessment of clinical status, investigators must rely on the use of standardized instruments for patient self-reporting of fatigue, mood disturbance, functional status, sleep disorder, global well-being, and pain. Further research is needed to develop better instruments for quantifying these domains in patients with CFS.
Shepherd C.		Chronic fatigue syndrome: a joint paediatric-psychiatric approach.	Arch Dis Child 1992 Nov;67(11):1410 comment on: Arch Dis Child. 1992 Apr;67(4):550-5	
Shepherd C.		Fluctuations in perceived energy and mood among patients with chronic fatigue syndrome.	J R Soc Med 1992 Sep;85(9):588 comment in: J R Soc Med. 1992 Oct;85(10):650 comment on: J R Soc Med. 1992 Apr;85(4):195-8	
Shepherd C.		Outcome in the chronic fatigue syndrome.	BMJ 1992 Aug 8;305(6849):365 comment on: BMJ. 1992 Jul 18;305(6846):147-52	
Shepherd C.		Immune responsiveness in chronic fatigue syndrome.	Postgrad Med J 1992 Jan;68(795):66-7 comment on: Postgrad Med J. 1991 Jun;67(788):532-7	
Shimizu T.	Dept. of Neurology, Teikyo University	[Neuro-psychiatric aspects of chronic	Nippon Rinsho 1992 Nov;50(11):2630-4	Chronic fatigue syndrome (CFS) is easily differentiated from various neurological organic disorders by conventional clinical examinations. The most important

	Medical School.	fatigue syndrome].[article in Japanese]		disease for distinguishment from CFS is fibromyalgia syndrome, in which the prominent and cardinal feature is a deprivation of stage 4 slow wave sleep. Experimentally, the sleep disturbance in controls can induce general myalgia, muscle tender points, severe fatigue and stiffness on awakening. The EEG abnormality is slow alpha wave contaminants on slow wave background, which is identical to EEG of CFS. The results clearly imply that CFS is not a hysterical or psychogenic disease, and that fibromyalgia may be a central fundamental of CFS. Fibromyalgia, however, has distinct features such as no antecedent inflammatory process and no endemics. Therefore, the syndrome has features distinct from, in addition to common features to CFS. It is also very difficult to distinguish CFS from depression. The above-mentioned features can be observed in depression. Now, study of brain blood flow or metabolism by PET or SPECT can be a possible tool for establishment of the CFS identity. Review Literature
Stoner BP, Corey GR.	Department of Medicine, Duke University Medical Center, Durham 27710.	Chronic fatigue syndrome. A practical approach.	N C Med J 1992 Jun;53(6):267-70	
Straus SE. Editorial		Defining the chronic fatigue syndrome.	Arch Intern Med 1992 Aug;152(8):1569-70 comment on: Arch Intern Med. 1992 Aug;152(8):1604-9	
Takahashi H, Imai K, Katanuma A, Sugaya T, Hisano K, Motoya S, Aoki S, Sugiyama T, Yachi A.	Department of Internal Medicine (Section I), Sapporo Medical College.	[A case of chronic fatigue syndrome who showed a beneficial effect by intravenous administration of magnesium sulphate].[article in Japanese]	Arerugi 1992 Nov;41(11):1605-10	We have treated a case of chronic fatigue syndrome with atopic diathesis was had suffered general malaise, low grade fever, swelling of the lymph nodes, myalgias and arthralgias for a long time. A 29-year-old female, who had been treated for atopic dermatitis for 5 years, complained of general malaise in May 1990. She was admitted to the nearest hospital in December 1990 because of low grade fever, swelling of the lymph nodes and an elevation of antinuclear antibody (2520x). She was transferred to our hospital in May 1991. A diagnosis of collagen disease was not compatible with her condition. In addition to general malaise, fever and lymph node swelling, headache, myalgias, muscle weakness, arthralgias and insomnia were observed, and a diagnosis of chronic fatigue syndrome was made based on the working case definition proposed by Holmes et al. Although eosinophilia, a high serum level of IgE, and elevation of RAST scores, low NK and ADCC activity, and a reduced level of NK cells in the peripheral blood were detected, serum antibodies to a number of viruses were in the normal range. Treatments with non-steroid anti-inflammatory drugs, minor tranquilizers and antidepressant drugs were not effective at all. An administration of magnesium sulphate was intravenously performed once a week in order to improve her condition, especially severe general malaise. After about 6-week's administration

				of magnesium sulphate, she noticed reduced easy fatigability and an improvement in her impaired daily activities. Finally she was able to leave the hospital in January 1992.(ABSTRACT TRUNCATED AT 250 WORDS)
Thoolen IM, de Vries TW.	Kinderkliniek Academisch Ziekenhuis Groningen.	[Chronically tired or the chronic fatigue syndrome in an adolescent].[article in Dutch]	Tijdschr Kindergeneeskd 1992 Jun;60(3):63-7	To fulfill the criteria of the chronic fatigue syndrome a patient must have new onset persistent or relapsing, debilitating fatigue or easy fatigability. The symptoms do not resolve with bedrest and are severe enough to reduce or impair average daily activity below 50% of the patient's premorbid activity level for a period of at least 6 months. Other clinical conditions that may produce similar symptoms must be excluded. Using a case history the (differential) diagnosis, treatment and prognosis of the chronic fatigue syndrome are discussed.
Uchida A.	Dept. Late Effect Studies, Kyoto University.	[Therapy of chronic fatigue syndrome].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2679-83	Chronic fatigue syndrome (CFS) is characterized by unexplained, debilitating fatigue or easy fatigability lasting longer than six months. While a number of clinical trials have been performed in CFS patients, there is currently no established therapy for CFS. Treatment with acyclovir of CFS patients is ineffective. Intravenous immunoglobulin therapy appears to be effective, though the results are controversial. Antidepressants might help the associated depression and anxiety but not other symptoms. Trials with magnesium have improved the well-being of patients. Restoration of NK activity by biological response modifiers, such as sizofirann, resulted in restoration of NK cell activity and recovery from CFS. Taken together, immunological abnormalities may be involved in CFS, and its restoration may produce clinical benefit in CFS. Review Literature
Uchida A.	Dept. Late Effect Studies, Kyoto University.	[Chronic fatigue immune dysfunction syndrome].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2625-9	Chronic fatigue syndrome (CFS) is characterized by unexplained, debilitating fatigue or easy fatigability lasting longer than six months. While a viral basis of infection is proposed to be the cause of CFS, other viral infections do not generally persist after several weeks. Immunological disorders, including abnormal functions and distributions of T lymphocytes, B lymphocytes, natural killer (NK) cells, and monocyte/macrophages, are described in CFS. NK cells are known to play an important role in host resistance against viral infection as well as in the regulation of the immune systems. Restoration of NK activity resulted in recovery from CFS. Taken together, immunological abnormalities, especially dysfunction of NK cells, may be involved in CFS. Review Literature
Ur E, White PD, Grossman A.	Department of Endocrinology, St. Bartholomew's Hospital, London, England.	Hypothesis: cytokines may be activated to cause depressive illness and chronic fatigue syndrome.	Eur Arch Psychiatry Clin Neurosci 1992;241(5):317-22	Abnormalities in the regulation of the hypothalamo-pituitary-adrenal (HPA) axis are a well recognised feature of endogenous depression. The mechanism underlying this phenomenon remains obscure although there is strong evidence suggesting excessive CRH activity at the level of the hypothalamus. We propose a novel hypothesis in which we suggest that the aetiological antecent to CRH hyperactivity is cytokine activation in the brain. It is now well established both that interleukins -1 and -6 are produced in a number of central loci and that

				cytokines are potent stimulators of the HPA axis. Hence, we suggest that activation of IL-1 and IL-6 by specific mechanisms (such as neurotropic viral infection) in combination with the consequent CRH-41 stimulation, may (via their known biological effects) underly many of the features found in major depression and other related disorders, particularly where chronic fatigue is a prominent part of the symptom complex. This theory has considerable heuristic value and suggests a number of experimental stratagems which may employed in order to confirm or reject it.
van Rensburg EJ.		Unacceptable trends in the diagnosis of chronic fatigue syndrome.	S Afr Med J 1992 Feb 1;81(3):172-3	
Vereker MI.	Paxton House Family and Young Person's Unit, Reading.	Chronic fatigue syndrome: a joint paediatric-psychiatric approach.	Arch Dis Child 1992 Apr;67(4):550-5 comment in: Arch Dis Child. 1992 Nov;67(11):1410	
Ware NC, Kleinman A.	Department of Social Medicine, Harvard Medical School, Boston, Massachusetts 02115.	Culture and somatic experience: the social course of illness in neurasthenia and chronic fatigue syndrome.	Psychosom Med 1992 Sep-Oct;54(5):546-60	An anthropological view of culture and somatic experience is presented through elaboration of the notion that illness has a social course. Contemporary anthropology locates culture in local worlds of interpersonal experience. The flow of events and processes in these local worlds influences the waxing and waning of symptoms in a dialetic involving body and society over time. Conversely, symptoms serve as a medium for the negotiation of interpersonal experience, forming a series of illness-related changes in sufferers' local worlds. Thus, somatic experience is both created by and creates culture throughout the social course of illness. Findings from empirical research on neurasthenia in China, and chronic fatigue syndrome (CFS) in the United States, corroborate this formulation. Attributions of illness onset to social sources, the symbolic linking of symptoms to life context, and the alleviation of distress with improvement in circumstances point to the sociosomatic mediation of sickness. Transformations occasioned by illness in the lives of neurasthenic and CFS patients confirm the significance of bodily distress as a vehicle for the negotiation of change in interpersonal worlds. An indication of some of the challenges anthropological thinking poses for psychosomatic medicine concludes the discussion.
Welch LS, Sokas R.	Division of Occupational and Environmental Medicine, George Washington University School of Medicine, Washington, DC 20037.	Development of multiple chemical sensitivity after an outbreak of sick-building syndrome.	Toxicol Ind Health 1992 Jul-Aug;8(4):47-50	Investigation of this outbreak raises some important points for future research. Although for various reasons the case ascertainment for MCS was not complete, the three MCS patients described here all had preexisting conditions that may have put them at risk. In addition, one person among the 20 described had chronic fatigue syndrome but did not develop MCS. Many of the persons described here continue to have ongoing complaints that are not MCS. Significant exacerbation of preexisting allergic disease and new onset of asthma occurred

				among those patients. As a group, they did not recover completely after the outbreak; several are no longer working in the building but in alternative work spaces. An important distinction should be made between individuals who met the definition used here for MCS and others who had significant exacerbation of some better-defined illness brought on by building conditions. New onset of MCS was a partial but not complete explanation of the clinical course for this group of 20 persons.
Wessely S.		The measurement of fatigue and chronic fatigue syndrome.	J R Soc Med 1992 Apr;85(4):189-90 comment in: J R Soc Med. 1992 Sep;85(9):588	
Wessely S. Publication Types: Comment Letter		Outcome in the chronic fatigue syndrome.	BMJ 1992 Aug 8;305(6849):365 comment in: BMJ. 1992 Sep 12;305(6854):649 comment on: BMJ. 1992 Jul 18;305(6846):147-52	
Whelton CL, Salit I, Moldofsky H.	Department of Psychiatry, University of Toronto, Toronto Hospital, Canada.	Sleep, Epstein-Barr virus infection, musculoskeletal pain, and depressive symptoms in chronic fatigue syndrome.	J Rheumatol 1992 Jun;19(6):939-43	Sleep physiology, viral serology and symptoms of 14 patients with chronic fatigue syndrome (CFS) were compared with 12 healthy controls. All patients described unrefreshing sleep and showed a prominent alpha electroencephalographic nonrapid eye movement (7.5-11.0 Hz) sleep anomaly (p less than or equal to 0.001), but had no physiologic daytime sleepiness. There were no group differences in Epstein-Barr virus (EBV) antibody titers. The patient group had more fibrositis tender points (p less than 0.0001), described more somatic complaints (p less than 0.0001), and more depressive symptoms (p less than 0.0001). Patients with CFS do not show evidence for a specific chronic EBV infection, but show altered sleep physiology, numerous tender points, diffuse pain, and depressive symptoms. These features are similar to those found in fibromyalgia syndrome.
Winters EG, Quinet RJ.	Dept of Internal Medicine, Ochsner Clinic, New Orleans, LA 70121.	Chronic fatigue syndrome.	J La State Med Soc 1992 Jun;144(6):260-70	The chronic fatigue syndrome (CFS) is a poorly understood condition with nonspecific signs and symptoms, especially debilitating fatigue. Most patients can pinpoint the onset of their illness and usually describe a flu-like state. The search for an etiologic agent has focused on a number of viruses such as Epstein-Barr, enteroviruses, retroviruses, and human herpesvirus-6. Evidence supports persistent viral infection in a small percentage of CFS patients. Immunologic abnormalities do exist in CFS, which indicate the presence of immune activation in CFS patients. Although abnormal muscle biopsies have been found in some patients with CFS, strength and endurance appear normal, but perception of exertion may be abnormal. Patients with chronic fatigue have a high incidence of

				premorbid and concurrent psychiatric disorders, and on physical examination many often have reproducible tender points similar to fibromyalgic patients. Clinical evaluation should rule out other potential causes of fatigue, but elaborate diagnostic tests are seldom required. Presently, no specific treatment exists for CFS. A cognitive behavioral approach with or without the use of tricyclics has been advocated. Patients should be encouraged to maintain functional status and should not be discouraged from exercise. Several medications have been tried but with no definite clinical benefit.
Wong R, Lopaschuk G, Zhu G, Walker D, Catellier D, Burton D, Teo K, Collins-Nakai R, Montague T.	Department of Medicine, University of Alberta, Edmonton, Canada.	Skeletal muscle metabolism in the chronic fatigue syndrome. In vivo assessment by 31P nuclear magnetic resonance spectroscopy.	Chest 1992 Dec;102(6):1716-22	BACKGROUND: Previous study of patients with chronic fatigue syndrome (CFS) has demonstrated a markedly reduced dynamic exercise capacity, not limited by cardiac performance and in the absence of clinical neuromuscular dysfunction, suggesting the possibility of a subclinical defect of skeletal muscle. METHODS: The in vivo metabolism of the gastrocnemius muscles of 22 CFS patients and 21 normal control subjects was compared during rest, graded dynamic exercise to exhaustion and recovery, using 31P nuclear magnetic resonance (NMR) spectroscopy to reflect minute-to-minute intracellular high-energy phosphate metabolism. RESULTS: Duration of exercise was markedly shorter in the CFS patients (8.1 +/- 2.8 min) compared with the normal subjects (11.3 +/- 4.3 min) (p = 0.005). There were large changes in phosphocreatine (PCr), inorganic phosphate (Pi), and pH from rest to clinical fatigue in all subjects, reflecting the high intensity of the exercise. The temporal metabolic patterns were qualitatively similar in the CFS patients and normal subjects. There were early and continuous changes in PCr and Pi that peaked at the point of fatigue and rapidly reversed after exercise. In contrast, pH was relatively static in early exercise, not declining noticeably until 50 percent of total exercise duration was achieved, and reaching a nadir at 2 min postexercise, before rapidly reversing. There were no differences in pH at rest (7.08 +/- 0.04 vs 7.10 +/- 0.04), exhaustion (6.85 +/- 0.17 vs 6.76 +/- 0.17) or early (6.64 +/- 0.25 vs 6.56 +/- 0.24) or late recovery (7.09 +/- 0.04 vs 7.10 +/- 0.05), CFS patients vs normal subjects, respectively (NS). Neither were there intergroup differences (NS) in PCr or Pi. Although, quantitatively, the changes in PCr, Pi, and pH were marked and similar in both groups from rest to exhaustion, the changes all occurred much more rapidly in the CFS patients. Moreover, adenosine triphosphate (ATP) was significantly (p = 0.007) less at exhaustion in the CFS group. CONCLUSIONS: Patients with CFS and normal control subjects have similar skeletal muscle metabolic patterns during dynamic exercise and reach similar clinical and metabolic end points. However, CFS patients reach exhaustion much more rapidly than normal subjects, at which point they also have relatively reduced intracellular concentrations of ATP. These data suggest a defect of oxidative metabolism with a resultant acceleration of glycolysis in the working skeletal muscles of CFS patients. This metabolic defect

				may contribute to the reduced physical endurance of CFS patients. Its etiology is unknown. Whether CFS patients' overwhelming tiredness at rest has a similar metabolic pathophysiology or etiology also remains unknown.
Wood C, Magnello ME, Sharpe MC.	Department of Biological Anthropology, University of Oxford.	Fluctuations in perceived energy and mood among patients with chronic fatigue syndrome.	J R Soc Med 1992 Apr;85(4):195-8 comment in: J R Soc Med. 1992 Sep;85(9):587 J R Soc Med. 1992 Sep;85(9):588	Patients currently suffering or recently recovered from chronic fatigue syndrome (CFS) were compared with each other and with a group of well-matched controls in a study of diurnal variation in levels of perceived mental and physical energy and positive and negative affect. Patients who were currently ill showed diurnal variation in patterns of energy, with maximum levels being recorded between 10.00 h and 12.00 h which were significantly higher ($P < 0.05$) than energy levels recorded on rising or retiring. This pattern was similar to the controls but average energy levels at each time point were lower ($P < 0.05$) among the ill patients. Recovered patients showed the same pattern, with mean energy levels falling between those of the ill patients and controls. Similar diurnal patterns were found for perceptions of positive, though not negative affect. Correlations between physical and mental energy and between both of these energy variables and positive affect were high ($r = 0.75$ to 0.85) in both controls and CFS patients. However, correlations with negative affect were low (eg $r = -0.10$) and non-significant. Total scores on the Hospital Anxiety and Depression Scale (HAD) were significantly higher ($P < 0.05$) among patients who were still ill than those who had recovered. Scores on the HAD Depression (but not Anxiety) subscale were also significantly higher among those who were still ill ($P < 0.01$). These findings may be of value in facilitating programmes of cognitive-behavioural modification intended to aid the recovery of patients with CFS.
Wood C.		Fluctuations in perceived energy and mood among patients with chronic fatigue syndrome.	J R Soc Med 1992 Oct;85(10):650 comment on: J R Soc Med. 1992 Sep;85(9):588	
Woodward CG, Cox RA.	Public Health Laboratory, Leeds, U.K.	Epstein-Barr virus serology in the chronic fatigue syndrome.	J Infect 1992 Mar;24(2):133-9	The antibody profiles against Epstein-Barr virus were studied in 136 patients presenting with chronic fatigue syndromes. These profiles were compared with a panel of sera from blood donors. The patients exhibited higher titres in a combined assay for antibodies to the Restricted (R) and Diffuse (D) components of the Early Antigen complex than controls (P less than 0.001) but titres against these antigens were not useful on an individual patient basis. The patients who displayed elevated titres of antibodies to Early Antigens did not differ clinically from those displaying titres in the control range. Four of nine patients who had increased antibodies to Early Antigens also had evidence of active enterovirus infection.
Wright B.		Chronic fatigue syndrome and	J R Soc Med 1992 Sep;85(9):588 comment	

		heterogeneity.	on: J R Soc Med. 1992 Apr;85(4):189-90	
Yamanishi K.	Research Institute for Microbial Diseases, Osaka University.	[Chronic fatigue syndrome and virus infection: human herpesvirus 6 (HHV-6) infection].[article in Japanese]	Nippon Rinsho 1992 Nov;50(11):2612-6	Chronic fatigue syndrome (CFS) is newly-recognized disease characterized by chronic and debilitating fatigue. It has been suggested that viral infection may be involved in this syndrome from the results of clinical examination, including increased activity of 2',5'-synthetase in leukocytes of patients. The following viruses have been reported as etiologic agents of this disease. First, many studies have found elevated levels of IgG to viral capsid antigen and early antigens to Epstein-Barr virus (EBV), but low titer or absence of antibody to EBV-associated nuclear antigen. Second, the enteroviruses have also been implicated as possible causative agent of CFS, because virus could be isolated from patients. Recently it was also reported that antibodies to human T-lymphotropic virus (HTLV) and HTLV type II (HTLV-II) gag sequence were detectable in patients. Finally several reports state that human herpesvirus 6 (HHV-6) could be isolated from CFS patients in the high frequency. In conclusion, it is still early to identify the etiologic agent from these reports, and more effort is needed. Review Literature
Zajdowicz TR.		Chronic fatigue syndrome and military service.	Mil Med 1992 Sep;157(9):A3-4	

1991				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Abbey SE, Garfinkel PE.	Department of Psychiatry, Toronto Hospital, Ont., Canada.	Neurasthenia and chronic fatigue syndrome: the role of culture in the making of a diagnosis.	Am J Psychiatry 1991 Dec;148(12):1638-46 comment in: Am J Psychiatry. 1992 Dec;149(12):1753;	Chronic fatigue syndrome is an increasingly popular diagnosis consisting of multiple psychiatric and somatic symptoms. It bears a striking resemblance to the nineteenth-century diagnosis of neurasthenia. Both disorders arose during periods characterized by a preoccupation with commerce and material success and major changes in the role of women. They illustrate the role of culture in the development of a new diagnosis that emphasizes a "medical" rather than "psychiatric" etiology. The authors argue that chronic fatigue syndrome will meet the same fate as neurasthenia--a decline in social value as it is demonstrated that the majority of its sufferers are experiencing primary psychiatric disorders or psychophysiological reactions and that the disorder is often a culturally sanctioned form of illness behavior.
Abbey SE, Garfinkel PE.	Department of Psychiatry, Toronto Hospital, Ontario, Canada.	Chronic fatigue syndrome and depression: cause, effect, or covariate.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S73-83	Depressed mood and the psychiatric diagnosis of major depressive episode (MDE) are common findings in patients with chronic fatigue syndrome (CFS). The relationship between depression and CFS is unclear and may be explained by one of four models: (1) CFS is an atypical manifestation of MDE; (2) depression is the result of CFS as either an organic mood syndrome or an adjustment reaction; (3) CFS and MDE are covariates; and (4) the diagnosis of MDE is artifactual. The evidence for these models is discussed. The potentially confounding effect of depression on tests of immune function and neuropsychological testing is described. The implications of these different models for the design of studies of CFS are examined.
Ablashi DV, Balachandran N, Josephs SF, Hung CL, Krueger GR, Kramarsky B, Salahuddin SZ, Gallo RC.	Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, Maryland 20892.	Genomic polymorphism, growth properties, and immunologic variations in human herpesvirus-6 isolates.	Virology 1991 Oct;184(2):545-52	Fifteen human herpesvirus-6 (HHV-6) isolates from normal donors and patients with AIDS, systemic lupus erythematosis, chronic fatigue syndrome, collagen-vascular disease, leukopenia, bone marrow transplants, Exanthem subitum (roseola), and atypical polyclonal lymphoproliferation were studied for their tropism to fresh human cord blood mononuclear cells, growth in continuous T cell lines, reactivity to monoclonal antibodies, and by restriction enzyme banding patterns. All isolates replicated efficiently in human cord blood mononuclear cells, but mitogen stimulation of the cells prior to infection was required. The ability to infect continuous T-cell lines varied with the isolates. Isolates similar to GS prototype infected HSB2 and Sup T1 cells and did not infect Molt-3 cells, whereas isolates similar to Z-29 infected Molt-3 cells but not HSB2 and Sup T1 cells. Some of the monoclonal antibodies directed against the HHV-6 (GS) isolate showed reactivity with all isolates tested, but others only reacted with HHV-6 isolates similar to the GS isolate and not with those similar to Z-29 isolate. Restriction enzyme analysis using EcoRI, BamHI, and HindIII revealed that HHV-6 isolates from roseola, bone marrow transplant, leukopenia, and an HIV-1-positive AIDS patient from Zaire (Z-29) were closely related but distinct from GS type

				HHV-6 isolates. Based on the above findings, we propose that, like herpes simplex virus types 1 and 2, the 15 HHV-6 isolates analyzed can be divided into group A (GS type) and group B (Z-29 type).
Ablashi DV, Salahuddin SZ, Josephs SF, Balachandran N, Krueger GR, Gallo RC.	National Cancer Institute, NIH, Bethesda, MD 20892.	Human herpesvirus-6 (HHV-6) (short review).	In Vivo 1991 May-Jun;5(3):193-9	Human Herpesvirus-6 is the etiological agent of Roseola infantum and approximately 12% of heterophile antibody negative infectious mononucleosis. HHV-6 is T-lymphotropic, and readily infects and lyses CD4+ cells. The prevalence rate of HHV-6 in the general population is about 80% (as measured by IFA) with an IgG antibody titer of 1:80. A lower prevalence, however, is observed in some countries. HHV-6 is reactivated in various malignant and non-malignant diseases as well as in Chronic Fatigue Syndrome and transplant patients. Furthermore, elevated antibody titers were also observed in lymphoproliferative disorders, auto-immune diseases and HIV-1 positive AIDS patients. There appears to be some strain variability in HHV-6 isolates. The GS isolates of HHV-6 (prototype) was resistant to Acyclovir, Gancyclovir, but its replication was inhibited by Phosphonoacetic acid and Phosphoformic acid. HHV-7 isolated from healthy individuals showed, by restriction analysis, that 6 out of 11 probes derived from two strains of HHV-6, cross-hybridized with DNA fragments, derived from HHV-7.
Ablashi DV, Zompetta C, Lease C, Josephs SF, Balachandra N, Komaroff AL, Krueger GR, Henry B, Lukau J, Salahuddin SZ.		Human herpesvirus 6 (HHV6) and chronic fatigue syndrome (CFS).	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:33-40	
Alisky JM, Iczkowski KA, Foti AA.	Chronic fatigue syndrome.		Am Fam Physician 1991 Jul;44(1):56, 61. Erratum in: Am Fam Physician 1991 Aug;44(2):406	
Anon		[Chronic fatigue syndrome].[article in Dutch]	Ned Tijdschr Geneeskd 1991 Dec 7;135(49):2347-9 comment on: Ned Tijdschr Geneeskd. 1991 Oct 26;135(43):2005-9	
Anon		Alleged link between hepatitis B vaccine and chronic fatigue syndrome.	Can Dis Wkly Rep 1991 Oct 5;17(40):215-6	
Anon		Magnesium and chronic fatigue syndrome.	Lancet 1991 May 25;337(8752):1295	

Anon		Magnesium and chronic fatigue syndrome.	Lancet 1991 May 4;337(8749):1094-5 comment on: Lancet. 1991 Mar 30;337(8744):757-60	
Anon		Chronic fatigue syndrome--false avenues and dead ends.	Lancet 1991 Feb 9;337(8737):331-2	
Anon		Chronic fatigue syndrome definition sparks off debate.	Nurs Times 1991 Jan 16-22;87(3):13 comment on: Nurs Times. 1990 Nov 21-27;86(47):40-3	
Anon		Chronic fatigue syndrome.	JAMA 1991 Jan 16;265(3):357-8 comment on: JAMA. 1990 Jul 4;264(1):48-53	
Anon		Chronic Fatigue Syndrome. Proceedings of a workshop. Toronto, Ontario, 28-29 September 1989. Overall	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:1-71	
Anon		Considerations in the design of studies of chronic fatigue syndrome. Pittsburgh, Pennsylvania, 15-16 September 1988. Overall	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S1-140	
Armon C, Kurland LT.	Department of Neurology, Mayo Clinic, Rochester, Minnesota 55905.	Chronic fatigue syndrome: issues in the diagnosis and estimation of incidence.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S68-72	This article critiques the current working definition of chronic fatigue syndrome. The concerns raised about the current working definition are the following: prolonged or excessive exertion is not addressed explicitly; duration and quality of bed rest are not specified; a socioeconomic ascertainment bias is present; data from history and physical findings are not clearly separated and are relegated to minor criteria; and the rigor of neurologic and psychiatric evaluations is not specified. We propose a flow chart that addresses the possible modes of evolution of chronic fatigue syndrome for patients; this chart may yield more homogeneous subgroups of individuals with this syndrome or enable some patients to avert the syndrome.
Arnason BG.	Department of	Nervous system-	Rev Infect Dis 1991 Jan-	This essay is based on the premise that certain individuals may have a biologically

	Neurology, University of Chicago, Illinois 60637.	immune system communication.	Feb;13 Suppl 1:S134-7	determined propensity to respond to infection that is manifested by the development of disease such as chronic fatigue syndrome; the sequence of events that leads to this response involves the immune system. Biochemical pathways between the immune and nervous systems are reviewed, and the role of various products in the systemic circulation, including interleukin-1, pituitary hormone, and catecholamines, is highlighted. This premise could be tested by measuring levels of these substances in carefully selected patients and controls.
Arya DK.		Chronic fatigue syndrome.	Br J Gen Pract 1991 Nov;41(352):480 comment on: Br J Gen Pract. 1991 Aug;41(349):324-6 Br J Gen Pract. 1991 Aug;41(349):339-42	
Balachandran N, Tirawatnapong S, Pfeiffer B, Ablashi DV, Salahuddin SZ.	Department of Microbiology, Molecular Genetics, and Immunology, University of Kansas Medical Center, Kansas City 66103.	Electrophoretic analysis of human herpesvirus 6 polypeptides immunoprecipitated from infected cells with human sera.	J Infect Dis 1991 Jan;163(1):29-34	Proteins of human herpesvirus 6 (HHV-6) eliciting human antibody responses were examined in serum from healthy adults and patients with AIDS, chronic fatigue syndrome, Hodgkin's disease, and Sjogren's syndrome. HHV-6 IgG antibody titers measured by immunofluorescence (IF) ranged from 1:10 to 1:1280. Lysates of HHV-6-infected and uninfected cells labeled with [35S]methionine, [3H]glucosamine, and 125I were immunoprecipitated with sera and analyzed electophoretically. Sera with IF titers greater than or equal to 1:20 immunoprecipitated greater than 20 [35S]methionine-labeled HHV-6 polypeptides of approximately 26-180 kDa. At least 10 HHV-6 glycoproteins and 8 HHV-6 polypeptides associated with the surfaces of infected cells were recognized by human sera. The approximate molecular masses of glycoproteins immunoprecipitated by human sera were similar to those immunoprecipitated by monoclonal antibodies. The labeling intensity of HHV-6 protein bands increased with increasing IF titer, and the effect was most prominent for HHV-6 glycopolypeptides. No reactivities with specific HHV-6 polypeptide(s) were characteristic of a given patient group. These findings suggest that HHV-6 glycoproteins are good targets for human antibody responses.
Barofsky I, Legro MW.	Institute of Social Oncology, Silver Spring, Maryland.	Definition and measurement of fatigue.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S94-7	Although fatigue is a key component of the chronic fatigue syndrome, its definition and measurement remain relatively undeveloped. Most research on fatigue has been oriented towards work or performance of tasks and has involved laboratory studies of healthy individuals, while the study of fatigue as encountered in clinical settings has received minimal attention from investigators. This paper recommends that the natural history of chronic fatigue in its various clinical presentations be studied and that standardized assessment tools be used in this process. An investigation of the tools available for the assessment of fatigue yielded single-item, unidimensional, and multidimensional

				instruments. Additionally, the apparent association between affective illness and the chronic fatigue syndrome is addressed, and the fact that this relationship depends on issues of measurement is explored.
Becker JT.	Department of Psychiatry, University of Pittsburgh School of Medicine, Pennsylvania.	Methodologic considerations in assessment of cognitive function in chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S112-3	Rigorous and standardized assessment of cognitive function is an important component of any multidisciplinary study of chronic fatigue syndrome. The present paper describes some methodologic issues that need to be addressed to maximize the yield from any neuropsychiatric evaluation of the syndrome.
Bell KM, Cookfair D, Bell DS, Reese P, Cooper L.	Monroe County Health Department, Rochester, New York 14692.	Risk factors associated with chronic fatigue syndrome in a cluster of pediatric cases.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S32-8	After seven pediatric cases of chronic fatigue syndrome (CFS) were diagnosed in a farming community in upstate New York, a questionnaire regarding symptoms and potential risk factors of CFS was distributed to all students enrolled in the same school district. Twenty-one students with symptoms of CFS were identified. Two controls per case matched for age and sex were randomly selected from questionnaire respondents. Health status was verified for all subjects by telephone, and diagnosis of CFS was confirmed by a physician. Information was collected on the following factors: symptoms of CFS among other family members; history of allergy/asthma; consumption of raw milk, raw eggs, raw cheese, or raw meat; water supply; exposure to animals; home heating source; proximity to farmland/orchards; tick bite; blood transfusion; camping; and appendicitis. Logistic-regression analyses indicated that the best model (characterized by symptoms among other family members, recent ingestion of raw milk, and history of allergy/asthma) produced significant estimates of relative risk (P less than .05) of 35.9, 44.3, and 23.3, respectively, for the three factors (corrections were made for the effect of the other covariates). These data suggest that a combination of host and environmental factors, including an infectious agent or agents, are involved in the etiology of CFS.
Bertram G, Dreiner N, Krueger GR, Ramon A, Ablashi DV, Salahuddin SZ, Balachandram N.	ENT Clinic Dortmud, University Witten-Herdecke, F.R.G.	Frequent double infection with Epstein-Barr virus and human herpesvirus-6 in patients with acute infectious mononucleosis.	1492: In Vivo 1991 May-Jun;5(3):271-9	Clinical infectious mononucleosis (IM) represents a benign self-limited form of lymphoproliferative disease which is usually caused by infection with Epstein-Barr virus (EBV). Microscopic characteristics of this lymphoproliferative disorder, however, are not ultimately specific for EBV infection, but can also be seen in infections with other lymphotropic viruses, especially of the herpesvirus family. Human herpesvirus-6 (HHV-6) infection can apparently be associated with a number of diseases also seen in EBV infection. Also, postinfectious chronic fatigue syndrome (PICFS) which may follow IM is in more than 60% of the cases accompanied by persistent active HHV-6 infection. We thus screened serologically 215 cases of acute IM for evidence for infection with EBV, HHV-6 and CMN. Patients were tentatively grouped into those having primary infection or reactivated (probably non-primary) infections. Cases were followed for two years to monitor changes in titers. Of all 215 cases, 211 (98.1%) were positive for EBV, 137 (63.7%) for primary infections, 21 (9.8%) for reactivated infection, and

				53 (24.6%) for latent EBV. Thirty-three (15.3%) cases had primary HHV-6 infection, 63 (29.3%) active or reactivated HHV-6 infection, and 71 (33.9%) latent HHV-6. Double active EBV and HHV-6 infection, including primary and reactivated infections, amounted to 89 (39.5%) cases. Cytomegalovirus (CMV) antibody titers were found in 81 (37%) cases, 48 (22.3%) of which indicated latent infection and 33 (15.3%) active infection. Only two cases had evidence of active CMV infection alone, 1 cases of active CMV and HHV-6 infection. Serologic titers in 12 (5.6%) cases indicated combined active infection with CMV, EBV and HHV-6.(ABSTRACT TRUNCATED AT 250 WORDS)
Blakely AA, Howard RC, Sosich RM, Murdoch JC, Menkes DB, Spears GF.	Department of Psychological Medicine, Otago Medical School, University of Otago, Dunedin, New Zealand.	Psychiatric symptoms, personality and ways of coping in chronic fatigue syndrome.	Psychol Med 1991 May;21(2):347-62	This study aimed to investigate the psychological characteristics of chronic fatigue syndrome (CFS: Holmes et al. 1988). A battery of psychometric instruments comprising the General Health Questionnaire (GHQ), the Beck Depression Inventory (BDI), the Minnesota Multiphasic Personality Inventory (MMPI) and the Lazarus Ways of Coping (WoC) inventory, was administered to a sample of clinically-defined CFS sufferers (N = 58), to a comparison group of chronic pain (CP) patients (N = 81) and to a group of healthy controls matched for sex and age with the CFS sample (N = 104). Considerable overlap was found between CFS and CP patients at the level of both physical and psychological symptoms. This raises the possibility that CFS sufferers are a sub-population of CP patients. However, while there was some commonality between CFS and CP patients in terms of personality traits, particularly the MMPI 'neurotic triad' (hypochondriasis, depression and hysteria), CFS patients showed more deviant personality traits reflecting raised levels on the first MMPI factor, emotionality. Moreover, results were not consistent with the raised emotionality being a reaction to the illness, but rather were consistent with the hypothesis that emotionality is a predisposing factor for CFS. The majority of CFS patients fell within four personality types, each characterized by the two highest MMPI scale scores. One type (N = 20) reported a lack of psychological symptoms or emotional disturbance contrary to the overall trend for the CFS sample. This group conformed to the ICD-10 classification of neurasthenia.
Brancati FL.		Intravenous immunoglobulin treatment of chronic fatigue syndrome.	Am J Med 1991 Sep;91(3):320-1 comment on: Am J Med. 1990 Nov;89(5):551-3 Am J Med. 1990 Nov;89(5):561-8	
Brodsky CM.	Department of Psychiatry, School of Medicine, University of California, San	Depression and chronic fatigue in the workplace. Workers' compensation and	Prim Care 1991 Jun;18(2):381-96	There is ample evidence that some forms of depression can be caused or aggravated by work. The relationship of work and chronic fatigue syndrome is questionable, but elements at work can aggravate the symptoms of chronic fatigue syndrome. The role of physicians who can support or discourage beliefs

	Francisco.	occupational issues.		about physical illness is all important, both by what they say and how they treat. In the process of interaction, they can promote or discourage disability. The role of the physician in the workplace is to determine if an illness is work related, if it is disabling, if it requires treatment, and what treatment. The physician must advise if the worker can continue in his or her usual and customary employment and, if not, if he or she can be vocationally rehabilitated from a medical standpoint. Conditions in which physical symptoms are unsupported by physical findings and have diagnostic labels that describe the disorder without indicating either cause or pathology are especially troubling for the physician who must decide if the patient's job caused the symptoms.
Buchwald D, Komaroff AL.	Department of Medicine, Harborview Medical Center, University of Washington School of Medicine, Seattle.	Review of laboratory findings for patients with chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S12-8	Various abnormalities revealed by laboratory studies have been reported in adults with chronic fatigue syndrome. Those most consistently reported include depressed natural killer cell function and reduced numbers of natural killer cells; low levels of circulating immune complexes; low levels of several autoantibodies, particularly antinuclear antibodies and antithyroid antibodies; altered levels of immunoglobulins; abnormalities in number and function of lymphocytes; and modestly elevated levels of two Epstein-Barr virus-related antibodies, immunoglobulin G to viral capsid antigen and to early antigen.
Buchwald D, Wener MH, Komaroff AL.	University of Washington, Seattle, WA.	Anti-neuronal antibody levels in chronic fatigue syndrome patients with neurologic abnormalities.	Arthritis Rheum 1991 Nov;34(11):1485-6	
Butler S, Chalder T, Ron M, Wessely S.	Department of Psychiatry, National Hospital for Neurology and Neurosurgery, Queen Square, London, UK.	Cognitive behaviour therapy in chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1991 Feb;54(2):153-8	Fifty patients fulfilling operational criteria for the chronic fatigue syndrome (CFS), and who had been ill for a mean of five years, were offered cognitive behaviour therapy in an open trial. Those fulfilling operational criteria for depressive illness were also offered tricyclic antidepressants. The rationale was that a distinction be drawn between factors that precipitate the illness and those that perpetuate it. Among the latter are cognitive factors such as the belief that physical symptoms always imply tissue damage, and behavioural factors such as persistent avoidance of activities associated with an increase in symptoms. Therapy led to substantial improvements in overall disability, fatigue, somatic and psychiatric symptoms. The principal problems encountered were a high refusal rate and difficulties in treating affective disorders. Outcome depended more on the strength of the initial attribution of symptoms to exclusively physical causes, and was not influenced by length of illness. These results suggest that current views on both treatment and prognosis in CFS are unnecessarily pessimistic. It is also suggested that advice currently offered to chronic patients, to avoid physical and mental activity, is counterproductive.
Byrne E.	Neurology Department,	The chronic fatigue	Clin Exp Neurol	The chronic fatigue syndrome is one of the most common medical problems in

	St. Vincent's Hospital, Melbourne.	syndrome: a reappraisal and unifying hypothesis.	1991;28:128-38	Western countries. Research work in virology, immunology, metabolic medicine and psychiatry in this area is reviewed and a disease model proposed. The chronic fatigue syndrome can be considered as a continuum ranging from cases with chronic viraemia on the one hand to instances of frank psychiatric illness on the other. In the majority of patients the fully evolved syndrome may involve an interaction of premorbid factors (psychological, immunological), environmental trigger factors (virus) and enhancing factors (emotional response to illness). A Venn diagram is a convenient way of expressing this concept.
Cassel W, Archer-Duste H.		The new epidemic: chronic fatigue syndrome.	Pa Nurse 1991 Feb;46(2):8-9	
Chao CC, Janoff EN, Hu SX, Thomas K, Gallagher M, Tsang M, Peterson PK.	Department of Medicine, Hennepin County Medical Center, Minneapolis, MN 55415.	Altered cytokine release in peripheral blood mononuclear cell cultures from patients with the chronic fatigue syndrome.	Cytokine 1991 Jul;3(4):292-8	Chronic fatigue syndrome (CFS) is an idiopathic illness associated with a variety of immunologic abnormalities. To investigate potential pathogenetic mechanisms, we evaluated serum levels and peripheral blood mononuclear cell (PBMC) production of selected cytokines and immunoglobulins. Serum bioactive transforming growth factor beta (TGF-beta) levels were higher (P less than 0.01) in patients with CFS (290 +/- 46 pg/mL) than in control subjects (104 +/- 18 pg/mL), but levels of other cytokines tested were not different. Lipopolysaccharide-stimulated release of interleukin 1 beta (IL-1 beta), IL-6, and tumor necrosis factor-alpha was increased (P less than 0.05) in PBMC cultures from patients with CFS versus control subjects; enhanced (P less than 0.01) IL-6 release to phytohemagglutinin was also observed. In contrast, TGF-beta release in response to lipopolysaccharide was depressed (P less than 0.01) in PBMC cultures derived from patients with CFS. No differences in IL-2 and IL-4 or immunoglobulin production were observed. The enhanced release of inflammatory cytokines by stimulated PBMC from patients with CFS suggests that these cells are primed for an increased response to immune stimuli. These data also suggest an association between abnormal regulation of TGF-beta production in vivo and in vitro with the immunologic consequence of CFS.
Cluff LE.	Robert Wood Johnson Foundation, Princeton, New Jersey.	Medical aspects of delayed convalescence.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S138-40	Disease and illness are not synonymous. In most instances, disease is demonstrable by anatomic, physiologic, biochemical, microbiologic, or immunologic abnormalities. Disease is a pathologic process. Not all persons with a disease are sick or ill. Symptoms of illness associated with a disease may be manifest or persist after the disease has disappeared. The absence of demonstrable disease, however, does not necessarily mean that symptoms of illness are unreal. Recovery from disease and recovery from illness are not always equated. Many factors, including personal characteristics and social circumstances, can be responsible for recovery from disease and illness. Chronic fatigue syndrome or symptoms of illness can persist in some patients but not in others after many different diseases.

Collignon P.		Immunoglobulin treatment for chronic fatigue syndrome.	Am J Med 1991 Oct;91(4):443-4 comment on: Am J Med. 1990 Nov;89(5):561-8	
Comtois R.	Hopital Notre-Dame, Montreal, Quebec.	[Chronic fatigue: myth or reality]?[article in French]	Union Med Can 1991 Jan-Feb;120(1):10-6	Chronic fatigue is one of the most common complaints. However, it can be a vexing problem in clinical practice. In contrast to serum cholesterol or blood pressure, fatigue may seem immeasurable. The management of fatigue is often complicated by the uncertainty surrounding of its cause and the frequent lack of specific therapy. Recently, criteria were established for the diagnosis of chronic fatigue syndrome. This working case definition does provide some guidance for the practicing physician.
Cooke RG.		The psychiatrist and chronic fatigue syndrome.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:13-5	
Cotton P.		Treatment proposed for chronic fatigue syndrome; research continues to compile data on disorder.	JAMA 1991 Nov 20;266(19):2667-8	
Covington EC.	Department of Psychiatry, Cleveland Clinic Foundation, Ohio.	Depression and chronic fatigue in the patient with chronic pain.	Prim Care 1991 Jun;18(2):341-58	Chronic benign pain is commonly associated with chronic fatigue and depression. Depression and chronic fatigue syndrome are also associated with each other and often include pain. Psychologic factors are prominent in these conditions, and they may share neurobiologic factors as well. Management requires separately addressing each component of patients' distress and usually includes physical rehabilitation, education, administration of nonhabituating medications and often counseling. Depression may be a favorable prognostic sign, as it suggests a treatable condition and provides incentive for recovery.
Cox IM, Campbell MJ, Dowson D.	Medical School, University of Southampton, UK.	Red blood cell magnesium and chronic fatigue syndrome.	Lancet 1991 Mar 30;337(8744):757-60 comment in: Lancet. 1991 Jul 6;338(8758):66 Lancet. 1991 May 4;337(8749):1094-5 Lancet. 1991 Sep 7;338(8767):641 Lancet. 1992 Jul 11;340(8811):124-5	The hypotheses that patients with chronic fatigue syndrome (CFS) have low red blood cell magnesium and that magnesium treatment would improve the wellbeing of such patients were tested in a case-control study and a randomised, double-blind, placebo-controlled trial, respectively. In the case-control study, 20 patients with CFS had lower red cell magnesium concentrations than did 20 healthy control subjects matched for age, sex, and social class (difference 0.1 mmol/l, 95% confidence interval [CI] 0.05 to 0.15). In the clinical trial, 32 patients with CFS were randomly allocated either to intramuscular magnesium sulphate every week for 6 weeks (15 patients) or to placebo (17). Patients treated with magnesium claimed to have improved energy levels, better emotional state, and less pain, as judged by changes in the Nottingham health profile. 12 of the 15 treated patients said that they had benefited from treatment, and in 7 patients energy score improved from the maximum to the minimum. By contrast, 3 of the

				17 patients on placebo said that they felt better (difference 62%, 95% CI 35 to 90), and 1 patient had a better energy score. Red cell magnesium returned to normal in all patients on magnesium but in only 1 patient on placebo. The findings show that magnesium may have a role in CFS. Randomized Controlled Trial
Crowley JP.		Chronic fatigue syndrome.	R I Med J 1991 Jul;74(7):310-1	
Dale JK, Di Bisceglie AM, Hoofnagle JH, Straus SE.	Medical Virology Section, Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.	Chronic fatigue syndrome: lack of association with hepatitis C virus infection.	J Med Virol 1991 Jun;34(2):119-21	Chronic fatigue syndrome (CFS) is a debilitating heterogeneous disorder lacking consistent, objective physical or laboratory abnormalities. Among the hypothetical etiologies for CFS are chronic viral infections. The present controlled seroprevalence study found that, among typical CFS patients, evidence of hepatitis C virus (HCV) infection is uncommon. Only one of 36 patients and none of 14 controls were anti-HCV positive. The positive patient had persistent aminotransferase elevations and prior posttransfusion hepatitis. Thus HCV infection is not a common feature of CFS and should not be routinely sought.
Daugherty SA, Henry BE, Peterson DL, Swarts RL, Bastien S, Thomas RS.	Department of Family Medicine, University of Nevada School of Medicine, Reno 89557.	Chronic fatigue syndrome in northern Nevada.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S39-44	The clinical and laboratory findings from studies of patients with chronic fatigue syndrome (CFS) from northern Nevada are summarized. Physicians caring for these patients have estimated that greater than 400 patients with CFS from northern Nevada and nearby communities in California were identified between 1984 and 1988. As a result of these studies, a cluster of clinical and laboratory features associated with the illness in moderately to severely affected patients has been identified: profound fatigue of prolonged duration; cervical lymphadenopathy; recurrent sore throat and/or symptoms of influenza; loss of cognitive function manifested by loss of memory and loss of ability to concentrate; myalgia; impairment of fine motor skills; abnormal findings on magnetic resonance imaging brain scan; depressed level of antibody to Epstein-Barr virus (EBV) nuclear antigen; elevated level of antibody to EBV early antigen restricted component; elevated ratio of CD4 helper to CD8 suppressor cells; and strong evidence of association of this syndrome with infection with human herpesvirus 6. More-serious and longer-lasting neurologic impairments, including seizures, psychosis, and dementia, have also been observed in some of these patients.
David AS, Wessely S, Pelosi AJ.	King's College Hospital, London.	Chronic fatigue syndrome: signs of a new approach.	Br J Hosp Med 1991 Mar;45(3):158-63 comment in: Br J Hosp Med. 1991 Oct;46(4):270	Persistent media highlighting of the plight of patients suffering from severe fatigue of unknown cause (postviral fatigue syndrome or myalgic encephalomyelitis) has at last been matched by professional attention. Recent research has started to clarify the roles of infective, neuromuscular and psychiatric factors in the illness, but pathophysiological mechanisms remain obscure.
Demitrack MA, Dale JK,	Clinical	Evidence for impaired	J Clin Endocrinol Metab	Chronic fatigue syndrome is characterized by persistent or relapsing debilitating

Straus SE, Laue L, Listwak SJ, Kruesi MJ, Chrousos GP, Gold PW.	Neuroendocrinology Branch, National Institute of Mental Health, National Institutes of Health, Bethesda, Maryland.	activation of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome.	1991 Dec;73(6):1224-34	fatigue for at least 6 months in the absence of a medical diagnosis that would explain the clinical presentation. Because primary glucocorticoid deficiency states and affective disorders putatively associated with a deficiency of the arousal-producing neuropeptide CRH can be associated with similar symptoms, we report here a study of the functional integrity of the various components of the hypothalamic-pituitary-adrenal axis in patients meeting research case criteria for chronic fatigue syndrome. Thirty patients and 72 normal volunteers were studied. Basal activity of the hypothalamic-pituitary-adrenal axis was estimated by determinations of 24-h urinary free cortisol-excretion, evening basal plasma total and free cortisol concentrations, and the cortisol binding globulin-binding capacity. The adrenal cortex was evaluated indirectly by cortisol responses during ovine CRH (oCRH) stimulation testing and directly by cortisol responses to graded submaximal doses of ACTH. Plasma ACTH and cortisol responses to oCRH were employed as a direct measure of the functional integrity of the pituitary corticotroph cell. Central CRH secretion was assessed by measuring its level in cerebrospinal fluid. Compared to normal subjects, patients demonstrated significantly reduced basal evening glucocorticoid levels (89.0 +/- 8.7 vs. 148.4 +/- 20.3 nmol/L; P less than 0.01) and low 24-h urinary free cortisol excretion (122.7 +/- 8.9 vs. 203.1 +/- 10.7 nmol/24 h; P less than 0.0002), but elevated basal evening ACTH concentrations. There was increased adrenocortical sensitivity to ACTH, but a reduced maximal response [F(3.26, 65.16) = 5.50; P = 0.0015). Patients showed attenuated net integrated ACTH responses to oCRH (128.0 +/- 26.4 vs. 225.4 +/- 34.5 pmol/L.min, P less than 0.04). Cerebrospinal fluid CRH levels in patients were no different from control values (8.4 +/- 0.6 vs. 7.7 +/- 0.5 pmol/L; P = NS). Although we cannot definitively account for the etiology of the mild glucocorticoid deficiency seen in chronic fatigue syndrome patients, the enhanced adrenocortical sensitivity to exogenous ACTH and blunted ACTH responses to oCRH are incompatible with a primary adrenal insufficiency. A pituitary source is also unlikely, since basal evening plasma ACTH concentrations were elevated. Hence, the data are most compatible with a mild central adrenal insufficiency secondary to either a deficiency of CRH or some other central stimulus to the pituitary-adrenal axis. Whether a mild glucocorticoid deficiency or a putative deficiency of an arousal-producing neuropeptide such as CRH is related to the clinical symptomatology of the chronic fatigue syndrome remains to be determined.
Demitrack MA, Greden JF. Review Review, Tutorial		Chronic fatigue syndrome: the need for an integrative approach.	Biol Psychiatry 1991 Oct 15;30(8):747-52	
Deulofeu R, Gascon J, Gimenez N, Corachan		Magnesium and chronic fatigue syndrome.	Lancet 1991 Sep 7;338(8767):641	

M.			comment on: Lancet. 1991 Mar 30;337(8744):757-60	
Dille JR.		Chronic fatigue syndrome.	Aviat Space Environ Med 1991 Oct;62(10):1008-9	
Evans AS.	Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, Connecticut 06510.	Chronic fatigue syndrome: thoughts on pathogenesis.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S56-9	Studies have shown that a proportion of patients with severe chronic infection due to Epstein-Barr virus (EBV) lack antibody to a component of EBV nuclear antigen. However, it is not clear whether this circumstance is one of cause or effect in regard to the pathogenesis of chronic fatigue syndrome (CFS); it is clearly not pathognomonic since it also occurs in persons infected with the human immunodeficiency virus and--rarely--in those with other EBV-related conditions. Stress and depression may be other pathogenetic mechanisms that could reactivate EBV and lead to CFS; examples of this phenomenon are given. The syndrome might also follow certain other viral infections as part of a process that has been called postinfectious neurasthenia. Currently, the cause(s) and cure of CFS, a common and distressing syndrome, are enigmatic and require multidisciplinary study.
Fark AR.	Department of Family Medicine, Burns Clinic Medical Center, Michigan, Royne City, MI 49712.	Infectious mononucleosis, Epstein-Barr virus, and chronic fatigue syndrome: a prospective case series.	J Fam Pract 1991 Feb;32(2):202, 205-6, 209 comment in: J Fam Pract. 1991 May;32(5):456	Epstein-Barr viral infection, specifically infectious mononucleosis, typically has a more protracted course than other acute viral illnesses. Some recent observers have additionally suggested the possibility that Epstein-Barr virus (EBV) is the etiologic infectious agent in chronic fatigue syndrome, based on the finding of higher proportions of elevated antibodies to the EBV early antigen in some patients complaining of chronic fatigue. Straus et al reported on 23 patients with chronic fatigue, 83% of whom exhibited persistently elevated antibodies in modest titer to the early antigen. Ten of these patients had never fully recovered from an episode of acute infectious mononucleosis. Other studies had noted similar associations between persistently elevated antibodies to EBV-specific antigens and chronic symptoms in patients who presented with chronic symptoms after mononucleosis. Three important antigen complexes, demonstrable by immunofluorescence procedures, are expressed in EBV-infected cells. The early antigen is thought to function perhaps in early replication of viral DNA. A late antigenic complex, the viral capsid antigen, may represent, in addition to structural capsid proteins, components of the viral enzymatic machinery for late phases of replication or transformation. The Epstein-Barr nuclear antigen is felt to function in viral transformation of host cells.
Furman JM.	Department of Otolaryngology, University of Pittsburgh, Pennsylvania.	Testing of vestibular function: an adjunct in the assessment of chronic fatigue	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S109-11	Patients with chronic fatigue syndrome (CFS) often complain of dysequilibrium that is nonspecific. The basis of this complaint is unknown but may be related to vestibular system abnormalities, in that an association between inner-ear deficits and infectious mononucleosis has been established in the medical literature. An

		syndrome.		overview of quantitative vestibular function testing is given, including vestibulo-ocular and vestibulospinal tests. The basic principles of caloric and rotational testing are provided, including the interaction between vision and the vestibular system. Moving-platform posturography is described. Preliminary results from quantitative vestibular function testing of a small group of individuals with CFS are provided.
Goldenberg DL.	Newton-Wellesley Hospital, Newton, Massachusetts.	Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome.	Curr Opin Rheumatol 1991 Apr;3(2):247-58	There continues to be an emerging body of literature related to fibromyalgia and the related conditions chronic fatigue syndrome and myofascial pain. During the past year, the most notable contributions included a large multicenter study providing new diagnostic criteria for the classification of fibromyalgia and clinical studies describing the overlap of fibromyalgia, chronic fatigue syndrome, and myofascial pain. Pathophysiologic studies were often preliminary and uncontrolled but the focus of these studies on abnormal nociception, neurohormones, and muscle metabolism provides an exciting hypothesis to unify pain, fatigue, and sleep disturbances, the primary symptoms of fibromyalgia. Unfortunately, new therapeutic trials were neither innovative nor especially encouraging.
Gorensek MJ.	Department of Infectious Disease, Cleveland Clinic Florida, Ft. Lauderdale, Florida.	Chronic fatigue and depression in the ambulatory patient.	Prim Care 1991 Jun;18(2):397-419	Fatigue, pain, and emotional upset remain the most common problems affecting humanity and for which we still know so very little. Chronic fatigue syndrome is most likely a number of as yet unproven various undifferentiated illnesses that are exceedingly difficult to distinguish from depression. There probably is a subset of patients with CFS who do have true immune dysfunction and persistent viral infection, and this particular group of patients should be further investigated. This group is the minority of patients who present with chronic fatigue. Although chronic fatigue syndrome may be the result of an organic illness in psychologically susceptible individuals, it remains most important to assess underlying psychologic factors that then need to be addressed. These factors may very likely have a profound effect on immune function, but more research is needed in this area. The diagnostic evaluation of patients with chronic fatigue syndrome should initially focus on causes for fatigue other than Epstein-Barr viral infection. Significant underlying medical conditions should be ruled out, and extensive inquiry into symptoms suggestive of depression and anxiety should be aggressively pursued. Treatment should include psychiatric support and counseling, good nutrition, adequate rest, and a gradual increase in activity. Anti-inflammatory agents and serotonin-replenishing antidepressants are helpful when muscle pain and tenderness are a major part of the patient's symptoms. Psychoactive drugs are useful when indicated. Low doses of antidepressants such as doxepin (10-25 mg at night) are generally well tolerated and have shown efficacy in numerous patients, although there are no reports of controlled trials.
Goudsmit EM,		Chronic fatigue	Br J Gen Pract 1991	

Macintyre A, Sullivan M.		syndrome.	Nov;41(352):479-80 comment in: Br J Gen Pract. 1992 Jan;42(354):39-40 comment on: Br J Gen Pract. 1991 Aug;41(349):339-42	
Gracious B, Wisner KL.	Department of Psychiatry, University of Pittsburgh School of Medicine, PA 15213.	Nortriptyline in chronic fatigue syndrome: a double blind, placebo-controlled single case study.	Biol Psychiatry 1991 Aug 15;30(4):405-8	
Grafman J, Johnson R Jr, Scheffers M.	Cognitive Neuroscience Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892.	Cognitive and mood-state changes in patients with chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S45-52	In this paper the cognitive and psychiatric impairments associated with chronic fatigue syndrome (CFS) and related disorders are reviewed. It is concluded that while acute mononucleosis and infection with Epstein-Barr virus occasionally result in impaired cognition, such changes have not yet been objectively verified in patients with CFS. However, when patients with CFS are carefully studied, concurrent or premorbid psychiatric disorders are revealed at a greater than chance level. Finally, some suggestions are offered regarding improved neuropsychological assessment of fatigue, concentration, and attention for patients with CFS. The findings to date, while suggesting that psychological predisposition may play a role in the expression of CFS, are still inconclusive regarding the etiology of CFS.
Grufferman S.	Department of Clinical Epidemiology and Preventive Medicine, University of Pittsburgh School of Medicine, Pennsylvania 15261.	Issues and problems in the conduct of epidemiologic research on chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S60-7	The epidemiologic research approach is perhaps most appropriate for initial studies of chronic fatigue syndrome since the syndrome is vaguely defined, scientific knowledge about it is limited, and an infectious etiology is suspected. Several priority needs appropriate for epidemiologic research are identified, including a refinement of diagnostic criteria; a greater understanding of the natural history of the syndrome; basic incidence, prevalence, and mortality statistics; information on whether asymptomatic cases exist; etiologic studies of possible heterogeneity of cases; investigations of clusters of cases; and determinations of whether patients with the syndrome have an increased risk of malignancy. Because of the lack of cogent etiologic hypotheses regarding the syndrome, case-control studies are identified as a high priority for research. The many difficulties encountered in conducting such research are discussed and approaches to dealing with these problems are suggested.
Gupta S, Vayuvegula B.	Division of Basic and Clinical Immunology, University of California, Irvine 92717.	A comprehensive immunological analysis in chronic fatigue syndrome.	Scand J Immunol 1991 Mar;33(3):319-27	A detailed analysis of cell-mediated and antibody-mediated immunity was performed in 20 CDC-defined patients with chronic fatigue syndrome (CFS) and 20 age- and sex-matched healthy controls. CD3+, CD4+, CD8+, and CD20+ lymphocytes were comparable in two groups. Natural killer cells as defined by

				CD16, CD56 and CD57 antigens were significantly reduced in CFS. A significant increase in the proportions of CD4+ ICAM 1+ T cells was observed in CFS. Monocytes from CFS displayed increased density (as determined by mean fluorescence channel numbers) of intercellular adhesion molecule 1 (ICAM-1) and lymphocyte function associated antigen 1 (LFA-1), but showed decreased enhancing response to recombinant interferon-gamma in vitro. The lymphocyte DNA synthesis in response to phytohaemoglobulin (PHA), Concanavalin A (Con A) and pokeweed mitogen (PWM) was normal but the response to soluble antigens was significantly reduced. Serum IgM, IgG, IgA, and IgG subclasses were normal. In vivo specific antibody response to pneumococcus vaccine was depressed in CFS. Forty percent of patients showed titres of anti-human herpes virus 6 (anti-HHV-6) antibody higher than that in the controls (greater than or equal to 1/80). These data suggest immunological dysfunction in patients with chronic fatigue syndrome. The significance of these observations is discussed.
Hawton KE, Hengeveld MW.	Warneford Hospital, Psychiatrische Universiteitskliniek, Oxford, Engeland.	[Chronic fatigue syndrome; psychiatric aspects].[article in Dutch]	Ned Tijdschr Geneeskd 1991 Oct 26;135(43):2014-7	
Hayden SP.	Department of Internal Medicine, Cleveland Clinic Foundation, Ohio 44195.	A practical approach to chronic fatigue syndrome.	Cleve Clin J Med 1991 Mar-Apr;58(2):116-20	Chronic fatigue may have several physical causes, but a psychiatric condition is often involved. A substantial minority of patients are not diagnosed by conventional tests and do not respond to antidepressant therapy. These patients should be referred for psychiatric opinion or observed for new developments. Extensive virologic testing and unorthodox treatment approaches have no scientific basis at present. Claims of dramatic new diagnostic tests or therapy should be treated with caution because of the long history of unsuccessful attempts to categorize chronic fatigue into one diagnosis and the strong placebo effect shown in controlled trials.
Hick JF.		The etiology of chronic fatigue syndrome.	Minn Med 1991 Sep;74(9):7-8 comment on: Minn Med. 1991 May;74(5):21-6	
Hickie I, Lloyd A, Wakefield D.		Chronic fatigue syndrome and depression.	Lancet 1991 Apr 13;337(8746):922-3 comment on: Lancet. 1991 Jan 19;337(8734):160-2	
Hilgers A, Krueger GR, Lembke U, Ramon A.	International Institute of Immunopathology, Inc. Cologne, Washington, DC.	Postinfectious chronic fatigue syndrome: case history of thirty-five patients in Germany.	In Vivo 1991 May-Jun;5(3):201-5	Thirty-five patients with chronic fatigue syndrome according to the criteria of Holmes were followed for periods of up to eight years. The most frequent symptoms were severe fatigue, arthralgias and myalgias, recurrent oropharyngitis and various psychiatric disorders. More than half of the patients

				suffered from neuropathy, lymphadenopathy, gastrointestinal complaints and recurrent low-grade fever. Recurrent or persistent activity of human herpesvirus -6 infection was seen in 73% of the patients and of Epstein-Barr virus in 34.4%. In addition, various other infections were diagnosed at lower frequency. Initial routine immunologic screening revealed various types of deficiencies, these were yet inconsistent and variable when different patients were compared with each other. Tentative treatments included in immunoglobulins, nonspecific immunostimulation and virostatic drugs. No consistently positive results were obtained with any treatment schedule although immunoglobulins appeared the most efficient measure. In addition, psychologic care of the patients is indicated, since disturbances in the psycho-neuroimmunologic regulation may play a significant role in the pathogenesis of the disease.
Holmes GP.	Epidemiology Office, Centers for Disease Control, Atlanta, Georgia 30333.	Defining the chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S53-5	The recently published working definition of the chronic fatigue syndrome (CFS) is a necessary first step toward a consistent effort to research this controversial illness. Before this definition was developed, cases often were defined vaguely, according to the perceptions and biases of the individual researchers, so that the results of some studies were unclear. However, few specific diagnostic parameters for CFS exist, and the new definition may not delineate a single clinicopathologic entity. Future efforts at researching this illness should be aimed at identifying parameters that differentiate CFS from psychiatric conditions such as major depression and from other defined chronic diseases. Because CFS may be the result of multiple disease processes, the separate study of well-defined subgroups of patients with CFS is appropriate. Such subgroups of patients are probably more likely to have common pathogenetic features than are patients with CFS as a whole group.
Ho-Yen DO, McNamara I.	Raigmore Hospital, Inverness.	General practitioners' experience of the chronic fatigue syndrome.	Br J Gen Pract 1991 Aug;41(349):324-6 comment in: Br J Gen Pract. 1991 Nov;41(352):480	In order to examine the prevalence of patients with symptoms fulfilling the criteria for the chronic fatigue syndrome an extensive survey was carried out of general practitioners on 10 local government lists in two health boards (91% response rate). At the same time practitioners' attitudes to the syndrome and their experience in terms of workload and the characteristics of patients affected were documented. The majority of general practitioners (71%) accepted the existence of chronic fatigue syndrome, but 22% were undecided. The doctors reported a prevalence among their patients of 1.3 per 1000 patients (range 0.3-2.7 for the 10 areas) with a peak in the 30-44 years age group. Female patients were more commonly affected than males (sex ratio 1.8:1.0), but the severity of illness and the use of general practitioner's time was the same among male and female patients. Patients in occupations where they were exposed to infection were affected (teachers and students, 22% of sample; hospital workers, 7%), but many patients were unskilled (8%) and skilled workers (9%). Patients suffering from the chronic fatigue syndrome appear to be a real and distinct group for

				general practitioners and may represent a substantial part of the workload of doctors in particular areas.
Hyde BM.		Myalgic encephalomyelitis (chronic fatigue syndrome): an historic perspective.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:5-8	
Joncas JH.		Search for an association between Epstein-Barr virus infection and the chronic fatigue syndrome.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:43-7	
Jones JF, Streib J, Baker S, Herberger M.	Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.	Chronic fatigue syndrome: I. Epstein-Barr virus immune response and molecular epidemiology.	J Med Virol 1991 Mar;33(3):151-8	Patients with chronic fatigue syndrome were compared to healthy seropositive control subjects in an open study and a case-control study analyzing spontaneous transformation rates of peripheral blood lymphocytes, EBV viral genome characteristics as determined by DNA restriction fragment polymorphisms, and antibody production by Western blot analysis. Thirty percent of patients versus 8% of control subjects underwent spontaneous transformation in the two studies. Viral genome patterns were overall similar to one another, with polymorphisms frequently present in BamHI B', K, H, and Y fragments. Only one line was found with the EBNA-2B genotype. Nineteen lines were found to contain viral DNA in the linear form suggesting active lytic replication. Western blot studies suggested that ill subjects made antibodies to lytic proteins more frequently than did healthy control subjects. Lack of control of EBV outgrowth in vitro is correlated with antibody evidence of active infection in vivo in some patients with chronic fatigue syndrome.
Jones JF.	Department of Pediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.	Serologic and immunologic responses in chronic fatigue syndrome with emphasis on the Epstein-Barr virus.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S26-31	Although patients with chronic fatigue syndrome (CFS) can be diagnosed by clinical criteria, the lack of specific laboratory criteria delays or prevents the diagnosis and contributes to the quasi-disease status of the syndrome. A resurgence of interest in the syndrome has followed reports suggesting that CFS may be associated with chronic active infection due to the Epstein-Barr virus. Analysis of reports to date shows that the mean titers of antibodies to viral capsid antigen and to early antigen are greater for patients with CFS than for healthy individuals; this is particularly evident in cases for which serial samples were tested. However, these differences do not prove the cause of CFS. Cell-mediated immune responses in patients with CFS vary from study to study, and the number and function of natural killer cells in those patients are the most variable factors. Rates of isolation of virus from saliva do not differ, but in one comparison study with a large number of subjects, more lymphocytes that

				contained virus were isolated from patients than from controls. Other viruses, such as the Coxsackie B virus, have been implicated as causes of CFS in studies from Great Britain. The use of a working definition of CFS and standardized tests to address abnormalities revealed by laboratory tests among homogeneous populations should allow determination of useful tests for the diagnosis of CFS and studies of its mechanisms.
Josephs SF, Henry B, Balachandran N, Strayer D, Peterson D, Komaroff AL, Ablashi DV.		HHV-6 reactivation in chronic fatigue syndrome.	Lancet 1991 Jun 1;337(8753):1346-7	
Katon WJ, Buchwald DS, Simon GE, Russo JE, Mease PJ.	Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle 98195.	Psychiatric illness in patients with chronic fatigue and those with rheumatoid arthritis.	J Gen Intern Med 1991 Jul-Aug;6(4):277-85 comment in: J Gen Intern Med. 1991 Jul-Aug;6(4):378-9	OBJECTIVES: To identify psychiatric differences between patients with chronic fatigue and those with rheumatoid arthritis and to investigate whether patients meeting Centers for Disease Control (CDC) criteria for chronic fatigue syndrome (CFS) can be differentiated from patients with chronic fatigue on measures of disability and psychosocial distress. DESIGN: Cross-sectional study comparing 98 patients with chronic fatigue with 31 patients with rheumatoid arthritis on structured psychiatric interviews and patient questionnaires. Nineteen patients meeting CDC criteria for CFS were compared with 79 patients with chronic fatigue not meeting CDC criteria on questionnaires measuring disability and psychosocial distress. SETTING: Consecutive patients with chronic fatigue were selected from a chronic fatigue clinic at the University of Washington, and 31 consecutive patients with rheumatoid arthritis were sampled from a private rheumatology practice. MAIN RESULTS: Patients with chronic fatigue had a significantly higher prevalence of lifetime major depression and somatization disorder than did patients with rheumatoid arthritis. Patients with chronic fatigue also had a significantly higher prevalence of current and lifetime psychiatric diagnoses. Only 19 of 98 patients with chronic fatigue met CDC criteria for CFS. Patients meeting CDC criteria for CFS could not be differentiated from the larger group of patients with chronic fatigue on any study variable. CONCLUSIONS: Patients with chronic fatigue have a significantly higher burden of psychiatric illness than do patients with rheumatoid arthritis. The psychiatric illness preceded the development of chronic fatigue in over half the patients. Centers for Disease Control criteria for CFS did not select a subset of chronic fatigue patients who could be differentiated on disability or psychosocial parameters from patients with chronic fatigue who did not meet CDC criteria.
Komaroff AL, Buchwald D.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School,	Symptoms and signs of chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S8-11	This review summarizes the symptoms and signs seen in patients with chronic fatigue syndrome (CFS). It is based on the authors' experience with two cohorts of approximately 510 patients with chronic debilitating fatigue and on the reported experience of other investigators with similar patients. The most

	Boston, Massachusetts 02115.			characteristic symptoms of CFS are the sudden onset of an infectious-type illness, the subsequent chronic and debilitating fatigue, and postexertional malaise; many patients also have recurrent fevers, pharyngitis, adenopathy, myalgias, sleep disorders, and cognitive impairment.
Kroenke K.	Department of Medicine, Uniformed Services University of Health Sciences, Bethesda, MD 20814.	Chronic fatigue syndrome: is it real?	Postgrad Med 1991 Feb 1;89(2):44-6, 49-50, 53-5 comment in: Postgrad Med. 1991 Nov 15;90(7):23-4	Epstein-Barr virus is no longer considered an important cause of chronic fatigue syndrome. Instead, the disease is probably related to an underlying psychiatric disorder, subtle immunologic dysfunction, or an interaction between these two factors. A carefully taken history, physical examination, and simple laboratory testing are usually sufficient to establish the diagnosis. Therapy with antidepressants or nonsteroidal anti-inflammatory drugs may be effective in selected patients. Thorough follow-up conducted with empathy and optimism is important in all cases.
Krueger GR, Ablashi DV, Josephs SF, Salahuddin SZ, Lembke U, Ramon A, Bertram G.	Immunopathology Laboratory, University of Cologne, F.R.G.	Clinical indications and diagnostic techniques of human herpesvirus-6 (HHV-6) infection.	In Vivo 1991 May-Jun;5(3):287-95	The sixth member of the human herpesvirus family, HHV-6, causes early childhood infection with subsequent latency and antibody prevalence of about 60-80%. Active infection is related to a number of acute and chronic diseases such as exanthem subitum, certain cases of infectious mononucleosis and other immunoproliferative syndromes, autoimmune disorders and so-called postinfectious chronic fatigue syndrome. The clinical diagnosis of HHV-6 associated diseases requires detailed clinical differential diagnostic procedures and meticulous serological testing with exclusion of other herpesvirus infections or cross-reactivity between such infections. Diagnostic efforts, however, are warranted by certain indications for therapeutic intervention. The current review summarizes indications, techniques and limitations for the serological diagnosis of HHV-6 infection.
Krupp LB, Mendelson WB, Friedman R.	Department of Neurology, State University of New York, Stony Brook 11794.	An overview of chronic fatigue syndrome.	J Clin Psychiatry 1991 Oct;52(10):403-10 comment in: J Clin Psychiatry. 1992 Aug;53(8):296	BACKGROUND: Psychological and immunologic factors both appear to contribute to chronic fatigue syndrome (CFS). By comparing CFS with other disorders in which fatigue is a prominent symptom, the association between fatigue, psychological vulnerability, depression, and immune function may be further defined. Recent data from psychological, neurologic, and immunologic studies that address these issues are reviewed. METHOD: Articles and abstracts covering CFS and related topics of fatigue, depression, and postinfectious syndromes were identified through MEDLINE and Index Medicus (1980-1990) and by bibliographic review of pertinent review articles. RESULTS: The 1988 definition of CFS by the Centers for Disease Control encompasses several conditions in which the major characteristic is severe fatigue associated with constitutional symptoms. Several studies have identified immune dysfunction in CFS patients, but the specificity of these findings remains unclear. Most studies have shown that CFS patients, compared with other patients with chronic medical illness, experience more disabling fatigue. Some investigators have found a higher incidence of concurrent and past psychiatric illness in CFS patients compared with other medical patients,

				thereby suggesting an underlying psychopathology in CFS. However, other studies have not found a higher than expected incidence of past depression in CFS patients and have further shown that many CFS patients have no identifiable psychopathology. CONCLUSION: CFS appears to be a heterogenous entity. Although there may be a high coincidence of major depression in CFS, a substantial proportion of patients lack any identifiable DSM-III-R psychiatric disorder yet still manifest the syndrome, thereby suggesting it has an autonomous entity. Despite the evolving nature of our current understanding of CFS, a rational diagnostic and therapeutic approach to CFS is possible.
Kulig JW.		Chronic Fatigue Syndrome and Fibromyalgia in Adolescence.	Adolesc Med 1991 Oct;2(3):473-484	A complaint of persistent, debilitating fatigue in an adolescent, accompanied by symptoms that meet the recently adopted criteria for chronic fatigue syndrome (CFS), presents a difficult challenge for the clinician. This article describes the diagnostic criteria for CFS and fibromyalgia, and discusses the epidemiology, etiology, and management of these conditions.
Kundu SK, Ahronheim GA, Menezes J.		Immunodysregulation and chronic fatigue syndrome.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:49-50	
Kutemeyer M.		[Comments on the review by Wilfrid A. Nix. Chronic fatigue syndrome--a new disease picture]?[article in German]	Nervenarzt 1991 Jan;62(1):64-6	
Lam RW.	Department of Psychiatry, University of British Columbia, Vancouver.	Seasonal affective disorder presenting as chronic fatigue syndrome.	Can J Psychiatry 1991 Nov;36(9):680-2	Although operational criteria have been recently proposed to better define chronic fatigue syndrome (CFS), it remains a controversial diagnosis. There are many overlapping symptoms between CFS and major depression. The author presents two patients with seasonal affective disorder, who responded to phototherapy and had previously been diagnosed as CFS. Because of the consequences of treatment, seasonal and non seasonal depression need to be ruled out in patients with chronic fatigue symptoms.
Landay AL, Jessop C, Lennette ET, Levy JA.	Department of Immunology/Microbiology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois.	Chronic fatigue syndrome: clinical condition associated with immune activation.	Lancet 1991 Sep 21;338(8769):707-12	There is much conflicting immunological and viral data about the causes of chronic fatigue syndrome (CFS); some findings support the notion that CFS may be due to one or more immune disorders that have resulted from exposure to an infectious agent. In the present study, flow cytometry and several different monoclonal antibodies recognising T, B, and natural killer (NK) cell populations as well as activation and cell adhesion antigens were used to study 147 individuals with CFS. Compared with healthy controls, a reduced CD8 suppressor cell population and increased activation markers (CD38, HLA-DR) on CD8 cells were found. The differences were significant ($p = 0.01$) in patient with major symptoms of the disease. These immunological indices were not observed in 80 healthy

				individuals, in 22 contacts of CFS patients, or in 43 patients with other diseases. No correlation of these findings in CFS patients with any known human viruses could be detected by serology. The findings suggest that immune activation is associated with many cases of CFS.
Lane TJ, Manu P, Matthews DA.	Department of Medicine, University of Connecticut School of Medicine, Farmington 06032.	Depression and somatization in the chronic fatigue syndrome.	Am J Med 1991 Oct;91(4):335-44 comment in: Am J Med. 1992 Jun;92(6):710 Am J Med. 1994 May;96(5):485-6	PURPOSE: To report the prevalence, clinical features, and diagnostic associations of the proposed chronic fatigue syndrome (CFS) in a cohort of patients with chronic fatigue and to assess the usefulness of a structured psychiatric interview for detecting previously unrecognized psychiatric morbidity in patients with CFS. PATIENTS AND METHODS: A consecutive sample of 200 adult patients with a chief complaint of chronic fatigue was prospectively evaluated in a referral-based clinic within a university general medicine practice. All patients received a thorough medical history, physical examination, diagnostic laboratory testing, and portions of the Diagnostic Interview Schedule, version III-A. The criteria for CFS were applied, and patients with CFS were compared with matched control subjects from the inception cohort. RESULTS: The 60 patients with CFS had similar likelihoods of current psychiatric disorders (78% versus 82%), active mood disorders (73% versus 77%), and preexisting psychiatric disorders (42% versus 43%) when compared with fatigued control subjects. Patients with CFS were more likely to have somatization disorder (p less than 0.001) and to attribute their illness to a physical cause (p less than 0.005) than fatigued controls. Patients with CFS also displayed functional symptoms, often lifelong, which are not part of the case definition of CFS. Depressive features in patients with CFS were similar to those of control subjects, but a trend toward suicidal behavior was noted. CONCLUSIONS: Patients with CFS have a high prevalence of unrecognized, current psychiatric disorders, which often predate their fatigue syndrome. Assessment of patients with CFS should include a structured psychiatric evaluation.
Leventhal LJ, Naides SJ, Freundlich B.	Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia.	Fibromyalgia and parvovirus infection.	Arthritis Rheum 1991 Oct;34(10):1319-24	An infectious cause of fibromyalgia (FM) has been hypothesized based upon the observed similarity of this entity and chronic fatigue syndrome. Three patients developed symptoms of FM after documented episodes of acute parvovirus B19 infections. B19 antibody determinations were obtained approximately 1 month after the symptoms began; both IgM and IgG titers were positive at that time. All 3 patients met criteria for FM. Polysomnography performed on 2 of the patients revealed profound alpha-wave intrusion throughout nonrapid eye movement sleep. A more careful search for viral infections in FM patients whose symptoms appear following a "flu-like" illness appears warranted.
Lewis SF, Haller RG.	Department of Physiology, University of Texas Southwestern Medical Center, Dallas.	Physiologic measurement of exercise and fatigue with special reference	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S98-108	Oxidative metabolism is the major source of energy for muscle activity, and maximal oxygen uptake (VO2max), the product of maximal cardiac output and maximal arteriovenous oxygen difference, indicates individual capacity for oxidative metabolism and performance of exercise by the large muscles.

		to chronic fatigue syndrome.		Strength, a function of muscle cross-sectional area, motor-unit recruitment, and neuromuscular coordination, is the ability to develop force in a single, brief, maximal-effort voluntary contraction of rested muscle. Weakness is a diminished ability of rested muscle to exert maximal force. Fatigue is a loss of maximal force-generating capacity that develops during muscular activity, likely originates within muscle itself, and persists until muscle is fully recovered. Individual perception of motor effort can be determined with standardized rating scales. These concepts are discussed in detail, their relevance to the pathophysiology of exercise in chronic fatigue syndrome is analyzed, and a general strategy of exercise evaluation pertinent to chronic fatigue syndrome is presented.
Lloyd A, Hickie I, Brockman A, Dwyer J, Wakefield D.		Cytokine levels in serum and cerebrospinal fluid in patients with chronic fatigue syndrome and control subjects.	J Infect Dis 1991 Nov;164(5):1023-4	
Lloyd AR, Gandevia SC, Hales JP.	Department of Clinical Neurophysiology, Prince Henry Hospital, Sydney, Australia.	Muscle performance, voluntary activation, twitch properties and perceived effort in normal subjects and patients with the chronic fatigue syndrome.	Brain 1991 Feb;114 (Pt 1A):85-98	The decrease in maximal force-generating capacity, the degree of central activation of the muscle, and the subjective perception of effort were measured during prolonged submaximal isometric exercise in 12 male patients suffering from the 'chronic fatigue syndrome' and 13 naive, healthy male subjects. Maximal voluntary isometric torque generated by the elbow flexors was measured before, and at 5 min intervals during an endurance sequence of 45 min of repetitive isometric contractions (6 s duration, 4 s rest interval) producing 30% of the initial maximal voluntary torque. Electrical stimuli were also delivered to the elbow flexors to measure the contractile force in the intervals between voluntary contractions. The degree of central motor activation during maximal voluntary contractions was assessed using a sensitive method of twitch interpolation. In addition, the perceived effort required to achieve the target submaximal contractions was recorded using a standardized self-report scale. A high degree of central activation was achieved in maximal contractions during the endurance sequence both in the patients (mean of maximal force 93.6%; SD 7.8%), and in the control subjects (mean 90.9%; SD 9.5%). The relative torque produced by either voluntary or electrically stimulated contractions was not significantly different between patients and control subjects throughout the test. There was no significant difference in the perceived exertion between the patients and control subjects. These findings support the concept that neither poor motivation, nor muscle contractile failure is important in the pathogenesis of 'fatigue' in patients with the chronic fatigue syndrome.
Lopis R.		A personal encounter with a mystery illness.	Aust Fam Physician 1991 Mar;20(3):316-7	I urge all practitioners to accept that 'chronic fatigue' patients have genuine symptoms. This disease can cause depression, but for most patients it is not caused by depression. I acknowledge that a depressed patient can develop the

				chronic fatigue syndrome in the same way that they can contract any other disease. If you are unable to diagnose a patient with these symptoms please refer them to a centre specialising in this devastating and poorly understood disease.
Lynch S, Main J, Seth R.		Definition of chronic fatigue syndrome (CFS)	Br J Psychiatry 1991 Sep;159:439-40 comment in: Br J Psychiatry. 1992 Jan;160:127-8 comment on: Br J Psychiatry. 1991 May;158:717	
Lynch S, Seth R, Montgomery S.	St Mary's Hospital Medical School, London.	Antidepressant therapy in the chronic fatigue syndrome.	Br J Gen Pract 1991 Aug;41(349):339-42 comment in: Br J Gen Pract. 1991 Nov;41(352):479-80 Br J Gen Pract. 1991 Nov;41(352):480	The chronic fatigue syndrome is a condition receiving increasing recognition. Symptoms of depression are not infrequent and may be persistent and severe enough to warrant treatment. The controversy over the use of antidepressant therapy in this condition may present a dilemma for the general practitioner considering possible treatments. This paper draws on the literature and on the authors' own observations of patients with the chronic fatigue syndrome to suggest guidelines for the use of antidepressant therapy.
Malleson PN.	Research Centre, University of British Columbia, Vancouver, Canada.	Pain syndromes, disability, and chronic disease in childhood.	Curr Opin Rheumatol 1991 Oct;3(5):860-6	Childhood disability and chronic disease are common, and their prevalence is increasing as children survive with conditions that were previously fatal. It is important that physicians in training learn about disability and handicap, and the functioning of multidisciplinary teams to manage these problems. Chronic ill-health is often very expensive to manage, and some serious and creative thinking about the best way to fund such health care is urgently needed. Pediatric rheumatologists are involved with the care of many children with chronic and recurrent musculoskeletal pain; however, they have not perhaps focused enough research effort on the investigation of pain and its management. Whether reflex neurovascular dystrophy, fibromyalgia, and chronic fatigue syndrome are part of a disease continuum is unclear, but it seems probable that psychosocial problems are often important contributing factors in all three conditions. Immunoglobulin subclass deficiencies are being increasingly delineated, occurring in chronic fatigue syndrome as well as many other disease states. Their clinical relevance still remains, for the most part, uncertain. Short stature occurs in many chronic illnesses, and the role of growth hormone treatment in these conditions is beginning to be investigated.
Mantysaari M.		Aerobic work capacity in chronic fatigue syndrome.	BMJ 1991 Jan 5;302(6767):50 comment on: BMJ. 1990 Oct 27;301(6758):953-6	
Matthews DA, Lane TJ, Manu P.	Division of General Medicine, University of	Antibodies to Epstein-Barr virus in patients	South Med J 1991 Jul;84(7):832-40	To clarify the role of Epstein-Barr virus (EBV) infection and the value of EBV antibody testing in evaluating patients with chronic fatigue, we studied 200

	Connecticut School of Medicine, Farmington.	with chronic fatigue.		consecutive patients with chronic fatigue (mean duration, 9 years). Complete EBV serologic panels were obtained for 154 patients, 35 (23%) of whom met serologic or clinical criteria for chronic or reactivated EBV infection. We compared these patients with chronic EBV infection (CEBV cases) to 35 age- and sex-matched patients who were selected from the same cohort of fatigued patients but who did not meet the criteria (CEBV control subjects). We found few differences between groups in demographic characteristics, clinical features, and symptoms; CEBV cases were more likely to meet criteria for the proposed chronic fatigue syndrome (14% vs 0%), and to report that they suffered from an influenza-like illness at the onset of their fatigue syndrome (34% vs 12%), that they lost their job because of their fatigue (37% vs 11%), and that their fatigue was improved by recreational activity (26% vs 3%). Physical examination and laboratory testing showed few abnormalities in either group. Psychiatric morbidity was common in both groups, including mood disorders (63% of CEBV cases vs 54% of CEBV controls), anxiety (11% vs 9%) and somatization disorder (9% in each group). We conclude that EBV serologic patterns have little clinical usefulness in evaluating patients with chronic fatigue.
Matthews DA, Manu P, Lane TJ.	Division of General Medicine, University of Connecticut Health Center, Farmington 06030.	Evaluation and management of patients with chronic fatigue.	Am J Med Sci 1991 Nov;302(5):269-77	Chronic fatigue is a common and disabling problem in primary care practice. The differential diagnosis of chronic fatigue is extensive and includes medical disorders, altered physiologic states (eg, pregnancy, exertion), psychiatric disorders, lifestyle derangements, drugs, and controversial entities (eg, chronic candidiasis, food allergies, environmental illness, and chronic fatigue syndrome). The most common diagnoses are psychiatric disorders, including mood, anxiety, and somatoform disorders. A comprehensive approach to diagnosis and management is necessary, including structured psychiatric interviewing, functional assessment, and elicitation of the patient's diagnostic beliefs. Patients often believe they are suffering from an organic medical disorder (eg, viral or immunologic) and resist psychiatric labelling of their symptoms and referral to mental health practitioners. Establishing and maintaining rapport, having a flexible approach, and demonstrating a personal concern for the patient is essential. Drug therapy for specific psychiatric and medical illnesses and cognitive-behavioral approaches for enhancing coping mechanisms are effective.
McBride SJ, McCluskey DR.	Department of Immunology, Queen's University & Royal Victoria Hospital, Belfast, UK.	Treatment of chronic fatigue syndrome.	Br Med Bull 1991 Oct;47(4):895-907	Chronic Fatigue Syndrome is a disorder which is characterised by profound fatigue together with a variety of other subjective clinical features which persist over a prolonged period of time. The aetiology remains at present uncertain and therefore rational therapeutic strategies are difficult to plan. This paper reviews currently used forms of treatment aimed at correcting the possible pathophysiological mechanisms and discusses the problems associated with the management of this condition.
McLaughlin B.		Virology laboratory	Can Dis Wkly Rep 1991	

		diagnosis of chronic fatigue syndrome.	Jan;17 Suppl 1E:51-5	
Meadows LM, Walther P, Ozer H.	Division of Medical Oncology, School of Medicine, University of North Carolina, Chapel Hill.	alpha-Interferon and 5-fluorouracil: possible mechanisms of antitumor action.	Semin Oncol 1991 Oct;18(5 Suppl 7):71-6	We have treated 17 patients with 5-fluorouracil (5-FU, 300 mg/m2/d by continuous ambulatory infusion for 8 weeks) and interferon alfa-2b (escalating doses to cohorts of three to five patients, given subcutaneously on a daily schedule at 2.0, 3.5, 5.0, and 10.0 x 10(6) IU/m2). The two major toxicities observed were mucositis, which occurred in 10 patients at 2 weeks and required interruption of therapy and 5-FU dose reduction, and chronic fatigue syndrome, which required reduction of the dose of interferon alfa-2b. Other toxicities seen included elevation in BUN/creatinine, elevation in liver function tests, alopecia, diarrhea, confusion, and myelosuppression. No toxic deaths occurred. Five responses were observed: two complete responses, two partial responses, and one minor response, all in patients with gastrointestinal malignancy; three of the responding patients had previously failed 5-FU-containing regimens. When we measured 5-FU plasma levels in nine of our patients, they were at or below 1 ng/mL in most patients; however, within 1 hour of administration of interferon alfa-2b, plasma levels rose 16-fold. This elevation of 5-FU levels persisted for at least 24 hours, and could not be accounted for on the basis of altered interleukin-6 levels. When the regimen was tested in eight patients with metastatic renal cell carcinoma as part of a pilot study, three partial responses were observed, and no patient developed disease progression while on treatment. The combination of 5-FU, given by continuous infusion, and interferon alfa-2b, given daily, appears worthy of advancement to phase II trials.
Menezes J, Ablashi DV.		Avenues for research in chronic fatigue syndrome etiology.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:65-6	
Middleton D, Savage DA, Smith DG.	Northern Ireland Tissue Typing Service, City Hospital, Belfast.	No association of HLA class II antigens in chronic fatigue syndrome.	Dis Markers 1991 Jan-Feb;9(1):47-9	
Mildon CA.		Clinical observations of chronic fatigue syndrome.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:17-9	
Miller G.	Department of Pediatrics, Yale University School of Medicine, New Haven, Connecticut 06510.	Molecular approaches to epidemiologic evaluation of viruses as risk factors for patients who have chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S119-22	One approach to understanding the chronic fatigue syndrome might be to carry out prospective studies of fatigue that occurs following infection with viral diseases of known etiology, such as influenza, hepatitis, and infectious mononucleosis. Among the viral parameters that should be evaluated are virus burden, variation of virus strain, sites of viral replication, and the state of the viral life cycle (e.g., latent or replicative). Immunologic studies should focus on the humoral and cellular responses to defined viral gene products to identify subtle,

				individual variations in immune recognition of specific viral subcomponents.
Miller JH.		Chronic fatigue syndrome and invalid pensions.	Med J Aust 1991 Feb 18;154(4):293	
Milton JD, Clements GB, Edwards RH.	Department of Medicine, University of Liverpool, UK.	Immune responsiveness in chronic fatigue syndrome.	Postgrad Med J 1991 Jun;67(788):532-7 comment in: Postgrad Med J. 1992 Jan;68(795):66-7	We have endeavoured to find immunological indications of chronic virus infection in patients with chronic fatigue syndrome (myalgic encephalomyelitis) and to investigate immune responsiveness to viruses in such patients in comparison with normal subjects and patients with muscular dystrophy. Levels of circulating IgM immune complexes were elevated (above the 95% normal control range) in 10 (17%) of 58 patients with chronic fatigue syndrome, which was not significantly different from the normal controls or from dystrophy controls (by Mann Whitney U test). Levels of IgG complexes were only increased in 10% of patients. Lymphocyte proliferation in response to concanavalin A (Con A), assessed by increase in 3H-thymidine incorporation, did not differ between 14 patients and 18 normal subjects. The proliferative response to Coxsackie B virus antigen did not differ between chronic fatigue patients and normal subjects when expressed either as an increase in counts or as a stimulation index. Adjustment of the counts in relation to the proliferation response to Con A, as an indication of the overall proliferative response of the cell preparation, did not reveal any hidden difference. IgM antibodies to Coxsackie B viruses were not found in any of 20 patients and in 1 of 20 dystrophy controls. Significant levels of neutralizing antibodies to Coxsackie B viruses 1-5 were found in 6 out of 19 (32%) patients compared with 4 out of 17 (24%) dystrophy controls, which does not differ from currently expected normal incidence. Antibody titres to other respiratory viruses were also not notably different between the patient and control groups.(ABSTRACT TRUNCATED AT 250 WORDS)
Munitz H, Hermesh H.		[Chronic fatigue syndrome, clinical significance].[article in Hebrew]	Harefuah 1991 Feb 1;120(3):164-5	
Murray RS.		Myth of the chronic fatigue syndrome.	West J Med 1991 Jul;155(1):68	
Pagano JS.	Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill 27599-2975.	Detection of Epstein-Barr virus with molecular hybridization techniques.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S123-8	The cord-blood transformation assay remains the standard method for detecting Epstein-Barr virus (EBV) in secretions. However, newer methods are much faster and more sensitive, although most are still regarded as research procedures. The most useful of these are Southern blot hybridization, particularly the variation that employs terminal genomic probe analysis; in situ cytohybridization; and polymerase chain reaction analyses. Use of these methods alone or in combination should disclose the infected cell type, whether the infection is productive or latent, and the presence of multiple strains of EBV. Such

				information may help establish whether EBV is a causal agent in chronic fatigue syndrome.
Peterson PK, Schenck CH, Sherman R.	Department of Medicine, Hennepin County Medical Center, Minneapolis.	Chronic fatigue syndrome in Minnesota.	Minn Med 1991 May;74(5):21-6 comment in: Minn Med. 1991 Sep;74(9):7-8	Chronic fatigue syndrome (CFS), an illness characterized by debilitating fatigue and a number of associated symptoms, was identified in 135 patients using the case definition provided in 1988. The demographic features of these patients, 97% of whom resided in Minnesota, were similar to those reported elsewhere. About three-fourths of the cases occurred between 1984 and 1989, and in 123 (91.1%), the illness began with what appeared to be an acute infection. Patients had been ill for an average of 4.3 years before enrollment in the study. Fatigue was their most troublesome symptom, although a majority of the patients rated most of the general symptoms and neuropsychological complaints associated with CFS as moderate or severe. Follow-up data obtained on 62 patients one year after initial evaluation revealed that none had completely recovered. However, about 40% reported some improvement in each of the CFS symptoms.
Plummer WP.		Chronic fatigue syndrome.	Br J Gen Pract 1991 Nov;41(352):480 comment on: Br J Gen Pract. 1991 Aug;41(349):324-6	
Pope HG Jr, Hudson JI.	McLean Hospital, Belmont, Massachusetts.	A supplemental interview for forms of "affective spectrum disorder".	Int J Psychiatry Med 1991;21(3):205-32	OBJECTIVE: Recent evidence suggests that a number of psychiatric and medical conditions may be members or candidate members of a larger family of conditions, which we have termed "affective spectrum disorder (ASD)." In order to facilitate further research into this concept, we drafted seven interview modules, using the format of the Structured Clinical Interview for DSM-III-R (SCID), designed to diagnose the following psychiatric and medical disorders: irritable bowel syndrome, narcolepsy, Tourette's disorder, migraine, fibromyalgia, chronic fatigue syndrome, and kleptomania. METHOD: Published operational diagnostic criteria for these seven disorders were sought in the literature. Questions in SCID format were then drafted in accordance with these operational criteria. Draft modules were then sent to experts familiar with each of the disorders and suggestions and revisions from these experts incorporated into the final modules. RESULTS: The complete supplemental interview is presented with this report. Preliminary experience with this interview in more than 100 patients tentatively suggests that it is reliable for diagnosing the disorders in question; however, a formal test-retest reliability assessment is still required. CONCLUSIONS: It is hoped that this supplemental interview, used in conjunction with the SCID, will be helpful in further studies of the epidemiology, pathogenesis, and treatment of these possible forms of affective spectrum disorder.
Purtilo DT.		Dual infections of the	Can Dis Wkly Rep 1991	The etiologic bases of CFS are undetermined at the present time. It is very

		immune system in patients with chronic active Epstein-Barr virus infection mimicking chronic fatigue syndrome.	Jan;17 Suppl 1E:29-32	important to distinguish the patients with CFS as defined by the Centers for Disease Control (CDC) case definition of Holmes et al. from patients with physical and laboratory findings suggesting dual infections and/or underlying immunodeficiency. Particularly fruitful might be a longitudinal immunovirologic study of patients who exhibit CFS following a well-documented viral infection.
Radvila A.	Medizinische Universitatspoliklinik, Inselspital, Bern.	[Intense fatigue in humans. Psychosocial and cultural aspects].[article in German]	Ther Umsch 1991 Nov;48(11):756-61	A differentiation between the normal sensation of tiredness and the symptom "fatigue" is often difficult. Both are influenced by cultural, social, psychological and biological factors, which can lead--interactively--to symptom formation. Psychiatric disorders frequently associated with fatigue are all forms of depression, somatization and anxiety disorders, chronic pain states and drug abuse among many others. In at least 2/3 of patients with the fashionable chronic fatigue syndrome--formerly called neurasthenia--a psychiatric diagnosis can be made, most of them also suffer from many symptoms attributes to the autonomous nervous system. The clinical approach should be cautious avoiding diagnostic and therapeutic overaction and therapy should emerge from a diagnosis properly assessed.
Rand KH.	University of Florida College of Medicine.	Chronic fatigue syndrome: fact or fiction.	Med Sect Proc 1991;:135-44	
Ray C. Review Review, Tutorial		Chronic fatigue syndrome and depression: conceptual and methodological ambiguities.	Psychol Med 1991 Feb;21(1):1-9	
Redmond CK.	Department of Biostatistics, University of Pittsburgh, Pennsylvania 15261.	Analysis of clinical, epidemiologic, and laboratory data on chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S90-3	Much of the research conducted on chronic fatigue syndrome (CFS) is exploratory. The researchers' overall goal is to use clinical, epidemiologic, and laboratory data to provide clues about the etiology of this syndrome. In preparation for this symposium, a review of numerous publications on CFS has indicated that the literature generally does not reflect the application of optimal statistical methods for exploration of data. Whenever the researchers' aim is to generate hypotheses, modern methods designed specifically for exploratory data analysis are likely to provide greater insights into any patterns of data than are the traditional approaches to hypothesis testing. In addition, the use of formal methods of data synthesis for ongoing and future research on CFS is a means of strengthening collaborative efforts and of improving the ability of researchers to interpret the evidence available that relates to specific etiologic factors. The inclusion on the research team of experienced biostatisticians, who would oversee the statistical methods and the development of innovative analyses, is recommended.

Salit IE, Abbey SE, Moldofsky H, Ichise M, Garfinkel PE.		Post-infectious neuromyasthenia (chronic fatigue syndrome): a summary of ongoing studies.	Can Dis Wkly Rep 1991 Jan;17 Suppl 1E:9-12	
Schiraldi O.		[Comments on the "chronic fatigue syndrome"].[article in Italian]	Recenti Prog Med 1991 May;82(5):305	
Schulte PA.	National Institute for Occupational Safety and Health, Centers for Disease Control, Cincinnati, Ohio 45226.	Validation of biologic markers for use in research on chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S87-9	Unresolved aspects of chronic fatigue syndrome can be addressed by research involving biologic markers. These may be any molecular, biochemical, physiological, or other biologic parameter obtainable from biologic specimens. The use of biologic markers in research requires their validation as dependent or independent variables. Additionally, other characteristics of markers such as reliability of assays, background level, confounding factors, interpretations, and legal and ethical implications should be considered before the use of markers in research. A checklist is provided for evaluating a biologic marker before its inclusion in research.
Serra E.		Chronic fatigue syndrome.	Br J Psychiatry 1991 May;158:717 comment in: Br J Psychiatry. 1991 Sep;159:439-40 comment on: Br J Psychiatry. 1990 Apr;156:534-40	
Shafran SD.	Division of Infectious Diseases, Walter C. MacKenzie Health Sciences Centre, University of Alberta, Edmonton, Canada.	The chronic fatigue syndrome	Am J Med 1991 Jun;90(6):730-9.	The chronic fatigue syndrome (CFS) was formally defined in 1988 to describe disabling fatigue of at least 6 months' duration of uncertain etiology. Reports of CFS have emerged from the United States, Canada, the United Kingdom, Australia, New Zealand, Israel, Spain, and France. The disease primarily affects individuals between 20 and 50 years of age, and there is a preponderance of females. Although a triggering infectious illness is reported by most patients with CFS, there is no convincing evidence causally linking any currently recognized infectious agent to CFS. Multiple minor immunologic aberrations are frequent but inconsistent and of uncertain significance. There is no consistent evidence for myopathy or physical deconditioning. Depression is found in approximately 50% of CFS patients, with depression preceding the physical symptoms in half of the cases. No therapy has been proved effective in controlled clinical trials with prolonged follow-up, although antidepressants have not been formally evaluated. The long-term prognosis of patients with CFS has not been well studied, but CFS appears to be a disease of prolonged duration with considerable

				morbidity but no mortality. Further research into the pathogenesis and treatment of CFS is necessary.
Sharpe MC, Johnson BA, McCann J.	Warneford Hospital, Oxford.	Mania and recovery from chronic fatigue syndrome.	J R Soc Med 1991 Jan;84(1):51-2	
Simpson LO.		Red cells in the chronic fatigue syndrome.	Med J Aust 1991 Jun 3;154(11):783	
Smalley RV, Anderson SA, Tuttle RL, Connors J, Thurmond LM, Huang A, Castle K, Magers C, Whisnant JK.	University of Wisconsin, Madison.	A randomized comparison of two doses of human lymphoblastoid interferon-alpha in hairy cell leukemia. Wellcome HCL Study Group.	Blood 1991 Dec 15;78(12):3133-41	One hundred thirty-eight patients with hairy cell leukemia were randomized to receive either a dose of 2.0 megaunits (MU)/m2 or a 10-fold lower dose of 0.2 MU/m2 of a highly purified natural alpha-interferon, administered daily for 28 days followed by a three times a week schedule. Ninety-seven of these patients had previously undergone splenectomy, but otherwise none of the patients had received prior therapy for their leukemia. The two doses were comparable in their effect on improving the neutrophil and platelet count, whereas the higher dose had a greater beneficial effect on the hemoglobin level and a greater antileukemic effect on the marrow. Acute toxicity in the form of a flu-like syndrome, neurologic side effects, neutropenia, and the need for platelet transfusions was observed less frequently in the low-dose group, as was the chronic fatigue syndrome. No neutralizing antibody activity was seen in the sera from 61 patients examined. Because of its beneficial effect on the neutrophil and platelet count and a lower degree of toxicity (ie, a superior therapeutic/toxicity ratio), the low dose is recommended as initial therapy in patients with hairy cell leukemia. This therapy may be followed by dose escalation once clinical improvement is observed. Randomized Controlled Trial
Smith JL.	Bascom Palmer Eye Institute, University of Miami School of Medicine, Florida.	Neuro-ocular Lyme borreliosis.	Neurol Clin 1991 Feb;9(1):35-53	Any patient who has a Bell's palsy (unilateral or bilateral), aseptic meningitis, chronic fatigue syndrome, atypical radiculoneuropathy, presenile dementia, atypical myopathy, or symptoms of atypical rheumatoid arthritis should be asked specifically about the following: visits to highly endemic areas, any known tick bites, any skin lesion suggestive of erythema migrans, any history of palpitations or of prior Bell's palsy, aching in joints (especially the knees), paresthesias, chronic fatigue and depression, forgetfulness, and eye problems. Any patient showing a chronic iritis with posterior synechiae, vitritis in one or both eyes, an atypical pars planitis-like syndrome, big blind spot syndrome, and swollen or hyperemic optic discs should be asked the same questions. The physician should send one red-top tube of blood containing 2 to 3 ml serum to Microbiology Reference Laboratory, 10703 Progress Way, Cypress, CA 90630-4714, requesting a Lyme/treponemal panel. For $90 the patient will receive an RPR test with titer, serum FTA-ABS test, serum Lyme IFA IgG and IgM, and a serum Lyme ELISA test. If these tests are within normal limits and the physician is still suspicious, a Western blot can be ordered on serum. A green top tube with fresh white blood

				cells sent out by overnight express on a Monday or Tuesday will produce a Lyme PCR and a lymphocyte stimulation test. Finally, R.K. Porschen, director of MRL Laboratory, will provide information on the urine antigen test on an investigational basis. A careful history with emphasis on the specific questions noted above, a complete neuro-ophthalmological and physical examination ruling out other causative problems, and the laboratory studies here discussed will usually provide sufficient data to choose therapy. Much further active research into Lyme borreliosis is an important priority in medicine.
Stern K.		Chronic fatigue syndrome. New disease on the horizon.	J Dent Hyg 1991 Jan;65(1):39-41	
Straus SE.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.	History of chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S2-7	Chronic fatigue syndrome is not a new medical condition. For centuries its confusing array of features has been attributed to numerous environmental, metabolic, infectious, immunologic, and psychiatric disturbances. This is a review and critique of many of these alternative diagnoses, sufficient to provide a historical background for current thinking about the disorder.
Strickland MC.	Department of Psychiatry, Cleveland Clinic Florida, Ft. Lauderdale, Florida.	Depression, chronic fatigue syndrome, and the adolescent.	Prim Care 1991 Jun;18(2):259-70	To summarize, CFS and depression present very real problems for adolescent patients, their families, and their physicians. The wealth of symptoms presented may signal the presence of any number of psychiatric or physiologic disorders. As part of the evaluation to rule out other maladies, the physician must identify the developmental issues and life stress events with which patients or their families are struggling. Helping patients to accept psychiatric referral to address these issues is indicated if it is thought that they may be contributing to the onset or maintenance of the symptoms. Referral is also indicated if a protracted clinical course evolves and the patient's normal course of growth and development appears to be in jeopardy.
Sumaya CV.	Department of Pediatrics, University of Texas Health Science Center, San Antonio.	Serologic and virologic epidemiology of Epstein-Barr virus: relevance to chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S19-25	Patients considered to have chronic fatigue syndrome (CFS) have been reported to exhibit an increased antibody response to Epstein-Barr virus (EBV) early antigen complex and capsid antigen, findings that suggest some relationship between EBV and CFS. However, the serologic findings have not been totally consistent among different study groups, and the antibody patterns in asymptomatic individuals may be similar. Moreover, patients with symptomatology indicative of CFS do not appear to have an abnormal burden of EBV in body fluids and manifest only a variable, mild degree of EBV-specific cell-mediated responses. The evidence is growing that the serologic findings of an enhanced EBV state in individuals with CFS-like manifestations, as well as the subsequent reports of increased antibody titers to other viruses, reflect a generalized underlying immunologic dysfunction in these patients. Future studies

				with criteria-defined CFS study groups in which determinations are made of antibody responses to newly identified EBV-associated nuclear antigen components and distinct EBV proteins in addition to specific virologic and immunologic analyses of EBV may be worthwhile as a means of clarifying the association between EBV and CFS.
Swanink CM, Galama JM, Vercoulen JH, Bleijenberg G, Fennis JF, van der Meer JW.	Instituut Medische Microbiologie, Academisch Ziekenhuis St Radboud, Nijmegen.	[Chronic fatigue syndrome. I. Somatological hypothesis].[article in Dutch]	Ned Tijdschr Geneeskd 1991 Oct 26;135(43):2005-9 comment in: Ned Tijdschr Geneeskd. 1991 Dec 7;135(49):2347-9 Ned Tijdschr Geneeskd. 1992 Jan 18;136(3):148	
Tavris DE.	Pennsylvania Department of Health.	Criteria for chronic fatigue syndrome.	Pa Med 1991 Jul;94(7):34	
Thase ME.	Department of Psychiatry, University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, Pennsylvania 15213.	Assessment of depression in patients with chronic fatigue syndrome.	Rev Infect Dis 1991 Jan-Feb;13 Suppl 1:S114-8	Assessment of the relationship of depression to chronic fatigue syndrome (CFS) is a complicated but important topic. This relationship may range from the misdiagnostic (i.e., depression misidentified as CFS) to the etiologic (i.e., CFS causes an organic affective syndrome). Assessment should focus on the symptoms and syndromes of depressive disorder, utilization of a single rating scale to assess presumed depression is discouraged, and alternate approaches to classification that allow for symptomatic overlap of a major depressive disorder and CFS are suggested. Careful attention needs to be given to the use of external validating criteria in empiric studies, such as natural history, clinical course (including treatment response), and family history.
Vercoulen JH, Swanink CM, Galama JM, Fennis JF, van der Meer JW, Bleijenberg G.	Afd. Medische Psychologie, Academisch Ziekenhuis St Radboud, Nijmegen.	[Chronic fatigue syndrome. II. Psychosocial hypothesis].[article in Dutch]	Ned Tijdschr Geneeskd 1991 Oct 26;135(43):2010-4	
Wachsmuth JR, MacMillan HL.	Department of Psychiatry, Hospital for Sick Children, Toronto, Ontario, Canada.	Effective treatment for an adolescent with chronic fatigue syndrome.	Clin Pediatr (Phila) 1991 Aug;30(8):488-90	
Wemm KM Jr, Trestman RL.		The effects of a laboratory stressor on natural killer cell function in chronic fatigue syndrome patients.	Psychosomatics 1991 Fall;32(4):470-1	

Wessely S. Review Review, Tutorial		Chronic fatigue syndrome.	J Neurol Neurosurg Psychiatry 1991 Aug;54(8):669-71 comment in: J Neurol Neurosurg Psychiatry. 1992 Jan;55(1):85	
Wood GC, Bentall RP, Gopfert M, Edwards RH.	Department of Medicine, Royal Liverpool Hospital.	A comparative psychiatric assessment of patients with chronic fatigue syndrome and muscle disease.	Psychol Med 1991 Aug;21(3):619-28	The psychiatric status of patients with chronic fatigue syndrome (N = 34) and muscle disease (N = 24) attending a general medical clinic was studied. Among fatigue patients 14 (41.2%) were cases and a further 9 (26.5%) were subcases of psychiatric disorder as defined by CATEGO. A variety of diagnoses was found. Significantly fewer of the muscle patients had a psychiatric disorder with 3 (12.5%) being cases and 1 (4%) a subcase. The relative risk of psychiatric disorder in patients with chronic fatigue syndrome compared to patients with muscle disease was 3.3:1.
Woods TO, Goldberg DP.	Mental Illness Research Unit, University of Manchester, UK.	Psychiatric perspectives: an overview.	Br Med Bull 1991 Oct;47(4):908-18	This chapter reviews the evidence concerning the importance of psychological and social factors in the aetiology and pathogenesis of chronic fatigue syndrome. The diagnosis is often offered to doctors by patients; and we consider attribution, stigma, collusion between doctor and patient, and abnormal illness behaviour in this context. We then give a brief description of a model for common mental disorders, and show how chronic fatigue syndrome relates to this model. It emerges that there are special vulnerability factors in these patients' personalities before the viral illness, but the disorder is seen as being released by the viral illness. By the time the disorder becomes established the original causal nexus is seen as no longer so important, and the disorder can be seen as a form of abnormal illness behaviour maintained by special factors. The implications for treatment are then considered.
Wylie B.		Muscle versus brain: chronic fatigue syndrome.	Med J Aust 1991 Feb 4;154(3):220 comment on: Med J Aust. 1990 Nov 5;153(9):530-4	
Wysenbeek AJ, Shapira Y, Leibovici L.	Department of Medicine B, Beilinson Medical Center, Petah Tiqva, Israel.	Primary fibromyalgia and the chronic fatigue syndrome.	Rheumatol Int 1991;10(6):227-9	Thirty-three primary fibromyalgia patients were investigated for chronic fatigue syndrome symptoms. Significant fatigue was reported by 21/33 patients (63.6%), and patients reported various flulike symptoms, yet only 7/33 patients (21.2%) fulfilled criteria for the chronic fatigue syndrome. Only one patient reported painful lymph glands and four patients reported fever. Thus, symptoms of painful glands or fever might serve as clinical indicators, distinguishing between fibromyalgia and the chronic fatigue syndrome.
Yeomans JD, Conway SP.	Department of Psychiatry, St Jame's University Hospital,	Biopsychosocial aspects of chronic fatigue syndrome (myalgic	J Infect 1991 Nov;23(3):263-9	Fifteen patients, with a primary complaint of chronic fatigue, were referred to a physician by their general practitioners. Psychological distress, measured by simple psychiatric rating scales was common, but specific psychiatric diagnoses,

	Leeds, U.K.	encephalomyelitis).		derived from a comprehensive diagnostic interview, occurred less frequently. One questionnaire (Montgomery-Asberg depression rating scale) found emotional distress in 93%, but the diagnostic instrument (Present State Examination) suggested depressive syndromes in only two patients (13%). There were significant occupational difficulties in 87%. No consistently abnormal indices of biochemical or immunological function were found, nor evidence of acute or chronic infection. Chronic fatigue syndrome (CFS) is associated with physical, psychological and social distress. The illness cannot be defined using just one of these dimensions. Such a unilateral approach has resulted in unnecessary controversy over the nature of the 'real' core of CFS. A problem-oriented approach, recognising the multi-factorial and overlapping cause and effect issues in CFS, may be of more benefit to patients.

1988-90				
Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Abbey SE, Garfinkel PE.	Toronto Hospital, Toronto General Division, Ontario.	Chronic fatigue syndrome and the psychiatrist.	Can J Psychiatry 1990 Oct;35(7):625-33	The number of patients who are identified as having chronic fatigue syndrome (CFS) has increased, and as a result, chronic fatigue syndrome has received widespread attention. Research has demonstrated that cognitive, affective and behavioural symptoms are prominent in CFS. Psychiatrists are therefore being asked to participate in the assessment and management of patients with this syndrome. This paper will provide an overview of the clinical characteristics of CFS and the current empirical findings related to its pathology, and will conclude with a discussion of the management of these patients. Publication Types: Review Review, Tutorial
Ablashi DV, Josephs SF, Buchbinder A, Hellman K, Nakamura S, Llana T, Lusso P, Kaplan M, Dahlberg J, Memon S, et al.	Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, MD.	Human B-lymphotropic virus (human herpesvirus-6).	J Virol Methods 1988 Sep;21(1-4):29-48	Human B-lymphotropic virus (HBLV), also known as human herpesvirus-6 (HHV-6) was first isolated in 1986 from AIDS patients and patients with other lymphoproliferative disorders. HBLV is distinct from known human herpesviruses, biologically, immunologically and by molecular analysis. HBLV can infect and replicate in fresh and established lines of hemopoietic cells and cells of neural origin, suggesting wide tropism. The prevalence of HBLV antibody in the normal population was 26% though clear differences between different populations were observed. The prevalence of HBLV antibody an elevated antibody titer was higher in sera from certain malignancies, Sjogren's syndrome and sarcoidosis. Antibody to HBLV was also elevated in AIDS patients and patients with chronic fatigue syndrome. HBLV-DNA was detected in some B-cell lymphomas. The broad in vitro tropism, combined with immunological and molecular evidence of HBLV infection in individuals raise the question of the pathogenicity of this virus in some diseases. Because in vitro co-infection of CD4 cells by HBLV and HIV leads to enhanced degeneration, this raises the possibility that infection in AIDS patients by both viruses can aggravate the HIV-induced immunodeficiency. Specific reagents and immunological and molecular assays are currently being investigated, which will aid in virus detection in cells from patients, and in elucidating the possible pathogenesis of HBLV.
Ablashi DV, Lusso P, Hung CL, Salahuddin SZ, Josephs SF, Llana T, Kramarsky B, Biberfeld P, Markham PD, Gallo RC.	Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, MD 20892.	Utilization of human hematopoietic cell lines for the propagation and characterization of HBLV (human herpesvirus 6).	Int J Cancer 1988 Nov 15;42(5):787-91	Details of the productive infection of established human cell lines of diverse origin by HBLV (also designated Human Herpesvirus 6) are described in this report. The infection and replication of HBLV in several T and B lymphoid and other cell lines was observed by electron microscopic examination, by the detection of viral antigen expression by indirect immunofluorescence assay (IFA) and by the presence of HBLV DNA by Southern blot hybridization. Several of these cell lines produced large amounts of virus. For this reason and because of the absence of other human herpesviruses, these lines have provided a valuable resource for the preparation of reagents and the development of assays for the detection and characterization of HBLV. The isolation and characterization of new

				HBLV isolates from patients with chronic fatigue syndrome were also facilitated by using some of the cell lines reported here. The host range of HBLV in established cell lines, therefore, does not appear to be limited to the B lymphocytes, as initially suggested by in vivo studies. The infection of T and B lymphocytes, megakaryocytes and neuronal cells in vitro suggests a need for the evaluation of diverse hematological and neurological disorders to shed light on a possible HBLV involvement.
Adolphe AB.		Chronic fatigue syndrome: possible effective treatment with nifedipine.	Am J Med 1988 Dec;85(6):892	
Altay HT, Toner BB, Brooker H, Abbey SE, Salit IE, Garfinkel PE.	Department of Psychology, York University, Ontario, Canada.	The neuropsychological dimensions of postinfectious neuromyasthenia (chronic fatigue syndrome): a preliminary report.	Int J Psychiatry Med 1990;20(2):141-9	Postinfectious neuromyasthenia (PIN) is a clinical syndrome of protracted and incomplete recovery after an apparent viral-like illness. Medical investigation yields few abnormalities which might account for the symptomatology. A substantial number of PIN patients complain of cognitive changes. Specific complaints include impaired attention, concentration and abstraction skills. This study was designed to systematically investigate whether the aforementioned subjective complaints could be quantified objectively using standard neuropsychological instruments. Results indicated that on all tests but one, the subjects' performances were significantly higher than those of their age matched groups in the normative data. Specifically, PIN patients scored significantly better than their age matched norms on tests of concentration, attention and abstraction. What is most striking is the discrepancy between the subjective complaints of cognitive impairment and the objective results of the subjects' performances on all tests. These findings suggest that psychological factors may play an important role in the cognitive functioning of individuals diagnosed with postinfectious neuromyasthenia.
Anon		Immunological abnormalities in the chronic fatigue syndrome.	Med J Aust 1990 Jan 1;152(1):50-2 comment on: Med J Aust. 1989 Aug 7;151(3):122-4	
Anon		Life insurance MDs sceptical when chronic fatigue syndrome diagnosed.	CMAJ 1990 Dec 15;143(12):1283-6 comment on: Can Med Assoc J. 1990 Sep 1;143(5):413-5	
Anon		Chronic fatigue syndrome.	Br J Psychiatry 1990 Sep;157:447-50 comment on: Br J Psychiatry. 1990	

			Apr;156:534-40	
Anon		[Chronic infection caused by Epstein-Barr virus and chronic fatigue syndrome].[article in Spanish]	Med Clin (Barc) 1990 Mar 3;94(8):315-6 comment on: Med Clin (Barc). 1989 Apr 29;92(16):619-22	
Anon		Acyclovir treatment of the chronic fatigue syndrome.	N Engl J Med 1989 Jul 20;321(3):187-9 Erratum in: N Engl J Med 1989 Oct 12;321(15):1057 comment on: N Engl J Med. 1988 Dec 29;319(26):1726-8	
Anon		Chronic fatigue syndrome [correction]	CMAJ 1989 Apr 15;140(8):897	
Anon		The Epstein-Barr virus and chronic fatigue syndrome.	JAMA 1989 Mar 3;261(9):1277-8 comment on: JAMA. 1988 Aug 19;260(7):971-3	
Anon		Chronic fatigue syndrome.	CMAJ 1989 Feb 15;140(4):361, 364 Erratum in: Can Med Assoc J 1989 Apr 15;140(8):897	
Anon		"The chronic fatigue syndrome".	Ann Intern Med 1988 Jul 15;109(2):166-7	
Bennett RM.	Division of Arthritis and Rheumatic Diseases, Oregon Health Sciences University, Portland 97201.	Confounding features of the fibromyalgia syndrome: a current perspective of differential diagnosis.	J Rheumatol Suppl 1989 Nov;19:58-61	Patients eventually diagnosed as having the fibromyalgia syndrome often have symptoms which suggest alternate diagnoses such as peripheral neuropathy, spondylitis, metabolic myopathy, polymyalgia, early rheumatoid arthritis, early systemic lupus erythematosus or a chronic fatigue syndrome. Delay in diagnosis of fibromyalgia often proves costly and frustrating to the patient and may lead to inappropriate therapy.
Berends GM, Peeters MF, Lepoutre JM, van Liebergen FJ, Kurstjens RM, Koolen MI.		[Chronic fatigue syndrome; is there a connection with the Epstein-Barr virus]?[article in Dutch]	Ned Tijdschr Geneeskd 1988 May 7;132(19):874-8	
Bosse D, Ades EW.	Biological Products	Immunotherapy and	J Clin Lab Immunol 1989	We examined the ability of in vitro addition of Interleukin-2 (IL-2) to differentially

	Branch, Centers for Disease Control, Atlanta, GA 30333.	enhanced antibody-dependent cell-mediated cytotoxicity using virally-infected target cells.	Jul;29(3):109-10	enhance antibody-dependent cell mediated cytotoxicity (ADCC) utilizing cultured Epstein-Barr virus infected cells and gammaglobulin (Sandoglobulin). We found significant enhancement of ADCC when IL-2 was added. Chronic Epstein-Barr virus or Chronic Fatigue Syndrome patients in a therapeutic gammaglobulin program may benefit from IL-2 given in vivo.
Bradley CA.		Psychiatric diagnoses and chronic fatigue syndrome.	J Clin Psychiatry 1990 Feb;51(2):86 comment on: J Clin Psychiatry. 1989 Feb;50(2):53-6	
Buchwald D, Sullivan JL, Leddy S, Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Boston 02115.	"Chronic Epstein-Barr virus infection" syndrome and polymyalgia rheumatica.	J Rheumatol 1988 Mar;15(3):479-82 comment in: J Rheumatol. 1989 Mar;16(3):414-5	Twenty-three patients with polymyalgia rheumatica (PMR) followed in an academic rheumatology practice frequently reported symptoms commonly found in the recently described "chronic fatigue syndrome" or "chronic Epstein-Barr infection syndrome." These symptoms persisted for months after treatment had reduced the severity of the myalgias and lowered the sedimentation rate: periodically disabling fatigue (33%), recurrent pharyngitis (30%), sleep disorder (65%) and arthralgias (70%). However, antibody titers to Epstein-Barr virus in the patients with PMR were not significantly different from those in age and sex matched control subjects.
Camps Bansell J, Prieto Valtuena J.		[Chronic fatigue syndrome].[article in Spanish]	An Med Interna 1990 Oct;7(10):497-9	
Cassel W, Archer-Duste H.		The new epidemic: chronic fatigue syndrome.	1631: Calif Nurse 1989 Apr;85(4):6-7	
Chao CC, Gallagher M, Phair J, Peterson PK.		Serum neopterin and interleukin-6 levels in chronic fatigue syndrome.	J Infect Dis 1990 Dec;162(6):1412-3	
Cheney PR, Dorman SE, Bell DS.		Interleukin-2 and the chronic fatigue syndrome.	Ann Intern Med 1989 Feb 15;110(4):321	
Coulter P.		Chronic fatigue syndrome: an old virus with a new diagnosis.	J Community Health Nurs 1988;5(2):87-95	
Cunningham L, Bowles NE, Lane RJ, Dubowitz V, Archard LC.	Department of Biochemistry, Charing Cross and Westminster Medical School, London, U.K.	Persistence of enteroviral RNA in chronic fatigue syndrome is associated with the abnormal production of equal	J Gen Virol 1990 Jun;71 (Pt 6):1399-402	A subgenomic restriction fragment from cDNA prepared from Coxsackie B2 virus (CVB2) RNA was subcloned into a riboprobe vector allowing the production of enteroviral group-specific RNA probes complementary to either the positive (genomic) or negative (template) strand of enteroviral RNA. These riboprobes were used to follow productive infection of cultured cells by CVB2; as expected, positive strand RNA was synthesized in approximately 100-fold excess over

		amounts of positive and negative strands of enteroviral RNA.		negative strand. RNA was extracted from muscle biopsy samples from patients with chronic fatigue syndrome and probed for the presence of enteroviral RNA. In cases where enteroviral RNA was detected the amounts of positive and negative strands of enteroviral RNA were approximately equal, in contrast to the situation in lytic infection of cultured cells. This suggests that enterovirus persistence in muscle is due to a defect in control of viral RNA synthesis.
Dale JK, Straus SE, Ablashi DV, Salahuddin ZS, Gallo RC, Nishibe Y, Inoue YK.		The Inoue-Melnick virus, human herpesvirus type 6, and the chronic fatigue syndrome.	Ann Intern Med 1989 Jan 1;110(1):92-3	
David A, Pelosi A, McDonald E, Stephens D, Ledger D, Rathbone R, Mann A.	Section of Epidemiology and General Practice, Institute of Psychiatry, London.	Tired, weak, or in need of rest: fatigue among general practice attenders.	BMJ 1990 Nov 24;301(6762):1199-202 comment in: BMJ. 1991 Jan 19;302(6769):181 BMJ. 1991 Jan 5;302(6767):50	OBJECTIVES--To determine the prevalence and associations of symptoms of fatigue. DESIGN--Questionnaire survey. SETTING--London general practice. PARTICIPANTS--611 General practice attenders. MAIN OUTCOME MEASURES--Scores on a fatigue questionnaire and reasons given for fatigue. RESULTS--10.2% Of men (17/167) and 10.6% of women (47/444) had substantial fatigue for one month or more. Age, occupation, and marital status exerted minor effects. Subjects attributed fatigue equally to physical and non-physical causes. Physical ill health, including viral infection, was associated with more severe fatigue. Women rather than men blamed family responsibilities for their fatigue. The profile of persistent fatigue did not differ from that of short duration. Only one person met criteria for the chronic fatigue syndrome. CONCLUSIONS--Fatigue is a common complaint among general practice attenders and can be severe. Patients may attribute this to physical, psychological, and social stress.
Denman AM.	Division of Immunological Medicine, Northwick Park Hospital, Harrow, Middlesex, UK.	The chronic fatigue syndrome: a return to common sense.	Postgrad Med J 1990 Jul;66(777):499-501	
Ewig S, Dengler HJ.	Medizinische Klinik der Universitat Bonn.	[Chronic fatigue syndrome].[article in German]	Klin Wochenschr 1990 Aug 17;68(16):789-96	Reports on conditions of chronic fatigue associated with other somatopsychic symptoms after acute viral infections have led to the hypothesis of a "chronic fatigue syndrome" (CFS). Historical disease descriptions, like e.g. "myalgic encephalomyelitits", were updated by means of modern virological diagnostic techniques and data analysis. Several viral agents like enteroviruses, Epstein-Barr virus, Human-Herpesvirus 6 and other herpesviruses have been implicated for possible underlying infections. A preliminary disease definition by the Center for Disease Control (CDC) seeks to provide a rational basis for further etiological studies. In fact, there is growing consensus that the syndrome comprises various separate disease entities and causative agents. Today we can tentatively differentiate a "chronic mononucleosis" after infection with Epstein-Barr virus, an etiologically undetermined "postviral fatigue syndrome" and a fatigue syndrome

				of the myalgic type after Coxsackie-B virus infection. Furthermore, a valid diagnosis of CFS must be based on the exclusion of defined other diseases and the awareness of dealing with a hypothetical concept. As a result, current knowledge does not yet allow specific therapeutic recommendations.
Gantz NM, Holmes GP.	University of Massachusetts Medical Center, Worcester.	Treatment of patients with chronic fatigue syndrome.	Drugs 1989 Dec;38(6):855-62	
Gin W, Christiansen FT, Peter JB.	Department of Clinical Immunology, Queen Elizabeth II Medical Centre, Nedlands.	Immune function and the chronic fatigue syndrome.	Med J Aust 1989 Aug 7;151(3):117-8	
Goldenberg DL, Simms RW, Geiger A, Komaroff AL.	Arthritis-Fibrositis Center, Newton-Wellesley Hospital, MA 02162.	High frequency of fibromyalgia in patients with chronic fatigue seen in a primary care practice.	Arthritis Rheum 1990 Mar;33(3):381-7	We administered a standardized history questionnaire and performed a tender point examination on 27 patients with debilitating fatigue of at least 6 months duration, seen in a primary care practice, as well as on 20 patients with fibromyalgia. Sixteen of the 27 patients with chronic fatigue met the full criteria for the working case definition of chronic fatigue syndrome (CFS). Eight patients with chronic fatigue denied having any current persistent, diffuse musculoskeletal pain, and their tender point scores were similar to those in 10 normal control subjects. In contrast, 19 patients with chronic fatigue (70%) had persistent, diffuse musculoskeletal pain. The results of their tender point examinations were similar to those of the patients with fibromyalgia. Thus, the majority of these patients with debilitating chronic fatigue, including those who met criteria for CFS, met the historical and tender point diagnostic criteria for fibromyalgia. The presence of current musculoskeletal pain will identify those CFS patients who have fibromyalgia.
Goldenberg DL.	Newton-Wellesley Hospital, Department of Medicine, Tufts University School of Medicine, MA 02162.	Fibromyalgia and its relation to chronic fatigue syndrome, viral illness and immune abnormalities.	J Rheumatol Suppl 1989 Nov;19:91-3	Fibromyalgia and chronic fatigue syndrome have similar clinical and demographic features. We found that most patients with chronic fatigue syndrome have a tender point examination similar to patients with fibromyalgia. Similar pathophysiologic mechanisms are also being explored in each syndrome, including a potential role for viral induced immune dysfunction.
Goodnick PJ.		Bupropion in chronic fatigue syndrome.	Am J Psychiatry 1990 Aug;147(8):1091	
Goodwin SD, Sproat TT, Russell WL.	College of Pharmacy, University of Florida, Gainesville.	Management of Lyme disease.	Clin Pharm 1990 Mar;9(3):192-205	The microbiology, transmission, epidemiology, pathogenesis, clinical manifestations, diagnosis, and treatment of Lyme disease are reviewed. Lyme disease, a tick-borne syndrome, was first described in 1975. The etiologic agent of Lyme disease is Borrelia burgdorferi, a slow-growing spirochete. Lyme disease is the most prevalent tick-borne disease in this country; endemic areas in the United States include the northeastern, north central, and western regions. Both infectious and immunologic mechanisms are important factors in the pathogenesis of Lyme disease. The primary mechanism, however, is thought to

				be infectious. Three stages of Lyme disease have been described; stage I, characterized by erythema chronicum migrans and flu-like symptoms; stage II, characterized by dermatologic, ophthalmologic, neurologic, and cardiac disorders; and stage III, characterized by arthritis, a multiple sclerosis-like syndrome, psychiatric disorders, and a chronic fatigue syndrome. Therapy with penicillin or tetracycline hastens the resolution of stage I symptoms. Treatment duration normally ranges between 10 days and three weeks. Tetracycline or doxycycline appears to be more effective than penicillin in preventing the development of late Lyme disease. Although intravenous penicillin G and ceftriaxone are both effective for the treatment of late Lyme disease, many clinicians consider ceftriaxone to be the agent of choice. Whether exposed patients from endemic areas should receive antimicrobial prophylaxis is controversial. Further clinical studies are needed to determine optimal therapy for the various stages of Lyme disease, particularly Lyme arthritis.
Greenberg DB.	Department of Psychiatry, Massachusetts General Hospital Cancer Center, Boston.	Neurasthenia in the 1980s: chronic mononucleosis, chronic fatigue syndrome, and anxiety and depressive disorders.	Psychosomatics 1990 Spring;31(2):129-37	In the 1980s, patients suffering from unexplained fatigue and what seemed like a prolonged attack of acute mononucleosis were given the diagnosis of chronic mononucleosis or chronic infection with the Epstein-Barr virus. Although the diagnosis has great appeal, the Epstein-Barr virus does not cause the syndrome (CFS) of chronic fatigue, which has been renamed and redefined chronic fatigue syndrome to remove the inference that the virus is its cause. From a historical perspective, both syndromes represent the 1980s equivalent of neurasthenia, a disease of fatigue that influenced the development of psychiatric nosology. Because patients with depression and anxiety also have chronic fatigue and because most patients with CFS have an affective disorder, the assessment of organic causes of this syndrome requires careful psychiatric diagnosis and treatment. Defining chronic fatigue syndrome as a medical disorder may deprive patients of competent treatment of their affective disorder.
Hellinger WC, Smith TF, Van Scoy RE, Spitzer PG, Forgacs P, Edson RS.	Division of Infectious Diseases and Internal Medicine, Mayo Clinic, Rochester, MN 55905.	Chronic fatigue syndrome and the diagnostic utility of antibody to Epstein-Barr virus early antigen.	JAMA 1988 Aug 19;260(7):971-3 comment in: JAMA. 1989 Mar 3;261(9):1277-8	Antibody to Epstein-Barr virus (EBV) early antigen has been said to be the most specific indicator of symptomatic chronic EBV infection. We studied the clinical utility of this serologic test in the evaluation of patients with chronic fatigue. Thirty patients with chronic fatigue and highly elevated titers of antibody to early antigen (greater than or equal to 1:160) were compared with 30 age- and sex-matched controls with no antibody to early antigen. There were no significant differences noted between patients and controls at the initial evaluation (symptoms, physical examination, laboratory data). Follow-up information, available for 15 matched pairs, showed no differences in outcome between patients and controls. We conclude that the antibody to EBV early antigen is not helpful in the clinical evaluation of patients with chronic fatigue.
Hickie I, Lloyd A, Wakefield D, Parker G.	Division of Psychiatry, Prince Henry Hospital,	The psychiatric status of patients with the	Br J Psychiatry 1990 Apr;156:534-40	The prevalence of psychiatric disorder in 48 patients with chronic fatigue syndrome (CFS) was determined. Twenty-two had had a major depressive (non-

	Sydney, Australia.	chronic fatigue syndrome.	comment in: Br J Psychiatry. 1990 Sep;157:447-50 Br J Psychiatry. 1991 May;158:717	endogenous) episode during the course of their illness, while seven had a current major (non-endogenous) depression. The pre-morbid prevalence of major depression (12.5%) and of total psychiatric disorder (24.5%) was no higher than general community estimates. The pattern of psychiatric symptoms in the CFS patients was significantly different to that of 48 patients with non-endogenous depression, but was comparable with that observed in other medical disorders. Patients with CFS were not excessively hypochondriacal. We conclude that psychological disturbance is likely to be a consequence of, rather than an antecedent risk factor to the syndrome.
Holland R.		Chronic fatigue syndrome.	CMAJ 1989 Sep 1;141(5):375 comment on: Can Med Assoc J. 1989 Jul 1;141(1):11-2	
Holland R.		Chronic fatigue syndrome.	CMAJ 1989 May 1;140(9):1016	
Holmes GP, Kaplan JE, Gantz NM, Komaroff AL, Schonberger LB, Straus SE, Jones JF, Dubois RE, Cunningham-Rundles C, Pahwa S, et al.	Division of Viral Diseases, Centers for Disease Control, Atlanta, Georgia.	Chronic fatigue syndrome: a working case definition.	Ann Intern Med 1988 Mar;108(3):387-9	The chronic Epstein-Barr virus syndrome is a poorly defined symptom complex characterized primarily by chronic or recurrent debilitating fatigue and various combinations of other symptoms, including sore throat, lymph node pain and tenderness, headache, myalgia, and arthralgias. Although the syndrome has received recent attention, and has been diagnosed in many patients, the chronic Epstein-Barr virus syndrome has not been defined consistently. Despite the name of the syndrome, both the diagnostic value of Epstein-Barr virus serologic tests and the proposed causal relationship between Epstein-Barr virus infection and patients who have been diagnosed with the chronic Epstein-Barr virus syndrome remain doubtful. We propose a new name for the chronic Epstein-Barr virus syndrome--the chronic fatigue syndrome--that more accurately describes this symptom complex as a syndrome of unknown cause characterized primarily by chronic fatigue. We also present a working definition for the chronic fatigue syndrome designed to improve the comparability and reproducibility of clinical research and epidemiologic studies, and to provide a rational basis for evaluating patients who have chronic fatigue of undetermined cause.
Holy J.		[Chronic fatigue syndrome].[article in Czech]	Cas Lek Cesk 1989 Apr 14;128(16):501	
Jones JF, Williams M, Schooley RT, Robinson C, Glaser R.	Department of Pediatrics National Jewish Center for Immunology and Respiratory Medicine, Denver, CO 80206.	Antibodies to Epstein-Barr virus-specific DNase and DNA polymerase in the chronic fatigue syndrome.	Arch Intern Med 1988 Sep;148(9):1957-60	In an attempt to examine further the association between active Epstein-Barr virus (EBV) infection and the chronic fatigue syndrome (chronic EBV syndrome, or chronic or atypical mononucleosis), antibodies acting against EBV-specific DNase and DNA polymerase, which are expressed only during virus replication, were assayed. Serum samples from 25 healthy EBV-seropositive individuals neutralized 3.5 +/- 5.1 U (mean +/- SD) of DNase activity and 14.7 +/- 8.5 U of DNA

				polymerase activity. From these values were selected upper limits of anti-EBV enzyme activity of 17.9 and 31.3 U neutralized in normal individuals, respectively (representing the 95% confidence limit). Serum samples from six groups of subjects representing a variety of EBV-related illnesses were then studied. Only patients with notably elevated anti-EBV antibody titers to viral capsid antigen (VCA) (greater than 10,000) had elevated levels of anti-EBV DNase (38 to 56 U neutralized) and anti-EBV DNA polymerase (72 to 106 U neutralized). Three additional patients and two geriatric controls with average anti-EBV early antigen/VCA titers had slightly elevated levels of antibody to EBV DNA polymerase. IgA anti-VCA, anti-early antigen antibodies, or both, were also detected in the same patients who had high EBV DNase and polymerase antibody levels. These antibody profiles are similar to those in patients with nasopharyngeal carcinoma. Since three of the six patients with elevated anti-EBV enzyme antibody levels developed fatal lymphomas, patients with chronic EBV and this antibody profile might be in another illness category at risk for malignant disease.
Jones JF.	Department of Paediatrics, National Jewish Center for Immunology and Respiratory Medicine, Denver, Colorado 80206.	Epstein-Barr virus and the chronic fatigue syndrome: a short review.	Microbiol Sci 1988 Dec;5(12):366-9	Chronic Fatigue Syndrome (CFS), previously known as neuroasthenia is often considered to be due to psychiatric causes. Evidence for a possible role for the Epstein-Barr virus in CFS is summarized. A plea is made for physicians to accept CFS as a non-psychiatric chronic illness to encourage further research into a clear definition of the syndrome.
Kaslow JE, Rucker L, Onishi R.	Division of Basic and Clinical Immunology, University of California Irvine Medical Center, Orange 92668.	Liver extract-folic acid-cyanocobalamin vs placebo for chronic fatigue syndrome.	Arch Intern Med 1989 Nov;149(11):2501-3	Chronic fatigue syndrome is a recently defined entity for which clinical criteria were proposed by the Centers for Disease Control, Atlanta, Ga. A frequently advocated treatment in Southern California is an injectable solution of bovine liver extract containing folic acid and cyanocobalamin (LEFAC). We conducted a double-blind, placebo-controlled, crossover trial of intramuscular LEFAC in 15 patients who met the Centers for Disease Control criteria for chronic fatigue syndrome. Although patients responded to placebo and LEFAC by several criteria of functional status, no significant difference was apparent between response to placebo and that to LEFAC. The placebo response appeared to be strong. Randomized Controlled Trial
Katz BZ, Andiman WA.	Department of Pediatrics, Yale University School of Medicine, New Haven, CT 06510.	Chronic fatigue syndrome.	J Pediatr 1988 Nov;113(5):944-7	
Klimas NG, Salvato FR, Morgan R, Fletcher MA.	Miami Veterans Administration Medical	Immunologic abnormalities in chronic	J Clin Microbiol 1990 Jun;28(6):1403-10	The chronic fatigue syndrome (CFS), formerly known as chronic Epstein-Barr virus syndrome, is a clinical state of some complexity and uncertain etiology. In order

	Center, Florida.	fatigue syndrome.		to characterize in a comprehensive manner the status of laboratory markers associated with cellular immune function in patients with this syndrome, 30 patients with clinically defined CFS were studied. All of the subjects were found to have multiple abnormalities in these markers. The most consistent immunological abnormality detected among these patients, when compared with normal controls, was low natural killer (NK) cell cytotoxicity. The number of NK cells, as defined by reactivity with monoclonal antibody NKH.1 (CD56), was elevated, but the killing of K562 tumor cells per CD56 cell was significantly diminished. Lymphoproliferative responses after stimulation with phytohemagglutinin and pokeweed mitogen were decreased in most patients when compared with those in normal controls, as was the production of gamma interferon following mitogen stimulation. Lymphocyte phenotypic marker analysis of peripheral blood lymphocytes showed that there were significant differences between patients with CFS and controls. There was an increase in the percentage of suppressor-cytotoxic T lymphocytes, CD8, and a proportionally larger increase in the number of CD8 cells expressing the class II activation marker. Most patients had an elevated number of CD2 cells which expressed the activation marker CDw26. The numbers of CD4 cells and the helper subset of CD4+CD29+ cells in patients with CFS were not different from those in controls. There was, however, a significant decrease in the suppressor inducer subset of CD4+ CD45RA+ cells.(ABSTRACT TRUNCATED AT 250 WORDS)
Komaroff AL, Geiger AM, Wormsely S.		IgG subclass deficiencies in chronic fatigue syndrome.	Lancet 1988 Jun 4;1(8597):1288-9	
Komaroff AL, Goldenberg D.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115.	The chronic fatigue syndrome: definition, current studies and lessons for fibromyalgia research.	J Rheumatol Suppl 1989 Nov;19:23-7	Chronic fatigue syndrome (CFS) is characterized by chronic, debilitating fatigue lasting greater than 6 months. Frequent chronic and recurrent findings include fever, pharyngitis, myalgias, adenopathy, arthralgias, difficulties in cognition and disorders of mood. In the majority of patients, the illness starts suddenly with an acute, "flu-like" illness. The following laboratory abnormalities are seen with some frequency, although none are seen in all patients: lymphocytosis, atypical lymphocytosis, monocytosis, elevation of hepatocellular enzymes, low levels of antinuclear antibodies, varying levels of antithyroid antibodies, partial hypergammaglobulinemia, elevated CD4:CD8 ratio, decreased cytolytic activity of natural killer cells, and low levels of immune complexes. Clinical and serologic studies suggest an association of CFS with all of the human herpesviruses, particularly Epstein-Barr virus (EBV) and the recently discovered human B lymphotropic virus (HBLV) or human herpesvirus 6; neither EBV nor HBLV has yet been shown to play a causal role in the illness. Preliminary evidence suggests that many of these features of CFS also are seen in patients with fibromyalgia.
Komaroff AL, Straus SE,		The chronic fatigue	Ann Intern Med 1989	

Gantz NM, Jones JF.		syndrome.	Mar 1;110(5):407-8	
Komaroff AL.	Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.	Chronic fatigue syndromes: relationship to chronic viral infections.	J Virol Methods 1988 Sep;21(1-4):3-10	Chronic fatigue syndrome (CFS) is a newly-recognized clinical entity characterized by chronic, debilitating fatigue lasting longer than six months. Common associated findings are chronic and recurrent fever, pharyngitis, myalgias, adenopathy, arthralgias, difficulties in cognition and disorders of mood. In the majority of patients, the illness starts suddenly with an acute, 'flu-like' illness. The following abnormalities are seen with some frequency although none are seen in all patients: lymphocytosis, atypical lymphocytosis, monocytosis, elevation of hepatocellular enzymes, low levels of antinuclear antibodies, low levels of immune complexes. Clinical and serologic studies suggest an association of CFS with all of the human herpesviruses, particularly Epstein-Barr virus (EBV) and the recently-discovered human B-lymphotropic virus (HBLV) or human herpesvirus-6; neither EBV nor HBLV has yet been shown to play a causal role in the illness.
Koo D.		Chronic fatigue syndrome. A critical appraisal of the role of Epstein-Barr virus.	West J Med 1989 May;150(5):590-6	The symptom complex currently designated the chronic fatigue syndrome was previously termed the chronic or chronic active Epstein-Barr virus syndrome or the chronic mononucleosis syndrome, prematurely assuming an etiologic role for the Epstein-Barr virus (EBV). This presumption derived from the fact that some patients with the chronic fatigue syndrome have very high or very low titers of certain antibodies to EBV. A review of seroepidemiologic patterns of response to EBV and of studies of patients with the chronic fatigue syndrome shows that these antibody titers overlap considerably both with those of controls or other healthy persons and with those of patients with other illnesses. Given the high prevalence of exposure to EBV, it would be difficult to determine whether the virus caused the syndrome or whether the antibody elevations resulted from the illness, even if distinct differences in titers existed. Other methodologic issues of control selection, laboratory test comparability, and differing case definitions pose problems in studying this syndrome. The recently published working case definition should facilitate the continuing search for causes.
Krueger GR, Sander C.	Institute of Pathology, University of Cologne, FRG.	What's new in human herpesvirus-6? Clinical immunopathology of the HHV-6 infection.	Pathol Res Pract 1989 Dec;185(6):915-29	Human herpesvirus-6 (HHV-6), formerly known as human B-lymphotropic virus (HBLV), was first isolated in 1986 from patients with lymphoproliferative disorders and AIDS. Antibody prevalence against HHV-6 varies between about 60-80% indicating a widespread latent infection. Although HHV-6 infects in vivo primarily T-lymphocytes, it is associated with similar diseases as in infection with Epstein-Barr virus (EBV), a clearly B-lymphotropic virus. Reactivation of latent HHV-6 infection in patients with subnormal host defense may cause persistent active infection with so-called postinfectious chronic fatigue syndrome (PICFS) or may contribute to other pathologies such as immune deficiency itself, autoimmune disorders or progressive lymphoproliferation. Coinfection of CD4 cells by HHV-6 and human immunodeficiency virus (HIV 1) in AIDS patients can aggravate HIV-induced acquired immune deficiency. These characteristics of the

				only recently detected new virus justify further intense investigation. Review Literature
Kruesi MJ, Dale J, Straus SE.	National Institute of Mental Health, Child Psychiatry Branch, Bethesda, Md 20892.	Psychiatric diagnoses in patients who have chronic fatigue syndrome.	J Clin Psychiatry 1989 Feb;50(2):53-6 Erratum in: J Clin Psychiatry 1989 Apr;50(4):148 comment in: J Clin Psychiatry. 1990 Apr;51(4):169 J Clin Psychiatry. 1990 Feb;51(2):86	Patients with persistent fatigue are often suspected of having psychiatric illnesses, particularly depression. The authors used the Diagnostic Interview Schedule to assess the lifetime prevalence of psychiatric disorders in 28 patients who met Centers for Disease Control case definition criteria for chronic fatigue syndrome. Compared with studies of the general population and studies of chronically medically ill patients who received the same structured interview, the rates of psychiatric illness in patients with the chronic fatigue syndrome appeared high. An examination of the medical histories of the 28 patients indicated that psychiatric disorders more often preceded the chronic fatigue than followed it.
Lechky O.		Life insurance MDs sceptical when chronic fatigue syndrome diagnosed.	CMAJ 1990 Sep 1;143(5):413-5 comment in: Can Med Assoc J. 1990 Dec 15;143(12):1283-6	
Levine PH, Krueger GR, Straus SE.	Environmental Epidemiology Branch, National Cancer Institute, NIH, Bethesda, MD 20892.	A postviral chronic fatigue syndrome: a round table.	J Infect Dis 1989 Oct;160(4):722-4	
Linde A, Hammarstrom L, Smith CI.		IgG subclass deficiency and chronic fatigue syndrome.	Lancet 1988 Apr 16;1(8590):885-6	
Linde A.		[Chronic fatigue syndrome--a diagnosis to be seriously considered]?[article in Swedish]	Lakartidningen 1989 May 3;86(18):1687-90	
Lloyd A, Hickie I, Wakefield D, Boughton C, Dwyer J.	Department of Infectious Diseases, Prince Henry Hospital, Sydney, Australia.	A double-blind, placebo-controlled trial of intravenous immunoglobulin therapy in patients with chronic fatigue syndrome.	Am J Med 1990 Nov;89(5):561-8 comment in: Am J Med. 1990 Nov;89(5):551-3 Am J Med. 1991 Jun;90(6):768 Am J Med. 1991 Oct;91(4):443-4 Am J Med. 1991 Sep;91(3):320-1	PURPOSE: The chronic fatigue syndrome (CFS) is characterized by profound fatigue, neuropsychiatric dysfunction, and frequent abnormalities in cell-mediated immunity. No effective therapy is known. PATIENTS AND METHODS: Forty-nine patients (40 with abnormal cell-mediated immunity) participated in a randomized, double-blind, placebo-controlled trial to determine the effectiveness of high-dose intravenously administered immunoglobulin G. The patients received three intravenous infusions of a placebo solution or immunoglobulin at a dose of 2 g/kg/month. Assessment of the severity of symptoms and associated disability, both before and after treatment, was completed at detailed interviews by a physician and psychiatrist, who were

				unaware of the treatment status. In addition, any change in physical symptoms and functional capacity was recorded using visual analogue scales, while changes in psychologic morbidity were assessed using patient-rated indices of depression. Cell-mediated immunity was evaluated by T-cell subset analysis, delayed-type hypersensitivity skin testing, and lymphocyte transformation with phytohemagglutinin. RESULTS: At the interview conducted by the physician 3 months after the final infusion, 10 of 23 (43%) immunoglobulin recipients and three of the 26 (12%) placebo recipients were assessed as having responded with a substantial reduction in their symptoms and recommencement of work, leisure, and social activities. The patients designated as having responded had improvement in physical, psychologic, and immunologic measures (p less than 0.01 for each). CONCLUSION: Immunomodulatory treatment with immunoglobulin is effective in a significant number of patients with CFS, a finding that supports the concept that an immunologic disturbance may be important in the pathogenesis of this disorder. Randomized Controlled Trial
Lloyd A, Wakefield D, Smith L, Isbister J, McGrath M, Collings A, Bajenov N.		Red blood cell morphology in chronic fatigue syndrome.	Lancet 1989 Jul 22;2(8656):217 comment in: Lancet. 1989 Sep 30;2(8666):805 comment on: Lancet. 1987 Aug 8;2(8554):328-9	
Lloyd AR, Hickie I, Boughton CR, Spencer O, Wakefield D.	Department of Immunology, Prince Henry Hospital, Little Bay, NSW.	Prevalence of chronic fatigue syndrome in an Australian population.	Med J Aust 1990 Nov 5;153(9):522-8	An epidemiological study was undertaken to provide the first reported estimate of the point prevalence of chronic fatigue syndrome in an Australian community. After a pilot study in a separate location, the population of the Richmond Valley, New South Wales, was sampled using a structured case-finding technique, which included notification from local medical practitioners, the use of a screening questionnaire and standardised interviews conducted by a physician and psychiatrist. In addition, investigations were performed to exclude alternative diagnoses and to assess cell-mediated immunity. Forty-two patients with chronic fatigue syndrome, with a female:male ratio of 1.3:1.0, were detected in a population of 114,000. The mean age at onset of symptoms was 28.6 years (SD, 12.3 years), and the median duration of symptoms from onset to sampling date was 30 months. The social status of the patients was distributed in accordance with that of the remainder of the population sampled, with no bias towards the middle or upper social classes. The disorder was causing considerable incapacity, with 43% of patients unable to attend school or work. The conservative estimate from this study suggests a prevalence on June 30 1988 of 37.1 cases per 100,000 (95% confidence interval [CI], 26.8-50.2). Chronic fatigue syndrome is an

				important disorder in this Australian community that affects young individuals from all social classes and causes considerable ill health and disability.
Lloyd AR, Wakefield D, Boughton CR, Dwyer JM.	Department of Immunology, Prince Henry Hospital, Little Bay, NSW.	Immunological abnormalities in the chronic fatigue syndrome.	Med J Aust 1989 Aug 7;151(3):122-4 comment in: Med J Aust. 1990 Jan 1;152(1):50-2	The chronic fatigue syndrome is a disorder of unknown aetiology which is characterized by debilitating fatigue. Recent evidence has suggested that viruses may persist in the tissues of patients with chronic fatigue syndrome. A concurrent immunological disturbance is likely to be associated with the persistence of viral antigens. Therefore, the humoral and cellular immunity of 100 patients who were suffering from chronic fatigue syndrome and that of 100 healthy, age- and sex-matched control subjects were compared. This study documents the frequent occurrence of abnormalities within the cellular and humoral immune systems of patients with well-defined chronic fatigue syndrome. Disordered immunity may be central to the pathogenesis of chronic fatigue syndrome. In patients with chronic fatigue syndrome, a significant (P less than 0.01) reduction was found in the absolute number of peripheral blood lymphocytes in the total T-cell (CD2), the helper/inducer T-cell (CD4) and the suppressor/cytotoxic T-cell (CD8) subsets. A significant (P less than 0.001) reduction also was found in T-cell function, which was measured: in vivo by delayed-type hypersensitivity skin-testing (reduced responses were recorded in 50 [88%] of 57 patients); and in vitro by phytohaemagglutinin stimulation. Reduced immunoglobulin (Ig) levels were common (56% of patients), with the levels of serum IgG3- and IgG1-subclasses particularly (P less than 0.05) affected.
Lloyd AR.	Department of Infectious Diseases, Prince Henry Hospital, Little Bay, NSW.	Muscle versus brain: chronic fatigue syndrome.	Med J Aust 1990 Nov 5;153(9):530-4 comment in: Med J Aust. 1991 Feb 4;154(3):220	
Luka J, Okano M, Thiele G.	Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha.	Isolation of human herpesvirus-6 from clinical specimens using human fibroblast cultures.	J Clin Lab Anal 1990;4(6):483-6	The isolation and characterization of human herpesvirus-6 (HHV-6) has been hindered by the lack of cell lines useful for its rapid propagation. Recently, we have reported that the MRC-5 cell line (human diploid lung fibroblasts) was susceptible for HHV-6 infection. In this study, we report on the isolation of HHV-6 from the peripheral blood or buffy coat of three chronic fatigue syndrome patients, one post-liver transplant patient, and one severe chronic active Epstein-Barr virus syndrome patient using the MRC-5 cell line. Additionally, it was observed by Southern blot hybridization studies that four of five isolates had different restriction enzyme fragment patterns than the isolate obtained from the National Institutes of Health with Eco RI. These data suggest the usefulness of the MRC-5 cell line in the isolation and characterization of HHV-6 from various patients.
Manu P, Lane TJ, Matthews DA.	University of Connecticut School of	The frequency of the chronic fatigue	Ann Intern Med 1988 Oct 1;109(7):554-6	STUDY OBJECTIVE: To determine the frequency of the chronic fatigue syndrome among patients with symptoms of fatigue. DESIGN: Prospective, cohort study.

	Medicine, Farmington.	syndrome in patients with symptoms of persistent fatigue.	Erratum in: Ann Intern Med 1988 Dec 15;109(12):997	SETTING: Referral clinic, based in a primary care general internal medicine faculty practice of a university medical center. PATIENTS: Consecutive sample of 135 patients (53 men, 82 women) with 6 months or more of debilitating fatigue. INTERVENTIONS: All patients had a complete history taken, had a physical examination and a comprehensive battery of blood tests, and were given the Diagnostic Interview Schedule of the National Institute of Mental Health, a highly-structured 260-item instrument designed to enable accurate psychiatric diagnoses. Other diagnostic studies (for example, sleep studies and electroencephalography) were ordered if necessary for individual patients. MEASUREMENTS AND MAIN RESULTS: Six of the one hundred thirty-five patients met criteria for chronic fatigue syndrome (95% CI, 0 to 10). Ninety-one (67%) patients (CI, 56 to 78) had clinically active psychiatric disorders and 4 (3%) patients (CI, 0 to 8) had medical disorders that were considered a major cause of their fatigue. Thirty-four (25%) patients (CI, 14 to 36) had insufficient symptoms or objective findings of the chronic fatigue syndrome. CONCLUSION: The chronic fatigue syndrome is rare among patients with symptoms of persistent fatigue. Most of these patients have psychiatric disorders.
Martin-Du-Pan R.		[Chronic fatigue syndrome, fibromyalgia and depression].[article in French]	Rev Med Suisse Romande 1990 Oct;110(10):923-8	
Matthews DA, Lane TJ, Manu P.		Definition of the chronic fatigue syndrome.	Ann Intern Med 1988 Sep 15;109(6):511-2	
Moldofsky H, Saskin P, Lue FA.	Department of Psychiatry, University of Toronto, ON, Canada.	Sleep and symptoms in fibrositis syndrome after a febrile illness.	J Rheumatol 1988 Nov;15(11):1701-4	Sleep physiology and symptoms of 9 patients with fibrositis syndrome secondary to a febrile illness were compared to 9 patients with fibrositis syndrome who did not attribute their symptoms to a febrile illness and to 10 healthy controls. Both patient groups showed an alpha EEG (7.5 to 11 Hz) nonrapid eye movement sleep anomaly, had similar observed tender points, and self-ratings of musculoskeletal pain. These findings suggest that patients with postfebrile fibrositis have a nonrestorative sleep disorder characteristic of patients with fibrositis syndrome and share similar symptoms with patients who have a "chronic fatigue syndrome."
Montague TJ, Marrie TJ, Klassen GA, Bewick DJ, Horacek BM.	Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada.	Cardiac function at rest and with exercise in the chronic fatigue syndrome.	Chest 1989 Apr;95(4):779-84	To evaluate a possible cardiac pathophysiology of the chronic fatigue syndrome, we compared the resting cardiac function and exercise performance of 41 patients to those of an age-matched and sex-matched normal control group. Persistent fatigue following an acute apparently viral illness was the major complaint of all patients; none had specific cardiac symptoms nor abnormal physical findings. Electrocardiographic spatial patterns were normal in the patients, and there were no differences in the body surface sum of positive T-wave integrals between the patients (240 microV.x 10(2) +/- 107 microV.s x10(2))

				and control (244 microV.x 10(2) +/- 108 microV.s x 10(2) subjects. Twenty-four hour ambulatory ECGs revealed no differences in sinus rates and incidences of ventricular dysrhythmias in the two populations. Left ventricular dimensions and systolic fractional shortening values were also similar in both groups; moreover none of the patients had segmental wall motion abnormalities. On graded exercise testing, 20 of 32 normal subjects achieved target (85 percent of age-maximum) heart rates, compared to four of 31 patients (p less than 0.001). The duration of exercise averaged 12 +/- 4 minutes for the normal subjects and 9+/- 4 minutes for the patients (p less than 0.01). The temporal profile of exercise heart rates was dissimilar in the two groups, with patients' rates consistently and progressively less than those of normal subjects. Peak heart rate averaged 152 +/- 16 beats per minute for the normal group vs 124 +/- 19 beats per minute for the patients (p less than 0.0001); in age-related terms, respectively, 82 +/- 6 percent of the maximum heart rate vs 66 +/- 10 percent (p less than 0.0001). Thus, patients with chronic fatigue syndrome have normal resting cardiac function but a markedly abbreviated exercise capacity characterized by slow acceleration of heart rate and fatigue of exercising muscles long before peak heart rate is achieved.(ABSTRACT TRUNCATED AT 250 WORDS)
Morte S, Castilla A, Civeira MP, Serrano M, Prieto J.		Production of interleukin-1 by peripheral blood mononuclear cells in patients with chronic fatigue syndrome.	J Infect Dis 1989 Feb;159(2):362	
Morte S, Castilla A, Civeira MP, Serrano M, Prieto J.		Gamma-interferon and chronic fatigue syndrome.	Lancet 1988 Sep 10;2(8611):623-4	
Nix WA.	Klinik und Poliklinik fur Neurologie, Johannes Gutenberg-Universitat, Mainz.	[Chronic fatigue syndrome--a new disease picture]?[article in German]	Nervenarzt 1990 Jul;61(7):390-6	The chronic fatigue syndrome has recently been more frequently diagnosed. Yet it is unknown if this syndrome represents a disease entity of its own or merely a diagnostic label for a miscellaneous group of disorders. Further investigations are needed to find out if the syndrome has an organic or psychosomatic aetiology, or a mixture of both. In the meantime it is the responsibility of the clinician to make this decision in each individual case.
Parras F, Salva F, Reina J, Gil J, Portela D, Alomar P.		[Chronic fatigue syndrome associated with Epstein-Barr virus infection].[article in Spanish]	Med Clin (Barc) 1989 Apr 29;92(16):619-22 comment in: Med Clin (Barc). 1990 Mar 3;94(8):315-6	Epstein-Barr virus (EBV) infection is ubiquitous and may result in multiple and widely different clinical features; the most common of these is infectious mononucleosis (IM). Recently, a group of patients has been included in the chronic EBV infection syndrome (EBVIS), with a sustained nonspecific syndrome consisting of asthenia, anorexia, low grade fever and changes in mood, associated with a viral infection not necessarily caused by EBV; this has been called chronic fatigue syndrome (CFS). We report a patient who fulfilled the

				criteria for CFS associated with EBV after an acute, well documented EBV infection. We discuss its etiological and pathophysiological implications, emphasizing the need for extreme caution in the diagnosis of CFS. A merely clinical diagnosis may hide severe mistakes.
Payne CB Jr, Sloan HE.		Pulmonary function and the chronic fatigue syndrome.	Ann Intern Med 1989 Nov 15;111(10):860	
Peterson PK, Shepard J, Macres M, Schenck C, Crosson J, Rechtman D, Lurie N.	Department of Medicine, Hennepin County Medical Center, Minneapolis, Minnesota 55415.	A controlled trial of intravenous immunoglobulin G in chronic fatigue syndrome.	Am J Med 1990 Nov;89(5):554-60 comment in: Am J Med. 1990 Nov;89(5):551-3	PURPOSE: Currently, there is no established therapy for chronic fatigue syndrome (CFS), a recently defined illness that has been associated with a variety of immunologic abnormalities. Based on the hypothesis that a chronic viral infection or an immunoregulatory defect is involved in the pathogenesis of CFS, the therapeutic benefit of intravenous immunoglobulin G (IV IgG) was evaluated in a group of patients with CFS. Additionally, serum immunoglobulin concentrations and peripheral blood lymphocyte subset numbers were measured at the outset of the study, and the effect of IV IgG therapy on IgG subclass levels was determined. PATIENTS AND METHODS: Thirty patients with CFS were enrolled in a double-blind, placebo-controlled trial of IV IgG. The treatment regimen consisted of IV IgG (1 g/kg) or intravenous placebo (1% albumin solution) administered every 30 days for 6 months. Participants completed a self-assessment form prior to each of the six treatments, which was used to measure severity of symptoms, functional status, and health perceptions. Patients were also asked to report adverse experiences defined as worsening of symptoms occurring within 48 hours of each treatment. RESULTS: Twenty-eight patients completed the trial. At baseline, all 28 patients complained of moderate to severe fatigue, and measures of social functioning and health perceptions showed marked impairment. Low levels of IgG1 were found in 12 (42.9%), and 18 (64.3%) had low levels of IgG3. At the end of the study, no significant therapeutic benefit could be detected in terms of symptom amelioration or improvement in functional status, despite restoration of IgG1 levels to a normal range. Major adverse experiences were observed in 20% of both the IV IgG and placebo groups. CONCLUSION: The results of this study indicate that IV IgG is unlikely to be of clinical benefit in CFS. In addition to the ongoing need for placebo-controlled trials of candidate therapies for CFS, an expanded research effort is needed to define the etiology and pathogenesis of this disorder.
Phillips H.		Chronic fatigue syndrome.	Med J Aust 1989 Mar 20;150(6):351-2	
Pinardi G, Scarlato G.	Istituto di Clinica neurologica, Universita, Ospedale maggiore Policlinico, Milano.	[The chronic fatigue syndrome. A multifactorial approach and the treatment	Recenti Prog Med 1990 Dec;81(12):773-7	The chronic fatigue syndrome is a poorly defined symptoms complex characterized primarily by chronic or recurrent debilitating fatigue and various combinations of other symptoms, including psychological symptoms, sore throat, lymph node pain, headache, myalgia, arthralgias. Psychological disturbances,

		possibilities].[article in Italian]		ranging from mild depression or anxiety to severe behavioral abnormalities, are always present. Chronic fatigue syndrome is the name that more accurately describes this symptom complex of unknown cause. A viral aetiology has long been hypothesized: many viruses are potential candidates, including any of the 23 Coxsackie A or 6 Coxsackie B viruses, herpes viruses, particularly Epstein-Barr virus and varicella. These studies, though interesting, remain unconvincing because of methodological flaws such as a poor case definition and inadequate control groups. This syndrome may represent an infection by a yet unidentified virus. It is more likely due to an abnormal immune response toward different intracellular pathogens. There is no treatment to ameliorate the chronic fatigue syndrome. Epidemiological studies are essential with explicit operational case definition before progress can be made in the management of this distressing disorder.
Portwood M.		More information on chronic fatigue syndrome.	Nurse Pract 1988 Sep;13(9):8	
Portwood MF.		Chronic fatigue syndrome--a diagnosis for consideration.	Nurse Pract 1988 Feb;13(2):11-2, 15-8, 23	Chronic fatigue syndrome (CFS) is an illness which may be mild or completely disabling. Clients who return with recurring non-related symptoms and no specific diagnosis may suffer from CFS. The symptoms of CFS are numerous and varied, including fatigue, malaise, myalgias, difficulty concentrating, headaches and sore throat. Patient complaints seem out of proportion to the physical findings, which may be normal. There is no cure for this chronic disease. Therapy is primarily symptomatic. The role of the health care provider is to recognize this confusing disorder and help the patient and family cope with its many effects.
Powell MA.		Epstein-Barr antibody titer and chronic fatigue syndrome.	J Am Acad Nurse Pract 1990 Jan-Mar;2(1):33-4	
Powell R, Dolan R, Wessely S.	National Hospital For Nervous Diseases, Queen Square, London, U.K.	Attributions and self-esteem in depression and chronic fatigue syndromes.	J Psychosom Res 1990;34(6):665-73	There is considerable overlap in symptomatology between chronic fatigue syndrome (CFS) and affective disorder. We report a comparison of depressive phenomenology and attributional style between a group of CFS subjects seen in a specialized medical setting, which included a high proportion with depression diagnosed by Research Diagnostic Criteria (RDC), and depressed controls seen in a specialized psychiatric setting. Significant symptomatic differences between the depressed CFS group and depressed controls were observed for features such as self-esteem and guilt as well as attribution of illness. All the CFS groups tended to attribute their symptoms to external causes whereas the depressed controls experienced inward attribution. This may have resulted from differences in the severity of mood disorder between the samples, but it is also suggested that an outward style of attribution protects the depressed CFS patients from cognitive changes associated with low mood but at the expense of greater vulnerability

				towards somatic symptoms such as fatigue.
Prieto J, Subira ML, Castilla A, Serrano M.	Department of Internal Medicine, University Clinic, School of Medicine, Pamplona, Spain.	Naloxone-reversible monocyte dysfunction in patients with chronic fatigue syndrome.	Scand J Immunol 1989 Jul;30(1):13-20	We studied monocyte function in 35 consecutive patients with chronic fatigue syndrome (CFS) and 25 healthy controls. Eighty-five per cent of the patients showed monocyte dysfunction characterized by marked reduction in the number of monocytes displaying immunoreactive cytoskeletal vimentin filaments, a low phagocytosis index, and a reduced expression of HLA-DR antigens. These values increased dramatically after incubation of the patients' monocytes with the opioid antagonist naloxone. Other immunological abnormalities also noted in the patients were low lymphocyte blastogenesis and diminished numbers of monocytes displaying receptors for Fc of IgG (FcR) and C3b (CR1). These findings suggest that an increased opioid activity acting through a classical receptor mechanism is active on monocytes from a high proportion of patients with CFS and that this represents a novel example of immunomodulation by opioid peptides in human disease. We suggest that endogenous opioids are involved in the pathogenesis of the chronic fatigue syndrome.
Pritchard C.		Fibrositis and the chronic fatigue syndrome.	Ann Intern Med 1988 Jun;108(6):906	
Read R, Spickett G, Harvey J, Edwards AJ, Larson HE.		IgG1 subclass deficiency in patients with chronic fatigue syndrome.	Lancet 1988 Jan 30;1(8579):241-2	
Reilly PA, Littlejohn GO.	Prince Henry's Hospital, Melbourne, Australia.	Fibromyalgia and chronic fatigue syndrome.	Curr Opin Rheumatol 1990 Apr;2(2):282-90	
Reiss GR.		Chronic fatigue syndrome.	J Clin Psychiatry 1990 Apr;51(4):169 comment on: J Clin Psychiatry. 1989 Feb;50(2):53-6	
Richards AJ.		Epstein-Barr virus and chronic fatigue syndrome.	J Rheumatol 1988 Oct;15(10):1595	
Riley MS, O'Brien CJ, McCluskey DR, Bell NP, Nicholls DP.	Department of Medicine, Royal Victoria Hospital, Belfast.	Aerobic work capacity in patients with chronic fatigue syndrome.	BMJ 1990 Oct 27;301(6758):953-6 comment in: BMJ. 1990 Nov 24;301(6762):1217 BMJ. 1991 Jan 5;302(6767):50	OBJECTIVE--To determine the aerobic work capacity of patients with the chronic fatigue syndrome and compare it with that of two control groups, and to assess the patients' perception of their level of activity before and during illness. DESIGN--A symptom limited exercise treadmill test with on line gas analysis and blood sampling was used. Subjects were assessed by one investigator, who was blind to the group which they were in. SETTING--Department of medicine, Royal Victoria Hospital, Belfast. SUBJECTS--13 Patients (10 women, three men) who fulfilled the diagnostic criteria for chronic fatigue syndrome. Two control groups of similar age, sex, and body weight: 13 normal subjects (10 women, three men)

				and seven patients (five women, two men) with the irritable bowel syndrome. MAIN OUTCOME MEASURES--Aerobic work capacity as assessed by several variables such as length of time on treadmill, heart rate, and biochemical measurements; Borg score; and visual analogue scores of perceived level of physical activity. RESULTS--The patients with the chronic fatigue syndrome had a reduced exercise capacity compared with that of the other subjects, spending a significantly shorter time on the treadmill. They had a significantly higher heart rate at submaximal levels of exertion and at stage III exertion had significantly higher blood lactate concentrations. Using a Borg score, they showed a significantly altered perception of their degree of physical exertion with a mean score of 8.2 compared with 6.6 and 5.3 for the normal subjects and patients with the irritable bowel syndrome respectively. Using a visual analogue scale they indicated that they had a greater capacity for activity before illness than had the patients with the irritable bowel syndrome, but the scores were not significantly different between the two groups. Both groups of patients indicated reduced activity at the time of testing. Normal controls and patients with the irritable bowel syndrome aspired to a greater level of activity than their current level, but the patients with the chronic fatigue syndrome aspired to a level similar to that which they had had before their illness. CONCLUSIONS--Patients with the chronic fatigue syndrome have reduced aerobic work capacity compared with normal subjects and patients with the irritable bowel syndrome. They also have an altered perception of their degree of exertion and their premorbid level of physical activity.
Roath S.		Blood cell morphology in chronic fatigue syndrome.	Lancet 1989 Sep 30;2(8666):805 comment on: Lancet. 1989 Jul 22;2(8656):217	
Rosen SD, King JC, Wilkinson JB, Nixon PG.	Department of Cardiology, Charing Cross Hospital, London.	Is chronic fatigue syndrome synonymous with effort syndrome?	J R Soc Med 1990 Dec;83(12):761-4	Chronic fatigue syndrome (CFS), including myalgic encephalomyelitis (ME) and postviral syndrome (PVS), is a term used today to describe a condition of incapacity for making and sustaining effort, associated with a wide range of symptoms. None of the reviews of CFS has provided a proper consideration of the effort syndrome caused by chronic habitual hyperventilation. In 100 consecutive patients, whose CFS had been attributed to ME or PVS, the time course of their illness and the respiratory psychophysiological studies were characteristic of chronic habitual hyperventilation in 93. It is suggested that the labels 'CFS', 'ME' or 'PVS' should be withheld until chronic habitual hyperventilation - for which conventional rehabilitation is available - has been definitively excluded.
Rosen SD, King JC, Wilkinson JB, Nixon PG.		Aerobic work capacity in chronic fatigue	BMJ 1990 Nov 24;301(6762):1217	

		syndrome.	comment on: BMJ. 1990 Oct 27;301(6758):953-6	
Ross GH, Rea WJ, Johnson AR.		Chronic fatigue syndrome.	CMAJ 1989 Jul 1;141(1):11-2 comment in: Can Med Assoc J. 1989 Sep 1;141(5):375	
Sawyer MH, Webb DE, Balow JE, Straus SE.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland.	Acyclovir-induced renal failure. Clinical course and histology.	Am J Med 1988 Jun;84(6):1067-71	Four patients with a chronic fatigue syndrome experienced five episodes of acute renal insufficiency associated with high-dose (500 mg/m2) intravenous acyclovir administered intravenously as one-hour infusions. Nephrotoxicity developed despite precautions to avoid volume contraction. Examination of the urinary sediment of three patients by polarizing microscopy showed birefringent needle-shaped crystals within leukocytes. In the most severely affected patient, a serum creatinine concentration of 8.6 mg/dl developed and the patient underwent percutaneous renal biopsy that revealed foci of interstitial inflammation without tubular necrosis. Urine, blood, and renal tissue levels of acyclovir were high. One patient was rechallenged with low-dose intravenous acyclovir and the four patients later received oral acyclovir, all without adverse effect. The combined data from these patients support crystalluria and obstructive nephropathy as a mechanism of acyclovir-induced renal failure in humans. This experience emphasizes the importance of maintaining adequate hydration during high-dose acyclovir therapy.
Schooley RT. Review, Academic		Chronic fatigue syndrome: a manifestation of Epstein-Barr virus infection?	Curr Clin Top Infect Dis 1988;9:126-46	
Shahar E, Lederer J.	Department of Family Medicine, Sackler School of Medicine, Tel-Aviv University, Israel.	Asthenic symptoms in a rural family practice. Epidemiologic characteristics and a proposed classification.	J Fam Pract 1990 Sep;31(3):257-61; discussion 261-2 comment in: J Fam Pract. 1991 Jan;32(1):14	Asthenic symptoms (eg, fatigue, lassitude, weakness) are of major concern in family practice setting, yet relatively little research has addressed this issue. A retrospective chart review over a 10-year period was conducted to better characterize these symptoms in a rural family practice providing health care to 508 adult patients. Asthenic complaints were recorded at least once in the medical charts of 164 patients (32%) with a preponderance of female patients. Peak prevalence occurred in the third decade of age and during the summer months. Associated symptoms, mainly pain and dizziness, were reported in 75% of the cases. A cause or diagnosis was not identified by the practicing physician in nearly 50% of the encounters; nevertheless, most episodes resolved spontaneously. Patients could be subclassified into three categories according to the recurrence pattern of their asthenic symptoms during the study period. The largest category (64%) included patients who had a single or two episodes and was thus termed "episodic asthenia." Forty-five patients (27%) with recurrent

				episodes (mean 4.4, range 3 to 10) were classified as having "recurrent episodic asthenia." A third small group (14 patients, 9%) with persistent complaints over the years but no evidence of the chronic fatigue syndrome were classified as having "chronic persistent asthenia." The proposed classification may help future research of asthenic symptoms in the family practice setting.
Simpson LO.		Are ME and chronic fatigue syndrome the same disease?	N Z Med J 1990 Jun 27;103(892):305 comment in: N Z Med J. 1990 Aug 8;103(895):378	
Spracklen FH.	Department of Medicine, University of Cape Town.	The chronic fatigue syndrome (myalgic encephalomyelitis)--myth or mystery?	S Afr Med J 1988 Nov 5;74(9):448-52	The chronic fatigue syndrome (CFS) or myalgic encephalomyelitis has caused great confusion, misunderstanding and perhaps even mismanagement of many persons presenting with a variety of combinations of ill-defined complaints. The history, possible pathogenesis and clinical features, of what is probably in most instances a post-viral infection syndrome, are reviewed. The recent Centers for Disease Control case definition is summarised and simplified. The need for such uniformity of definition, acceptable to most workers in the field, is emphasised in order to facilitate further studies into the cause, diagnosis, course and treatment of CFS. The difficulty in treating this condition and the currently recommended management are described. Double-blind controlled studies are essential in assessing any proposed new treatment.
Straus SE, Dale JK, Peter JB, Dinarello CA.		Circulating lymphokine levels in the chronic fatigue syndrome.	J Infect Dis 1989 Dec;160(6):1085-6	
Straus SE, Dale JK, Tobi M, Lawley T, Preble O, Blaese RM, Hallahan C, Henle W.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, Bethesda, Md 20892.	Acyclovir treatment of the chronic fatigue syndrome. Lack of efficacy in a placebo-controlled trial.	N Engl J Med 1988 Dec 29;319(26):1692-8	Twenty-seven adults with a diagnosis of the chronic fatigue syndrome were enrolled in a double-blind, placebo-controlled study of acyclovir therapy. The patients had had debilitating fatigue for an average of 6.8 years, accompanied by persisting antibodies to Epstein-Barr virus early antigens (titers greater than or equal to 1:40) or undetectable levels of antibodies to Epstein-Barr virus nuclear antigens (titers less than 1:2) or both. Each course of treatment consisted of intravenous placebo or acyclovir (500 mg per square meter of body-surface area) administered every eight hours for seven days. The same drug was then given orally for 30 days (acyclovir, 800 mg four times daily). There were six-week observation periods before, between, and after the treatments. Three patients had acyclovir-induced nephrotoxicity and were withdrawn from the study. Of the 24 patients who completed the trial, similar numbers improved with acyclovir therapy and with placebo (11 and 10, respectively). Neither acyclovir treatment nor clinical improvement correlated with alterations in laboratory findings, including titers of antibody to Epstein-Barr virus or levels of circulating immune complexes or of leukocyte 2',5'-oligoadenylate synthetase. Subjective

				improvement correlated with various measures of mood. We conclude that acyclovir, as used in this study, does not ameliorate the chronic fatigue syndrome. We believe that the clinical improvement observed in most patients reflected either spontaneous remission of the syndrome or a placebo effect.
Straus SE, Dale JK, Wright R, Metcalfe DD.	Medical Virology Section, National Institute of Allergy and Infectious Diseases, Bethesda, MD 20892.	Allergy and the chronic fatigue syndrome.	J Allergy Clin Immunol 1988 May;81(5 Pt 1):791-5	The chronic fatigue syndrome is a heterogeneous disorder characterized by easy fatigability, feverishness, diffuse pains, and depression. Many patients also report inhalant, food, or drug allergies. This article reviews the clinical features of the syndrome and hypotheses of its pathogenesis, especially those regarding the Epstein-Barr virus and cellular immune mechanisms. Also summarized are recent studies of the validity of atopic complaints in the syndrome. The results of epicutaneous skin testing demonstrated a high correlation with history in 24 patients. Atopy coexists with the chronic fatigue syndrome in greater than 50% of patients.
Straus SE. Editorial		Intravenous immunoglobulin treatment for the chronic fatigue syndrome.	Am J Med 1990 Nov;89(5):551-3 comment in: Am J Med. 1991 Sep;91(3):320-1 comment on: Am J Med. 1990 Nov;89(5):554-60 Am J Med. 1990 Nov;89(5):561-8	
Subira ML, Castilla A, Civeira MP, Prieto J.		Deficient display of CD3 on lymphocytes of patients with chronic fatigue syndrome.	J Infect Dis 1989 Jul;160(1):165-6	
Swartz MN.		The chronic fatigue syndrome--one entity or many?	N Engl J Med 1988 Dec 29;319(26):1726-8 comment in: N Engl J Med. 1989 Jul 20;321(3):187-9	
Valdini A.	Department of Family Medicine, State University of New York, Stony Brook 11794.	Selections from current literature: chronic fatigue syndrome.	Fam Pract 1990 Jun;7(2):152-5	
Wakefield D, Lloyd A, Brockman A.	Department of Immunopathology and Infectious Diseases, Prince Henry Hospital, Sydney, Australia.	Immunoglobulin subclass abnormalities in patients with chronic fatigue syndrome.	Pediatr Infect Dis J 1990 Aug;9(8 Suppl):S50-3	
Wessely S, David A,		Management of chronic	J R Coll Gen Pract 1989	Simple rehabilitative strategies are proposed to help patients with the chronic

Butler S, Chalder T.		(post-viral) fatigue syndrome.	Jan;39(318):26-9 comment in: J R Coll Gen Pract. 1989 Apr;39(321):171-3 J R Coll Gen Pract. 1989 May;39(322):213-4	fatigue syndrome. A model is outlined of an acute illness giving way to a chronic fatigue state in which symptoms are perpetuated by a cycle of inactivity, deterioration in exercise tolerance and further symptoms. This is compounded by the depressive illness that is often part of the syndrome. The result is a self-perpetuating cycle of exercise avoidance. Effective treatment depends upon an understanding of the interaction between physical and psychological factors. Cognitive behavioural therapy is suggested. Cognitive therapy helps the patient understand how genuine symptoms arise from the frequent combination of physical inactivity and depression, rather than continuing infection, while a behavioural approach enables the treatment of avoidance behaviour and a gradual return to normal physical activity.
Wigley RD.		Chronic fatigue syndrome, ME and fibromyalgia.	N Z Med J 1990 Aug 8;103(895):378 comment on: N Z Med J. 1990 Jun 27;103(892):305	

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Authors	**Author Address**	**Title**	**Publication**	**Abstract**
Acheson ED.		Benign myalgic encephalomyelitis.	Lancet 1957 Apr 20;272(6973):834–5	
Acheson ED.		The clinical syndrome variously called benign myalgic encephalomyelitis, Iceland disease and epidemic neuromyasthenia.	Am J Med 1959 Apr;26(4):569–95	
Behan PO.		Post-infectious encephalomyelitis: some aetiological mechanisms.	Postgrad Med J 1978 Nov;54(637):755–9	The possibility that acute disseminated encephalomyelitis (ADEM) and epidemic myalgic encephalomyelitis ('epidemic neuromyasthenia') may share a common pathogenesis is examined and many factors common to the two diseases are described. It is suggested that further study of ADEM may help our understanding of epidemic myalgic encephalomyelitis.
Behan PO.		Epidemic myalgic encephalomyelitis.	Practitioner 1980 Aug;224(1346):805–7	
Bell EJ, McCartney RA.		A study of Coxsackie B virus infections, 1972-1983.	J Hyg (Lond) 1984 Oct;93(2):197–203	The results of a twelve-year study of Coxsackie B virus (CBV) infections in patients with a variety of acute and chronic illnesses are reported. CBVs were isolated from only 123 patients most of whom were children with respiratory illness. Virus diagnosis in adults was based mainly on the detection of significant rising or static high neutralizing antibody titres. Between 1972 and 1979 most investigations centred on patients with suspected viral heart disease, 12% of whom were found to have diagnostically significant CBV titres. In studies on patients with definite myo-pericarditis the number positive increased to 33%. In 1980 clinical interest switched to the possible role of CBV in myalgic encephalomyelitis (ME), an illness of diverse symptomatology. Investigation of suspected cases of ME in 1983 showed that 16% were serologically positive compared to 4% of normal adults in the West of Scotland. In patients with well-documented ME this figure rose to 41%. The demand by clinicians for CBV neutralizing antibody tests has increased over the past twelve years and continues to escalate annually, especially in patients with chronic relapsing illness.
Bhatia BB, Chandra S, Bhushan C.		Benign myalgic encephalomyelitis.	J Indiana State Med Assoc 1958 Oct;31(8):327–8	
Bishop J.		Epidemic myalgic encephalomyelitis.	Med J Aust 1980 Jun 14;1(12):585–6, 609	
Blackmore RJ.		Myalgic encephalomyelitis and	N Z Med J 1986 Jul 9;99(805):513	

		Immunovir.		
Blattner RJ.		Benign myalgic encephalomyelitis (Akureyri disease, Iceland disease).	J Pediatr 1956 Oct;49(4):504–6	
Bornstein B, Bechar M, Lass H.		Benign myalgic encephalomyelitis. (Report of five cases).	Psychiatr Neurol (Basel) 1960 Mar;139:132–40	
Buchwald D, Sullivan JL, Komaroff AL.		Frequency of 'chronic active Epstein-Barr virus infection' in a general medical practice.	JAMA 1987 May 1;257(17):2303–7	Twenty-one percent of 500 unselected patients, aged 17 to 50 years, seeking primary care for any reason were found to be suffering from a chronic fatigue syndrome consistent with "chronic active Epstein-Barr virus (EBV) infection," They had been experiencing "severe" fatigue, usually cyclic, for a median of 16 months (range, six to 458 months), associated with sore throat, myalgias, or headaches; 45% of the patients were periodically bedridden; and 25% to 73% reported recurrent cervical adenopathy, paresthesias, arthralgias, and difficulty in concentrating or sleeping. The patients had no recognized chronic "physical" illness and were not receiving psychiatric care. While antibody titers to several EBV-specific antigens were higher in patients than in age- and sex-matched controls subjects, the differences generally were not statistically significant. A chronic fatigue syndrome consistent with the chronic active EBV infection syndrome was prevalent in our primary care practice. However, our data offer no evidence that EBV is causally related to the syndrome. Indeed, we feel that among unselected patients seen in a general medical practice currently available EBV serologic test results must be interpreted with great caution.
Byrne E, Trounce I, Dennett X.		Chronic relapsing myalgia (?Post viral): clinical, histological, and biochemical studies.	Aust N Z J Med 1985 Jun;15(3):305–8	Two patients with persistent myalgia characterised by onset after an ill-defined systemic illness, marked fluctuations in the severity of the symptoms, and normal neuromuscular examination with the exception of variable muscle tenderness on deep palpation, may have a forme fruste of myalgic encephalomyelitis. Differentiation from psychogenic muscle pain is important in management. Muscle histology revealed non-specific Type II fibre atrophy. Mitochondrial respiration was assayed polarographically in intact organelles in vitro and revealed a mild depression of State 3 respiration rates with Site I and Site II substrates.
Caligiuri M, Murray C, Buchwald D, Levine H, Cheney P, Peterson D, Komaroff AL, Ritz J.	Division of Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA, USA.	Phenotypic and functional deficiency of natural killer cells in patients with chronic fatigue syndrome.	J Immunol 1987 Nov 15;139(10):3306–13	Natural killer (NK)3 cells are large granular lymphocytes that appear to play a significant role in the host's defense against viral infection. We performed an extensive phenotypic and functional characterization of NK cells on 41 patients with the chronic fatigue syndrome (CFS), or "chronic active Epstein-Barr virus infection" syndrome, and on 23 age- and sex-matched asymptomatic control subjects in an attempt to further characterize this illness. These studies demonstrated that a majority of patients with CFS have low numbers of

				NKH1+T3- lymphocytes, a population that represents the great majority of NK cells in normal individuals. CFS patients had normal numbers of NKH1+T3+ lymphocytes, a population that represents a relatively small fraction of NK cells in normal individuals. When tested for cytotoxicity against a variety of different target cells, patients with CFS consistently demonstrated low levels of killing. After activation of cytolytic activity with recombinant interleukin 2, patients were able to display increased killing against K562 but most patients remained unable to lyse Epstein-Barr virus-infected B cell targets. Additional cytotoxicity experiments were carried out utilizing anti-T3 monoclonal antibody to block killing by NKH1+T3+ cells. These experiments indicated that the NK cell that appears to be responsible for much of the functional activity remaining in patients with CFS belongs to the NKH1+T3+ subset, which under normal circumstances represents only approximately 20% of the NK cell population.
Church AJ.		Myalgic encephalomyelitis “an obscene cosmic joke”?	Med J Aust 1980 Apr 5;1(7):307–8	
Church AJ.		Myalgic encephalomyelitis.	Med J Aust 1980 Aug 23;2(4):224	
Daikos GK, Garzonis S, Paleologue A, Bousvaros GA, Papadoyannakis N.		Benign myalgic encephalomyelitis: an outbreak in a nurses’ school in Athens.	Lancet 1959 Apr 4;1(7075):693–6	
Deisher JB.		Benign myalgic encephalomyelitis (Iceland disease) in Alaska.	Northwest Med 1957 Dec;56(12):1451–6	
Fegan KG, Behan PO, Bell EJ.		Myalgic encephalomyelitis — report of an epidemic.	J R Coll Gen Pract 1983 Jun;33(251):335–7	
Galpine JF, Brady C.		Benign myalgic encephalomyelitis.	Lancet 1957 Apr 13;272(6972):757–8	
Galpine JF.		Benign myalgic encephalomyelitis.	Br J Clin Pract 1958 Mar;12(3):186–8 passim	
Goodwin CS.		Was it benign myalgic encephalomyelitis?	Lancet 1981 Jan 3;1(8210):37–8	
Gow PJ.		Myalgic encephalomyelitis.	N Z Med J 1984 Sep 12;97(763):620	
Gow PJ.		Myalgic encephalomyelitis.	N Z Med J 1984 Dec 12;97(769):868	
Greene IM.		Benign myalgic	J Fla Med Assoc 1958	

		encephalomyelitis; syndrome mimicking anterior poliomyelitis.	Apr;44(10):1105–6	
Gsell O.		[Encephalitis myalgica epidemica, a poliomyelitis-like disease; epidemic neuromyasthenia, benign myalgic encephalomyelitis.] [Article in German.]	Schweiz Med Wochenschr 1958 May 17;88(20):488–91	
Gsell O.		[Benign myalgic encephalomyelitis, epidemic pseudoneurasthenia.] [Article in German.]	Schweiz Med Wochenschr 1963 Feb 2;93:197–200	
Innes SG.		Encephalomyelitis resembling benign myalgic encephalomyelitis.	Lancet 1970 May 9;1(7654):969–71	
Keighley BD, Bell EJ.		Sporadic myalgic encephalomyelitis in a rural practice.	J R Coll Gen Pract 1983 Jun;33(251):339–41	
Kendell RE.		The psychiatric sequelae of benign myalgic encephalomyelitis.	Br J Psychiatry 1967 Aug;113(501):833–40	
Layzer RB.		Myoglobinaemia in benign myalgic encephalomyelitis.	Lancet 1981 Mar 21;1(8221):670	
Klajman A, Pinkhas B, Rannon L.		[An outbreak of an epidemic of benign myalgic encephalomyelitis.] [Article in Hebrew.]	Harefuah 1960 May 15;58:314–5	
Lyle WH.		Encephalomyelitis resembling benign myalgic encephalomyelitis.	Lancet 1970 May 23;1(7656):1118–9	
Matthew C.		Myalgic encephalomyelitis.	N Z Med J 1986 Sep 10;99(809):678	

Matthew C.		Myalgic encephalomyelitis and the doctor.	N Z Med J 1987 Sep 9;100(831):569	
Maurizi CP.		Raphe nucleus encephalopathy (myalgic encephalomyelitis, epidemic neuromyasthenia).	Med Hypotheses 1985 Apr;16(4):351–4	An injury to the dorsal raphe nucleus by Coxsackie B viruses is suggested as the cause of the disease sometimes called myalgic encephalomyelitis. The signs and symptoms are consistent with a serotonin deficiency in the dorsal raphe nucleus and the disease has a predisposition for women in nursing. Stress and underlying tryptophan deficiencies are considered as contributory factors.
May PG, Donnan SP, Ashton JR, Ogilvie MM, Rolles CJ.		Personality and medical perception in benign myalgic encephalomyelitis.	Lancet 1980 Nov 22;2(8204):1122–4	In an outbreak of benign myalgic encephalomyelitis in a girls' school all the residential pupils, both those affected and those unaffected, were investigated. Special virological tests were essentially negative, but it seemed that a few girls had had a viral infection. Psychological testing showed that among younger girls the patients were more neurotic than the others. Girls with various disorders were found to have been classified as having the same disorder, because of what has been called altered medical perception. The conclusions of an international symposium on this condition were not substantiated.
McCartney RA, Banatvala JE, Bell EJ.		Routine use of mu-antibody-capture ELISA for the serological diagnosis of Coxsackie B virus infections.	J Med Virol 1986 Jul;19(3):205–12	The role of coxsackie B viruses (CBV) in myo/pericarditis has been well documented; however, interpretation of static high neutralising antibody titres in individual patients has always been difficult. In introducing the mu-antibody capture ELISA test for the detection of CBV-specific IgM, we hoped to overcome this problem. A regimen for the routine serological diagnosis of CBV infections was introduced, using the CBV IgM ELISA as a screening test, followed by neutralisation tests (NT) to confirm the positive results. Seven hundred and sixty patients and 304 healthy adult controls were tested. The percentage CBV IgM positive in each of the clinical categories myo/pericarditis (33%) chest pain (22%), myalgic encephalomyelitis (31%), myalgia/Bornholm (19%) and controls (9%) was similar to those found in previous studies using NT alone. Cross-reactions with other enteroviruses, including hepatitis A (Enterovirus 72), were observed but did not prove to be a problem in the illness studied, since most involved adults. Both homotypic and heterotypic CBV IgM responses were found. Matching IgM and NT indicated a recent CBV infection. Positive IgM with negative NT titres suggested a recent infection with an enterovirus other than a CBV.
McEvedy CP, Beard AW.		Concept of benign myalgic encephalomyelitis.	Br Med J 1970 Jan 3;1(687):11–5	
Mourad S, Chidiac J.		Benign myalgic encephalomyelitis in Lebanon.	J Med Liban 1969;22(6):735–40	
Mukherjee TM, Smith		Abnormal red-blood-cell	Lancet 1987 Aug	

K, Maros K.		morphology in myalgic encephalomyelitis.	8;2(8554):328–9. Comment in Lancet 1989 Jul 22;2(8656):217	
Pampiglione G, Harris R, Kennedy J.		Electro-encephalographic investigations in myalgic encephalomyelitis.	Postgrad Med J 1978 Nov;54(637):752–4	The main EEG features are described of thirty-six young adults who were examined at the Royal Free Hospital between 1960 and 1964 and twelve children seen at the Hospital for Sick Children, Great Ormond Street, London, between 1957 and 1977. It is important in the future, if a plan is considered for the study of a fresh epidemic, to include systematic EEG studies covering a period of 2 to 3 years. The EEG alterations found in this limited survey, though modest, would suggest that cerebral function was disturbed with somewhat variable distribution by an insidious illness which has not yet been identified.
Parish JG.		Benign myalgic encephalomyelitis.	Br J Psychiatry 1973 Jun;122(571):735	
Parish JG.		Myalgic encephalomyelitis.	Lancet 1981 Apr 25;1(8226):950–1	
Parish G.		Myalgic encephalomyelitis: faulty fibres?	Nurs Mirror 1981 Oct 7;153(15):41–2	
Pool JH, Walton JN, Brewis EG, Uldall PR, Wright AE, Gardner PS.		Benign myalgic encephalomyelitis in Newcastle upon Tyne.	Lancet 1961 Apr 8;1:733–7	
Price JL.		Myalgic encephalomyelitis.	Lancet 1961 Apr 8;1:737–8	
Ramsay AM.		Benign myalgic encephalomyelitis.	Br J Psychiatry 1973 May;122(570):618–9	
Ramsay AM, Dowsett EG, Dadswell JV, Lyle WH, Parish JG.		Icelandic disease (benign myalgic encephalomyelitis or Royal Free disease).	Br Med J 1977 May 21;1(6072):1350	
Ramsay AM, Rundle A.		Clinical and biochemical findings in ten patients with benign myalgic encephalomyelitis.	Postgrad Med J 1979 Dec;55(654):856–7	Ten patients in whom the clinical findings were consistent with the syndrome variously described as ‘benign myalgic encephalomyelitis’, ‘epidemic neuromyasthenia’, ‘Royal Free disease’ and ‘Icelandic disease’ were investigated for blood levels of myoglobin and various enzymes. Although there is no clinical resemblance between the two diseases, the biochemical pattern bears a close similarity to that found in Duchenne muscular dystrophy (DMD) though differing sharply in that no rise in creatinine kinase levels was found. These findings are discussed with particular reference to recent suggestions that the permeability of cell membranes may be impaired by changes in intracellular energy mechanisms.
Ramsay M.		Myalgic encephalomyelitis: a	Nurs Mirror 1981 Oct 7;153(15):40–1	

		baffling syndrome.		
Ronchi W.		[A new drug in the therapy of chronic fatigue syndrome.] [Article in Italian.]	Minerva Med. 1959 Nov 28;50:3884–5.	
Rowlandson PH, Stephens JA.		Cutaneous reflex responses recorded in children with various neurological disorders.	Dev Med Child Neurol 1985 Aug;27(4):434–47	Cutaneous reflex responses were recorded from tibialis anterior or first dorsal interosseous muscles of children with hemiplegia, spinal-cord compression, necrotizing sacroid granulomatosis, acute encephalomyelitis, myalgic encephalomyelitis, and a group of children attending the Learning Difficulties Clinic. Abnormalities of response are reported and are compared with the different reports in the literature of abnormal reflex EMG responses recorded by various methods. It is concluded that cutaneo-muscular reflex testing may have a part to play in the diagnosis of difficult paediatric problems
Simpson LO, Shand BI, Olds RJ.		Blood rheology and myalgic encephalomyelitis: a pilot study.	Pathology 1986 Apr;18(2):190–2	The blood rheology of EDTA-anticoagulated blood samples from blood donors and subjects considered to have myalgic encephalomyelitis was assessed by multiple shear rate viscometry and by multiple-pressure filterability. Although average viscosities of the two groups were different, the differences did not reach statistical significance. In contrast, the data from multiple-pressure filtration of whole blood showed significant differences between females at the lowest (2.5 cm of water) filtration pressure. It appears that the acute phase of the disorder is associated with changes in blood rheology which could impair microcirculatory blood flow. In contrast, the chronic state does not appear to be associated with rheological abnormalities.
Staines D.		Myalgic encephalomyelitis hypothesis.	Med J Aust 1985 Jul 22;143(2):91	
Taerk GS, Toner BB, Salit IE, Garfinkel PE, Ozersky S.		Depression in patients with neuromyasthenia (benign myalgic encephalomyelitis).	Int J Psychiatry Med 1987;17(1):49–56	Neuromyasthenia (benign myalgic encephalomyelitis) is a term used to describe a protracted and incomplete recovery phase following viral-like illnesses. There are few significant physical findings or abnormal laboratory determinations. Although depressive symptoms have been observed in individuals with neuromyasthenia, systematic psychological investigations based on a standardized interview technique have not been reported. This study was designed to investigate the prevalence of psychiatric disorders and psychiatric symptoms in a group of patients presenting with neuromyasthenia. The study consisted of three parts: a structured psychiatric interview (The National Institute of Mental Health Diagnostic Interview Schedule), a self-report measure (The Beck Depression Inventory) and Dexamethasone Suppression Test. Results indicated that relative to a matched comparison group of non-clinical volunteers, a significant percentage (67%) of neuromyasthenic patients met criteria for major depression. Even more striking was the observation that 50 percent of the sample had a

				major depressive episode prior to the development of neuromyasthenia. These findings suggest that sporadic neuromyasthenia may be the result of an organic illness in psychologically susceptible individuals.
Walther H.		[Epidemic myalgic encephalomyelitis.] [Article in German.]	Schweiz Rundsch Med Prax 1972 Apr 11;61(15):469–80	
Wookey C.		Epidemic myalgic encephalomyelitis.	Br Med J 1978 Jul 15;2(6131):202	
[No authors listed]		Myalgic encephalomyelitis.	N Z Med J 1985 Jan 23;98(771):20–1	
[No authors listed]		Myalgic encephalomyelitis.	N Z Med J 1984 Nov 14;97(767):782	
[No authors listed]		Myalgic encephalomyelitis.	N Z Med J 1984 Oct 10;97(765):698–9	
[No authors listed]		Know your organizations: the Myalgic Encephalomyelitis Association.	Health Visit 1982 Jul;55(7):350	
[No authors listed]		Epidemic myalgic encephalomyelitis.	Br Med J 1978 Jun 3;1(6125):1436–7	
[No authors listed]		Benign myalgic encephalomyelitis.	Med J Aust 1970 Jul 4;2(1):3	
[No authors listed]		[Benign epidemic myalgic encephalomyelitis.] [Article in Italian.]	Recenti Prog Med 1957 Nov;23(5):525–31	
[No authors listed]		EPIDEMIC myalgic encephalomyelitis.	Br Med J 1957 Oct 19;33(5050):927–8	